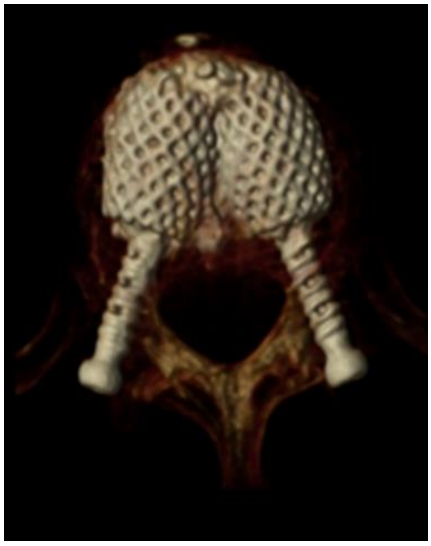
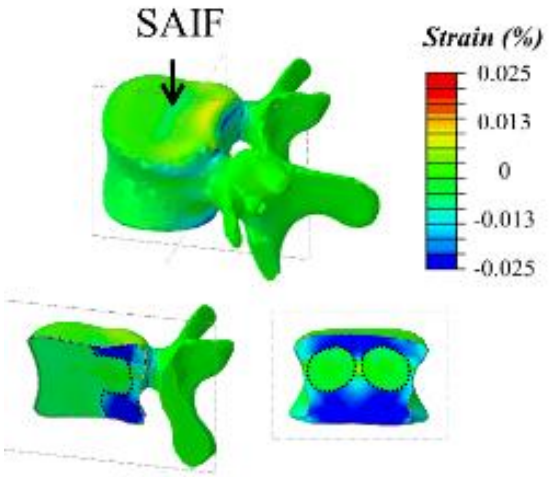
Stent-screw-assisted internal fixation (SAIF)

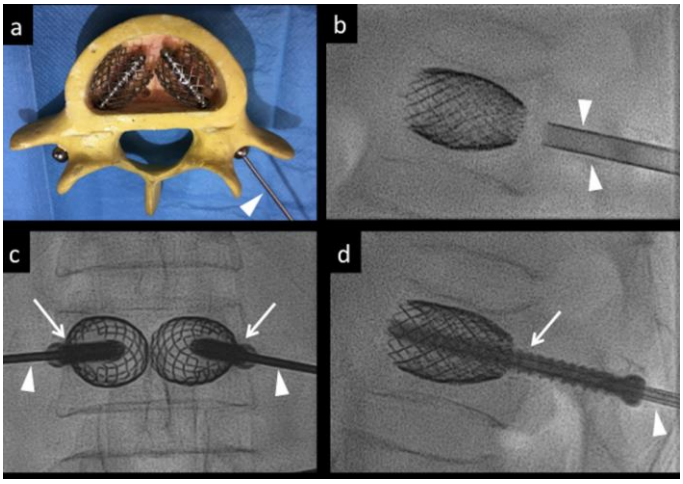
STENT-SCREW-ASSISTED INTERNAL FIXATION

SAIF

MINIMALLY-INVASIVE VERTEBRAL BODY RECONSTRUCTION
IN EXTENSIVE NEOPLASTIC AND OSTEOPOROTIC LESIONS







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Stent-Screw Assisted Internal Fixation (SAIF):

Minimally Invasive Vertebral Body Reconstruction in Extensive Neoplastic and Osteoporotic Lesions

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Dissertation

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Chapter 1

General Introduction and Outline of the Thesis

General Introduction

Fragility fractures of the spine as a result of decreased bone strength are often encountered in patients with osteoporosis or spinal metastases. These so-called vertebral compression fractures (VCFs) affect 10.7/1000 persons per year in women and 5.7/1000 persons per year in men among population over 50 years of age in Europe,[1] and are often secondary to osteoporosis or low bone mass.[2,3]

An estimated number of 500,000 new fractures occur every year in Europe. In Europe, osteoporotic fractures account for the loss of two million disability-adjusted life years, which is more than accounted for by, e.g., hypertensive heart disease.[4]

The medical costs of VCFs is very high and is projected to grow with aging of the population. Although VCFs can be asymptomatic, most patients experience substantial pain and suffering, significantly decreasing their mobility and quality of life.[5] After an incident VCF there is a 20% risk of an additional fracture occurring within the next year.[6] When fractured, the vertebra is commonly deformed by disproportionate height loss from the anterior vertebral body resulting in wedging.[7,8] Wedge accumulation over multiple thoracolumbar levels may lead to subsequent spinal deformity, causing an increased thoracolumbar kyphosis and decreased lumbar lordosis. The increased anterior spinal loading in degenerative thoracolumbar hyperkyphosis has been associated with a downward spiral of additional vertebral compression fractures, also known as the “vertebral fracture cascade”.[9] Thoracolumbar hyperkyphosis in turn severely impacts afflicted individuals’ health in terms of physical function, pulmonary function, pain and disability, postural control during walking, and even mortality (Figure 1).[10–14] From the biomechanical point of view, osteoporotic VCFs can occur spontaneously or due to trauma, generally a compressive load injury mechanism involving the vertebral body. The anterior and middle column of the spine mainly consist of cancellous bone and together support about 80% of the overall spinal load (i.e. muscle forces and body weight) and are most commonly affected. The spectrum of severity ranges from mild and stable compression fractures, affecting the disc-endplate region and leading only to minor deformity, to unstable fractures with a high-degree of osseous fragmentation, collapse deformity, middle column involvement, pedicular fractures, and kyphotic deformity (Figure 2).[15–18]

Figure 1

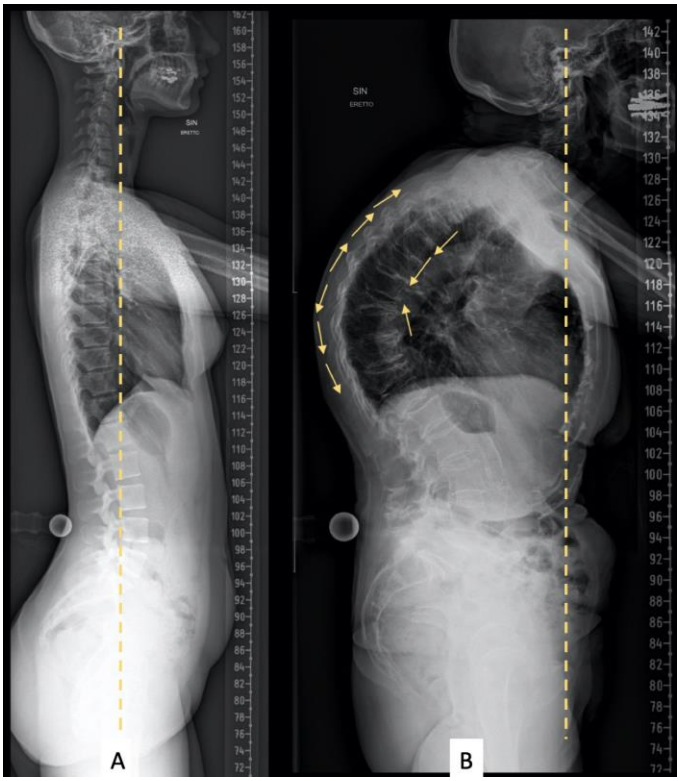

Figure 1. Standing full spine lateral radiograms showing sagittal balance of a patient with a normal spine (A) and in a patient with hyper-kyphotic spinal deformity consequent to multiple chronic thoracolumbar compression fractures (B).

Figure 2

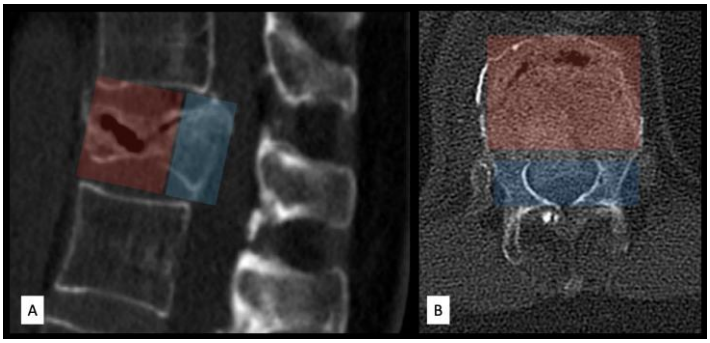

Figure 2. Osteoporotic fracture with burst morphology, high degree of fragmentation and severe deformity. Sagittal (A) and axial CT scan (B) demonstrate an intra-somatic cleft filled with gas. The fracture involves both the anterior column (red area) and the middle column (blue area), causing posterior wall retropulsion with spinal canal narrowing.

The underlying poor bone quality represents a risk-factor and might prevent osseous healing, potentially evolving toward the creation of osteonecrotic clefts[19–21] and,

together with the detrimental effect of the increased bending momentum due to kyphosis at the fracture level,[22] might be responsible for fracture progression. It is reported that between 15 to 35% of VCFs does not have a good outcome with conservative non-operative management resulting in persistent pain, chronic non-union, increased kyphosis, instability and ultimately neurologic compromise.[23,24]

A morphological classification of osteoporotic vertebral fractures, the OF classification, has been recently proposed[25] by the German Society for Orthopedics and Trauma (Figure 3).

Figure 3

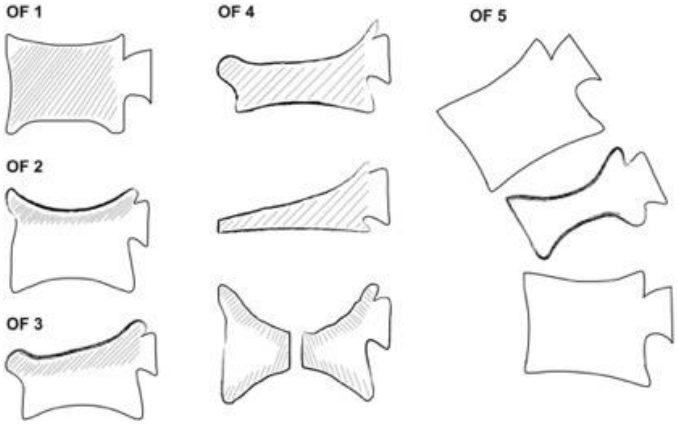

Figure 3. Schematic representation of the 5 OF subtypes (OF 1-5) of osteoporotic vertebral compression fractures following AOSpine-DGOU classification.

Treatment of osteoporotic VCFs should aim to relieve pain and break the downward spiral of recurrent VCFs and to prevent the subsequent progression of kyphosis and resultant global sagittal malalignment. Furthermore, it should intend to prevent or slow down the decline in postural control, thereby limiting the increased risk of falling in these patients.

Another important cause of decrease in spinal bone strength that can result in VCFs is represented by primary and metastatic neoplastic involvement of the vertebrae. An increasingly encountered problem in patients affected by cancer is, in fact, the occurrence of spinal metastases.

Spinal metastases are an increasing societal health burden secondary to an aging population and improvements in systemic therapy with consequent longer survival. Estimates indicate that 100,000 or more people in the USA have symptomatic spinal metastases requiring treatment. Advances in systemic therapy have increased the number of

patients requiring treatment for spine metastases each year, estimated to exceed 3/10,000 new patients annually[26,27] at a per-person cost of $60,000 or more for surgically treated patients.[28]

The probability that an elderly patient (60–79 years old) is affected by bone metastases compared to a middle-aged patient (40–59 years old) is four times higher in men and three times higher in women. While pain is the most frequent symptom, 10% of cancer patients will develop weakness, sensory disturbances, bowel or bladder dysfunction, and gait disturbance from compromised stability or spinal cord compression. Spinal instability may cause severe disability and neurological deficit that eventually impact patients' survival. The Spine Oncology Study Group defines spinal instability as a "loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads". Metastases compromise the mechanical integrity of the vertebra and make it susceptible to fracture. The spinal instability neoplastic score (SINS) can be used to suggest the need of stabilization of a fractured vertebra or of prophylactic stabilization of an impending collapse situation.[29] The extent of lytic destruction of the vertebra can be graded by the Tomita scale.[30] The lesions classified as Tomita 4 to 6 deserve particular interest as far as the optimal choice of treatment is concerned, since these lesions feature extensive osseous destruction, not only of the trabecular portions of the vertebra, but also of the cortical boundaries and of the posterior wall. These lesions commonly present an extra-compartmental extent, with possible invasion of the epidural space and compression of neural elements, which is graded by the epidural spinal cord compression (ESCC) scale.[31]

The optimal treatment of VCFs is debated, and varies depending on the cause, either benign osteoporotic or neoplastic, on the patients' characteristics and comorbidities, on the presence of pain, and on the fracture morphology, with or without underlying instability and spinal alignment deformity. Additionally neurological impairment caused by neural compression is a major determinant in treatment strategy.[27,32,33]

In the absence of neural compression and spinal instability an initial conservative approach consisting of analgesics and bracing may be considered. Systemic medical treatment for osteoporosis is also crucial to reduce the risk of subsequent fractures. In metastatic spinal involvement, in addition to the above cited regimens, radiation treatment

has long been one of the main pillars of treatment for local control of disease and pain palliation, with or without specific ever evolving chemiotherapeutic regimens.

However, none of these medical non-invasive measures offer restoration of spinal stability. Since in case of instability preventing neurological injury and spinal deformity is of paramount importance, if conservative measures have failed, invasive treatments, including open or minimally invasive surgery, and interventional percutaneous procedures can be considered.[34]

Vertebral augmentation (VA) has been extensively used for pain palliation and stabilization of VCF due osteoporosis, and tumors.[34–36]

Percutaneous vertebroplasty (VP) was first described in the treatment of an aggressive cervical vertebral hemangioma in 1987 by Galibert *et al*.[37] In 1989, a landmark paper was published by Lapras *et al* in which the authors described their experiences with VP in the treatment of osteoporotic fractures.[38] The decade following these two publications witnessed further expansion of their technique and the introduction of additional devices including balloon kyphoplasty (BKP), which was developed as a tool intended for fracture reduction and vertebral height restoration.[39] In the last thirty years hundreds of studies were published on this subject. Only one randomized controlled trial investigated the role of cement augmentation versus non-operative management in neoplastic vertebral fractures, showing significant benefit on pain and quality of life in this population.[40] Several randomized controlled trials instead investigated the role of cement augmentation in patients with osteoporotic VCFs. These trials compared different techniques of vertebral augmentation, vertebral augmentation to non-operative management, and vertebral augmentation to a sham procedure. Despite ongoing debate and controversies on the methods and the results of these studies, a recent meta-analysis provided evidence in favor of the cement augmentation treatment of VCFs, which was associated with greater improvement in pain intensity compared to non-operative management, and which was unrelated to the development of adjacent-level fractures. This result was considered, also in consideration of the minimal invasiveness of the treatment, and of its minimal complication risk, a therapeutic level I of evidence.[41] Meanwhile, innovation has resulted in the availability of vertebral body implant-based technology (instrumented

or armed kyphoplasty),[42] biologic cements, and radiofrequency ablative technologies, permitting the treatment of a wider array of patients with more complex presentations including osteoporotic, traumatic, and neoplastic lesions.[43,44]

In this thesis we are focusing on an alternative new minimally invasive treatment of selected extensive osteolytic metastatic spinal lesions and of severe osteoporotic fractures.

1.1 Treatment of neoplastic osteolysis

To prevent or arrest vertebral collapse in patients with lesions affecting the weight-bearing portions of the vertebrae, posterior surgical fixation is widely used, but should be accompanied by anterior column stabilization, either by corpectomy and cage interposition with bone grafting, or by cement augmentation[45] Corpectomy and grafting is an effective treatment but is an invasive procedure that has significant morbidity risk, especially in fragile patients.[46,47] Multilevel posterior fixation, however, may not be feasible in patients with advanced disease, multilevel lesions and poor bone quality.

The choice of the optimal treatment should also be based on the general health status of the patient, and on the patient's prognosis, and is ideally discussed in a multidisciplinary manner. Generally, surgical fixation combined with corpectomy and grafting can be considered in patients with unstable (SINS >6) solitary spinal metastasis, in good general health, and with a relatively long life expectancy.[48]

To prevent or arrest vertebral collapse, stand-alone vertebral augmentation is considered a viable option, with a much less invasive profile, to achieve pain palliation and reinforce the anterior column, in case there is integrity of the cortical bone boundaries, no advanced vertebral body collapse nor hyperkyphosis. [35,40,49–51] Cases with advanced vertebral body structure loss pose a challenge to vertebral augmentation;[35] in fact, cement distribution in these highly destroyed vertebral bodies might be unpredictable, uneven, or result in early extra-vertebral leaks leading to insufficient augmentation and stabilization, or to clinical complications including vascular migration or neural compression.

Figure 4

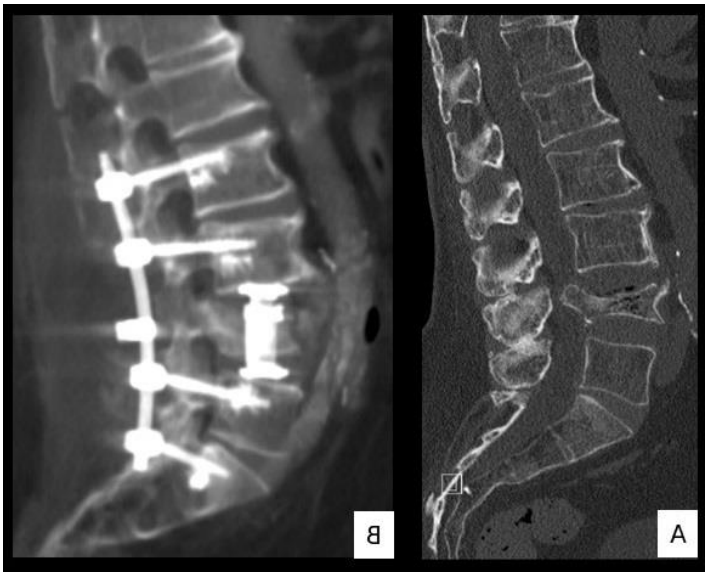

Figure 4: Surgical treatment of a L4 fracture with crush deformity. Reformatted sagittal CT scan (A) demonstrates the fracture, with multi-fragmented morphology, severe vertebral body height loss and posterior wall retropulsion of L4. Post-operative reformatted sub-volume sagittal CT scan (B) shows a 360° stabilization after an anterior approach for corpectomy and vertebral body reconstruction with a metallic cage, guaranteeing support for the anterior column, and posterior fixation with pedicular screws and rods two levels above and two levels below the fracture level.

