Surgical treatment for apical vaginal prolapse

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SACROCOLPOPEXY · SACROHYSTEROPEXY
SACROSPINOUS FIXATION

Anique van Oudheusden

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Surgical treatment for apical vaginal prolapse: sacrocolpopexy, sacrohysteropexy, and sacrospinous fixation
Thesis, Maastricht University, The Netherlands

ISBN 978-94-6483-252-5 • NUR 877

Author and layout thesis: Anique van Oudheusden
Cover, propositions, and invitation: Marloes Sijm © • www.studiosijm.nl
Illustrations: Cas van Cruchten
Printing thesis: Ridderprint • www.ridderprint.nl

máxima mc

Financial support for the publication of this thesis was kindly provided by:
Bayer / Bridea Medical / ChipSoft / Goodlife / Máxima MC / Medical Dynamics / Medsim / Theramex Netherlands B.V.

A digital version of this thesis can be found on:
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PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Maastricht,
op gezag van de Rector Magnificus, prof. dr. Pamela Habibović
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen op dinsdag 10 oktober 2023 om 13:00 uur

door

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Contents

CHAPTER 1

General introduction & outline of this thesis

General introduction

Pelvic organ prolapse

Pelvic organ prolapse (POP) refers to the downward displacement of a pelvic organ.[1] It is a frequently occurring health issue, especially concerning elderly women.[2, 3] POP can cause bothersome symptoms that may include vaginal bulge, pelvic pressure, and symptoms related to bladder or bowel dysfunction.[4, 5] In addition to mechanical discomfort, POP may negatively affect sexuality, body image, and quality of life and it is one of the most common reasons for gynaecological surgery.[5-7] Pelvic floor disorders are caused by complex pathophysiological mechanisms and have very different presentations, making them difficult to define. 'Anatomical prolapse with descent of at least one of the vaginal walls to or beyond the vaginal hymenal ring with maximal Valsalva effort, and second, the presence either of bothersome characteristic symptoms or of functional or medical compromise' has recently been adopted as the clinical definition of POP.[8]

POP can occur in the anterior, posterior, or apical compartment of the vagina, but is not limited to one compartment at once. Prolapse of the anterior vaginal wall is the most common form of POP, detected twice as often as posterior vaginal prolapse and three times more common than apical prolapse.[9] The prevalence of POP among women of whom both objective and subjective data are available is estimated between 25 – 35%.[5] Long-term prevalence of vaginal vault prolapse (VVP) has been reported in 23% of women who were treated for uterine prolapse by vaginal hysterectomy, compared with 4% in women who underwent a laparoscopic hysterectomy for another reason.[10] Moreover, the overall incidence of POP is still rising as a result of ageing and increasing obesity rates.[3]

APICAL PROLAPSE

The normal female anatomy is presented in Figure 1; in a sagittal plane, the main organs of the genital tract are shown. Uterine prolapse is shown in Figure 2; in this picture the uterus is descended beyond the hymen. Figure 3 shows an example of post-hysterectomy vaginal vault prolapse. Pelvic organ support depends on the combination of function of connective tissue attachments (endopelvic fascia), tensile strength of the tissues, and muscular support (levator ani muscle). This support is divided by three levels, as shown in Figure 4.[11] Disruption of one of these structures can lead to loss of support and POP. The main cause of the apical prolapse is the weakness of the uterosacral / cardinal ligament complex. This is the first, and most upper, level of Delancey's three levels of pelvic support.[11, 12]

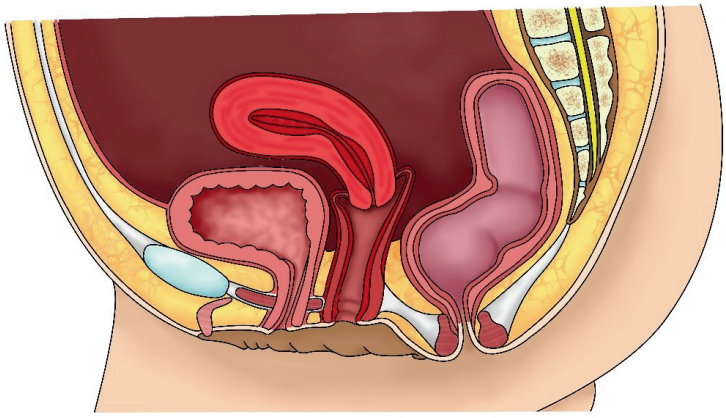

Figure 1. Female genital tract

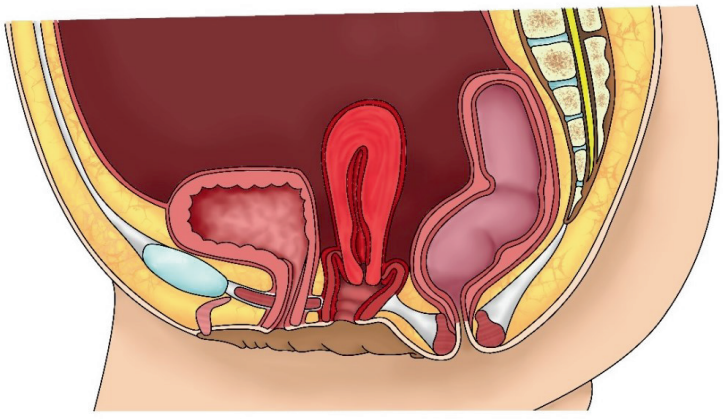

Figure 2. Uterine prolapse

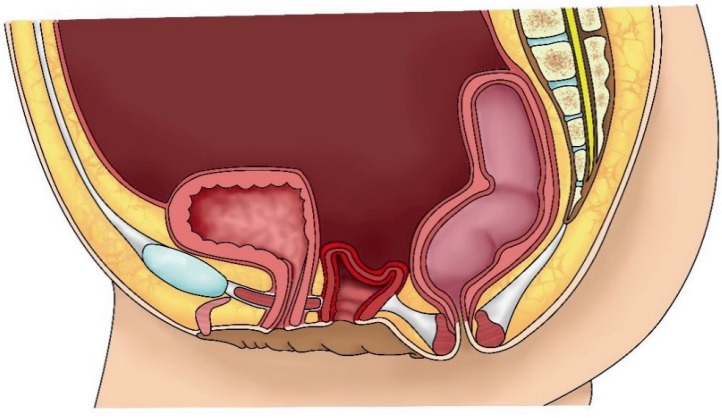

Figure 3. Vaginal vault prolapse

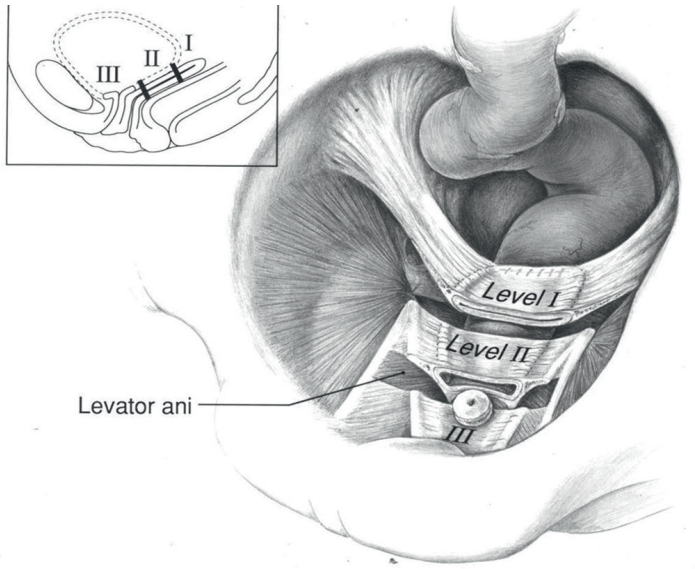

Figure 4. Delancey's levels of support
Level 1: support of the upper third of the vagina / uterus by the uterosacral and cardinal ligaments to the sacrum and the lateral pelvic side wall
Level 2: paravaginal attachments of the middle half of the vagina to the arcus tendinous fascia pelvis
Level 3: the fusion of the lower third of the vagina to the perineal membrane and perineal body
(From: DeLancey JO. Anatomic aspects of vaginal eversion after hysterectomy. Am J Obstet Gynecol. 1992)

Most reported symptoms

The symptom that most strongly correlates with and is most specific for the presence of POP, is a feeling of vaginal bulging or a vaginal bulge that can be seen or felt.[8, 9, 13] Table 1 shows the various dysfunction symptoms patient suffering from POP can report, categorised by compartment or function. Women with POP report a wide range of (dysfunctional) symptoms, although these symptoms are not exclusive to POP. Therefore, it is difficult to establish causality between POP and the described symptoms.

LOWER URINARY TRACT SYMPTOMS

Lower urinary tract symptoms (LUTS) are commonly reported in women with POP. More than 50% of women reported storage symptoms, which manifested as overactive bladder, urinary frequency, urgency, or nocturia. Symptoms of obstructive, difficult, or incomplete voiding were also reported with a prevalence > 50%. Approximately 40% of women has urgency and / or stress urinary incontinence.[14] However, also women without POP report LUTS, suggesting that urinary symptoms are likely to be co-incidental rather than causally related. The exceptions are the symptoms of splinting to void and obstructive voiding, which are more prevalent in women with POP.[14]

BOWEL SYMPTOMS

Cross-sectional studies demonstrated that the prevalence of anal incontinence are similar in women with and without POP, 19% and 18%, respectively.[14] Splinting vagina or perineum to start or complete defaecation, or obstructive defaecation, has an increasing prevalence as the POP-Q stage rises (8% – 15% in patients with POP-Q stage 0 – I, and 21% – 38% in patients with POP-Q stage II – IV).[14, 15]

SEXUAL DYSFUNCTION

Obstructed penetration, or difficulty getting past the vaginal bulge, was the most reported sexual dysfunction symptom, with a prevalence of 73%. In women with POP-Q stage IV a prevalence of sexual dysfunction of 100% was described.[14] Dyspareunia is reported to be present in between 16 to 30% of women with POP. Avoidance of coitus because of vaginal bulge was frequently reported, with a prevalence of 32%, versus 5% in women without POP. Increasing severity of POP is associated with a greater prevalence, ranging from 5% in women with POP-Q stage I to 44% in women with POP-Q stage IV.[14] For many patients, vaginal bulge from POP is the reason they do not feel sexually attractive or do not feel 'normal' in the vaginal area, *i.e.,* they suffer from a decreased body image.[9, 14]

PAIN

Low back pain is the most frequently reported pain in women with POP, with a prevalence of around 45%. Women with POP had twice the prevalence of low back pain compared with women without POP. However, causality between back pain and POP has yet to be established, as it is one of the symptoms least likely to improve after surgery for POP.[14] Abdominal pain also has a high prevalence, ranging between 11 and 45%. Pelvic pain is significantly more present in patients with POP, compared with patients without POP, 28% versus 6%, respectively. Further research is needed to correlate the degree of prolapse to pain and its severity.[14]

PERCEPTION OF POP

The perception of POP as a disease state is influenced by various factors including age, ethnicity, level of education, and socio-cultural issues. The patient's desire to seek help for their POP would likewise be influenced by these factors. Not all women with the same stage of POP will experience the same level of bother. The frequency and severity of symptoms associated with POP that impair quality of life are often the driving force for health-care-seeking behaviour. Despite this, there is poor help-seeking behaviour of women with POP and associated pelvic floor disorders (PFD).[17]

Pathophysiology of POP

The pathophysiology of pelvic organ prolapse is multifactorial and not fully understood yet. Several mechanisms have been described in literature. Family studies have shown a heritable component; pregnancy and vaginal childbirth are widely accepted risk factors; and increasing age has also been identified as an etiologic link in the development of POP.[18]

Table 1. Symptoms associated with pelvic organ prolapse[1, 9, 14, 16]

Symptom group	Specific symptom
Vaginal symptoms	▪ Seeing or feeling a bulge ▪ Sensation of vaginal bulging or protrusion ▪ Pelvic or vaginal pressure ▪ Heaviness in pelvis or vagina
Urinary symptoms (LUTS)	▪ Urinary incontinence ▪ Urinary urgency and / or frequency ▪ Overactive bladder ▪ Nocturia ▪ Weak or prolonged urinary stream ▪ Feeling of incomplete emptying ▪ Manual reduction of prolapse to start or complete voiding ▪ Position change to start or complete voiding
Bowel symptoms	▪ Incontinence of flatus or stool ▪ Feeling of incomplete emptying ▪ Hard straining to defaecate ▪ Urgency to defaecate ▪ Digital evacuation to complete defaecation ▪ Splinting vagina or perineum to start or complete defaecation
Sexual symptoms	▪ Dyspareunia ▪ Obstructed penetration ▪ Decreased sensation ▪ Decreased arousal or orgasm ▪ Decreased body image ▪ Anorectal of urinary dysfunction during coitus
Pain	▪ Pain in vagina, bladder, or rectum ▪ Pelvic or low back pain

GENETICS

A recent meta-analysis shows there are four possible genetic polymorphisms that show a moderate to weak association with POP.[19] All of these are associated with either supportive tissue or sex hormone activity. This may explain some part of the association with inheritable POP but does not yet represent information that can aid in clinical evaluation and screening of patients at risk to develop POP or in prognostic prediction of those individuals who have or may develop POP.[18-20]

PREGNANCY, LABOUR, AND DELIVERY

Vaginal delivery, and particularly forceps-assisted vaginal delivery, is strongly predictive of future development of POP, as defined by both being associated with symptoms and signs on physical examination, with the first delivery conferring the greatest risk. Nulliparity and delivery by caesarean section only are strongly protective compared with any vaginal delivery. This suggests that pregnancy alone does not increase risk for the future development of POP, but vaginal delivery does.[18, 21]

AGE AND MENOPAUSE

Increasing age plays a role in the development of POP. Every additional year is responsible for a 10% increase in the risk to develop POP.[22] It is difficult to distinguish age from menopause as independent risk factors. There is evidence of an association between declining oestrogen levels and the quality of pelvic floor muscle and connective tissue, yet the direct link between menopause and POP cannot be established.[18, 22]

Objective quantification of POP

For both clinical and scientific purposes, there are several objective and subjective measurement systems to describe, quantify, and stage POP.

PELVIC ORGAN PROLAPSE QUANTIFICATION

In an effort to quantify prolapse, the Porges and the Baden-Walker systems have been developed in the 1960s and 1970s. However, these systems lacked precision and the inter-observer reliability was poor, which made them difficult to use in research studies and in clinical settings.[8, 23, 24] The Pelvic Organ Prolapse Quantification (POP-Q) system has been developed as an objective site-specific system for describing, quantifying, and staging pelvic support in women. The POP-Q system was developed between 1993 and 1995, with the final version being published in 1996, after it was formally adopted by the International Continence Society (ICS), the American Urogynaecologic Society (AUGS), and the Society of Gynaecologic Surgeons (SGS).[25] The POP-Q system has demonstrated good inter- and intra-observer reliability.[26] The POP-Q has become widely accepted for clinical research and is recommended for clinical use by the American College of Obstetricians and Gynaecologists (ACOG).[27-29] The system provides an outline to describe site-specific vaginal topography using six anatomical points and three length measurements, as is shown in Figure 5. Stages of prolapse, from 0 – IV, are given based on the leading edge of vaginal descent relative to the hymen, as can be found in Table 2. The degree of prolapse may be worse after a lengthy time in the upright position.[1]

Subjective quantification of POP

In the studies described in this thesis, several validated questionnaires were used to assess disease-specific quality of life, vaginal bulge symptoms, micturition, defaecation, and sexuality. The questionnaires can be found in CHAPTER 14 as an appendix.

PATIENT GLOBAL IMPRESSION OF IMPROVEMENT

Patient satisfaction, comparing their situation postoperatively to their situation before surgery, was quantified with the Patient Global Impression of Improvement (PGI-I).[30] The PGI-I consists of one question on a seven-point Likert scale, ranging from 'very much worse' to 'very much better'. 'Much better' or 'very much better' was considered affirmative and presented as dichotomous outcome of a positive score.[31]

UROGENITAL DISTRESS INVENTORY, DEFECATORY DISTRESS INVENTORY, AND INCONTINENCE IMPACT QUESTIONNAIRE

Disease-specific quality of life was quantified with the Urogenital Distress Inventory (UDI),[32] the Defecatory Distress Inventory (DDI),[33] and the Incontinence Impact Questionnaire (IIQ).[32] The UDI and DDI, containing 19 and 11 items respectively, indicate whether complaints of micturition, prolapse, or defecation are present and to what extent they are bothersome. These questions are scored on a four-point Likert scale ranging from 'no bother' to 'greatly bothersome'. The IIQ consists of 13 questions and shows the disease-specific quality of life for urine incontinence, also using a four-point Likert scale. The score of each domain ranges from 0 to 100, high score indicates increasingly bothersome symptoms (UDI and DDI) and a poorer quality of life (IIQ).[32, 33]

Bothersome bulge symptoms were measured using the Urogenital Distress Inventory (UDI). A positive answer on any of the following questions is scored as a subjective recurrence: 'Do you experience a sensation of bulging or protrusion from the vagina?' and 'Do you have a bulge or something protruding that you can see in the vagina?', in combination with a response 'moderately bothersome', or 'greatly bothersome' to the question 'how much does this bother you?'[32]

PELVIC ORGAN PROLAPSE / URINARY INCONTINENCE SEXUAL FUNCTION QUESTIONNAIRE

Sexual functioning, using the Prolapse / Incontinence Sexual Questionnaire (PISQ), containing 12 questions.[34, 35] The PISQ covers three domains: behavioural-emotive, physical, and partner-related. These items are scored on a five-point Likert scale ranging from 0 (always) to 4 (never). Items 1 – 4 are reversely scored and a total of 48 is the maximum score; higher scores indicate better sexual function.[34, 35]

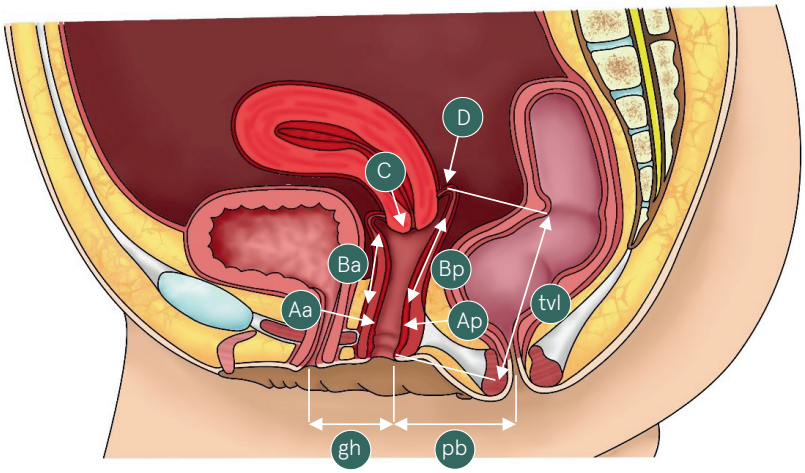

Figure 5. The Pelvic Organ Prolapse Quantification (POP-Q) system[25]
POP-Q point Aa: located in the midline of the anterior vaginal wall 3 cm proximal to the external urethral meatus
POP-Q point Ba: the most distal position of any part of the upper anterior vaginal wall from the vaginal cuff to point Aa
POP-Q point C: the most distal edge of the vaginal cuff (hysterectomy scar)
POP-Q point gh (genital hiatus): measurement from the middle of the external urethral meatus to the posterior margin of the hymen
POP-Q point pb (perineal body): measurement from the posterior margin of the hymen to the mid-anal opening
POP-Q point tvl (total vaginal length): length of the vagina (centimetres) from the vaginal cuff to the hymen
POP-Q point Ap: located in the midline of the posterior vaginal wall 3 cm proximal to the hymen
POP-Q point Bp: the most distal position of any part of the upper posterior vaginal wall from the vaginal cuff to point Ap
POP-Q point D: location of the posterior fornix in women who still have a cervix

Table 2. The five stages of pelvic organ support[1, 8, 25]

Stage	Description
0	No prolapse
I	Most distal prolapse is > 1 cm above the hymen
II	Most distal prolapse is between 1 cm above and 1 cm beyond hymen
III	Most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
IV	Complete eversion, or eversion at least within 2 cm of the total vaginal length

PELVIC FLOOR DISABILITY INDEX

Pelvic Floor Disability Index (PFDI-20) is another validated questionnaire to investigate pelvic floor symptoms.[36, 37] It consists of three subcategories: Pelvic Organ Prolapse

Distress Inventory (POPDI-6), Colorectal-Anal Distress Inventory (CRADI-8), and Urinary Distress Inventory (UDI-6). Total score ranges from zero to 300, the higher the score the greater the dysfunction. The score quantifies complaints and bother over the past three months. The Dutch Urogynaecology Workgroup also advises gynaecologists to use this questionnaire to access their patients POP symptoms in daily practice.

EUROQOL

General health-related quality of life is measured by the EuroQol (EQ-5D-3L and EQ-VAS) questionnaire; it is used to evaluate health utilities and the corresponding quality adjusted life years (QALYs).[38]

Treatment options

Treatment is unnecessary in women with prolapse who are asymptomatic. Treatment is offered if women with POP develop bothersome symptoms attributable to the prolapse.[9] Some women with advanced POP (prolapse beyond the hymen) only have few symptoms and report little or no bother. In these cases, expectant management is advised. Although POP rarely presents as a life-threatening disease, significant morbidity can result from advanced untreated POP that causes bladder outlet obstruction and obstructive uropathy.[8]

CONSERVATIVE TREATMENT

Conservative management options for POP with demonstrated efficacy include pelvic floor muscle training (PFMT) and pessary use.[9, 39, 40] In general, one of these options is offered to patients with symptomatic POP before considering surgery. They are particularly useful for women with a mild degree of prolapse, those who wish to have more children, who are frail and elderly, and those unwilling or not suitable to undergo surgery.[9, 39] Studies with one and two years of follow-up, comparing surgery and pessary use show better results after surgery.[41, 42] Therefore it is also justified and understandable when patients opt for a surgical treatment without trying a conservative option first.

SURGICAL TREATMENT

The main goal of POP surgery is to restore normal pelvic anatomy, eliminate POP symptoms, and normalise bowel, bladder, and sexual function.[9] About one in eight women with POP undergo surgery by the age of 80.[43] Of those who receive prolapse surgery, 13% will require a repeat operation within five years, and 29% will undergo another surgery for genital prolapse or a related condition at some point during their life.[2, 44]

There are several surgical treatment options of apical compartment prolapse. For a long time, vaginal hysterectomy was the preferred treatment for uterine prolapse worldwide.[45] However, recent studies have shown that a uterine-preserving treatment is non-inferior to a hysterectomy at 12 months follow-up.[46, 47] After five years of follow-up, a sacrospinous hysteropexy is superior to hysterectomy in the treatment of uterine descent in terms of recurrences of the apical compartment.[48] A hysterectomy may disrupt important supportive structures of the pelvic floor and a hysterectomy alone often fails to give the right support, subsequently increasing the risk of future vaginal vault prolapse.[49]

This dissertation focusses on two approaches, abdominal versus vaginal treatments. Laparoscopic sacrohysteropexy and vaginal sacrospinous hysteropexy in the treatment for uterine prolapse and laparoscopic sacrocolpopexy and sacrospinous fixation as treatment for vaginal vault prolapse.

LAPAROSCOPIC SACROCOLPOPEXY

Sacrocolpopexy is an abdominal approach in the surgical treatment of post-hysterectomy vaginal vault prolapse (Figure 6). The sacrocolpopexy was first described by Lane in 1962.[50, 51] It is defined as suspension of the vaginal apex to the anterior longitudinal ligament of the sacrum, using a graft.[51] A microporous, monofilament, light-weight polypropylene mesh is the most used type of mesh nowadays. The graft is attached to the sacral promontory on one side and on both the anterior and posterior vagina on the other side. Sacrocolpopexy is associated with lower risk of awareness of prolapse, recurrent prolapse on examination, and repeat surgery for prolapse than a variety of vaginal interventions.[31] This surgery can be performed via laparotomy, laparoscopically, or robotically. In the research described in this thesis all sacrohysteropexies and sacrocolpopexies were performed laparoscopically, with exception of CHAPTERS 2 and 3.

LAPAROSCOPIC SACROHYSTEROPEXY

Sacrohysteropexy is an abdominal procedure that suspends the uterus without removal of the uterus. Although some gynaecologists prefer to perform a supracervical hysterectomy followed by a sacrocervicopexy. Sacrohysteropexy is the suspension of the uterine cervix to the anterior longitudinal ligament of the sacrum using a graft.[51]

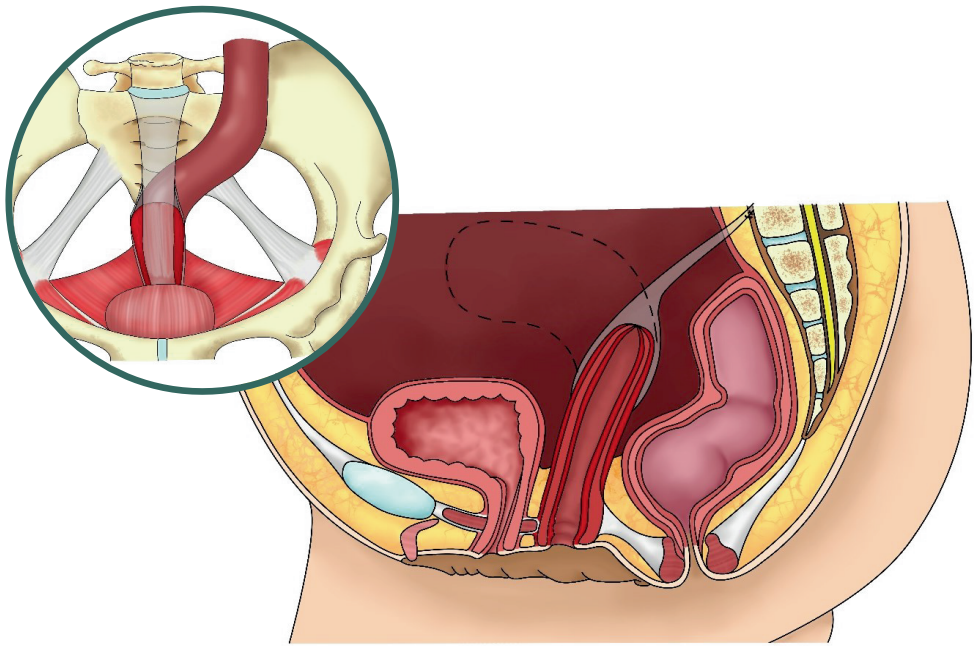

Figure 6. Sacrocolpopexy / sacrohysteropexy

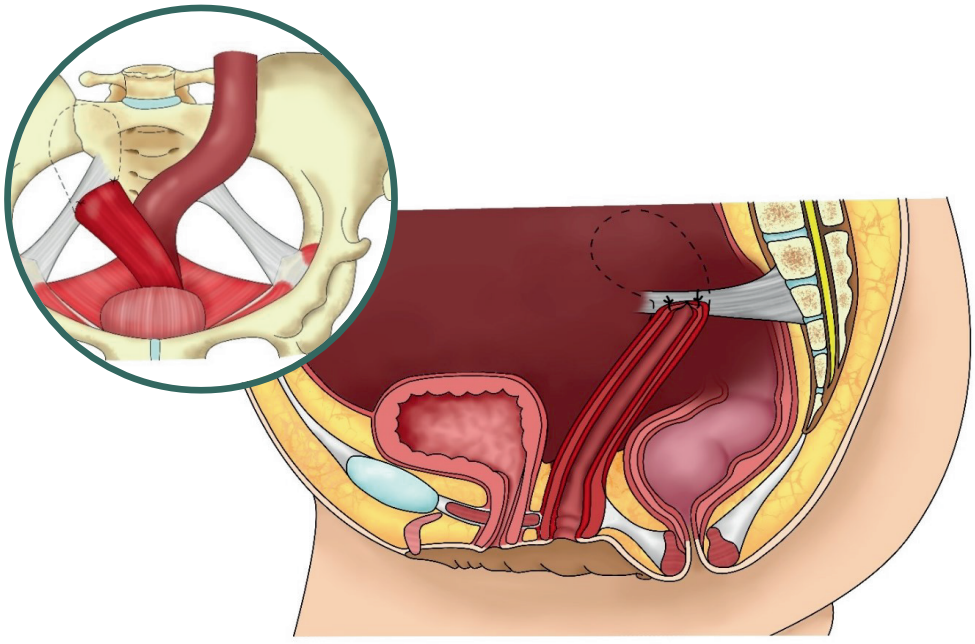

Figure 7. Vaginal sacrospinous fixation / sacrospinous hysteropexy

VAGINAL SACROSPINOUS FIXATION

Vaginal sacrospinous fixation (VSF) as treatment for post-hysterectomy vaginal vault prolapse is defined as suspension of the vaginal apex to the unilateral sacrospinous ligament (SSL) using sutures (Figure 7).[51] The surgical procedure was first described by Sederl, a German gynaecologist, in 1958.[52] Typically, the vaginal apex is attached to the right SSL at least 2 cm medial to the ischial spine, to reduce the risk of pudendal nerve damage.[53] VSF can be performed under direct visualisation of the SSL or an instrument can be used for suture placement by 'palpation' alone, such as the i-stitch®, Endo Stitch®, and Capio® devices.[51] It is the most performed surgical treatment for vaginal vault prolapse in the Netherlands. VSF is preferred as first choice surgical treatment by 66% of Dutch gynaecologists, followed by 14% who chose laparoscopic sacrocolpopexy as first choice surgical treatment for vaginal vault prolapse.[54]

VAGINAL SACROSPINOUS HYSTEROPEXY

Vaginal sacrospinous hysteropexy (SSHP) as treatment for uterine prolapse is one of the most performed surgeries for primary uterine descent. During this vaginal surgery the cervix is lifted towards one of the sacrospinous ligaments and attached with sutures, resulting in suspension of the uterus. The SSHP (with uterus present) procedure has great similarities with the VSF (post-hysterectomy). Several studies show that SSHP is a safe procedure for the treatment of uterovaginal prolapse and severe complications are rarely seen during and after this surgery.[46, 48, 55-57]

Aim and outline of this thesis

Various treatment options exist in the treatment of apical prolapse. However, prospective comparative trials are rare. The aim of this thesis is to examine which treatment is the most optimal, in terms of effectiveness and safety, for women suffering from uterovaginal prolapse or post-hysterectomy vaginal vault prolapse.

This thesis aims to answer the following questions:

- What are the short-term and long-term outcomes of laparoscopic versus open abdominal sacrocolpopexy in the treatment of vaginal vault prolapse? (CHAPTERS 2 and 3)
- Which treatment is the most optimal for patients with uterine prolapse, laparoscopic sacrohysteropexy or vaginal sacrospinous hysteropexy? (CHAPTERS 4 and 5)

- Which treatment is the most optimal for patients with post-hysterectomy vaginal vault prolapse, laparoscopic sacrocolpopexy or vaginal sacrospinous fixation? (CHAPTERS 6 and 7)
- Which patient-related and physician-related factors are of importance for Dutch gynaecologists, when surgically treating patients with apical prolapse? (CHAPTER 8)

Outline of this thesis

The results of a randomised controlled trial, which compared laparoscopic sacrocolpopexy and open abdominal sacrocolpopexy in the treatment of post-hysterectomy vault prolapse, at 12 months follow-up, are described in **CHAPTER 2** (SALTO trial).

CHAPTER 3 provides the long-term follow-up of the SALTO trial, which compared laparoscopic sacrocolpopexy with open abdominal sacrocolpopexy.

In **CHAPTER 4** a retrospective study with long-term follow-up is described, which compared laparoscopic sacrohysteropexy with vaginal sacrospinous hysteropexy.

Whether laparoscopic sacrohysteropexy is non-inferior to vaginal sacrospinous hysteropexy for women with uterine prolapse POP-Q stage 2 or higher, is provided in **CHAPTER 5**. These are the results of a randomised trial with a follow-up period of 12 months (LAVA trial).

CHAPTER 6 provides a study protocol of a randomised controlled trial to investigate outcomes after laparoscopic sacrocolpopexy compared with vaginal sacrospinous fixation (SALTO-2 study protocol).

CHAPTER 7 presents the results of a randomised controlled trial and a prospective cohort study, comparing laparoscopic sacrocolpopexy and vaginal sacrospinous fixation in the treatment of POP-Q stage ≥ 2 vaginal vault prolapse, with a follow-up time of 12 months (SALTO-2 trial).

Which surgical treatment Dutch gynaecologists prefer when treating patients with apical prolapse and which factors play a role in their choices is answered in **CHAPTER 8**. These are the results of a qualitative study.

CHAPTER 9 contains a general discussion, clinical implications and future perspectives.

CHAPTER 10 includes the impact paragraph, which explains the significance of this thesis.

CHAPTER 11 summarises this dissertation in English and in **CHAPTER 12** a Dutch summary is provided.

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CHAPTER 2

Laparoscopic sacrocolpopexy compared with open abdominal sacrocolpopexy for vault prolapse repair: a randomised controlled trial

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International Urogynaecology Journal. 2017 Oct;28(10):1469-1479.

Abstract

INTRODUCTION AND HYPOTHESIS

The objective was to evaluate the functional outcome after laparoscopic sacrocolpopexy versus open sacrocolpopexy in women with vault prolapse.

METHODS

A multicentre randomised controlled trial was carried out at four teaching and two university hospitals in the Netherlands in women with symptomatic vault prolapse requiring surgical treatment. Participants were randomised for laparoscopic or open sacrocolpopexy. Primary outcome was disease-specific quality of life, measured using the Urogenital Distress Inventory (UDI) questionnaire at 12 months follow-up. Secondary outcomes included anatomical outcome and perioperative data. We needed 74 participants to show a difference of 10 points on the prolapse domain of the UDI 12 months after surgery (power of 80%, α error 0.05).

RESULTS

Between 2007 and 2012, a total of 74 women were randomised. Follow-up after 12 months showed no significant differences in domain scores of the UDI between the two groups. After 12 months, both groups reported a UDI score of 0.0 (IQR 0 – 0) for the domain 'genital prolapse', which was the primary outcome. There were no significant differences between the two groups (p = 0.93). The numbers of severe complications were 4 in the laparoscopic group versus 7 in the open abdominal group (RR 0.57; 95% CI 0.50 – 2.27). There was less blood loss and a shorter hospital stay after laparoscopy; 2 (IQR 2 – 3) versus 4 (IQR 3 – 5) days, which was statistically different. There was no significant difference in anatomical outcome at 12 months.

CONCLUSION

Our trial provides evidence to support a laparoscopic approach when performing sacrocolpopexy, as there was less blood loss and hospital stay was shorter, whereas functional and anatomical outcome were not statistically different.

TRIAL REGISTRATION

Dutch trial register NTR3276.

Introduction

Post-hysterectomy vaginal vault prolapse has a reported incidence of 0.36 to 3.6 per 1,000 woman years or a cumulative incidence of 0.5%.[1, 2] Abdominal sacrocolpopexy (ASC) is the most effective treatment for vaginal vault prolapse, with success rates of 93 – 99%, and is now considered the first-choice treatment for vaginal vault prolapse.[3-8] Sacrocolpopexy is a procedure designed to treat apical compartment prolapse, including uterine or vaginal vault prolapse, in addition to multi-compartment prolapse.[9, 10]

According to a Cochrane review on the subject, ASC led to a lower rate of recurrent vault prolapse and dyspareunia compared with vaginal sacrospinous ligament fixation.[3] Nevertheless, ASC is also associated with a longer operative time, recovery period, and higher cost.[11]

Laparoscopic sacrocolpopexy (LSC) was first reported in 1994.[12] Since then, it has gained in popularity, before any clinical advantage over the open abdominal procedure was proven. Although the literature regarding LSC was limited and prospective comparative randomised trials were lacking, LSC has been widely adopted by pelvic reconstructive surgeons. LSC has potential advantages over laparotomy, as morbidity, hospital stay, postoperative pain, and recovery are all supposed to be less. Moreover, the aesthetic result is better after minimally invasive sacrocolpopexy. However, the laparoscopic approach is more challenging and the literature reports a long learning curve associated with this technique.[13, 14] More importantly, it is unknown if the laparoscopic mesh fixation to the promontory results in an equal anatomical outcome, as it has been stated that as part of the laparoscopic approach, the fixation point is higher, which could result in a more vertical position of the vagina.

Previous studies comparing LSC with ASC showed less blood loss and a significantly shorter hospital stay in the laparoscopic group.[15-17] A randomised controlled trial comparing laparoscopic with open abdominal sacrocolpopexy in patients with a symptomatic vault prolapse, which was published during the follow-up period of our trial, reported significantly less blood loss, a higher haemoglobin level, and a shorter hospital stay in favour of the laparoscopic group. There was no significant difference in anatomical outcome between the two groups. The exclusion criteria of the published study were very strict, and only patients with at least a grade 2 vault prolapse, a BMI less than 35, and without urinary stress incontinence were included.[15] This does not match the patient population of the general practice. Our trial creates a realistic reflection of daily practice.

Considering the lack of evidence, we performed a randomised trial comparing LSC with ASC using disease-specific quality of life as the primary outcome.

Materials and methods

We performed a multicentre randomised controlled trial comparing LSC and ASC in four teaching and two university hospitals in the Netherlands. All hospitals take part in the Dutch consortium for women's health. The consortium is a collaborative network in clinical studies in the field of obstetrics and gynaecology. The study was approved by the ethical committee of the Máxima Medical Centre in Veldhoven (file number NL12130.015.06) and the Board of Directors of all participating hospitals, and was registered in the Dutch Trial Register (NTR3276).

Eligible women with vault prolapse who met the inclusion criteria were counselled about the trial. Vault prolapse was defined as a post-hysterectomy prolapse of the apical compartment. After written informed consent was given, randomisation was performed by an independent research secretariat located in Amsterdam after a phone call or e-mail by the coordinating investigator. The treatment allocation was done by opaque sealed envelopes in a 1:1 ratio to either LSC or ASC. Women received a randomised case number to ensure that their data would be treated anonymously. No changes were made to the protocol after trial commencement, other than including more participating centres.

We included women with a history of hysterectomy presenting with symptomatic vaginal vault prolapse, with or without concomitant cystocele and rectocele, who chose to undergo surgery. Women who had undergone previous surgical correction of a vault prolapse were excluded, in addition to women with a contraindication for a surgical intervention because of their general physical condition.

Surgical intervention

The intervention was either abdominal or laparoscopic sacrocolpopexy following randomisation. To exclude a learning curve for both surgical interventions and procedure bias, all participating gynaecologists had to have performed at least 50 procedures before the start of the study. The procedures were standardised as much as possible to confirm consistency. Participants received a bowel preparation the day before the operation. Prophylactic antibiotics were given peroperatively (metronidazole / cefazolin). As prophylaxis for thromboembolism per- and postoperatively subcutaneous low

molecular weight heparin was administered.

ABDOMINAL SACROCOLPOPEXY

ASC was performed by a laparotomy under general anaesthesia, preferably using a Pfannenstiel incision. The peritoneum from the promontory to the vault was incised to expose the rectovaginal and vesicovaginal fascia, extending to the sacral promontory. A type 1 polypropylene mesh was used, which was cut into two pieces 3 cm wide and approximately 15 cm long. One piece of the mesh was attached between the vagina and the bladder anteriorly, and another as far down the posterior vaginal wall as possible using Ethibond, non-absorbable, synthetic and multifilament sutures from Ethicon. The mesh was fixated to the anterior part of the vaginal vault with four stitches, and six stitches were used to fixate the mesh posteriorly. The two meshes were sutured to each other, after which only the posterior mesh was fixed to the longitudinal vertebral ligament by staples or non-absorbable sutures, depending on surgeon preference. Excess mesh was trimmed and removed. The mesh was peritonealised.

LAPAROSCOPIC SACROCOLPOPEXY

LSC was performed under general anaesthesia with four trocars, one for the scope and three side trocars. The essence of the procedure was the same as for the abdominal procedure. The vaginal vault was elevated with a vaginal probe. The peritoneum from the promontory to the vault was incised laparoscopically by scissors to expose the rectovaginal and vesicovaginal fascia. One piece of type 1 polypropylene mesh was attached anteriorly and another as low as possible on the posterior vaginal wall. The sutures, size of the mesh, and its fixation were the same as in the abdominal procedure. The mesh was attached to the sacral promontory using staples and was peritonealised. All centres used polypropylene meshes and the same sutures.

Perioperative assessment

When stress incontinence was diagnosed preoperatively, it was up to the patient and her gynaecologist whether incontinence surgery was performed during the same procedure or in a second operation after evaluation of the sacrocolpopexy on the stress urine incontinence. A tension-free vaginal tape was used if incontinence surgery was indicated. No Burch colposuspensions were performed. Both procedures could be completed with any necessary concomitant vaginal operation after the vault suspension had been carried out. The decision to perform additional prolapse surgery was made by the surgeon after the sacrocolpopexy was completed.

A urethral catheter was left in situ and was removed the first day postoperatively or as clinically indicated. If the procedure was complicated by a bladder lesion, the catheter

was removed after one week. In the case of urinary retention after removal of the catheter on the first day, the catheter was reinserted for another day.

Outcome measures

Women were sent a questionnaire preoperatively, at 3 – 6 months postoperatively, and 12 months postoperatively. Women were asked to undergo a pelvic examination preoperatively and at 6 weeks and 12 months postoperatively. The observer was an independent researcher / resident, who had not performed the surgery. The researcher was not blinded to the type of surgery.

The primary outcome of the study was functional outcome, which was evaluated using the Urogenital Distress Inventory (UDI) at 12 months follow-up.[18] The UDI is a validated questionnaire evaluating prolapse-related symptoms. The questionnaires also contain versions of the Defecatory Distress Inventory (DDI),[19] the Incontinence Impact Questionnaire (IIQ),[18] the Patient Global Impression of Improvement (PGI-I),[20] and questions about sexuality, which were secondary outcomes. Other secondary outcomes were procedure time, amount of estimated blood loss, hospital stay, perioperative complications, reinterventions, and long-term complications. Reintervention included incontinence or prolapse surgery. All collected data were registered in a case report form. Another secondary outcome was the composite outcome of success, defined as no prolapse beyond the hymen, no bothersome bulge symptoms, and no repeat surgery or pessary use for recurrent prolapse within 12 months.[20, 21] Remaining study parameters were body mass index, pre- or postmenopausal status, use of oestrogens, combined prolapse surgery, and stress urinary incontinence procedures. The anatomical outcome using the Pelvic Organ Prolapse Quantification system (POP-Q)[22] was the secondary endpoint. A pelvic examination was performed to evaluate the anatomical results of the prolapse repair.

SAMPLE SIZE

A difference between the two surgical techniques of 10 points between the two groups on the prolapse domain of the UDI 12 months after surgery was considered to be clinically relevant. Assuming a standard deviation of the score on this domain of 15 points, we needed 74 participants to show a statistically significant difference in the primary outcome (power of 80%, α error 0.05).[23]

STATISTICAL ANALYSIS

The trial was a prospective, randomised controlled trial conducted with the aim of determining the superiority of the primary endpoint (prolapse domain of the UDI) in the laparoscopic sacrocolpopexy group. Analysis was by intention to treat. The domain

scores were calculated for the UDI, DDI, and IIQ. To examine differences between groups we used an unpaired *t* test or Mann-Whitney *U* test for continuous variables depending on the distribution, whereas a Pearson's Chi-squared test was used for dichotomous variables. We used two-sided significance tests, and a p value <0.05 was considered to indicate statistical significance. For dichotomous outcomes, we calculated relative risks and 95% confidence intervals. We used the statistics package SPSS version 22 (IBM, Armonk, NY, USA).

Results

The results are reported by means of the IUGA / ICS recommendations for reporting outcomes of surgical procedures for pelvic organ prolapse[24] and the CONSORT statement (www.consort-statement.org). Between 2007 and 2012, we randomised 37 women to the LSC group and 37 to the ASC group (Figure 1). One woman randomised to the laparoscopy group was very satisfied with a pessary, which she received to cover the time until the operation, and she cancelled surgery. In the abdominal group, one patient underwent a sacrospinous fixation of the vault prolapse because she was not happy with the randomisation result. Both women were included in the intention to treat analysis. In the laparoscopic group one procedure was combined with concomitant vaginal surgery, versus three in the open group. In both groups one procedure was combined with a tension-free vaginal tape (TVT-O). In the laparoscopic group, no concomitant vaginal prolapse surgery was performed, whereas in the open group, two procedures were combined with a posterior colporrhaphy.

At 12 months follow-up, there were 14 questionnaires missing, of which 11 participants (15.5%) were unwilling to complete the questionnaires; one participant did not receive the intervention, one participant postponed the procedure until the end of the study period for private reasons and had not yet completed the one-year follow-up, and one patient died five days after the intervention because of a complication of the intervention.

The number of missing questionnaires is presented in Figure 1. All non-responders were contacted by telephone and most of them explained that they were doing well, which was a reason not to return the questionnaires. Patient characteristics of responders and non-responders were comparable.

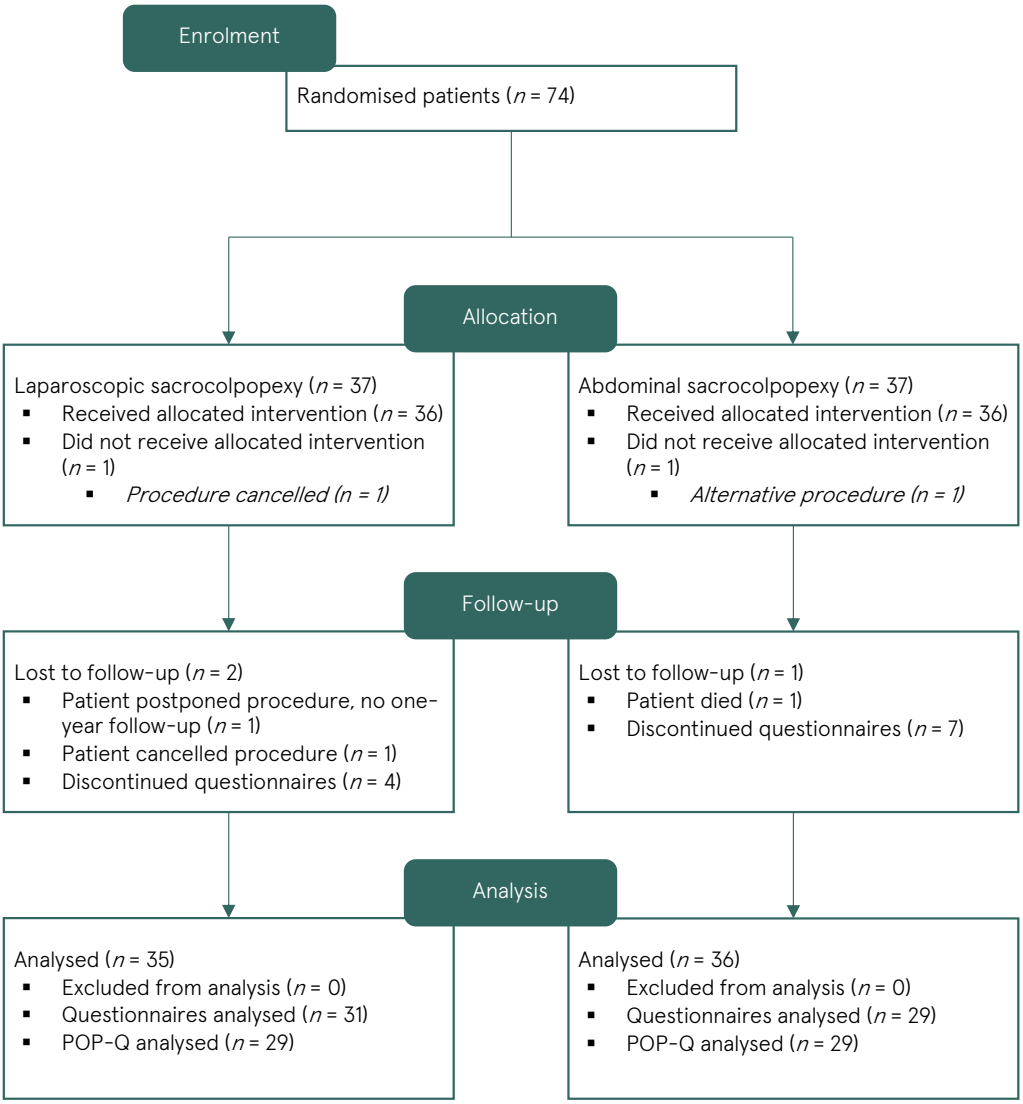

Figure 1. Flow diagram of the study population

Table 1 shows the baseline characteristics of the study population. The median age of the study population was 65.2 years (IQR 61 – 71 years) in the laparoscopic group and 66.7 years (IQR 64 – 73 years) in the abdominal group. Other baseline characteristics were also comparable, including the preoperative POP-Q stage.

Table 2 shows UDI, DDI and IIQ scores before surgery and 12 months after surgery. Both groups reported a UDI score of 0.0 (IQR 0 – 0) for the domain 'genital prolapse' ($p = 0.93$) after 12 months, which was the primary outcome. The domain 'pain and discomfort' showed a score of 0.0 (IQR 0 – 29) for the laparoscopic group versus 8.3 (IQR 0 – 33) for the abdominal group ($p = 0.15$). The UDI domain scores improved significantly for both groups at 12 months post-surgery ($p < 0.001$). At 12 months follow-up, the PGI-I score of 'very much better' was 25% (8/31) for the laparoscopy group, and 26% (7/27) for the open abdominal group. When we added the score of 'much better' the percentages were 71% (22/31) and 74% (20/27), which was not statistically different ($p = 0.563$).

