Valorisation

Addendum

Valorisation:

“the process of creating value from knowledge, by making knowledge suitable and/or available for social (and/or economic) use and by making knowledge suitable for translation into competitive products, services, processes and new commercial activities” (Maastricht promotie-reglement, 2013).
The primary goal of this paragraph is to highlight the social and economic relevance and value of the improvement of QOR and reduction of APSP after surgery as reported in this thesis. In this context we will first address the social and economic burden of poor Quality of Recovery (QOR) and Acute Postsurgical Pain (APSP) after day surgery. From this, we will describe the potential and value of our findings in view of the improvement of QOR and reduction of APSP after day surgery, not only for health care policy makers but also for outpatient clinic managers, individual surgeons and anaesthesiologists. It needs to be emphasized that our findings in the field of pre-operative prediction of APSP after day surgery and our insights in the field of pain medication adherence after day surgery may be the base for future policy change. Finally, we will discuss the innovative aspects of this thesis and the steps we have taken to disseminate our findings not only in scientific literature but also into daily practice in Dutch and Belgian outpatient clinics.

Social and economic burden of poor QOR and protracted APSP after day surgery

From Figure 1 in the introduction of this thesis (Chapter 1) we can conclude that poor QOR and protracted APSP after day surgery are both characterized by various dimensions including a significant social dimension. Furthermore, the impact of poor QOR and protracted APSP on psychosocial outcome cannot be underestimated. Poor QOR and protracted APSP may elicit anxiety or depression and may interfere with the mobility and self-care of the patient which can impede the development and maintenance of social relationships.
It is easily understandable that improving QOR and reducing APSP after day surgery will reduce health-care costs and will have a beneficial effect on social outcome after day surgery. Then the first objective must be to measure the effect of various procedures to control and eventually improve QOR and reduce APSP. Thus, our objective in the first part of this thesis was to assess QOR and APSP four days after a wide range of surgical procedures performed in an ambulatory setting (Chapter 2) \(^1\).

The results of the study presented in Chapter 2 \(^3\) suggest that QOR four days after day surgery is poor in almost half of all patients (47.8%) and good in only a minority of patients (17.3%). The analysis of QOR also shows a clear procedure-related variation (Chapter 2) \(^3\). In selected groups such as shoulder surgery, laparoscopic cholecystectomy and hernia repair, the incidence of poor outcome is even higher than 47.8%. Furthermore, almost 40% of all patients
have mobility problems, more than 30% of patients experiences problems with self-care and more than 60% with usual activities after day surgery. A minority of patients expresses concerns related to anxiety/depression.

The results of the additional material, presented in the addendum of Chapter 2 (p50), suggest that the prevalence of outpatients suffering moderate to severe APSP four days after day surgery is still very high. There also is a clear procedure-related variation in incidence of moderate to severe APSP. In selected groups such as shoulder surgery and bone surgery, even more than 55% of patients experiences moderate to severe pain four days after day surgery.

Consequently, as related to objective 1 we conclude that there is a huge potential for reducing health-care costs and increasing the beneficial effect on social outcome after day surgery by improving QOR and reducing APSP.

**Prediction models and adherence to pain therapy in relation to improvement of QOR and reduction of APSP after day surgery**

In the second part of this thesis, we tried to develop and test the role of prediction and prediction models as well as the adherence to pain therapy as new strategies to reduce APSP and, in a more protracted way, to improve QOR after day surgery (Chapters 3 to 5).

Chapter 3 describes the external validation of a previously published prediction model to pre-operatively detect those patients at risk for moderate to severe acute postoperative pain (APSP) after day surgery. Since we were not able to directly validate the previously published model, we first improved this model and then internally validated this improved version of the model. This improved prediction model will be valuable when implemented in the regular preoperative anesthesia evaluation of the outpatient. Identification of patients at high risk for moderate to severe APSP enables the physician to plan a tailor-made effective postoperative analgesic regimen and a more comprehensive follow-up program for these patients. In practice, this includes use of multi-modal analgesic techniques, regular telephone follow-up and even planned overnight stay. Moreover, it enables better patient information provision and adequate use of resources for selected patients with increased risk profile. Thus, health care policy makers should advocate for the implementation of our improved prediction model in daily practice. This can be achieved with the development of a convenient medical soft-
ware application. After input of not only patient demographics, but also other patient-related predictive factors as well as data related to the type of surgery, this application can easily calculate the risk for APSP with the regression formula of the modified prediction model (see Chapter 3).

Based on the results of our study on prevalence of patient non-adherence and partial adherence to acute pain therapy at home after day surgery (Chapter 4), we advocate implementation of interventions to improve analgesic adherence such as better patient education, telephone follow-up, electronic reminders and monitoring systems, e.g. Short Message Service text messaging and real-time medication monitoring linked to smart pill containers. Regular assessments of analgesic adherence by telephone follow-up also have the advantage that it can be combined with assessments of pain relief by prescribed analgesics. If necessary, analgesic therapy can be tailored to individual patient needs.