1.2 Treatment of osteoporotic fractures

Based on the OF classification of osteoporotic VCFs, guidelines on the minimally invasive percutaneous augmentation versus surgical management of those fractures have been issued.[33] Specifically, these guidelines maintain a potential choice between balloon kyphoplasty augmentation and surgical stabilization for fractures classified as OF 3, while firmly advise on surgical stabilization for most severe osteoporotic fractures, classified OF 4 or 5. Still wide variability of therapeutic approaches remain, based on different schools and practices. A recent review, compiled by authors from different European, American and Asian institutions, thereby combining and armonizing different approaches, advise on cement augmentation, either with vertebroplasty of with balloon kyphoplasty for patients who continue to have severe pain and who do not respond to conservative treatment, while advice toward spinal instrumentation for patients who have chronic vertebral pseudoarthrosis with instability or neurological deficit, intractable pain with collapsed vertebra, and kyphotic deformity.[32,52]

Cement vertebral augmentation is widely used to treat fragility fractures, to alleviate pain, restore axial load capability of the vertebral body (VB) and arrest fracture progression.[53] Ideally, vertebral body reconstruction, height restoration and homogeneous cement augmentation should be obtained with bone cement filling the two anterior thirds of the vertebral body from superior to inferior disc-endplates on both sides of midline, especially for the most severe of these fractures. However, vertebroplasty is not intended to restore vertebral body structure or height and balloon kyphoplasty has not been proven to guarantee sufficient height restoration, either due to the fact that the balloon tamps expand following the path of least resistance, or due to the deflation effect, which is the loss of fracture reduction occurring after balloon removal and prior to cement injection. Moreover, the PMMA cement does not have adhesive properties to ensure stability in highly fragmented osseous structures, and the cement might distribute into the fractured vertebral body in a heterogeneous and unpredictable manner.

Following vertebral augmentation, refracture of the treated vertebral body is a well-known and reported event.[6,54–57] This occurrence might be asymptomatic or be accompanied by pain recurrence.

A less frequent event is the re-fracture of the middle column, at the junction between middle and posterior third of the vertebral body where most commonly the junction between cement-augmented and non-augmented vertebral body is located. These fractures are characterized by involvement and retropulsion of the posterior wall and eventually result in catastrophic splitting and separation between augmented anterior portion of the vertebral body and middle column (Figure 5). This may also be accompanied by a kyphotic deformity at the incident level. Such fractures are not frequent and are largely unreported but when they do occur they pose a real therapeutic challenge.[58,59]

The importance of the middle column stability might be indeed largely underestimated since the load-bearing capacity of the vertebra is usually referred to the anterior column as a whole structure, totally neglecting the important role of the middle column.

Figure 5

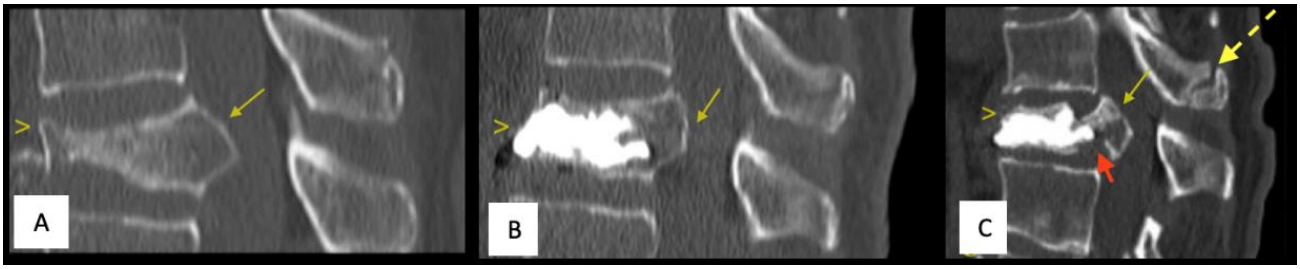

Fig. 5: Middle column collapse after vertebroplasty. Pre-treatement sagittal CT scan (A) demonstrates severe collapse with middle column injury and posterior wall retropulsion (yellow arrows) of L1. Sagittal CT images after vertebroplasty (B) shows good cement filling of the vertebral body with a good recovery of vertebral body height and reduction of the posterior wall retropulsion (B); the fractured middle column remains non-augmented. The CT scan after two months (C) shows refracture with splitting of the anterior and middle column (red arrow), collapse of the middle column and worsening of the posterior wall retropulsion, as well as a fracture of the spinous process (dashed yellow arrow) of T12.

Furthermore, the middle column, with the posterior third of the vertebral body, the posterior wall, and the pediculo-somatic junctions remains relatively non-augmented, even after satisfactory cement augmentation due to the safety measure to avoid cement dispersion too close to the posterior wall. The middle column, after cement augmentation, if observed on an axial post-procedure CT image, might be regarded as a “bare area”, not reinforced, and therefore a potential point of weakness of the vertebra (Figure 6).

Figure 6

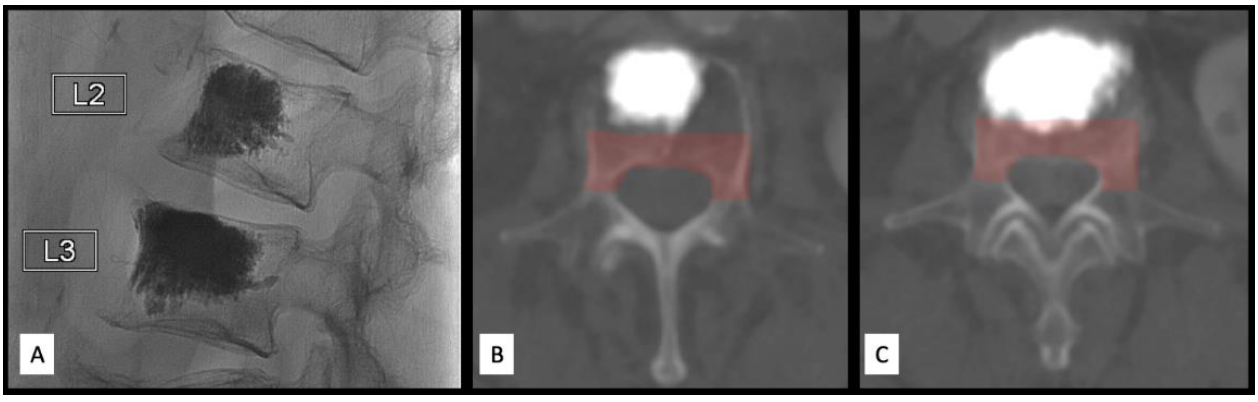

Figure 6. Bare area after vertebral augmentation. Conventional vertebral augmentation of L2 and L3. Lateral fluoroscopy image (A) and axial CT images (B, C) show a good filling of the anterior column with relative lack of cement augmentation of the bony structures of the middle column, namely the posterior third of the vertebral body, the posterior wall and the pedicles (red areas).

Some authors have recommended cement augmentation of the pedicles and pediculo-somatic junction, the so-called pediculoplasty,[60] but it should be considered that main stress forces at the level of the pedicles and pediculo-somatic junction are tensile, and PMMA is known to have optimal resistance to compressive loads rather than to tensile ones.[61]

Standard vertebral augmentation might therefore represent an undertreatment in osteoporotic fractures with middle column involvement.

1.3 Armed Kyphoplasty

The use of vertebral body stents (VBS) has been proposed to overcome the deflation effect observed with the standard balloon kyphoplasty.[62–67] The VBS consists of a barrel-shaped metallic mesh that is expanded and deployed in the vertebral body upon balloon expansion, and is then filled with bone cement. In extreme osteolysis, in the most severely fragmented vertebral fractures, and in severely collapsed vertebral bodies, the metallic mesh, the barrel shape, and the large support surface of VBS might serve to achieve height restoration, as an internal vertebral body scaffold, and as an effective device to contain bone cement within the vertebral body. The use of percutaneous transpedicular screws, in conjunction with cement augmentation, has been described to treat osteoporotic and neoplastic VCFs.[68,69]

The combination of metallic devices, such as stents and screws, that help restore the structure of the vertebral body from within, with the use of fluid cement augmentation, might replace the traditional concept of cement augmentation with a more advanced concept of “armed concrete” non-fusion vertebral stabilization.

In conclusion, there is a need to fill the gap, in the treatment armamentarium continuum of severe osteoporotic and neoplastic vertebral fractures, between standard vertebral augmentation techniques and surgical stabilization. Minimal invasiveness, percutaneous technique, and image-guidance should be pursued. Such a new technique should provide fracture reduction, kyphosis correction, and restoration of load bearing capacity. An effective non-fusion vertebral body reconstruction, through internal fixation, could obviate the need of an external surgical fixation, with its intrinsic drawbacks in patients with poor bone quality, and the invasiveness and morbidity of an anterior column stabilization through corpectomy and grafting in fragile patients.

Outline of Thesis

The aim of this thesis was to investigate the Stent-screw-assisted Internal Fixation (SAIF) technique procedural steps, its potential applications, the biomechanical rationale and clinical experience, with safety and feasibility, in severe neoplastic and osteoporotic vertebral lesions.

We addressed the following research questions (RQ):

- **RQ1**: can VBS be used safely and efficiently to reconstruct the anterior column in extreme osteolysis of the vertebral body?
- **RQ1** is addressed in Chapter 1, via a study retrospectively analyzing the results of a VBS-cement treatment to reconstruct the morphology of the anterior column destroyed by extreme osteolysis.
- **RQ2**: how can VBS-cement complex be integrated by transpedicular screws? which applications could be addressed by this new technique, called SAIF?
- **RQ2** is addressed in Chapter 2, illustrating the technical procedural steps of SAIF, its rationale, its potential clinical applications
- **RQ3:** What is the biomechanical rationale of SAIF in the stabilization of extreme osteolytic lesion of the vertebral body? How would SAIF compare to surgical posterior fixation?
- **RQ3** is addressed in Chapter 3a, featuring a biomechanical demonstration, on a finite element analysis of a lytic vertebra model, of the rationale of SAIF stabilization, in comparison with a posterior surgical fixation model
- **RQ4:** is SAIF clinically safe and efficient to treat extreme osteolysis lesions of the vertebral body?
- **RQ4** is addressed in Chapter 3b, a clinical series of patients affected by extreme osteolysis of a vertebra, treated with SAIF
- **RQ5**: is there a biomechanical rationale to explain the re-fractures of the middle column after cement augmentation in osteoporotic vertebrae? The bare area concept. How would SAIF compare to standard vertebral augmentation in stabilizing the middle column?

- **RQ5** is addressed in Chapter 4a featuring a biomechanical demonstration, on a finite element analysis of an osteoporotic vertebra model, of the presence of a so-called “bare area”, at the level of the middle column, which represents a weak point, prone to re-fracture following cement augmentation of the anterior column. The biomechanical simulation compares the stabilization obtained with SAIF with that of standard vertebral augmentation
- **RQ6:** is SAIF clinically safe and efficient to treat severe osteoporotic fractures of the vertebral body?
- **RQ6** is addressed in Chapter 4b, a clinical series of patients affected by severe osteoporotic fractures treated with SAIF
- **RQ7**: is the frequently associated posterior wall retropulsion a contraindication to the SAIF procedure?
- **RQ7** is addressed in Chapter 5. This Chapter includes description of a technique to create a true cavity in the vertebral body, in those vertebrae with extreme osteolysis and posterior wall dehiscence, before performing SAIF. Another study in this Chapter investigates on the results of armed kyphoplasty in VCFs with posterior wall retropulsion.
- **RQ8**: what is the efficacy of SAIF as compared to surgical stabilization in unstable (OF3-5) osteoporotic fractures?
- **RQ8** is addressed in Chapter 6, with a study design of a randomized controlled trial comparing SAIF to surgical stabilization of severe unstable osteoporotic fractures

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Chapter 2

Vertebral Body Stent Augmentation to Reconstruct the Anterior Column in Neoplastic Extreme Osteolysis

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Abstract

Objectives

Extensive lytic lesions of the vertebral body (VB) increase risk of fracture and instability and require stabilization of the anterior column.

Vertebral augmentation is an accepted treatment option, but when osteolysis has extensively destroyed the VB cortical boundaries (a condition herein defined as “extreme osteolysis”) the risk of cement leakage and/or insufficient filling is high. Vertebral Body Stents (VBS) might allow partial restoration of VB height, cement containment and reinforcement, but their use in extreme osteolysis has not been investigated. Our study retrospectively assessed feasibility and safety of VBS augmentation in patients with ‘extreme osteolysis’ of the VB.

Methods

We retrospectively analyzed 41 treated vertebrae (from T1 to L5). VB reconstruction was assessed on post-procedure CT and rated on a qualitative 4-point scale (poor-fair-good-excellent). Clinical and radiological follow-up was performed at 1 month and thereafter at intervals following oncological protocols.

Results

VBS augmentation was performed at 12 lumbar and 29 thoracic levels, with bilateral VBS in 23/41. VB reconstruction was judged satisfactory (good or excellent) in 37/41 (90%) of levels. Bilateral VBS received higher scores than unilateral ($P=0.057$, Pearson’s X^2). We observed no periprocedural complications. Cement leaks (epidural or foraminal) occurred at 5/41 levels (12.2%) without clinical consequences. Follow-up data were available for 27/29 patients, extending beyond 6 months for 20 patients (7–28 months, mean 15.3 months). VBS implant stability was observed in 40/41 cases (97%).

Conclusions

Our results support the use of VBS as a minimally-invasive, safe and effective option to reconstruct the anterior column in prominent VB osteolysis.

Introduction

Spinal osteolysis may cause instability, leading to fractures and neural compression [1]. Stability restoration is therefore of paramount importance in the treatment of spinal lytic tumors.

While radiation and systemic therapies are used to achieve tumor-control and pain palliation, invasive treatments are often required to prevent or arrest vertebral collapse in patients with lesions affecting the weight-bearing portions of the vertebrae, including the vertebral body (VB). Posterior surgical fixation is widely used in such cases, but should be accompanied by anterior column stabilization, either with corpectomy and grafting, or with cement vertebral augmentation (VA)[2]. Posterior fixation, however, may not be feasible in patients with advanced disease, multilevel lesions, and poor bone quality. Corpectomy and grafting is an effective treatment but is an invasive procedure that has significant morbidity risk, especially in fragile patients [3,4].

Stand-alone VA is considered a viable option to achieve pain palliation and reinforce the anterior column[5-7], but when the osteolysis causes extensive destruction of the cortical boundaries of the VB, a condition here defined as “extreme osteolysis” (EO), the injection of cement may be challenging or impossible [8-9].

The Vertebral-Body-Stent (VBS) (DePuySynthes-Johnson&Johnson®) is a balloon-expandable barrel-shaped metallic device, which is inserted via mono- or bi-pedicular access. Upon expansion, the VBS keeps the created cavity open after balloon-deflation until cement is injected. Introduced for treatment of vertebral compression fractures, the use of VBS in extensive neoplastic osteolysis has not been investigated and recommended[10-15]. Nevertheless, in EO of the VB, the VBS might serve as a stabilizing implant by virtue of its large support-surface, its potential to achieve VB height restoration and to help contain the injection of cement (Fig. 1S). The purpose of this study was to assess feasibility and safety of VB-reconstruction using VBS in EO. The durability of the results was assessed recording the rate of subsequent spine surgery at target levels.

Materials and methods

This is a retrospective study on a prospectively-maintained database of a consecutive series of patients with neoplastic EO of one or more VBs, treated with VBS (March 2013 - November 2016). EO was defined as an extensive lytic lesion of the VB, with wide cortical destruction, combining, to variable extent, involvement of the posterior wall, the anterolateral boundaries, and the disc-endplates (types 4-6 according to the scoring system of Tomita et al.[16]). The study was approved by the local ethics committee. Patients were informed of the investigative use of VBS to treat their condition and provided informed consent.

All patients underwent pre-procedure spinal-CT and gadolinium-enhanced MRI at the target-level to define extent of osteolysis, degree of vertebral collapse (< or > 50%), and presence of epidural mass (EM) (see Fig. 1S).

All target-lesions were deemed to be unstable or potentially unstable according to their SINS score [17].

Therapeutic decisions for each patient were reached by a multidisciplinary spine-tumor board, defining indications and timing of invasive, radiation, and chemotherapy treatments.

VBS procedure

All procedures were performed under biplane fluoroscopic-guidance. The VBS was implanted through trans-pedicular 7G trocar; a unilateral stent was inserted in cases of lateralized lytic lesion or of a small VB.

When deemed necessary, prior to VBS deployment, a cavity was created in the VB using a coaxial osteotomic curette (Medtronic, Minneapolis, MN, USA), followed by vacuum-suction.

VBSs were expanded and implanted in the VB by hydraulic ballon-inflation. Following balloon-deflation and removal, high-viscosity PMMA (Vertaplex HV, Stryker, Kalamazoo, MI, USA) was injected under *fluoroscopic* monitoring, to obtain VBS filling and, when possible, interdigitation into adjacent trabecular bone . In multilevel osteolysis, when indicated, further vertebrae were subjected to VA during the same procedure, at adjacent or distant levels. Patients were allowed to stand and walk as early as three hours after the procedure, and most commonly discharged the same day.

Assessment of VB-reconstruction and follow-up

VB-reconstruction was assessed on post-procedure plain-films and CT. CT-datasets were reconstructed with a bone algorithm with 3 mm and 10 mm thick MIP images in three orthogonal planes, and reviewed by a neuroradiologist (AC) and a neurosurgeon (PS). Extra-vertebral cement leaks were recorded. Based on the restoration of VB height, the position of the stents in the VB, and the cement filling of the lytic cavities and adjacent trabecular spaces, an overall score of VB-reconstruction success was assigned, under consensus, on the basis of an a-priori-defined, qualitative, four-grade scale, rating the VB-reconstruction as poor, fair, good, or excellent. Poor indicated failure to achieve sufficient augmentation of the anterior column whereas excellent indicated appropriate stent expansion to fill the lytic lesion and reconstruct the destroyed portion of the VB, satisfactory height restoration, and cement filling (Fig. 1). An excellent result would appear as an internal prostheses of the affected VB. Good and excellent ratings were considered satisfactory results.