Table 1. Baseline characteristics

	Laparoscopic sacrocolpopexy (*n* = 37)	**Open abdominal sacrocolpopexy (*n* = 37)**
Age (years)		
Median (IQR)	65 (61 – 71)	67 (64 – 73)
Body mass index (kg/m^2)		
Mean (range)	25.3 (18 – 32)	25.9 (21 – 33)
Parity		
No./total no. of patients (%)		
0	1/34 (2.9)	0/34 (0.0)
1	3/34 (8.8)	2/34 (5.9)
2	14/34 (41.2)	14/34 (41.2)
3	13/34 (38.2)	9/34 (26.5)
≥4	3/34 (8.8)	9/34 (26.5)
Menopausal status		
No./total no. of patients (%)		
Premenopausal	1/36 (2.8)	0/37 (0.0)
Postmenopausal	35/36 (97.2)	37/37 (100.0)
Urinary incontinence		
No./total no. of patients (%)		
None	20/35 (57.1)	15/35 (42.9)
Stress	2/35 (5.7)	3/34 (8.8)
Urgency	4/35 (11.4)	4/35 (11.4)
Combined	9/35 (25.7)	13/35 (37.1)
Oestrogens use		
No./total no. of patients (%)		
None	3/29 (10.3)	5/29 (17.2)
Local/Systemic	26/29 (89.7)	24/29 (28.8)
History of gynaecological surgery		
No./total no. of patients (%)		
TVH only	13/36 (36.1)	7/34 (20.6)
TVH & ACR	3/36 (8.3)	7/34 (20.6)
TVH & PCR	1/36 (2.8)	2/34 (5.9)
TVH & ACR/PCR	11/36 (30.6)	4/34 (11.8)
TVH & later ACR & mesh	1/36 (2.8)	0/34 (0)
TVH & ACR & later PCR	0/36 (0)	1/34 (2.9)
TAH only	3/36 (8.3)	11/34 (32.4)
TAH & PCR	1/36 (2.8)	2/34 (5.9)
Laparoscopic hysterectomy	2/36 (5.6)	0/34 (0)
Supracervical hysterectomy	1/36 (2.8)	0/34 (0)

Table 1 (continued). Baseline characteristics

	Laparoscopic Sacrocolpopexy (n = 37)			Open Abdominal Sacrocolpopexy (n = 37)		
Preoperative POP-Q stage No./total no. of patients (%)						
Apical compartment						
Stage 0	0/32 (0)			1/34 (2.9)		
Stage 1	9/32 (28.1)			14/34 (41.2)		
Stage 2	9/32 (28.1)			9/34 (26.5)		
Stage 3	7/32 (21.9)			4/34 (11.8)		
Stage 4	7/32 (21.9)			6/34 (17.6)		
Anterior compartment						
Stage 2-4	24/30 (80)			21/32 (65.6)		
Posterior compartment						
Stage 2-4	10/28 (35.7)			20/32 (62.5)		
POP-Q measurements	**Aa**	**Ba**	**C**	**Aa**	**Ba**	**C**
	-0.5 ± 1.4 (-3 – 2)	0.8 ± 2.3 (-3 – 4)	1.1 ± 3.1 (-6 – 6)	-.5 ± 1.9 (-3 – 3)	0.3 ± 3.1 (-5 – 8)	-0.1 ± 4.4 (-8 – 10)
	gh	**pb**	**tvl**	**gh**	**pb**	**tvl**
	3.8 ± 0.8 (2 – 5)	2.7 ± 0.5 (2 – 3)	7.9 ± 1.3 (6 – 11)	3.7 ± 0.8 (3 – 5)	3.1 ± 0.7 (2 – 4)	8.3 ± 1.5 (4 – 10)
	Ap	**Bp**	**D**	**Ap**	**Bp**	**D**
	-1.5 ± 1.8 (-3 – 3)	-0.6 ± 2.6 (-3 – 4)	-	-0.5 ± 1.8 (-3 – 3)	0.4 ± 3.0 (-4 – 8)	-

POP-Q stage 1: most distal prolapse is > 1 cm above the hymen
POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen
POP-Q stage 3: most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
POP-Q stage 4: total prolapse
TVH transvaginal hysterectomy, *TAH* total abdominal hysterectomy, *ACR* anterior colporrhaphy, *PCR* posterior colporrhaphy, *POP-Q* pelvic organ prolapse quantification

Clinical outcomes are presented in Table 3. In the LSC group blood loss was 86 ml (IQR 10 – 100) versus 200 ml (IQR 100 – 300) in the ASC group ($p < 0.001$). Hospital stay was two days (IQR 2 – 3) versus four days (IQR 3 – 5; $p < 0.001$). Duration of surgery (125 versus 115 min; $p = 0.31$), number of complications during surgery (5.6% versus 0%, $p = 0.15$), and number of complications during admission (5.6% versus 18.9%, $p = 0.06$) were not statistically significantly different.

The laparoscopic group contains fewer complications, four in the laparoscopic group versus seven in the open group, which is not significantly different (RR 0.57; 95% CI 0.50 – 2.27). In the open abdominal group the complications that occurred were more severe. One complication concerned a 79-year-old woman who presented with cardiac arrhythmia on the third day after surgery. She was diagnosed with sepsis and a bowel perforation was suspected. A relaparotomy was performed and the diagnose bowel perforation could be confirmed. She developed pneumonia and due to multi-organ failure, she died on the fifth day after surgery. The complication was considered a calamity and was reported to the health care inspectorate.

Table 2. Domain scores disease-specific quality of life

	Before surgery		12 months after surgery		*p* value
	LSC (*n* = 34)	ASC (*n* = 31)	LSC (*n* = 31)	ASC (*n* = 29)	
Urogenital distress inventory (UDI)					
Overactive bladder	33.3 (11 – 56)	44.4 (22 – 50)	0.0 (0 – 11)	5.6 (0 – 19)	0.30
Urinary incontinence	16.7 (0 – 50)	16.7 (0 – 42)	16.7 (0 – 33)	16.7 (0 – 33)	0.52
Obstructive micturition	0.0 (0 – 33)	16.7 (0 – 58)	0.0 (0 – 13)	0.0 (0 – 0)	0.28
Genital prolapse	66.7 (58 – 92)	66.7 (33 – 67)	0.0 (0 – 0)	0.0 (0 – 0)	0.92
Pain	16.7 (0 – 50)	33.3 (17 – 33)	0.0 (0 – 29)	8.3 (0 – 33)	0.15
Recurrent bladder infections					0.50
No./total no. of patients (%)					
Never	22/34 (64.7)	17/30 (56.7)	26/31 (83.9)	21/28 (75)	
Once	8/34 (23.5)	4/30 (13.3)	4/31 (12.9)	4/28 (14.3)	
2 – 4 times	1/34 (2.9)	5/30 (16.7)	0/31 (0)	2/28 (7.1)	
> 4 times	3/34 (8.8)	4/30 (13.3)	1/31 (3.2)	1/28 (3.6)	
Incontinence de novo					
No./total no. of patients (%)					
Urge incontinence			2/31 (6.5)	3/29 (10.3)	0.23
Stress incontinence			5/31 (16.1)	4/29 (13.8)	0.69
Defecatory distress inventory (DDI)					
Obstipation	0.0 (0 – 17)	0.0 (0 – 17)	0.0 (0 – 17)	0.0 (0 – 17)	0.76
Obstructive defecation	4.2 (0 – 17)	8.3 (0 – 25)	0.0 (0 – 8)	0.0 (0 – 8)	0.56
Pain	0.0 (0 – 0)	0.0 (0 – 0)	0.0 (0 – 0)	0.0 (0 – 17)	0.03
Faecal incontinence	0.0 (0 – 17)	8.3 (0 – 33)	0.0 (0 – 0)	0.0 (0 – 17)	0.13
Flatus incontinence	33.3 (0 – 67)	33.3 (0 – 67)	0.0 (0 – 33)	0.0 (0 – 17)	0.48
Incontinence impact questionnaire (IIQ)					
Physical	25.0 (0 – 50)	0.0 (0 – 33)	0.0 (0 – 25)	0.0 (0 – 17)	0.66
Mobility	11.1 (0 – 33)	33.3 (11 – 44)	0.0 (0 – 28)	11.1 (0 – 25)	0.37
Social	11.1 (0 – 22)	11.1 (0 – 33)	0.0 (0 – 6)	0.0 (0 – 11)	0.47
Embarrassment	0.0 (0 – 17)	16.7 (0 – 17)	0.0 (0 – 8)	0.0 (0 – 17)	0.90
Emotional	11.1 (0 – 33)	22.2 (0 – 33)	0.0 (0 – 22)	0.0 (0 – 25)	0.54
Sexuality					
No./total no. of patients (%)					
Sexually active	20/32 (62.5)	14/31 (45.1)	26/28 (92.8)	26/28 (92.8)	1.00
Dyspareunia					0.23
Not at all	11/31 (35.5)	5/31 (16.1)	14/26 (53.8)	10/28 (35.7)	
Moderately	0/31 (0)	3/31 (9.7)	3/26 (11.5)	3/28 (10.7)	
Somewhat	4/31 (12.9)	4/31 (12.9)	1/26 (3.8)	0/28 (0)	
Quite a bit	2/31 (6.5)	1/31 (3.2)	0/26 (0)	0/28 (0)	
Not applicable	14/31 (45.2)	18/31 (58.1)	8/26 (30.8)	15/28 (53.6)	
Frequency coitus					0.66
Never	17/32 (53.1)	18/31 (58.1)	11/28 (39.3)	15/28 (53.6)	
<1 / month	4/32 (12.5)	5/31 (16.1)	3/28 (10.7)	4/28 (14.3)	
1 – 2 / month	4/32 (12.5)	3/31 (9.7)	9/28 (32.1)	6/28 (21.4)	
1 / week	6/32 (18.8)	3/31 (9.7)	4/28 (14.3)	1/28 (3.6)	
> 1 / week	1/32 (3.1)	2/31 (6.5)	1/28 (3.6)	2/28 (7.1)	

Data are given in medians (IQR), unless stated otherwise
LSC laparoscopic sacrocolpopexy, *ASC* abdominal sacrocolpopexy

Two other women in the open abdominal group had wound dehiscence, which needed surgical repair. One procedure carried out in the laparoscopic group had to be converted because of bleeding coming from the promontory. The total estimated blood loss of this procedure was 1,200 ml.

Table 3. Clinical outcome

	Laparoscopic Sacrocolpopexy (*n* = 36)	**Open Abdominal Sacrocolpopexy (*n* = 37)**	***p* value**
Operative time (minutes)			
Median (IQR)	125 (108 – 135)	115 (94 – 129)	0.31
Estimated blood loss (ml)			
Median (IQR)	86 (10 – 100)	200 (100 – 300)	<0.001
Hospital stay (days)			
Median (IQR)	2 (2 – 3)	4 (3 – 5)	<0.001
Complications during surgery			0.15
No./total no. of patients (%)	2/36 (5.6)	0/36 (0)	
Bladder lesion (conversion)	1	0	
Bleeding (conversion)	1	0	
Complications during admission			0.06
No./total no. of patients (%)	2/36 (5.6)	7/37 (18.9)	
Fatal bowel perforation	0	1	
Wound dehiscence	0	2	
Pulmonary embolism	0	1	
Ileus	0	3	
Wound infection	1	0	
Pyelonephritis (re-admission)	1	0	

Table 4 shows the surgical reinterventions for pelvic organ prolapse and occult / new urinary incontinence. In the laparoscopy group, there were seven women in whom a reintervention for prolapse or incontinence was performed, versus four in the open surgery group (RR 1.75; 95% CI 0.81 – 3.91). In both groups, three women had surgery for stress urinary incontinence. The laparoscopic group had four reinterventions for recurrent POP versus one in the open group (RR 4, 95% CI 0.84 – 5.73). All surgical reinterventions concerned the posterior compartment. No pessaries were placed as a reintervention. At 12 months follow-up, two participants in the laparoscopic group developed de novo urge incontinence, and five participants developed de novo stress incontinence, versus three and four respectively in the open abdominal group, according to the questionnaires. There was no significant difference in these results between the groups.

There were no significant differences between the groups in anatomical results 12 months postoperatively according to the POP-Q, as shown in Table 5. At the 12-months

Table 4. Surgical reinterventions for pelvic organ prolapse and occult / new urinary incontinence

	Laparoscopic Sacrocolpopexy (*n* = 36)	Open Abdominal Sacrocolpopexy (*n* = 37)	*p* value
Reintervention			
No./total no. of patients (%)	7/36 (16.7)	4/37 (10.8)	0.12
Incontinence surgery	3/36 (8.3)	3/37 (8.1)	1.00
TVT-S	1	0	
TVT-O	1	3	
TOT	1	0	
Prolapse surgery	4/36 (11.1)	1/37 (2.7)	0.17
Rectopexy	1	0	
PCR	2	0	
Enterocele repair	1	0	
Posterior VM	0	1	

TVT tension-free vaginal tape (*S* secur, *O* obturator), *TOT* trans obturator tape, *PCR* posterior colporrhaphy, *VM* vaginal mesh

postoperative follow-up visit no mesh or suture exposures were seen during vaginal examination in the two groups. No other complications were seen at the 12-months follow-up visit.

We asked our population at the 12-months follow-up visit about their complaints and four of the participants mentioned (unexplained) pelvic pain; one in the laparoscopic group and three in the open abdominal group. In all four of these participants, pelvic pain was already present before the surgery, but it turned out to be worse 12 months after the procedure. If we look at the questionnaires, eight participants in the laparoscopic group versus 13 in the abdominal group had pelvic pain after 12 months, which was not a significant difference ($p = 0.056$).

The composite outcome of success was 83.8% (31/37) for the laparoscopy group and 89.2% (33/37) in the open abdominal group. In both groups, there were no recurrences of stage 2 or higher of the apical compartment. Two patients in the laparoscopy group had bothersome bulge symptoms compared with four in abdominal group. Five participants of the laparoscopy group were re-operated for POP, versus one in the abdominal group.

According to the questionnaires, in both groups more participants became sexually active, there was less dyspareunia, and the coitus frequency was increased at 12 months postoperatively (Table 2). There were no significant differences between the groups.

Table 5. 12 months postoperative POP-Q

	Laparoscopic Sacrocolpopexy (*n* = 29)			Open Abdominal Sacrocolpopexy (*n* = 29)			*p* value		
Postoperative POP-Q stage No./total no. (%)									
Apical compartment							0.13		
Stage 0	23/29 (79.3)			27/29 (93.1)					
Stage 1	6/29 (20.7)			2/29 (6.9)					
Stage 2	0/29 (0)			0/29 (0)					
Stage 3	0/29 (0)			0/29 (0)					
Stage 4	0/29 (0)			0/29 (0)					
Anterior compartment							0.87		
Stage 2-4	8/29 (27.6)			7/29 (24.1)					
Posterior compartment							0.65		
Stage 2-4	8/29 (27.6)			10/29 (34.5)					
POP-Q measurements	**Aa**	**Ba**	**C**	**Aa**	**Ba**	**C**	**Aa**	**Ba**	**C**
	-0.5 ± 1.4 (-3–2)	0.8 ± 2.3 (-3–4)	1.1 ± 3.1 (-6–6)	-.5 ± 1.9 (-3–3)	0.3 ± 3.1 (-5–8)	-0.1 ± 4.4 (-8-10)	0.54	0.64	0.54
	gh	**pb**	**tvl**	**gh**	**pb**	**tvl**	**gh**	**pb**	**tvl**
	3.8 ± 0.8 (2–5)	2.7 ± 0.5 (2–3)	7.9 ± 1.3 (6–11)	3.7 ± 0.8 (3–5)	3.1 ± 0.7 (2–4)	8.3 ± 1.5 (4–10)	0.17	0.62	0.76
	Ap	**Bp**	**D**	**Ap**	**Bp**	**D**	**Ap**	**Bp**	**D**
	-1.5 ± 1.8 (-3–3)	-0.6 ± 2.6 (-3–4)	-	-0.5 ± 1.8 (-3–3)	0.4 ± 3.0 (-4–8)	-	0.48	0.45	-

System involves quantitative measurements of various points of vaginal wall with hymen as reference point. Degree of prolapse of anterior vaginal wall (Aa and Ba), posterior vaginal wall (Ap and Bp) and uterus (C) is measured in centimetres above or proximal to hymen (negative number) of beyond or distal to the hymen (positive number), with plane of hymen defined as zero. Point A represents the descent of a measurement point 3 cm proximal to the hymen on the anterior (Aa) and posterior (Ap) vaginal wall. B is the most descended edge on the anterior (Ba) and posterior (Bp) vaginal wall
POP-Q stage 1: most distal prolapse is > 1 cm above the hymen
POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen
POP-Q stage 3: most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
POP-Q stage 4: total prolapse
POP-Q pelvic organ prolapse quantification

Discussion

Main findings

We performed a multicentre randomised trial that compared laparoscopic and open abdominal sacrocolpopexy in patients with a vaginal vault prolapse. There were no significant differences in quality of life related to micturition, prolapse, and defecation in the two groups. Anatomical results were similar at 12 months after surgery. In the laparoscopic group, there was less blood loss during the procedure and the hospital stay was shorter.

Quality of life was the primary outcome in our trial. In both groups, the functional outcomes of the UDI domain scores were significantly improved, which supports previous findings of a high success rate for sacrocolpopexy.[3-5] Disease-specific quality of life was statistically equal after both laparoscopic and open abdominal sacrocolpopexy. These results are in line with those of a randomised controlled trial by Freeman et al. comparing open abdominal with laparoscopic sacrocolpopexy, which was published recently.[15] In this study, there was also less blood loss and a shorter hospital stay after laparoscopy.

We chose disease-specific quality of life, using the UDI questionnaire, as the primary outcome of our study. As outcome definitions for evaluating prolapse surgery were improved after the start of the trial, after a publication by Barber et al.,[25] we added the combined outcome measure (recurrent pelvic organ prolapse stage ≥ 2 in the apical compartment, with bothersome bulge symptoms, and reinterventions), at 12 months of follow-up. This outcome measure was not specified in the study protocol.

There was no significant difference in anatomical outcome between the two groups in this trial.[15] These results correspond to the outcomes of our study. The results of similar functional and anatomical effects, and less blood loss and shorter hospital stay were also found in two other comparative cohort studies.[16, 17]

We showed that sacrocolpopexy is an effective surgical treatment for women with a symptomatic vault prolapse. Although the focus of the sacrocolpopexy is mainly the apical and the anterior compartments, the posterior compartment improves as well. Besides anatomical improvement, patients have better scores on all domains of the disease-specific quality of life questionnaires.

There was a trend towards fewer complications in the laparoscopic group (11% versus 18.9%, RR 0.57; 95% CI 0.50 – 2.27). The complications in the open group were much more severe, including re-laparotomies and a fatal bowel perforation. The study by Freeman et al. did not show any significant differences in complication rates either: 5.6% (2/26) in the laparoscopic vs 7.4% (2/27) in the open group. Complications in the laparoscopic group included opening of the vagina and one bladder injury. In the open group an area of mesentery of the small bowel became detached and this required the resection of 10 cm of small bowel. In one other case, there was excessive bleeding from the sacrum, which required haemostatic bone wax.[15]

One reason for our unexpected higher complication rate may be accurate documentation during a prospective trial. The trial consists of an unselected study

population, in contrast with retrospective cohort studies. Furthermore, patients were referred from other centres for the sacrocolpopexy, which may influence the complexity of the patient population. Despite these possible explanations, it is still unusual that so many severe and rare complications occurred during this trial.

We did not see any mesh or suture exposures in our study population. Other trials reported rates of mesh-related complications of between 3 and 11%.[5-8] Our absence of mesh complications may be because our follow-up time was only one year, which is relatively short for the development of exposures.

The anatomical results of the initial surgery were similar, but participants who had undergone laparoscopic surgery had more reinterventions. The laparoscopic group had four reinterventions for recurrent POP versus one in the open group (RR 4, 95% CI 0.84 – 5.73), all concerning the posterior compartment. An explanation could be that two open procedures were combined with a posterior colporrhaphy in the same session versus no concomitant vaginal POP surgery in the laparoscopic group.

The inclusion period of our trial was five years, which is a long period for a multicentre trial with six participating centres. Many patients and gynaecologists preferred the laparoscopic procedure and the laparoscopic sacrocolpopexy was already being implemented in many participating centres, despite the fact that its clinical effectiveness was still unknown. Unfortunately, not all eligible patients were documented. Most participants were randomised in the last three years of the study by including more centres. Moreover, many procedures were performed by the same surgeon, as this gynaecologist visited some of the other sites to perform the laparoscopic sacrocolpopexy for the study population. The other procedures were performed by experienced surgeons who had been trained to perform the procedure the same way. This resulted in a homogeneous operation technique and frequent performance of the procedure.

Strengths and limitations

We performed a randomised controlled trial, which is considered the best type of study to assess the effectiveness of a procedure. Another strength of our trial is that procedures were all performed by experienced gynaecologists, with a track record of more than 50 sacrocolpopexy procedures. A trial of Deprest et al. showed that it takes 60 procedures to effectively limit complications, owing to the challenging suture and dissection skills that are needed for this technique.[14] The laparoscopic sacrocolpopexy is a challenging, level 4 procedure. The laparoscopic technique has an advantage over an open abdominal procedure with regard to dissection, which is easier during laparoscopy

because of the increased visual field. However, stitching is more difficult compared with the open technique because of a decreased degree of movement and two-dimensional vision. As a large number of patients are needed to acquire sufficient surgical skills, this procedure should only be performed by experienced surgeons.

A limitation of our study was the relatively high percentage of loss to follow-up (15.5%). The number of missing questionnaires was equal in the two groups. All non-responders were contacted by telephone and most of them explained that they were doing well, which was a reason not to return the questionnaires. However, patient characteristics of responders and non-responders were comparable; thus, we do not believe that the loss to follow-up has greatly affected our results.

Another limitation is that the patients and staff were not blinded to the intervention. Although patients were encouraged by the medical care staff to recover quickly and to not extend their admission for unnecessary reasons, there is still a chance of bias because of the type of incision that was used. This could affect the length of the hospital stay; however, two versus four days still constitutes a large difference of two days. Furthermore, the hospital stay was prolonged by the extended (re)admission because of several complications in the abdominal group.

Interpretation

In conclusion, this randomised controlled trial comparing laparoscopic and open abdominal sacrocolpopexy showed no significant differences in functional and anatomical outcome, but there was less blood loss and a shorter hospital stay when the procedure was performed using the laparoscopic approach. Although this superiority study did not show a significant difference in the primary outcome (UDI prolapse domain), there is still evidence to support a laparoscopic approach as there was less blood loss, the hospital stay was shorter, and the anatomical and combined outcomes were not statistically different. Therefore, we recommend further implementation of the laparoscopic approach. However, given the learning curve, we advise low-volume centres to refer patients to a centre with laparoscopic expertise.

Conclusion

Our trial provides evidence to support a laparoscopic approach when performing sacrocolpopexy, as there was less blood loss and the hospital stay was shorter, whereas functional and anatomical outcomes were not statistically different.

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CHAPTER 3

Laparoscopic sacrocolpopexy versus abdominal sacrocolpopexy for vaginal vault prolapse: long-term follow-up of a randomised controlled trial

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Abstract

INTRODUCTION AND HYPOTHESIS

The objective of this study was to evaluate long-term outcomes of laparoscopic sacrocolpopexy (LSC) versus abdominal sacrocolpopexy (ASC) for vaginal vault prolapse (VVP).

METHODS

Long-term follow-up of a multicentre randomised controlled trial (SALTO-trial). 74 women were randomly assigned to LSC (*n* = 37) or ASC (*n* = 37). Primary outcome was disease-specific quality of life, measured with validated questionnaires. Secondary outcomes included anatomical outcome, composite outcome of success, complications, and retreatment.

RESULTS

We analysed 22 patients in the LSC group and 19 patients in the ASC group for long-term follow-up, with a median follow-up of 109 months (9.1 years). Disease-specific quality of life did not differ after long-term follow-up with median scores of 0.0 (LSC: IQR 0 – 17; ASC: IQR 0 – 0) on the 'genital prolapse' domain of the UDI in both groups (p = 0.175). Anatomical outcomes were the same for both groups on all points of the POP-Q. The composite outcome of success for the apical compartment is 78.6% (*n* = 11) in the LSC group and 84.6% (*n* = 11) in the ASC group (p = 0.686). Mesh exposures occurred in 2 patients (12.5%) in the LSC group and 1 patient (7.7%) in the ASC group. There were 5 surgical reinterventions in both groups (LSC: 22.7%; ASC: 26.3%, p = 0.729).

CONCLUSIONS

At long-term follow-up no substantial differences in quality of life, anatomic results, complications, or reinterventions between LSC and ASC were observed. Therefore, the laparoscopic approach is preferable, considering the short-term advantages.

TRIAL REGISTRATION

Dutch Trial Register NTR6330, 18 January 2017.

Introduction

The prevalence of vaginal vault prolapse (VVP), requiring apical surgery, has been reported in 23% of women who underwent vaginal hysterectomy for pelvic organ prolapse (POP).[1] The risk of developing VVP increases in the years after hysterectomy, especially in women whose initial hysterectomy was performed for POP.[2, 3] Pelvic floor symptoms due to POP can have a severe impact on women's quality of life, requiring an effective treatment.[4]

Sacrocolpopexy is one of the surgical options in the treatment of VVP, with success rates between 93 and 99%.[5-8] Sacrocolpopexy is associated with a lower risk of awareness of prolapse, recurrent prolapse on examination, repeat surgery for prolapse, and dyspareunia than other vaginal interventions for POP.[9] Previously, the results of the SALTO trial were published.[10, 11] In this multicentre RCT, we compared laparoscopic sacrocolpopexy (LSC) with abdominal sacrocolpopexy (ASC) as treatment for VVP, with a follow-up time of 12 months. The results showed less blood loss, a shorter hospital stay, and less related morbidity in favour of the laparoscopic group. There was a significant improvement in quality of life in both groups.[10, 11]

Evidence for long-term clinical outcomes of LSC versus ASC is essential to reach consensus on the optimal surgical treatment, adequate patient selection and preoperative counselling. Therefore, this follow-up study was performed to evaluate the long-term outcome in terms of disease-specific quality of life of patients who participated in the SALTO trial.

Materials and methods

Study design

Details of the SALTO trial were published previously.[10, 11] In short, a multicentre randomised controlled trial was performed, comparing LSC and ASC as treatment for VVP, in four teaching hospitals and two university hospitals in the Netherlands. Eligible women with vault prolapse who met the inclusion criteria were informed about the trial, and randomised after consent. Inclusion criteria were women with a history of hysterectomy presenting with symptomatic vaginal vault prolapse, with or without concomitant cystocele or rectocele, who chose to undergo surgery.

This observational long-term follow-up study was approved by the ethical research committee (METC) of the Máxima Medical Centre (file number METC W17.015, CCMO NL60618.015.17) and by the board of directors of each of the participating hospitals, separately from the original SALTO trial. This trial was registered in the Dutch Trial Register (NTR6330). The study was developed and described in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement.[12] The results are reported by means of the joint International Urogynaecological Association (IUGA) / International Continence Society (ICS) recommendations for reporting outcomes of surgical procedures for pelvic organ prolapse.[13]

Primary and secondary outcomes

The primary outcome of this trial was long-term disease-specific quality of life, measured with the Urogenital Distress Inventory (UDI). The primary outcome in our follow-up study is similar to the original SALTO trial. Secondary outcomes were the effects of the surgical treatment on POP-related functional symptoms such as micturition, defecation, sexuality, and patient satisfaction, using validated questionnaires. Moreover, long-term complications such as mesh exposure and retreatment were evaluated. Surgical retreatment was categorised according to the joint IUGA / ICS recommendations for reporting outcomes. Surgeries were subdivided into repeat surgery for the apical compartment, surgery for a different site (anterior or posterior compartment), surgery for complications, and surgery for non-POP-related conditions (*e.g.*, stress urinary incontinence).[13, 14]

More outcome definitions were used in the literature after the initial SALTO study.[14] To make studies more comparable, we have added several secondary outcome measures. We analysed composite outcome of success, defined as no POP beyond the hymen (apical compartment), absence of bothersome bulge symptoms, and no repeat surgery. Additionally, we examined surgical failure, which meant prolapse POP-Q ≥ stage 2 (in the apical compartment or in any compartment) or surgical reintervention. Last, anatomical failure (POP-Q ≥ stage 2) was evaluated.[13-15]

Data collection

All patients from the initial SALTO trial were sent a letter to ask for participation in this observational follow-up study. When they failed to respond, they were called and asked to participate. All participants gave new informed consent to participate in the long-term follow-up trial. They were asked to fill in various Dutch validated questionnaires and were invited to visit an outpatient clinic to undergo pelvic examination. The observer was an independent researcher, gynaecologist or resident who had not performed the surgery

and was trained in the POP-Q examination.[16] The observer was not blinded to the type of surgery, because of visible abdominal scars.

Disease-specific quality of life was tested with the UDI,[17] the Defecatory Distress Inventory (DDI),[18] and the Incontinence Impact Questionnaire (IIQ).[17] The UDI and DDI, containing of 19 and 11 items respectively, indicate whether complaints of micturition, prolapse, or defecation are present and to what extent these complaints are bothersome. These questionnaires consist of four-point Likert scales, ranging from 'no bother' to 'greatly bothersome'. The result of the IIQ questionnaire, composed of 13 questions, shows the disease-specific quality of life for urine incontinence. The score of each domain ranges from 0 to 100, a high score indicates more frequent or more bothersome symptoms (UDI and DDI), and hence, a poorer quality of life (IIQ). Patient satisfaction of their postoperative condition was verified by the Patient Global Impression of Improvement (PGI-I). The PGI-I is a seven-point Likert scale answering the question: 'check the number that best describes what your postoperative condition is like now, compared with what it was before you had the surgery'.[19] 'Much better' or 'very much better' was considered affirmative and presented as dichotomous outcome.[9] Furthermore, we evaluated sexual functioning using the Prolapse / Incontinence Sexual Questionnaire (PISQ), containing 12 questions. These items were scored on a five-point Likert scale ranging from 0 (always) to 4 (never), for which higher score indicates better sexual function.[20, 21]

Bothersome bulge symptoms were measured using the UDI. A positive answer to any of the following questions is scored as a subjective recurrence: 'Do you experience a sensation of bulging or protrusion from the vagina?' and 'Do you have a bulge or something protruding that you can see in the vagina?', in combination with a response 'moderately bothersome' or 'greatly bothersome' to the question 'how much does this bother you?'.

Interventions

LAPAROSCOPIC SACROCOLPOPEXY

Laparoscopic sacrocolpopexy was performed under general anaesthesia using four trocars, one for the scope and three side trocars. The vaginal vault was elevated with a vaginal probe. The peritoneum from the promontory to the vault was incised laparoscopically by scissors to expose the rectovaginal and vesicovaginal fascia. A type 1 polypropylene mesh was used, which was cut into two pieces; 3 cm wide and approximately 15 cm long. One piece of the mesh was attached anteriorly and another as low as possible on the posterior vaginal wall, using non-absorbable multifilament sutures. The mesh was fixated to the anterior part of the vaginal vault with four stitches,

and six stitches were used to fixate the mesh posteriorly. The mesh was attached to the sacral promontory using staples and was peritonealised.[10]

ABDOMINAL SACROCOLPOPEXY

The ASC was performed by a laparotomy under general anaesthesia, preferably using a Pfannenstiel incision. The essence of the procedure was the same as for the laparoscopic procedure. The peritoneum from the promontory to the vault was incised to expose the rectovaginal and vesicovaginal fascia, extending to the sacral promontory. One piece of type 1 polypropylene mesh was attached between the vagina and the bladder anteriorly, and another as far down the posterior vaginal wall as possible. The sutures, the size of the mesh, and its fixation were the same as in the laparoscopic approach. The two meshes were sutured to each other, after which only the posterior mesh was fixed to the longitudinal vertebral ligament by staples or non-absorbable sutures, depending on the surgeon's preference. The mesh was peritonealised. All centres used polypropylene meshes and the same sutures.[10]

Sample size

Sample size calculation was performed for the initial SALTO trial and 74 patients were included accordingly.[10] Loss to follow-up from the initial trial was taken into account and a response rate of 60% was estimated. A difference of 15 points between the two groups on the 'genital prolapse' domain from the UDI was considered a clinically relevant difference. The standard deviation of the UDI score was 15.8.[22] With an α level of 0.05 and a 60% response rate, the calculated power would be 83% and was considered to be adequate.

Statistical analysis

The domain scores were calculated for the UDI, DDI, IIQ, PISQ, and PGI-I questionnaires. To examine differences between the two groups the independent-samples t test was used for continuous variables. The Mann-Whitney U test was used in the case of non-normally distributed variables. For dichotomous variables, Pearson's Chi-squared test was used. The log-rank test was used for survival analysis of the time to surgical retreatment. Two-sided significance tests were used, and a p value of less than 0.05 was considered to be statistically significant. All statistical analyses were performed using IBM SPSS for Windows (version 25).

Results

In the original trial 74 women were randomly assigned to LSC (*n* = 37) or ASC (*n* = 37) between 2007 and 2012. Figure 1 shows the flow diagram of the study population. In total 71 participants were eligible for long-term follow-up, 36 participants in the LSC group and 35 patients in the ASC group. We included 22 patients (61.1%) from the LSC group and 19 patients (54.3%) from the ASC group. Fourteen patients (38.9%) were lost to follow-up in the LSC group versus 16 patients (45.7%) in the ASC group; nine patients died and eight patients were not able to participate owing to old age or serious health conditions (unrelated to pelvic floor symptoms, *e.g.*, terminal stage cancer). Nine patients were not willing to participate in this follow-up study. For most of them it was too much of a burden, none reported any POP-related complaints. In the LSC group one patient was lost to follow-up in the initial trial owing to postponed surgery but agreed to participate now. Meanwhile, she received the allocated intervention (LSC).

Table 1 shows the baseline characteristics and perioperative data of the patients in the SALTO trial. The median duration of follow-up was 109 months (9.1 years), 105 months (8.75 years) in the LSC group and 111 months (9.25 years) in the ASC group. In the LSC group 88.2% (*n* = 30) had two vaginal deliveries or more, compared with 94.1% (*n* = 32) in the ASC group. Also, the majority is postmenopausal at the time of surgery (LSC: 97.2%, *n* = 35; ASC: 100%, *n* = 37).

The primary outcome of long-term disease-specific quality of life, measured with the UDI, was not different between groups. The median score for the domain 'genital prolapse' was 0 (IQR 0 – 17) in the LSC group as well as in the ASC group (IQR 0 – 0; *p* = 0.175). On the other domains of the UDI, DDI, and IIQ, there we did not observe any statistically significant differences, as is shown in Table 2. An improvement of 'much better' or 'very much better' on the PGI-I was reported by 11 patients (57.9%) in the LSC group, and 10 patients (58.8%) in the ASC group (*p* = 0.955). Sexual function was the same in both groups, with total PISQ scores of 34.2 (range 19 – 45) and 32.5 (range 28 – 37) in the LSC and ASC group, respectively (*p* = 0.132). Thirty percent (*n* = 6) of the participants in the LSC group were sexually active, compared with 63% (*n* = 20) before surgery. In the ASC group there was also a reduction, from 45% (*n* = 14) to 10.5% (*n* = 2). Four patients were reported to have dyspareunia, two patients in each group (*p* = 0.102). Two patients also reported this preoperatively, one in each group. From one patient, preoperative data on sexuality are missing (ASC group) and the other patient was not sexually active before surgery (LSC group). Therefore, it was unclear whether the reported dyspareunia of these two patients occurred after surgery.

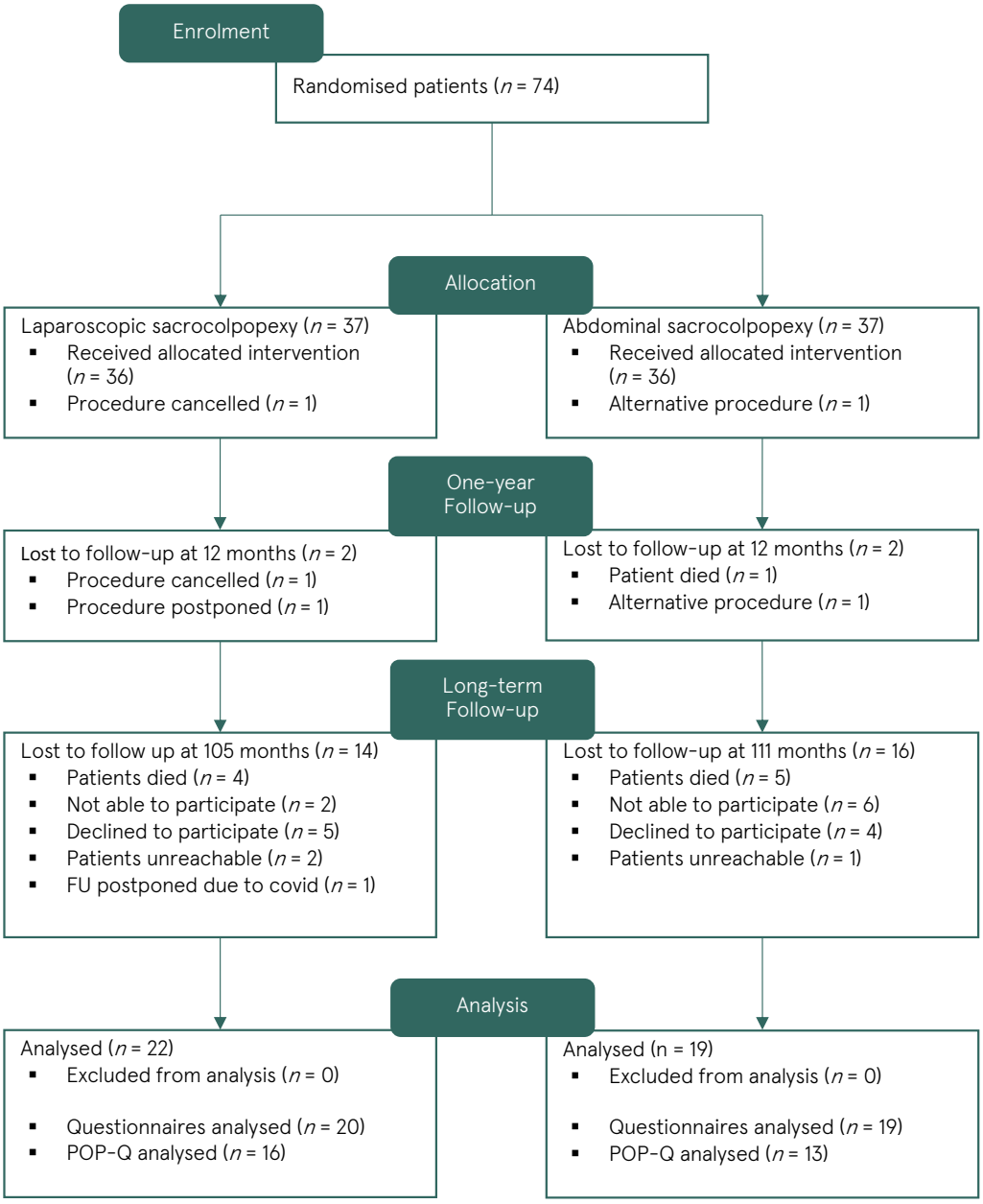

Figure 1. Flow diagram of study population

Table 1. Baseline characteristics and perioperative data

	Laparoscopic sacrocolpopexy (*n* = 37)	**Abdominal sacrocolpopexy (*n* = 37)**	***p* value**
Age at time of inclusion (years)			
Median (IQR)	65 (61 – 71)	67 (64 – 73)	N.A.
Parity No./total no. of patients (%)			N.A.
0	1/34 (2.9)	0/34 (0.0)	
1	3/34 (8.8)	2/34 (5.9)	
2	14/34 (41.2)	14/34 (41.2)	
3	13/34 (38.2)	9/34 (26.5)	
≥4	3/34 (8.8)	9/34 (26.5)	
Body mass index at time of inclusion (kg/m^2)			
Mean (range)	25.3 (18 – 32)	25.9 (21 – 33)	N.A.
Menopausal status			
No./total no. of patients (%)			N.A.
Premenopausal	1/36 (2.8)	0/37 (0.0)	
Postmenopausal	35/36 (97.2)	37/37 (100.0)	
Urinary incontinence			
No./total no. of patients (%)			N.A.
None	20/35 (57.1)	15/35 (42.9)	
Stress	2/35 (5.7)	3/34 (8.8)	
Urgency	4/35 (11.4)	4/35 (11.4)	
Combined	9/35 (25.7)	13/35 (37.1)	
POP-Q stage apical compartment (point C)			
No./total no. of patients (%)			N.A.
Stage 0	0/32 (0)	1/34 (2.9)	
Stage 1	9/32 (28.1)	14/34 (41.2)	
Stage 2	9/32 (28.1)	9/34 (26.5)	
Stage 3	7/32 (21.9)	4/34 (11.8)	
Stage 4	7/32 (21.9)	6/34 (17.6)	
POP-Q stage 2-4			
No./total no. of patients (%)			N.A.
Anterior compartment prolapse (Ba ≥ -1)	24/30 (80)	21/32 (65.6)	
Posterior compartment prolapse (Bp ≥ -1)	10/28 (35.7)	20/32 (62.5)	
Follow-up duration (months)			
Median (IQR)	105 (87 – 126)	111 (79 – 117)	N.A.
Age at time of long-term follow-up (years)			
Median (IQR)	71 (68 – 76)	76 (67 – 78)	0.549
Operative time (minutes)			
Median (IQR)	125 (108 – 135)	115 (94 – 129)	0.31
Estimated blood loss (ml)			
Median (IQR)	86 (10 – 100)	200 (100 – 300)	**< 0.001**
Hospital stay (days)			
Median (IQR)	2 (2 – 3)	4 (3 – 5)	**< 0.001**
Complications during surgery			
No./total no. of patients (%)	2/36 (5.6)	0/36 (0.0)	0.15
Bladder lesion (conversion)	1	0	
Bleeding (conversion)	1	0	

Table 1 (continued). Baseline characteristics and perioperative data.

	Laparoscopic sacrocolpopexy (*n* = 37)	Abdominal sacrocolpopexy (*n* = 37)	*p* value
Complications during admission			
No./total no. of patients (%)	2/36 (5.6)	7/37 (18.9)	0.06
Fatal bowel perforation	0	1	
Wound dehiscence	0	2	
Pulmonary embolism	0	1	
Ileus	0	3	
Wound infection	1	0	
Pyelonephritis (re-admission)	1	0	

POP-Q stage 1: most distal prolapse is > 1 cm above the hymen
POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen
POP-Q stage 3: most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
POP-Q stage 4: total prolapse
POP-Q pelvic organ prolapse quantification, *IQR* interquartile range

As shown in Table 3, the composite outcome of success for the apical compartment was 78.6% (*n* = 11) in the LSC group and 84.6% (*n* = 11) in the ASC group (*p* = 0.686). Surgical failure for the apical compartment was also statistically comparable, with 12.5% (*n* = 2) in the LSC group and 0% (*n* = 0) in the ASC group (*p* = 0.186). Anatomical failure and prolapse beyond the hymen also showed the same results for both groups (*p* = 0.186 and *p* = 0.359 respectively for the apical compartment).

Last, Table 3 shows the reinterventions. In both groups five participants had surgical treatment, 22.7% in the LSC group and 26.3% in the ASC group (*p* = 0.729). Three patients in the LSC group and four patients in the ASC group underwent further surgery due to a bothersome cystocele or rectocele. One patient in the LSC group had de novo stress urine incontinence, for which she received a mid-urethral sling. Mean time to surgical reintervention (Figure 2) was comparable in the two groups (LSC 41.2 months (SEM 22.7) versus ASC 55.8 months (SEM 13.5), *p* = 0.814). Two patients had surgery to remove the mesh, owing to severe complications. One patient presented with complaints of vaginal mesh exposure. The mesh got infected and extensive surgery was performed, 5.6 years (67 months) after she had undergone the ASC. During surgery it was discovered that the mesh fistulated through the vaginal vault. Adhesiolysis and resection of part of the ileum was performed. There was no descensus of the vaginal vault (POP-Q point C: -7) and an asymptomatic rectocele (POP-Q point Bp: 0) was left untreated. This surgery was otherwise uncomplicated and the patient made a good recovery. After four years, this patient had no POP-related complaints or pain. In the LSC group one patient also had a vaginal exposure and the mesh was infected. A robot-assisted procedure was performed to remove the mesh, 10.2 years (122 months) after she had undergone the LSC. The

Table 2. Functional outcome and quality of life at long-term follow-up

	Before surgery		Long-term follow-up		*p* value
	LSC (*n* = 34)	**ASC (*n* = 31)**	**LSC (*n* = 20)**	**ASC (*n* = 19)**	
Patient satisfaction (PGI-I)					
'Very much better' or 'Much better'	N.A.	N.A.	11/19 (57.9)	10/17 (58.8)	0.955
Vaginal bulge symptoms					0.345
No bother [a]	3/29 (10.3)	3/30 (10)	14/20 (70)	18/19 (94.7)	
'Moderately bothersome or 'greatly bothersome'	26/29 (89.7)	25/30 (83.3)	3/20 (15)	0/19 (0)	
Urogenital distress inventory (UDI)					
Overactive bladder	33.3 (11 – 56)	44.4 (22 – 50)	16.7 (3 – 33)	22.2 (0 – 44)	0.762
Urinary incontinence	16.7 (0 – 50)	16.7 (0 – 42)	25.0 (0 – 33)	16.7 (0 – 42)	0.828
Obstructive micturition	0.0 (0 – 33)	16.7 (0 – 58)	0.0 (0 – 17)	0.0 (0 – 33)	0.901
Genital prolapse	66.7 (58 – 92)	66.7 (33 – 67)	0.0 (0 – 17)	0.0 (0 – 0)	0.175
Pain	16.7 (0 – 50)	33.3 (17 – 33)	0.0 (0 – 17)	16.7 (0 – 33)	0.061
Defecatory distress inventory (DDI)					
Obstipation	0.0 (0 – 17)	0.0 (0 – 33)	0.0 (0 – 17)	0.0 (0 – 17)	1.000
Obstructive defecation	4.2 (0 – 17)	8.3 (0 – 25)	0.0 (0 – 8)	8.3 (0 – 17)	0.531
Pain	0.0 (0 – 0)	0.0 (0 – 0)	0.0 (0 – 0)	0.0 (0 – 0)	0.749
Faecal incontinence	0.0 (0 – 17)	8.3 (0 – 33)	0.0 (0 – 29)	16.7 (0 – 33)	0.478
Flatus incontinence	33.3 (0 – 67)	33.3 (0 – 67)	16.7 (0 – 58)	0 (0 – 33)	0.396
Incontinence impact questionnaire (IIQ)					
Physical	25.0 (0 – 50)	0.0 (0 – 33)	0.0 (0 – 13)	0.0 (0 – 15)	0.897
Mobility	11.1 (0 – 33)	33.3 (11 – 44)	8.3 (0 – 23)	16.7 (8 – 42)	0.127
Social	11.1 (0 – 22)	11.1 (0 – 33)	0.0 (0 – 8)	0.0 (0 – 17)	0.967
Embarrassment	0.0 (0 – 17)	16.7 (0 – 17)	0.0 (0 – 13)	0.0 (0 – 13)	0.989
Emotional	11.1 (0 – 33)	22.2 (0 – 33)	0.0 (0 – 8)	8.3 (0 – 17)	0.322
Sexual function (PISQ)					
Sexually active	20/32 (62.5)	14/31 (45.1)	6/20 (30)	2/19 (10.5)	0.132
Dyspareunia	6/16 (37.5)	8/13 (61.5)	2/6 (33.3)	2/2 (100)	0.102
PISQ-12 total score Mean (range)	-	-	34.2 (19 – 45)	32.5 (28 - 37)	0.857
Behavioural-emotive	-	-	10.0 (6 – 15)	9.5 (9 – 10)	0.857
Physical	-	-	15.2 (4 – 20)	14.5 (11 – 18)	0.643
Partner-related	-	-	9.0 (6 – 10)	8.5 (8 – 9)	0.429

Values are given in median (interquartile range, IQR) or in number of participants / total number of participants (percentages), unless stated otherwise
Percentages were calculated using non-missing data
UDI and DDI; each item: 0 = no bothersome symptoms; 100 = most bothersome symptoms
IIQ; each item: 0 = best quality of life; 100 = worst quality of life
PISQ-12 total score: 0 = worst sexual function; 48 = best sexual function
PISQ-12 behavioural-emotive (items 1 – 4): 0 = worst function; 16 = best function
PISQ-12 physical (items 5 – 9): 0 = worst function; 20 = best function
PISQ-12 partner-related (items 10 – 12): 0 = worst function; 12 = best function
LSC laparoscopic sacrocolpopexy; *ASC* abdominal sacrocolpopexy; *PGI-I* Patient Global Impression of Improvement; *UDI* Urogenital Distress Inventory; *DDI* Defecatory Distress Inventory; *IIQ* Incontinence Impact Questionnaire; *PISQ* Prolapse / Incontinence Sexual Questionnaire
[a] Not all participants reported bothersome POP symptoms on the UDI questionnaire. They did so, however, at the outpatient clinic before inclusion in this trial

patient fully recovered from this complication. One patient from the ASC group had a diagnostic laparoscopy owing to complaints of abdominal pain. In each group, three patients were reported to have had pelvic floor physical therapy after the initial surgery (LSC 14.3% versus ASC 15.8%; p = 0.894). The initial sacrocolpopexy was without perioperative complications for both patients.

Table 3. Outcome for pelvic organ prolapse (POP) after long-term follow-up.

	Laparoscopic sacrocolpopexy (n = 16)	**Abdominal sacrocolpopexy (n = 13)**	***p* value**
Composite outcome of success [a]			
Apical compartment	11/14 (78.6)	11/13 (84.6)	0.686
Any compartment	7/14 (50)	10/13 (76.9)	0.148
Surgical failure [b]			
Apical compartment	2/16 (12.5)	0/13 (0)	0.186
Any compartment	9/16 (56.3)	9/13 (69.2)	0.474
Anatomical failure [c]			
Apical compartment (C ≥ -1)	2/16 (12.5)	0/13 (0)	0.186
Anterior compartment (Ba ≥ -1)	6/16 (37.5)	5/13 (38.5)	0.958
Posterior compartment (Bp ≥ -1)	6/16 (37.5)	6/13 (46.2)	0.638
Prolapse beyond hymen			
Apical compartment (point C > 0)	1/16 (6.3)	0/13 (0)	0.359
Anterior compartment (point Aa or Ba > 0)	3/16 (18.8)	1/13 (7.7)	0.390
Posterior compartment (point Ap or Bp > 0)	0/16 (0)	0/13 (0)	-
Reinterventions			
Surgical reintervention [d]	5/22 (22.7)	5/19 (26.3)	0.729
Time to surgical reintervention (months) mean (SEM)	41.2 (22.7)	55.8 (13.5)	0.814
Repeat surgery	0/22 (0)	0/19 (0)	
Surgery different site	3/22 (13.6)	4/19 (21.1)	
ACR	1	2	
PCR	2	2	
Surgery for complications	1/22 (4.5)	2/19 (5.2)	
Mesh removal	1	1	
Diagnostic laparoscopy	0	1	
Surgery for non-POP-related conditions	1/22 (4.5)	0/19 (0)	
MUS	1	0	
Pessary treatment	0/22 (0)	0/19 (0)	-
Physical therapy	3/21 (14.3)	3/19 (15.8)	0.894

All data are given in number of participants / total participants (percentages). Percentages were calculated using non-missing data
POP-Q stage 1: most distal prolapse is > 1 cm above the hymen
POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen
POP-Q stage 3: most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
POP-Q stage 4: total prolapse
POP-Q pelvic organ prolapse quantification; *ACR* anterior colporrhaphy; *PCR* posterior colporrhaphy; *VSF* vaginal sacrospinous fixation; *MUS* mid-urethral sling; *SEM* standard error of the mean
[a] No POP beyond hymen (in apical compartment or any compartment), absence of bothersome bulge symptoms, and no surgical reintervention or pessary treatment
[b] Prolapse POP-Q ≥ stage 2 (in apical compartment or in a any compartment) or repeat surgery or pessary treatment
[c] POP-Q ≥ stage 2
[d] One patient in the ASC group had surgery for complications and primary surgery for a different site

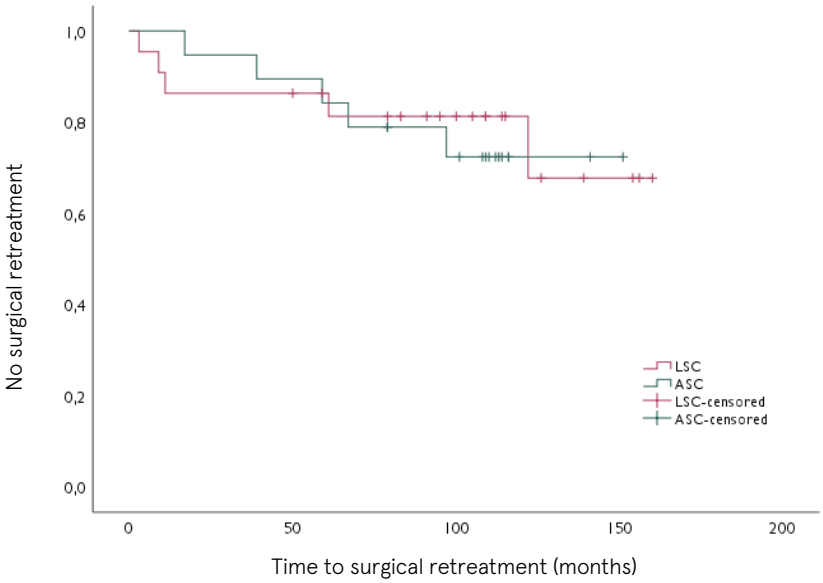

Figure 2. Survival analysis for time to surgical retreatment

Time (months) to surgical retreatment, $p = 0.814$

Table 4 shows the mean POP-Q scores. Point C is at -4.7 in the LSC group (SD ± 3.9, range -8 – 8) and at -5.8 in the ASC group (SD ± 1.5, range -8 – -3), $p = 0.353$. The larger standard deviation is due to one patient in the LSC group, who had a stage 4 vaginal vault prolapse at long-term follow-up with 'greatly bothersome' vaginal bulge symptoms.