Although a combination of paracetamol with non-steroidal anti-inflammatory drugs (NSAID’s) and weak opioids as rescue analgesics is the current gold standard in multimodal pain treatment for patients at home after painful day surgery, there are still some limitations. A major limitation is the fact that NSAID’s cannot be prescribed in up to 25% of all patients because of numerous contraindications. Obviously, these patients are at risk and without alternative pain treatment options will likely suffer from prolonged moderate to severe pain after painful day surgery. This prolonged APSP and resulting poor QOR will have a significant negative economic and social impact on the patient. Hence, we present the results of a randomised controlled trial comparing clinical efficacy, patient satisfaction and side-effect profile of an analgesic regimen based on paracetamol and Controlled Released (CR) oxycodone with an analgesic regimen based on paracetamol with NSAID’s for pain treatment at home after painful day surgery. As the alternative pain treatment of paracetamol/CR oxycodone for either 1 or 2 days was found to be equally effective in reducing postoperative pain as compared to a combination of the present gold standard (paracetamol/NSAID) with comparable patient satisfaction level, we suggest that paracetamol/CR oxycodone should be included in the guidelines for postoperative pain treatment. Paracetamol/CR oxycodone pain treatment at home may act as a valuable alternative for the current paracetamol/NSAID gold standard, particularly in patients with a contraindication for NSAID’s.
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Clinicians are increasingly reluctant to prescribe opioids for pain relief at home after day surgery in an attempt to avoid respiratory depression and to minimize the risk for opioid-related side-effects and the emergence of an opioid addiction. Consequently, it is pivotal to expand the arsenal of non-opioid analgesics for pain relief at home after day surgery. Therefore, in the third part of this thesis, we proposed a study protocol for a double-blind, randomized controlled, non-inferiority trial comparing a combination of metamizole and paracetamol to a combination of ibuprofen (an NSAID) and paracetamol in the treatment of APSP at home after painful day surgery.

Innovative aspects and transfer of knowledge

Innovative aspects of the various studies in this thesis can easily be summarized: Chapter 2 describes the first study to date to analyze a wide spectrum of possible predictors of poor QOR after day surgery, including patient characteristics, type and duration of surgery and anesthesia, social and psychological factors. An improved prediction model to pre-operatively detect those patients at risk for moderate to severe acute postoperative pain (APSP) after day surgery is presented in Chapter 3. Chapter 4 presents the first large prospective cohort study to date assessing both prevalence and possible predictors of patient non-adherence to pharmacological acute pain therapy at home after day surgery. The assessment of the efficacy of CR oxycodone for pain treatment at home after painful day surgery as described in Chapter 5 is new. The study protocol presented in Chapter 6 is the first study protocol to date dedicated to assess if a combination of metamizole and paracetamol is non-inferior to a combination of ibuprofen (an NSAID) and paracetamol in the treatment of APSP at home after painful day surgery.

These innovative and new findings on prevalence and prediction of APSP and QOR but also of non-adherence to pain therapy have been published in peer-reviewed papers and presented at various scientific meetings (the European Anaesthesiology Congresses in Berlin (2015) and in London (2016)). All research as described in this thesis has been published as open access articles to promote the dissemination of the knowledge among the scientific community.
With respect to the implementation of our results we are in search of funding to finance the development of a medical software application that allows to calculate the risk for APSP based on the regression formula of the improved prediction model. We are also in close contact with the guideline steering committee of the Dutch Society of Anesthesiology, the Society of Anesthesia and Resuscitation of Belgium and the Belgian Society of Ambulatory Surgery. These organizations translate the latest evidence into guidelines for practical use. These guidelines need to be implemented and are consequently used by anesthesiologists and outpatient clinic managers as a reference for treating patients and organizing care in an ambulant setting. Our goal is to further implement the use of a medical software application in daily practice in Dutch and Belgian outpatient clinics which then allows a very precise calculation of the risk for development of APSP. Those patients with a calculated high risk for APSP will then be treated with multi-modal analgesic techniques. At the same time those patients will receive regular telephone follow-up, will receive interventions to improve analgesic adherence such as better patient education, and will receive electronic reminders and monitoring systems, e.g. Short Message Service text messaging and real-time medication monitoring linked to smart pill containers.

In conclusion: the implementation of the innovative aspects as described in this thesis are likely to result in further improvement of QOR and reduction of APSP after day surgery. This in turn will significantly reduce health-care costs and will have a beneficial effect on social outcome after day surgery. Furthermore, better outpatient care may further extend the criteria for performing very complex and painful procedures in an ambulatory setting and as a result will also have a cost-saving effect.
References