Patients were followed up at 1 month clinically and with upright spine-plain films. Thereafter the patients underwent routine oncological clinical and imaging follow-up. From these records, spine images could be derived and assessed at intervals in accordance with oncological follow-up protocols, or when clinical conditions prompted referral for spinal imaging. Imaging follow-up was evaluated to assess significant new findings at the treated and adjacent levels.

Statistics

Descriptive statistics for clinical and demographic data were expressed as mean, or as median ± range.

Implant outcomes were stratified according to the VB-reconstruction score, into the following categories: poor, fair, good, or excellent. Differences between categories in the degree of height-reduction and tumor histotype (metastases vs. multiple myeloma-plasmocytoma) were tested using Pearson's X^2. The same test was employed to assess differences in the VB-reconstruction scores and cement leak occurrence when treated levels were classified on the basis of bilateral or unilateral VBS. The existence of a relationship between patients' SINS and VB reconstruction scores was investigated by using Spearman's rho test. A P-value of less than 0.05 was considered statistically significant. Analyses were conducted using SPSS Version 20.0.0 (IBM, Armonk, NY, USA).

Results

Population

The study group included 29 patients and procedures to treat 41 levels with EO between T1 and L5. SINS score ranged between 7 and 18 (mean 10.7; median 10).
A summary of patients' characteristics, and features of the lytic lesions is provided in Table 1.
One patient had a neurological deficit due to spinal cord compression, and another patient had radicular sciatic pain before the procedure.

Technical results

Conscious-sedation was used in 17/29 patients, and general anesthesia in 12/29. VBS procedures were performed as a stand-alone intervention in 26/29 cases (36 levels), with a percutaneous posterior surgical fixation in 1/29 cases (1 level), and after laminectomy and posterior surgical fixation in 2/29 cases (4 levels). VBS was bilateral at 23/41 levels, and unilateral at 18/41 levels. Cavity-creation was performed at 35/41 levels.
During the same procedure, additional VA with cement-only was performed at adjacent or distant vertebral levels (affected by lytic lesions, but not defined as EO) in 20/29 cases, at a total of 63 levels.
Cement leakage was detected in 14/41 cases (34%), without clinical consequences. There were no other clinical intraprocedural complications. No patients showed new or worsening neurological deficit.
VB-reconstruction by VBS was judged excellent at 31/41 (75%), good at 6/41 (15%) fair at 4/41 (10%), and poor at 0/41 of the treated levels, leading to a satisfactory result (excellent or good rating) in 37/41 (90%) of cases. Table 1S summarizes the technical results.
VB-reconstruction scores did not correlate with degree of height-reduction, SINS-score, and tumor-histotype. The occurrence of cement leaks did not correlate with unilateral or bilateral implants. Only the difference in the VB-reconstruction score between bilateral and unilateral implants approached statistical significance (P=0.057, Pearson's X^2), as shown on Table 2S.

Follow-up results

Clinical and imaging follow-up at 1 month post-procedure was available for 27/29 patients (39/41 treated levels). Due to deaths from unrelated causes, follow-up data at 6 months or more (7–28 months, mean 15.3 months) were available on 20 patients (28/41 levels).

Spine stability at the target-levels was observed until the last available follow-up in 40/41 cases (97%). In one patient, ventral mobilization of the VBS-implants at T1 was noted at 1-month follow-up, causing transient dysphagia. Only one patient in this series required subsequent spinal surgery at the target-level, six months post-VBS, due to an adjacent-level fracture.

Four patients showed mild adjacent-level impaction fracture, without clinical consequences. One patient developed radicular pain 3 months post-procedure, with a new disc-herniation adjacent to a target-level, and was treated conservatively.

Local progression of disease was observed in two patients (2/41 levels, 4.9%), at 3 and 23 months post-procedure, respectively, with increased EM, but without neurological sequelae.

Discussion

In our series of patients with EO in whom VBS was used to reconstruct and augment the VB, technical success was achieved in 90% of cases, regardless of tumor histology, with no significant clinical complications, and with stable results at follow-up. Subsequent target-level spine surgery occurred in 1/29 patients.

Treatment indications

All patients had a SINS score indicating unstable or potentially unstable vertebral lesions. The main aim of the procedure was reconstruction and augmentation of the anterior column in VBs that had fractured or were at risk of collapse.

In patients with EO of the VB, surgery is considered the standard treatment to restore stability. A posterior fixation should be combined to corpectomy and grafting, with placement of different cages, cement or autologous bone [3]. This approach, however, is associated with significant morbidity and is mostly indicated in patients with solitary spinal metastasis, in good general health, and with a long life expectancy [18]. Moreover, surgical fixation might not be the ideal solution in patients with multilevel metastatic involvement or poor bone quality.

Augmentation procedures, such as vertebroplasty and kyphoplasty, either as stand-alone procedures [19], following radiofrequency ablation [20], or in combination with posterior fixation [21], might be contraindicated or unfeasible in the presence of EO. Extensive loss of cortical boundaries integrity may favor extra-vertebral cement leakage, potentially resulting in compression of neural structures and/or insufficient filling of the vertebral lytic lesion. This is likely to lead to unsatisfactory augmentation and reinforcement of the anterior column [8,22,23]. VBS, introduced for the treatment of vertebral compression fractures [10–15], has not been investigated nor recommended in patients with EO, and cranial to T6.

In this study, VBS was chosen as a stand-alone procedure when deemed clinically appropriate and when surgery was contraindicated, or in combination with a posterior surgical approach, as an alternative to a surgical reconstruction of the anterior column with a cage. In our series a combined VBS and posterior surgical fixation was chosen in three patients presenting spinal lesions with high SINS scores (13-18). In patients with multilevel involvement, the decision on which levels to treat to prevent or to arrest a fracture was based on the extent and location of the lytic lesions suggesting biomechanical risk of collapse [24].

Due to its minimal invasiveness, and minimal recovery time, VBS could be more deliberately offered as a palliative treatment, as with patients having a poor prognosis and/or a low Tokuhashi score [25].

VBS technique

When the lytic lesion was felt to have a solid soft-tissue consistency during insertion of the trocar, we performed curettage with a coaxial osteotome, followed by vacuum-suction through an 8G cannula (Fig. 2S). In our opinion, the creation of a cavity in the VB reduces the risks of displacement of solid tumoral tissue through the dehiscent cortical boundaries, namely the posterior wall, and of epidural PMMA leak.

In unilateral VBS implant cement-only VA was performed through the contralateral pedicle, to ensure bilateral and homogeneous augmentation.

The injected PMMA-volume varied according to the size of the lytic lesions, trabecular compliance, stent expansion, and distribution of injected cement.

Efficacy of the procedure

Vertebral body reconstruction

The main goal of the VBS procedure and the primary endpoint of our analysis was the reconstruction of the VB, which is important for restoration of axial load-bearing capability of the anterior column [12]. This was attempted by creating a construct similar to “armed-concrete” in the VB with metallic stents and PMMA. With their large support-surface, filled with PMMA, VBS could provide primary reinforcement of the anterior column, and their tight mesh may help achieve cement-containment (Figs 2 and 3S). Where necessary and possible, we tried to restore the VB-height, to favor a more physiological biomechanical condition.

In the absence of a validated system, a neuroradiologist and a neurosurgeon assigned under consensus an arbitrary VB-reconstruction score. This was based on a qualitative overall assessment of the post-procedure plain-films and CT-images, taking into account stents’ placement, expansion, cement filling, and VB height-restoration. The reconstruction achieved was judged satisfactory in 90% of levels. The VB-height as seen on post-procedure CT was substantially maintained at follow-up in 40/41 levels. More subtle phenomena of bone

remodeling/subsidence around the solid implants of VBS and PMMA were observed, but had no significant impact on stability, spinal alignment, or patients' symptoms. Reconstruction at four treated levels was judged unsatisfactory (fair), based on post-procedure CT-images assessment; all four levels had received a unilateral VBS implant, and 3/4 were lumbar levels. Out of these patients, only one required subsequent posterior surgical stabilization, one had died before 6-month follow-up but had no instability complications, and the remaining two had an unremarkable follow-up. Although low scores for VB-reconstruction seemed not to correlate with a poor outcome in terms of stability at follow-up, this might be due to the small number of patients concerned, and bilateral implant, when possible, seems to offer more satisfactory VB-reconstruction results, especially in the larger lumbar vertebrae. Successful VB-reconstruction might relate to the restoration of the load-bearing capability of the anterior column, as suggested by the observed stability of the target-levels at follow-up. Moreover, in the available late follow-up CT-exam, formation of a new cortical bone shell was noted around the VBS and in some cases intervertebral osseous fusion was observed (Fig. 3), implying achievement of stability.

Other studies have assessed the use of VBS to restore VB-height and alignment in osteoporotic fractures. In contrast to balloon-kyphoplasty, the VBS system maintains the restored VB-height because the stent remains expanded in the VB after balloon-deflation [12]. In our opinion VBS has other potential advantages in patients with EO. The metallic mesh guarantees a reasonably uniform and predictable barrel-shaped balloon-expansion, while a "non-armed" compliant balloon might expand following the path of least-resistance in a severely altered anatomy, where residual bone, sclerosis, and lytic soft-tissue lesions coexist. The barrel-shape of the VBS, with its large support-surface, provides mechanical support and recreates VB walls, such as in lateral or endplates dehiscent cortical boundaries; furthermore, the metallic mesh helps contain the viscous PMMA cement (see Figs 1, 2, 3S). When bilateral VBSs are fully deployed in the VB they resemble a solid and efficient VB-prosthesis, offering a scaffold for the subsequent PMMA filling, and respecting the intervertebral disc spaces, which are usually untouched by the neoplastic lesions. In the follow-up period we observed five patients with a new compression-fracture adjacent to the VBS-treated target-level. Only one required treatment with VA and surgical stabilization due to worsening focal scoliosis; the others were asymptomatic and did not require interventions. Adjacent new fractures are a known phenomenon, and might be attributable to multilevel metastatic involvement, or primary or secondary osteoporosis.

There might also be a concomitant effect of altered biomechanics, caused primarily by the target-level fracture and, to a lesser degree by the fixation of the fracture, which is likely to increase the stiffness of the treated level [26-29].
In several cases we performed VA with cement-only at adjacent or distant levels, either due to multilevel osteolysis, or for prophylaxis (Fig. 3).

Pain palliation

Pain palliation was a concurrent indication for treatment in most of our patients, but did not represent an endpoint of this study. Precise assessment of pain palliation is usually difficult while evaluating different treatment modalities, and is even more challenging in a retrospective study. Moreover, many patients had multilevel spinal and extra-spinal metastatic involvement, and therefore may have had pain with multifactorial etiologies [23]. Also, some patients may not have had any significant pain from the target vertebral lesion and may have undergone treatment solely for stabilization purposes, to avoid or arrest fracture. Finally, patients also received different treatment regimens of radiotherapy, chemotherapy, supportive care (including steroids and analgesic drugs), and concomitant VA at adjacent or distant levels. Nevertheless, clinical charts recording oncology follow-up reported clinically-significant pain amelioration solely attributed to the VBS–VA procedure in 17/29 patients (with no new or changed therapeutic regimen). In 4/29 cases, pain amelioration was attributable to the procedure in combination with a new or changed regimen of chemotherapy or radiotherapy (it was impossible to determine whether one of these therapeutic measures or a combination of them was responsible for the pain palliation), while in 4/29 patients no significant pain amelioration was noted after the procedure. The remaining 4/29 patients had no definite pre-procedure pain clearly attributable to the vertebral target-lesion. The pain palliation offered by a VA procedure, in this case performed with VBS, might have some advantages over standard radiation therapy alone. Beside dose constraints in patients who have already been irradiated, radiotherapy benefits on pain might be delayed by weeks or months [30] and about 20–30% of patients are non-responders [31,32]. In addition, radiation cannot ensure immediate stabilization of the affected vertebra, since treatment might be followed by a phase of increased vertebral fragility and fracture risk [33]. Nevertheless, we are not proposing an exclusive role for VBS but rather a complementary role to multimodal treatment with radiation and/or chemotherapy to achieve rapid pain relief, immediate reinforcement of the anterior column, and local disease control. Indeed,

the multimodal approach might have been the key to the low rate (4.9%) of local disease-progression at the treated levels, observed in this series.

Complications

No clinically-significant intra- or periprocedural complications were observed. Post-procedure CT showed PMMA leaks in 34% of cases (epidural or foraminal leak in 12.2% levels), all without clinical consequences.

Previous studies reported a lower rate of extra-vertebral PMMA leakage for VBS than for vertebroplasty [10–11,17] but the patients mostly did not have neoplastic lesions, which carry higher leakage risk. As far as we know, there are no data about the rate of PMMA leakage in patients with EO of the VB treated with VBS. A previous study[34] reported a low complication rate (1.7%) during VA of neoplastic lytic lesions with dehiscent posterior wall, and our results seem to support the use of VBS as a safe procedure even in patients with EO.

In our series, there were 21/41 levels with an EM, visible on pre-procedure MRI, and we observed no worsening of neurological status post-procedure. We believe that cavity-creation in the VB, and fracture reduction, with re-expansion of the collapsed VB in a cranio-caudal direction, might have had a role in preventing clinically-significant soft-tissue migration in the central canal.

At 1-month follow-up, one patient exhibited ventral mobilization of the two stents implanted at the T1 level, causing mild dysphagia. The posterior half of the stents remained between C7 and T2 vertebral bodies, still ensuring support, and flexion–extension plain-films showed no mobility of the stents, and maintenance of spinal alignment. A conservative approach was chosen. At 3-month follow-up the dysphagia had resolved and there was no further mobilization of the stents, which also remained stable at the 6- and 8-month follow-up. It is certainly conceivable that the stents might mobilize in the absence of an intact VB cortical shell, but our results so far show this to be an unusual occurrence. Nevertheless, to obviate this potential problem, a system to anchor the VBS to the pedicle(s) is under evaluation at our center.

Limitations

The limitations of our study mainly relate to its retrospective design, rather arbitrary inclusion criteria, and heterogeneous follow-up. It also lacked a control-group, either of patients treated conservatively or with a standard surgical technique. However, the patients

included in this study had all suffered a fracture or were at significant risk of developing a vertebral fracture, and were deemed unsuitable for a standard surgical intervention, namely for an anterior stabilization surgery. The scale adopted to assess the efficacy of VB-reconstruction in the absence of alternatives in literature was qualitative, arbitrary and not validated, but rating reflected the consensus opinion of a neuroradiologist and a neurosurgeon. Nevertheless, this study is the result of a prospectively-established database; all treated cases were included and management and follow-up reflected a multidisciplinary established clinical practice. This study can represent a first step, and a larger study might provide stronger information upon which to base vertebral augmentation procedures in such challenging cases.

Conclusion

Extreme VB neoplastic osteolysis poses a treatment challenge in a group of fragile patients. In our study, the use of percutaneous VBS proved to be a minimally invasive, feasible, safe and effective technique to augment and ultimately provide stability to the anterior spinal column, with durable results. It might therefore be considered as a valuable option, as a stand-alone intervention or in combination with a posterior surgical approach of decompression and stabilization.

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Competing Interest: None declared.

Contributorship Statement

All authors contributed to the presented work by substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work and drafting the work or revising it critically for important intellectual content and final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Sharing Statement: N/A

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Figures and tables

Figure 1

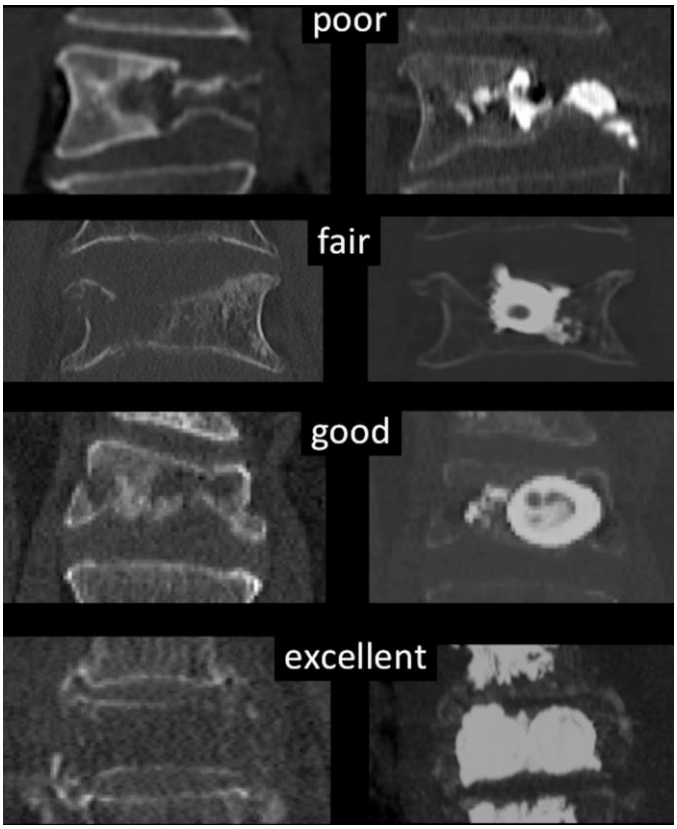

Figure 1. Examples of vertebral body reconstruction illustrating our qualitative four-point scale: coronal reformatted pre- (left column) and post-procedure (right column) CT images of four patients. In the first row a case of poor reconstruction is shown (from a patient who was not part of this study): simple cement augmentation was ineffective in attaining height restoration, and due to an early tendency towards cement leakage, only partial cement filling of the lytic cavities was achieved. In the second row, a case of fair reconstruction is shown: this right-lateralized lytic lesion was treated with a unilateral Vertebral Body Stent (VBS) implant; no significant height restoration was attained and large areas of vertebral body remain non-augmented. In the third row, a case of good reconstruction is shown: a rather left-lateralized lytic lesion was treated with a unilateral VBS implant; the stent expansion is satisfactory, crossing the midline, with ensuing height restoration, cement stent-filling and adjacent interdigitation, but the right side of the vertebral body is scarcely augmented. In the fourth row, a case of excellent reconstruction is shown: this extremely extensive osteolysis with moderate vertebral body collapse was treated with a bilateral VBS implant, well centered, with appropriate expansion from inferior to superior disc endplates, achieving height restoration, with optimal cement filling and interdigitation. *Note:* Coronal views are shown as these are the most illustrative ones, but plain films and triplanar CT images were also considered during assessment.