Three mesh exposures and three suture exposures were described, and are shown in Table 5. Two mesh exposures, one in each group, were part of the complications described above. The other mesh exposure was in the LSC group and was left untreated, because it was only minor and without complaints. One patient in the LSC group and two patients in the ASC group had a suture exposure. The suture exposure for the patient in the LSC group was discovered at the follow-up visit for this study. She complained of vaginal blood loss and dyspareunia. After removal of this suture at the outpatient clinic she had no more complaints. In the ASC group, one suture exposure was discovered during an earlier visit of the patient to the outpatient clinic because of POP complaints, due to a rectocele. The suture was removed during subsequent vaginal surgery (posterior colporrhaphy). The suture exposure of the second patient in the ASC group was discovered by coincidence during vaginal examination for this follow-up study; the patient experienced no complaints and no treatment was performed.

Table 4. Pelvic Organ Prolapse Quantification (POP-Q) measurements

	1 year follow-up			Long-term follow-up		
	LSC (*n* = 29)	**ASC (*n* = 29)**	***p* value**	**LSC (*n* = 16)**	**ASC (*n* = 13)**	***p* value**
Aa	-1.3 ± 1.8 (-3 – 2)	-1.1 ± 1.6 (-3 – 3)	0.829	-1.4 ± 2.0 (-3 – 3)	-1.6 ± 1.5 (-3 – 2)	0.719
Ba	-1.3 ± 1.8 (-3 – 2)	-1.3 ± 1.3 (-5 – 8)	0.947	-1.3 ± 2.0 (-3 – 3)	-1.7 ± 1.3 (-3 – 1)	0.550
C	-5.6 ± 2.3 (-8 – 0)	-5.1 ± 1.5 (-8 – -3)	0.621	-4.7 ± 3.9 (-8 – 8)	-5.8 ± 1.5 (-8 – -3)	0.353
GH	3.6 ± 0.7 (3 – 5)	4.0 ± 0.8 (3 – 5)	0.262	3.4 ± 1.0 (2 – 5)	3.6 ± 1.1 (1 – 5)	0.538
PB	3.1 ± 0.7 (2 – 4)	3.3 ± 0.7 (2 – 4)	0.624	3.0 ± 0.5 (2 – 4)	3.1 ± 0.6 (2 – 4)	0.723
TVL	7.8 ± 0.6 (7 – 9)	7.9 ± 1.6 (4 – 10)	0.896	7.7 ± 0.8 (6 – 9)	8.1 ± 1.4 (6 – 10)	0.394
Ap	-1.5 ± 1.3 (-3 – 0)	-1.6 ± 1.3 (-3 – 3)	0.840	-1.8 ± 1.2 (-3 – 0)	-1.8 ± 1.2 (-3 – 0)	0.924
Bp	-1.5 ± 1.3 (-3 – 0)	-1.6 ± 1.3 (-4 – 8)	0.840	-1.8 ± 1.2 (-3 – 0)	-1.7 ± 1.3 (-3 – 0)	0.571

POP-Q point Aa: located in the midline of the anterior vaginal wall three cm proximal to the external urethral meatus
POP-Q point Ba: the most distal position of any part of the upper anterior vaginal wall from the vaginal cuff to point Aa
POP-Q point C: the most distal edge of the vaginal cuff (hysterectomy scar)
POP-Q point GH (genital hiatus): measurement from the middle of the external urethral meatus to the posterior margin of the hymen
POP-Q point PB (perineal body): measurement from the posterior margin of the hymen to the mid-anal opening
POP-Q point TVL (total vaginal length): length of the vagina (centimetres) from the vaginal cuff to the hymen
POP-Q point Ap: located in the midline of the posterior vaginal wall 3 cm proximal to the hymen
POP-Q point Bp: the most distal position of any part of the upper posterior vaginal wall from the vaginal cuff to point Ap

Table 5. Complications after long-term follow-up

	Laparoscopic sacrocolpopexy (*n* = 16)	**Abdominal sacrocolpopexy (*n* = 13)**	***p* value**
Complications	3/16 (18.8)	4/13 (30.8)	0.452
Mesh exposure with infection	1/16 (6.3)	1/13 (7.7)	
Mesh exposure	1/16 (6.3)	0/13 (0)	
Suture exposure	1/16 (6.3)	2/13 (15.4)	
Abdominal pain	0/16 (0)	1/13 (7.7)	

All data are given in number of participants / total participants (percentages)

Discussion

Main findings

This observational long-term follow-up study of a multicentre randomised controlled trial shows that there was no difference in disease-specific quality of life whether after

laparoscopic or after abdominal sacrocolpopexy, with median scores of 0.0 (LSC: IQR 0 – 17; ASC: IQR 0 – 0) on the 'genital prolapse' domain of the UDI in both groups (p = 0.175). This corresponds with our previously published SALTO trial and LAS trial, both comparing the laparoscopic and the abdominal procedure, with one-year follow-up.[10, 23]

Composite outcome of success, surgical failure, and anatomical failure were the same in both groups for all compartments. We found no relation between the type of surgery and the compartment of the recurrence. Also, no relation was found between the preoperative POP-Q stage and the compartment of the recurrence. Some patients had a recurrence in the same compartment as they did preoperatively; others did not.

In our study, mesh exposures were reported in 12.5% and 7.7% in the LSC and ASC groups respectively. A retrospective cohort study from 2019 reports exposure rates of 1.4%.[24] We expect this to be an underestimation of the exposure rate, as they detected only patients with bothersome exposures. Three prospective cohort studies reported an exposure rate of 2.9%, 3.7%, and 4.5%. These studies had a shorter follow-up time, median of 60 months (5 years) instead of the 109 months (9.1 years) in our study, which could explain why they reported lower exposure rates.[25-27] Three suture exposures were found in our study population. In the SALTO trial non-resorbable sutures were used, which might contribute to these exposures. Nowadays, it is common practice to use resorbable sutures, which might lead to fewer suture exposures.[28] There were no other surgery-related risk factors in our study population, such as concomitant hysterectomy.[29]

Patient satisfaction on the PGI-I is 57.9% (n = 11) in the LSC group and 58.8% (n = 10) in the ASC group (p = 0.955). This seems lower than patient satisfaction reported in other long-term follow-up studies.[27, 30] These studies report trials with a median follow-up time of five and six years, compared with the nine years of our follow-up. The lower satisfaction in our trial might be due to a longer period of follow-up. It is understandable that patients find it more difficult to compare their situation now and before surgery, solely considering POP complaints after a longer period of time. The PGI-I asks patients to describe their postoperative condition, compared with how it was before surgery. Perhaps this question was not specific enough for the participants. Moreover, the PGI-I was only validated for a follow-up duration of 12 months.[19]

Strengths and limitations

We performed a randomised controlled trial, which is considered to yield the highest level of evidence when comparing two different treatment options. One of the main strengths of our study is the duration of follow-up, with a median of 109 months (9.1

years), which may be stated as 'very long' (> 5 years) duration of follow-up, according to the IUGA / ICS joint report on the terminology for reporting outcomes of surgical procedures for pelvic organ prolapse.[13] To our knowledge, there is no other comparative study with similar or longer duration of follow-up for the laparoscopic versus the open abdominal approach to sacrocolpopexy. Another strength of our study is that we reported on additional outcomes; such as combined outcome measure, objective outcome, and subjective outcome.[14, 15] By conforming to more commonly used clinical outcomes, our data are easy to interpret and could be used for meta-analyses in the future.

One of the limitations of our study is the relatively high rate of loss-to-follow-up. However, the statistical power remains >80% for the primary outcome measure disease-specific quality of life. From the 36 eligible patients in the LSC group, 14 patients (38.9%) were lost to follow-up, compared with 16 patients (45.7%) of the 35 eligible participants in the ASC group. Nine patients died and eight patients were not able to participate owing to old age or serious health issues, which was beyond our control. Perhaps the SARS-CoV-2 pandemic added to the loss-to-follow-up; however, we have no complete data on this matter. Other studies reported attrition rates of 46% at five years,[31] rising to 62% at seven years.[6] Loss to follow-up generally increases as review time climbs.[9] Although we opted for a higher response rate, our loss to follow-up is not more than could be expected.

Most of our study population were postmenopausal and multiparous, with two or more vaginal births. This makes our results mainly applicable for patients with comparable characteristics.

Interpretation

The laparoscopic approach to sacrocolpopexy is preferable, compared with the open abdominal technique, mainly because of better short-term outcomes. The laparoscopic approach has less blood loss and a shorter hospital stay.[10, 32] Functional outcomes, complications, and retreatment were comparable for both techniques.[10, 23, 32] After a median follow-up of 109 months (9.1 years) the results are in line with the results after short-term follow-up. Therefore, laparoscopic sacrocolpopexy proves to be an effective and safe treatment for vaginal vault prolapse. More is known about patient-related and surgery-related risk factors for developing mesh exposure after sacrocolpopexy. Patients should be counselled accordingly and gynaecologists should consider adjusting their technique to minimize the risk of mesh-related complications.[29, 33] LSC is a difficult procedure with a long learning curve; therefore, we believe this surgery should be

performed by experienced surgeons and centralised care is preferable when the volumes are low.

Conclusion

At long-term follow-up there was no substantial difference in disease-specific quality of life, anatomical results on the POP-Q, complications as mesh or suture erosions, and reinterventions between the LSC and the ASC groups. Therefore, the laparoscopic approach of sacrocolpopexy is preferable, considering the previously discovered advantages in the short term.

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CHAPTER 4

Laparoscopic sacrohysteropexy versus vaginal sacrospinous hysteropexy as treatment for uterine descent: comparison of long-term outcomes

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International Urogynaecology Journal. 2023 Jan;34(1):211-223.

Abstract

INTRODUCTION AND HYPOTHESIS

Pelvic organ prolapse (POP) is a frequent occurring health issue, especially concerning elderly women. The objective of this study is to examine the long-term outcomes of laparoscopic sacrohysteropexy (LSH) and vaginal sacrospinous hysteropexy (SSHP) for treatment of uterine prolapse.

METHODS

A retrospective study of patients who underwent a LSH or SSHP. Validated questionnaires and an outpatient examination visit were used to investigate the effects of both surgical treatments. The primary outcome was the composite outcome of success for the apical compartment, defined as no recurrence of uterine prolapse (POP-Q measurement C ≤ 0), no subjective recurrence of POP, and / or not requiring therapy for recurrent prolapse. Secondary outcomes were peri- and postoperative data, anatomical failure, prolapse beyond hymen, subjective outcomes, and disease-specific quality of life.

RESULTS

We included 105 patients, 53 in the LSH group and 52 in the SSHP group. The overall response rate of the questionnaires was 83% (n = 87) after a mean follow-up time of 4.5 years (54.2 months; 95% CI 44.8 – 64.2 months) in the LSH group and 2.5 years (30.1 months; 95% CI 29.3 – 31.5 months) in the SSHP group. There were no clinically relevant differences between the study groups in composite outcome of success (p = 0.073), anatomical failure of the apical compartment (p = 0.711), vaginal bulge symptoms for which patients consulted professionals (p = 0.126), and patient satisfaction (p = 0.741). The operative time was longer in the LSH group (117 minutes; interquartile range (IQR) 110 – 123), compared with the SSHP group (67 minutes; IQR 60 – 73) (p < 0.001). The duration of hospital stay was also longer in the LSH group (4 days) than in the SSHP group (3 days) (p = 0.006).

CONCLUSIONS

LSH and SSHP seem to be equally effective after long-term follow-up in treating uterine prolapse in terms of objective and subjective recurrence.

Introduction

Many women suffer from pelvic organ prolapse (POP). The prevalence of POP has been reported as 40 – 60% in parous women.[1-4] Due to the higher life expectancy in women, the incidence of POP is expected to increase. The lifetime risk of women undergoing a single surgery for POP or urinary incontinence is 19 – 20% at the age of 85.[5, 6] Vaginal hysterectomy (VH) is the most used surgical treatment worldwide for patients with symptomatic uterovaginal prolapse,[7] although a hysterectomy may cause nerve damage and disrupt important supportive structures of the pelvic floor. [8] In addition, a hysterectomy alone often fails to give the right support. Recurrence of POP in women who underwent a hysterectomy for pelvic organ prolapse has been reported in 11.6%.[9] A more recent study examined the long-term prevalence of POP after hysterectomy, with a median follow-up of 16 years. The prevalence of vaginal vault prolapse was 23% in women after vaginal hysterectomy for POP, defined as POP requiring apical surgery during the follow-up period or ≥ stage 2 during POP-Q examination.[10]

There is an increasing amount of evidence in favour of surgical options with uterus preservation compared with vaginal hysterectomy in the treatment of uterine descent.[4, 11] Various surgical techniques for the treatment of uterine prolapse with uterus preservation have been described, including vaginal, abdominal, and laparoscopic procedures. One of these procedures is the vaginal sacrospinous hysteropexy (SSHP). During this procedure the cervix is lifted towards one of the sacrospinous ligaments and attached with sutures, resulting in suspension of the uterus. Several studies show that SSHP is a safe procedure for the treatment of uterovaginal prolapse and severe complications are rarely seen during and after this surgery.[4, 11-15] Also, it has been shown that uterus preservation by SSHP is non-inferior to VH with suspension of the uterosacral ligaments, after a follow-up period of 12 months.[4] In a randomised controlled trial of 208 participants and a follow-up time of five years, significantly fewer anatomical recurrences of the apical compartment with bothersome bulge symptoms or repeat surgery were found after SSHP compared with VH with uterosacral ligament suspension. After hysteropexy a higher proportion of women had a composite outcome of success.[11]

The laparoscopic sacrohysteropexy (LSH) is another surgical option for uterovaginal prolapse with uterine preservation. During a laparoscopic procedure a mesh is attached to the cervix and the other side of the mesh is fixated to the promontory by sutures or tackers, to elevate the uterus. In a randomised controlled trial of 126 patients, LSH was equally effective compared with SSHP as surgical treatment of the apical compartment after 12 months of follow-up. Following LSH, bothersome overactive bladder and faecal

incontinence were more frequent, but dyspareunia was reported less frequently. However, the follow-up time in this publication of the trial was only 12 months.[15]

Both uterovaginal suspension techniques seem to be an effective procedure with low risk of complications for patients with uterovaginal prolapse. However, evidence comparing LSH to SSHP for uterine prolapse with long-term follow-up is lacking. We wondered what the long-term effects of LSH and SSHP would be and therefore performed a retrospective trial with a long-term follow-up and evaluated whether one of the two surgeries is preferable to treat apical prolapse.

Materials and methods

Study design

We performed a retrospective cohort study in the Máxima Medical Centre (MMC), a teaching hospital in the Netherlands. The ethical research committee of the MMC waived the need for approval (file number 2014-12). After assessment of the study protocol, the committee judged that the rules laid down in the medical Research Involving Human Subjects Act did not apply to this research proposal. This study was developed and described in accordance with the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines.[16] The results are reported by means of the IUGA / ICS recommendations for reporting outcomes of surgical procedures for pelvic organ prolapse.[17]

The study population consisted of patients who underwent a LSH between 2003 and 2013 or a SSHP between 2009 and 2011 for primary treatment of uterine prolapse. The SSHP was introduced in our hospital in 2009. Both techniques were performed by experienced gynaecologists, who had completed their learning curves. If indicated, the LSH or SSHP was combined with concomitant surgery such as an anterior or posterior colporrhaphy (both performed vaginally) or a mid-urethral sling (MUS). Additional surgery was included in the duration of the operative time. The choice of treatment was left to the discretion of the gynaecologist and based on the preference of the patient and gynaecologist. Patients with a history of hysterectomy were excluded.

Outcome measures

The primary outcome was the composite outcome of success for the apical compartment, defined as no recurrence of uterine prolapse (POP-Q measurement C ≤ 0),[18, 19] no bothersome bulge symptoms, and / or not requiring retreatment for recurrent

prolapse (either surgery or conservative treatment).[20] A positive answer on any of the following questions of the Urinary Distress Inventory (UDI) questionnaire is scored as a subjective recurrence: 'Do you experience a sensation of bulging or protrusion from the vagina?' and 'Do you have a bulge or something protruding that you can see in the vagina?' in combination with a response 'slightly bothersome' to 'greatly bothersome' to the question 'how much does this bother you?'

Secondary outcomes were anatomical failure (POP-Q ≥ stage 2 in any compartment), prolapse beyond hymen (POP-Q measurements > 0), reinterventions; subjective outcomes, and disease-specific quality of life. Furthermore, patient characteristics, preoperative morbidity, postoperative complications, and follow-up data were evaluated.

Surgical interventions

The laparoscopic sacrohysteropexy (LSH) was performed under general anaesthesia. A uterine manipulator was used. After insufflation, four laparoscopic ports were placed: one 10-mm umbilical, two 5-mm lateral ports, and one 12-mm disposable trocar suprapubic. The ureter was identified on the right side. The peritoneum was incised from the sacral promontory to the level of the cervico-uterine junction. The vesico-uterine peritoneum was incised, and the bladder was dissected from the cervix. A bifurcated polypropylene type-1 monofilament microporous non-absorbable mesh was fixated to the posterior side of the cervix with four sutures. An inverted Y-shaped mesh was attached with four sutures to the anterior side of the cervix. Both ends of the Y-shaped mesh were perforated through the broad ligament and sutured to the posterior mesh, dorsally of the uterus. The end of the posterior mesh was attached to the sacral promontory using staples and was peritonealised.

The sacrospinous hysteropexy (SSHP) was conducted under general or spinal anaesthesia. After hydrodissection, the posterior vaginal wall was opened and the right sacrospinous ligament was exposed by blunt dissection, via the pararectal space. Breisky retractors were inserted for clear vision of the ligament. Two non-absorbable sutures were passed through the sacrospinous ligament, 2 cm medial to the ischial spine. Then, the sutures were placed through the posterior side of the cervix, resulting in suspension of the uterus. The vaginal wall was closed with absorbable sutures. Concomitant anterior or posterior vaginal wall repair or anti-incontinence surgery was performed if indicated with either the LSH or the SSHP.

Peri- and postoperative care

All patients were given a transurethral catheter and antibiotic prophylaxis (cefazolin and metronidazole) during surgery. The catheter was removed the next day or after the second day in case of an anterior colporrhaphy. After a SSHP, an intravaginal gauze packing was placed until the next day to reassure haemostasis. Thrombosis prophylaxis (subcutaneous injection of low molecular weight heparin) was prescribed during admission.

All patients were seen for follow-up six weeks after surgery as part of regular postoperative care. Evaluation of the POP symptoms and anatomical results, using the Pelvic Organ Prolapse Quantification (POP-Q), were registered. Information from possible additional follow-up visits was acquired from patients' files.

Data collection

In 2014, two to eleven years after POP surgery, all women who had undergone a SSHP or a LSH were contacted by mail and asked to fill in various Dutch validated questionnaires. Disease- specific quality of life was tested by the Patient Global Impression of Improvement (PGI-I);[21] Urinary Distress Inventory (UDI),[22] Defecatory Distress Inventory (DDI),[23] and Incontinence Impact Questionnaire (IIQ).[22] The UDI and DDI, containing of 19 and 11 items, respectively, indicate whether complaints of micturition, prolapse, or defecation are present and to what extent they are bothersome. These questions are designed using a four-point Likert scale ranging from 'not at all' to 'greatly'. The IIQ consists of 13 questions and shows the disease-specific quality of life for urine incontinence, also using a four-point Likert scale. The score of each domain ranges from 0 to 100, high score indicates increasingly bothersome symptoms (UDI and DDI) and a poorer quality of life (IIQ).

Furthermore, we evaluated sexual functioning, using the Prolapse / Incontinence Sexual Questionnaire (PISQ), containing 12 questions. The PISQ covers three domains: behavioural-emotive, physical, and partner-related. These items are scored on a five-point Likert scale ranging from 0 (always) to 4 (never). Items 1 - 4 are reversely scored, and a total of 48 is the maximum score; higher scores indicate better sexual function.[24, 25]

If patients did not return the questionnaires, we contacted them by telephone and sent the questionnaires again. The follow-up time for patients was recorded from surgery until completion of the questionnaire. For the non-responders, the follow-up time was calculated from surgery until the time of the last data collection from patients' files.

The follow-up consult consisted of an evaluation of prolapse symptoms and possible long-term complications combined with a vaginal examination to evaluate anatomical results using the POP-Q. Long-term complications included suture and mesh exposures as well as chronic pain symptoms. We asked the patient whether they had consulted a physician because of prolapse-related complaints or had a retreatment elsewhere. These follow-up visits were performed by a researcher, who was trained and authorised for POP-Q examination. The gynaecologists who had performed the POP surgeries were not involved in the evaluation in order to maintain objectivity.

Statistical analysis

The LSH group and SSHP group were compared using the Student's *t* test for normally distributed data and the Mann-Whitney *U* test for skewed data. For categorical data the Pearson's Chi-squared and Fisher tests were used. Follow-up time, age, and preoperative stage of uterine prolapse were evaluated as confounders in a logistic and linear regression analysis. Changes for > 10% in Exp(B) or β were viewed as confounding and further investigated in multivariable regression analysis. The statistical analysis was completed in Statistical Package for the Social Sciences (SPSS) 25.0 database for Windows.

Results

One hundred five patients were eligible for inclusion: 53 in the LSH group and 52 in the SSHP group, as shown in Figure 1. The questionnaires were completed by 44 (83.0%) patients in the LSH group and 43 (82.7%) patients in the SSHP group. Twenty-nine (54.7%) patients from the LSH group and 33 (63.5%) from the SSHP group came to our outpatient clinic for a POP-Q examination. Eighteen (17.1%) patients were lost to follow-up for various reasons; two patients had severe cognitive problems, four patients could not be contacted because of missing addresses or telephone numbers, and 12 patients were not willing to participate in a follow-up study. The mean follow-up time of this study is 4.5 years (54.2 months; 95% CI 44.8 – 64.2 months) in the LSH group and 2.5 years (30.1 months; 95% CI 29.3 – 31.5 months) in the SSHP group, which is significantly different, $p < 0.001$.

Table 1 shows the baseline characteristics of the study population. It shows significant differences in age at time of surgery as well as the age at time of follow-up. The LSH group was younger, with a mean age of 52.2 years (95% CI 48.8 – 22.6) at baseline and 56.7 years (95% CI 53.2 – 60.3) at follow-up, compared with the SSHP group, whose mean

age was 60.7 years (95% CI 57.3 – 64.1) at baseline and 63.7 years (95% CI 60.0 – 67.3) at follow-up, $p = 0.001$ and $p = 0.008$, respectively. In the LSH group there were more participants with a POP-Q stage ≥3 of the apical and anterior compartments compared with the SSHP group, $p = 0.006$ and $p = 0.003$, respectively. There was no difference in stage of posterior vaginal wall prolapse at baseline, $p = 0.125$.

Table 2 displays the perioperative data and complications. The LSH group had a significantly longer mean surgery time of 117 minutes (IQR 110 – 123), compared with the SSHP group, which had a mean operative time of 67 minutes (IQR 60 – 73), $p < 0.001$. Mean estimated amount of blood loss in the LSH group was less, 60 millilitres (95% CI 44 – 74) compared with the blood loss in the SSHP group of 168 millilitres (95% CI: 131 – 205), $p < 0.001$. Duration of hospital stay in the LSH group was significantly longer than in the SSHP group, four days versus three days, $p = 0.006$.

There was significantly less perioperative concomitant surgery in the LSH group (32.1% additional surgery) compared with the SSHP group (88.5% additional surgery), $p < 0.001$. In the LSH group there were four additional procedures because of POP complaints and three procedures because of stress urine incontinence. In nine cases (17%) the concomitant surgery was not related to POP complaints; four patients (7.5%) had a sterilisation with Filshie-clips; three patients (5.7%) had a bilateral salpingo-oophorectomy; one patient (1.9%) had a correction of an abdominal herniation; one patient (1.9%) had a hysteroscopic polypectomy. In the SSHP group 41 patients (78.8%) had an anterior colporrhaphy as concomitant surgery; in eight cases (15.4%) this was combined with a posterior colporrhaphy, perineorrhaphy and / or mid-urethral sling. Three patients (5.8%) had a posterior colporrhaphy; one patient (1.9%) had a posterior colporrhaphy combined with a mid-urethral sling; and one patient (1.9%) had a vaginal mesh (Prolift anterior).

Like the perioperative complications, the postoperative complications were not significantly different. Mesh exposure happened during the follow-up period after a LSH in three cases (5.7%). In all cases excision of the exposure was necessary. In one participant (1.9%) of the SSHP group, the sutures were visible and needed to be shortened in the outpatient clinic. De novo dyspareunia occurred in one patient (1.9%) in the LSH group, versus three patients in the SSHP group (5.8%), $p = 0.299$. In six (11.3%) of the women in the LSH group, chronic abdominal pain was reported, whereas in the SSHP group none of the participants said they had this complaint. One patient already had abdominal complaints before surgery, one patient had heavy menstrual bleeding due to uterine fibroids, one patient had irritable bowel syndrome, and three patients reported de novo abdominal pain (5.7%).

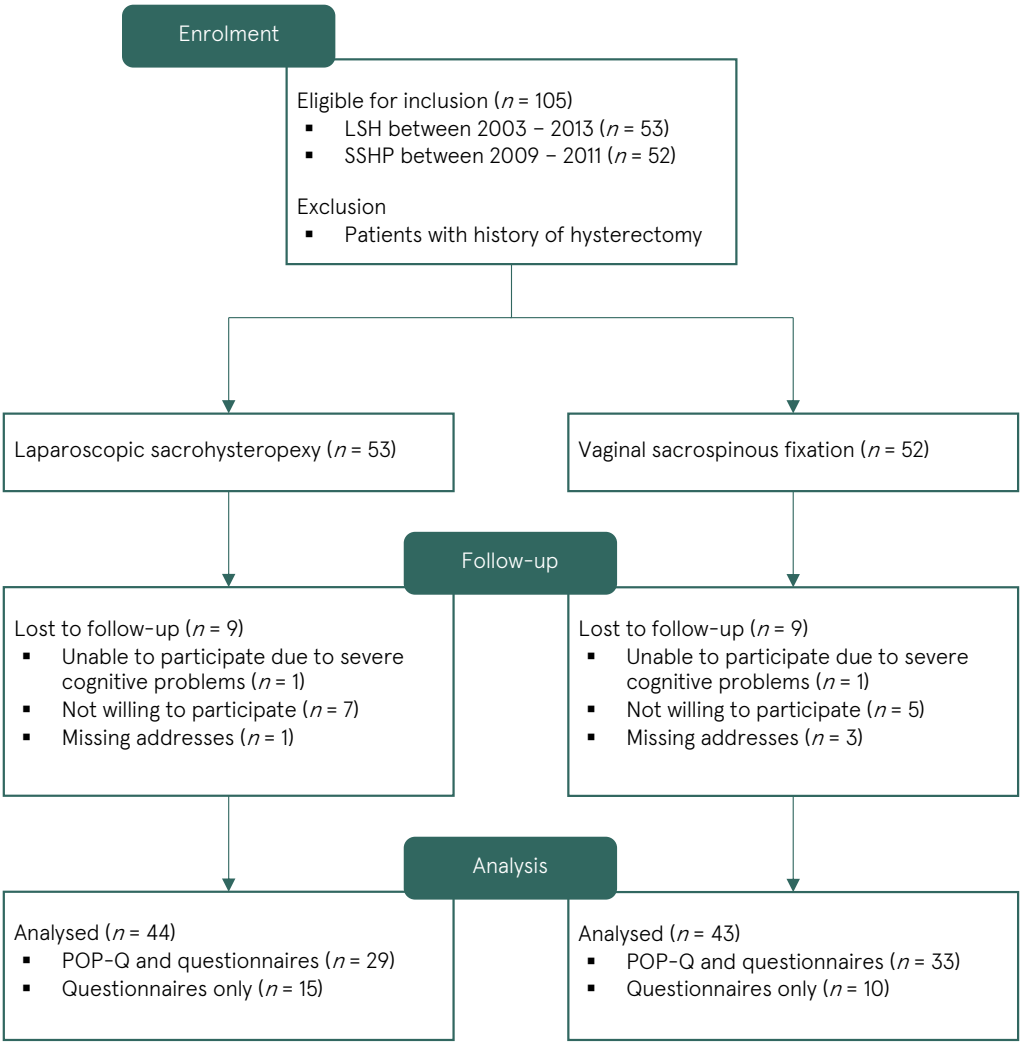

Figure 1. Flow diagram of the study population

Table 1. Baseline characteristics

	Laparoscopic sacrohysteropexy (n = 53)	Vaginal sacrospinous hysteropexy (n = 52)	p value
Age during surgery (years)			**0.001**[a]
Mean (95% CI)	52.2 (48.8 – 55.6)	60.7 (57.3 – 64.1)	
Age at follow-up (years)			**0.008**[a]
Mean (95% CI)	56.7 (53.2 – 60.3)	63.7 (60.0 – 67.3)	
Parity			0.792[b]
No./total no. of patients (%)			
0	2/42 (4.8)	1/43 (2.3)	
1	3/42 (7.1)	3/43 (7.0)	
2	26/42 (61.9)	27/43 (62.8)	
3	10/42 (23.8)	9/43 (20.9)	
≥4	1/42 (2.4)	3/43 (7.0)	
Body mass index (kg/m²)			0.835[a]
Mean (95% CI)	24.9 (23.9 – 26.0)	25.1 (24.1 – 26.2)	
History of gynaecological surgery			0.234[b]
No./total no. of patients (%)			
None	39/53 (73.6)	46/52 (88.4)	
ACR/PCR	10/53 (18.9)	6/52 (11.5)	
Vaginal sacrospinous hysteropexy	2/53 (3.8)	-	
Laparoscopic sacrohysteropexy	1/53 (1.9)	-	
Manchester Fothergill	1/53 (1.9)	-	
POP-Q stage apical compartment (point C)			**0.006**[b]
No./total no. of patients (%)			
1	2/52 (3.8)	5/51 (9.8)	
2	23/52 (44.2)	34/51 (66.7)	
3	20/52 (38.5)	12/51 (23.5)	
4	7/52 (13.5)	0/51 (0.0)	
POP-Q stage anterior compartment (point Ba)			**0.003**[b]
No./total no. of patients (%)			
0	4/44 (9.1)	5/48 (10.4)	
1	7/44 (15.9)	0/48 (0.0)	
2	7/44 (15.9)	22/48 (45.8)	
3	25/44 (56.8)	21/48 (43.8)	
4	1/44 (2.3)	0/48 (0.0)	
POP-Q stage posterior compartment (point Bp)			0.125[b]
No./total no. of patients (%)			
0	7/38 (18.4)	19/45 (42.2)	
1	15/38 (39.5)	10/45 (22.2)	
2	11/38 (29.0)	12/45 (26.7)	
3	5/38 (13.2)	5/45 (11.1)	
Duration of follow-up (months)			**<0.001**[a]
Mean (95% CI)	54.2 (44.8 – 64.2)	30.1 (29.3 – 31.5)	

ACR anterior colporrhaphy, *PCR* posterior colporrhaphy
[a] Student's *t* test
[b] Pearson's Chi-squared test

Table 2. Perioperative data and complications

	Laparoscopic sacrohysteropexy (n = 53)	Vaginal sacrospinous hysteropexy (n = 52)	p value
Operative time (minutes)			**<0.001[c]**
Median (IQR)	117 (110 – 123)	67 (60 – 73)	
Estimated blood loss (ml)			**<0.001[a]**
Mean (95% CI)	60 (44 – 74)	168 (131 – 205)	
Hospital stay (days)			**0.006[a]**
Mean (95% CI)	4 (3.5 – 4.2)	3 (3.0 – 3.5)	
Perioperative complications			0.396[b]
No./total no. of patients (%)			
One or more complications	2/53 (3.8)	1/52 (1.9)	
Bleeding	1/53 (1.9)	-	
Alternative mesh fixation	1/53 (1.9)	-	
Anaesthesia-induced complication	-	1/52 (1.9)	
Concomitant surgery	17/53 (32.1)	46/52 (88.5)	**<0.001[b]**
No./total no. of patients (%)			
None	36/53 (67.9)	6/52 (11.5)	
ACR	-	33/52 (63.5)	
PCR	1/53 (1.9)	3/52 (5.8)	
ACR + PCR	-	4/52 (7.5)	
Perineorrhaphy	3/53 (5.7)	-	
ACR + perineorrhaphy	-	3/52 (5.8)	
PCR + MUS	-	1/52 (1.9)	
ACR + PCR + MUS	-	1/52 (1.9)	
VM	-	1/52 (1.9)	
MUS	3/53 (5.7)	-	
Other than for POP/UI	9/53 (17.0)	-	
Postoperative complications < 2 weeks			0.458[b]
No./total no. of patients (%)			
One or more complications	7/53 (13.2)	12/52 (23.1)	
Ileus	1/53 (1.9)	-	
Abdominal wall hematoma	1/53 (1.9)	-	
Retroperitoneal hematoma	-	1/52 (1.9)	
Urinary tract infection	2/53 (3.8)	1/52 (1.9)	
Urinary retention (> 150 ml)	2/53 (3.8)	7/52 (13.5)	
Anaemia	-	4/52 (7.5)	
Postoperative complications > 2 weeks			0.381[b]
No./total no. of patients (%)			
One or more complications	12/53 (22.6)	9/52 (17.3)	
Recurrent urinary tract infection	-	2/52 (3.8)	
Urinary retention (> 150 ml)	1/53 (1.9)	1/52 (1.9)	
De novo dyspareunia	1/53 (1.9)	3/52 (5.8)	
Bottom pain	-	2/52 (3.8)	
Constipation	2/53 (3.8)	-	
Abdominal pain	6/53 (11.3)	-	
Exposure mesh	3/53 (5.7)	-	
Erosion sutures	-	1/52 (1.9)	

ACR anterior colporrhaphy, *PCR* posterior colporrhaphy, *MUS* mid-urethral sling, *VM* vaginal mesh (Prolift anterior), *POP* pelvic organ prolapse, *UI* urine incontinence

[a] Student's *t* test

[b] Pearson's Chi-squared test

[c] Mann-Whitney *U* test

The composite outcome of success for the apical compartment was 41.4% in the LSH group compared with 72.7% in the SSHP group (p = 0.073), as is shown in Table 3. There were no significant differences between the study groups concerning anatomical failure of the apical compartment in long-term follow-up (p = 0.711). Also, conservative and surgical reinterventions show no significant differences between the two study groups; p = 0.158 and p = 0.242, respectively (Figure 2). Regression analysis for composite outcome of success and anatomical failure showed no confounding for duration of follow-up, age, or preoperative POP-Q stage of uterine descent.

In the LSH group, 18 patients (34.6%) consulted a physician because of prolapse-related complaints (in our hospital or elsewhere) as opposed to 11 patients (21.2%) in the SSHP group (p = 0.126), according to the questionnaire. Sixteen versus six patients in the LSH and SSHP groups (37.2% versus 14.6%), respectively, reported recurrence of POP according to the UDI questionnaire (p = 0.019). Subsequently, vaginal bulge symptoms occurred significantly more in the LSH group; recurrence of POP had an odds ratio (OR) of 3.46 when comparing LSH to SSHP (p = 0.022). However, after correcting for the confounder duration of follow-up the OR was 2.73 and not statistically significant (p = 0.080).

The POP-Q results, after a mean follow-up duration of 4.5 years (54.2 months) in the LSH group and 2.6 years (30.1 months) in the SSHP group are shown in Table 4. Point Bp on the posterior wall of the vagina was significantly more descended in the LSH group (mean -2.2; SD ± 1.1) compared with the SSHP group (mean -2.8; SD ± 0.4; p = 0.031). The difference in the posterior compartment between the two groups was present at 6 weeks follow-up as well as during long-term follow-up. Point Bp was positioned more cranially in the SSHP group compared with the LSH group based on linear regression (β -.111, p = 0.051). No confounders were found. The other points of the POP-Q were not statistically different. Point C was -6.2; SD ± 1.7 in the LSH group versus 6.0; SD ± 1.5 in the SSHP group, p = 0.501.

The PGI-I in Table 5 did not show a difference in patient satisfaction; 75.0% (n = 33) of patients in the LSH group said their postoperative condition is 'very much better' or 'much better' now compared with 71.8% (n = 28) in the SSHP group (p = 0.741). The disease-specific quality of life from the UDI questionnaire showed a significantly higher score in the domain 'genital prolapse' in the LSH group with a mean score of 13.8 versus a mean score of 5.4 in the SSHP group (β -8.35; p = 0.044). After correcting for the confounder duration of follow-up time in linear regression analysis the β was -4.11 and not significantly different between the two study groups, p = 0.316. Age and POP-Q stage

Table 3. Recurrences of POP and retreatment after surgery

	LSH (*n* = 53)	SSHP (*n* = 52)	*p* value
Composite outcome of success for the apical compartment	12/29 (41.4)	24/33 (72.7)	0.073[a]
Anatomical failure			
During follow-up consultation at 6 weeks			
Anterior compartment (Ba ≥ -1)	3/26 (11.5)	6/45 (13.3)	0.827[a]
Apical compartment (C ≥ -1)	0/33 (0.0)	0/46 (0.0)	-
Posterior compartment (Bp ≥ -1)	4/17 (23.5)	1/33 (3.0)	**0.040[a]**
During follow-up consultation at long-term follow-up			
Anterior compartment (Ba ≥ -1)	25/28 (89.3)	25/33 (75.8)	0.171[a]
Apical compartment (C ≥ -1)	1/28 (3.6)	1/33 (3.0)	0.711[a]
Posterior compartment (Bp ≥ -1)	6/26 (23.1)	0/33 (0.0)	**0.006[a]**
Prolapse beyond hymen			
During follow-up consultation at 6 weeks			
Anterior compartment (Ba > 0)	1/26 (3.8)	3/45 (6.7)	0.619[a]
Apical compartment (C > 0)	0/33 (0.0)	0/46 (0.0)	-
Posterior compartment (Bp > 0)	2/17 (11.8)	0/33 (0.0)	**0.044[a]**
During follow-up consultation at long-term follow-up			
Anterior compartment (Ba > 0)	16/29 (55.2)	17/33 (51.5)	0.773[a]
Apical compartment (C > 0)	1/29 (3.4)	0/33 (0.0)	0.282[a]
Posterior compartment (Bp > 0)	3/27 (11.1)	0/33 (0.0)	**0.049[a]**
Vaginal bulge symptoms			
Symptoms for which patient consulted professional	18/52 (34.6)	11/52 (21.2)	0.126[a]
Time to consulted professional (months) Median (IQR)	22.0 (10.5 – 55.0)	28.0 (25.0 – 31.0)	0.306[b]
Recurrence POP on UDI questionnaire*	16/43 (37.2)	6/41 (14.6)	**0.019[a]**
Conservative retreatment	15/52 (28.8)	6/52 (11.5)	0.158[a]
Physical therapy	12/52 (23.1)	5/52 (9.6)	
Pessary treatment	2/52 (3.8)	1/52 (1.9)	
Combined	1/52 (1.9)	0/52 (0.0)	
Surgical retreatment	7/53 (13.2)	2/52 (3.8)	0.242[a]
SSHP + ACR + PCR	1/53 (1.9)	-	
VH + ACR	1/53 (1.9)	-	
VH	-	1/52 (1.9)	
MUS	1/53 (1.9)	-	
ACR	2/52 (3.8)	-	
VM	2/52 (3.8)	-	
Manchester Fothergill + ACR	-	1/52 (1.9)	
Time to surgical reintervention (months) Median (IQR)	12.0 (6.9 – 34.4)	9.2 (5.2 – 11.5)	0.164[b]

All data is given in number / total number of patients (percentage), unless stated otherwise
SSHP vaginal sacrospinous hysteropexy, *ACR* anterior colporrhaphy, *PCR* posterior colporrhaphy, *VH* vaginal hysterectomy, *MUS* mid-urethral sling, *VM* vaginal mesh (Prolift anterior)
* Bulge symptoms on UDI questionnaire: 'Slightly bothersome' to 'greatly bothersome'
[a] Pearson's Chi-squared test
[b] Log-rank test

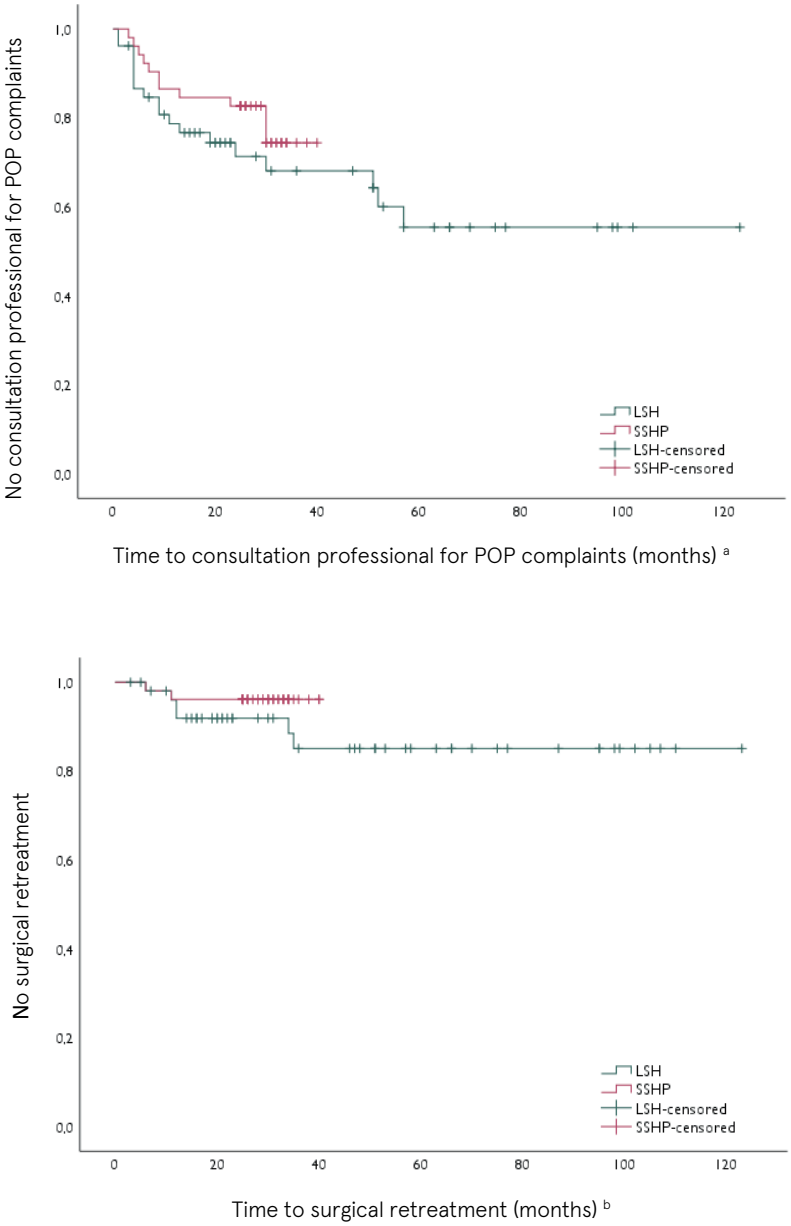

Figure 2. Survival analysis of consultation professional for POP complaints and surgical retreatment.

[a] Time (months) to consultation professional for POP complaints, $p = 0.306$
[b] Time (months) to surgical retreatment, $p = 0.164$

Table 4. POP-Q long-term follow-up

	Laparoscopic sacrohysteropexy (*n* = 27)	Vaginal sacrospinous hysteropexy (*n* = 33)	*p* value
Aa	-0.4 ± 1.8 (-3 – 3)	-0.6 ± 1.4 (-3 – 3)	0.559
Ba	-0.2 ± 1.5 (-3 – 5)	0.6 ± 2.3 (-3 – 4)	0.580
C	-6.2 ± 1.7 (-8 – 0)	-6.0 ± 1.5 (-8 – -1)	0.501
GH	3.7 ± 0.7 (2 – 5)	3.7 ± 0.7 (2 – 5)	0.888
PB	3.0 ± 0.2 (3 – 4)	3.0 ± 0.2 (3 – 4)	0.865
TVL	9.4 ± 0.7 (8 – 11)	9.5 ± 0.7 (9 – 12)	0.626
Ap	-2.3 ± 1.0 (-3 – 0)	-2.8 ± 0.4 (-3 – -2)	0.077
Bp	-2.2 ± 1.1 (-3 – 0)	-2.8 ± 0.4 (-3 – -2)	**0.031**
D	-7.4 ± 1.6 (-9 – -2)	-7.3 ± 1.3 (-9 – -3)	0.522

Data are means ± standard deviation (range lowest – highest)

of uterovaginal prolapse were not confounders. More patients in the LSH group were sexually active, compared with the SSHP group, 83.3% and 56.1%, respectively ($p = 0.007$). For the sexually active women a PISQ score was calculated, which showed a total score of 37.4 in the LSH group and 36.8 in the SSHP group ($p = 0.722$). Also, in the three subdomains of the PISQ no statistical differences were found between the two groups.

Discussion

Main findings

We performed a retrospective study in a teaching hospital in the Netherlands and included 105 patients who underwent a LSH or a SSHP for uterine prolapse. After correcting for confounding factors, LSH and SSHP seem to be equally effective in treating uterine prolapse, composite outcome measures and reported vaginal bulge symptoms. There were no clinically relevant differences in terms of anatomic recurrence of apical prolapse, POP symptoms for which patients consulted professionals, re-operation rates, and disease-specific quality of life. The operative time and hospital stay were significantly longer in the LSH group, whereas the estimated blood loss was more in the SSHP group.

Surgery time was longer for the LSH procedure, despite the higher rates of concomitant surgery that was performed during SSHP for the other compartments. This finding was to be expected and correlates to the literature, since LSH is a more complex laparoscopic procedure.[2] Blood loss was significantly less during LSH. However, the difference between the two groups was only around 100 ml estimated blood loss; therefore, it is not clinically relevant. This amount of blood loss is concordant with other literature.[2, 26] Hospital stay was longer in the LSH group (four days) compared with the SSHP group (three days). Since the procedures were performed, between 2003 and 2013,

Table 5. Domain scores for disease-specific quality of life

	Laparoscopic sacrohysteropexy (*n* = 53)	Vaginal sacrospinous hysteropexy (*n* = 52)	*p* value
Patient satisfaction (PGI-I)			
No./total no. of patients (%)			
'Very much better' or 'Much better'	33/44 (75.0)	28/39 (71.8)	0.741
Urogenital distress inventory (UDI)			
Overactive bladder	8.3 (3.8 – 12.9)	13.7 (7.4 – 19.9)	0.165
Urinary incontinence	7.5 (4.2 – 10.9)	9.8 (5.0 – 14.6)	0.425
Obstructive micturition	7.7 (3.5 – 12.0)	11.0 (4.9 – 17.0)	0.369
Genital prolapse	13.8 (7.2 – 20.3)	5.4 (0.5 – 10.3)	0.044
Pain	17.1 (10.2 – 23.9)	8.8 (2.5 – 15.1)	0.081
Defecatory distress inventory (DDI)			
Obstipation	5.6 (1.8 – 9.3)	4.9 (1.5 – 8.3)	0.798
Obstructive defecation	7.5 (3.3 – 11.8)	4.8 (0.6 – 8.6)	0.324
Pain	3.7 (1.3 – 7.6)	2.4 (0.8 – 5.2)	0.610
Faecal incontinence	4.8 (1.1 – 8.4)	3.3 (0.8 – 7.7)	0.610
Incontinence impact questionnaire (IIQ)			
Physical	8.5 (3.7 – 13.4)	10.4 (3.5 – 17.2)	0.657
Mobility	7.1 (3.9 – 10.2)	12.0 (5.4 – 18.7)	0.176
Social	4.0 (1.2 – 6.8)	6.9 (1.3 – 12.4)	0.353
Embarrassment	5.3 (1.7 – 8.9)	9.3 (1.8 – 16.7)	0.334
Emotional	6.9 (2.9 – 11.0)	10.2 (3.3 – 17.1)	0.405
General quality of life	83.6 (79.8 – 87.5)	78.4 (73.4 – 83.5)	0.097
Sexual function			
Sexually active	35/42 (83.3)	23/41 (56.1)	**0.007**
No./total no. of patients (%)			
PISQ-12 Total score	37.4 (35.5 – 39.3)	36.8 (33.9 – 39.7)	0.722
Behavioural-emotive	11.3 (10.2 – 12.3)	11.1 (9.6 – 12.4)	0.874
Physical	17.4 (16.3 – 18.5)	16.7 (15.0 – 18.4)	0.482
Partner-related	9.1 (8.6 – 12.4)	8.6 (7.8 – 9.3)	0.214

All data are means (95% confidence interval), unless otherwise indicated.
UDI and DDI; each item: 0 = no bothersome symptoms; 100 = most bothersome symptoms
IIQ; each item: 0 = best quality of life; 100 = worst quality of life
PISQ-12 total score: 0 = worst sexual function; 48 = best sexual function
PISQ-12 behavioural-emotive (items 1 – 4): 0 = worst function; 16 = best function
PISQ-12 physical (items 5 – 9): 0 = worst function; 20 = best function
PISQ-12 partner-related (items 10 – 12): 0 = worst function; 12 = best function

hospital protocols in the Netherlands have been changed, and admission after these surgeries is usually shorter nowadays.

The risk of vaginal mesh exposure in our study for the LSH group was 5.7% (*n* = 3) over a mean follow-up time of 4.5 years. In the literature, mesh exposure of 1 – 3% after LSH has been reported.[27] This lower incidence of mesh exposure is probably due to a shorter period of follow-up. Our follow-up time is much longer, and exposures occur more often after a longer period of follow-up, as is seen in a study with seven-year follow-up and exposure rate of 10.5%.[28]

In six (11.3%) of the women of the LSH group, chronic abdominal pain was reported, whereas in the SSHP group none of the participants stated to have this complaint. However, only half of those patients reported de novo abdominal pain (5.7%); in three patients a different cause was identified. The abdominal pain was not severe enough to perform a diagnostic laparoscopy or refer to another specialty (*e.g.,* a surgeon). Other studies did not report on abdominal pain as a long-term outcome measure.[15, 28-31]

Postoperatively, point Bp on the posterior wall of the vagina had descended significantly more in the LSH group compared with the SSHP group. The difference in the posterior compartment was already present at six-week follow-up. However, the difference for point Bp is only 0.6 cm, and just one re-operation was done for the posterior compartment in the LSH group, which suggests that the difference in the posterior compartment might not be clinically relevant. Also, in a randomised controlled trial there seems to be a difference in anatomical failure for the posterior compartment (LSH 18.2% versus SSHP 6.9%). Although this is not statistically significant, it may show a trend and corresponds to our results.[15]

Strengths and limitations

The strength of this study is that the composite outcome of success of the apical compartment has been used as primary outcome. Barber's publication underlines the importance of an outcome which includes objective and subjective POP correction as well as retreatment.[20] Another strength is the long follow-up time of 4.5 years (54.2 months; 95% CI 44.8 – 64.2 months) in the LSH group and 2.6 years (30.1 months; 95% CI 29.3 – 31.5 months) in the SSHP group. There are no prospective comparative studies which have comparable length of follow-up.[15] To evaluate the effectiveness of a surgical treatment for POP, a long follow-up time is desirable.[20]

There are also some limitations to this study. Due to the retrospective design, the two study groups are significantly different regarding the baseline characteristics and the duration of follow-up time. However, the primary outcome regression models were used to eliminate three confounders: duration of follow-up, age, and stage of POP. In addition, patient selection occurred, since in our clinic SSHP is less likely to be performed in young sexually active women compared with older postmenopausal women given the higher rate of dyspareunia de novo after SSHP. Also, there is a time difference between the two surgical procedures of > five years (LSH 2003 – 2013 and SSHP 2009 – 2011), which can influence the study results. Although we believe this is not the case in our study, it is an important aspect to address. All surgeons had completed their learning curve before the start of our study. Moreover, during this period there were no significant changes or improvements in surgical equipment or procedures, expecting better outcomes.

In the LSH group more women were sexually active compared with the SSHP group, postoperatively. The difference in sexual activity might be explained by the significantly lower age in the LSH group. De novo dyspareunia occurred in both groups but showed no statistically difference: 1.9% (n = 1) in the LSH group versus 5.8% (n = 3) in the SSHP group (p = 0.299). A randomised controlled trial on the topic found more dyspareunia after the SSHP.[15] The PISQ scores also showed no significant differences between the groups.

Conclusion

In conclusion, the LSH and SSHP are equally effective based on objective and subjective recurrence rates after correction for confounding factors. The operative time and hospital stay were significantly longer in the LSH group, whereas the estimated blood loss was more in the SSHP group. Peri- and postoperative complications are equal. The risk of vaginal mesh exposure is 3.8% after a mean follow-up time of 54.2 months. LSH as a treatment for uterine descent is promising; however, the long-term follow-up of a randomised controlled trial is needed to compare the effectiveness of these interventions for uterine prolapse.

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CHAPTER 5

Hysteropexy in the treatment of uterine prolapse stage 2 or higher: laparoscopic sacrohysteropexy versus sacrospinous hysteropexy – a multicentre randomised trial (LAVA trial)

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Abstract

OBJECTIVE

To investigate whether laparoscopic sacrohysteropexy (LSH) is non-inferior to vaginal sacrospinous hysteropexy (SSHP) in the surgical treatment of uterine prolapse.

DESIGN

Multicentre randomised controlled, non-blinded non-inferiority trial.

SETTING

Five non-university teaching hospitals in the Netherlands, one university hospital in Belgium.

POPULATION

126 women with uterine prolapse stage 2 or higher undergoing surgery without previous pelvic floor surgery.

METHODS

Randomisation in a 1:1 ratio to LSH or SSHP, stratified per centre and severity of the uterine prolapse. The predefined inferiority margin was an increase in surgical failure rate of 10%.

MAIN OUTCOME MEASURES

Primary outcome was surgical failure, defined as recurrence of uterine prolapse (POP-Q ≥ 2) with bothersome bulging / protrusion symptoms and / or repeat surgery or pessary at 12 months postoperatively. Secondary outcomes were anatomical recurrence (any compartment), functional outcome, and quality of life.

RESULTS

LSH was non-inferior for surgical failure (*n* = 1, 1.6%) compared with SSHP (*n* = 2, 3.3%, difference -1.7%, 95% CI -7.1 – 3.7) 12 months postoperatively. Overall anatomical recurrences and quality of life did not differ. More bothersome symptoms of overactive bladder (OAB) and faecal incontinence were reported after LSH. Dyspareunia was more frequently reported after SSHP.

CONCLUSION

LSH was non-inferior to SSHP for surgical failure of the apical compartment at 12 months follow-up. Following LSH, bothersome OAB and faecal incontinence were more frequent, but dyspareunia was less frequent.

TRIAL REGISTRATION

Dutch trial register NTR4029.

Introduction

Pelvic organ prolapse (POP) is a common health problem associated with a significant impairment in quality of life.[1] The lifetime risk of undergoing surgery for POP or urinary incontinence is 20% by the age of 80 years.[2] As result of an ageing population, a significant increase in both the number of women with POP and those seeking care for POP is expected to occur over the next 20 – 40 years.[3] Consequently, surgical rates for POP and urinary incontinence in the USA are estimated to increase with 42.7% by 2050.[3]

Traditionally, uterine prolapse is treated by vaginal hysterectomy and suspension of the vaginal vault, despite the fact that the uterus is not the cause but only a passive structure in the development of prolapse.[4, 5] However, uterus preservation techniques are gaining interest and more of these operations have been done in recent years.[6-9] In concert with this, more women express a preference for uterine preservation.[10-12] Women may want to avoid hysterectomy because they feel the uterus is important for a sense of self-esteem and plays a role in sexual satisfaction, the added surgical risk of hysterectomy, and / or a desire to preserve fertility.[10, 12, 13] In addition, data showing an added value of hysterectomy over uterus preservation are lacking.

Several studies have demonstrated that uterine suspension is as effective and safe as prolapse surgery, including vaginal hysterectomy.[13-16] Laparoscopic, robotic, abdominal, and vaginal procedures have been described to suspend the uterus. To date, no randomised controlled trials (RCTs) are available comparing these different routes.[13] Surgical access route and method of uterus suspension mostly depend on the preference of the surgeon. Whether these operations have comparable anatomical and functional outcomes remains unclear.

Vaginal sacrospinous hysteropexy (SSHP) is the most studied technique for uterus suspension and its efficacy has been demonstrated in several RCTs.[15-17] However, laparoscopic sacrohysteropexy (LSH) has not been compared directly in a randomised trial against SSHP, although it seems to be increasingly popular.[7, 18] Therefore, we tested the hypothesis that LSH is non-inferior to SSHP regarding surgical failure at 12 months of follow-up.

Methods

Study design

The trial protocol of this study has been published previously.[19] The study was approved by the ethics committee of the Isala Hospital (file number NL43801.075.13) and all additional centres, and was registered in the Dutch Trial Register (NTR4029). Briefly, all women with uterine prolapse at stage 2 or higher (uterine prolapse 1 cm above the hymen and beyond) and opting for surgical treatment were invited to participate. Women with coexisting anterior and / or posterior vaginal wall prolapse or concomitant incontinence surgery were also eligible. Exclusion criteria were previous pelvic floor or prolapse surgery, known cervical dysplasia / malignancy, language barriers, the wish to preserve fertility, presence of immunological or haematological disorders potentially interfering with postoperative recovery, contraindications for laparoscopic surgery (*e.g.,* ileus, risk of severe adhesions), suspect findings of uterus and / or ovaries on ultrasound causing symptoms and / or requiring surgical treatment, abnormal uterine bleeding requiring surgical treatment, postmenopausal bleeding in the past year, and unwillingness to return for follow-up. Participants were randomly assigned to LSH or SSHP.

Before enrolment, gynaecological examination was performed including pelvic ultrasound to exclude uterine or ovarian disease, a cervical smear test and vaginal inspection in 45° semi-upright position for staging uterovaginal prolapse using the pelvic organ prolapse quantification system (POP-Q).[20]

Five non-university teaching hospitals in the Netherlands and one university hospital in Belgium participated in this study. In order to standardise surgery, a detailed protocol was developed for both operations during a specific study masterclass in which all centres participated. All procedures were performed according to this standardised protocol using the same materials (*e.g.,* sutures, mesh). To eliminate a learning curve effect, each surgeon should have performed at least 20 procedures of each, prior to the recruitment of the first patient for this study.

Written information was provided to eligible women and informed consent was obtained. Participants were then randomly assigned in a 1:1 ratio to either SSHP or LSH using a web-based computer application with generated computer randomisation tables in blocks of four. Randomisation was stratified per centre and severity of the uterine prolapse (POP-Q stage 2, 3, or 4). Surgeons and women were not blinded to the allocated surgical procedure. A physician trained in urogynaecology who was not involved in the management of patients performed the follow-up at 12 months.

Primary and secondary outcomes

The primary outcome was a composite outcome of surgical failure of the apical compartment at 12 months follow-up, defined as recurrence of uterine prolapse (POP-Q ≥ stage 2) with bothersome bulging / protrusion symptoms and / or requiring therapy, whether it was repeat surgery or pessary.[21] Additional outcomes were anatomical failure in any compartment (POP-Q ≥ stage 2 in any compartment); surgical success defined as no prolapse beyond the hymen, no bothersome bulge symptoms, or therapy for recurrent prolapse within 12 months; and overall surgical failure, which was defined as POP-Q ≥ stage 2, pessary use, or repeat surgery for recurrent prolapse in any compartment within 12 months. Other secondary outcomes were functional outcome, quality of life, and sexual functioning.

Data collection

Pelvic organ prolapse (POP) measurements using the POP-Q system were performed at baseline, at six weeks, and six and 12 months after surgery. At those visits, women completed questionnaires regarding health-related and disease-specific quality of life (short form-36, EuroQol 5D, urogenital distress inventory, defecatory distress inventory and incontinence impact questionnaire).[22-25] We defined the presence of bothersome bulge symptoms after surgery as any positive answer to any of the following two questions from the urogenital distress inventory: 'Do you experience a sensation of bulging or protrusion from the vagina' and 'Do you have a bulge or something protruding that you can see in the vagina?' in combination with a response 'somewhat bothered' to 'very much bothered' to the question 'how much does this bother you?' To assess sexual functioning, the 12-item pelvic organ prolapse / urinary incontinence sexual questionnaire was used.[26] Data were entered and registered using a web-based application facilitated by the Isala.

Interventions

Women received perioperative antibiotics, thrombosis prophylaxis, a bladder catheter, and postoperative analgesia according to local hospital protocols. LSH was performed under general anaesthesia. For SSHP, patients received general or spinal anaesthesia, according to patient or physician preference. Participants were advised to abstain from heavy physical duties for six weeks.

VAGINAL SACROSPINOUS HYSTEROPEXY

The posterior vaginal wall was incised and separated from the rectum. The right ischial spine was localised digitally. After retractor positioning, the sacrospinous ligament was exposed through blunt dissection. Under direct vision, two permanent sutures (Prolene

1/0, Ethicon Inc., Sommerville, NJ, USA) were placed through the right sacrospinous ligament at least 2 cm from the ischial spine. After placing the polypropylene sutures through the posterior aspect of the cervix, these were tightened to redress the uterus. Finally, the posterior vaginal wall was closed using absorbable sutures. Concomitant anterior or posterior colporrhaphy and anti-incontinence surgery were performed if indicated.

LAPAROSCOPIC SACROHYSTEROPEXY

First a uterine manipulator (Clearview, Clinical Innovations LLC, Murray, UT, USA) was placed. After placing four laparoscopic ports (umbilical, suprapubic, two lateral ports) and creating a pneumoperitoneum, the peritoneum over the sacral promontory was incised. The broad ligament at the level of the cervico-uterine junction was opened. The vesico-uterine peritoneum was incised, and the bladder dissected distally for 2 – 3 cm. The arms of a bifurcated polypropylene flat mesh (Gynemesh, Ethicon Inc., Sommerville, NJ, USA) were introduced bilaterally through windows created in the broad ligaments. Non-absorbable sutures were placed through the arms of the mesh and the anterior (2 – 3 sutures) and posterior (4 sutures) aspect of the cervix, respectively. The mesh was attached to the sacral promontory using three 5.3 x 3.7 mm titanium staples (Endoscopic Multifeed Stapler-20, Ethicon Inc., Sommerville, NJ, USA). The peritoneum was then closed using a resorbable running suture (Vicryl 2.0, Ethicon Inc., Sommerville, NJ, USA). After removing the laparoscopic ports, the wounds were closed. If indicated, anterior and / or posterior vaginal wall repair was performed laparoscopically (by extended dissection) or vaginally afterwards (anterior and / or posterior colporrhaphy). Furthermore, anti-incontinence surgery was performed if necessary.

Statistical analysis

Sample size calculation was based on the primary outcome. We assumed a failure rate of 3% based on outcomes of SSHP in a previous prospective study.[17] The non-inferiority margin was set at 10%. This means that when the upper limit of the 95% confidence interval (CI) for the estimated difference in recurrence rate after LSH versus SSHP exceeded 10%, LSH would be regarded as inferior to SSHP. Assuming an absolute recurrence risk of 3% in both groups and a two-sided α risk of 0.05, with two groups of 55 women each, the trial had 80% power with a prespecified non-inferiority margin of 10%. Considering a 10% loss to follow-up, we required 124 women, 62 in each study arm.

Data were analysed primarily according to an intention to treat (ITT) principle. However, a per protocol (PP) analysis was done as well. In case of missing data on anatomical outcome at 12 months, this was reported, and we applied the last observation carried forward (LOCF) strategy with data at the six-month follow-up if available. If these data

were not available, data of six weeks follow-up was used. If the six-week follow-up was missing, we left the women out of the ITT-LOCF analysis. In case of missing questionnaires, we obtained information on the presence or absence of bothersome bulge symptoms from the 12-month follow-up visit. As sensitivity analysis, we applied conservative imputation (worst-case scenario, failure) in which all patients lost to follow-up at the 12-month visit were regarded as having experienced a recurrence.

The PP-analysis was performed on the primary and secondary outcomes for anatomical and surgical failure. This analysis included women who completed the entire treatment protocol as originally planned, with availability of the POP-Q scores at 12 months and absence of major deviations from the protocol.

For exploratory purposes of the results, Pearson's Chi-squared or Fisher's exact test was used to compare proportions and a Mann-Whitney *U* test was used to compare continuous variables between the groups. A p value of < 0.05 was considered to be significant. In case of statistical significance, linear regression was used to assess confounding with baseline values. All statistical analyses were performed using SPSS for Windows (version 24.0.0.1, SPSS Statistics UK, SPSS Inc, Chicago, IL, USA).

Results

In total, 126 women were randomly assigned to LSH (n = 64) or SSHP (n = 62) between August 2013 and September 2016. Figure 1 displays the flowchart of this study. Seven protocol deviations occurred. Five women received SSHP instead of LSH (crossovers). Reasons for crossover were intra-abdominal adhesions making mesh placement difficult (n = 2), excessive intra-abdominal fat tissue with impaired visualization of the promontory (n = 1), an enlarged uterus reaching up to the promontory (n = 1), and perforation of the vaginal wall during dissection (n = 1). In one woman allocated to LSH, it was not impossible to attach the mesh to the promontory due to extremely hard tissue. Consequently, a Manchester Fothergill procedure was performed. Finally, in one woman an endometrial polyp was removed during LSH. Histopathological examination demonstrated endometrial carcinoma. Two months after surgery, a total laparoscopic hysterectomy was performed.

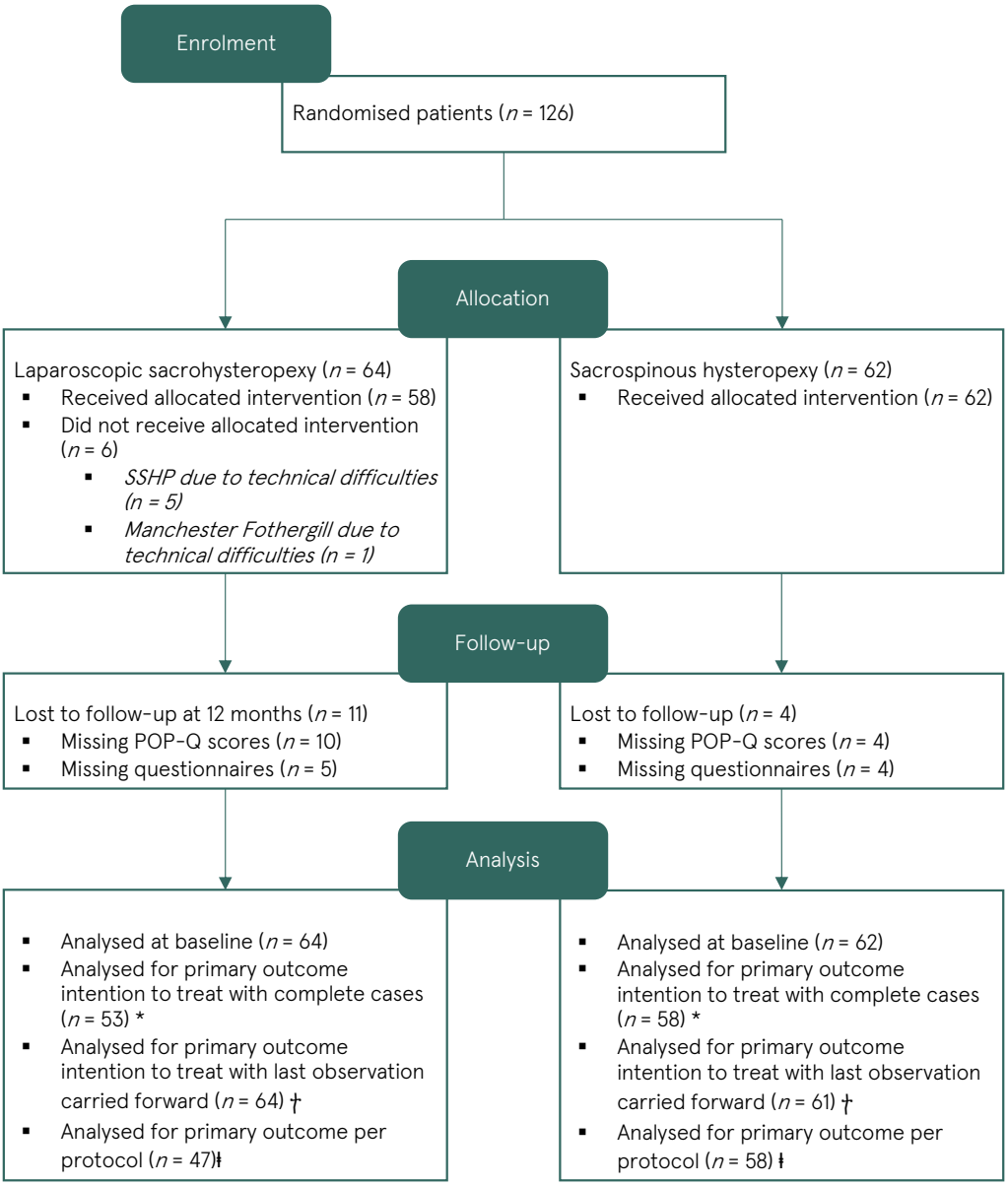

Figure 1. Flow diagram of the study population

* Intention to treat complete cases: only patients with complete follow-up (*e.g.,* POP-Q and questionnaire) were analysed according to allocation. Six patients allocated to LSH received a vaginal procedure and were analysed in the laparoscopic group.

† Intention to treat with last observation carried forward: missing data was imputed with data at the six months follow-up visit if available (*n* = 12) or, in case these data is also missing, data of 6 weeks follow-up visit (*n* = 2). In one patient allocated to the SSHP, no follow-up data was available.

‡ Per protocol analysis: 6 patients did not receive intended treatment. Excluded per protocol analysis: lost to follow-up at 12 months (*n* = 15) and major protocol deviations (*n* = 7).

Baseline characteristics and prolapse staging were comparable between groups (Table 1). In the SSHP group, there were significantly more additional anterior vaginal wall repairs (SSHP: *n* = 61, 98.4%; LSH: *n* = 55, 85.9%, *p* = 0.010), but not posterior repairs (SSHP: *n* = 14, 22.6%; LSH: *n* = 13, 20.3%). In the SSHP group, all anterior vaginal wall repair was performed by anterior colporrhaphy, whereas in the LSH group the majority of the anterior repair was performed laparoscopically (*n* = 44, 80%; vaginally *n* = 11, 20%). When looking at posterior repair, women in the SSHP group underwent posterior colporrhaphy (*n* = 12, 86%) or perineorrhaphy (*n* = 2, 14%). In the LSH group, posterior repair was performed laparoscopically (*n* = 5, 38%), by posterior colporrhaphy (*n* = 5, 38%) or by perineorrhaphy (*n* = 3, 23%). Three associated tension-free vaginal tapes were placed, two after LSH (3.1%) and one (1.6%) after SSHP.

Table 2 presents the results on the primary outcome and the additional definitions of surgical failure. Regarding the primary outcome, LSH was non-inferior to SSHP: LSH 1.6% (*n* = 1) versus SSHP 3.3% (*n* = 2), difference -1.7% (95% CI -7.1 – 3.7) for the ITT-LOCF approach. Non-inferiority of the LSH was also shown in the ITT analysis with complete cases and the PP analysis. The worst-case scenario did not lead to different conclusions. No difference was found in overall surgical failure, composite outcome of success, and anatomical failure. Most anatomical failures occurred in the anterior compartment.

Table 3 provides details on the functional outcomes. After LSH, significantly more bothersome symptoms of overactive bladder (OAB) were reported: UDI score LSH: 11 (interquartile range (IQR) 0 – 22); SSHP 0 (IQR 0 – 11), *p* = 0.012. De novo OAB occurred in two women (4.0%) after LSH. However, 28% (14/50) of women after LSH who were already suffering from OAB before surgery reported persistent OAB symptoms after surgery, as compared with 13.5% (7/52) of women after SSHP.

Significantly more bothersome symptoms of faecal incontinence following LSH were reported: DDI score LSH: 0 (IQR 0 – 17); SSHP: 0 (IQR 0 – 0), *p* = 0.017. Persistent faecal incontinence was reported in 3.4% (2/58) of women after SSHP, as compared with 10.2% (6/59) of women after LSH. De novo faecal incontinence was reported in five women (8.5%) after LSH compared with four women (6.9%) after SSHP.

Quality of life and sexual functioning did not differ. In the laparoscopic group, 84% (42/50) of the women were sexually active as compared with 75.5% (40/53) in the vaginal group. Of the sexually active women, 13 of 39 women (33.3%) of the SSHP group reported dyspareunia, which is almost three times as often compared with the laparoscopic group (5/37, 13.5%, *p* = 0.042). De novo dyspareunia was found in respectively five women (13.2%, SSHP) and three women (8.1%, LSH, not significant).

Table 1. Baseline characteristics and pelvic measurements of women

	Laparoscopic sacrohysteropexy (*n* = 64)	**Vaginal sacrospinous hysteropexy (*n* = 62)**
Mean (SD) age (years)	61.08 (9.8)	60.76 (10.7)
Mean (SD) body mass index (kg/m2)	26.6 (3.4)	26.6 (2.9)
Comorbidity		
Cardiovascular disease	29 (45.3)	19 (30.6)
Respiratory disease	4 (6.3)	4 (6.5)
Diabetes Mellitus	3 (4.7)	4 (6.5)
Current smoker (self-reported)	5 (7.8)	7 (11.3)
Median (range) number of vaginal deliveries	2 (1 – 10)	2 (1 – 5)
Median (range) number of caesarean deliveries	0 (0 – 1)	0 (0 – 1)
POP-Q stage uterine prolapse (point C)*		
2	45 (70.3)	39 (62.9)
3	18 (28.1)	19 (30.6)
4	1 (1.6)	4 (6.5)
POP-Q stage 2-4		
Anterior prolapse (Ba ≥ -1)	59 (92.2)	56 (90.3)
Posterior prolapse (Ba ≥ -1)	14 (22)	16 (25.8)
Prolapse beyond hymen		
Apical (POP-Q C > 0)	30 (46.6)	28 (45.2)
Anterior (POP-Q Ba > 0)	51 (81)	45 (72.6)
Posterior (POP-Q Bp > 0)	2 (3.2)	3 (4.8)
Vaginal bulge symptoms		
Any	56/62 (90.3)	56/59 (94.9)
Bothersome	54/62 (87.1)**	56/59 (94.9)

Values are numbers (percentages) unless stated otherwise
Percentages were calculated using non-missing data All patients were analysed as allocated
POP-Q pelvic organ prolapse quantification
* System involves quantitative measurements of various points of vaginal wall with hymen as reference point. Degree of prolapse of anterior vaginal wall (Aa and Ba), posterior vaginal wall (Ap and Bp) and uterus (C) is measured in centimetres above or proximal to hymen (negative number) of beyond or distal to the hymen (positive number), with plane of hymen defined as zero. Point A represents the descent of a measurement point 3 cm proximal to the hymen on the anterior (Aa) and posterior (Ap) vaginal wall. B is the most descended edge on the anterior (Ba) and posterior (Bp) vaginal wall
POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen
POP-Q stage 3: most distal prolapse is > 1 cm beyond hymen, but no further than 2 cm less than total vaginal length
POP-Q stage 4: total prolapse
** Not all women reported bothersome prolapse symptoms at baseline. The questionnaire was provided after women consented to participate, therefore amount of bother as reported at outpatient clinic could differ.

One year after surgery, 86.2% (*n* = 50) of the women were satisfied with the results of LSH, which is comparable with the satisfaction after SSHP (89.7%, *n* = 52). In both groups, a large majority would recommend the surgery to someone else (LSH: *n* = 50, 87.7%; SSHP: *n* = 52, 89.7%).

Table 2. Outcomes for pelvic organ prolapse at 12 months follow-up

	Laparoscopic sacrohysteropexy	Vaginal sacrospinous hysteropexy	Difference (95% CI)
Primary outcome			
Surgical failure [a]			
ITT analysis with complete cases	1/54 (1.9)	2/58 (3.4)	-1.6 (-7.5 – 4.3)
ITT analysis with LOCF	1/64 (1.6)	2/61 (3.3)	-1.7 (-7.1 – 3.7)
Per protocol analysis	1/47 (2.1)	2/58 (3.4)	-1.3 (-7.6 – 4.9)
Overall surgical failure [b]			
ITT analysis with complete cases	39/57 (68.4)	37/58 (63.8)	4.6 (-12.7 – 21.9)
ITT analysis with LOCF	42/64 (65.6)	38/61 (62.3)	3.3 (-13.5 – 20.2)
Per protocol analysis	35/50 (70)	37/58 (63.8)	6.2 (-11.5 – 23.9)
Composite outcome success [c]			
ITT analysis with complete cases	44/55 (80.0)	48/58 (82.8)	-2.8 (-17.1 – 11.6)
ITT analysis with LOCF	53/64 (82.8)	51/61 (83.6)	-0.8 (-13.9 – 12.3)
Per protocol analysis	38/49 (77.6)	48/58 (82.8)	-5.2 (-20.4 – 10.0)
Anatomical failure [d]			
Overall anatomical failure	35/55 (63.6)	36/58 (62.1)	1.6 (-16.3 – 19.4)
Apical compartment	2/55 (3.6)	2/58 (3.4)	0.2 (-6.6 – 7.0)
Anterior compartment	28/55 (50.9)	33/58 (56.9)	-6.0 (-24.3 – 12.4)
Posterior compartment	10/55 (18.2)	4/58 (6.9)	11.3 (-0.8 – 23.4)
Prolapse beyond hymen [e]			
Apical (POP-Q C > 0)	0/64 (0)	1/61 (1.6)	-1.6 (-4.8 – 1.5)
Anterior (POP-Q Ba > 0)	6/64 (9.4)	5/61 (8.2)	1.2 (-8.7 – 11.1)
Posterior (POP-Q Bp > 0)	0/64 (0)	0/61 (0)	-
Repeat surgery [e]			
Overall repeat surgery	2/64 (3.1)	3/61 (4.9)	-1.8 (-8.7 – 5.1)
Apical compartment	0/64 (0)	2/61 (3.3)	-3.3 (-7.7 – 1.2)
Anterior compartment	2/64 (3.1)	1/61 (1.6)	1.5 (-3.1 – 1.6)
Posterior compartment	0/64 (0)	0/61 (0)	-
Primary surgery different site [f]	0/64 (0)	0/61 (0)	-
Surgery for non-prolapsed conditions [e]			
Anti-incontinence	4/64 (6.3)	2/61 (3.3)	3.0 (-4.5 – 10.4)
Hysterectomy	1/64 (1.6)	0/61 (0)	-

Values are numbers (percentages) of women unless states otherwise
ITT intention to treat, *LOCF* last observation carried forward, *POP-Q* pelvic organ prolapse quantification
Percentages were calculated using non-missing data
[a] Recurrent apical prolapse POP-Q ≥2 with bothersome symptoms or repeat surgery or pessary for apical prolapse
[b] Prolapse POP-Q stage ≥2 (any compartment) or repeat surgery or pessary use
[c] No prolapse beyond hymen (any compartment), absence of bothersome bulge symptoms, and no repeat surgery or pessary use
[d] Prolapse POP-Q stage ≥ 2
[e] ITT with LOCF
[f] Reoperation for pelvic organ prolapse in non-operated compartment

Table 3. Functional outcome and quality of life after laparoscopic sacrohysteropexy versus vaginal sacrospinous hysteropexy at 12 months follow-up

	Before surgery		12 months after surgery		*p* value
	LSH (*n* = 62)	SSHP (*n* = 59)	LSH (*n* = 59)	SSHP (*n* = 58)	
Urogenital distress inventory (UDI) [a]					
Overactive bladder	22 (6 – 44)	22 (11 – 47)	11 (0 – 22)	0 (0 – 11)	0.012
Urinary incontinence	25 (0 – 33)	17 (0 – 33)	17 (0 – 33)	0 (0 – 17)	0.057
Obstructive micturition	16 (0 – 33)	33 (0 – 50)	0 (0 – 17)	0 (0 – 0)	0.188
Genital prolapse	58 (33 – 67)	67 (33 – 67)	0 (0 – 0)	0 (0 – 0)	0.251
Pain	17 (0 – 33)	33 (0 – 50)	0 (0 – 17)	0 (0 – 17)	0.691
Defecatory distress inventory (DDI) [a]					
Obstipation	0 (0 – 17)	0 (0 – 17)	0 (0 – 0)	0 (0 – 0)	0.779
Obstructive defecation	0 (0 – 17)	0 (0 – 8)	0 (0 – 8)	0 (0 – 8)	0.758
Pain	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	0.123
Faecal incontinence	0 (0 – 17)	0 (0 – 0)	0 (0 – 17)	0 (0 – 0)	0.017
Flatus incontinence	33 (0 – 67)	33 (0 – 33)	33 (0 – 33)	0 (0 – 33)	0.144
Incontinence impact questionnaire (IIQ) [b]					
Physical	33 (0 – 33)	33 (0 – 33)	0 (0 – 0)	0 (0 – 0)	0.746
Mobility	22 (6 – 39)	22 (0 – 44)	0 (0 – 17)	0 (0 – 11)	0.616
Social	0 (0 – 17)	0 (0 – 22)	0 (0 – 0)	0 (0 – 0)	0.740
Embarrassment	16 (0 – 17)	0 (0 – 33)	0 (0 – 0)	0 (0 – 0)	0.862
Emotional	11 (0 – 33)	11 (0 – 33)	0 (0 – 11)	0 (0 – 0)	0.298
Short form-36 [c]					
Physical functioning	70 (55 – 85)	70 (50 – 85)	90 (78 – 95)	90 (79 – 95)	0.434
Social functioning	88 (75 – 100)	88 (63 – 100)	100 (88 – 100)	100 (88 – 100)	0.512
Role limitations physical	75 (29 – 100)	75 (0 – 100)	100 (100 – 100)	100 (75 – 100)	0.776
Role limitations emotional	100 (83 – 100)	100 (92 – 100)	100 (100 – 100)	100 (100 – 100)	0.857
Mental health	84 (68 – 88)	80 (68 – 92)	88 (76 – 92)	87 (76 – 96)	0.809
Vitality	65 (54 – 78)	70 (50 – 80)	75 (60 – 80)	80 (69 – 90)	0.097
Bodily pain	78 (57 – 90)	78 (45 – 90)	90 (78 – 100)	100 (78 – 100)	0.629
General health perception	70 (60 – 80)	70 (54 – 81)	75 (60 – 90)	78 (64 – 90)	0.928
Health change	50 (25 – 50)	50 (25 – 5 0)	75 (50 – 100)	75 (50 – 100)	0.693
PISQ-12 [d]	35 (32 – 39)	35 (32 – 40)	39 (37 – 42)	39 (34 – 42)	0.252

Values are medians (interquartile ranges) of domain scores unless stated otherwise
LSH laparoscopic sacrohysteropexy, *SSHP* vaginal sacrospinous hysteropexy
All patients were analysed as allocated
p value for exploratory purposes: Mann Whitney *U* test of LSH versus SSHP
[a] 0 = no symptoms or not bothersome to 100 = most bothersome symptoms
[b] 0 = best quality of life to 100 = worst quality of life
[c] 0 = worst quality of life to 100 = best quality of life
[d] 0 = poorest sexual functioning, 48 = best sexual function

Discussion

Main findings

Laparoscopic sacrohysteropexy was non-inferior to SSHP for surgical failure in the middle compartment one year after surgery, both following ITT and PP analysis. There was no difference in anatomical and surgical failure in other compartments either in quality of life or sexual function. There were, however, more bothersome symptoms of OAB after LSH, which seems mostly due to persistence of preoperative OAB symptoms. These findings implicate that OAB symptoms seem to improve more after SSHP. Several studies suggest that OAB might be caused by the presence of a prolapse due to the loss of normal support of the bladder, which could interfere with bladder emptying and sensory urgency.[27, 28] However, in this subgroup, we found no difference in anterior vaginal wall prolapse at 12 months follow-up. De novo OAB occurred solely after LSH, albeit in only two women. After laparoscopic sacrocolpopexy, de novo OAB seems to occur more often, with incidences varying between 2.5 – 11.3%.[27-29] The polypropylene-mesh implantation is associated with de novo OAB.[30] Mesh shortening (retraction) is thought to play a role. In our study, determination of mesh shortening was not evaluated.

More bothersome faecal incontinence was reported after LSH than after SSHP. It is suggested that extensive dissection between the posterior vagina and the rectum exacerbates or causes defecatory dysfunction due to damage of the inferior hypogastric nerve.[31, 32] Furthermore, one of the causes of faecal incontinence is posterior compartment prolapse.[33] However, in this subgroup posterior vaginal wall prolapse was not observed.

Dyspareunia was reported almost three times as often after SSHP than after LSH. The vaginal surgical route might contribute to the high rate of dyspareunia after SSHP. Vaginal POP surgery may be accompanied by vaginal narrowing and scarring as well as damage of the vascularization and innervation of the vaginal wall, which can lead to sexual dysfunction, including dyspareunia.[34]

Anatomical failure of the anterior compartment was found in half of the women after both LSH and SSHP. This finding is in line with other studies regarding SSHP with incidences of anatomical failure in this compartment of 47% and 51%.[15, 17] The risk for recurrent prolapse of the anterior vaginal wall after SSHP is thought to be related to the change in vaginal axis to a more posterior and horizontal position.[35] In our study however no difference in anatomical recurrence of anterior vaginal wall prolapse was found between SSHP and LSH.

We found a relatively high crossover rate from LSH to SSHP. Nevertheless, all gynaecologists participating in this trial were fully trained in advanced laparoscopic urogynaecology procedures and performed LSH on a regular base prior to the start of this study. Reasons for crossover were adhesions, excessive intra-abdominal tissue, an enlarged uterus, and perforation of the vaginal wall during dissection.

Due to different definitions of the primary outcome and the usage of different questionnaires to analyse functional outcome and quality of life, it is difficult to make a comparison with other studies.[21] In addition, studies on the outcome of LSH are limited, typically pooling data with outcomes after the sacrocolpopexy (either for vault prolapse or concomitant (subtotal) hysterectomy), making it hard to separate outcomes.

There are, however, several RCTs that compare SSHP with vaginal hysterectomy.[15, 17] In these, SSHP is as effective as vaginal hysterectomy for the treatment of uterine prolapse. Our findings are in line with those studies, though we observed a higher overall surgical failure after SSHP at one-year follow-up (62.3% versus 51%).[15] This might be caused by a higher incidence of prolapse of the anterior compartment in our study group (56.9% versus 47%), whereas the rates of concomitant anterior colporrhaphy were comparable (98.4% and 97%). This may be attributed to the large variation in surgical technique of anterior colporrhaphy, though other factors may play a role as well.[36] Compared with the RCT of Dietz et al. we found less anatomical recurrences of the apical compartment (3.4% versus 21%) after SSHP.[17] The latter number is rather high for SSHP.[15, 16, 37] In the RCT of Dietz et al, performed between 2001 and 2005, SSHP was perhaps a relatively novel technique for those surgeons. The differences between anatomical recurrence might be explained by more experience nowadays.

In a prospective study by Price et al, one surgical failure (2%) of the apical compartment was observed at 10-week follow-up, compared with 1.9% in our study.[38] In a prospective observational study, three women (2%) required reoperation for apical support for symptomatic prolapse at a mean follow-up of 2.1 years.[39] In our study, no reoperation of the apical compartment was observed at a follow-up of 12 months, probably due to the shorter follow-up. Furthermore, our findings are mainly in line with a randomised study comparing LSH to vaginal hysterectomy.[40] However, we found lower reoperation rates of the apical compartment at one-year follow-up (0% versus 6%). Differences in sample size (37 versus 59) and subtle differences in surgical protocol might explain this finding.

Strengths and limitations

Strengths of this study are the randomised multicentre design and the large sample size. Also, prior to first enrolment, all study centres participated in a masterclass where both surgeries were discussed in detail and a standardised approach was demonstrated. The primary outcome was defined as prolapse of the apical compartment in combination with bothersome bulge symptoms or repeat surgery or pessary use for recurrent prolapse. It is known that treatment success varies widely depending on the definition of surgical success. However, definitions of treatment success that require patient-reported outcome are more clinically relevant and meaningful to the patient than those that include anatomical criteria only.[21]

We acknowledge some limitations. First, our findings are based on a short-term follow-up. However, a recent cohort study demonstrated that the highest risk for undergoing repeat surgery for POP is within the first year.[41] Another limitation is the relatively high loss to follow-up in the laparoscopic group, with an eventual number of women with data available lower than what was required (< 55 women). Two women withdrew the informed consent due to intercurrent illness, and nine did not report at 12 months, hence observations at 6 months were used. At that time, no anatomical recurrence of the apical compartment was observed.

Interpretation

This study provides evidence that on the short-term LSH is as effective as SSHP for the treatment of uterine prolapse. The subtle differences in secondary outcomes may help in the process of shared-decision making and choose the optimal surgical route for a specific patient. Symptoms of OAB seem to improve more after SSHP than after LSH. Furthermore, persistent faecal incontinence was reported more frequently after LSH than after SSHP. As treatment options are limited and are associated with side-effects, faecal incontinence is a devastating outcome.[42, 43] Dyspareunia occurred more frequently after SSHP.

There is a wide variation in LSH techniques on several key points, such as level of dissection, mesh type, and tension of the mesh.[44] This variation could play a role in both anatomical and functional results. Well-designed trials regarding the procedure are needed to provide evidence for the best surgical technique.

Conclusion

Twelve months after the index procedure, LSH was non-inferior to SSHP for bothersome bulging / protrusion symptoms and / or therapy for recurrent prolapse in the middle compartment. Following LSH, bothersome OAB and faecal incontinence were more frequent, yet dyspareunia was less frequent.

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CHAPTER 6

Laparoscopic sacrocolpopexy versus vaginal sacrospinous fixation for vaginal vault prolapse, a randomised controlled trial: SALTO-2 trial, study protocol

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BMC Women's Health. 2017 Jul 26;17(1):52.

Abstract

BACKGROUND

Hysterectomy is one of the most performed surgical procedures during lifetime. Almost 10% of women who have had a hysterectomy because of prolapse symptoms, will visit a gynaecologist for a surgical correction of a vaginal vault prolapse thereafter. Vaginal vault prolapse can be corrected by many different surgical procedures. A Cochrane review comparing abdominal sacrocolpopexy to vaginal sacrospinous fixation considered the open abdominal procedure as the treatment of first choice for prolapse of the vaginal vault, although operation time and hospital stay is longer. Literature also shows that hospital stay and blood loss are less after a laparoscopic sacrocolpopexy compared with the abdominal technique. To date, it is unclear which of these techniques leads to the best operative result and the highest patient satisfaction. Prospective trials comparing laparoscopic sacrocolpopexy and vaginal sacrospinous fixation are lacking. The aim of this randomised trial is to compare the disease-specific quality of life of the laparoscopic sacrocolpopexy and vaginal sacrospinous fixation as treatment of vaginal vault prolapse.

METHODS

We will perform a multicentre prospective randomised controlled trial. Women with a post-hysterectomy symptomatic, POP-Q stage ≥ 2, vaginal vault prolapse will be included. Participants will be randomised to the laparoscopic sacrocolpopexy group or the vaginal sacrospinous fixation group. Primary outcome is disease-specific quality of life at 12 months follow-up. Secondary outcomes will be the effect of the surgical treatment on prolapse related symptoms, sexual functioning, procedure related morbidity, hospital stay, postoperative recovery, anatomical results using the POP-Q classification after one- and five-years follow-up, type and number of reinterventions, costs, and cost-effectiveness. Analysis will be performed according to the intention to treat principle and not as a per protocol analysis. With a power of 90% and a level of 0.05, the calculated sample size necessary is 96 patients. Taking into account 10% attrition, a number of 106 patients (53 in each arm) will be included.

DISCUSSION

The SALTO-2 trial is a randomised controlled multicentre trial to evaluate whether the laparoscopic sacrocolpopexy or vaginal sacrospinous fixation is the first-choice surgical treatment in patients with a POP-Q stage ≥ 2 vault prolapse.

Background

Hysterectomy is one of the most performed surgical procedures during a women's lifetime. Almost 10% of women who have had a hysterectomy because of prolapse symptoms, will visit a gynaecologist for a surgical correction of a vaginal vault prolapse (VVP) thereafter. VVP can be corrected by many different surgical procedures. These symptoms are directly related to the prolapse and contain of pelvic pressure, bulging of the vaginal wall, dropping sensation in the vagina, or backache. Other symptoms that are often present, are symptoms of the bladder, bowel and sexual problems.[1] These symptoms could affect the quality of life of these women severely. Therefore, an effective treatment is required.

The incidence of post-hysterectomy VVP requiring surgical treatment, has been estimated at 36 per 10,000 person-years.[2] The longer the time after hysterectomy, the higher the risk of vault prolapse. If the initial reason for hysterectomy was genital prolapse the risk increases significantly.[1–3] Women tend to get older and older and due to this improved life expectancy, there will be an enormous extra demand for future prolapse surgery.

Surgery for pelvic organ prolapse, including VVP, focuses on the correction of the normal anatomy of the vagina, resulting in normal function of the bladder and bowel. To date, a variety of surgical interventions to treat VVP surgically have been described.[4] These procedures can be performed vaginally or abdominally. The abdominal route can be performed as an open or laparoscopic sacrocolpopexy (LSC). The vaginal approach includes the vaginal sacrospinous fixation (VSF), which was first reported in 1958.[5] This is probably the most performed treatment modality of VVP at the moment. In a questionnaire of the International Urogynaecological Association (IUGA), which was performed in 2002, VSF was the most performed surgical correction for the VVP, as 78% of the responders reported the VSF as the first-choice treatment for VVP.[6] The LSC technique was developed in the footsteps of the abdominal sacrocolpopexy, and has been implemented since then.[7]

No randomised controlled trials comparing LSC and VSF have been performed. A Cochrane review showed that abdominal sacrocolpopexy is better compared with VSF. The recurrence rate of VVP was lower after an abdominal sacrocolpopexy (RR 0.23, 95% CI 0.07 – 0.77) and dyspareunia was less (RR 0.39, 95% CI 0.18 – 0.86). However, the rates of recurrence surgery for prolapse showed no statistical difference (RR 0.46, 95% CI 0.19 – 1.11). The VSF has a shorter operation time, lower costs, and an earlier return to daily

activities.[8] In none of the included studies disease-specific quality of life was the primary outcome. Furthermore, in some of the studies no power analysis was done.

A cohort study comparing laparoscopic to abdominal sacrocolpopexy shows a significant reduction in hospitalization (1.8 ± 1.0 days versus 4.0 ± 1.8 days; $p < 0.001$).[9] A prospective cohort study comparing laparoscopic to abdominal sacrocolpopexy that we performed prior to this study revealed a significant reduction in blood loss (77 ml (± 182) versus 192 ml (± 126) respectively, $p = <.001$), hospital stay (2.4 days versus 4.2 days respectively, $p = <.001$), and less procedure related morbidity (RR 0.24, 95%-CI 0.07 – 0.80, $p = 0.009$).[10] The laparoscopic procedure seems to have advantages over the abdominal procedure.

Since prospective trials comparing LSC and VSF are lacking, we plan to perform an RCT. The aim of this randomised trial is to compare the disease-specific quality of life of the LSC and VSF as the treatment of VVP.

Methods / study design

Study design

The SALTO-2 trial is a randomised controlled multicentre trial and will be performed to compare LSC versus VSF for VVP. The follow-up time will be one and five years. The trial will be a non-blinded trial, because it is impossible to blind the participating women and medical staff for the allocated technique, since one procedure will be performed vaginally and the other one laparoscopically, leaving small abdominal scars. However, a physician blinded for the intervention will perform follow-up examination. This will be another physician than the surgeon who performed the operation. The study design is presented in Figure 1.

Objectives

The objective of this study is to determine whether LSC in women with vault prolapse, POP-Q stage 2 or higher, improves outcomes in terms of disease-specific quality of life, recurrence of prolapse, complications, hospital stay, postoperative recovery, sexual functioning, costs, and costs-effectiveness, compared with VSF.

Hypothesis

Based on the literature, we expect that the LSC will be equally or more successful in correction of vault prolapse and its related disease-specific quality of life compared with VSF.

Participating hospitals

The trial will be performed in several teaching and academic hospitals in the Netherlands. The nine participating centres are Máxima Medical Centre, Isala Medical Centre, Spaarne Gasthuis, Catharina Hospital, Maastricht University Medical Centre +, Gelre Hospital, Radboud University Medical Centre, Sint Lucas Andreas Hospital, VU Medical Centre, and Martini Hospital. Before the start of the trial, a masterclass was organised to reach consensus on the details of operation technique of the LSC and VSF and evaluate the operation skills of the participating surgeons. All participating gynaecologists performed at least twenty-five procedures before the beginning of the trial to exclude a learning curve.

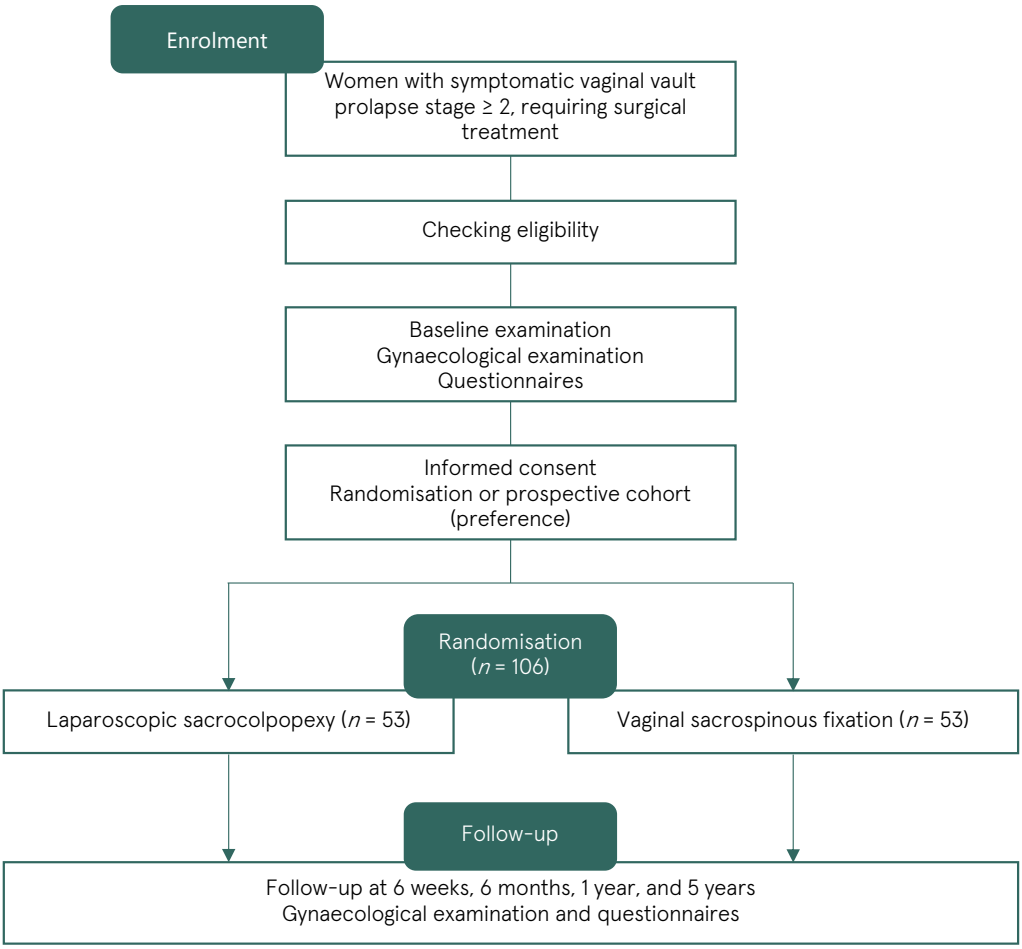

Figure 1. Flow diagram of the study design

During this master class, which was attended by many experienced surgeons, several surgical steps of both procedures were discussed (for the sacrocolpopexy: type of mesh, type of sutures, number of sutures, dissection technique, re-peritonealisation, (no) obliteration of Douglas pouch. For the VSF: (no) hydro dissection type and number of sutures, concomitant prolapse surgery). Decisions which techniques should be used were made and recorded to reduce practice variation as much as possible and to carry out a uniform operation technique during the inclusion period.

Study population and recruitment

All patients with a symptomatic post-hysterectomy VVP stage 2 or higher (according to POP-Q classification) who need surgical treatment are eligible for the study.

INCLUSION CRITERIA

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Symptomatic vault prolapse POP-Q ≥ stage 2 which needs surgical treatment.
- Eligible for both surgical treatments.
- Patients must be able to read Dutch.

EXCLUSION CRITERIA

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Previous surgical treatment of vault prolapse.
- Contraindication for a surgical intervention.
- Incapacitated patients, illiterate patients or patients with other language barriers.