Figure 2

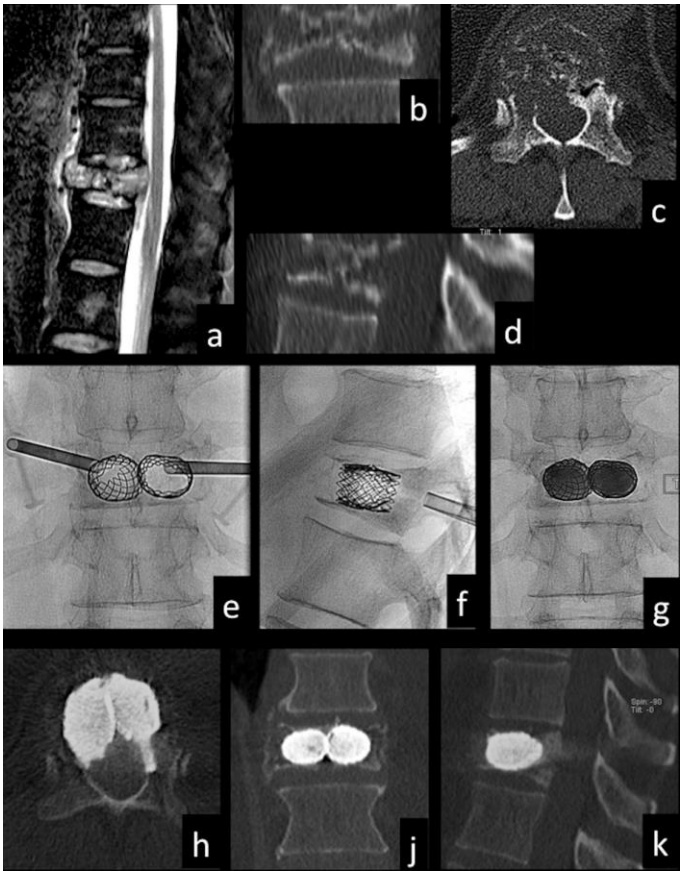

Figure 2. Plasmocytoma with extreme osteolysis of the T11 vertebral body. Fat-suppressed T2-W sagittal MR (a) and multiplanar target level CT (b–d) images show a pathologically fractured vertebral body, with extensive dehiscence of cortical boundaries. Intraprocedural fluoroscopic images (e–f) show the large support surface offered by the Vertebral Body Stent (VBS) scaffold in the vertebral body. After PMMA filling of the VBS, post-procedural fluoroscopic (g) and CT (h–k) images show the satisfactory height restoration, leak-free cement deposition, and anterior column reconstruction.

Figure 3

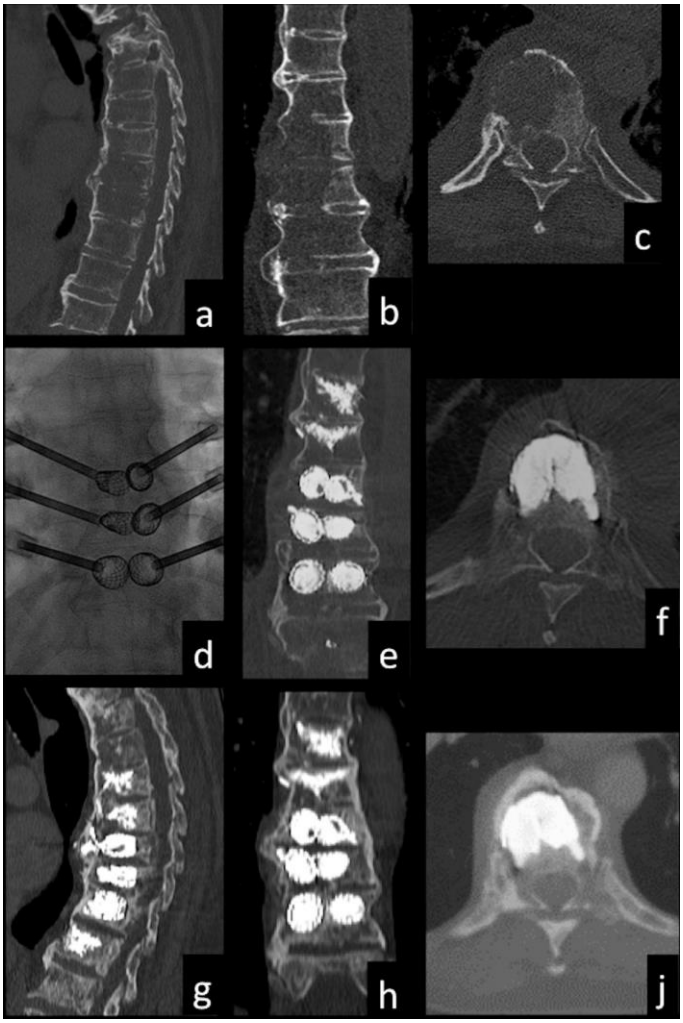

Figure 3. Multilevel breast cancer with metastatic vertebral involvement. This patient had multiple lytic lesions of adjacent mid-thoracic vertebral bodies (a–c), three of which showed extreme osteolysis threatening impending collapse, and were treated with Vertebral Body Stents (VBS) (d–f), while standard vertebral augmentation was performed at three additional levels that showed non-extreme osteolysis. CT images from a follow-up total-body CT 8 months after the procedure (g–j) show preserved stability, diffuse osteosclerosis, incorporating the VBS, and intervertebral fusion in response to oncological therapy.

Supplementary material

Figure 1S

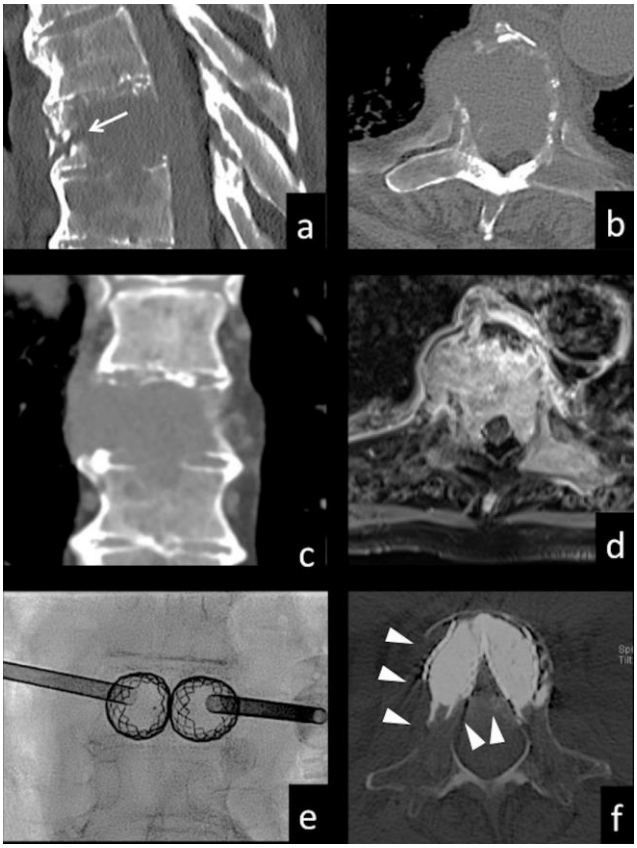

Figure 1S. Characterization of metastatic extreme osteolysis of the T8 vertebral body with multiplanar CT images (a–c) and enhanced fat-suppressed axial T1-W MRI (d). The lesion is characterized by widespread disruption of cortical boundaries and invasion of the central canal by an epidural mass. The height of the vertebral body is preserved but there are signs of pathological fracture (arrow on a) and impending collapse. Fluoroscopic A-P view (e) shows the Vertebral Body Stents (VBS) deployed in the vertebral body after deflation of the balloons. Post-procedural axial CT (f) displays the metallic stents filled with radio-opaque PMMA in a case of extreme osteolysis of a lumbar vertebral body; the boundaries provided by the metallic stents create a scaffold and contain the cement, avoiding leaks through the largely eroded antero-lateral and posterior walls of the vertebral body (arrowheads).

Figure 2S

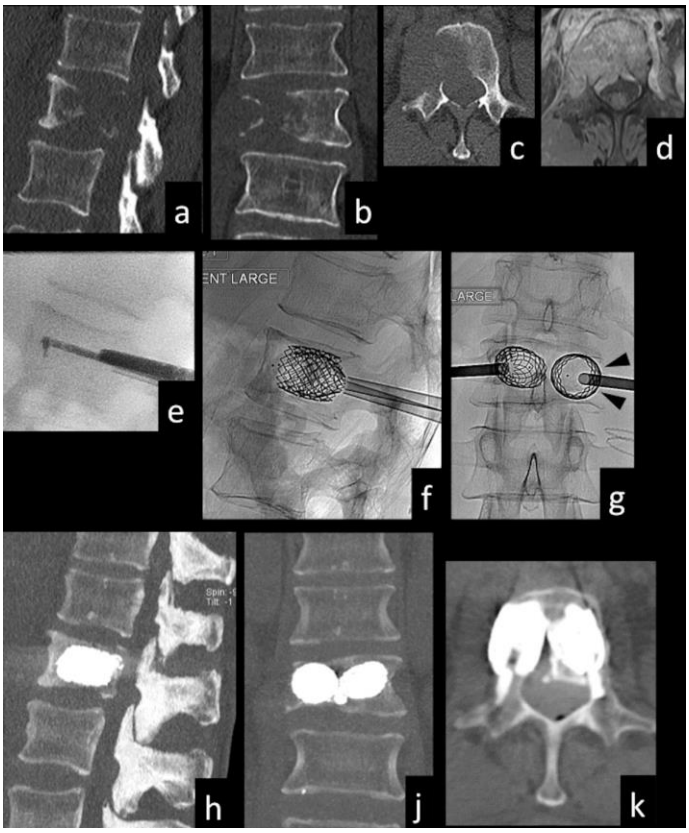

Figure 2S. Renal cell cancer: L1 metastasis. Multiplanar CT (a–c) and enhanced fat-suppressed T1-W axial MR (d) images show the extreme destructive lesion of the right side of the vertebral body and pedicle, with pathological fracture and presence of epidural mass. Intra-procedural fluoroscopic images show the use of a coaxial osteotomic curette (e) followed by vacuum suction (not shown) to create a cavity in the vertebral body, in order to accommodate the stent expansion (f–g). Note how the stent on the right-hand side recreates a lateral wall boundary (arrowheads in g). CT images at 6 months post-procedure (h–k) show the support offered to the anterior column by the cement-filled Vertebral Body Stent, well embedded in a vertebral body that has reconstituted osseous boundaries following oncological treatment.

Figure 3S

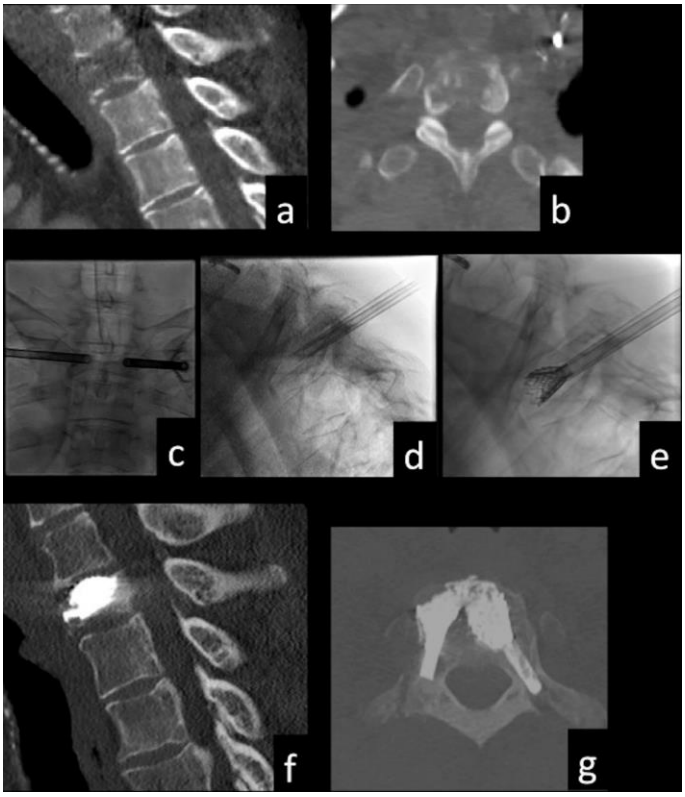

Figure 3S. Lung cancer: extreme osteolysis of the T2 vertebral body. Pre-procedure CT (a–b) shows a compression fracture and extensive cortical erosion of the whole vertebral body. Bilateral small-size Vertebral Body Stents were deployed through the transpedicular approach (c–e) and contained the subsequent PMMA injection. Optimal results in terms of vertebral body reconstruction and absence of leaks are shown by the post-procedure CT (f–g).

Table 1

Characteristics of the study population and features of the lytic lesions

Patients **Age** (years)	29 (M/F 15/14) 44–83 (mean 67.7)
Treated levels Lumbar Thoracic	41 *(1.4 mean, range 1–3 lvs/pt)* 12 29
Histotype Solid tumor metasta-ses Multiple myeloma Plasmocytoma	No. of lvs 26 11 4
SINS score	7- 18 (*mean 10.7, median 10*)
Vertebral collapse <50% >50%	No. of lvs 19 22
Epidural mass	21 lvs

No.: number; pt: patient. lvs: levels

Table 1S

Summary of technical results

Anesthesia General Local and i.v. sedation	 12/29 pts 17/29 pts
Stand-alone VBS **VBS-PS** **L + PS + VBS**	26/29 pts 1/29 pts 2/29 pts
VBS Unilateral Bilateral	41 lvs 18/41 lvs 23/41 lvs
Cavity creation	35/41 lvs
Cement leak Epidural space Neuroforamen Disc space Perivertebral space	14/41 (31%) lvs 4 1 2 7
VB reconstruction score Poor Fair Good Excellent	 0/41 (0%) lvs 4/41 (10%) lvs 6/41 (15%) lvs 31/41 (75%) lvs

L, laminectomy; PS, posterior surgical stabilization; VB, vertebral body; VBS, Vertebral Body Stenting. pts: patients. lvs: levels.

Table 2S

Summary of the VB reconstruction rankings and number of cases with cement leak, separately for the unilateral and bilateral approaches.

	Fair	**Good**	**Excellent**	**Cement Leak**
Unilateral (N=14)	4	4	6	3
Bilateral (N=27)	-	2	25	11
P (Pearsons's X^2)	0.057			0.478

Chapter 3

Stent-Screw Assisted Internal Fixation. The SAIF Technique to Augment Severe Osteoporotic and Neoplastic Vertebral Body Fractures

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Abstract

Objectives

To describe a new technique to obtain minimally-invasive, yet efficient vertebral body (VB) re-construction, augmentation, and stabilization in severe osteoporotic and neoplastic fractures, combining two pre-existing procedures. The implant of vertebral body stents (VBS) is followed by insertion of percutaneous, fenestrated, cement-augmented pedicular screws, that act as anchors to the posterior elements for the cement-stent complex. The screws reduce the risk of stent mobilization in a non-intact VB cortical shell, and bridge middle column and pedicular fractures. This procedure results in a 360° non-fusion form of vertebral internal fixation that may empower vertebral augmentation and potentially avoid corpectomy in challenging fractures.

Procedure details and applications

This report provides step-by-step procedural details, rationale, and proposed indications for this procedure. The procedure is entirely percutaneous, under fluoroscopic guidance. Through trans-pedicular trocars the VBS are inserted, balloon-expanded and implanted in the VB. Over k-wire exchange the trans-pedicular screws are inserted inside the stents' lumen, and cement is injected through the screws to augment the stents, and fuse the screws to the stents. This technique may find appropriate applications for the most severe osteoporotic fractures, with large clefts, high-degree fragmentation and collapse, middle column and pedicular involvement, and in extensive neoplastic lytic lesions.

Conclusions

Stent-Screw Assisted Internal Fixation (*SAIF*) technique might represent a minimally-invasive option to obtain VB reconstruction and restoration of axial load capability, in severe osteoporotic and neoplastic fractures, potentially obviating more invasive surgical interventions, in situations that would pose significant challenges to standard vertebroplasty or balloon-kyphoplasty.

Introduction

Vertebral augmentation (VA) has been extensively used for pain palliation and stabilization of vertebral body fractures due to trauma, osteoporosis, and tumors [1-3]. The introduction of the Vertebral Body Stent (VBS) (DePuySynthes-Johnson&Johnson®) further empowers these techniques. VBS is a balloon-expandable barrel-shaped metallic cage, which is percutaneously inserted via uni- or bi-pedicular access. Upon expansion, the VBS maintains the cavity through balloon-deflation and subsequent cement injection. Introduced for treatment of vertebral compression fractures[4-10], VBS has been used in neoplastic fractures[11] as well. Most recently, it has been tested in cases of extensive osteolysis of the vertebral body, to reconstruct the anterior column[12].

VBS has several potential advantages over traditional non-instrumented augmentation, in that the rigid stent remains expanded after balloon-deflation thus maintaining the restored vertebral body (VB) height[7]. The VBS metallic mesh virtually guarantees a predictable and reasonably uniform barrel-shaped balloon-expansion, whereas a compliant balloon often follows the path of least-resistance. The barrel-shape of the VBS, with its large support-surface, provides mechanical support, scaffolds the VB from within, and where necessary, recreates VB walls, such as in dehiscent or fragmented cortical boundaries. Further, the metallic mesh helps contain the injected cement in the created cavity. These characteristics potentially favor the use of VBS in the most severe vertebral fractures, such as highly fragmented osteoporotic fractures, or neoplastic fractures with prominent cortical osteolysis.