Patients with co-existing anterior / posterior defects or concomitant incontinence surgery can be included. Patients need to agree to return the questionnaires and visit the follow-up appointments.

Patients who don't want to participate in the trial because of a preference for one of both surgical options will be asked for a cohort group and requested to complete the questionnaires as well. This cohort group will be compared with the study population to analyse whether a patient's preference will affect the quality of life.

Assessment for eligibility will be performed by a gynaecologist of the participating hospital. Women eligible for this trial will be counselled for the trial. Subsequently, written patient information is provided, which contains information on the objectives, design,

methods, possible advantages and disadvantages of the study treatments, and information that non-co-operation with the study or withdrawal will not have consequences for their treatment. Before randomisation, written informed consent will be obtained.

Interventions

VAGINAL SACROSPINOUS FIXATION

The patient is placed in lithotomy position. The sacrospinous ligament will be accessed through an incision following the length of the posterior vaginal wall, extending up to the vaginal vault. Blunt dissection is used to open the right pararectal space and locate the ischial spine. A 'window' is created through the rectal pillar, large enough for two fingers. Just lateral to the rectum and above the puborectal muscle, the right sacrospinous ligament-coccygeus muscle complex will be exposed. Three Breisky specula will be positioned, whereafter two Prolene 1-0 sutures will be placed under direct vision. These two permanent non-absorbable sutures will be put into the sacrospinous ligament at about 0.5 cm apart, with the lateral suture being placed about 2 cm from the ischial spine. The sutures will be attached to the vault on the suture line where the vault was closed after hysterectomy seeking the part with most connective tissue or ligament remains.

LAPAROSCOPIC SACROCOLPOPEXY

Patients do not receive bowel preparation the day before the operation. Looking at the design of this surgical intervention, the main goal of sacrocolpopexy is to reconstitute an adequate, durable system of support and suspension of the vagina by replacing the impaired and / or detached native fascial tissue with a synthetic non-absorbable prosthesis. The LSC will be performed under general anaesthesia with four trocars, one for the scope and three side trocars. The vaginal vault will be lifted using a vaginal probe. The peritoneum will be dissected to expose the vesicovaginal and rectovaginal fascia, extending to the sacral promontory. Preparation of the rectovaginal and vesicovaginal fascia will be done as far down as possible. The preparated tissue and the size of the mesh will be measured and documented. One side of the polypropylene mesh will be attached anteriorly of the vaginal wall, and the other side as far down posteriorly as possible using absorbable sutures. As little as possible stitches will be used. Depending on the surgeon's preference, the mesh will be attached to the sacral promontory using staples or non-absorbable sutures. The mesh will be peritonealised at several points. The pouch of Douglas will not be obliterated.

The VSF can be performed under spinal or general anaesthesia, depending on the patient's and anaesthesiologist's preferences. The laparoscopic procedure will be performed under general anaesthesia. Both procedures will be completed with any

additional vaginal surgery, if indicated, after the vault suspension has been carried out. For example anterior and posterior colporrhaphy may be performed during the same procedure. No vaginal mesh augmented procedures are allowed.

In both groups, prophylactic antibiotics and thrombosis prophylaxis will be given perioperatively. An indwelling urine catheter will be left in-situ and will be removed the first day postoperatively or as clinically indicated. Prolonged catheterisation will be recorded. If necessary, patients will receive analgesics according to the local hospital protocol. Patients are advised to withhold from heavy physical work for a minimal period of six weeks.

In case clinically indicated (complication or technical challenge to continue the procedure), the surgeon could convert to the other intervention. Participants will be analysed according to the intention to treat principle.

Data collection

Participants will be followed preoperatively, until one- and five-years post procedure. At follow-up, several aspects will be evaluated:

- Clinical examination of the prolapse using POP-Q.
- UDI, the Dutch validated version of the Urogenital Distress Inventory, questionnaire comprising 17 questions, to assess the presence and experienced discomfort of pelvic floor problems. The UDI consists of 5 domains: discomfort / pain, urinary incontinence, overactive bladder, genital prolapse, and obstructive micturition. The total UDI score is defined as the average of the 5 domain scores, and can be used to assess cost effectiveness by measuring quality of life.[11]
- DDI, the Defecatory Distress Inventory is a standardised questionnaire measuring defecatory symptoms. The questions cover the following sections: obstructive defecation, constipation, faecal incontinence, and pain related to defecation. Patients have more bothersome symptoms if they have a high score on a particular section.[12]
- IIQ, the Incontinence Impact Questionnaire is a disease-specific quality of life questionnaire covering five sections: physical functioning, mobility, emotional functioning, social functioning, and embarrassment.[11]
- EQ-5D, EuroQol, is a general quality of life questionnaire, to evaluate health utilities and the corresponding quality adjusted life years (QALYs). This is the difference in quality of life caused by the treatment multiplied by the duration of treatment effect.[13, 14]
- Medical cost questionnaire.

- PISQ, Pelvic Organ Prolapse / Incontinence Sexual Questionnaire, to analyse sexual function in participants with urinary incontinence and / or pelvic organ prolapse.[15]
- PGI-I, Patient Global Impression of Improvement, to evaluate the postoperative condition as compared with the condition before the surgical intervention. A single question is used to rate the condition, and the answer can be given on a scale from 1. 'Very much better' to 7. 'Very much worse'.[16]
- Preoperative urodynamic examination is only necessary when clinically indicated.
- During the first 6 weeks postoperatively (including the hospitalization), participants are asked to keep a diary, which includes the following sections: postoperative pain measured by Visual Analogue Score (VAS), used pain medication and the RI-10 recovery questionnaire. RI-10, the Recovery Index 10 is a questionnaire evaluating postoperative recovery. The questionnaire consists of 10 items using five-point Likert scales.[17]
- To evaluate postoperative recovery and satisfaction three questions are added to the 12-month questionnaire:
    1. Are you satisfied with the postoperative result?
       Answers: yes / no / don't know
    2. Did the operation improve your symptoms?
       Answers: yes / no / don't know
    3. Would you recommend the surgery to a friend?
       Answers: yes / no / don't know

Randomised participants will be scheduled for follow-up visits preoperatively, at 6 weeks, one year, and five years postoperatively. During these outpatient visits a physical examination, including POP-Q, will be performed and complications will be detected. The follow up visit at one and five years will be performed by a physician blinded for the intervention. This will not be the surgeon who performed the operation.

Table 1. Overview of data being recorded

	POP-Q	UDI DDI IIQ	EQ-5D	Costs	PISQ	PGI-I	Diary	Satisfaction
Baseline	x	x	x	x	x	-	-	-
6 weeks	x	-	-	x	-	-	x	-
6 months	-	x	x	x	x	-	-	-
1 year	x	x	x	x	x	x	-	x
5 years	x	x	x	x	x	x	-	x

Postoperative recovery will be assessed by asking the patients to keep a diary during their hospital stay and in the first 6 weeks postoperative. The diary consists of the several sections: VAS pain score, pain medication and the RI-10 recovery questionnaire. A part of the questionnaire of the economic evaluation is also added to the diary.

Secondary outcomes will be the effect of the surgical treatment on prolapse related symptoms, postoperative recovery, procedure related morbidity, sexual function, quality of life, anatomical results using the POP-Q classification until one year follow-up, type and number of reinterventions, costs, cost-effectiveness, and long-term complications. Other study parameters are:

- procedure time
- blood loss
- hospital stay
- postoperative pain medication
- postoperative pain scores (visual analogue scale)
- perioperative complications

Other study parameters are baseline values or parameters which might intervene with the main study parameter, like duration of symptoms, medical history, parity, body mass index, education / profession, smoking, atrophy, pre- or postmenopausal status, use of oestrogens or hormone replacement therapy, previous prolapse or stress incontinence surgery, previous pessary therapy, combined prolapse- or stress incontinence surgery and type of sutures and mesh during the intervention.

In case of loss to follow-up, participants will be contacted by telephone and asked for the reason for not returning the questionnaires or returning for follow-up visits. If necessary, the general practitioner will be contacted to gather additional information. Characteristics of responders and non-responders will be compared.

Economic evaluation

The costs of both surgical treatments will be compared. The direct costs of the LSC and VSF, like costs of operating time and use of materials, will be taken into account. Moreover, medication for postoperative pain reduction, length of hospital stay and admission for complications or reinterventions will be assessed. The economic evaluation will be conducted from a societal perspective, including direct medical and direct non-medical costs. Home care, consisting of both professional care as well as informal or family care will be evaluated. We will use a patient questionnaire to collect all the information of the additional home care. This questionnaire is added to the diary

which will be kept by all patients. Productivity losses will not be included in the economic evaluation, since most of the participants will be over 55 years of age. To gather medical costs a case record form will be used. Cost components will be valued according to standard Dutch guidelines for economic evaluation (CVZ 2004). Actual costs will be estimated for the LSC and VSF and informal care will be valued by using shadow prices. These data will be used to perform a cost-effectiveness analysis.

To perform a cost-utility analysis, we will use the EuroQol questionnaire (EQ-5D). This is a disease non-specific quality of life questionnaire, to derive health utilities and the corresponding quality adjusted life years (QALYs). This is the change in quality of life induced by the treatment multiplied by the duration of treatment effect. QALYs can then be related to medical costs to arrive at a final common denominator of cost / QALY.

Primary and secondary outcomes

The primary outcome is the functional effect by evaluating disease-specific quality of life at 12 months follow-up using the Dutch validated version of the Urogenital Distress Inventory (UDI). Secondary outcomes will be the effect of the surgical treatment on other prolapse related symptoms as defecation and sexual problems and the anatomical results using the Pelvic Organ Prolapse Quantification (POP-Q) at one- and five-years follow-up. Other secondary outcomes are procedure related parameters as procedure time, estimated amount of blood loss, length of hospitalization, postoperative pain medication, postoperative pain score (visual analogue scale) and perioperative complications, postoperative recovery, general quality of life, type and number of reinterventions, costs, cost-effectiveness, and long-term complications. Another secondary outcome will be the success rate according to Barbers' criteria. Success is defined as no prolapse of the vault beyond the hymen, no bothersome bulge symptoms (vaginal bulging and protrusion according to the validated questionnaire), and no repeat surgery or pessary use for recurrent vault prolapse.[18]

Sample size calculation

We will consider the score of the UDI genital prolapse domain as primary endpoint. A difference between both surgical techniques of 10 points on the genital prolapse domain of the UDI one year after surgery, will be considered a clinically relevant difference between both groups.[19] The standard deviation of the score on this domain is 15 points.[19] With a power of 90% and a level of 0.05, the calculated sample size necessary is 96 (48 in each group). The analysis will be performed by intention to treat. Odds ratios and 95% confidence intervals are calculated for all terms that are included in the regression

model. Domain scores will be analysed using repeated measurement analysis. Taking into account 10% attrition, a number of 106 patients (53 in each arm) will be included.

Randomisation

The trial represents a multi-centre randomised controlled design. Eligible patients with vault prolapse who meet the inclusion criteria will be randomised when informed consent is signed. The treatment allocation ratio is 1:1 to either LSC or VSF. Stratified randomisation will be used to achieve approximate balance of participating centres across study groups. The investigators or the participating surgeons are not aware of these series. Randomisation will be performed by the coordinating researcher, after which the procedure can be planned. For randomisation, opaque sealed envelopes will be used in order to conceal the allocation. To evaluate data anonymously, participants will receive a case number at randomisation. Blinding for allocation of treatment is impossible because of the laparoscopic or vaginal approach which requires a different introduction and anaesthesia technique. However, the follow up visit at one and five years will be performed by a physician blinded for the intervention.

Statistical analysis

DATA ANALYSIS

Data will be analysed based on intention to treat principle and stratified for centre. If the treatment effect is homogenous across centres, we will also perform an un-stratified analysis. To examine differences between groups we use an unpaired T-test for continuous variables and a Chi-square or, if opportune, a Fisher's exact test for dichotomous variables.

For differences in UDI, DDI and IIQ domain scores, a repeated measurement analysis will be performed. Repeated measurements analysis provides information of the results over time. Two-sided significance tests will be used throughout. A p value of <0.05 will be considered to be statistically significant. Time to reintervention will be compared with Cox regression and Kaplan Meier analysis. The statistical package used was SPSS 22.

Ethics

The study will be carried out in accordance with the principles of the Declaration of Helsinki. The SALTO-2 trial was approved in March 2014 (version 3.1.) by the Ethics Committee of the Máxima Medical Centre Veldhoven (METC 1324) and the local Ethics Committees of the participating centres. Informed consent will be obtained before participants will be randomised. Participants are currently being recruited and enrolled. The date of first enrolment was 27.09.2013. If any important modifications will be made

to the protocol, an amendment will be presented to the Medical Ethics Committee of the Máxima Medical Centre Veldhoven for consideration.

Discussion

LSC and VSF are generally performed procedures in pelvic care clinics all over the world. Although there is some literature about both surgical procedures, there is much heterogeneity in study populations and interventions. Furthermore, quality of life, which is the most relevant outcome to evaluate the effect of prolapse surgery, was no primary outcome of any of these studies[5, 6,10]. In our opinion the question which surgical intervention leads to the highest patient satisfaction for women with a stage 2 or higher VVP is still unanswered. Prospective trials comparing disease-specific quality of life after VSF and LSC are lacking. Therefore, a sufficiently powered randomised controlled trial with long-term follow-up is required to provide evidence-based decisions on the preferred treatment.

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CHAPTER 7

Laparoscopic sacrocolpopexy versus vaginal sacrospinous fixation for vaginal vault prolapse: a randomised controlled trial and prospective cohort (SALTO-2 trial)

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BJOG. 2023 May; Online publication ahead of print.

Abstract

OBJECTIVE

To determine whether laparoscopic sacrocolpopexy (LSC) or vaginal sacrospinous fixation (VSF) is the most optimal surgical treatment in patients with POP-Q ≥ stage 2 vaginal vault prolapse (VVP).

DESIGN

Multicentre randomised controlled trial (RCT) and prospective cohort study alongside.

SETTING

Seven non-university teaching hospitals and two university hospitals in the Netherlands.

POPULATION OF SAMPLE

Patients with symptomatic post-hysterectomy vaginal vault prolapse, requiring surgical treatment.

METHODS

Randomisation in a 1:1 ratio to LSC or VSF. Evaluation of prolapse was done using the pelvic organ prolapse quantification (POP-Q). All participants were asked to fill in various Dutch validated questionnaires 12 months postoperatively.

MAIN OUTCOME MEASURES

Primary outcome was disease-specific quality of life. Secondary outcomes included composite outcome of success and anatomical failure. Furthermore, we examined peri-operative data, complications, and sexual function.

RESULTS

A total of 179 women, of whom 64 women were randomised and 115 women participated in a prospective cohort. Disease-specific quality of life did not differ after 12 months between the LSC and VSF group in the RCT and the cohort (RCT: $p = 0.887$; cohort: $p = 0.704$). The composite outcomes of success for the apical compartment, in the RCT and cohort, were 89.3% and 90.3% in the LSC group and 86.2% and 87.8% in the VSF group, respectively (RCT: $p = 0.810$; cohort: $p = 0.905$). There were no differences in number of reinterventions and complications between both groups (reinterventions RCT: $p = 0.934$; cohort: $p = 0.120$; complications RCT: $p = 0.395$; cohort: $p = 0.129$).

CONCLUSION

LSC and VSF are both effective treatments for vaginal vault prolapse, after a follow-up period of 12 months.

TRIAL REGISTRATION

Dutch Trial Register NTR3977.

Introduction

In gynaecology, hysterectomy is one of the most frequently performed surgeries and is a risk factor for developing bothersome vaginal vault prolapse (VVP), which needs surgical repair.[1-3] Long-term prevalence of VVP has been reported in 23% of women who were treated for uterine prolapse by vaginal hysterectomy.[4] Moreover, the overall incidence of pelvic organ prolapse (POP) is still rising as a result of ageing and increasing obesity rates.[5]

Several abdominally and vaginally performed surgical interventions to treat VVP are available. In a previous RCT, we compared laparoscopic sacrocolpopexy (LSC) to open abdominal sacrocolpopexy (ASC). The laparoscopic procedure showed clear advantages.[6-8] Among Dutch gynaecologists, the vaginal sacrospinous fixation (VSF) is the first choice surgical treatment for VVP.[9] The VUE trial, a multicentre RCT comparing LSC with VSF for VVP, showed no evidence that an abdominal procedure was more clinically effective after short-term follow-up.[10] More prospective trials are needed to validate these results and attain the highest level of evidence..

In a Cochrane review and a meta-analysis on the treatment of apical prolapse, women with and without a uterus were included, as well as studies on open abdominal and laparoscopic sacrocolpopexy.[11, 12] To reduce heterogeneity, it is important to conduct a trial specifically for women with post-hysterectomy apical prolapse and compare only two surgical treatments which have been described precisely. Therefore, we performed an RCT with a prospective cohort alongside, to compare the disease-specific quality of life after the LSC with the VSF in the treatment of VVP.

Methods

Study design

The protocol of the SALTO-2 trial has been published previously.[13] The study was registered in the Dutch Trial Register (NTR3977) and it was approved by the medical ethical research committee of the Máxima Medical Centre (file number 1324). Patients were not involved in the development of this study.

Patients who were willing to participate in a clinical trial, but did not agree to be randomised, were treated according to their own preference and took part in our

prospective cohort, which followed the same study protocol. The RCT was stopped before the targeted sample size was achieved, mainly because of a strong patient preference for one of the surgical techniques.

Seven non-university teaching hospitals and two university hospitals in the Netherlands participated in this trial. In order to standardise surgery, a protocol was developed for LSC and VSF during a study masterclass.[13-15] Each surgeon needed to have performed at least 25 procedures of both the LSC and VSF prior to the start of patient recruitment in their hospital.

All patients with a symptomatic post-hysterectomy VVP POP-Q ≥ stage 2, who opted for surgical treatment were eligible for the study. Both surgical treatments had to be suitable for the patient. Concomitant surgery for POP or for stress urinary incontinence was allowed. Patients who had previous surgery for VVP or patients who had contra-indications for a surgical intervention were excluded from participation.

Eligible patients received written information about the study and after informed consent was signed, patients were randomised in a 1:1 ratio to LSC or VSF using a web-based computer application. Randomisation was stratified per centre in blocks of six. Patients and doctors were not blinded for the allocated surgery.

Primary and secondary outcomes

The primary outcome was disease-specific quality of life. Secondary outcomes were the effects of the surgical treatment on POP-related symptoms as micturition, defaecation, and sexual function. We also analysed composite outcome of success, defined as no POP beyond the hymen, absence of bothersome bulge symptoms, and no surgical retreatment or pessary treatment. Additionally, we examined anatomical failure (prolapse POP-Q ≥ stage 2).[15-17] Finally, we assessed clinical outcomes as operative time, estimated amount of blood loss, length of hospital stay, and complications.

Data collection

Anatomical evaluation of POP was done using the pelvic organ prolapse quantification (POP-Q) prior to surgery, after six weeks, and one year postoperatively.[18] All participants were asked to fill in various Dutch validated questionnaires 12 months postoperatively.

Disease-specific quality of life was measured with the Urogenital Distress Inventory (UDI),[19] the Defecatory Distress Inventory (DDI),[20] and the Incontinence Impact Questionnaire (IIQ).[19] The UDI and DDI indicate whether complaints of micturition,

prolapse, or defaecation are present and to what extent they are bothersome. The IIQ shows the disease-specific quality of life for urine incontinence. The score of each domain ranges from 0 to 100, high scores indicate more or more bothersome symptoms (UDI and DDI) and a poorer quality of life (IIQ). Bothersome bulge symptoms were measured using the UDI. A positive answer on any of the following questions was scored as subjective awareness of prolapse: 'Do you experience a sensation of bulging or protrusion from the vagina?' and 'Do you have a bulge or something protruding that you can see in the vagina?', in combination with a response 'moderately bothersome', or 'greatly bothersome' to the question 'how much does this bother you?'

Patient satisfaction was assessed using the Patient Global Impression of Improvement (PGI-I) one year postoperatively, a seven-point Likert scale ranging from 'very much better' to 'very much worse'.[21] 'Much better' or 'very much better' was considered affirmative and presented as dichotomous outcome.[11] Furthermore, we evaluated sexual functioning, using the Prolapse / Incontinence Sexual Questionnaire (PISQ). A total of 48 is the maximum score; higher score indicates better sexual function.[22, 23] Dyspareunia was recorded affirmative with a reply of 'sometimes', 'usually', or 'always' to the question 'do you feel pain during sexual intercourse?'.

Interventions

All patients received peri-operative antibiotics, thrombosis prophylaxis during admission, a bladder catheter, and postoperative analgesia according to local hospital protocols.

LAPAROSCOPIC SACROCOLPOPEXY

The LSC was performed under general anaesthesia. After insufflation, four laparoscopic ports were placed: one umbilical trocar for the scope and three side trocars. The vaginal vault was lifted using a vaginal probe. The peritoneum over the sacral promontory was incised and dissected further to expose the vesicovaginal and rectovaginal fascia. Preparation of the vesicovaginal and rectovaginal fascia was done as far caudally as possible, to correct for coexistent anterior compartment or posterior compartment prolapse. One side of the Y-shaped polypropylene mesh was attached anteriorly of the vaginal wall, and the other side on the posterior side of the vaginal wall, using absorbable sutures. The mesh was attached to the sacral promontory using staples, tackers, or non-absorbable sutures. Lastly, the mesh was peritonealised.

VAGINAL SACROSPINOUS FIXATION

For the VSF, patients received general or spinal anaesthesia. The sacrospinous ligament was accessed through an incision following the length of the posterior vaginal wall, extending up to the vaginal vault. Blunt dissection was used to open the right pararectal

space and to locate the ischial spine. Just lateral to the rectum and above the puborectal muscle, the right sacrospinous ligament-coccygeus muscle complex was dissected bluntly. Three Breisky retractors were positioned, whereafter two non-absorbable sutures were passed through the sacrospinous ligament, 2 cm medial to the ischial spine. The sutures were attached to the top of the vagina, at the point where the most connective tissue remained. The posterior vaginal wall was closed with absorbable sutures.

Sample size

Sample size calculation for the RCT was based on the primary outcome. A difference of 10 points on the UDI questionnaire 'genital prolapse' between the LSC group and VSF group postoperatively was considered clinically relevant.[24] The standard deviation was estimated to be 15 points. With a power of 90%, a significance level of .05, and an attrition rate of 10%, the calculated sample size was 106 (53 in each group).

Statistical analysis

In case of missing data on the UDI, DDI, and IIQ questionnaires, we performed multiple imputation (MI) with fully conditional specification. The number of imputations was set to the percentage of incomplete patient data.

Data from the RCT were analysed based on the intention to treat principle. Dichotomous or categorical data were presented as number of participants with corresponding percentages. Between-group differences were tested using logistic regression analysis, adjusted for variables that differed between groups at baseline to a clinically meaningful extent. Results were presented as odds ratio (OR) including 95% confidence interval (CI). Continuous data were presented as mean with standard error of the mean (SEM) and analysed with multivariable linear regression. Analyses on RCT data were corrected for difference in POP-Q stage of the posterior compartment.

In the prospective cohort we used the same statistical techniques but corrected for the difference in POP-Q stage of the apical compartment. Both studies were analysed separately first, and a fixed-effect meta-analysis was then used to combine results into a single inference for the primary outcome and principal secondary outcomes. A p-value of $< .05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows 25 except for the meta-analysis, which was performed in R version 4.0.4.

Results

Between September 2013 and June 2019, 64 women were included in the RCT (LSC: *n* = 33; VSF: *n* = 31) and 115 women (LSC: *n* = 46; VSF *n* = 69) were included in the prospective cohort. Figure 1 shows the flow diagram of this study. Baseline characteristics are shown in Table 1. In the RCT, more women in the VSF group had a posterior compartment beyond the hymen (LSC: 18.2%, *n* = 6; VSF: 41.9%, *n* = 13). In the cohort study, the LSC group included more participants with a vaginal vault prolapse beyond the hymen (LSC 54.3%, *n* = 25; VSF 29.0%, *n* = 20; *p* = 0.001). Some patients did not have a stage 2 VVP, which occurred more frequently in the cohort (LSC: *n* = 6; VSF: *n* = 17) than in the RCT (LSC: *n* = 3; VSF: *n* = 3).

RCT

Disease-specific quality of life is shown in Table 2 and did not differ at 12 months between the LSC and the VSF groups, according to the UDI. Participants scored an average of 8.5 points (SEM 5.2) on the domain 'genital prolapse' in the LSC group, compared to 10.9 points (SEM 4.5) in the VSF group (*p* = 0.887). Most participants had no bother of vaginal bulge symptoms (LSC 89.7%, *n* = 26; VSF 76.7%, *n* = 23; *p* = 0.299. Constipation was statistically significantly different, according to the DDI. Patients in the LSC group scored 10.4 points (SEM 3.0), compared to 2.4 points (SEM 1.0) in the VSF group (*p* = 0.033). Patients in both groups were similarly satisfied with the results, according to the PGI-I questionnaire (LSC 78.6%, *n* = 22; VSF 80.0%, *n* = 24; *p* = 0.778). After 12 months, mean PISQ scores (Table S1) showed no difference in sexual function between groups (LSC: 36.4 points (SEM 1.1); VSF: 38.6 points (SEM 1.2); *p* = 0.221). Three patients reported de novo dyspareunia one year postoperatively; two patients (11.8%) in the LSC group and one patient (7.1%) in the VSF group (*p* =.713).

The composite outcome of success, shown in Table 3, for the apical compartment was comparable in both groups; 89.3% (*n* = 25) in the LSC group and 86.2% (*n* = 25) in the VSF group (*p* = 0.810). There was no substantial difference in the number of reinterventions between both groups (LSC 25.8%, *n* = 8; VSF 23.3%, *n* = 7; *p* = 0.934). Surgical reinterventions for the apical compartment were only performed in the VSF group; three LSCs were done because of recurrences within one year. In the LSC group one surgery was performed because of a recurrent cystocele, a vaginal mesh was placed.

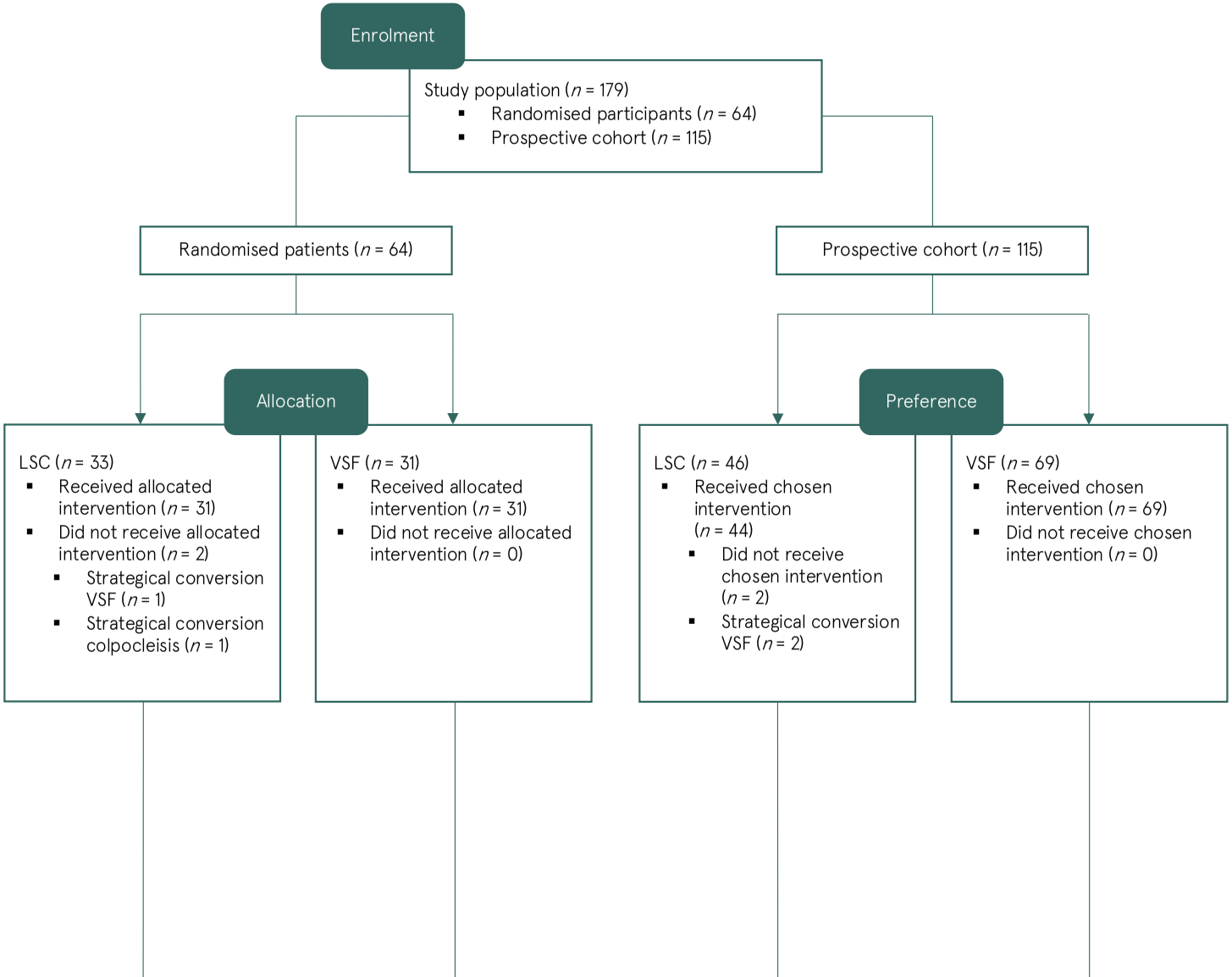
Table S2 displays the perioperative data. Mean operative time was significantly shorter in the VSF group (LSC: 130.5 minutes (SEM 5.2); VSF: 66.1 minutes (SEM 4.0); *p* < 0.001). There was more concurrent surgery in the VSF group (LSC: 9.1%, *n* = 3; VSF: 80.6%, *n* = 25; p <

0.001) which mainly consisted of anterior colporrhaphies (64.5%, *n* = 20) and posterior colporrhaphies (22.6%, *n* = 7). There were no differences in adverse events (Table S3). In the LSC group there was a bladder lesion, which was diagnosed and treated during surgery. This patient had an uneventful recovery the first six weeks postoperatively. After one year, a mesh erosion was ruled out with cystoscopy as she was treated with a mid-urethral sling for stress urinary incontinence. In the VSF group two bleedings of more than 1000 ml occurred. One bleeding was solved with clips and the other one conservatively. POP-Q measurements, as shown in Table S4, showed a difference in the anterior and apical compartments in favour of the LSC.

Cohort

Disease-specific quality of life (Table 2) did not significantly differ between the LSC and the VSF group pre-operatively or after 12 months, on any of the five domains of the UDI. Participants scored an average of 7.0 (SEM 3.3) points on the domain 'genital prolapse' in the LSC group, compared to 9.1 (SEM 3.3) points in the VSF group (p = 0.704). Most participants had no bother of vaginal bulge symptoms (LSC 91.2%, n = 31; VSF 91.8%, n = 45; p = 0.592). Patients in both groups were similarly satisfied with the results, according to the PGI-I questionnaire (LSC 88.2%, n = 30; VSF 72.3%, n = 34; p = 0.081). At one year follow-up mean PISQ scores (Table S1) showed no difference in sexual function between groups (LSC: 34.5 points (SEM 1.0); VSF: 35.0 points (SEM 0.6); p = 0.649). De novo dyspareunia occurred in two patients (22.2%) form the LSC group, versus three patients (27.3%) from the VSF group (p = 0.795).

The composite outcome of success for the apical compartment, presented in Table 3, was comparable in both groups; 90.3% (n = 28) in the LSC group and 87.8% (n = 36) in the VSF group (p = 0.905). Anatomical failure for the apical compartment was also equal in both groups (LSC 0.0%, n = 0; VSF 4.9%, n = 3; p = 0.279). There was no difference in number of reinterventions between both groups (LSC 24.4% n = 10; VSF 14.8%, n = 9; p = 0.120). In both groups three patients had further surgery, of which two patients in the VSF group had repeat surgery for the apical compartment. In the other cases it concerned surgery for a different compartment or surgery for non-POP-related conditions (*e.g.,* stress urinary incontinence).


Enrolment
Study population (n = 179)
Randomised participants (n = 64)
Prospective cohort (n = 115)
Randomised patients (n = 64)
Prospective cohort (n = 115)
Allocation
Preference
LSC (n = 33)
Received allocated intervention (n = 31)
Did not receive allocated intervention (n = 2)
Strategical conversion VSF (n = 1)
Strategical conversion colpocleisis (n = 1)
VSF (n = 31)
Received allocated intervention (n = 31)
Did not receive allocated intervention (n = 0)
LSC (n = 46)
Received chosen intervention (n = 44)
Did not receive chosen intervention (n = 2)
Strategical conversion VSF (n = 2)
VSF (n = 69)
Received chosen intervention (n = 69)
Did not receive chosen intervention (n = 0)

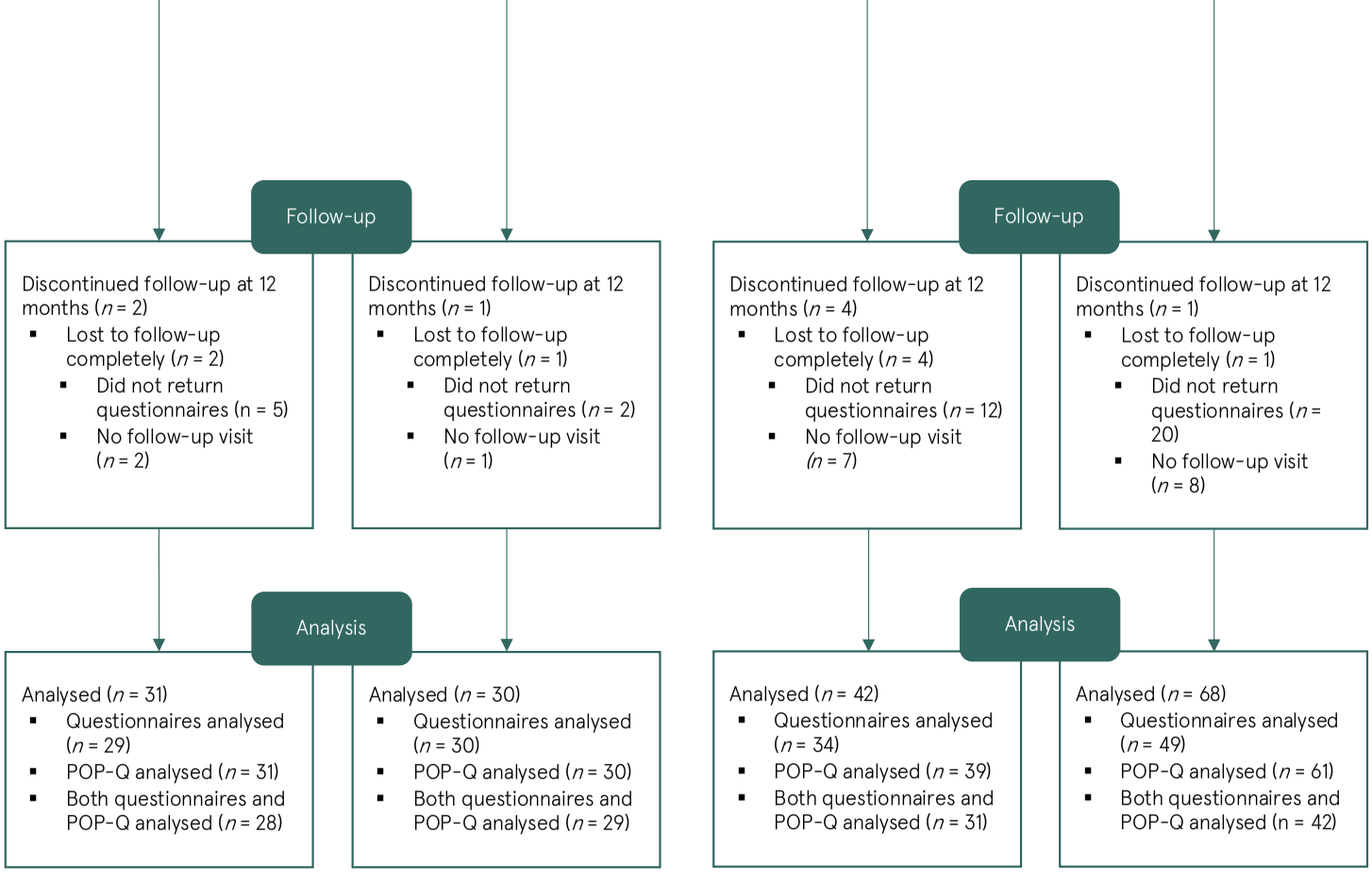


Figure 1. Flow diagram of study population

Table 1. Baseline characteristics

	Randomised Controlled Trial		Prospective Cohort		
	LSC (*n* = 33)	**VSF (*n* = 31)**	**LSC (*n* = 46)**	**VSF (*n* = 69)**	***p* value**
Age (years)	61.7 (9.7)	66.0 (11.8)	64.4 (10.6)	66.1 (8.4)	0.375
Body mass index (kg/m^2)	26.3 (4.0)	25.8 (3.2)	25.5 (3.6)	26.2 (3.7)	0.350
Parity					0.449
0	1/32 (3.1)	0/30 (0.0)	1/44 (2.3)	2/63 (3.2)	
1	4/32 (12.5)	2/30 (6.7)	3/44 (6.8)	6/63 (9.5)	
2	18/32 (56.3)	19/30 (63.3)	25/44 (56.8)	29/63 (46.0)	
3	7/32 (21.9)	7/30 (23.3)	10/44 (22.7)	20/63 (31.7)	
≥4	2/32 (6.3)	2/30 (6.7)	5/44 (11.4)	6/63 (9.5)	
Menopausal status					0.062
Premenopausal	7/33 (21.2)	4/31 (12.9)	5/46 (10.9)	2/69 (2.89)	
Postmenopausal	26/33 (78.8)	27/31 (87.1)	41/46 (89.1)	67/69 (97.1)	
Urinary incontinence					0.317
None	16/33 (48.5)	18/31 (58.1)	22/45 (48.9)	45/69 (65.2)	
Stress	4/33 (12.1)	3/31 (9.7)	4/45 (8.9)	5/69 (7.2)	
Urgency	7/33 (6)	2/31 (6.5)	9/45 (20.0)	11/69 (15.9)	
Combined	6/33 (18.2)	8/31 (25.8)	10/45 (22.2)	8/69 (11.6)	
Prolapse beyond hymen					
Apical compartment (C > 0)	15/33 (45.5)	17/30 (56.7)	25/46 (54.3)	20/69 (29.0)	**0.001**
Anterior compartment (Ba > 0)	18/33 (54.5)	17/30 (56.7)	31/46 (67.4)	45/69 (65.2)	0.724
Posterior compartment (Bp > 0)	6/33 (18.2)	13/31 (41.9)	15/46 (32.6)	19/68 (27.9)	0.418

Values are means (standard deviation (SD)) or in number of participants / total number of participants (percentages)
Percentages were calculated using non-missing data
LSC laparoscopic sacrocolpopexy, *VSF* vaginal sacrospinous fixation

Table S2 displays the perioperative data. The operative time was significantly shorter in the VSF group (LSC: 147.1 minutes (SEM 5.3); VSF: 58.5 minutes (SEM 2.5); $p < 0.001$). There was more concomitant surgery in the VSF group (LSC 28.3%, $n = 13$; VSF 87.0%, $n = 60$; p<.001). The POP-Q measurements in Table S4 showed a difference pre-operatively on point C (LSC 1.7 (SEM 0.5); VSF 0.0 (SEM 0.3); $p = 0.003$). After 12 months of follow-up there also were statistically significant differences. Both the apical as the anterior compartments showed a difference in favour of the LSC.

Pooled data

Figure 2 shows the forest plot of the pooled data (RCT and prospective cohort) for the primary outcome, disease-specific quality of life. The domain score 'genital prolapse' on the UDI was not statistically significantly different (mean difference 1.57, 95% CI (-6.18; 9.32), $p = 0.692$). The composite outcome of success (Figure S1) was not statistically significantly different (OR 0.86, 95% CI (0.26; 2.80), $p = 0.800$). The data for the DDI domain 'constipation' showed a difference in the RCT in favour of the VSF, but not in the prospective cohort. Once pooled (Figure S2), no statistically significant difference between both groups was found (mean difference -5.60, 95% CI (-11.41; 0.22), $p = 0.059$). Last, the outcome reinterventions (Figure S3) was pooled and also showed no significant difference (OR 0.86, 95% CI (0.26; 2.80), $p = 0.225$).

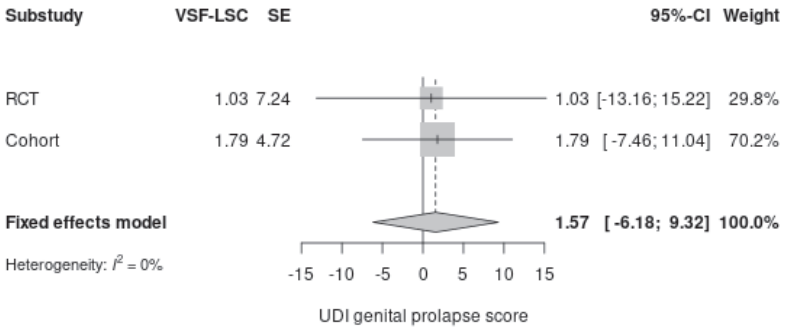


Figure 2. Forest plot Urinary Distress Inventory (UDI) domain 'genital prolapse'

Table 2. Disease-specific quality of life at 12 months follow-up

	Randomised Controlled Trial				
	Before surgery		12 months after surgery		
	LSC (*n* = 33)	**VSF (*n* = 31)**	**LSC (*n* = 29)**	**VSF (*n* = 30)**	***p* value**
UDI					
Genital prolapse	55.5 (6.5)	57.2 (5.7)	8.5 (5.2)	10.9 (4.5)	0.887
Overactive bladder	32.3 (4.5)	30.7 (3.8)	15.2 (4.6)	14.0 (3.5)	0.817
Urinary incontinence	22.9 (4.2)	23.9 (4.4)	20.6 (4.3)	14.4 (2.9)	0.365
Obstructive micturition	31.4 (4.7)	28.6 (5.2)	12.7 (4.9)	13.0 (4.4)	0.823
Pain	31.1 (4.6)	21.2 (4.2)	15.7 (4.4)	11.5 (3.3)	0.473
DDI					
Constipation	15.4 (3.7)	10.1 (3.4)	10.4 (3.0)	2.4 (1.0)	**0.033**
Obstructive defecation	11.9 (2.1)	11.9 (2.2)	8.7 (2.6)	3.2 (1.3)	0.070
Pain	10.0 (3.4)	5.2 (2.4)	5.3 (3.3)	2.6 (2.3)	0.494
Faecal incontinence	6.6 (2.3)	9.2 (2.7)	4.4 (3.1)	6.1 (2.9)	0.676
Flatus incontinence	40.0 (6.7)	39.7 (5.6)	32.7 (7.1)	26.6 (5.1)	0.817
IIQ					
Physical	45.4 (3.1)	41.2 (3.8)	30.8 (3.1)	29.6 (2.4)	0.837
Mobility	45.8 (2.3)	41.8 (3.5)	33.7 (1.8)	30.3 (1.3)	0.373
Social	35.0 (2.2)	34.6 (3.0)	28.1 (2.1)	27.2 (1.5)	0.824
Embarrassment	34.6 (1.9)	34.0 (2.6)	29.0 (1.8)	26.7 (0.8)	0.292
Emotional	42.5 (2.4)	38.4 (2.5)	32.4 (1.7)	28.6 (1.3)	0.117
Vaginal bulge symptoms					
Any	27/30 (90.0)	26/29 (89.7)	3/29 (10.3)	7/30 (23.3)	0.299
Bothersome	26/30 (86.7)	24/29 (82.8)	3/29 (10.3)	3/30 (10.0)	1.000
PGI-I					
Satisfaction	-	-	22/28 (78.6)	24/30 (80.0)	0.778

Values are given in mean (SEM) or in number of participants / total number of participants (percentages). Percentages were calculated using non-missing data
LSC laparoscopic sacrocolpopexy, *VSF* vaginal sacrospinous fixation, *UDI* urogenital distress inventory, *DDI* defecatory distress inventory, *IIQ* incontinence impact questionnaire, *PGI-I* patient global impression of improvement
* Not all participants reported bothersome POP symptoms on the UDI questionnaire. They did so, however, at the outpatient clinic before inclusion in this trial
UDI and DDI; each item: 0 = no bothersome symptoms; 100 = most bothersome symptoms. IIQ; each item: 0 = best quality of life; 100 = worst quality of life

Table 2 (continued). Disease-specific quality of life at 12 months follow-up

	Prospective Cohort					
	Before surgery			12 months after surgery		
	LSC (*n* = 46)	**VSF (*n* = 69)**	***p* value**	**LSC (*n* = 34)**	**VSF (*n* = 49)**	***p* value**
UDI						
Genital prolapse	70.1 (3.6)	63.3 (4.0)	0.290	7.0 (3.3)	9.1 (3.3)	0.704
Overactive bladder	41.4 (4.9)	39.7 (4.4)	0.609	24.0 (4.9)	27.7 (4.4)	0.798
Urinary incontinence	27.2 (4.7)	26.6 (3.7)	0.929	17.9 (4.7)	21.4 (3.9)	0.650
Obstructive micturition	36.6 (5.5)	36.8 (4.8)	0.751	13.3 (4.3)	19.3 (3.9)	0.360
Pain	30.1 (5.2)	33.3 (4.3)	0.867	25.5 (5.5)	22.3 (4.3)	0.491
DDI						
Constipation	13.5 (3.8)	15.9 (3.0)	0.936	14.3 (4.6)	13.2 (3.3)	0.931
Obstructive defecation	13.7 (3.3)	16.1 (2.7)	0.976	9.2 (2.8)	10.7 (2.5)	0.637
Pain	10.0 (3.0)	12.3 (3.2)	0.605	12.1 (3.9)	8.8 (3.1)	0.400
Faecal incontinence	15.2 (4.2)	13.8 (3.5)	0.647	10.9 (4.0)	11.8 (3.2)	0.816
Flatus incontinence	42.0 (5.3)	37.1 (4.3)	0.553	30.2 (6.0)	30.2 (6.0)	0.934
IIQ						
Physical	46.0 (3.5)	47.8 (2.8)	0.873	42.4 (4.0)	38.9 (3.3)	0.583
Mobility	50.0 (3.6)	49.2 (2.9)	0.518	42.3 (3.4)	39.6 (2.9)	0.521
Social	40.7 (3.0)	39.3 (2.7)	0.581	34.0 (3.0)	33.2 (2.4)	0.766
Embarrassment	39.9 (3.4)	42.6 (2.8)	0.542	35.4 (2.6)	35.2 (2.3)	0.977
Emotional	46.7 (3.5)	46.0 (3.0)	0.734	37.6 (3.0)	37.7 (2.1)	0.988
Vaginal bulge symptoms						
Any	37/37 (100.0)	50/53 (94.3)	0.266	3/34 (8.8)	4/49 (8.2)	0.592
Bothersome	37/37 (100.0)	48/53 (90.6)	0.075	3/34 (8.8)	4/49 (8.2)	0.592
PGI-I						
Satisfaction	-	-	-	30/34 (88.2)	34/47 (72.3)	0.081

Table 3. Outcome for POP at 12 months postoperatively

	Randomised Controlled Trial			
	LSC (*n* = 31)	**VSF (*n* = 30)**	**aOR (95% CI)**	***p* value**
Composite outcome of success[a]				
Apical compartment	25/28 (89.3)	25/29 (86.2)	0.81 (0.15; 4.50)	0.810
Any compartment	25/28 (89.3)	22/29 (75.9)	0.39 (0.08; 1.89)	0.244
Bulge complaints/reintervention[b]				
Apical compartment	25/28 (89.3)	25/29 (86.2)	0.81 (0.15; 4.50)	0.810
Any compartment	25/28 (89.3)	25/29 (86.2)	0.81 (0.15; 4.50)	0.810
Anatomical failure[c]				
Apical compartment (C ≥ -1)	0/31 (0.0)	1/30 (3.3)	-	0.492
Anterior compartment (Ba ≥ -1)	9/31 (29.0)	17/30 (56.7)	2.91 (0.97; 8.68)	0.056
Posterior compartment (Bp ≥ -1)	7/31 (22.6)	3/30 (10)	0.31 (0.07; 1.44)	0.135
Any compartment (C, Ba, or Bp ≥ -1)	14/31 (45.2)	19/30 (63.3)	1.81 (0.62; 5.26)	0.275
Prolapse beyond hymen				
Apical compartment (C > 0)	0/31 (0.0)	0/30 (0.0)	-	-
Anterior compartment (Ba > 0)	1/31 (3.2)	4/30 (13.3)	4.69 (0.46; 47.68)	0.192
Posterior compartment (Bp > 0)	0/31 (0.0)	0/30 (0.0)	-	-
Any compartment (C, Ba, or Bp > 0)	1/31 (3.32)	4/30 (13.3)	4.69 (0.46; 47.68)	0.192
Reinterventions				
Any reintervention	8/31 (25.8)	7/30 (23.3)	1.05 (0.31; 3.56)	0.934
Further surgery	6/31 (19.4)	5/30 (16.7)		
Repeat surgery				
LSC	-	3/30 (10)		
Surgery different site				
ACR	-	-		
PCR	-	-		
VM	1/31 (3.2)	-		
Surgery for complications				
DLS	1/31 (3.2)	-		
Non-POP-related surgery				
MUS	4/31 (12.9)	2/30 (6.7)		
Pessary treatment*	-	-		
PFMT*	2/31 (6.5)	2/30 (6.7)		

All data is given in number of participants / total number of participants (percentages).
Percentages were calculated using non-missing data
LSC laparoscopic sacrocolpopexy, *VM* vaginal mesh, *MUS* mid-urethral sling, *PFMT* pelvic floor muscle therapy, *ACR* anterior colporrhaphy, *PCR* posterior colporrhaphy
[a] No POP beyond hymen (in apical compartment or any compartment), absence of bothersome bulge symptoms, and no repeat surgery or pessary treatment
[b] Absence of bothersome bulge symptoms and no repeat surgery or pessary treatment
[c] POP-Q ≥ stage 2
* One patient had pessary treatment as well as pelvic floor physical therapy

Table 3 (continued). Outcome for POP at 12 months postoperatively

	Prospective Cohort			
	LSC (n = 31)	**VSF (n = 30)**	**aOR (95% CI)**	***p* value**
Composite outcome of success[a]				
Apical compartment	28/31 (90.3)	36/41 (87.8)	0.91 (0.18; 4.63)	0.905
Any compartment	26/31 (83.9)	35/41 (85.4)	0.995 (0.24; 4.10)	0.995
Bulge complaints/reintervention[b]				
Apical compartment	28/31 (90.3)	36/41 (87.8)	0.91 (0.18; 4.63)	0.905
Any compartment	26/31 (83.9)	36/41 (87.8)	1.41 (0.33; 6.02)	0.647
Anatomical failure[c]				
Apical compartment (C ≥ -1)	0/39 (0.0)	3/61 (4.9)	-	0.279
Anterior compartment (Ba ≥ -1)	14/39 (35.9)	32/61 (52.5)	1.67 (0.70; 3.93)	0.248
Posterior compartment (Bp ≥ -1)	8/39 (20.5)	4/61 (6.6)	0.36 (0.09; 1.40)	0.140
Any compartment (C, Ba, or Bp ≥ -1)	20/39 (51.3)	33/61 (54.1)	1.03 (0.44; 2.40)	0.941
Prolapse beyond hymen				
Apical compartment (C > 0)	0/39 (0.0)	1/61 (1.6)	-	1.000
Anterior compartment (Ba > 0)	1/39 (2.6)	5/61 (8.2)	3.53 (0.36; 34.21)	0.277
Posterior compartment (Bp > 0)	1/39 (2.6)	1/61 (1.6)	0.74 (0.04; 13.66)	0.838
Any compartment (C, Ba, or Bp > 0)	2/39 (5.1)	6/61 (9.8)	2.21 (0.39; 12.46)	0.370
Reinterventions				
Any reintervention	10/41 (24.4)	9/61 (14.8)	2.37 (0.80; 7.02)	0.120
Further surgery	3/41 (7.3)	4/61 (6.6)		
Repeat surgery				
LSC	-	2/61 (3.3)		
Surgery different site				
ACR	-	2/61 (3.3)		
PCR	1/41 (2.4)	-		
VM	1/41 (2.4)	-		
Surgery for complications				
DLS	-	-		
Non-POP-related surgery				
MUS	1/41 (2.4)	-		
Pessary treatment*	1/41 (2.4)	1/61 (1.6)		
PFMT*	6/41 (14.6)	4/61 (6.6)		

Discussion

Main findings

We performed a multicentre RCT with a prospective cohort alongside, to compare LSC with VSF as treatment for vaginal vault prolapse. Disease-specific quality of life did not differ after 12 months between the LSC and VSF groups in the RCT and the prospective cohort. The domain 'genital prolapse' on the UDI showed a statistically significant and clinically relevant reduction in both the LSC as the VSF group, which is comparable to other studies after one year of follow-up.[7, 15, 25]

The composite outcome of success for the apical compartment did not differ significantly between groups. Neither did anatomical failure, nor prolapse beyond the hymen. However, we observed a clinically relevant difference in the RCT for the anterior compartment: anatomical failure occurred in 29.0% of patients (n = 9) in the LSC group, compared to 56.7% of patients (n = 17) in the VSF group (p = 0.056). This difference was less pronounced in the prospective cohort. The VUE trial, a multicentre RCT comparing LSC to VSF for vault prolapse, also showed more anatomical recurrences in the anterior compartment after VSF compared with LSC.[10]

No difference was found in reinterventions between both groups in the RCT; in the LSC group eight reinterventions were done (25.8%), compared to seven in the VSF group (23.3%), p = 0.934. The cohort showed comparable data, with ten reinterventions in the LSC group (24.4%) and nine reinterventions in the VSF group (14.8%), p = 0.120. There was also no statistically significantly difference when only reinterventions for recurrent POP were taken into account. However, only in the VSF groups repeat surgery for the apical compartment was done, five LSCs were performed. Probably, due to a lack of power in the RCT we could not prove statistically relevance, but we consider it to be clinically relevant. The VUE trials showed 4% reinterventions for the apical compartment in the VSF group versus 1% in the LSC group, this was also not statistically different.[10] Two reviews showed more reinterventions in patients who underwent the VSF, compared to the sacrocolpopexy. However, these results are less comparable to the results of our trial, because also patients with a uterine descent were included as well as different approaches to the sacrocolpopexy (abdominal and robot).[11, 12]

Strengths and limitations

To our knowledge, this is one of the first two randomised trials to compare LSC to VSF for vaginal vault prolapse. We presented the results of the RCT and the cohort separately, for an objective representation of the data, with various outcome measures.

The results are a valuable addition to the existing literature, and moreover, it enables a meta-analysis of randomised patients.

One of the main strengths of our study is that both procedures were discussed during a masterclass in which all hospitals participated, in order to reduce differences in surgical techniques.[13] This makes the groups more homogenous and easier to compare and rule out differences due to various surgical methods.

Our study has several limitations as well. Due to the strong treatment preferences of many patients, mainly because of a fear for mesh, we were able to randomise only 64 women instead of the intentional 106 women. Therefore, we stopped the inclusion of patients prematurely, which lead to underpowered outcomes of our randomised study. To compensate for this fact, we also added the results of the prospective cohort and pooled the primary outcome measure and the principal secondary outcomes.

Another limitation is that not all patients met the inclusion criterium of VVP POP-Q ≥ stage 2. In these cases, patients had a cystocele and / or rectocele POP-Q ≥ stage 2 and a VVP POP-Q stage 1. These patients had bothersome POP-related symptoms and requested surgical treatment. We did not exclude them, because they had an indication for surgical treatment, it reflects daily practice, and it is in line with the VUE trial.[10]

Last, we do not have complete data on the patients who were assessed for eligibility or patients who declined participation. Although we do know that most of the patients in the prospective cohort did not want to be randomised because of a certain preference. In some other cases the gynaecologist alleged a certain treatment to be more suitable.

Interpretation

Our study shows that LSC and VSF are both effective treatments for VVP after a one-year follow-up. However, LSC and VSF are very different types of surgery, which could explain that gynaecologists as well as patients have a certain preference, which made it hard to include enough patients in the RCT. Moreover, the negative publicity about mesh was also a major reason why patients did not want to be randomised. Since the outcomes of both groups are comparable, it is imaginable that other factors play a role in the choice of surgical treatment for VVP. Shorter operation time and possibility to use spinal analgesia possibly make VSF more appropriate for elderly patients or patients with comorbidity. Also, the VSF is easier to learn compared to the LSC, which makes it more widely available for patients.[12]

The VUE trial showed similar results to our trial.[10] Subjective POP complaints were equal in both groups 12 months postoperatively. Prolapse beyond the hymen was also the same between both groups. There was no difference in complaints of constipation. These results are all in line with our study. Although the VUE study group has published an elaborate report on all outcomes, they did not provide combined outcome measures.[16, 17] Combined outcome measures such as composite outcome of success can reveal differences between both study groups, because it shows the results per patient more specifically.

In the first year of follow-up only reinterventions for the apical compartment were done in the VSF groups (*n* = 5, 5.5%). However, for a patient it most likely does not matter if the recurrence is in the same compartment as the initial prolapse or in another. Surgery for a different site (anterior or posterior compartments) was done in both the LSC and the VSF groups (LSC: *n* = 3, 4.3%; VSF: *n* = 2, 2.2%). Results from trials like the SALTO-2 trial can help patients make an informed decision about their treatment for VVP. Long-term follow-up of this trial is of essence to identify recurrence rates, need for further POP treatment, and complications.

Conclusion

LSC and VSF are both effective treatments for VVP, at 12 months follow-up. There is no difference between both groups in disease-specific quality of life or vaginal bulge symptoms. There are no statistically significant differences in surgical reinterventions, although there might be a clinically relevant difference in surgical reinterventions for the apical compartment, favouring LSC.

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Supplementary Figures & Tables

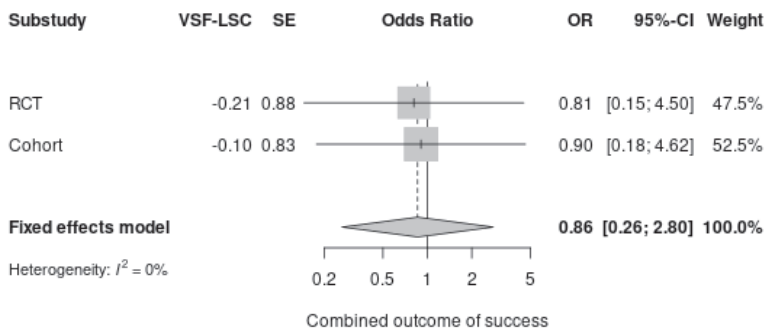

Figure S1. Forest plot combined outcome of success

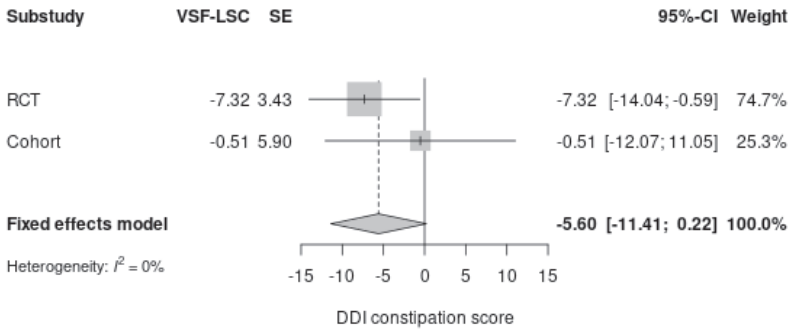

Figure S2. Forest plot Defecatory Distress Inventory (DDI) domain 'constipation'

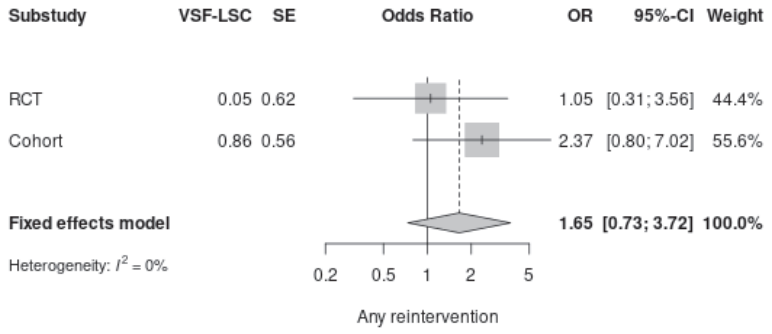

Figure S3. Forest plot any reintervention

Table S1. Sexual function at 12 months follow-up

	Randomised Controlled Trial				
	Before surgery		12 months after surgery		
	LSC (*n* = 33)	**VSF (*n* = 31)**	**LSC (*n* = 29)**	**VSF (*n* = 30)**	***p* value**
PISQ					
Sexually active	21/30 (70.0)	18/29 (62.1)	17/29 (58.6)	14/30 (46.7)	0.358
Dyspareunia	14/21 (66.7)	16/18 (88.9)	16/17 (94.1)	13/14 (92.9)	0.374
De novo dyspareunia	-	-	2/17 (11.8)	1/14 (7.1)	0.713
PISQ-12 score	31.5 (1.2)	33.9 (1.6)	36.4 (1.1)	38.6 (1.2)	0.221
Behavioural-emotive	9.1 (0.6)	10.8 (0.7)	10.3 (0.6)	11.5 (0.6)	0.191
Physical	14.3 (0.7)	15.1 (0.9)	17.5 (0.5)	18.3 (0.5)	0.290
Partner-related	7.7 (0.5)	7.9 (0.5)	8.6 (0.3)	8.6 (0.7)	0.972

Values are given in mean (SEM) or in number of participants / total number of participants (percentages). Percentages were calculated using non-missing data
LSC laparoscopic sacrocolpopexy, *VSF* vaginal sacrospinous fixation, *PISQ* prolapse / incontinence sexual questionnaire
PISQ-12 Total score: 0 = worst sexual function; 48 = best sexual function
PISQ-12 Behavioural-emotive (items 1 – 4): 0 = worst function; 16 = best function
PISQ-12 Physical (items 5 – 9): 0 = worst function; 20 = best function
PISQ-12 Partner-related (items 10 – 12): 0 = worst function; 12 = best function

Table S2. Perioperative data

	Randomised Controlled Trial			Prospective Cohort		
	LSC (*n* = 33)	**VSF (*n* = 31)**	***p* value**	**LSC (*n* = 46)**	**VSF (*n* = 69)**	***p* value**
Operative time (minutes)	130.5 (5.2)	66.1 (4.0)	*<.001*	147.1 (5.3)	58.5 (2.5)	*<.001*
Estimated blood loss (ml)	35.2 (5.7)	141.3 (48.5)	*.292*	57.7 (13.2)	73.5 (9.2)	*.164*
Hospital stay (days)	2.2 (0.1)	2.1 (0.1)	*.453*	2.2 (0.1)	2.1 (0.1)	*.393*
Concomitant surgery						
Any concomitant surgery	3/33 (9.1)	25/31 (80.6)	*<.001*	13/46 (28.3)	60/69 (87.0)	*<.001*
ACR	-	14/31 (45.2)		1/46 (2.2)	32/69 (46.4)	
PCR	1/33 (3.0)	3/31 (9.7)		-	3/69 (4.3)	
ACR + PCR	-	2/31 (6.5)		-	9/69 (13.0)	
Perineorrhaphy	1/33 (3.0)	-		7/46 (15.2)	4/69 (5.8)	
ACR + perineorrhaphy	-	3/31 (9.7)		-	6/69 (8.7)	
PCR + perineorrhaphy	-	-		1/46 (2.2)	1/69 (1.4)	
ACR + PCR + perineorrhaphy	-	1/31 (3.2)		-	3/69 (4.3)	
Enterocele repair	-	1/31 (3.2)		-	2/69 (2.9)	
PCR + Enterocele repair	-	1/31 (3.2)		-	-	
MUS + perineorrhaphy	1/33 (3.0)	-		-	-	
BSO	-	-		3/46 (6.5)	-	
Surgical procedure	-	-		1/46 (2.2)	-	

Table S1 (continued). Sexual function at 12 months follow-up

	Prospective Cohort					
	Before surgery			12 months after surgery		
	LSC (*n* = 46)	**VSF (*n* = 69)**	***p* value**	**LSC (*n* = 34)**	**VSF (*n* = 49)**	***p* value**
PISQ						
Sexually active	16/37 (43.2)	25/53 (47.2)	0.592	17/34 (50.0)	23/49 (46.9)	0.911
Dyspareunia	9/16 (56.3)	21/25 (84.0)	0.050	13/17 (76.5)	20/23 (87.0)	0.388
De novo dyspareunia	-	-	-	2/9 (22.2)	3/11 (27.3)	0.795
PISQ-12 score	30.8 (1.6)	31.9 (0.8)	0.705	34.5 (1.0)	35.0 (0.6)	0.649
Behavioural-emotive	9.9 (0.8)	9.5 (0.5)	0.608	9.1 (0.6)	9.9 (0.5)	0.305
Physical	12.6 (1.1)	14.1 (0.8)	0.256	17.2 (0.7)	17.2 (0.6)	0.967
Partner-related	8.3 (0.7)	8.3 (0.3)	0.917	8.3 (0.6)	8.0 (0.4)	0.705

Table S3. Complications

	Randomised Controlled Trial			Prospective Cohort		
	LSC (*n* = 33)	**VSF (*n* = 31)**	***p* value**	**LSC (*n* = 46)**	**VSF (*n* = 69)**	***p* value**
Complications during surgery						
Any complication	1/33 (3.0)	3/31 (9.7)	0.395	3/46 (6.5)	1/69 (1.4)	0.129
Bleeding > 1 L	-	2/31 (6.5)		-	-	
Bladder lesion	1/33 (3.0)	-		1/46 (2.2)	1/69 (1.4)	
Vaginal lesion	-	-		1/46 (2.2)	-	
Bended ureter	-	1/31 (3.2)		-	-	
Bleeding trocar incision	-	-		1/46 (2.2)	-	
Complications during admission						
Any complication	2/33 (6.1)	2/31 (6.5)	0.676	1/46 (2.2)	5/69 (7.2)	0.240
Urinary tract infection	1/33 (3.0)	-		1/46 (2.2)	-	
Urinary retention	1/33 (3.0)	2/31 (6.5)		-	3/69 (4.3)	
Pain buttocks	-	-		-	1/69 (1.4)	
Atrial fibrillation	-	-		-	1/69 (1.4)	
Complications until 6 weeks postoperatively						
Any complication	5/32 (15.6)	3/31 (9.7)	0.488	3/46 (6.5)	12/69 (17.4)	0.238
Urinary tract infection	3/32 (9.4)	3/31 (9.7)		2/46 (4.3)	6/69 (8.7)	
Pain buttocks	-	-		-	6/69 (8.7)	
Abdominal pain	1/32 (3.1)	-		-	-	
Wound infection	1/32 (3.1)	-		-	-	
Mesh exposure vaginally	-	-		1/46 (2.2)	-	

Values are given in mean (standard error of mean (SEM)) or in number of participants / total number of participants (percentages). Percentages were calculated using non-missing data
LSC laparoscopic sacrocolpopexy, *VSF* vaginal sacrospinous fixation, *ASC* abdominal sacrocolpopexy, *ACR* anterior colporrhaphy, *PCR* posterior colporrhaphy, *MUS* mid-urethral sling, *BSO* bilateral salpingo-oophorectomy

Table S4. POP-Q measurements

	Randomised Controlled Trial				
	Before surgery		12 months after surgery		
	LSC (*n* = 33)	**VSF (*n* = 31)**	**LSC (*n* = 31)**	**VSF (*n* = 30)**	***p* value**
Aa	0.2 (0.3)	0.2 (0.4)	-1.8 (0.2)	-0.9 (0.3)	**0.014**
Ba	0.9 (0.4)	1.1 (0.5)	-1.8 (0.2)	-1.0 (0.3)	**0.031**
C	0.6 (0.4)	1.3 (0.5)	-7.1 (0.3)	-6.0 (0.4)	**0.025**
GH	4.0 (0.1)	4.0 (0.1)	3.8 (0.2)	3.5 (0.1)	0.135
PB	3.0 (0.1)	3.0 (0.1)	3.2 (0.1)	3.2 (0.1)	0.647
TVL	8.2 (0.2)	8.2 (0.2)	8.4 (0.3)	8.1 (0.3)	0.200
Ap	-1.4 (0.3)	-0.5 (0.3)	-2.0 (0.2)	-2.3 (0.1)	0.105
Bp	-1.2 (0.3)	0.6 (0.5)	-2.0 (0.2)	-2.3 (0.1)	0.067
D	-	-	-	-	-

Table S4 (continued). POP-Q measurements

	Prospective cohort					
	Before surgery			12 months after surgery		
	LSC (*n* = 46)	**VSF (*n* = 69)**	***p value***	**LSC (*n* = 39)**	**VSF (*n* = 61)**	***p* value**
Aa	1.0 (0.3)	0.6 (0.2)	0.224	-1.7 (0.2)	-1.1 (0.1)	**0.009**
Ba	1.7 (0.4)	1.2 (0.3)	0.226	-1.7 (0.2)	-1.1 (0.2)	**0.017**
C	1.7 (0.5)	0.0 (0.3)	**0.003**	-7.0 (0.2)	-6.0 (0.3)	**0.016**
GH	4.1 (0.2)	4.1 (0.1)	0.988	3.5 (0.1)	3.4 (0.1)	0.953
PB	2.9 (0.1)	3.0 (0.1)	0.558	3.1 (0.1)	3.1 (0.1)	0.518
TVL	8.6 (0.2)	8.3 (0.1)	0.166	8.7 (0.2)	8.4 (0.1)	0.189
Ap	-0.8 (0.3)	-1.0 (0.2)	0.566	-1.9 (0.2)	-2.3 (0.1)	0.257
Bp	0.2 (0.5)	-0.7 (0.3)	0.068	-1.9 (0.2)	-2.3 (0.1)	0.347
D	-	-	-	-	-	-

Values are means (standard error of the mean)
LSC laparoscopic sacrocolpopexy, *VSF* vaginal sacrospinous fixation
POP-Q point Aa: located in the midline of the anterior vaginal wall 3 cm proximal to the external urethral meatus
POP-Q point Ba: the most distal position of any part of the upper anterior vaginal wall from the vaginal cuff to point Aa
POP-Q point C: the most distal edge of the vaginal cuff (hysterectomy scar)
POP-Q point GH (genital hiatus): measurement from the middle of the external urethral meatus to the posterior margin of the hymen
POP-Q point PB (perineal body): measurement from the posterior margin of the hymen to the mid-anal opening
POP-Q point TVL (total vaginal length): length of the vagina (centimetres) from the vaginal cuff to the hymen
POP-Q point Ap: located in the midline of the posterior vaginal wall 3 cm proximal to the hymen
POP-Q point Bp: the most distal position of any part of the upper posterior vaginal wall from the vaginal cuff to point Ap

CHAPTER 8

Gynaecologists' perspectives on surgical treatment for apical prolapse: a qualitative study

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International Urogynaecology Journal. 2023 July; Online publication ahead of print.

Abstract

INTRODUCTION AND HYPOTHESIS

Vaginal sacrospinous fixation (VSF) without mesh and sacrocolpopexy (SCP) with mesh are the most frequently performed surgical procedures for apical prolapse in the Netherlands. There is no long-term evidence suggesting the optimal technique, however. The aim was to identify which factors play a role in the choice between these surgical treatment options.

METHODS

A qualitative study using semi-structured interviews amongst Dutch gynaecologists was carried out. An inductive content analysis was performed with Atlas.ti.

RESULTS

Ten interviews were analysed. All gynaecologists performed vaginal surgeries for apical prolapse, six gynaecologists perform SCP themselves. Six gynaecologists would perform VSF for a primary vaginal vault prolapse (VVP); three gynaecologists preferred a SCP. All participants prefer a SCP for recurrent VVP. All participants have stated that multiple comorbidities could be a reason to choose VSF, as this procedure is considered less invasive. Most participants choose a VSF in the case of older age (6/10) or higher body mass index (7/10). All treat primary uterine prolapse with vaginal, uterine-preserving surgery.

CONCLUSIONS

Recurrent apical prolapse is the most important factor in advising patients which treatment they should undergo for VVP or uterine descent. Also, the patient's health status and the patient's own preference are important factors. Gynaecologists who do not perform the SCP in their own clinic are more likely to perform a VSF and find more reasons not to advise a SCP. All participants prefer a vaginal surgery for a primary uterine prolapse.

Introduction

Pelvic organ prolapse (POP) is a frequently occurring health issue and is expected to increase as age and obesity rates are rising.[1] The lifetime risk of women undergoing surgery for POP has reported to be 20% by the age of 80 years.[2] Traditionally, uterine prolapse has been treated with vaginal hysterectomy (VH). Interest in uterine-preserving treatments is gaining, as more literature on this matter has been published.[3-7] Women prefer uterus preserving prolapse surgery in the absence of substantial benefit of VH.[8] Besides POP, there are other reasons for performing a hysterectomy, including heavy menstrual bleeding or cervix dysplasia. The prevalence of vaginal vault prolapse (VVP) in women who underwent a VH for pelvic organ prolapse has been reported in 23% of the cases. In women who had a hysterectomy for another reason, laparoscopically or vaginally, the prevalence of VVP was 4.4% and 5.8% respectively.[9]

Vaginal sacrospinous fixation (VSF) without mesh and sacrocolpopexy (SCP) with mesh are the most frequently performed surgical procedures for apical prolapse in the Netherlands.[10] Several randomised trials have been conducted to compare laparoscopic and vaginal treatments for apical prolapse. The LAVA trial (n = 126) showed non-inferiority of the laparoscopic sacrohysteropexy (LSH) compared with the vaginal sacrospinous hysteropexy (SSHP), in the treatment of uterine descent, for bothersome bulge symptoms, after 12 months of follow-up.[4] The results of the VUE study (vault trial, n = 208) showed no differences between the laparoscopic sacrocolpopexy (LSC) and the VSF, as treatment for VVP, in terms of efficacy, quality of life, or adverse events at one year follow-up.[11] The SALTO-2 trial (n = 64) also reported no differences between LSC and VSF on anatomical and functional outcome, in the treatment of VVP, at one year follow-up. This trial, however, intended to include 106 women and was stopped prematurely. The main reason for not including the targeted sample size was a patients' preference for one of the two surgeries.[12, 13]

LSC and VSF are very different procedures; thus, it is conceivable that gynaecologists also have a certain preference. A previously conducted clinical practice survey showed no standardised method for the treatment of VVP. The VSF appeared to be the first-choice treatment of VVP among Dutch gynaecologists.[10] However, it is unclear what factors contribute to their preference. There are no specific patient characteristics known to favour one technique over the other. The aim of this qualitative study was to identify the factors that influence Dutch gynaecologists in making their choice and counselling patients.

Materials and methods

Study design

A qualitative study consisting of semi-structured interviews was conducted amongst Dutch gynaecologists. All interviews were performed by one researcher (AVO); no other people were present during the interviews. The researcher knew some of the participants, but there was no work relationship or dependency of any sort. Participants were contacted by e-mail and the interview took place by a 20 to 30 minutes videoconference call. Respondents were asked beforehand, with a short digital questionnaire, which surgeries they performed; how many of those surgeries they perform per year; and how many procedures they had carried out in total. In order to represent various perspectives on this matter gynaecologists were selected in different types of hospitals, *i.e.,* university hospitals, non-university teaching hospitals, and non-university non-teaching hospitals.

The Medical Ethical Research Committee of the Zuyderland Medical Centre (METC Z) exempted the need for ethical review (file number METCZ20220042), because it was not subject to the Medical Research Involving Human Subjects Act (WMO).[14] This study was developed and described in accordance with the consolidated criteria for reporting qualitative research (COREQ).[15]

Data collection

A list of topics was drawn up and tested in a pilot interview (AVO, MW, and LM), prior to the start of the study. Minor alterations were made and then the study started. At the start of each interview, the participant was asked what their first-choice surgical treatment for primary and recurrent VVP would be. Open-ended questions were used to explore the experiences of the participant and investigate which factors were important in deciding on the optimal surgical treatment. Last, participants were asked to give their top five factors that were of importance in their decision.

Data processing and analysis

The interviews were recorded and thereafter fully transcribed, with the use of Amberscript.com. The transcripts were coded and analysed by two researchers (AVO and LM), using the qualitative analysing tool Atlas.ti 9.0.23 for Windows. Disagreements during coding were few and were discussed until consensus was reached between the two researchers. Data are presented as numbers and are discussed qualitatively. The top five factors were reversely scored, 5 points for the most important factor, 4 points for the second most important factor, and so on.

Results

Saturation of data was reached after eight interviews, *i.e.,* no new factors were mentioned during the interviews. Two additional interviews were held to confirm saturation. In total, ten gynaecologists participated in study. No one declined participation or dropped out prematurely. Characteristics of respondents are shown in Table 1. Four of the participants were subspecialised urogynaecologists. All gynaecologists perform post-hysterectomy sacrospinous fixation (VSF), vaginal sacrospinous hysteropexy (SSHP), and vaginal hysterectomy (VH). SCP and sacrohysteropexy (SHP) are performed by six participants themselves, laparoscopically or robot assisted. Three gynaecologists have to refer to another hospital for SCP and SHP.

All topics were categorised in the following themes: type of prolapse, patient-related factors, surgery-related factors, and physician-related factors. The code tree with themes, subthemes, and topics is presented in Supplementary figure 1.

Preferred treatment for vaginal vault prolapse

Table 2 shows the first-choice treatment for the different types of prolapse for all gynaecologists and subdivided into groups depending on whether they must refer to another hospital for this procedure. Six gynaecologists would perform a VSF for a primary VVP; three gynaecologists preferred a SCP; and one gynaecologist has no specific preference. When the previous hysterectomy was carried out as treatment for uterine prolapse, two gynaecologists would still advise a VSF, whereas five other participants would prefer a SCP. All participants would prefer a SCP after a previous treatment for VVP. Whether the VVP is a recurrent apical prolapse or a recurrent VVP, is the most important factor for most participants (Table 3).

Patient-related factors

Patients' medical / surgical history is the second most important factor for gynaecologists to consider. All participants have stated that certain comorbidities or abdominal surgical history could be a reason for choosing VSF.

QUOTE 1: "We perform a treatment to improve quality of life, which should never result in more morbidity thereafter. Sometimes it is inevitable of course, but you should do everything to minimize that risk. For some patients a vaginal procedure is much safer, *e.g.,* patients with cardiac or pulmonary comorbidity."

High age and high body mass index are factors that were interpreted differently by some participants. In some cases, gynaecologists prefer to perform a VSF in patients who are older (6/10), *e.g.,* over 80 or 85 years of age; as opposed to one gynaecologist who prefers the SCP in that case. The same goes for higher BMI; seven gynaecologists opt for a VSF, compared with two gynaecologists who chose a sacrocolpopexy.

Table 1. Characteristics of respondents

	Respondents (*n* = 10)
Sex	
Female	7/10
Male	3/10
Age (years), median (IQR)	50.5 (45.5 – 52.5)
Hospital type	
Academic teaching hospital	2/10
Non-academic teaching hospital	6/10
Non-academic non-teaching hospital	2/10
Experience as a gynaecologist (years), median (IQR)	13.5 (8.5 – 16.3)
Specialty	
Urogynaecologist	4/10
Gynaecologist with urogynaecological focus	6/10
Procedure performed	
VSF / SSHP / VH	10/10
Modified Manchester	9/10
Sacrocolpopexy / sacrohysteropexy performed by participant [a]	6/10
Sacrocolpopexy / sacrohysteropexy performed by colleague [a]	1/10
No sacrocolpopexy / sacrohysteropexy performed in hospital [a]	3/10
Combining laparoscopic / vaginal surgery (perineoplasty) [b]	3/10
Procedures performed in total	
VSF	
1 – 100	3/10
> 100	7/10
SSHP	
1 – 100	2/10
> 100	8/10
Modified Manchester	
1 – 100	4/10
> 100	6/10
Vaginal hysterectomy	
1 – 100	2/10
> 100	8/10
LSC / LSH	
0	4/10
1 – 100	5/10
> 100	1/10
RSC / RSH	
0	9/10
1 – 100	-
> 100	1/10

No./No. of total respondents, unless stated otherwise
VSF vaginal sacrospinous fixation of post-hysterectomy vaginal vault prolapse, *SSHP* vaginal sacrospinous hysteropexy, *VH* vaginal hysterectomy, *LSC* laparoscopic sacrocolpopexy, *RSC* robotic sacrocolpopexy; *LSH* laparoscopic sacrohysteropexy, *RSH* robotic sacrohysteropexy
[a] Sacrocolpopexy and sacrohysteropexy, performed per laparoscopy, robot, or abdominally
[b] Combining sacrocolpopexy or sacrohysteropexy with vaginal surgery for pelvic organ prolapse.

QUOTE 2: "A higher BMI is just the reason to do a sacrocolpopexy. It is a more effective treatment, because there is a lower chance of recurrence."

QUOTE 3: "When a patient has morbid obesity, and too much visceral fat, sacrocolpopexy can be a technically difficult procedure. In that case I would prefer a sacrospinous fixation."

When considering surgical treatment for POP, regardless of the type of surgery, all gynaecologists emphasise that patients should have enough bothersome complaints. The extent of bulge symptoms is not relevant in their choice between a VSF or SCP. However, the kind of complaints can be of importance when choosing a specific procedure for some participants. Urgency, severe constipation, or (chronic) pelvic pain are reasons to opt for a VSF instead of SCP, stated four respondents. One participant was hesitant to perform a VSF on a patient with pelvic pain or trigger points in the course of the pudendal nerve or the sacrospinous ligament.

QUOTE 4: "When a patient has severe urgency complaints, I do not believe you should do a treatment with mesh. When someone has constipation, there is a chance of worsening after a sacrohysteropexy."

QUOTE 5: "When I palpate the sacrospinous ligament and it hurts, I counsel the patient differently. In the case of a primary vault prolapse, the patient has to have pelvic floor physical therapy first to relieve these pain symptoms, before I would perform a vaginal sacrospinous fixation."

A lower or higher pelvic organ prolapse quantification (POP-Q) stage only matters for two participants. Three gynaecologists pay attention to the vaginal length, they prefer sacrocolpopexy when the vaginal length is short in order to prevent a bridging suture or overcorrection of the prolapse in VSF.

Surgery-related factors

The VSF can be performed with spinal analgesia, whereas general anaesthesia is needed for a SCP. Three participants, who only perform VSF, said that it is an advantage to be able to perform a VSF with spinal analgesia. Five gynaecologists do not believe that it is of importance, or they leave it up to the anaesthesiologist to decide whether general anaesthesia can be administered; those are all gynaecologists who perform the LSC in their own hospital.

Table 2. First choice surgical treatment for the type of prolapse

	VSF	LSC/RSC	No preference
Surgical treatment of first choice for VVP			
VVP after hysterectomy for other reason than prolapse	6/10	3/10	1/10
Performing SCP / SHP in same hospital	3/10	3/10	1/10
Referring to other hospital for SC	3/10	-	-
VVP after hysterectomy for prolapse	2/10	5/10	3/10
Performing SCP / SHP in same hospital	-	5/10	2/10
Referring to other hospital for SC	2/10	-	1/10
Recurrent VVP after previous surgical treatment for VVP	-	10/10	-

No./no. of total respondents
VVP vaginal vault prolapse, *VSF* vaginal sacrospinous fixation of post-hysterectomy vaginal vault prolapse, *SCP* sacrocolpopexy (either laparoscopic sacrocolpopexy or robotic sacrocolpopexy), *SHP* sacrohysteropexy (either laparoscopic sacrocolpopexy or robotic sacrocolpopexy)

Table 3. Top five factors influencing choice of treatment given by gynaecologists

Factors	Total number of points	Number of times mentioned
Recurrent prolapse	39	8
Comorbidity / surgical history	29	7
Age	14	6
Patient's preference / fear of mesh	13	5
Body mass index	12	4
Higher POP-Q stage	8	2
Time till recurrence	8	2
Chronic pelvic pain	4	2
Type of complaints (*e.g.*, urgency, pain)	4	1
Sustainability	4	1
Sexual function	3	1
Combination with rectopexy	2	1
Concomitant cystocele	1	1
No need for referral to another hospital	1	1

Other surgery-related factors were subcategorised into perioperative factors and postoperative factors. Nine participants stated SCP to be a more invasive procedure owing to a longer surgical time, a higher risk of complications, and the prolonged Trendelenburg position.

Postoperative factors that were mentioned are a lower recurrence rate or higher efficacy for the SCP (7/10) and a higher chance of recurrent cystocele for the VSF (2/10). One gynaecologist said that de novo dyspareunia was a result of SCP, whereas three gynaecologists said that it was a result of VSF. Two participants argued that de novo dyspareunia can be a result of both procedures.

QUOTE 6: "Dyspareunia is always a bit tricky. We quite often see dyspareunia after sacrospinous fixation. On the other hand, in the case of pre-existent dyspareunia, you rather would not place a mesh."

Physician-related factors

Gynaecologists who need to refer patients for a sacrocolpopexy all (4/10) stated that they experience no barriers to doing so. One respondent did say that they preferred to treat a patient in their own hospital. Two participants said that most patients want to stay in their own hospital for surgical treatment for their prolapse, so they tend to choose the surgery that can be performed by their own gynaecologist.

QUOTE 7: "I do not experience a barrier in referring patients, as we have great collaboration in our region. However, patients prefer to be treated in their own hospital. So, it seems they are the ones experiencing a barrier."

QUOTE 8: "The Dutch Medical Treatment Contracts Act (WBGO) demands that patients are informed of all treatment options, whether you can perform them yourself or not."

Uterine descent

All participants preferred a vaginal, uterine-preserving, treatment as first-choice surgery for primary uterine prolapse. The main reason is that they do not see an indication for the use of mesh for a first prolapse, as there are successful autologous tissue options. Comparable reasons were mentioned as the factors that play a role in the VVP, such as SCP is regarded as a more invasive procedure, carrying greater risks of mesh-related complications, and the risk of chronic pain. Which specific surgery they prefer is mainly based on their own clinical experience. Vaginal hysterectomy was only performed when there were other complaints, such as pre-malignancies, heavy menstrual bleeding, or the patient's explicit wish to have their uterus removed.

A recurrent uterine prolapse is the main reason for considering a SHP. Two participants would prefer a SHP in the case of a recurrence. Six participants do not have a strong preference and would counsel a patient for a SHP or another vaginal treatment, which could be a VH, modified Manchester (MM), SSHP left sided or bilaterally, or uterosacral ligament suspension (USLS). Two gynaecologists, who only perform vaginal surgery, would perform another vaginal treatment, either a SSHP after an MM or an MM after a SSHP. Similar factors to the post-hysterectomy vault prolapse are important to the participants, such as the patient's health status. Anatomical characteristics of the uterine

descent were of more interest than in the choice of the surgical treatment for VVP; *e.g.*, the quality of the uterosacral ligaments or whether there is an elongated cervix. Furthermore, time until the recurrence is important or whether the stitches through the sacrospinous ligament of the former VSF were torn out.

Discussion

Main findings

A qualitative study was performed to reveal the factors that are important for Dutch gynaecologists in counselling their patients with apical prolapse. The results show that, for the treatment of primary VVP (*i.e.*, no recurrence), some have a preference for VSF, some for SCP, and others have no preference. Recurrent VVP is the most important factor for choosing a SCP, for most gynaecologists (8/10). Second, comorbidity and surgical history are considered of relevance to both surgical procedures (7/10). Further patient-related factors that play a role are age, BMI, and patients' own preferences.

In the treatment for primary uterine prolapse all participants prefer a vaginal uterine-preserving treatment. In the case of a recurrent uterine prolapse, the surgical treatment preferences diverge greatly. The main reason for not choosing SCP is reluctance with regard to the use of mesh, as there are effective options with native tissue. Apparently, most gynaecologists conform to the Dutch guideline for the use of mesh implants in the treatment of POP and urinary incontinence, which states that abdominally placed mesh is more difficult and riskier than vaginal native tissue procedures.[16] In the case of recurrent uterine descent or additional complaints (*e.g.,* severe cervical dysplasia or heavy menstrual bleeding) a VH is preferred by the gynaecologists in our study.

Age is a known risk factor for the development of POP, but age as risk factor for recurrent POP is contradictory in the literature.[17, 18] A recent updated systematic review, however, defined younger age as a statistically significant risk factor for recurrent prolapse.[19] This last finding would suggest advising the surgical intervention with the lowest recurrence rates for younger patients. Some reviews and cohort studies suggest better outcomes for sacrocolpopexy.[20-22] However, this is not yet confirmed with long-term follow-up from RCTs directly comparing LSC with VSF.[11]

Overweight and obese women are more likely to develop POP, compared with women with a BMI within the normal range.[23] For POP recurrence, BMI was not statistically significant as a risk factor. However, the authors state that a slight trend could be

observed in the categorical variables BMI > 30 versus BMI ≤ 30.[19] Also a higher POP-Q stage before surgery (stage 3 or 4) was listed as a risk factor for POP recurrence.[18, 19] This was only mentioned by one participant to play a role in selection of surgical treatment.

Some participants consider spinal analgesia to be beneficial compared with general anaesthesia, especially for elderly patients. However, there seems to be no literature supporting this theory.[24-26]

Strengths and limitations

The main strength of this qualitative study is that the semi-structured interviews enabled us to examine this topic in more depth. We used the list of topics from the pilot interview and open-ended questions to explore factors and answers more in detail. This study only included Dutch gynaecologists, so it mainly reflects Dutch clinical practice. However, all described surgical techniques are used internationally and therefore this study is still of interest to a broader audience.

During the interviews it became clear that participants had a different interpretation of the term 'recurrence', when talking about post-hysterectomy vault prolapse. Some gynaecologists considered a vault prolapse after hysterectomy for POP to be a recurrence, whereas others thought a vault prolapse after previous surgical treatment for VVP to be a recurrence. This could have influenced the answers given by the gynaecologists, although this misunderstanding was discovered during the first interview and the interpretation of 'recurrence' was clarified at the beginning of the following interviews.

Interpretation

Most gynaecologists first set an indication for the type of surgery based on whether or not there is a recurrent prolapse. To come to a final decision, most gynaecologists look at multiple factors combined. For example, this could lead to an 85-year-old patient with a recurrent vault prolapse, obesity, and multiple comorbidities undergoing a VSF instead of a sacrocolpopexy, whereas a 60-year-old patient with a recurrent VVP who has a very active lifestyle could undergo a sacrocolpopexy. When a sacrocolpopexy is the preferred option, it seems that the most important factors for the final choice between the procedures are (relative) contra-indications for sacrocolpopexy.

Gynaecologists who do not perform the sacrocolpopexy themselves or in their own hospital, find more factors important in favour of the VSF. They all see a benefit in the possibility of spinal analgesia, whereas in the other group only one participant stated this.

It seems that they are more likely to perform a VSF in the case of an apical recurrence. RCTs investigating the optimal surgical treatments for apical prolapse have not demonstrated superiority of a certain surgery. Therefore, it seems reasonable that gynaecologists consider certain patient-related and surgery-related factors to make a choice between treatments. Nevertheless, patients should be able to make a fully informed decision and doctors should aim to reduce practice pattern variability.

This study focuses on gynaecologists' preferences. Future research on patients' preferences on the different kinds of treatments for VVP would be even more interesting. Furthermore, it would be helpful to incorporate factors that are truly of importance in a personalised decision aid to make the choice between procedures.

Conclusions

Recurrent apical prolapse is the most important factor in advising patients on which treatment they should undergo for VVP or uterine descent. Also, patients' comorbidities, surgical history, age, BMI, and the patient's own preference are important factors. Gynaecologists who do not perform the sacrocolpopexy in their own clinic are more likely to perform a VSF and find more reasons not to advise a patient to undergo a SCP. All participants prefer a vaginal surgery for a primary uterine prolapse.

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Supplementary Figure

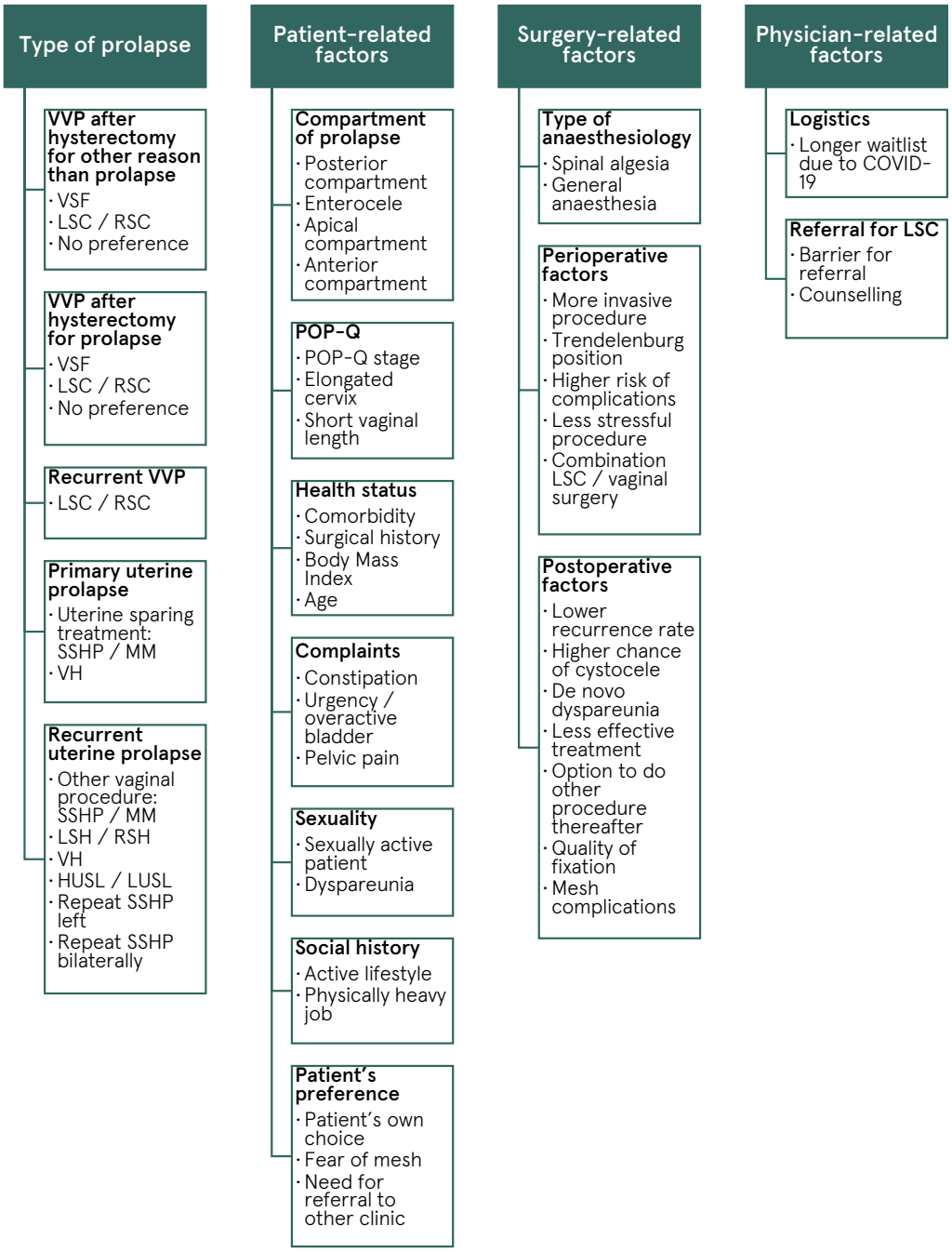

Figure S1. Code Tree

CHAPTER 9

General discussion & future perspectives

General discussion

This dissertation focuses on the surgical treatment of apical vaginal prolapse. We aimed to answer the following research questions:

- What are the short-term and long-term outcomes of laparoscopic versus open abdominal sacrocolpopexy in the treatment of vaginal vault prolapse?
- Which treatment is the most optimal for patients with uterine prolapse, laparoscopic sacrohysteropexy or vaginal sacrospinous hysteropexy?
- Which treatment is the most optimal for patients with post-hysterectomy vaginal vault prolapse, laparoscopic sacrocolpopexy or vaginal sacrospinous fixation?
- Which patient-related and physician-related factors are of importance for Dutch gynaecologists, when surgically treating patients with apical prolapse?

In this chapter, the main outcomes of the studies are summarised, the clinical implications will be discussed, and future perspectives are given.

Surgical approach to sacrocolpopexy

In order to answer the question whether laparoscopic sacrocolpopexy (LSC) or open abdominal open sacrocolpopexy (ASC) is the preferred technique in terms of effectiveness and risks, we performed the SALTO trial; a multicentre randomised controlled trial, which compared LSC with ASC in the treatment of post-hysterectomy vaginal vault prolapse (VVP). On average, patients had less blood loss and a shorter hospital stay after the laparoscopic procedure, compared with the abdominal technique. There was no substantial difference in disease-specific quality of life, anatomical outcome, the quantity of complications, and the number of surgical reinterventions, at 12 months follow-up (CHAPTER 2). We also examined the long-term effects of both surgical treatments. The long-term outcomes of patients from the SALTO trial were studied after a median follow-up of 9.1 years. Also, after long-term follow-up, no substantial differences were found in disease-specific quality of life, anatomical outcome, the quantity of complications, and the number of surgical reinterventions. Therefore, the laparoscopic approach of sacrocolpopexy (SCP) is the preferred technique, compared with the open procedure, considering the advantages on short term (CHAPTER 3).

INTERPRETATION IN LIGHT OF OTHER EVIDENCE

Two other RCTs have been published on this matter; the LAS trial in 2013 and an Italian trial in 2016.[1, 2] The LAS trial has shown clinical equivalence at one year follow-up. The

Italian study has shown comparable outcomes for the apical compartment, but more recurrences in the anterior compartment in the LSC group, at twelve months follow-up. In the SALTO trial, no difference was found in the anterior compartment; the LAS trial did not report these outcomes.

Although the SALTO trial found no differences in effectiveness between the laparoscopic and the abdominal technique, a review has recently been published which concluded that ASC is the preferred option in some cases.[3] Current evidence was assessed regarding efficacy and the complication rates of SCP compared with sacrospinous ligament fixation in the treatment of apical prolapse. Both laparoscopic and open abdominal procedures were included. Also, patients with uterine descent and post-hysterectomy VVP were included in this review. The abdominal and vaginal procedures were compared. The review showed that both SCP and VSF offer a sufficient alternative to the restoration of apical support. VSF was associated with a lower success rate, higher recurrence rate, higher dyspareunia rate, shorter operative time, and lower complication rate. Advantages of SCP were found in studies using the open abdominal technique, the minimally invasive technique showed no differences on recurrence or success rate. When anatomical durability and sexual function is a priority, the authors conclude that ASC may be the preferred option. When considering factors of mesh exposure, operative time, gastrointestinal complications, haemorrhage, and wound infections, VSF may be the better option.[3] Theories on why LSC had poorer results than the ASC are speculative and without citation: first, insufficient pulling of the mesh; second, mesh displacement. One of the main limitations of this publication is that LSC and ASC were never directly compared in this review and no network meta-analysis was performed. A network meta-analysis, also known as multiple treatment comparison, is a statistical technique that allows comparison of several treatments in the same meta-analysis simultaneously.[4, 5] The advantage is that it facilitates indirect comparisons of multiple interventions that have not been studied in a head-to-head fashion in the included studies.[6] However, as they did not perform such an analysis, we cannot conclude that the ASC is better than the LSC based on their study. Moreover, both patients with and without uterus were included. In order to make a reliable comparison, those patient categories should be analysed separately, as it is a different condition and research outcomes can vary. Studies presented in this thesis should be included in future reviews and meta-analyses.

In 2016, a review was published examining minimally invasive sacrocolpopexy (MISC) versus ASC.[7] Robot sacrocolpopexy and laparoscopic sacrocolpopexy were both included in the MISC group. Twelve papers were included, of which one RCT, two prospective cohort studies, and nine retrospective cohort studies. No differences were found in the number of overall complications or mesh exposure rates. The length of

hospital stay was significantly shorter and the amount of estimated blood loss was significantly less, in favour of the MISC group. No differences were found in disease-specific quality of life, after short-term to long-term follow-up. The results of this review are in line with the results of the SALTO trial.

MESH-RELATED COMPLICATIONS

Concerns regarding the use of vaginal mesh for prolapse have led to questions about the safety and efficacy of abdominally placed mesh.[8] The main long-term complications for vaginal mesh have proven to be mesh exposure, erosion, or pain.[8, 9] Although mesh-related complications after SCP are uncommon, mesh exposure can have an important impact on the patient's quality of life.[10] Clinical presentation is variable according to location and severity of the defect. Symptoms include pain, dyspareunia, 'hispareunia' (partner reporting pain during sexual intercourse), vaginal bleeding or discharge, recurrent infection or abscess formation.[10, 11] Symptoms may occur even years after primary surgery, which is why long-term follow-up of studies like the SALTO trial are important. Mesh exposure can be asymptomatic, and, in those cases, it can only be found by physical examination with inspection of vaginal tissue.

The overall occurrence of mesh exposure after MISC is low and is being estimated at 3.5%.[10] In the long-term follow-up of the SALTO trial, mesh exposures are reported in 12.5% (n = 2) and 7.7% (n = 1) in the LSC and ASC group, respectively. Due to the high loss to follow-up, the data could be less reliable and give a distorted image. Mesh-related complications of LSC in a retrospective cohort study showed a prevalence of 0.7%, with a median follow-up of 51 months.[12] We believe that this is an underestimation of the exposure rate, as they only detected patients with bothersome exposures. Three prospective cohort studies reported exposure rates of 2.9%, 3.7%, and 4.5%. These studies had a shorter follow-up time, with a median of 60 months instead of the 109 months in our study, that could explain the lower reported exposure rates.[13-15] One study showed a mesh exposure rate of 10.5%, following ASC, at seven years follow-up and is more in line with the SALTO study.[16] These results underline the importance of long-term follow-up, which includes an anamnesis specifically focusing on mesh-related complications and gynaecological examination as part of the study protocol.[10, 17, 18]

In the past years we have learned more about patient-related and surgery-related risk factors for developing mesh-related complications.[10, 19, 20] Patient-related risk factors include smoking, a history of diabetes mellitus, immunosuppression, menopausal status, and severe vaginal atrophy. Surgery-related risk factors include using non-resorbable sutures, concomitant total hysterectomy, and perioperative complications. Especially the risk factors that we can influence with interventions should be taken into account

when counselling patients about SCP and the possible complications on the short- and long-term. Some gynaecologists have already switched to using only resorbable sutures; others should consider doing this.