Despite the advantages enumerated above, in the most severe osteolytic or neoplastic fractures the implanted VBS may only be partially contained by the non-intact cortical shell. In that situation, the VBS could potentially be expected to mobilize[6,12], leading to adverse events. Other potential issues in the VBS treatment of these lesions is the frequent association with middle column and pedicular fractures, in the face of which VBS augmentation might represent an under-treatment.

The aim of this manuscript is to describe a new technique, combining the VBS implant to the insertion of percutaneous trans-pedicular cannulated fenestrated screws, followed by

cement deposition through the screw, with the intent to anchor the VBS-cement implant to the posterior elements, reduce the risk of VBS mobilization, bridge middle column and pedicular fractures.

This Stent-Screw-Assisted Internal Fixation (SAIF) technique, as opposed to the standard surgical external fixation achieved with screws and rods bypassing the index level, might represent a minimally invasive image-guided 360° non-fusion form of vertebral reconstruction and stabilization in severe osteoporotic and neoplastic thoraco-lumbar vertebral fractures.

Procedural details

This is a technical note describing the procedural details, and potential applications, of a new technique, combining the use of two established and already reported procedures and devices[7,13-14]. The Institutional Review Board approved this investigation, and the patients signed a required informed consent to undergo the procedure.

Figure 1 shows SAIF model, instrumentarium, main procedural steps and schematic drawings, while figures 2-4 report SAIF in three different clinical scenarios, representing examples of potential clinical applications of the technique.

Procedural Instructions for Bilateral SAIF

The patient is placed under general anesthesia and turned prone. Intravenous antibiotic prophylaxis is administered . Under fluoroscopic guidance, a 4.5 mm (7G) caliber trocar, included in the VBS access kit, is positioned via trans-pedicular access at the pediculo-somatic junction, bilaterally, as per a standard Balloon Kyphoplasty (BKP), with an oblique latero-medial orientation[15] (Fig. 1). Particular care is observed to insert the trocar parallel to the anticipated alignment of the original “pre-fracture” endplates, to allow the most efficient vertebral height restoration during VBS expansion (Fig. 4). Manual drills are placed co-axially through trocars to creates the necessary space for the balloon-mounted vertebral body stent which are then inserted on each side in the VB. The stents are expanded, as desired and possible, by balloon inflation with a manual hydraulic pump, using saline or contrast, trying to obtain fracture reduction and height restoration. The balloons are deflated and removed, while the expanded stents remain in place (Fig. 1). At this point the trocars are removed leaving a k-wire (1.4 x 350 mm, blunt tip) in place. The tract is not dilated. Over the k-wire, through the same 6-8 mm skin stab incision, a low-profile manual screw-driver (Fig. 4) is used to place percutaneous

transpedicular fenestrated cannulated screw (injection pin, 2B1, Milan-Italy) of desired length (34-55 mm) and caliber (5 or 6 mm), as planned on the basis of the pre-procedure CT axial images. The screw is inserted into the lumen of the stent, until the bulbous head reaches the dorsal cortex of the posterior elements. The screw-driver is removed, and over the same k-wire a 14G, 210 mm long cannula with luer-lock hub, is inserted in the screw for upcoming cement injection (Fig. 1). The screws have multiple fenestrations at the distal tip, and along their entire threaded stem, to allow and optimize cement dispersion. The cannula fits within the screw lumen and the position of the injection cannula can be adjusted along the entire stem, from the distal tip to its proximal end, to manage the desired site of cement injection (Fig. 1). The injection cannula is compatible with all commercially available PMMA cements and with any luer-lock injection system. PMMA injection is monitored with real time fluoroscopy in lateral view with intermittent antero-posterior checks. Most commonly cement is injected in the distal third of the screw and is seen permeating from the screw fenestrations inside the stents' lumen, and after stents' filling, either overflowing to the adjacent stent, or to the anterior open end of the stent, or interdigitating through the mesh into the adjacent trabecular spaces. Cement injection is halted if extravertebral leaks occur or if cement approaches the posterior wall. When cement injection is deemed complete the injection cannula is retracted and the screw left in place. When the PMMA hardens, the screws are fixed in the VBS-cement complex implant, and anchor it to the pedicles and posterior elements' cortex. There is no need to apply suture stitches since the stab incisions are very small. The patients are allowed to stand and walk as early as three hours after the procedure and, if clinically conditions allow, may be discharged the same day.

Applications

We propose the SAIF technique to perform vertebral augmentation in severe osteoporotic fractures, such as those characterized by crush deformity, advanced collapse (Genant grade 3)[16], high degree of osseous fragmentation (McCormack comminution grade 2 and 3)[17], large osteonecrotic cleft, middle column and pedicular fractures, or more in general in those vertebral fractures with advanced loss of integrity and quality of trabecular and cortical bone (Fig. 4). Similarly, in neoplastic lesions (Figg. 2-3), SAIF might be considered to augment extensive osteolytic lesions with dehiscent cortical boundaries (Tomita extracompartmental lesion type 4-6)[18], fractured, or at risk of impending collapse.

Discussion

SAIF is a previously undescribed technique, combining implant of Vertebral Body Stents and cement augmentation through percutaneous pedicular screws. In the aggregate, VBS and screws become a solid construct; the screws anchor the VBS to the posterior elements, and potentially bridge and stabilize middle column and pedicular fractures. This represents an advance over traditional augmentation in that also the middle column is stabilized.

Vertebral augmentation, performed with vertebroplasty or BKP has limitations in complex osteoporotic fractures with advanced bone loss, and in extensive lytic lesions[19-21]. Cement distribution in these highly destroyed VBs might be unpredictable, uneven, or even result in early extravertebral leak, leading to insufficient augmentation and stabilization, or to clinical complications, if central vascular migration or neural compression occur. Middle column fractures characterize potentially unstable fractures, and augmentation of the anterior column alone might represent an undertreatment. In addition, frequently associated pedicular fractures represent a treatment dilemma, and cement augmentation is biomechanically inefficient on structures that bear tensile forces[22].

These injuries are commonly considered for a surgical treatment of stabilization, that may include corpectomy performed through anterior or antero-lateral approach. At the same time, this approach carries significant invasiveness and morbidity risk[23-24], especially in elderly patients affected by osteoporosis or neoplastic diseases. Therefore, a minimally invasive treatment option remains desiderable.

In vertebral lesions with severely altered osseous structure the SAIF technique offers a VB reconstruction by the VBS metallic cages and cement. These bilateral implants scaffold the VB offering a large support surface along the disc-endplates, help contain cement along dehiscent cortical boundaries (Fig. 3), and, filled with cement, become a structure of “armed concrete”, able to bear the axial load in a solid and uniform manner in the VB. Cement flowing from one stent to the other, either interdigitating through the mesh, or passing through the anterior open ends, creates a solid bridge between the two VBS (Figg. 2 and 4), and the screws that are cemented inside the stents represent the anchors to the most commonly intact posterior elements, largely limiting the risk of VBS mobilization. The whole construct, with the two stents interconnected by the bridge, and the two screws as anchors, might be

regarded as an internal VB prosthesis fixed to the neural arch (Fig. 2). Insertion of a unilateral screw can also be considered, especially in neoplastic cases, when one of the two pedicles is involved by lytic destruction and would not offer a good anchoring.
As opposed to a surgical corpectomy, grafting and posterior instrumentation, the disc spaces and the mobility of the spinal functional units are spared. Nevertheless, when indicated, SAIF can be combined with a posterior surgical instrumentation. Inserting screws with a rod connecting system, the screws at the target level might even be connected to the bars of a posterior instrumentation. The whole SAIF procedure is image-guided, percutaneous and minimally invasive, performed through two small skin stab incisions. The addition of the screws to the VBS is entirely performed over a k-wire, enhancing its safety and rapidity. The cement injection through the screws into the VB can be adjusted at operator's preferences, sliding the injection cannula along the screw stem. Recovery is more typical of a percutaneous procedure, so that most patients are allowed to stand after few hours, and return to their normal activities within 24 hours from the procedure. Moreover, in neoplastic patients, SAIF does not interfere with chemotherapy or radiation treatment.

Risks and contraindications for the SAIF procedure are the same as for vertebroplasty, BKP or VBS.
The additional procedure time and material costs that SAIF requires are justified in consideration of the patient selection, challenging features of the treated lesions, short hospitalization, and fast patient's recovery, especially if compared to a standard surgical procedure.

We do not utilize nor recommend VBS and SAIF in young patients with traumatic fractures, in which bone quality is supposed to be good, and large volume implants in the VB with VBS and PMMA may halt spontaneous osseous healing.

In conclusion SAIF technique might represent a minimally invasive treatment option to reconstruct the VB and restore axial load capability in severe osteoporotic or neoplastic fractures, potentially obviating the need for a more invasive surgical procedure of corpectomy and grafting. Biomechanical and clinical studies are needed to further prove this concept.

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Figures

Figure 1

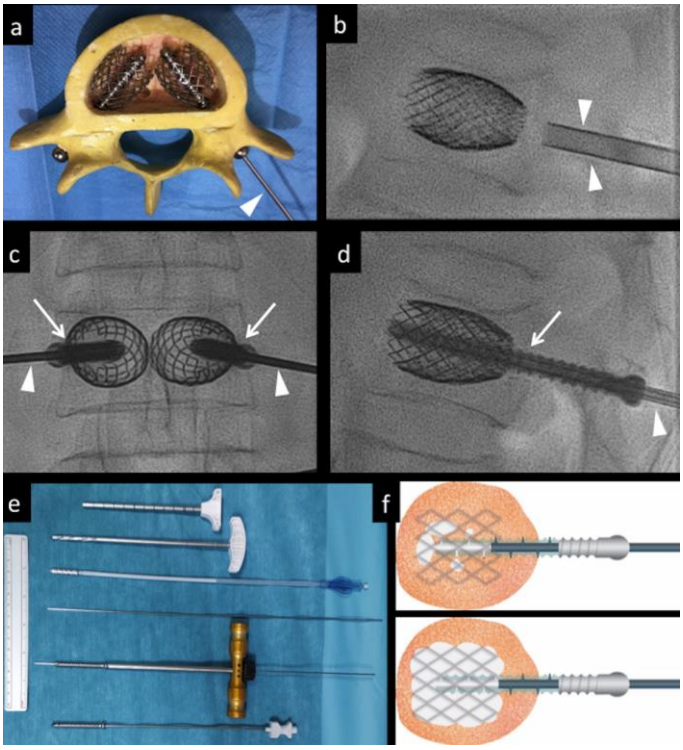

Figure 1. SAIF technique. In a) a model representation of the SAIF implants in a lumbar vertebra. Bilateral vertebral body stents expanded and implanted, with transpedicular fenestrated screws inserted in their lumen. Cement injection through the screws inside the stents would follow, via the injection cannula (arrowhead), but is not shown to maintain visibility of the implants. In b-d) the main fluoroscopy-guided procedural steps of SAIF before cement injection. In b) a lateral fluoroscopic view showing the stents that have been inserted and expanded in the vertebral body through the bilateral transpedicular access cannulae (arrowheads). In c) and d) antero-posterior and lateral views respectively showing that the cannulae have been replaced, via k-wire exchange, with transpedicular cannulated fenestrated screws (arrows) inside the stents; over the same k-wire a cannula for cement injection is inserted inside each screw (arrowheads). In e) the main strumentarium for SAIF technique is shown; from top to bottom the 7G trocar, the manual coaxial drill, the balloon-mounted stent, the k-wire, the screw mounted on a screw-driver, over a k-wire, and the 14G cement injection luer lock cannula inserted in the screw. In f) a schematic drawing showing how the fitting cannula (in blue) can be positioned along the screw stem, so that cement (in white) flows through the screw fenestrations distal to the cannula tip, and fills the stent lumen.

Figure 2

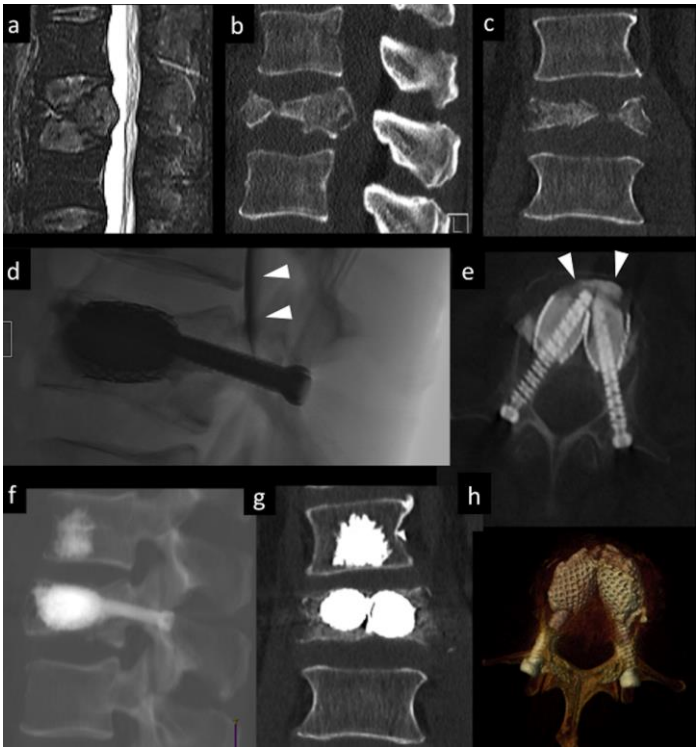

Figure 2. SAIF technique in a L2 hepatocarcinoma metastatic fracture. Patient with hepatocarcinoma, 56 yo, M, with disabling drug-resistant mechanical back pain, and evidence on MR (a) and CT (b-c) of a severely collapsed and fragmented L2 vertebral body fracture, with involvement of middle column and posterior wall retropulsion, but without neurological deficit. In d) a lateral fluoroscopic view in prone position shows the result of SAIF, with pedicular screws inside the stents, filled by PMMA cement augmentation. There is residual intra-dural contrast agent from intra-operative myelographic control (arrowheads). There is significant height restoration of the vertebral body, and optimal stent cement augmentation, in absence of extra-vertebral leaks. Post procedure CT (e-h) shows the vertebral body reconstruction by the stents, the cement bridge along the anterior aspect of the stents (arrowheads on e), and the screws cemented inside the stents, anchoring to the posterior elements. Prophylactic vertebral augmentation was performed at L1. The patient reported rapid and sustained pain relief, and was discharged the same day, after 6 h of observation. He expired 5 months later but until his death he had no further back pain or issues.

Figure 3

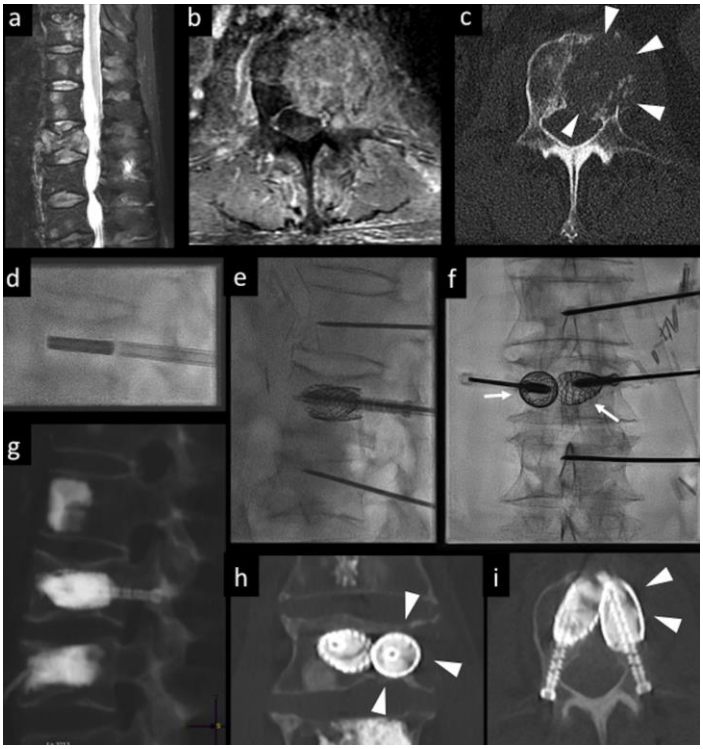

Figure 3. SAIF technique in a L2 renal cell cancer large lytic lesion. Patient with renal cell cancer, 64 yo, M, with severe mechanical axial back pain. MRI with sagittal fat-suppressed T2-W (a), and axial fat-suppressed contrast-enhanced T1-W (b) images show pathological fracture with partial collapse of the L2 vertebral body, on a large vertebral and extra-compartmental enhancing soft tissue mass, centered in the left side of the vertebral body, crossing midline, extending to the left pedicle, ventral epidural space and perivertebral space on the left, toward the psoas. Multilevel metastatic spinal involvement is also noted. Correspondant axial CT image (c) shows the lytic nature of the lesion with largely dehiscent cortical borders at the posterior and left antero-lateral walls (arrow-heads on c). Standard vertebral augmentation would pose significant risk of early extra-vertebral cement leak and insufficient stabilization due to the extensive cortical osteolysis. SAIF fluoroscopic intra-procedural images (d-f) show insertion of stents, their balloon expansion, and insertion of screws; additional 14 G needles are inserted at L1 and L3 for standard augmentation. To be noted the slight left-sided lateralization of the stents (arrows on f) to obtain maximum protection of the left hemibody, predominantly involved by the lytic lesion. Post-procedure CT (g-i) , after cement-augmentation, shows how the stents with cement have reconstructed the destroyed portion of the vertebral body and now offer support to bear axial load. The stents' walls recreate vertebral body walls along the disc-endplates and lateral aspect of the vertebral body (arrowheads on h and i), and limit the risk of cement leak. The screws anchor the stents-cement complex to the posterior elements, minimizing the risk of displacement. The patient reported significant pain relief, was able to stand and walk the same day, and already after three days underwent radiation treatment for local disease control.