ROBOT SACROCOLPOPEXY

Another technique is the robot-assisted sacrocolpopexy (RSC). Robotic surgical systems have been developed with the goal of facilitating technically difficult procedures. Hence, many surgeons have turned to robotic-assisted surgery to offer patients a minimally invasive approach to SCP. In 2011 the first RCT comparing RSC to LSC was published. Results showed that an RSC results in a longer operating time, increased postoperative pain, and significant added expense with no clear advantage in pelvic floor function or anatomy one year after surgery, compared with LSC.[21] Another RCT was published in 2014, concluding higher costs or RSC than LSC, while short-term outcomes and complications are similar. It also showed longer duration of surgery, slightly higher pain scores one week after surgery, and a somewhat slower recovery to normal activities.[22] Lastly, in 2019 an RCT was published, which showed comparable outcomes for the RSC and the LSC, with 100% anatomic correction of the apical compartment in both groups.[23] Recently, two systematic reviews have been published on this topic. Both stating that RSC and LSC have equivalent clinical outcomes. There were no differences in complication rates or mesh exposures.[24, 25] RSC was associated with a lower conversion rate compared with LSC. This might be due to the better 3D view, better range of motion with instrument articulation, tremor filtration, and improved ergonomics.[26, 27] Considering these results, both RSC and LSC seem good strategies for performing SCP, both with some advantages and disadvantages.

Laparoscopic sacrohysteropexy versus vaginal sacrospinous hysteropexy

A retrospective study and a multicentre randomised controlled trial were conducted to examine which treatment, laparoscopic sacrohysteropexy (LSH) or vaginal sacrospinous hysteropexy (SSHP), is the most optimal for patients with uterine prolapse. The long-term follow-up of our retrospective study shows that LSH and vaginal SSHP are equally effective, based on objective and subjective recurrence rates (CHAPTER 4). The LAVA trial, a multicentre randomised controlled trial, in which LSH and SSHP in the treatment of uterine prolapse stage 2 or higher are compared, showed that LSH was non-inferior to SSHP for surgical failure of the apical compartment. There were no differences in overall anatomical recurrences and disease-specific quality of life. More bothersome symptoms of overactive bladder and faecal incontinence were reported after LSH. Dyspareunia was more frequently reported after SSHP (CHAPTER 5).

INTERPRETATION OF THE RESULTS

Anatomical outcomes from the retrospective analysis were in line with the data from the RCT. The LAVA trial showed some differences in secondary outcomes, however. There were more overactive bladder symptoms (OAB) in the LSH group, which was likely due to persistence of preoperative OAB symptoms. Furthermore, faecal incontinence was more common in the LSH group. In the retrospective cohort we found no differences in OAB symptoms or faecal incontinence. Although there was a statistically significant difference on these domains on the UDI and DDI questionnaires in the RCT, it is questionable whether these differences were clinically relevant, because the difference in median scores was less than 15 points between both groups. LSH was compared with vaginal mesh hysteropexy in an RCT, which was published in 2017. It showed similar results for the laparoscopic approach, compared to our studies. However, it also did not show a difference on the CRADI (Colorectal-Anal Distress Inventory) and UDI questionnaires, which we found in our study.[28]

Dyspareunia was less frequent in the LSH group, which is consistent with some previous research, but it is not confirmed in all studies.[29-32] In the retrospective cohort, less women in the LSH group had dyspareunia as well, although this was not statistically different. More women were sexually active in the LSH group of the retrospective cohort study (83.3%), compared with the SSHP group (56.1%), $p = 0.007$. It is unclear why a difference was found in the number of patients who were sexually active; it could be because of more dyspareunia in the SSHP group, higher age in the SSHP group, or a selection bias.

Once differences in secondary outcomes are confirmed with future research, they can be used to personalize treatment options for patients and counsel them about individualised risks. *I.e.,* a patient who is sexually active, might have a better outcome in terms of sexual function after a LSH compared with a SSHP.

DYSPAREUNIA

Women consider preservation of sexual activity and improvement of sexual function as important goals after surgery for POP. When women with POP were asked to prioritize the importance of outcomes after surgery, they ranked improvement in sexual function just below resolution of bulge symptoms and improvement in physical function.[33] A systematic review comparing different approaches to pelvic floor repair concluded that PISQ scores were not different between LSH and native tissue repairs. Dyspareunia was reported more often after vaginal mesh procedures, but not more frequently after laparoscopic or native tissue procedures.[30] Another review concluded that sexual function generally improves or remains unchanged after all types of reconstructive POP surgeries and does not worsen for any surgery type. Prevalence of total dyspareunia was

lower after all POP surgery types, and de novo dyspareunia was considered low, ranging from 0 to 9%.[31] This might be explained by the fact that vaginal POP surgery may be accompanied by vaginal narrowing and scarring as well as damage of the vascularisation and innervation of the vaginal wall, which can lead to sexual dysfunction including dyspareunia.[34] A recent multivariable regression analysis found only that preoperative dyspareunia was associated with postoperative dyspareunia. This underscores the need to ask specifically for sexual function and proceed with caution in a patient reporting dyspareunia at baseline, who then is at risk of persistent dyspareunia.[30, 32]

Laparoscopic sacrocolpopexy versus vaginal sacrospinous fixation

We performed a multicentre randomised controlled trial in which we included women with a symptomatic (post-hysterectomy) vaginal vault prolapse, POP-Q ≥ stage 2. A prospective cohort ran alongside. We published the protocol of this trial in CHAPTER 6. The results of the SALTO-2 trial show that both LSC and VSF are effective treatment options for post-hysterectomy vaginal vault prolapse (CHAPTER 7). Although, there seem to be more reinterventions for the apical compartment in the VSF group.

INTERPRETATION IN LIGHT OF OTHER EVIDENCE

The VUE trial, a multicentre RCT comparing LSC with VSF as treatment for vaginal vault prolapse was conducted in the UK and published in 2020.[35] It showed similar results to our trial. Subjective POP complaints were similar in both groups 12 months postoperatively. Prolapse beyond the hymen also did not differ substantially between both groups. These results are all in line with our study. Although the VUE study group has published an elaborate report on all outcomes, they did not provide combined outcome measures as recommended by Barber.[36, 37] Combined outcome measures such as composite outcome of success and surgical failure can reveal differences between both study groups, because it shows the results per patient more specifically.

The FIGO working group 'Pelvic Floor Medicine and Reconstructive Surgery' describes the different treatments for apical prolapse based on the literature evidence, the cost-effectiveness, the degree of difficulty and summed them up with an expert's recommendation. They stated that vaginal procedures are well described procedures with favourable outcomes and cost-benefit profiles. SCP has a high-effectivity; data on the route of performance and long-term outcomes of comparative trials are awaited. The costs with mesh implants are higher compared to the surgeries with autologous tissue or any conservative treatment and further studies are recommended to evaluate the cure rates in the span of decades.[38]

LONG-TERM OUTCOMES

With great interest we await the long-term outcomes of the SALTO-2 trial. Recently, a multicentre retrospective cohort study was published with a follow-up of up to 14.8 years.[39] The cohort included 9,681 women with apical prolapse, who underwent SCP (ASC and LSC), uterosacral ligament suspension (HUSLS and LUSLS), vaginal sacrospinous fixation, or colpocleisis between 2006 – 2018. Colpocleisis and SCP offered the most durable obliterative and reconstructive prolapse repairs. Reoperations for recurrent prolapse per 1,000 patient-years were 1.4 and 4.8, respectively. For VSF and USLS the reintervention rates were 13.9 and 9 per 1,000 patient-years. In the VSF group 28.6% of reinterventions was for the apical compartment. In the SCP group, 6% of reinterventions was performed for the apical compartment. SCP offered the most durable repair, but also the highest rate of reoperation for complications in 3.3% of patients. Reported reoperations included incisional hernia repair, diagnostic laparoscopy or laparotomy, mesh excision, fistula repair, and wound incision and drainage or debridement.

Long-term safety and efficacy of laparoscopically placed mesh for apical prolapse has been a question of interest, especially since the concerns regarding the use of vaginal mesh and lack of long-term outcomes on this matter. A recently published, retrospective cohort study, showed long-term safety of abdominally placed mesh with low levels of mesh exposure (2.6%) or long-term pain (3.2%), after a median follow-up of six years. This study has a high heterogeneity of procedures included: a mixture of LSC or LSH with or without additional rectopexy was assessed. The efficacy of apical support with mesh is commendable with 98% objective cure rate (POP-Q stage < 2) and 80% subjective cure rate (PGI-I questionnaire) at long-term follow-up.[8]

Patient-related and physician-related factors in the treatment of apical prolapse

Lastly, we conducted a qualitative study amongst Dutch gynaecologists. Using semi-structured interviews, we investigated what patient-related and physician-related factors were considered important when surgically treating patients, suffering from apical prolapse. Most gynaecologists prefer a VSF for primary VVP, whereas all participants would advise a SCP for a recurrent VVP. Most important factors on which their decisions are based are whether it is a recurrent apical prolapse, patient's health status, and patient's own preference. It seems that gynaecologists who only perform a VSF in their hospitals, are more likely to perform a VSF and find more reasons not to advise a SCP. All participants prefer a vaginal surgery for a primary uterine prolapse.

INTERPRETATION IN LIGHT OF OTHER EVIDENCE

In a previous Dutch study, the preferred surgical treatment for VVP was VSF (66%), the second choice was SCP (27%). This study, however, did not investigate why gynaecologists have a certain preference.[40] There are numerous effective surgical treatment options with native tissue, which is the main reason that gynaecologists do not see an indication for the use of mesh in the treatment of primary uterine descent. This is in accordance with the Dutch guideline for the use of mesh implants in the treatment of POP and urinary incontinence, which states that abdominally placed mesh is more difficult and risky than vaginal native tissue procedures.[41] Age and obesity are known risk factors for the development of POP.[42-44] Age has also been appointed as risk factor for recurrence, however a high BMI has not.[45] This would suggest to advise the surgical intervention with the lowest recurrence rates for younger patients.

Native tissue vaginal repairs offer decreased morbidity compared with mesh-augmented SCP; however, SCP has greater anatomic success. Surgical restoration of the vaginal apex can be accomplished via a variety of approaches and techniques. When deciding on the proper surgical intervention, the surgeon must carefully calculate the risks and benefits of each procedure while incorporating the patient's individual medical and surgical risk factors.[46] It would be helpful to determine which factors are truly of importance, so patients can get a personalised decision aid to make the choice between different procedures.

GYNAECOLOGISTS' PERSPECTIVES ON TREATMENT OF UTERINE DESCENT

The SAVE U trail showed that uterus preserving procedures have comparable results after one year, and a better anatomical outcome compared with vaginal hysterectomy after five years follow-up. SSHP is the preferred treatment for uterine descent.[47, 48] The management of POP in the Netherlands has changed between 2011 and 2017: the number of surgical interventions decreased, which was mostly due to less performed hysterectomies, in line with the previously described study outcomes.[47-49] An alternative uterus preserving technique, besides SSHP, is the modified Manchester (MM). Recently, the SAM trial was conducted in the Netherlands, a multicentre RCT comparing the MM to SSHP as treatment for uterus prolapse.[50] The results have not been published yet. A qualitative study, published in 2021, showed that Dutch gynaecologists' preference is mainly based on their own experience and background. Also, most gynaecologists reported that their counselling was biased toward one of the two surgeries, mostly based on their own experiences.[51] One of the main reasons for practice pattern variation is the absence of clearly defined guidelines or lack of evidence for optimal treatment.[49] Therefore, it is important to gain clear evidence on the optimal treatment options for POP. It would also be interesting if there was literature on why certain patient-related

and surgical factors are important in the treatment of POP. Better understanding and convincing evidence would most likely lead to less practice pattern variation and uniform counselling of patients.

ORGANISATION OF UROGYNAECOLOGICAL CARE

The Dutch Urogynaecology Workgroup (Werkgroep Bekkenbodem, WBB), part of the Dutch Society of Obstetrics and Gynaecology (Nederlandse Vereniging voor Obstetrie en Gynaecologie, NVOG), stimulates regional collaboration and regularly planned meetings within the region to discuss complicated cases and interesting or new research evidence. Furthermore, the WBB has made some recommendations for the use of mesh as treatment for POP. They advise to be cautious with the use of mesh and warn for an opportunistic implementation of SCP.[41] It is important that gynaecologists performing SCP have enough experience with the procedures and they perform a certain number of sacrocolpopexies per year, *e.g.,* ten LSCs per year as first or second surgeon. Above all, every patient should be informed about all treatment options, even if you do not perform a certain treatment yourself.

Future perspectives

Pathophysiological mechanisms

Further understanding of the pathophysiological mechanisms responsible for the development of POP is crucial to advance new therapeutic options. For instance, establishing whether there is an association between menopause and POP is relevant because of its therapeutic potential.[52] While few mechanistic studies into the role of ageing and the pathophysiology of POP exist, there are several candidate pathways to inspire future research based on the nine 'hallmarks' of ageing: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication.[53] These hallmarks provide a conceptual framework for the study of the mechanisms of ageing with the potential to significantly improve the treatment or prevention of POP as an age-related disease.

Many of the reported symptoms in patients with POP, are also reported by women who do not suffer from POP.[54] Therefore, that those symptoms are caused by POP cannot always be established (yet). It is important to conduct further research and clarify the pathophysiological mechanism of the (dysfunctional) symptoms. This will mainly be

important to inform patients about what to expect from surgical treatment. Patient satisfaction could possibly improve when they know what can be expected.

Tissue engineering

Tissue engineering refers to combining cells, extra-cellular matrix, and biologically active molecules into functional tissues. The goal of tissue engineering is to assemble such fully functional constructs that restore, maintain, or improve damaged tissue or a whole organ. Regenerative medicine is a broad field that includes tissue engineering, but also incorporates the idea of self-healing (*i.e.,* where the body uses its own systems, sometimes with help from added biological material from outside the body, to recreate cells or rebuild organs). Both tissue engineering and regenerative medicine continue to evolve greatly. Currently, tissue engineering plays a relatively small role in patient treatment, procedures are still experimental and very costly.

A new approach for treating women with POP could be found in tissue engineering.[55] It has made superior progress in POP treatment, and biological scaffolds have received considerable attention. Nevertheless, pelvic floor reconstruction still faces severe challenges, including the construction of ideal scaffolds, the selection of optimal seed cells, and growth factors.[56] Different cells and scaffolds have their own advantages and disadvantages, which can produce therapeutic effects on PFD. Therefore, mores studies with longer follow-up are needed to select the most effective and safe cells and materials for PFD repair.[57] Existing POP treatment is symptom-based. When new techniques can actually interfere in the pathophysiological mechanisms, it could be a game changer for both patients and doctors in the treatment of POP.

Pregnancy and childbirth

One of the main risk factors for developing pelvic floor dysfunction (PFD) is vaginal childbirth. Pregnant women are generally not aware of the risks. A risk calculator (UR-CHOICE) has been developed to inform pregnant women about the risks of developing POP, urinary incontinence, and / or anal incontinence.[58] A qualitative study was conducted to investigate whether pregnant women want to know about the PFD risks.[59] Women's PFD knowledge was limited, meaning they were unlikely to raise PFD risk with healthcare professionals. Women believed it was important to know their individual PFD risk and that knowledge would motivate them to undertake preventative activities. Healthcare professionals believed it was important to discuss PFD risk. However, limited time and concerns over increased caesarean section rates prevented this in all but high-risk women or those that expressed concerns.[59] The UR-CHOICE calculator could support discussion to consider preventative PFD activities and to enable women to be

more prepared should PFD occur. A randomised trial is needed to test the effectiveness of an intervention which includes the UR-CHOICE calculator in reducing PFD. Also, this qualitative study should be repeated in the Netherlands to establish that Dutch patients have the same meaning as patients from New Zealand do.

Core outcome sets

At this moment one of the main challenges in urogynaecological literature is the availability of many different reported outcome measures. In our studies we reported the outcomes as suggested by Barber and IUGA / ICS standards.[36, 37, 60, 61] These outcome measures still leave room for own interpretation. Patient-reported outcome measures should be uniform and internationally agreed upon. Moreover, there should be a recommendation on the used validated questionnaires, so results from different studies can be compared and pooled and heterogeneity reduced.

There is a project group working on standardising outcome sets globally: CHORUS, an International Collaboration for Harmonising Outcomes, Research, and Standards in Urogynaecology and Women's Health.[62] Core outcome sets (COS) represent the minimum outcomes as well as outcome measures that should be evaluated and reported in research. The development and establishment of COS does not mean that research outcomes should be restricted to the particular COS. While research can and should investigate other outcomes, the COS that will be reported, will allow comparisons of outcomes as well as robust systematic reviews and meta-analysis.[62] One of the first steps in this process is to publish systematic reviews to identify a wide variation in outcomes and outcome measures for various types of PFD, *e.g.,* apical prolapse.[63] Next, international, multi-perspective online Delphi surveys will be undertaken. Lastly, dissemination and implementation of the COS within an international context will be the endpoint of the COS development process.

The International Urogynaecology Consultation (IUC) project, an initiative by IUGA, aims to select and bring the world's most renowned experts together to produces best practice documents and consensus papers based on a selection of articles containing the most up-to-date scientific evidence concerning POP, urogenital pain, and sexual function.[64] Four chapters, containing a total of 16 systematic reviews will be published: chapter 1 – defining POP; chapter 2 – evaluation of the patient with POP; chapter 3 – conservative treatment of the patient with POP; and chapter 4 – surgical treatment of the patient with POP. The IUC project is much broader than the previously described CHORUS project, but they also published a review on patient-reported outcome measures (PROs) and patient-reported goals (PRGs) as part of the second chapter.[65]

It would be favourable to have an established set of outcome measures for reporting research on treating POP. This would also streamline the development of study protocols and data collection. Last, it would enable meta-analyses and systematic reviews and reduce heterogeneity.

Ongoing studies

- LAVA trial (laparoscopic sacrohysteropexy versus vaginal sacrospinous hysteropexy) five-year follow-up.
- SALTO-2 trial (laparoscopic sacrocolpopexy versus vaginal sacrospinous fixation) five-year follow-up.
- Laparoscopic sacrocolpopexy for the treatment of repeat cystocele or multi-compartment prolapse.

Future studies

- Updated systematic review and meta-analysis of published RCTs and prospective comparative studies on the treatment of apical prolapse.
- Systematic review and meta-analysis and of LSC versus VSF for post-hysterectomy vaginal vault prolapse.
- Patient reported outcome measures for POP, aiming to use the same outcome measures when reporting surgical outcomes for POP worldwide.
- Further understanding of pathophysiological mechanisms and the possibilities of tissue engineering in the treatment of POP.
- Validation of UR-CHOICE in the Netherlands.
- Alternative procedures for the treatment of vaginal apical prolapse, such as:
  - High uterosacral ligament suspension (HUSLS),[66]
  - Laparoscopic uterosacral ligament suspension (LUSLS),[67]
  - Vaginal – natural orifice translumenal endoscopic surgery (V-NOTES),[68, 69]
  - Laparoscopic lateral suspension (LLS).[70]

General conclusion

According to this thesis, several conclusions can be made:

- Laparoscopic sacrocolpopexy is the preferred technique, compared to open abdominal sacrocolpopexy, based on short-term advantages. Results, in terms of recurrences and complication rates, are similar after long-term follow-up.
- Laparoscopic sacrohysteropexy and vaginal sacrospinous hysteropexy are comparable in their effectiveness for women with uterine prolapse, according to the results of a retrospective study and a randomised controlled trial with one year follow-up.
- Laparoscopic sacrocolpopexy and vaginal sacrospinous fixation are both effective surgical treatment options at twelve months follow-up, in the treatment of vaginal vault prolapse. Although, there seems to be a clinically relevant difference in surgical reinterventions for the apical compartment in favour of the LSC.
- Preferred treatment options for vaginal vault prolapse differ amongst Dutch gynaecologists. Most important factors on which their decisions are based are whether it is a recurrent apical prolapse, patient's health status, and patient's own preference.

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CHAPTER 10

Impact paragraph

Impact paragraph

Pelvic organ prolapse (POP) is a frequently occurring health issue, which can cause bothersome symptoms that may include vaginal bulge, pelvic pressure, and symptoms related to bladder or bowel dysfunction.[1-4] In addition, POP may negatively affect sexuality, body image, and quality of life.[4, 5] The prevalence has been reported as high as 25 – 60% in parous women.[1, 2, 6, 7] Moreover, the overall incidence of POP is still rising as a result of ageing and increasing obesity rates.[2] The lifetime risk of women undergoing a single surgery for POP or urinary incontinence is 19 – 20%.[8, 9]

The relevance of research on the treatment of POP is self-explanatory when considering factors as the high and increasing prevalence, the impact of the symptoms, and the need for treatment. In this chapter the main outcomes of our studies will be summarised. Furthermore, the importance of this thesis and how it can contribute scientifically and societally will be explained.

Aim of the thesis and main outcomes

The aim of this dissertation was to investigate which surgical treatment options are the most optimal for patients with post-hysterectomy vaginal vault prolapse or patients with uterine descent. In addition, we examined which patient-related and physician-related factors are important to Dutch gynaecologists when surgically treating patients with apical prolapse.

Based on our research discussed in this thesis, we conclude the following:

- Laparoscopic sacrocolpopexy is the preferred technique compared to open abdominal sacrocolpopexy for the treatment of post-hysterectomy vaginal vault prolapse, based on short-term advantages. On average, patients had less blood loss and a shorter hospital stay after the laparoscopic procedure, compared with the abdominal technique. There was no difference in disease-specific quality of life, anatomical outcome, the quantity of complications, and the number of surgical reinterventions at one-year follow-up and after long-term follow-up (CHAPTERS 2 and 3).
- Laparoscopic sacrohysteropexy and vaginal sacrospinous hysteropexy are comparable in their effectiveness for women with uterine prolapse, as we have shown with the results of a retrospective study and a randomised trial at one year follow-up. In both studies, there were no differences in overall anatomical recurrences and disease-specific quality of life (CHAPTERS 4 and 5).

- Laparoscopic sacrocolpopexy and vaginal sacrospinous fixation are both effective surgical treatment options at twelve months follow-up, in the treatment of vaginal vault prolapse. Although, there seems to be a clinically relevant difference in surgical reinterventions for the apical compartment in favour of the LSC (CHAPTERS 6 and 7).
- Preferred treatment options for vaginal vault prolapse differ amongst Dutch gynaecologists. Most important factors on which their decisions are based are whether it is a recurrent apical prolapse, patient's health status, and patient's own preference (CHAPTER 8).

Scientific and societal impact

Mainly, two surgical routes can be utilised in the treatment of middle compartment prolapse; the vaginal route (vaginal sacrospinous fixation (VSF) for vaginal vault prolapse and vaginal sacrospinous hysteropexy (SSHP) for uterine descent) and the abdominal route (sacrocolpopexy and sacrohysteropexy).

The SALTO trial has confirmed the effectiveness of laparoscopic sacrocolpopexy (LSC) for vaginal vault prolapse, as it is as successful as the open abdominal technique (ASC) after short- and long-term follow-up. This minimally invasive procedure has already been widely implemented, but a prospective comparative trial with long-term follow-up was lacking. Also, this long-term follow-up of an RCT is an addition to the existing literature by presenting the clinical outcomes (disease-specific quality of life, anatomical results, bulge symptoms) as well as the long-term complications (mesh exposures) after LSC and ASC. Consequently, the ASC should no longer be performed, unless there is a specific reason to do so, *e.g.,* a technical issue or a complication which arises during the laparoscopy.

We conducted two other randomised controlled trials about the surgical treatment of apical prolapse and the results at 12 months follow-up were presented. The LAVA trial was the first RCT to compare LSH to SSHP in the treatment of uterine descent. The SALTO-2 trial is one of the first two RCTs to compare LSC to VSF for post-hysterectomy vaginal vault prolapse. Unique to both trials is that they have specifically defined inclusion criteria concerning uterine descent or post-hysterectomy vault prolapse. In previously published review articles, both women with and without a uterus were included and compared, which may affect the outcome of those reviews.[7, 10] These results are important to inform patients of what to expect after prolapse surgery. Based on these studies, there is not one surgical treatment favourable compared to the other. Although, in the SALTO-2 trial, there seems to be a clinically interesting difference in the number

of surgical reinterventions in favour of the LSC. When this finding is confirmed and indeed statistically significant after long-term follow-up, it is advisable to perform LSC in women who have a higher chance of recurrence.

It is known that POP recurrence or mesh complications can arise after many years. Therefore, reliable long-term results are also needed, and they are to be expected from our trials in a few years. Moreover, a meta-analysis of several RCTs including our trials should be performed in the nearby future to achieve the highest level of evidence and confirm the results of our studies by combining them with other evidence.

The results of our qualitative study show that gynaecologists who do not perform the sacrocolpopexy in their own clinic are more likely to perform a VSF and seem to find more reasons not to advise a sacrocolpopexy. On the other hand, patients from gynaecologists who do perform sacrocolpopexy in their clinics are perhaps more likely to undergo a treatment with mesh. This difference can partly be considered practice pattern variation (PPV). PPV is the variance in care which cannot be clarified by the specifics of the medical condition. PPV can lead to under- and overtreatment and therefore could introduces unnecessary risks of surgery, or patients might not receive adequate treatment for their medical condition.[11, 12] Our qualitative study can improve awareness of this issue and is relevant in order to develop plans and actions that can lead to reduce PPV. More research is needed to investigate which factors are truly of importance, so patients can get a personalised decision aid to make the choice between different treatment options. If PPV can be further reduced in the future, it could lead to less health care expenses, as PPV is associated with higher costs.[11, 13]

Activities leading to greater involvement

In order to inform other health care workers, our data is published in peer-reviewed journals and presented at global and nationwide conferences. It can be used for review articles, meta-analyses, and guidelines. To enable this, we selected outcome measures that are similar to those in other trials (*e.g.,* combined outcome of success, anatomical failure, prolapse beyond the hymen, and disease-specific quality of life). For patients and health care professionals, guidelines are one of the most important outcomes in daily practice. The Dutch 'Prolapse' guideline dates from 2014 and is ready to be updated. Although some modules have been updated in recent years, more new studies can be added. The data presented in the guideline should be adjusted into personalised decision aids for patients.

Learning more about pelvic floor disorders (PFD), which includes POP, is very important for patients. Many women suffer from bothersome or functional symptoms, without

realising that the problem is very common and there are several treatment options available. There are numerous international and national resources that make an effort to inform women about the condition and the different treatment options. These include the patient leaflets from IUGA (many also available in Dutch),[14] several Dutch websites (*e.g.,* www.bekkenbodem4all.nl, www.bekkenbodemwijzer.nl, and www.degynaecoloog.nl) [15-17] and social media platforms (*e.g.,* Instagram).[18] This information is easily accessible for both doctors and patients. Moreover, it is especially important to empower women to search for their preferred personalised solution of POP. Even if their gynaecologist does not offer this specific treatment. Studies like ours can contribute to the content of the information and even more important to the knowledge of women.

Impact of this thesis

In this thesis, the search for the most optimal treatment of apical prolapse has been expanded. It is clear that there is no longer a place for an intended open abdominal sacrocolpopexy. The LAVA trial and the SALTO-2 trial show no superior surgical technique in the treatment of uterine descent or vaginal vault prolapse, respectively. Until further evidence is published, all techniques can be used in the treatment of apical prolapse, provided that the patient made a fully informed decision.

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CHAPTER 11

Summary

Summary

This chapter summarises the findings of the research described in this dissertation and highlights the most important findings.

Introduction

CHAPTER 1 provides a general introduction on pelvic organ prolapse (POP) and its treatment options. Pelvic organ prolapse (POP) refers to the downward displacement of a pelvic organ. It is a frequently occurring health issue, especially concerning elderly women. POP can cause bothersome symptoms that may include vaginal bulge, pelvic pressure, and symptoms related to bladder or bowel dysfunction. In addition to mechanical discomfort, POP may negatively affect sexuality, body image, and quality of life and it is one of the most common reasons for gynaecological surgery. Pelvic floor disorders are caused by complex pathophysiological mechanisms and have very different presentations, making them difficult to define. 'Anatomical prolapse with descent of at least one of the vaginal walls to or beyond the vaginal hymenal ring with maximal Valsalva effort, and second, the presence either of bothersome characteristic symptoms or of functional or medical compromise' has recently been adopted as the clinical definition of POP.

POP can occur in the anterior, posterior, or apical compartments of the vagina, but is not limited to one compartment at once. This thesis focusses on the apical compartment, thus uterine descent and post-hysterectomy vaginal vault prolapse.

The main goal of POP surgery is to restore normal pelvic anatomy and eliminate POP symptoms, which may subsequently restore bowel, bladder, and sexual function. Various treatment options exist in the treatment of apical prolapse, including sacrocolpopexy, sacrohysteropexy, and vaginal sacrospinous fixation. However, prospective comparative trials are rare. The aim of this thesis was to examine which treatment is the most optimal, in terms of effectiveness and safety, for women suffering from uterovaginal prolapse or post-hysterectomy vaginal vault prolapse.

What are the short-term and long-term outcomes of laparoscopic versus open abdominal sacrocolpopexy in the treatment of vaginal vault prolapse?

CHAPTER 2 describes the results of the multicentre randomised controlled SALTO trial, which compares laparoscopic sacrocolpopexy (LSC) to open abdominal sacrocolpopexy (ASC) in the treatment of post-hysterectomy vaginal vault prolapse. In this study, 74 patients with symptomatic vault prolapse, requiring surgical repair, were included and randomly assigned to LSC (n = 37) or ASC (n = 37). Follow-up after 12 months showed no significant differences in disease-specific quality of life, measured with the Urogenital Distress Inventory (UDI). The 'genital prolapse' domain on the UDI scored a median of 0.0 in both groups (IQR 0 – 0), p = 0.93. Patients had less blood loss and a shorter hospital stay after the laparoscopic procedure, compared with the abdominal technique. There was no substantial difference in the rate of complications between both groups. Moreover, we did not find a difference in anatomical outcome after one year, meaning that none of the patients had a POP-Q ≥ stage 2 prolapse of the apical compartment. In the LSC group, 7 surgical reinterventions were done, compared with 4 in the ASC group, of which none for the apical compartment. The number of surgical reinterventions was not statistically different. The composite outcome of success was 83.8% (n = 31) for the LSC group and 89.2% (n = 33) in the ASC group. Considering these results, we concluded that this trial provides evidence to support a laparoscopic approach when performing a sacrocolpopexy.

CHAPTER 3 presents the long-term follow-up of the SALTO trial. Patients were asked to participate in this observational follow-up study to examine disease-specific quality of life, anatomical outcome, retreatment, and long-term complications. We included 22 patients (61.1%) in the LSC group and 19 patients (54.3%) in the ASC group. There were 14 (38.9%) patients lost to follow-up in the LSC group versus 16 patients (45.7%) in the ASC group. The median duration of follow-up was 109 months (9.1 years). Disease-specific quality of life did not differ after long-term follow-up with median scores of 0.0 (LSC: IQR 0 – 17 versus ASC: IQR 0 – 0) on the 'genital prolapse' domain of the UDI in both groups (p = 0.175). Patient satisfaction, according to the PGI-I was also not statistically different (LSC: 57.9% versus ASC: 58.8%, p = 0.955). Anatomical outcomes were the same for both groups on all points of the POP-Q. The composite outcome of success for the apical compartment is 78.6% (n = 11) in the LSC group and 84.6% (n = 11) in the ASC group (p = 0.686). Mesh exposures occurred in two patients (12.5%) in the LSC group and one patient (7.7%) in the ASC group. There were five surgical reinterventions in both groups (LSC: 22.7%; ASC: 26.3%, p = 0.729). At long-term follow-up there was no substantial difference

in disease-specific quality of life, anatomic results on the POP-Q, complications as mesh or suture exposure, and reinterventions between the LSC and the ASC groups. Therefore, the laparoscopic approach of sacrocolpopexy is preferable, considering the previously discovered advantages on short-term.

Which treatment is the most optimal for patients with uterine prolapse, laparoscopic sacrohysteropexy or vaginal sacrospinous hysteropexy?

CHAPTER 4 shows the long-term outcomes of laparoscopic sacrohysteropexy (LSH) compared with vaginal sacrospinous hysteropexy (SSHP) as treatment for uterine descent. This is a retrospective study of patients who underwent a LSH between 2003 and 2013 or a SSHP between 2009 and 2011 for primary treatment of uterine prolapse. We included 105 patients, 53 in the LSH group and 52 in the SSHP group. Patients were asked to fill out several validated Dutch questionnaires to investigate disease-specific quality of life. Furthermore, they were asked to visit the outpatient clinic for a pelvic examination to examine anatomical outcomes. The median duration of follow-up was 4.5 years in the LSH group and 2.5 years in the SSHP group. There were no statistically differences between the study groups in composite outcome of success (POP-Q point C ≤ 0, no bulge symptoms, and / or no retreatment); 41.4% in the LSH group compared with 72.7% in the SSHP group (p = 0.073). Anatomical failure of the apical compartment (POP-Q point C > 1) occurred in one patient in each group (p = 0.711). Vaginal bulge symptoms for which patients consulted professionals happened in 34.6% of patients in the LSH group, compared with 21.2% in the SSHP group (p = 0.126). Last, no difference in patient satisfaction was found; 75% of patients in the LSH group were satisfied and 71.8% of patients in the SSHP group were satisfied (p = 0.741). The operative time was longer in the LSH group (117 minutes; IQR 110 – 123), compared with the SSHP group (67 minutes; IQR 60 – 73) (p < 0.001). The duration of hospital stay was also longer in the LSH group (4 days) than in the SSHP group (3 days) (p = 0.006). We concluded that LSH and SSHP are equally effective in the treatment of uterine prolapse, based on objective and subjective recurrence rates, after correction for confounding factors.

CHAPTER 5 provides the results of the LAVA trial, a multicentre randomised controlled non-blinded non-inferiority trial. In total, 126 women with uterine prolapse stage 2 or higher were randomly allocated between a laparoscopic sacrohysteropexy (LSH; n = 64) or a vaginal sacrospinous hysteropexy (SSHP; n = 62). LSH was non-inferior to vaginal SSHP regarding surgical failure at 12 months follow-up, in the intention to treat analysis. The failure rate was 1.6% (n = 1) in the LSH group, versus 3.3% in the SSHP group (n = 2);

difference -1.7%; 95% CI for difference -7.1 – 3.7. Non-inferiority of LSH was confirmed in the per protocol analysis. There were no differences in overall anatomical recurrences and quality of life. More bothersome symptoms of overactive bladder and faecal incontinence were reported after LSH. Dyspareunia was more frequently reported after SSHP. Based on the analysis at 1-year follow-up, we concluded that LSH was non-inferior to SSHP for surgical failure of the apical compartment.

Which treatment is the most optimal for patients with vaginal vault prolapse, laparoscopic sacrocolpopexy or vaginal sacrospinous fixation?

CHAPTER 6 shows the SALTO-2 research protocol, a randomised trial which compares laparoscopic sacrocolpopexy (LSC) to vaginal sacrospinous fixation (VSF) for the treatment of vaginal vault prolapse. Hysterectomy is one of the most performed gynaecological surgical procedures during lifetime. Many women who have had a hysterectomy because of prolapse symptoms will visit a gynaecologist for a surgical correction of a vaginal vault prolapse thereafter. Vaginal vault prolapse can be corrected by different surgical procedures. A Cochrane review comparing abdominal sacrocolpopexy (ASC) to VSF considered the abdominal procedure as the treatment of first choice for prolapse of the vaginal vault, although operation time and hospital stay is longer. Literature also shows that hospital stay and blood loss are less after a LSC compared with the abdominal technique. However, it is unclear which of these techniques leads to the best operative result and the highest patient satisfaction. Prospective trials comparing LSC and VSF are lacking. The aim of this randomised trial is to compare the disease-specific quality of life of the LSC versus the VSF as the treatment of vaginal vault prolapse. We will perform a multicentre prospective randomised controlled trial. Women with a post-hysterectomy symptomatic, POP-Q ≥ stage 2, vaginal vault prolapse will be included. Participants will be randomly allocated to either the LSC or the VSF group. The primary outcome will be disease-specific quality of life at 12 months follow-up. Secondary outcomes will be the effect of the surgical treatment on prolapse related symptoms, sexual functioning, procedure related morbidity, hospital stay, postoperative recovery, anatomical results using the POP-Q classification, and reinterventions. With a power of 90% and a level of 0.05, the calculated sample size necessary is 96 patients. Taking into account 10% attrition, a number of 106 patients (53 patients in each group) will be included.

CHAPTER 7 describes the outcome of the SALTO-2 trial, a multicentre randomised controlled trial and prospective cohort alongside, which compared laparoscopic

sacrocolpopexy with vaginal sacrospinous fixation in the treatment of vaginal vault prolapse POP-Q stage 2 or higher. Data from both studies was initially analysed separately, whereafter a meta-analysis was carried out to combine results for the primary outcome and principal secondary outcomes. In total, 179 women were included in the study, of whom 64 women were randomised and 115 women participated in a prospective cohort. The RCT was stopped prematurely, mainly because of strong patient preference hampering inclusion. Disease-specific quality of life did not differ after 12 months between the LSC and VSF group in the RCT and the cohort (RCT: p = 0.887; cohort: p = 0.704; meta-analysis: mean difference 1.57; 95% CI (-6.18 – 9.32), p = 0.692). The composite outcome of success for the apical compartment, in the RCT and prospective cohort, was 89.3% and 90.3% in the LSC group and 86.2% and 87.8% in the VSF group (RCT: p = 0.810; cohort: p = 0.905; meta-analysis: OR 0.86; 95% CI (0.26 – 2.80), p = 0.800). There were no statistically relevant differences in number of complications between the LSC and the VSF (RCT: p = 0.395; cohort: p = 0.129). Also, reinterventions did not differ statistically significantly differ between both groups (RCT: p = 0.934; cohort: p = 0.120), although there seems to be a clinically relevant difference in surgical reinterventions for the apical compartment in favour of the LSC. LSC and VSF are both effective treatments for vaginal vault prolapse, after a follow-up time of 12 months.

Which patient-related and physician-related factors are of importance for Dutch gynaecologists when treating patients with apical prolapse surgically?

CHAPTER 8 provides information on why Dutch gynaecologists prefer a certain surgical treatment for apical prolapse. These are the results of a qualitative study, in which we conducted semi-structured interviews. Ten Dutch urogynaecologists or gynaecologists with a special interest in urogynaecology participated. All gynaecologists performed vaginal surgeries for apical prolapse, seven gynaecologists perform sacrocolpopexy themselves or a colleague in their hospital does. Six gynaecologists would perform a VSF for a primary vaginal vault prolapse, in women who have never been operated for POP before; three gynaecologists preferred a sacrocolpopexy. All participants prefer a sacrocolpopexy for recurrent VVP, *i.e.,* after previous surgery for post-hysterectomy vault prolapse. All participants have stated that multiple comorbidities could be a reason to choose VSF, as this is considered less invasive than sacrocolpopexy. Most participants would choose a VSF in case of higher age (6/10) or higher body mass index (7/10). Gynaecologists who do not perform the sacrocolpopexy in their own clinic are more likely to perform a VSF and seem to find more reasons not to advise a sacrocolpopexy. In case

of a primary uterine prolapse, all participants prefer a vaginal, uterine-preserving approach in the surgical treatment of primary uterine prolapse.

Discussion & Impact Paragraph

CHAPTER 9 describes the general discussion, clinical implications of this research and future perspectives. According to this thesis, several conclusions can be made:

- Laparoscopic sacrocolpopexy is the preferred technique, compared to open abdominal sacrocolpopexy, based on short-term advantages. Results, in terms of recurrences and complication rates, are similar after long-term follow-up.
- Laparoscopic sacrohysteropexy and vaginal sacrospinous hysteropexy are comparable in their effectiveness for women with uterine prolapse, according to the results of a retrospective study and a randomised controlled trial with one year follow-up.
- Laparoscopic sacrocolpopexy and vaginal sacrospinous fixation are both effective surgical treatment options at twelve months follow-up, in the treatment of vaginal vault prolapse. Although, there seems to be a clinically relevant difference in surgical reinterventions for the apical compartment in favour of the LSC.
- Preferred treatment options for vaginal vault prolapse differ amongst Dutch gynaecologists. Most important factors on which their decisions are based are whether it is a recurrent vaginal vault prolapse, patient's health status, and patient's own preference.

The importance of this thesis and how it can contribute scientifically and societally is described in **CHAPTER 10**. The relevance of research on the treatment of POP is evident when considering factors as the high and increasing prevalence, the impact of the symptoms, and the need for treatment. The results of our studies are an addition to the existing literature because they show new information, which can be used for counselling and help patients making evidence-based decisions.

CHAPTER 12

Dutch summary

Nederlandstalige samenvatting (Dutch summary)

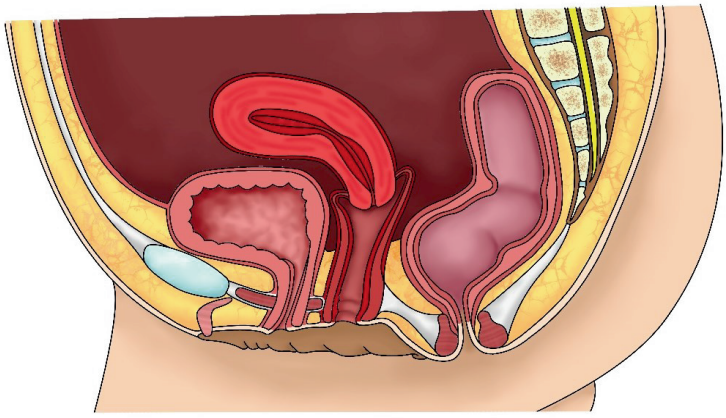
Dit hoofdstuk geeft een Nederlandstalige samenvatting van dit proefschrift en beschrijft de belangrijkste bevindingen van het onderzoek naar de operatieve behandeling van verzakking van de baarmoeder of vaginatop (middelste compartiment).

Introductie & overzicht thesis

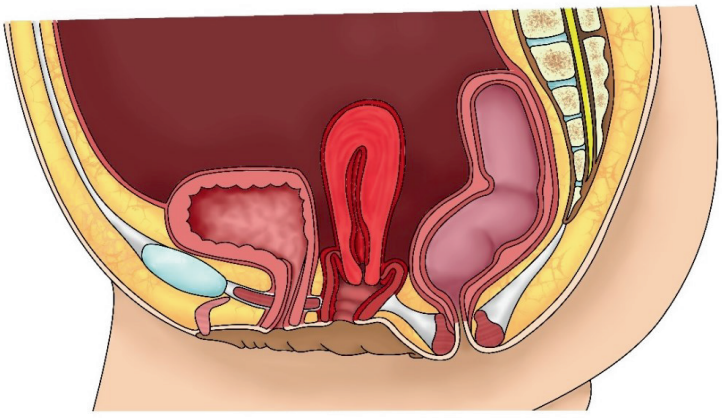
HOOFDSTUK 1 geeft een algemene introductie over genitale prolaps (verzakking) en de mogelijkheden voor behandeling. Genitale prolaps betekent dat er sprake is van een verzakking van de blaas (voorste compartiment), de baarmoeder (descensus uteri, middelste / apicale compartiment), de endeldarm (achterste compartiment) of de vaginatop (na verwijdering van de baarmoeder, tevens middelste / apicale compartiment). Prolaps is een veel voorkomend gezondheidsprobleem, vooral bij oudere vrouwen. Prolaps kan hinderlijke klachten geven, zoals het voelen van een uitstulping, een zwaar gevoel in de schede, een balgevoel, rugpijn en blaas- en darmklachten. Naast mechanische klachten kan een prolaps ook invloed hebben op seksualiteit, het zelfbeeld en de kwaliteit van leven. Een genitale prolaps is een van de voornaamste redenen voor gynaecologische chirurgie. Bekkenbodem aandoeningen worden veroorzaakt door complexe mechanismen, die nog niet volledig duidelijk zijn. Risicofactoren voor het ontwikkelen van een verzakking zijn onder andere een eerdere vaginale bevalling, prolaps bij familieleden en leeftijd.

De klinische definitie van genitale prolaps is als volgt: ‘Anatomische prolaps met verzakking van ten minste één van de compartimenten tot of voorbij het hymen (maagdenvlies) bij maximale Valsalva (maximale opgebouwde druk door op de handrug te blazen), in combinatie met de aanwezigheid van typische hinderlijke klachten of functionele klachten.’

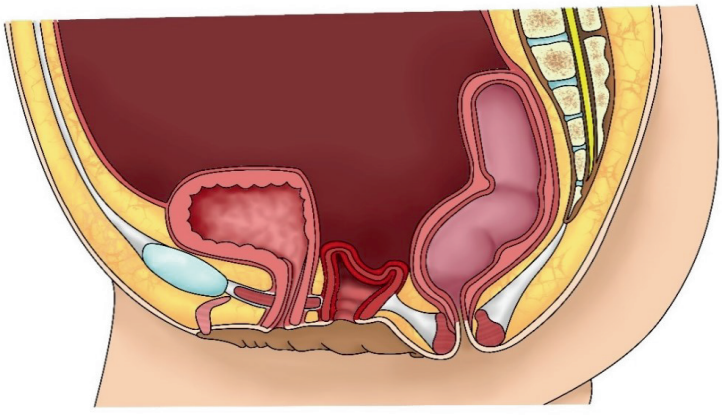
Figuur 1 is een schematische weergave van de anatomie van de vrouwelijke genitalia. Dit proefschrift richt zich op het middelste compartiment. Dat wil zeggen descensus uteri (verzakking van de baarmoeder, Figuur 2) en vaginatop prolaps (verzakking van de vaginatop, nadat de baarmoeder werd verwijderd, Figuur 3).



Figuur 1. Anatomie vrouwelijke genitalia

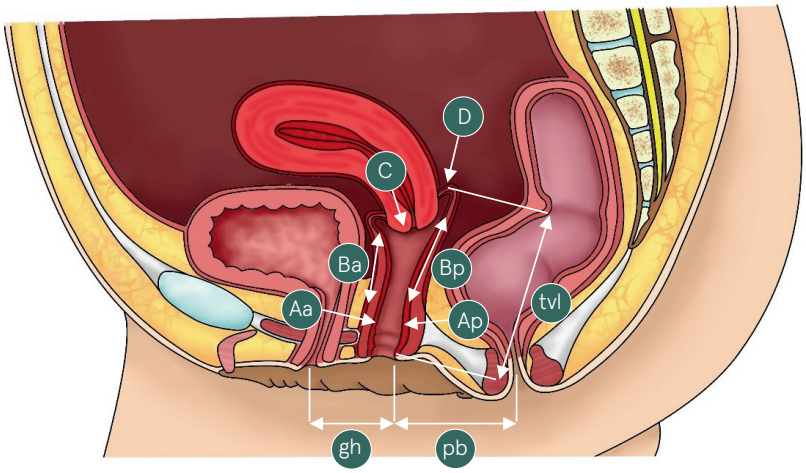


Figuur 2. Descensus uteri



Figuur 3. Vaginatop prolaps

Om een prolaps vast te stellen, wordt onder andere een POP-Q (Pelvic Organ Prolapse Quantification) onderzoek verricht. Bij dit gynaecologische onderzoek vraagt de gynaecoloog aan de patiënte op de handrug te blazen (Valsalva). Hierdoor wordt de prolaps (beter) zichtbaar en kan deze worden gemeten en geclassificeerd worden, van stadium 0 t/m 4. Figuur 4 toont een uitleg van de POP-Q.

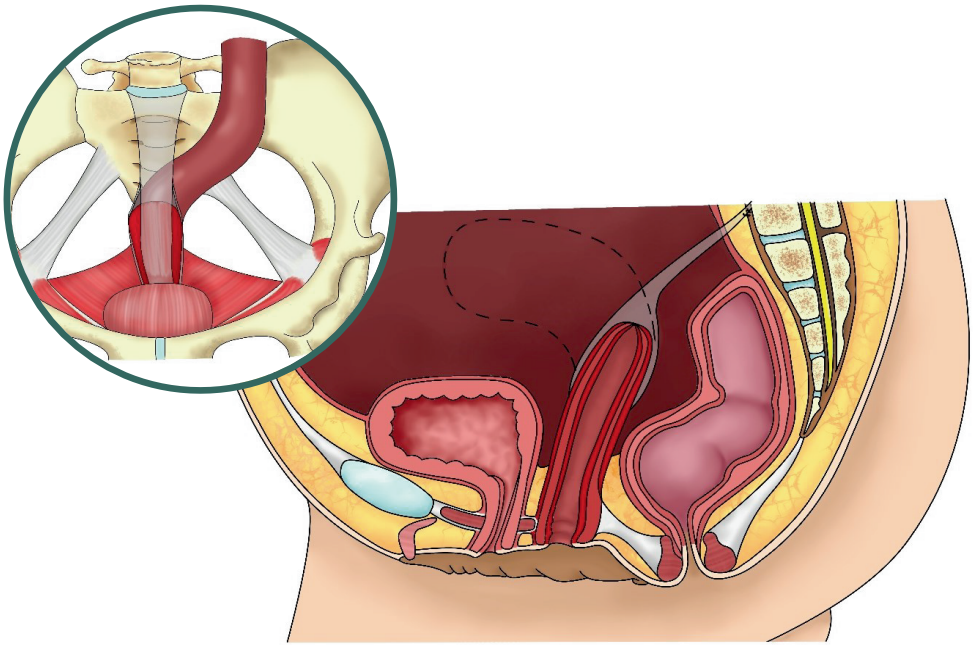


Figuur 4. Pelvic Organ Prolapse Quantification (POP-Q) systeem

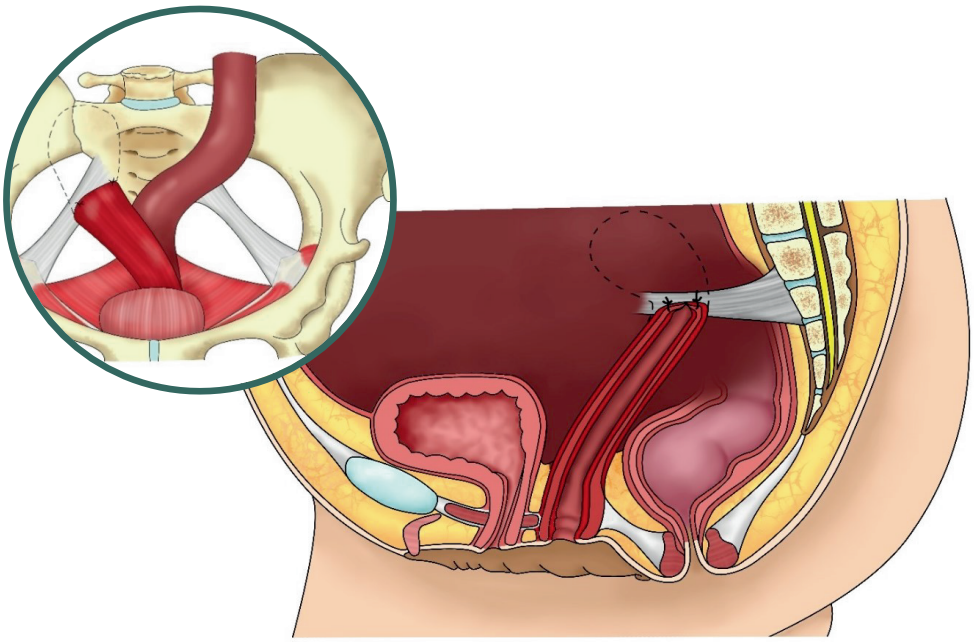
Aa: punt op de vaginavoorwand, 3 cm proximaal van de meatus urethrae (ingang plasbuis).
Ba: het meest distale deel van het bovenste gedeelte van de vaginavoorwand.
C: meest distale deel van de cervix (baarmoederhals).
GH: genitale hiatus, gemeten vanaf de meatus urethrae tot aan middenachter het hymen (maagdenvlies).
PB: perineum, de achterste grens van de hiatus genitalis tot aan de anus.
TVL: totale vaginale lengte, gemeten van het hymen tot punt D.
Ap: punt op de vagina-achterwand, 3 cm proximaal van het hymen.
Bp: het meest distale deel van het bovenste gedeelte van de vagina-achterwand.
D: fornix posterior (hoogste punt achter de baarmoederhals) bij een uterus in situ.