Figure 4

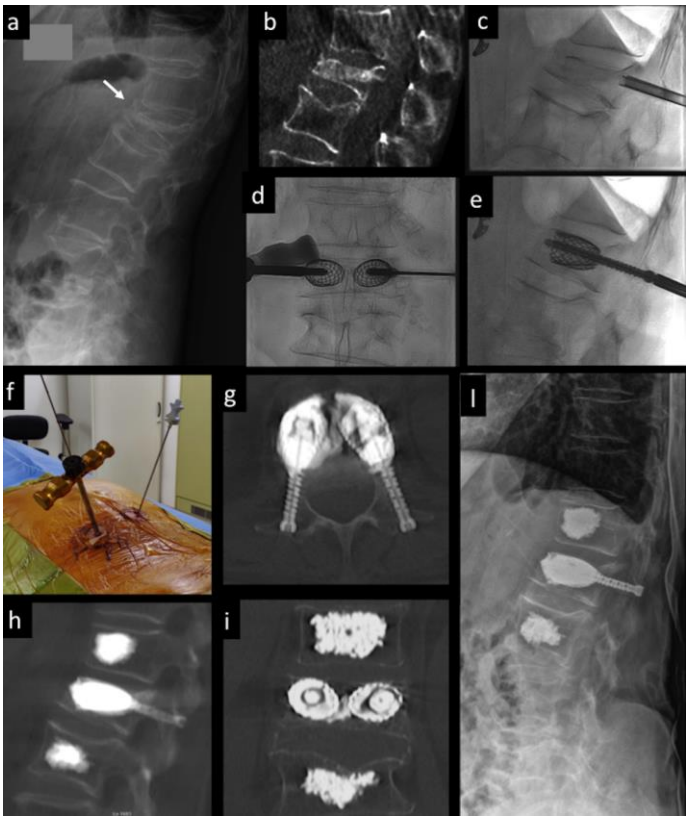

Figure 4. SAIF technique in a osteoporotic fracture with vertebra plana deformity. A 75 yo F patient, with known osteoporosis, following a fall from her height reported severe back pain. Imaging revealed a mild L1 compression fracture. Despite best medical conservative treatment disabling pain persisted and at 14 days, follow-up standing plain films revealed progression to vertebra plana deformity (arrow on a), with severe junctional kyphosis (Cobb angle 28°), which was keeping the patient bed-ridden. CT confirmed the fracture (b), slightly reduced in the supine position, suggesting a mobile fracture, and milder compression fractures at T12 and L2. Procedural fluoroscopic images show the trocar access parallel to the anticipated alignment of the original “pre-fracture” endplates (c), to allow the most efficient vertebral height restoration during vertebral stent expansion and screw insertion (d-e). Image (f) shows the operation field corresponding to the (d) fluoroscopic image, with the low-profile screw driver over the k-wire on the left, and the cement injection cannula already inserted in the screw on the right. Post-procedure CT images (g-i) show the obtained height restoration and internal vertebral body reconstruction and fixation of L1, and standard cement augmentation at T12 and L2; the stents are interconnected by a “bridge “ of cement, and are anchored to the posterior elements by the screws. Patient was then able to stand and walk with significantly reduced pain, and standing plain films at 1 month follow-up (l) showed stability of the implants and of the height restoration, with markedly reduced junctional kyphosis (Cobb angle 15°).

Chapter 4

Stent-screw Assisted Internal Fixation (SAIF) of Severe Lytic Spinal Metastases: a Comparative Finite Element Analysis on SAIF Technique

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Abstract

Objective

A new Stent-screw Assisted Internal Fixation (SAIF) minimally invasive cement-augmentation technique has been introduced to treat patients with extensive osteolytic lesions of the vertebral body. The aim of the current Finite Element (FE) study, employing a spine model with an extensive osteolytic defect, was to assess the effect of the SAIF technique in reducing strains in the vertebral body in comparison with a standard surgical short posterior fixation.

Methods

Different FE models of a L1-S1 spine were developed, representing an intact condition (reference configuration), an extensive osteolysis condition, and its treatment, respectively with stand-alone SAIF, SAIF and posterior fixation, and with stand-alone posterior fixation. Each model was loaded to reproduce standing and upper body bending. Principal strains were calculated on the superior endplate, anterior and posterior cortical walls. A paired Wilcoxon test with a 0.05 significance level was performed to statistically analyze the results.

Results

Median strains on the bony structures increased in the osteolysis model compared to the intact model and SAIF technique was effective in reducing such strains under standing and flexion conditions. Additional posterior fixation, combined to SAIF technique, produced minimal further reduction of the median strains on the bony structures. Stand-alone posterior fixation only shielded the osteolytic vertebra avoiding excessive displacements, but failed in restoring the axial stiffness to values typical of the intact vertebra.

Conclusions

The new SAIF technique resulted effective in restoring the load-bearing capacity of the extensively osteolytic vertebra; additional posterior fixation provided only further minor advantages.

Key Words: Extensive Osteolysis (EO); Finite Element Model (FEM); Screw-Stent Assisted Internal Fixation (SAIF); spinal metastases; spine biomechanics

Introduction

Extensive neoplastic osteolytic lesions within the vertebral body (VB) reduce the load bearing ability of the anterior and middle spinal columns, leading to fracture, instability and potential neurological deficit[1].

Surgical spinal stabilization, including anterior column reinforcement and posterior instrumentation, provides an effective method to prevent this cascade[2]. However, the surgical approach involves the performance of corpectomy and grafting. It is highly invasive and brings significant morbidity in fragile patients. Moreover, posterior stabilization using pedicle screws and rods may not be appropriate in case of multilevel metastatic involvement or poor bone quality[3,4]. VB cement augmentation is often considered, due its minimal invasiveness for reinforcement of the anterior column[5], as a stand-alone measure or combined with posterior instrumentation, but it may not be feasible in case of extensive disruption of the osseous cortical boundaries of the VB. In such conditions of extreme osteolysis (EO) there is a risk of cement leakage outside the VB, that may lead to neurological complications or insufficient augmentation[6]. Vertebral body stenting (VBS), based on balloon-expandable metallic cages (stents) and cement-augmentation, may represent a further option allowing fracture reduction and VB reconstruction, while reducing the risk of cement-leakage[6,7], but stent-cement complex mobilization has been reported[8], and is certainly a concern in cases of EO[7].

A new Stent-screw Assisted Internal Fixation (SAIF, Figure 1) technique has been recently proposed to overcome these issues[9]. This minimally invasive` technique combines the advantages of VBS cement-augmentation and the usage of cannulated/fenestrated pedicle screw to reconstruct/restore the load bearing capacity of the anterior spine, and anchor the stents to the posterior neural arch, generally less extensively affected by the metastases.

In the biomechanical literature, much effort has been made to characterize the mechanical behaviour of lytic defects with finite element models (FEM) and experimental tests. The defect size/volume, its shape and location are key factors to predict the risk of VB fracture[10,11,12], while axial load is considered the most challenging loading condition[13]. As far as vertebral augmentation is concerned, the cement volume and its elastic modulus are considered more important factors than its shape or distribution[14], a full height restoration is indicated as a key factor to reduce the stress on the surrounding bony structures[15], while cement bridging both

endplates provides adequate strength[16]. Other experimental study demonstrated that VBS allows a complete restoration of the VB height, while restoring its overall stiffness and strength[17]. No biomechanical analysis on the new SAIF technique has been published. The aim of the current FEM study, employing a lumbar spine model with an EO defect at L3, was to compare the effect of the new SAIF technique in restoring the load bearing capacity of the anterior spinal column, and in reducing bone strains, in comparison with a standard surgical short posterior fixation.

Materials and Methods

Different FEM lumbar spine models were created to conduct a comparative analysis.

Intact and EO models

An intact non-linear FEM representing the L1-S1 spine segment of a healthy 40 year-old human male without spinal pathology nor defects[18] was used as a reference, and named the “intact model”. The model (Figure 2), complete with vertebral bodies, intervertebral discs and ligaments, has already been validated by comparison with experimental in-vitro measurements regarding kinematics, overall compressive stiffness, and strains reached on each vertebra[15].
To exclude any effect due to the boundary conditions, the middle vertebra (L3) was selected as the level of interest to reproduce the lytic defect as a low modulus (5 MPa) linear elastic isotropic region[10]. To quantify the reliability of the EO model in reproducing the published in-vitro experiments on a two functional spinal units (FSUs) segment, where a defect was artificially created in the middle vertebra[19], the intact L2-L4 sub-segment was initially considered. A defect matching the size of the defect described by Groenen[19] was introduced at L3, assigning adequate material properties[10] to the elements representing the defect and those representing the vertebra. To evaluate its overall axial stiffness, the segment was loaded with an axial force while the caudal vertebra was totally constrained.
After performing the validation simulations on a L2-L4 segment, the subsequent comparative analyses were performed on the complete L1-S1 segment, introducing in L3 a severe EO defect involving 100% of the trabecular bone volume and the right pedicle: this model was named “EO model” (Figure 2).

SAIF model

To describe the SAIF technique on the EO model (Figure 2), the cannulated screw CAD model (2B1 SRL, Milan, Italy) was properly positioned through the right pedicle of the L3 vertebra using ICEM CFD (Ansys Inc), followed by boolean operations and remeshing of all parts using tetrahedral elements. Attention was paid in maintaining a good compromise between mesh refinement and the computational cost; for the same reason, the metallic cage of the stent was not included in the model, assuming it gives a negligible contribution to the overall compressive stiffness of the treated vertebra compared to the PMMA bone cement that completely fills and surrounds the stents. To reproduce anterior cement augmentation with optimal endplate-to-endplate filling[16], linear elastic material properties typical of PMMA (E= 2.5GPa, Poisson ratio of 0.44)[20] were assigned to the anterior 2/3 of the VB (about 20ml), while the titanium screw was modelled with a 110 GPa elastic modulus[21].

Posterior fixation models (FIX and SAIF+FIX)

Bilateral posterior spinal fixation on the EO model was reproduced introducing titanium pedicle screws at L2 and L4 levels, bridged by a titanium 5.5mm straight spinal rods[21]. Embedding elements technique was used to constrain the screw within the pedicles, while a tie constraint was assumed at screw-rod interface[21,22,23]. This model, named “FIX model”, intended to represent a standard surgical short posterior stabilization (Figure 2). To study the advantages of supplemental posterior fixation coupled to the new SAIF technique, the bilateral instrumentation was introduced also on the SAIF model, named “SAIF+FIX model” (Figure 2).

Comparative FE analyses

Each model was loaded to reproduce standing (500N axial follower load) and upper body bending (1175N axial follower load + 7.5Nm flexion moment), keeping the sacrum constrained[24,25]. All simulations were run in ABAQUS Standard 2017 (Dassault Systèmes Ri, Simulia Corp, Providence, RI, USA).

To investigate the effect of the new SAIF technique in restoring the load bearing capacity of the anterior spine, the axial stiffness of the SAIF-treated vertebra and the strain distribution on the surrounding bony structures were compared with the intact, the untreated EO, the FIX and the SAIF+FIX conditions. Principal strains values, possibly related to bone fracture risk[26,27]

were calculated on set of elements within selected regions of interest of L3, namely the superior endplate (EP), the anterior and posterior cortical walls. To determine any statistical difference between the median values collected on each region of interest a paired Wilcoxon test with a 0.05 significance level was performed. Box plot representation, showing 25–75% interquartile ranges, median bar and whiskers indicating the 5–95% range (with a cross indicating the average value), was used to allow qualitative comparison. To point out any mechanical issue related to the usage of the cannulated screw, the maximum von Mises stresses were evaluated and compared across the SAIF models.

Results

Intact and EO model

The overall axial stiffness predicted for the L2-L4 sub-segment was within the range of experimental values reported by Groenen et al.[19], demonstrating the capability of the EO model in delivering realistic results.

In the complete L1-S1 models, the intact L3 vertebra exhibited an axial stiffness of 12.8 kN/mm and the median strains remained relatively low with the superior EP undergoing mainly tensile strains, and the anterior and posterior walls undergoing compression in standing (Table 1, Figures from 3 to 5). In upper body flexion (Table 2) the tensile strains generally increased on the superior EP, anterior and posterior wall, while the compression remained relatively low on the superior EP and posterior wall (Figures 3 and 5), and increased on the anterior wall (Figure 4).

The axial stiffness of the vertebra was reduced by 74% in the simulated EO defect compared to the intact condition (Table 1), while the median strains on the bony structures were significantly increased up to one order of magnitude on the superior EP and on the posterior wall of the EO model compared to the intact model (Table 1, 2, Figures 3 and 5). The strains were 2 to 16 times greater during standing and 1.5 to 15 times greater during flexion, with the anterior wall being the least affected and the superior EP being the most affected.

SAIF technique stand-alone effectively recovered the axial stiffness of the treated vertebra. SAIF technique was effective in significantly ($p<0.05$) reducing the median strains on the bony structures by 95% on the superior EP and by 70% on the anterior and posterior cortical walls compared to the untreated EO condition in standing (Table 1, Figures from 3 to 5).

In flexion the strain reduction was again significant, beyond 91% on the superior EP, about 85% on the posterior wall, and 40% on the anterior wall (Table 2, Figures from 3 to 5).

Supplemental posterior fixation coupled to SAIF technique (SAIF+FIX) increased the axial stiffness by two orders of magnitude with statistically significant ($p<0.05$) effects in further reduction of the median strains on the posterior wall of 14%, while the strains increased by 10% on the anterior wall in standing (Table 1, Figures 4 and 5). During flexion the trend in SAIF+FIX was opposite, with a relative strain increase of 5% on the posterior wall and a decrease of 11% on the anterior wall when compared to SAIF model (Table 2, Figures 4 and 5).

Short posterior fixation alone (FIX) only shielded the EO vertebra avoiding excessive displacements, but failed in restoring the axial stiffness to values typical of the intact vertebra. Additionally, it was significantly less effective than SAIF technique in reducing the strains on the bony structures, with statistically significant ($p>0.05$) percentage reduction of median values of about 35% only on the superior EP and on the posterior wall compared to the EO model in standing (Table 1, Figures 3 and 5). In flexion, the strain significantly decreased only on the superior EP of about 25%, while it remained comparable or slightly increased on the remaining structures (Table 2, Figures from 3 to 5).

The highest von Mises stress value predicted on the cannulated screw was 47MPa and it was reached in the SAIF model.

Discussion

The new SAIF technique allows a minimally invasive percutaneous reconstruction of the vertebral body disrupted by extreme osteolysis. The VBS reduces the fracture, creates an internal VB scaffold, and helps contain PMMA cement, while the augmented screw anchors the stent-cement complex to the posterior elements, preventing its mobilization, thereby representing a non-fusion form of internal fixation[7,9].

The current study aimed at testing the biomechanical rationale of SAIF technique, both in terms of restoration of the load bearing capacity of the VB (i.e. axial stiffness) and of the reduction of the fracture risk (i.e. principal strains) on the bony structures.

Our model successfully described the loss of axial stability of the VB due to the presence of a large lytic defect within the L3 vertebra, in nice agreement with the experimental in-vitro tests on cadaveric specimen simulating a bone defect[19]. This idea is well documented by the clinical literature reporting an increased fracture risk in case of extensive osteolysis, justifying the need for an immediate and effective treatment of stabilization[1,3,4].

According to our models, the SAIF technique effectively restored the load bearing capability of the VB to values typical of an intact spine and significantly reduced the strains on all bony structures (beyond 90% on the superior EP and the posterior wall, about 40% on the anterior wall) compared to the untreated EO condition. Moreover, the SAIF technique was significantly more effective than fixation, which only partially shielded the metastatic vertebra without being capable to reduce the strains on all the considered structures. In particular, when fixation was considered, during standing the anterior wall was exposed to significantly higher tensile strains and to similar compressive strains compared to the untreated EO condition, while, in flexion, which is considered even more risky than standing for the occurrence of VB collapse, also the posterior wall was exposed to relatively high strains, potentially indicating a higher fracture risk.

The supplementation of the SAIF technique with posterior fixation only lead to a marginal decrease of the strains on the bony structures (about 5% on the superior EP and the posterior wall, about 16% on the anterior wall). This relatively small advantage should be weighted on the higher invasiveness of a surgical posterior fixation technique, and the potential interference with initiation of radiation treatment. For the same reason, other potentially relevant, but highly invasive, surgical strategies based on long segment stabilization, corpectomy and vertebral body cages implantation were excluded from the current analysis.

The scenario represented by the SAIF model could represent a worst-case condition in the context of use of the proposed technique. In fact, standard SAIF technique implies bilateral screw insertion. The choice to test a SAIF model with unilateral screw was made to test the SAIF technique in the most challenging situation, as in cases where local anatomy precludes bilateral screws insertion. In these cases, it is important to implant the stents in an adjacent "kissing configuration" to facilitate the creation of a PMMA cement bridge between the two VBS-cement complex, so that a unilateral screw can effectively anchor and stabilize the VBS-cement complex to the vertebral neural arch.

The choice to simulate also upper body flexion, known as a high-demanding activity correlated to the risk of VB fracture, has been made once more in order to fully represent a *worst-case* condition to which the patient can be subjected: in this situation results must be interpreted looking at compressive strains on the anterior cortical wall in which a higher bone fracture risk is expected. In this region SAIF efficiently reduces (-65%) compressive strains while posterior fixation alone was less effective (-32%): the multiple usage of SAIF and posterior fixation furtherly enhances the reduction obtained by SAIF, but only to a limited extent (further -7%).

It is important to report that, in all these *worst-case* configurations, the maximum stress on the cannulated pedicle screw, even when surrounded by a pedicle affected by the osteolysis, were much lower than the typical yield point for Titanium alloy (about 750 MPa), thus assessing its mechanical reliability for this specific application.

The approach used in the current paper does not catch inelastic phenomena and failure modes related to vertebral body collapse. However, it allows a comparison across different instrumentation strategies assuming that only elastic deformations occur upon loading, as confirmed by the reported strain values never exceeding the maximum bone strength (strain equal to about 1%). The shape and volume of the treated L3 vertebral body were assumed to be equal to the intact condition, which relates to the high volume (20 ml) of cement in the VB assumed to be injected in the SAIF model. This choice may more closely represent a preventive treatment of the vertebra, rather than a partially collapsed condition[15], while allowing to investigate the full potential of the SAIF technique assuming a perfect height restoration with optimal endplate-to-endplate cement filling[16]. Nevertheless, the current approach has the advantage to precisely control specific study parameters (e.g. defect volume, material properties, loading conditions), that may present a wide variability in a real clinical setting and may involve a confounding effect on the results. This is a limitation of the present study.

Future FEM studies could be addressed to evaluate the usage of the SAIF technique at multiple thoraco-lumbar spinal levels typical of metastatic conditions. Moreover, the model could be easily upgraded to describe an osteoporotic condition, where the SAIF technique could represent a valuable mini-invasive surgical option[9]. Finally, it will be surely important to compare the results of the current study with long-term prospective or retrospective clinical study as the results will become available.

Conclusion

In our FEM simulations the new SAIF technique was effective in restoring the load bearing capacity of the EO vertebra, while significantly reducing the strain on the surrounding bony structures. Additional posterior fixation only provided minor advantages. The present study provides a solid biomechanical rationale to support the usage of the technique for the treatment of vertebrae affected by extensive osteolysis.

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Figures and tables

Figure 1

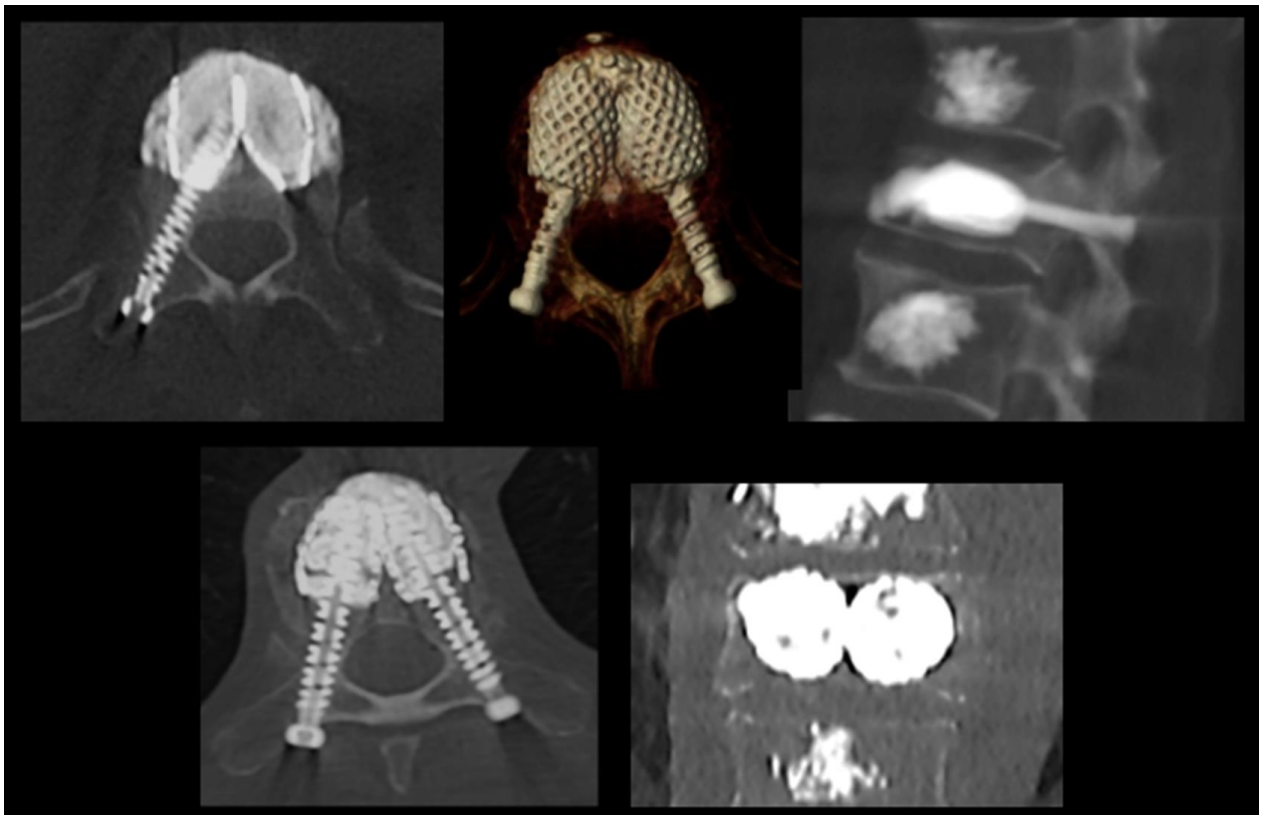

Figure 1: multiplanar reformatted and 3D volume rendering CT images of vertebrae treated with the new Stent-screw Assisted Internal Fixation (SAIF) technique. The VBS balloon-expandable stents are inserted in the vertebral body through trans-pedicular access; uni-pedicular or bipedicular fenestrated screw(s) are percutaneously inserted in the stent(s). Stents are then filled with cement through the screw(s). The stent-cement complex augments the vertebral body, while the screw(s) anchor the construct to the posterior elements.

Figure 2

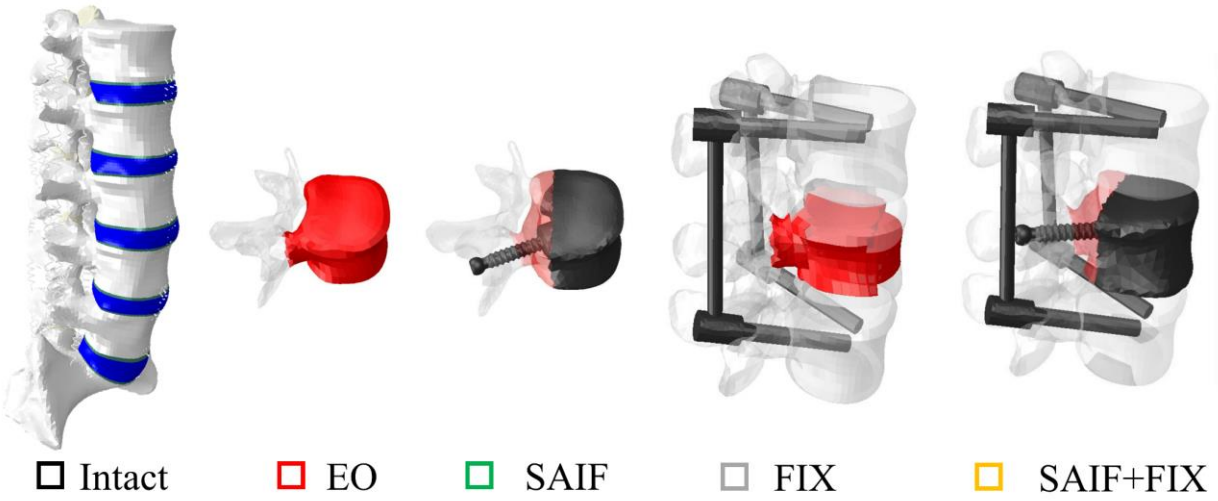

Figure 2. L1-S1 FEMs considered in the study: for clarity the L3 VB is not shown in the L1-S1 model but separate for EO and SAIF models, as is the L2-L4 segment for SAIF+FIX and FIX. The osteolysis involving the trabecular osseous component is represented in red, bone cement and implants in dark grey.

Figure 3

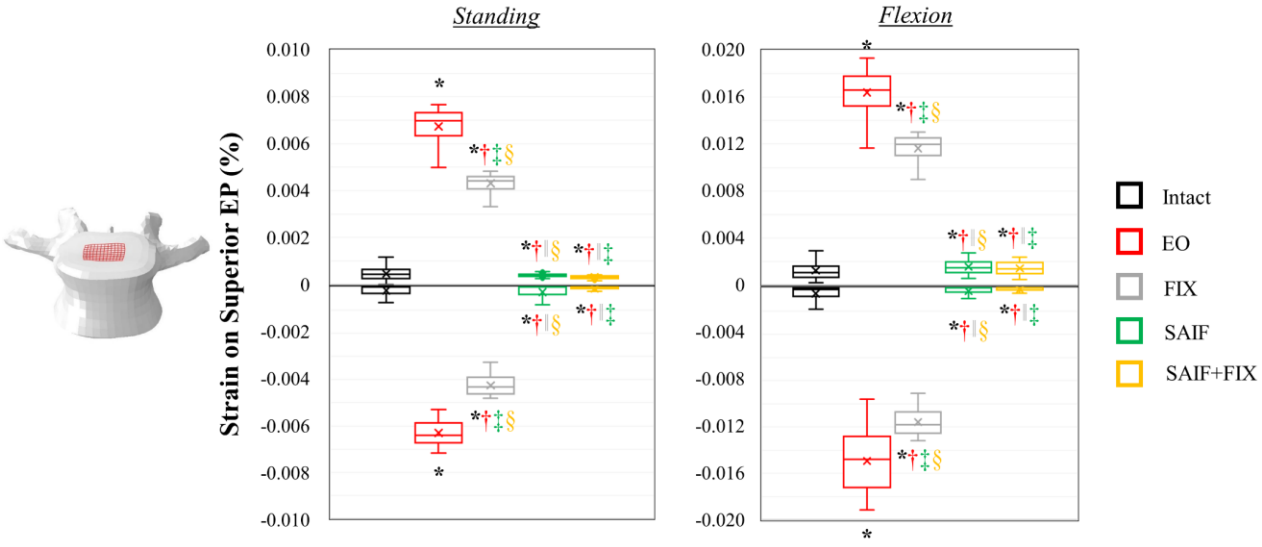

Figure 3. Box plots representing the strains on the superior EP for all simulated configurations. *, †, ǁ, ‡, §: indicate significant differences ($p<0.05$) in median values compared to intact, EO, FIX, SAIF and SAIF+FIX models, respectively.

Figure 4

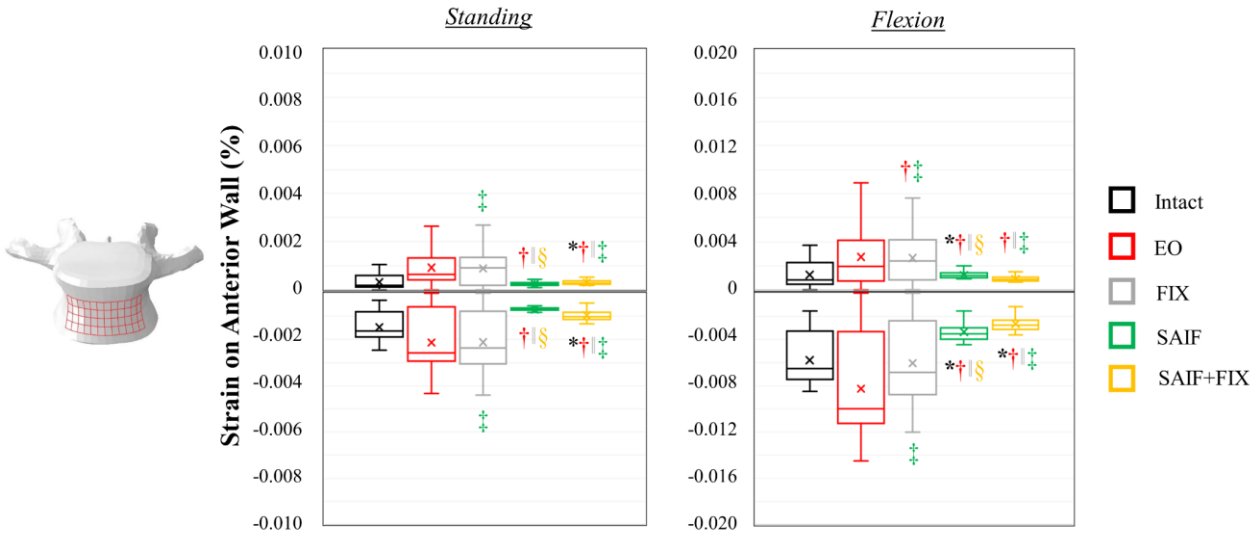

Figure 4. Box plots representing the strains on the anterior wall for all simulated configurations. *, †, ǁ, ‡, §: indicate significant differences ($p<0.05$) in median values compared to intact, EO, FIX, SAIF and SAIF+FIX models, respectively.

Figure 5

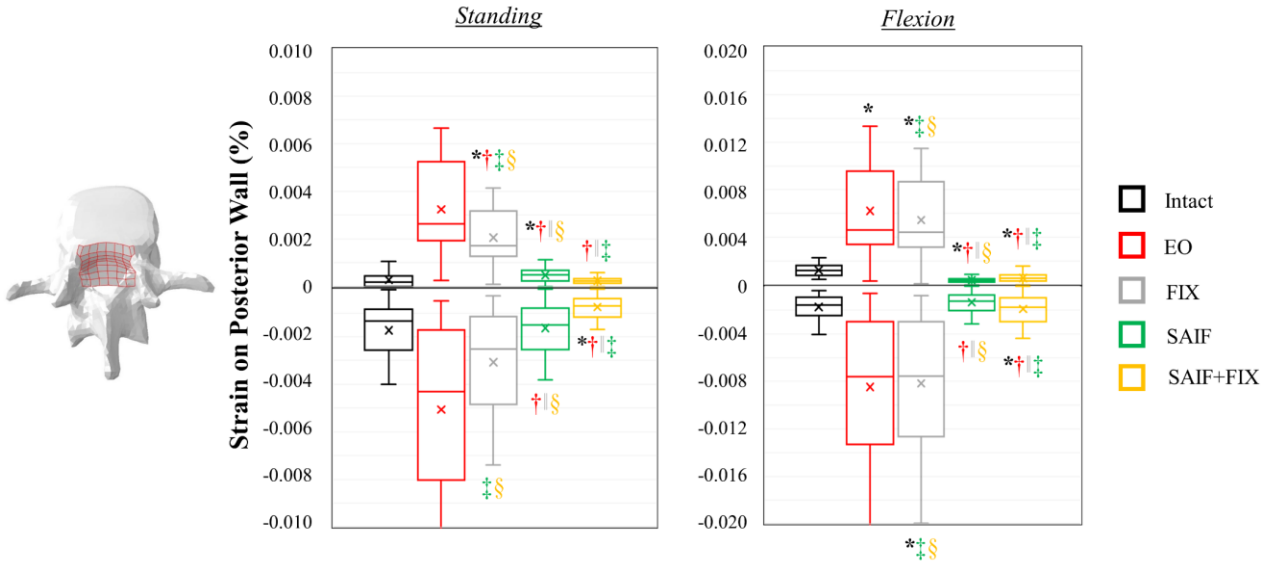

Figure 5: Box plots representing the strains on the anterior wall for all the simulated configurations. *, †, ǁ, ‡, §: indicate significant differences ($p<0.05$) in median values compared to intact, EO, FIX, SAIF and SAIF+FIX models, respectively.

Table 1

Median of the principal strains and axial stiffness obtained during standing in each configuration.

		Standing				
		INTACT	**EO**	**SAIF**	**FIX**	**SAIF+FIX**
Superior EP	**Max Principal Strain (%)**	0.004	0.070 (*)	0.004 (*,†,‖,§)	0.044 (*,†,‡,§)	0.003 (*,†,‖,‡)
	Min Principal Strain (%)	-0.001	-0.064 (*)	-0.001 (*,†,‖,§)	-0.043 (*,†,‡,§)	-0.001 (*,†,‖,‡)
Anterior wall	**Max Principal Strain (%)**	0.002	0.006	0.002 (†,‖,§)	0.009 (‡)	0.003 (*,†,‖,‡)
	Min Principal Strain (%)	-0.016	-0.027	-0.007 (†,‖,§)	-0.024 (‡)	-0.010 (*,†,‖,‡)
Posterior wall	**Max Principal Strain (%)**	0.002	0.026	0.005 (*,†,‖,§)	0.017 (*,†,‡,§)	0.002 (†,‖,‡)
	Min Principal Strain (%)	-0.013	-0.043	-0.014 (†,‖,§)	-0.025 (‡,§)	-0.007 (*,†,‖,‡)
Axial Stiffness (kN/mm)		12.8	3.3	6.3	6.3	535.4

*, †, ‖, ‡, § indicate significant differences ($p<0.05$) in median values compared to intact, EO, FIX, SAIF and SAIF+FIX models.

Table 2

Median of the principal strains obtained during flexion in each configuration.

		Flexion				
		INTACT	**EO**	**SAIF**	**FIX**	**SAIF+FIX**
Superior EP	**Max Principal Strain (%)**	0.010	0.166 (*)	0.014 (*,†,‖,§)	0.120 (*,†,‡,§)	0.014 (*,†,‖,‡)
	Min Principal Strain (%)	-0.001	0.149 (*)	-0.001 (*,†,‖,§)	-0.118 (*,†,‡,§)	-0.001 (*,†,‖,‡)
Anterior wall	**Max Principal Strain (%)**	0.008	0.020	0.012 (*,†,‖,§)	0.024 (†, ‡)	0.009 (†,‖,‡)
	Min Principal Strain (%)	-0.065	0.100	-0.035 (*,†,‖,§)	-0.068 (‡)	-0.028 (*,†,‖,‡)
Posterior wall	**Max Principal Strain (%)**	0.012	0.046 (*)	0.004 (*,†,‖,§)	0.045 (*,‡,§)	0.006 (*,†,‖,‡)
	Min Principal Strain (%)	-0.014	0.076	-0.013 (†,‖,§)	-0.076 (*,‡,§)	-0.018 (*,†,‖,‡)

*, †, ‖, ‡, § indicate significant differences ($p<0.05$) in median values compared to intact, EO, FIX, SAIF and SAIF+FIX models.

Chapter 5

Stent-Screw–Assisted Internal Fixation (SAIF): Clinical Report of a Novel Approach to Stabilizing and Internally Fixating Vertebrae Destroyed by Malignancy

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Abstract

Objective

Severe lytic cancerous lesions of the spine are associated with significant morbidity and treatment challenges. Stabilization and restoration of the axial load capability of the vertebral body (VB) are important to prevent or arrest vertebral collapse. Percutaneous stent screw–assisted internal fixation (SAIF), which anchors a VB stent/cement complex with pedicular screws to the posterior vertebral elements, is a minimally invasive, image-guided, 360° internal fixation technique that can be utilized in this patient cohort. The purpose of this study was to assess the feasibility, safety, and stabilization efficacy of VB reconstruction via the SAIF technique in a cohort of patients with extensive lytic vertebral lesions, who were considered to have an unstable or potentially unstable spine according to the Spinal Instability Neoplastic Score (SINS).