Er zijn verschillende chirurgische behandelopties. Het belangrijkste doel van prolaps chirurgie is het herstellen van de normale anatomie, het oplossen van de verzakkingsklachten en de blaas-, darm- en seksuele functie verbeteren. Ongeveer één op acht vrouwen met genitale prolaps tot een leeftijd van tachtig jaar ondergaat ooit een operatie hiervoor. In dit proefschrift ligt de focus op de volgende chirurgische behandelingen: de sacrocolpopexie, de sacrohysteropexie (Figuur 5), de vaginale sacrospinale fixatie en de vaginale sacrospinale hysteropexie (Figuur 6).

Een sacrocolpopexie is een procedure om een verzakking van de vaginatop te herstellen bij vrouwen die in het verleden een baarmoederverwijdering hebben ondergaan. De operatie herstelt de normale positie en functie van de vagina. Een variant hierop is de sacrohysteropexie die een verzakte baarmoeder corrigeert. Deze ingreep verloopt op vergelijkbare wijze als de sacrocolpopexie. De sacrocolpopexie wordt verricht onder narcose via kijkbuisjes (laparoscopie) of een snede in de buik (laparotomie). Allereerst wordt de vagina van de blaas losgemaakt aan de voorzijde en van de endeldarm aan de achterzijde. Een kunststof matje (mesh) wordt over het vagina oppervlak aan de voor- en achterzijde gelegd en vastgemaakt met hechtingen. De mesh wordt daarna bevestigd aan het heiligbeen (sacrum). Tot slot wordt het matje bedekt door het buikvlies (peritoneum).



Figuur 5. Sacrocolpopexie / Sacrohysteropexie



Figuur 6. Vaginale sacrospinale fixatie / sacrospinale hysteropexie

Een vaginale sacrospinale fixatie of een sacrospinale hysteropexie is een operatie bedoeld om de vaginatop of baarmoeder weer te ondersteunen. Via een snede in de vagina worden eerst hechtingen gelegd door een stevige band (het sacrospinale ligament) in het bekken en daarna door de baarmoederhals of vaginatop. De hechtingen zijn blijvend en onoplosbaar. Het gevormde littekenweefsel ondersteunt de vagina of baarmoeder.

Er is relatief weinig wetenschappelijk bewijs dat aantoont wat de beste behandeling is van descensus uteri en vaginatop prolaps. Het doel van dit proefschrift is te onderzoeken welke behandeling het meest optimaal is voor vrouwen die last hebben van een descensus uteri of vaginatop prolaps, aan de hand van onderstaande vragen:

- Wat zijn de korte en lange termijn uitkomsten van laparoscopische versus laparotomische sacrocolpopexie als behandeling van vaginatop prolaps? (HOOFDSTUK 2 en 3)
- Welke behandeling is het meest optimaal voor patiënten met een descensus uteri, laparoscopische sacrohysteropexie of vaginale sacrospinale hysteropexie? (HOOFDSTUK 4 en 5)

- Welke behandeling is het meest optimaal voor patiënten met een vaginatop prolaps, laparoscopische sacrocolpopexie of vaginale sacrospinale fixatie? (HOOFDSTUK 6 en 7)
- Welke patiënt-gerelateerde en arts-gerelateerde factoren zijn bij Nederlandse gynaecologen van belang wanneer zij patiënten advies geven over een chirurgische behandeling van descensus uteri en vaginatop prolaps? (HOOFDSTUK 8)

Wat zijn de korte en lange termijn uitkomsten van laparoscopische versus laparotomische sacrocolpopexie als behandeling van vaginatop prolaps?

HOOFDSTUK 2 geeft de resultaten weer van de SALTO studie. Dit is een multicenter gerandomiseerd onderzoek, waarbij de laparoscopische sacrocolpopexie (LSC; operatie met kijkbuisjes) met de laparotomische sacrocolpopexie (ASC; operatie via snede in de buik) wordt vergeleken als behandeling van vaginatop prolaps. Aan het onderzoek namen 74 patiënten met een vaginatop prolaps deel, die in aanmerking kwamen voor chirurgische behandeling. Zij werden willekeurig ingedeeld (gerandomiseerd) in de LSC (n = 37) of ASC (n = 37) groep. Follow-up na 12 maanden liet geen verschil zien in ziektespecifieke kwaliteit van leven en prolaps gerelateerde klachten. Patiënten hadden minder bloedverlies en een kortere ziekenhuisopname na de laparoscopische procedure, vergeleken met de laparotomische techniek. Er was geen verschil in het aantal complicaties tussen beide groepen. Eén jaar na de ingreep was er ook geen verschil in anatomische uitkomst. Geen enkele patiënte had noemenswaardige prolaps van het middelste compartiment (POP-Q stadium 2 of hoger). In de LSC groep werden 7 chirurgische re-interventies verricht, vergeleken met 4 in de ASC groep. Dit was niet statistisch significant verschillend. De gecombineerde uitkomstmaat van succes (geen verzakkingsklachten, geen prolaps voorbij het hymen en geen re-interventie) was 83,3% (n = 31) in de LSC groep en 89,2% (n = 33) in de ASC groep. Gezien de resultaten van deze studie, concluderen wij dat de laparoscopische techniek de voorkeur heeft wanneer men een sacrocolpopexie verricht, omdat de uitkomst voor de patiënte vergelijkbaar is, maar gepaard gaat met minder bloedverlies en een kortere opname.

In **HOOFDSTUK 3** worden de lange termijn resultaten van de SALTO studie beschreven. Alle patenten uit de initiële SALTO studie werden uitgenodigd voor deelname in deze vervolgstudie, om de kwaliteit van leven, het anatomisch resultaat en het voorkomen van lange termijn complicaties te onderzoeken. Tweeëntwintig patiënten (61,1%) werden geïncludeerd uit de LSC groep en 19 patiënten (54,3%) uit de ASC groep. De mediane

follow-up duur bedroeg 109 maanden (9,1 jaar). Ziektespecifieke kwaliteit van leven verschilde niet na lange termijn follow-up. Patiënttevredenheid was ook niet statistisch significant verschillend tussen de groepen. Anatomische uitkomsten waren hetzelfde voor beide groepen op alle punten van de POP-Q. De gecombineerde uitkomstmaat van succes voor het middelste compartiment (geen verzakkingsklachten, geen vaginatop prolaps voorbij het hymen en geen re-interventie) is 78,6% (*n* = 11) in de LSC groep en 84,6% (*n* = 11) in de ASC groep. Mesh exposure (wanneer het matje in de vagina bloot komt te liggen) trad op bij twee patiënten (12,5%) in de LSC groep en één patiënte (7,7%) in de ASC groep. Er waren vijf chirurgische re-interventies in beide groepen. Bij lange termijn follow-up werd geen relevant verschil gevonden in kwaliteit van leven, anatomisch resultaat, complicaties en reïnterventies tussen beide groepen. Daarom heeft de laparoscopische benadering de voorkeur boven de laparotomische benadering, gezien de eerder gevonden voordelen na korte termijn follow-up.

Welke behandeling is het meest optimaal voor patiënten met een descensus uteri, laparoscopische sacrohysteropexie of vaginale sacrospinale hysteropexie?

HOOFDSTUK 4 beschrijft de lange termijn uitkomsten van de laparoscopische sacrohysteropexie (LSH) versus de sacrospinale hysteropexie (SSHP) als behandeling van descensus uteri. Het is een retrospectieve studie van patiënten die een LSH ondergingen tussen 2003 en 2013 of een SSHP tussen 2009 en 2011 als primaire behandeling van uterusprolaps. Er werden 105 patiënten geïncludeerd, 53 patiënten in de LSH groep en 52 patiënten in de SSHP groep. De gemiddelde follow-up duur bedroeg 4,5 jaar in de LSH groep en 2,5 jaar in de SSHP groep. Er was geen statistisch significant verschil in de gecombineerde uitkomstmaat van succes (geen verzakkingsklachten, geen prolaps voorbij het hymen en geen re-interventie); 41,4% in de LSH groep, vergeleken met 72,7% in de SSHP groep. Anatomisch falen van het middelste compartiment trad op bij één patiënte in elke groep. Klachten die zouden kunnen passen bij een verzakking, waarvoor patiënten contact zochten met een medisch professional gebeurde in 34,6% van de patiënten in de LSH groep, versus 21,2% in de SSHP groep. Ook werd er geen verschil gevonden in patiënttevredenheid; 75% van de patiënten in de LSH vergeleken met 71,8% van patiënten in de SSHP groep waren tevreden. De gemiddelde operatietijd was langer in de LSH groep (117 minuten) dan in de SSHP groep (67 minuten). De opnameduur was ook langer in de LSH groep (4 dagen) dan in de SSHP groep (3 dagen). We concludeerden dat de LSH en de SSHP beiden nagenoeg even effectieve behandelingen zijn voor descensus uteri.

In **HOOFDSTUK 5** worden de resultaten van de LAVA studie gepresenteerd, een multicenter gerandomiseerd non-inferioriteit onderzoek (type studie die onderzoekt of een alternatieve behandeling niet slechter is dan een bestaande behandeling). In totaal werden 126 patiënten met descensus uteri stadium 2 of hoger geïncludeerd en ondergingen een laparoscopische sacrohysteropexie (LSH; *n* = 64) of een vaginale sacrohysteropexie (SSHP; *n* = 62). LSH was non-inferieur aan SSHP wat betreft chirurgisch falen na 12 maanden follow-up. Dit betekent dat de LSH niet onderdoet voor de SSHP. De behandeling slaagde niet bij 1,65% (*n* = 1) van de patiënten in de LSH groep, versus 3,3% in de SSHP groep (*n* = 2). Er was geen verschil in anatomisch recidief (het opnieuw optreden van prolaps) en kwaliteit van leven. Meer hinderlijke overactieve blaas klachten en fecale incontinentie (ongewenst verlies van ontlasting) werd gerapporteerd na LSH. Dyspareunie (pijn bij gemeenschap) werd vaker gerapporteerd na SSHP. Op basis van de analyse na 1 jaar follow-up, concluderen we dat de LSH non-inferieur is aan SSHP in geval van chirurgisch falen van het apicale compartiment.

Welke behandeling is het meest optimaal voor patiënten met een vaginatop prolaps, laparoscopische sacrocolpopexie of vaginale sacrospinale fixatie?

HOOFDSTUK 6 is het onderzoeksprotocol van de SALTO-2 studie, een gerandomiseerd onderzoek, welke laparoscopische sacrocolpopexie (LSC) vergelijkt met vaginale sacrospinale fixatie (VSF) als behandeling van vaginatop prolaps. Hysterectomie (baarmoederverwijdering) is een van de meest uitgevoerde gynaecologische operaties. Veel vrouwen, die een hysterectomie ondergingen vanwege descensus uteri, komen later in aanmerking voor een operatieve correctie van een vaginatop prolaps. Vrouwen met symptomatische vaginatop prolaps, POP-Q stadium 2 of hoger, kunnen worden geïncludeerd. Patiënten worden willekeurig geloot (gerandomiseerd) tussen LSC en VSF. De primaire uitkomstmaat is ziektespecifieke kwaliteit van leven na 12 maanden follow-up. Secundaire uitkomsten zijn het effect van de chirurgische behandeling op prolaps-gerelateerde klachten, seksueel functioneren, morbiditeit, ziekenhuisopname, postoperatief herstel, anatomische uitkomst (POP-Q), complicaties en re-interventies. Er wordt beoogd 106 patiënten te includeren (53 in elke groep).

In **HOOFDSTUK 7** presenteren we de resultaten van de SALTO-2 studie. Dit is een multicenter gerandomiseerd onderzoek (RCT) met daarnaast een prospectief cohort (groep waarin patiënten worden behandeld volgens hun eigen voorkeur), welke laparoscopische sacrocolpopexie (LSC) vergelijkt met vaginale sacrospinale fixatie (VSF),

als behandeling van vaginatop prolaps. Data van de RCT en het cohort werd eerst separaat geanalyseerd en erna werd een meta-analyse verricht van de primaire uitkomstmaat en de belangrijkste secundaire uitkomstmaten, om de resultaten te combineren. In totaal werden 179 vrouwen geïncludeerd in de studie, van wie 64 werden gerandomiseerd en 115 deelnamen aan het prospectieve cohort. De RCT werd voortijdig gestopt, met name vanwege een sterke voorkeur van de patiënten voor een bepaalde operatie. Na 12 maanden follow-up verschilde ziektespecifieke kwaliteit van leven niet tussen de LSC en VSF in de RCT en in het cohort. De gecombineerde uitkomst van succes voor het middelste compartiment was vergelijkbaar in zowel de RCT als het cohort. Er was geen statistisch significant verschil in het aantal complicaties tussen de LSC en de VSF groep. Ook het aantal re-interventies verschilde niet tussen beide groepen, hoewel er een klinisch relevant verschil leek te zijn tussen chirurgische re-interventies voor het apicale compartiment, in het voordeel van de LSC. Op basis van deze resultaten concludeerden we dat de LSC en de VSF beide effectieve behandelingen zijn voor vaginatop prolaps, na een follow-up duur van 12 maanden.

Welke patiënt-gerelateerde en arts-gerelateerde factoren zijn bij Nederlandse gynaecologen van belang wanneer zij patiënten advies geven over een chirurgische behandeling van descensus uteri en vaginatop prolaps?

De voorkeur van gynaecologen voor een bepaalde chirurgische behandeling beschrijven we in **HOOFDSTUK 8**. Dit zijn de resultaten van een kwalitatieve interview studie. Tien Nederlandse gynaecologen, met speciale interesse in de urogynaecologie, namen deel aan de studie. Alle gynaecologen verrichten vaginale operaties voor apicale prolaps; zeven gynaecologen voeren zelf de sacrocolpopexie uit of het wordt gedaan door een collega in hun ziekenhuis. Zes gynaecologen zouden een VSF adviseren voor een vaginatop prolaps bij vrouwen die niet eerder voor prolaps zijn geopereerd. Drie gynaecologen prefereerden de sacrocolpopexie. Alle deelnemers adviseerden een sacrocolpopexie voor een recidief vaginatop prolaps, dat wil zeggen na een eerdere chirurgische ingreep voor vaginatop prolaps (bijvoorbeeld een VSF). Alle deelnemers vinden meerdere comorbiditeiten eventueel reden om een VSF te verrichten, omdat deze ingreep als minder invasief wordt beschouwd dan een LSC. Meeste deelnemers vinden ook hogere leeftijd (6/10) of hogere BMI (7/10) een reden om een VSF te verrichten. Gynaecologen die niet in hun eigen ziekenhuizen een sacrocolpopexie kunnen verrichten, zijn meer geneigd een VSF te doen en vinden hiervoor ook meer

argumenten. In het geval van een eerste descensus uteri, verrichten alle deelnemers vaginale chirurgie, zonder gebruik van mesh.

Discussie & Impact

HOOFDSTUK 9 beschrijft de algemene discussie, klinische implicaties van dit onderzoek en toekomstperspectieven. Aan de hand van dit proefschrift kunnen de volgende conclusies worden getrokken:

- Laparoscopische sacrocolpopexie heeft de voorkeur ten opzichte van laparotomische sacrocolpopexie, gebaseerd op uitkomsten na korte termijn follow-up. Het aantal recidieven en complicaties zijn vergelijkbaar tussen beide groepen na lange termijn follow-up.
- Laparoscopische sacrohysteropexie en vaginale sacrospinale hysteropexie zijn vergelijkbaar in hun effectiviteit als behandeling van descensus uteri, op basis van de resultaten van een retrospectief onderzoek en een gerandomiseerde studie met één jaar follow-up.
- Laparoscopische sacrocolpopexie en vaginale sacrospinale fixatie zijn beide effectieve chirurgische behandelingen voor vaginatop prolaps na 12 maanden follow-up. Er is mogelijk wel sprake van een klinisch relevant verschil in de chirurgische re-interventies voor het apicale compartiment, in het voordeel van de LSC.
- Nederlandse gynaecologen verschillen van mening over de geprefereerde chirurgische behandeling van prolaps in het apicale compartiment. Ze baseren hun advies op het feit of het een recidief prolaps betreft, de algehele gezondheid van de patiënte en de voorkeur van de patiënte zelf.

Het belang van dit proefschrift en hoe het kan bijdragen aan de wetenschap en de maatschappij, staat beschreven in **HOOFDSTUK 10**. De hoge en toenemende prevalentie van prolaps en de impact van klachten op het leven van een vrouw, maken dit onderzoek relevant. De resultaten van onze studies zijn een toevoeging aan de reeds bestaande literatuur, omdat ze nieuwe informatie tonen, welke gebruikt kan worden bij de uitleg aan patiënten.

CHAPTER 13

List of abbreviations & questionnaires

List of abbreviations

In alphabetical order

ACOG	American college of obstetricians and gynaecologists
ACR	Anterior colporrhaphy
ASC	Abdominal sacrocolpopexy
AUGS	American urogynaecology society
CCMO	Centrale commissie mensgebonden onderzoek
CI	Confidence interval
CONSORT	Consolidated standards of reporting trials
COREQ	Consolidated criteria for reporting qualitative research
CRADI-8	Colorectal-Anal Distress Inventory
DDI	Defaecatory Distress Inventory
EQ-5D	EuroQol questionnaire
EQ-VAS	EuroQol Visual Analog Scale
HUSLS	High uterosacral ligament suspension
ICS	International continence society
IIQ	Incontinence Impact Questionnaire
IQR	Inter quartile range
ITT	Intention to treat
IUGA	International urogynaecology association
LSC	Laparoscopic sacrocolpopexy
LSH	Laparoscopic sacrohysteropexy
LOCF	Last observation carried forward
LUSLS	Laparoscopic uterosacral ligament suspension
LUTS	Lower urinary tract symptoms
METC	Medische ethische toetsingscommissie
MF	Manchester Fothergill
MM	Modified Manchester
MUS	Mid urethral sling
NTR	Nationaal trial register
NVOG	Nederlandse vereniging voor obstetrie en gynaecologie
OAB	Overactive bladder
PCR	Posterior colporrhaphy
PFDI-20	Pelvic floor disability index

PFMT	Pelvic floor muscle training
PGI-I	Patient Global Impression of Improvement
PISQ	Pelvic Organ Prolapse / Urinary Incontinence Sexual Function Questionnaire
POP	Pelvic Organ Prolapse
POPDI-6	Pelvic Organ Prolapse Distress Inventory
POP-Q	Pelvic Organ Prolapse Quantification
PP	Per protocol
QALYs	Quality adjusted life years
RCT	Randomised controlled trial
RR	Relative risk
RSC	Robotic sacrocolpopexy
RSH	Robotic sacrohysteropexy
SCP	Sacrocolpopexy
SD	Standard deviation
SEM	Standard error of the mean
SGS	Society of Gynaecologic Surgeons
SHP	Sacrohysteropexy
SPSS	Statistical Package for the Social Sciences
SSHP	Sacrospinous hysteropexy
SSL	Sacrospinous ligament
STROBE	Strengthening the reporting of observational studies in epidemiology
TAH	Total abdominal hysterectomy
TLH	Total laparoscopic hysterectomy
TOT	Trans obturator tape
TVH	Transvaginal hysterectomy
TVT	Tension free vaginal tape
TVT-O	Tension free vaginal tape - obturator
TVT-S	Tension free vaginal tape - secur
UDI	Urogenital Distress Inventory
UI	Urinary incontinence
VH	Vaginal hysterectomy
VM	Vaginal mesh
VSF	Vaginal sacrospinous fixation
VVP	Vaginal vault prolapse
WBB	Werkgroep bekkenbodem (Dutch urogynaecology workgroup)

Questionnaires

PGI-I (Patient Global Impression of Improvement)

---

*Deze vraag geeft een globale indruk over de mate van verbetering die de behandeling bij u heeft teweeg gebracht. Omcirkel het getal dat het meeste op uw **huidige** situatie van toepassing is.*

U heeft een behandeling ondergaan voor uw plas en / of verzakkingsklachten.
Kies uit het onderstaande rijtje het antwoord dat het beste weergeeft hoe uw situatie **nu** is ten opzichte van de situatie zoals doe was voor dat u werd behandeld.

- ☐ Heel veel beter
- ☐ Veel beter
- ☐ Beetje beter
- ☐ Geen verandering
- ☐ Beetje slechter
- ☐ Veel slechter
- ☐ Heel veel slechter

EQ-5D en EQ-VAS (EuroQol)

De volgende 6 vragen hebben betrekking op uw huidige gezondheidstoestand. Kruis bij elke vraag de zin aan, die het best past bij uw eigen gezondheidstoestand ***vandaag****.*

---

1. Mobiliteit

- ☐ Ik heb geen problemen met lopen
- ☐ Ik heb enige problemen met lopen
- ☐ Ik ben bedlegerig

2. Zelfzorg

- ☐ Ik heb geen problemen om mijzelf te wassen of aan te kleden
- ☐ Ik heb enige problemen om mijzelf te wassen of aan te kleden
- ☐ Ik ben niet in staat mijzelf te wassen of aan te kleden

3. Dagelijkse activiteiten (bv werk, studie, huishouden, gezin- en vrijetijdsactiviteiten)

- ☐ Ik heb geen problemen met mijn dagelijkse activiteiten
- ☐ Ik heb enige problemen met mijn dagelijkse activiteiten
- ☐ Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren

4. Pijn / klachten

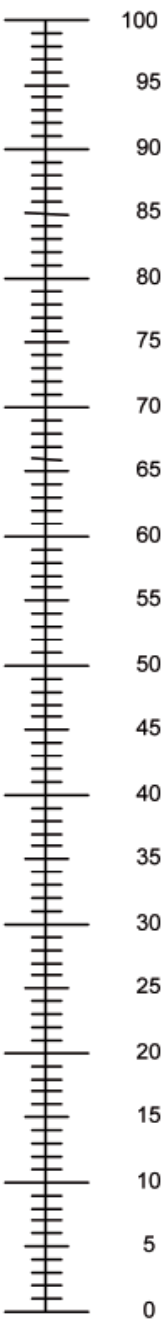
- ☐ Ik heb geen pijn of andere klachten
- ☐ Ik heb matige pijn of andere klachten
- ☐ Ik heb zeer ernstige pijn of andere klachten

5. Stemming

- ☐ Ik ben niet angstig of somber
- ☐ Ik ben matig angstig of somber
- ☐ Ik ben erg angstig of somber

6. Om mensen te helpen bij het aangeven hoe goed of hoe slecht een gezondheidstoestand is, hebben we een meetschaal (te vergelijken met een thermometer) gemaakt. Op de meetschaal hiernaast betekent '100' de beste gezondheidstoestand die u zich kunt voorstellen, en '0' de slechtste gezondheidstoestand die u zich kunt voorstellen.

We willen u vragen op deze meetschaal aan te geven hoe goed of hoe slecht volgens u uw eigen gezondheidstoestand vandaag is. Zet een kruis op de meetschaal welke volgens u aangeeft hoe goed of hoe slecht uw gezondheidstoestand vandaag is.



UDI (Urogenital Distress Inventory)

Vrouwen met ongewenst urineverlies en / of een verzakking hebben aangegeven dat ze de volgende klachten hadden. Kunt u aangeven welke klachten u op dit moment ook heeft en hoeveel last u daar van heeft. Beantwoord svp alle vragen, ook als u geen klachten heeft.

---

1. **a.** Vindt u dat u vaak moet plassen?

☐ Ja ☐ Nee (ga naar vraag 1c)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Hoe veel keer plast u gemiddeld per dag? ..... keer

2. **a.** Als u moet plassen, voelt u dan altijd een sterke aandrang?

☐ Ja ☐ Nee (ga naar vraag 3)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

3. **a.** Hebt u ongewenst urineverlies als u aandrang voelt om te plassen?

☐ Ja ☐ Nee (ga naar vraag 4)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Zo ja, hoe vaak verliest u ongewild urine?

☐ Dagelijks

☐ Paar keer per week

☐ 1 Keer per week

☐ 1 Keer per maand

☐ 1 Keer per jaar

4. **a.** Hebt u ongewenst urineverlies bij lichamelijke inspanning, hoesten of niezen?

☐ Ja ☐ Nee (ga naar vraag 5)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Zo ja, hoe vaak verliest u ongewild urine?

☐ Dagelijks

☐ Paar keer per week

☐ 1 Keer per week

☐ 1 Keer per maand

☐ 1 Keer per jaar

5. **a.** Heeft u wel eens ongewenst urineverlies zonder dat u aandrang voelt of zonder dat u zich lichamelijk inspant?

☐ Ja ☐ Nee (ga naar vraag 6)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

6. **a.** Verliest u ongewenst wel eens kleine hoeveelheden urine (druppels)?

☐ Ja ☐ Nee (ga naar vraag 7)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

7. **a.** Verliest u ongewenst wel eens grote hoeveelheden urine?

☐ Ja ☐ Nee (ga naar vraag 8)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

8. **a.** Hebt u moeite uw blaas leeg te plassen?

☐ Ja ☐ Nee (ga naar vraag 9)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

9. **a.** Hebt u wel eens het gevoel dat de blaas na het plassen niet helemaal leeg is?

☐ Ja ☐ Nee (ga naar vraag 10)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

10. **a.** Hebt u wel eens een drukkend gevoel onder in de buik?

☐ Ja ☐ Nee (ga naar vraag 11)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

11. **a.** Hebt u wel eens pijn onder in de buik of in de schaamstreek?

☐ Ja ☐ Nee (ga naar vraag 12)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

12. **a.** Hebt u wel eens het gevoel dat er iets uit de vagina stulpt?

☐ Ja ☐ Nee (ga naar vraag 13)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

13. **a.** Hebt u wel eens gezien dat er iets uit de vagina stulpt?

☐ Ja ☐ Nee (ga naar vraag 14)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

14. Hoe vaak hebt u het afgelopen jaar een blaasontsteking gehad?

☐ Nooit

☐ 1 Keer

☐ Tussen de 2 en 4 keer

☐ Meer dan 4 keer

15. **a.** Moet u ’s nachts meer dan 1 keer plassen?

☐ Ja ☐ Nee (ga naar vraag 16)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

16. **a.** Plast u wel eens in bed?

☐ Ja ☐ Nee (ga naar vraag 17)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

17. **a.** Heeft u wel eens pijn tijdens het plassen?

☐ Ja ☐ Nee (ga naar vraag 18)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

18. **a.** Heeft u wel eens een zwaar of drukkend gevoel in het bekkengebied?

☐ Ja ☐ Nee (ga naar vraag 19)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

19. **a.** Heeft u wel eens een ongemakkelijk gevoel in het bekkengebied als u staat of als u zich lichamelijk inspant?

☐ Ja ☐ Nee

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

DDI (Defecatory Distress Inventory)

De volgende verschijnselen zijn beschreven door vrouwen met klachten van de stoelgang. Geeft u aan welke verschijnselen u tegenwoordig herkent en hoeveel last u daarvan heeft.

---

1. **a.** Hebt u minder dan driemaal per week ontlasting?

☐ Ja ☐ Nee (ga naar vraag 2)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

2. **a.** Moet u om ontlasting te krijgen in meer dan een kwart van de keren persen?

☐ Ja ☐ Nee (ga naar vraag 3)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

3. **a.** Hebt u wel eens aandrang tot ontlasting terwijl er dan op het toilet geen ontlasting komt?

☐ Ja ☐ Nee (ga naar vraag 4)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

4. **a.** Hebt u wel eens het gevoel dat er iets uit de anus hangt of er iets voor zit?

☐ Ja ☐ Nee (ga naar vraag 5)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

5. **a.** Ervaart u pijn tijdens de aandrang tot ontlasting?

☐ Ja ☐ Nee (ga naar vraag 6)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

6. **a.** Ervaart u pijn tijdens of vlak na de ontlasting?

☐ Ja ☐ Nee (ga naar vraag 7)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

7. **a.** Verliest u wel eens dunne ontlasting zonder dat u daar controle over heeft?

☐ Ja ☐ Nee (ga naar vraag 8)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Hoe vaak komt het voor?

☐ Dagelijks

☐ Paar keer per week

☐ 1 Keer per week

☐ 1 Keer per maand

☐ 1 Keer per jaar

8. **a.** Verliest u wel eens vaste ontlasting zonder dat u daar controle over heeft?

☐ Ja ☐ Nee (ga naar vraag 9)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Hoe vaak komt het voor?

☐ Dagelijks

☐ Paar keer per week

☐ 1 Keer per week

☐ 1 Keer per maand

☐ 1 Keer per jaar

9. **a.** Verliest u wel eens windjes zonder dat u daar controle over heeft?

☐ Ja ☐ Nee (ga naar vraag 10)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

c. Hoe vaak komt het voor?

☐ Dagelijks

☐ Paar keer per week

☐ 1 Keer per week

☐ 1 Keer per maand

☐ 1 Keer per jaar

10. **a.** Moet u wel eens via de schede mee drukken om ontlasting te krijgen?

☐ Ja ☐ Nee (ga naar vraag 10)

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

11. **a.** Moet u de ontlasting wel eens met de vingers via de anus verwijderen?

☐ Ja ☐ Nee

b. Zo ja, hoeveel last heeft u hier van?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

IIQ (Incontinece Impact Questionnaire)

Sommige vrouwen vinden dat ongewenst urineverlies en / of een verzakking en / of problemen met de ontlasting hun activiteiten, relaties en gevoelens kunnen beïnvloeden. De vragen in onderstaande lijst gaan over aspecten van uw leven die door uw probleem beïnvloed of veranderd kunnen zijn. Geef voor iedere vraag het antwoord aan dat het beste beschrijft hoe zeer uw activiteiten, relaties en gevoelens beïnvloed worden door uw urineverlies en / of verzakking en / of problemen met de ontlasting.

Hoeveel invloed heeft ongewenst urineverlies en / of verzakking en / of problemen met de ontlasting gehad op:

1. Uw vermogen om huishoudelijk werk te doen (koken, schoonmaken, wassen)
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

2. Uw vermogen om klein onderhoud of reparaties te verrichten in en om het huis
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

3. Boodschappen doen en winkelen
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

4. Reizen met auto of openbaar vervoer over een afstand van minder dan 20 minuten
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

5. Ergens naar toe gaan als u niet helemaal zeker weet of er daar toiletten zijn
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

6. Bezoek krijgen van vrienden en kennissen
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

7. Relaties met vrienden en kennissen
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

8. Vermogen om een seksuele relatie te hebben
☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

9. Geestelijke / emotionele gezondheid

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

10. Wordt u in uw activiteiten beperkt door angst dat anderen u ruiken?

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

Hebt u als gevolg van uw probleem de volgende gevoelens?

11. Nervositeit of ongerustheid

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

12. Frustratie

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

13. Zich gegeneerd voelen

☐ Helemaal niet ☐ Een beetje ☐ Nogal ☐ Heel erg

PISQ-12 (Pelvic Organ Prolapse/Urinary Incontinece Sexual Function Questionnaire)

De volgende vragen gaan over het seksueel leven van u en uw partner. Alle informatie is strikt vertrouwelijk. Uw vertrouwelijke antwoorden zullen alleen worden gebruikt om artsen inzicht te geven in wat belangrijk is voor patiënten in hun seksueel leven. Kruist u alstublieft het hokje aan dat voor u het beste antwoord is op de vraag. Bij het beantwoorden van de vragen gaat u uit van uw seksueel leven van de afgelopen 6 maanden.

---

1. Bent u seksueel actief?

☐ Ja (ga verder met het invullen van de vragenlijst)

☐ Nee (de volgende vragen zijn niet voor u van toepassing)

2. Hoe vaak verlangt u naar seks? Dit verlangen kan bestaan uit het willen hebben van seks, het plannen van seks, gevoelens van frustratie door een gebrek aan seks, enzovoorts.

☐ Dagelijks

☐ Wekelijks

☐ Maandelijks

☐ Minder dan 1 keer per maand

☐ Nooit

3. Heeft u een orgasme tijdens geslachtsgemeenschap met uw partner?

☐ Altijd

☐ Meestal

☐ Soms

☐ Zelden

☐ Nooit

4. Voelt u zich seksueel opgewonden tijdens seksuele activiteiten met uw partner?

☐ Altijd

☐ Meestal

☐ Soms

☐ Zelden

☐ Nooit

5. Hoe tevreden bent u ver de afwisseling in seksuele activiteiten in uw huidige seksleven?

☐ Zeer tevreden
☐ Redelijk tevreden
☐ Noch tevreden, noch ontevreden
☐ Redelijk ontevreden
☐ Zeer ontevreden

6. Heeft u pijn tijdens geslachtsgemeenschap?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

7. Heeft u ongewenst urineverlies tijdens seksuele activiteiten?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

8. Wordt u in uw seksuele activiteiten beperkt door angst voor ongewenst verlies van ontlasting of urine?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

9. Vermijdt u geslachtsgemeenschap vanwege een uitstulping in de vagina (verzakking van blaas, endeldarm of vagina)?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

10. Wanneer u seks heeft met uw partner, heeft u dan negatieve emotionele reacties, zoals angst, afkeer, schaamte of schuldgevoel?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

11. Heeft uw partner een erectieprobleem dat uw seksuele activiteiten beïnvloedt?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

12. Heeft uw partner een probleem met voortijdige zaadlozing dat uw seksuele activiteiten beïnvloedt?

☐ Altijd
☐ Meestal
☐ Soms
☐ Zelden
☐ Nooit

13. Hoe intens zijn de orgasmen die u in de afgelopen 6 maanden heeft gehad in vergelijking met orgasmen in het verleden?

☐ Veel minder intens
☐ Minder intens
☐ Dezelfde intensiteit
☐ Meer intens
☐ Veel meer intens

14. **a.** Bent u tevreden met uw seksueel functioneren?

☐ Ja, ik ben tevreden

☐ Nee (ga door met vraag 14.b.)

b. Levert dit stress op voor u en / of stress in uw relatie?

☐ Altijd

☐ Meestal

☐ Soms

☐ Zelden

☐ Nooit

PFDI-20 (Pelvic Floor Disability Index)

	Klachten	Nee	Ja, maar geen last van	Ja, beetje last van	Ja, behoorlijk last van	Ja, veel last van
1.	Heeft u gewoonlijk een drukkend gevoel onder in de buik?					
2.	Heeft u doorgaans een zwaar of doof gevoel in het bekkengebied?					
3.	Heeft u gewoonlijk een uitstulping of komt er iets naar buiten, dat u kunt zien of voelen in het gebied van uw vagina?					
4.	Moet u doorgaans op de vagina of rond de endeldarm drukken om ontlasting te hebben of om het af te kunnen maken?					
5.	Heeft u gewoonlijk het gevoel dat u uw blaas niet volledig leeg plast?					
6.	Heeft u ooit met uw vingers op een uitstulping moeten drukken in het gebied van de vagina om te kunnen plassen of om het plassen af te kunnen maken?					
7.	Heeft u het gevoel dat u te veel moet persen om ontlasting te kunnen hebben?					
8.	Heeft u het gevoel dat uw darmen nog niet helemaal leeg zijn na de ontlasting?					
9.	Heeft u gewoonlijk ongecontroleerd ontlastingverlies als uw ontlasting goed gevormd is?					

10.	Heeft u gewoonlijk ongecontroleerd ontlastingverlies als uw ontlasting dun is?					
11.	Heeft u gewoonlijk ongecontroleerde winderigheid uit uw endeldarm?					
12.	Heeft u doorgaans pijn tijdens de ontlasting?					
13.	Ervaart u een sterk aandranggevoel en moet u zich haasten naar het toilet voor de ontlasting?					
14.	Komt een deel van uw darmen wel eens door de anus en stulpt die uit tijdens of na de ontlasting?					
15.	Moet u gewoonlijk vaak plassen?					
16.	Heeft u doorgaans urineverlies dat verband houdt met een gevoel van aandrang; oftewel een sterk gevoel dat u naar het toilet moet gaan?					
17.	Heeft u gewoonlijk urineverlies dat verband houdt met hoesten, niezen of lachen?					
18.	Heeft u doorgaans kleine hoeveelheden urineverlies (druppels)?					
19.	Heeft u gewoonlijk moeite uw blaas te legen?					
20.	Heeft u doorgaans pijn of ongemak in de onderbuik of rond het kruis?					

CHAPTER 14

Publications, acknowledgements & curriculum vitae

Publications

Journals

A.M.J. van Oudheusden, M. Weemhoff, L.F. Menge, B.A.B. Essers. Gynaecologists' perspectives on surgical treatment for apical prolapse: a qualitative study. International Urogynaecology Journal. 2023. Online publication ahead of print.

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Dankwoord (Acknowledgements)

Het is voltooid! Er waren momenten waarop dit punt ontzettend ver weg leek, maar het is gelukt en daar ben ik onwijs blij mee. Uiteraard was dit nooit geslaagd zonder de hulp en input van vele mensen.

Allereerst wil ik graag alle **patiënten** bedanken voor deelname aan de studies. Het is niet niks het lot te laten bepalen welke ingreep je ondergaat. Bedankt voor het invullen van alle vragenlijsten en de bezoeken aan het ziekenhuis.

Professor dr. M.Y. Bongers, Marlies, veel dank voor je eindeloze geduld en motiverende begeleiding. Wat is het fijn om één van jouw promovendi te zijn, jij gaat voor ons door het vuur. Al sinds mijn tijd als semi-arts voel ik me door jou gesteund en heb je me altijd van eerlijk en nuttig advies voorzien. De snelheid waarmee je reageert op mijn mails en berichtjes is ongelooflijk; hiermee zorg je ervoor dat het tempo hoog blijft en er geen onnodige vertraging ontstaat.

Dr. A.L.W.M. Coolen, Anne Lotte, al sinds onze eerste ontmoetingen in Thailand en op het ULV maak je me enthousiast voor de (uro)gynaecologie. Zoals jij al in je eigen dankwoord schreef, hebben we inderdaad andere talenten binnen de wetenschap, waarmee we elkaar goed aanvullen en laten we die in de toekomst blijven benutten in een fijne samenwerking.

Dr. S.M.J. van Kuijk, Sander, sinds jouw betrokkenheid bij dit project ging alles aanzienlijk vlotter. Met jouw hulp hebben de analyses de juiste statistische benadering gekregen en je weet het ontzettend geduldig en begrijpelijk uit te leggen. Daarnaast geef je parels van feedback, zoals: 'hysterectomie veroorzaakt POP, en wordt behandeld door hysterectomie?' en 'absence of evidence is not evidence of absence.'

Drs. J. Veen, Joggem, de eerste stappen in de urogynaecologie zette ik bij jou. Zo leerde ik onder andere dat bepaalde POP-Q metingen simpelweg onmogelijk zijn. Jouw 'opvoeding' op de verloskamers heeft er o.a. voor gezorgd dat geen enkele patiënte zonder rectaal toucher postpartum de deur uit gaat. Veel dank voor jouw kritische en originele feedback op de artikelen, hier werden ze inhoudelijk echt beter van.

Dr. M. Weemhoff, Mirjam, hoewel geen officiële rol, ben je gedurende een groot deel van het traject van dichtbij betrokken geweest. Altijd kon ik bij jou terecht om even te sparren

over het onderzoek of andere zaken, zoals carrière keuzes en sollicitaties. Onze preferentiestudie was heel leuk om te doen en het is een mooi stuk geworden.

Beoordelingscommissie **prof. dr. R.F.P.M. Kruitwagen**, **prof. dr. N.D. Bouvy**, **dr. K.J.B. Notten** en **prof. dr. C.H. van der Vaart**, hartelijk dank voor het kritisch lezen en beoordelen van mijn manuscript.

Alle **coauteurs**, veel dank voor jullie hulp tijdens de studies en jullie input voor de artikelen. **Gynaecologen van de preferentiestudie** (CHAPTER 8), dank jullie wel voor de boeiende en interessante gesprekken over de chirurgische behandeling van apicale prolaps. **Mèlanie van IJsselmuiden**, super dat we zowel de LAVA als de SALTO-2 in het BJOG hebben gepubliceerd!

Paranimfen **Anouk van den Bosch** en **Lieke Claassen**, afgelopen jaren hebben we vele life events gedeeld samen en staan we altijd voor elkaar klaar. Het is dan ook fantastisch dat jullie op 10 oktober aan mijn zijde staan als paranimf. We hebben elkaar leren kennen tijdens onze studententijd in Maastricht en ik zou het hele dankwoord kunnen vullen met mooie herinneringen uit die tijd en ook erna. Intussen hebben jullie zelf ook besloten te gaan promoveren en ik verheug me natuurlijk al op jullie promoties!

Al sinds 2012 is de **Zeikerds** een inspirerende onderzoeksgroep. Inmiddels zijn we letterlijk en figuurlijk gegroeid en hebben we verschillende samenwerkingen met collega's uit het land. Fijn om hier deel van te mogen zijn. **Carolien Vermeulen**, ik kijk uit naar jouw promotie volgend jaar! **Ingrid van Hooff**, hartelijk dank voor de hulp bij de logistiek van de SALTO studies, je bent een topper en onmisbaar voor onderzoekers in het MMC!

(WESP) studenten **Hilde Hoskam**, **Ivon Terink**, **Evi Swolfs**, **Leah Menge** en **Josephine Eissing**. Veel dank voor jullie bijdrage aan de onderzoeken en de artikelen in dit proefschrift. Dankzij jullie hulp kwam dit boek steeds verder richting de eindstreep.

Marloes Sijm, dank je wel voor de mooie stationary voor mijn promotie, stelling 10 wordt hiermee probleemloos verdedigd. **Cas van Cruchten**, dank je wel voor de prachtige illustraties voor de inleiding en de samenvatting van dit proefschrift. Hierdoor is het ook voor niet-medici duidelijk waar dit onderzoek over gaat.

Kees van den Bosch en **Julia Rupert**. Dank jullie wel voor het lezen van het voorwoord en de samenvatting en jullie kritische feedback hierop.

Collega-AIOS, in het bijzonder onze intervisie groep en Zuyderland opleidingsmaatjes **Nicole Alers**, **Anouk van den Bosch**, **Suzanne Dedden**, **Jeanny de Groot**, **Imke Kessels**, **Dorien Koppes**, **Guusje de Krom**, **Julia van der Meulen** en **Anne van Tetering**. Het is superfijn om met jullie alle perikelen van ons werk te delen, ingrijpende situaties te bespreken en elkaar te stimuleren in onze carrières. Laten we dit samen voortzetten! Nicole, dank voor je kritische blik op de lay-out van dit proefschrift, fijn dat jij hierin minstens net zo perfectionistisch bent als ik.

Mentoren **Jacques Maas**, **Anika Dam**, **Paul Kampschöer**, **Lennie van Hanegem** en **Jan Willem van der Steeg**. Allemaal waren jullie op een ander moment in mijn carrière, en ook in mijn leven, betrokken bij dit traject. Veel dank voor jullie eerlijke en inspirerende adviezen, voor jullie luisterend oor en de heerlijke etentjes! Jan Willem, jouw idee om 3 maanden schrijftijd in te zetten in het laatste jaar van de opleiding was precies wat ik nodig had om dit project tot een goed einde te brengen.

Gynaecologen, arts-assistenten, verloskundigen en verpleegkundigen van het **Máxima MC**, **VieCuri MC**, **Zuyderland MC**, **Maastricht UMC+** en het **Jeroen Bosch Ziekenhuis**. Heel erg bedankt voor de fijne ANIOS- en opleidingstijd. Jullie begeleiding en onze samenwerking heeft me gevormd tot de gynaecoloog die ik nu ben.

Vakgroep Gynaecologie van het VieCuri MC, **Roosmarie de Bie**, **Dieuwke Boskamp**, **Petra Bourdrez**, **Claire La Chapelle**, **Rafli van de Laar**, **Frouke Notten**, **Annemieke van Wijck** en **Ella Wijnen**. Dank jullie wel voor de fijne start in Venlo (zowel als ANIOS, AIOS en recent als gynaecoloog) en voor de ruimte om mijn proefschrift af te ronden. Claire, het is fijn dat je ook zo gemotiveerd en enthousiast bent om de bekkenzorg in het VieCuri verder vorm te geven. Ons eerste gezamenlijke IUGA-congres belooft veel moois voor toekomstige congressen!

Lieve **vrienden** en **familie**, hoewel er niet per se een direct verband is tussen jullie en dit onderzoek, zijn de momenten met elkaar van onschatbare waarde. Door alle ontspannen borrels, etentjes, weekendjes weg, vakanties en nog veel meer, lukt het om op de andere momenten hard te werken en maximaal te shinen. Ik realiseer me dat onderstaande lijst niet compleet is.

Voetbalvrouwen **Anouk**, **Charlotte**, **Elles**, **Julia** en **Lieke**. Ik ben super dankbaar voor onze fijne vriendschap. Iedereen is heel anders en dat maakt het juist heel leuk. De groep wordt sinds 2020 langzaam uitgebreid met Pieter, Jonne, Joep, Cleo en binnenkort nog een meisje, bijzonder om deze life events samen te kunnen delen.

Werkgroep INKOM 2012, **Arno**, **Sjanneke**, **Martijn** en **Jochem**. 2012 blijft voor altijd een bijzonder jaar, een aaneenschakeling van hoogtepunten en geweldige herinneringen. Hoewel het plaatsvond voorafgaand aan dit promotietraject, heb ik veel dingen geleerd en meegenomen in mijn latere carrière. De frequentie van onze WGI 2012-dagen is weliswaar wat afgenomen, maar als we elkaar zien is het altijd een feestje!

Ellis en **Ton**, dank jullie voor de onvoorwaardelijke steun die jullie me altijd hebben gegeven. Toen ik m'n studie geneeskunde een jaar wilde stoppen voor een fulltime bestuursjaar waren al mijn voorbereide argumenten niet meer nodig, maar ging mama me juist overtuigen waarom ik dit inderdaad moest gaan doen en papa had blindelings vertrouwen in het hele plan, hoe bijzonder is dat! En ook op andere momenten hebben jullie me altijd gesteund in wat ik wilde gaan doen, als ik er maar gelukkig van werd. Nooit werd ik afgeremd of spraken jullie hardop je twijfels uit. Dit heeft er mede voor gezorgd dat ik sta waar ik nu sta. **Chris**, 'amice', dankjewel dat je zo een fijne bonusvader bent. Ik geniet van onze discussies en gesprekken over zeer uiteenlopende onderwerpen, waarbij ons gezamenlijke talent als amateur-psychiater tot de hoogtepunten behoort. **Max**, we zijn heel verschillend en bewandelen een ander pad, maar ik ben dankbaar voor onze fijne band en dat we er voor elkaar zijn!

Omi en **Papoe**, wat ontzettend fijn dat jullie er zijn. Ook door jullie heb ik me altijd in mijn keuzes gesteund en gestimuleerd gevoeld. Dankzij het enthousiasme van Papoe ben ik in Maastricht gaan studeren, want: 'wat moest ik nou toch, daar helemaal in Limburg?'

Ton en **Eugenie**, **Wendy** en **Huub**, dank voor het warme welkom in jullie familie en de interesse in mijn werk en onderzoek.

Lieve **Eric**, het is superfijn samen met jou te zijn! Qua promotietraject ben je op het goede moment ingestapt en was je bij de successen om deze samen te vieren. Toen jij zag dat mijn onderzoek in een stroomversnelling kwam gedurende de 3 maanden schrijftijd tijdens mijn opleiding, stelde jij voor om extra verlof op te nemen, zodat het daadwerkelijk binnen afzienbare tijd af zou komen. Dank voor je support en stimulatie om het beste uit mezelf te halen. Met jou is het leven een feestje en daarmee voel ik me heel rijk.

Curriculum Vitae

Anique van Oudheusden werd geboren op 6 januari 1988 te Goirle. In 2006 slaagde ze voor het Atheneum aan het Mill-Hill College te Goirle. Zij begon datzelfde jaar met de studie Geneeskunde aan de Universiteit van Maastricht. Voor haar keuze-coschap ging zij in 2009 naar Maleisië, alwaar zij een stage Obstetrie en Gynaecologie volgde. Tussen het vijfde en zesde jaar van de studie was Anique voorzitter van Werkgroep INKOM 2012; een fulltime bestuursjaar in opdracht van de Universiteit van Maastricht. Zij voltooide haar opleiding tot basisarts in oktober 2013 in het Máxima MC te Veldhoven met een semi-arts stage in de urogynaecologie. Hier startte zij met het onderzoek, wat uiteindelijk heeft geleid tot dit proefschrift. Aansluitend begon zij daar als ANIOS (arts-assistent niet-in-opleiding) Obstetrie & Gynaecologie. Zij vervolgde haar carrière in het VieCuri MC te Venlo. In januari 2016 startte zij met de opleiding tot gynaecoloog in het Zuyderland MC te Heerlen (opleiders dr. P.E.A.M. Mercelina-Roumans en dr. H.J.M.M. Mertens). Het tweede en derde jaar van de opleiding werd voortgezet in het Maastricht UMC+ (opleider prof. dr. R.F.P.M. Kruitwagen). In 2019 won zij de award voor 'Clinicus van het jaar', verkozen door coassistenten tot beste begeleider van het coschap moeder-kind (arts-assistent, academisch). Ze keerde gedurende 2 jaar terug naar het Zuyderland MC (opleider dr. M.M.L.H. Wassen) en differentieerde in de urogynaecologie. De opleiding continueerde zij in het Jeroen Bosch Ziekenhuis te 's-Hertogenbosch (opleider dr. I.P.M. Gaugler-Senden) met een differentiatie minimaal invasieve chirurgie. De opleiding rondde zij af in het VieCuri MC te Venlo (opleider dr. I. Van Gestel) in augustus 2022. Sinds 1 maart 2023 werkt zij daar als gynaecoloog met aandachtsgebieden urogynaecologie en minimaal invasieve chirurgie. Anique woont samen met Eric in Sittard.

Urogynaecological Research Group
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