Methods and results

This study was a retrospective assessment of a prospectively maintained database of a consecutive series of patients with neoplastic extensive extracompartmental osteolysis (Tomita type 4–6) of the VB treated with the SAIF technique. VB reconstruction was assessed on post-procedure plain radiographs and CT by two independent raters. Technical and clinical complications were recorded. Clinical and imaging follow-ups were assessed.

Thirty-five patients with extensive osteolytic metastatic lesions of the VB underwent 36 SAIF procedures. SAIF was performed as a stand-alone procedure in 31/36 cases and was associated with posterior surgical fixation in 5/36 (4/5 with decompressive laminectomy). In 1 case an epidural cement leak required surgical decompression. VB reconstruction was categorized as satisfactory (excellent or good rating) by the two raters in 34/36 cases (94.5%) with an interrater reliability of 94.4% (Cohen’s kappa of 0.8). Follow-up, ranging from 1 to 30 months, was available for 30/36 levels. Long-term follow-up (6–30 months, mean 11.5 months) was available for 16/36 levels. Stability during follow-up was noted in 29/30 cases.

Conclusions

SAIF provides 360° non-fusion internal fixation that stabilizes the VB in patients with extensive lytic lesions that would otherwise be challenging to treat.

Keywords extreme osteolysis; pathological fracture; vertebral body stents; pedicular screws; stabilization; internal fixation; stent screw–assisted internal fixation; SAIF; oncology. Abbreviations EO = extreme osteolysis; ESCC = epidural spinal cord compression; PMMA = polymethyl methacrylate; SAIF = stent-screw–assisted internal fixation; SINS = Spinal Instability Neoplastic Score; VA = vertebral augmentation; VB = vertebral body; VBS = VB stent.

EXTENSIVE neoplastic osteolysis of the vertebral body (VB) can significantly impact the load-bearing capacity of the spine,[38] leading to instability, fractures, and potential neurological deficit.[34] While percutaneous augmentation procedures have traditionally focused on pain palliation, mechanical stabilization is an independent surgical indication.

Surgical treatment is effective at restoring the mechanical stability of the anterior and posterior columns,[39] but instrumented fusion may not always be appropriate in cases of multilevel metastatic involvement or in patients with poor bone quality. Moreover, corpectomy and grafting, which reinforce the anterior column, are invasive and can lead to significant morbidity, especially in medically fragile patients.[6, 22, 25,44]

Vertebral augmentation (VA), performed with vertebroplasty or balloon kyphoplasty, is a minimally invasive option that reinforces the anterior column,[4] but when osteolysis causes extensive destruction of the cortical boundaries of the VB, there is risk of cement leakage, possibly resulting in neural compression or insufficient augmentation of the VB.[4,21] In the present study, we address the stabilization of such lesions, characterized by “extreme osteolysis” (EO) with wide circumferential discontinuity of the cortical boundaries of the VB, corresponding to extracompartmental type 4–6 lytic lesions in the Tomita classification (Fig. 1).[41]

VB stents (VBSs) are barrel-shaped, balloon-expandable metallic cages that can be used to reduce the vertebral fracture,[15,43] reconstruct the VB, and aid in cement augmentation of EO cases.[9] Nevertheless, in a VB with extensive cortical dehiscence, there is risk of VBS/cement mobilization before new bone apposition occurs.[9]

The recently described percutaneous stent screw–assisted internal fixation (SAIF),[8] whereby the VBS/cement complex is anchored with pedicular screws to the posterior vertebral elements, is a minimally invasive image-guided, 360° internal fixation technique. It can be performed as a stand-alone procedure or in combination with a posterior surgical approach to stabilize the anterior column. We hypothesized that SAIF can be successfully employed in EO as a means of VB reconstruction and restoration of axial load capability with the aim of obviating the need for a more invasive corpectomy and grafting. The purpose of this study was to assess the feasibility, safety, and stabilization efficacy of VB reconstruction via the SAIF technique in a cohort of patients with EO of the VB, who were considered to have an unstable or potentially unstable spine according to the Spinal Instability Neoplastic Score (SINS).[18]

Methods

Patients

This is a retrospective analysis of a single-center, prospectively maintained database of a consecutive series of patients with neoplastic EO of one or more thoracolumbar VBs treated with SAIF between May 2015 and September 2018. The study was authorized by the Ethics Committee of Canton Ticino].

All patients underwent pre-procedure CT and gadolinium-enhanced MRI of the spine at the target level to define the extent of lytic lesions, the degree of vertebral collapse (≤ or >50%), and the presence of an associated epidural mass defined as epidural spinal cord compression (ESCC) grade[5] between 1b and 3. All target lesions were deemed to be unstable or potentially unstable according to the SINS.[18]

An individualized clinical decision on the treatment plan for each patient was reached by a multidisciplinary spine tumor board composed of medical and radiation oncologists, spine surgeons, and neuroradiologists, who defined indications for and the timing of invasive treatment, radiation, and chemotherapy. Informed consent was obtained for all procedures.

SAIF Procedure

SAIF procedural details have been previously described.[8] Briefly, all procedures were performed percutaneously while the patient was under general anesthesia, with the aid of biplane fluoroscopic guidance. When deemed necessary, cavity creation was performed utilizing curettage and vacuum suction (Q-VAC technique).[35] Following transpedicular implant of the VBS(s) and placement of uni- or bilateral pedicular screws, cement augmentation was performed through the screw(s) with high-viscosity polymethyl methacrylate (PMMA; VertaPlex HV, Stryker) under real-time fluoroscopy.

In cases of multilevel lytic lesions, when deemed appropriate, additional vertebrae at adjacent or distant levels were treated with cement-only VA during the same session. Patients undergoing a stand-alone SAIF procedure were allowed to stand and walk without spinal braces as early as 3 hours after the procedure. Most SAIF procedures were performed in a day surgery outpatient setting.

Assessment of VB Reconstruction, Complications and Follow-Up

VB reconstruction was assessed with postprocedure plain radiographs and CT scans. CT data sets were reconstructed utilizing a bone algorithm with 3- and 10-mm-thick maximum intensity projection (MIP) images in three orthogonal planes. A neuroradiologist (A.C.) and a neurosurgeon (P.S.) independently reviewed the postprocedure images to assess the technical results, assigning a VB reconstruction "score." We applied a previously published, qualitative 4-grade scale (poor, fair, good, excellent),[9] based on the overall assessment of correct placement and expansion of the implants, cement filling of the lytic cavities, and restoration of the VB height. A poor grade was characterized as a failure to achieve sufficient augmentation of the anterior column, whereas an excellent grade indicated stent expansion and cement distribution filling the lytic lesion and reconstructing the destroyed portion of the VB, satisfactory height restoration, and correct screw positioning.

Intraprocedural complications, including potentially significant cement leaks, and misplacement of the screws were recorded.

At 1 month after treatment, patients were followed up with clinical examination and upright spine radiographs. Patients underwent routine oncological clinical and imaging follow-up with CT, PET-CT, MRI, or plain radiography, as clinically indicated. Those clinical charts and imaging studies were reviewed as part of this study. Imaging follow-up data were evaluated to assess the recurrence of vertebral collapse, new or worsening spinal deformity of the treated segment, mobilization of the implants, signs of subsidence, new vertebral fractures at adjacent levels, and local tumor progression. Patients were referred to the multidisciplinary spine tumor board for any recurrent or new spinal events.

Statistical Analysis

Analyses were conducted using SPSS version 20.0.0 (IBM Corp.). Descriptive statistics for clinical and demographic data were expressed as the mean or median and range. VB reconstruction results were judged according to the following scale: poor, fair, good, or excellent. Excellent and good ratings were considered as satisfactory results[9].Cohen's kappa coefficient (□) was used to assess the proportion of agreement of the two independent raters beyond that expected by chance,[11] and the classification by Landis and Koch[32] was used to

define the agreement level: poor, < 0.00; slight, 0.00–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; substantial, 0.61–0.80; or almost perfect, 0.81–1.00.

Results

In 35 patients, 36 SAIF procedures were performed to treat 36 levels with EO. A summary of patient characteristics and features of the lytic lesions is provided in Table 1, whereas technical results and periprocedural complications are summarized in Table 2.

Technical Results

SAIF procedures were performed as a stand-alone intervention in 31/36 cases, in conjunction with percutaneous posterior surgical fixation in 1/36 cases, and after decompressive laminectomy and posterior surgical fixation in 4/36 cases. Bilateral VBS implants were utilized in 33/36 levels (92%), and a unilateral VBS implant was used in 3/36 levels (8%). Bilateral screws were utilized in 18/36 levels (50%), and unilateral screws were used in 18/36 levels (50%). Cavity creation in the VB with Q-VAC[35] was performed in 29/36 levels.
During the same procedure, cement-only VA was performed at adjacent or distant vertebral levels (i.e., affected by lytic lesions, but not defined as EO) in 22/35 patients, at a total of 61 levels.

VB Reconstruction

VB reconstruction scores assigned by the two raters were respectively excellent at 27/36 (75%) and 28/36 (78%) levels, good at 7/36 (19.4%) and 6/36 (16.7%), fair at 2/36 (5.6%) and 2/36 (5.6%), and poor at none of the treated levels, with satisfactory results (excellent or good rating) in 34/36 cases (94.5%) for both raters. The interrater reliability was 94.4% with a Cohen’s kappa of 0.8 indicating strong interrater reliability.

Procedural and Periprocedural Safety

An extravertebral cement leak was visible at 12/36 levels (33%) on postprocedure CT, with an epidural or a foraminal location in 7/36 levels (19%). In 1 case the epidural cement leak caused the postprocedural onset of an L2 sensory and motor deficit necessitating

emergent L2 decompressive hemilaminectomy, with complete resolution of symptoms. In another case a small epidural leak caused transient, self-resolving L5 radicular pain. The remaining cement leaks were asymptomatic. No other patients experienced worsening of their neurological status after the procedure. One patient with a preexisting neurological deficit due to spinal cord compression underwent SAIF associated with laminectomy and posterior instrumentation and did not experience worsening of his neurological condition. One patient who had undergone SAIF combined with laminectomy and surgical stabilization subsequently developed a pulmonary embolism on day 1 postprocedure, with no evidence of PMMA emboli, and died on day 2. No other periprocedural clinical complications occurred.

Follow-Up Results and Non-neurological Complications

A summary of follow-up results is provided in Table 3. Postprocedure clinical and imaging follow-up was available at 1 month for 30/36 treated levels, at 3 months for 24/36 levels, and at 6 months or later (range 6–30 months, mean 11.5 months) for 16/36 levels.

In 1 patient treated with unilateral-screw SAIF, the nonanchored VBS mobilized dorsally, toward the neuroforamen, 1 month postprocedure in the context of an unrecognized preexisting vertebral osteomyelitis. This required surgical removal, curettage, and stabilization. Implant stability was otherwise observed in all remaining cases until the last available follow-up. Mild subsidence of the treated VB around the VBS/cement complex was observed during follow-up in 5/30 levels (17%) with available follow-up, without the onset of new symptoms. Intervertebral osseous fusion was noted in 4/16 levels (25%) with long-term follow-up (≥ 6 months). Local disease progression was observed in 2/30 levels (7%) at 3 and 5 months postprocedure, respectively, not affecting local spinal stability. No new fractures were noted at adjacent levels at the follow-up imaging.

Discussion

In this series of patients with EO and an SINS indicating potentially or frankly unstable lesions, the SAIF technique proved to be a feasible and safe minimally invasive procedure for VB reconstruction and stabilization, with durable results at follow-up. These clinical results seem to confirm recently published biomechanical data on a finite element analysis (FEM) of the SAIF technique applied to a vertebra affected by EO.[31] SAIF was effective in recovering the axial stiffness and reducing the strains of the treated vertebra in the tested scenario. In contrast, a short posterior fixation was unable to significantly restore stiffness and stability. Posterior fixation combined with SAIF showed only minor additional effects as compared to those obtained with SAIF alone. These biomechanical results clearly underscore the importance of anterior column support during stabilization of osteolytic lesions of the VB.

Vertebroplasty and/or balloon kyphoplasty are widely used for pain palliation in cancer-related vertebral compression fractures,[19,24,26] but when stability is a concern, posterior spinal instrumentation is warranted.[33] Stand-alone VA is relatively contraindicated in the presence of vertebra plana, osseous comminution, posterior wall dehiscence, or wide cortical erosions. In fact, these were exclusion criteria in a prospective randomized controlled trial comparing kyphoplasty to nonsurgical management in cancer patients with vertebral fractures.[1,4] While VA is sometimes done in these situations for pain palliation, such procedures do not address the instability.

VBS augmentation has been reported as a viable option to reconstruct the anterior column in EO,[9] but when the VB's cortical boundaries are widely dehiscent, there is risk of VBS mobilization.[9,28] Misplaced or dislocated stents outside the VB can cause serious complications such as injury to the nerve roots, spinal cord, lumbar plexus, great vessels, pleura, or mediastinal organs.[40] For these reasons, at the institution at which this study was undertaken, the patients with EO would have been treated with anterior column reconstructive surgery combined with posterior instrumentation. Percutaneous image-guided screw fixation is an emerging procedure for osteosynthesis using cannulated cement-augmented screws, demonstrating promising results in the fixation of osteolytic bone metastasis in the spine and other skeletal locations.[7,13,14,20,30,36]

The patients considered to be eligible for SAIF are medically fragile] fragile, which often limits the indication for corpectomy, anterior stabilization, and open posterior instrumentation.

Beyond that, poor bone quality due to multilevel metastatic involvement and/or osteoporosis represents a condition predisposing to instrumentation failure.

This is the first reported series of patients with EO spinal lesions treated with the SAIF technique[8] in which screws were used in combination with VBSs in EO spinal lesions with the intent to obtain 360° nonfusion internal VB fixation. A VBS was used to restore VB height, scaffold the VB, help cement containment, and reinforce the anterior column extensively destroyed by the lytic lesion. The addition of the screws guaranteed anchoring of the VBS/PMMA implant to the generally intact posterior elements, bridging the middle column and preventing their mobilization. The combined use of VBS, PMMA, and pedicular screws can represent a VB prosthesis in these extensively destroyed metastatic lesions and can be used as a stand-alone technique or combined with posterior instrumentation and/or decompressive laminectomy or separation surgery, potentially obviating the need for corpectomy and grafting.

In this series, all patients were evaluated by multiple specialists in the setting of a multidisciplinary spine tumor board with extensive experience in the treatment of oncological disease. After that consultation, when deemed appropriate and if reconstructive anterior column surgery was contraindicated, SAIF was performed as a stand-alone procedure (Figs. 2–4) or was combined with a posterior surgical approach for external fixation (Fig. 5) and decompressive laminectomy. Even in this challenging cohort, characterized by higher SINS (12–14) and higher ESCC grades (2–3), anterior and posterior stabilization was performed, avoiding more invasive surgical reconstruction of the anterior column and meaningful morbidity risks.[6,16] In this study, the SAIF group was not compared to a control group, as the patients in this series were in a very challenging clinical position with other clinical conditions and severe lesions of the VB that posed contraindications to standard augmentation procedures, making a more invasive anterior column surgery less palatable.[2]

SAIF Technique

SAIF was preferentially performed with bilateral VBS implants to offer more satisfactory VB reconstruction results.[9] Ideally, the SAIF technique should be performed with bilateral screw fixation (Figs. 2 and 4), but when EO involved one of the two pedicles, a unilateral screw was inserted through the intact pedicle to ensure osseous anchoring to the VBS/cement complex (Figs. 3 and 5). Especially in these cases, the VBSs should be positioned converging

toward the midline of the VB so that, upon expansion, the two stents could have a “kissing configuration,” favoring the creation of a PMMA bridge between the two VBSs. The screw anchor and cement bridge ensure stability of the construct. In 3 cases, given the presence of mixed lytic and sclerotic components in the VB, a unilateral VBS was implanted in the lytic area. The injected PMMA volume varied according to the size of the lytic lesions, trabecular compliance, stent expansion, and cement distribution. The goal is to obtain optimal cement filling and interdigitation in the nonlytic adjacent trabecular bone whenever possible. Techniques utilized to limit PMMA leakage and/or displacement of the soft tissue include the creation of a cavity,[8,10,35] the use of high-viscosity PMMA,[3,10] the containment effect of the VBS mesh,[9] and real-time fluoroscopic control during cement injection. These approaches were considered particularly relevant, as these patients had highly destructive lesions typically with a dehiscent posterior wall and the frequent coexistence of an epidural mass.

There were 22/36 levels with a high degree of vertebral collapse and 23/36 levels with an epidural mass on preprocedure MRI. Although MRI postprocedure was not routinely performed to assess soft-tissue encroachment of the central canal, there was no worsening of neurological status postprocedure. We hypothesize that cavity creation and fracture reduction, with reexpansion of the collapsed VB in a craniocaudal direction, may have had a role in preventing clinically significant soft-tissue migration in the central canal. All screws were positioned within the pedicles and in the VBS under fluoroscopic guidance, with no screw loosening observed at follow-up. The screws implanted in the SAIF technique are not connected to external fixation bars; thus, there are no strong stress forces on the screws that can predispose to screw loosening.

SAIF Stabilization Efficacy

The main aim of the SAIF procedure is VB reconstruction to restore axial load-bearing capability while avoiding more invasive traditional surgery in this compromised cohort. A previously published qualitative score based on postprocedure plain radiographs and CT images was used to assess the reconstruction:[9] the construct was judged satisfactory when appropriate placement of the devices, VBS expansion, and cement filling restored VB height and achieved reconstruction of the destroyed VB, appearing as a 360° nonfusion internal fixation of the affected VB. VB reconstruction was judged satisfactory (good or excellent) in 94.5% of cases by the two raters, with high interrater agreement.

Follow-up, ranging from 1 to 30 months, was available for 30 treated levels. At follow-up, the implants were stable with no VBS mobilization in 29/30 cases. The screw anchoring may represent a means of avoiding VBS mobilization in conjunction with other technical measures, such as a PMMA bridge, cement interdigitation, and optimized implant(s) positioning. In the late follow-up CT studies (≥ 6 months post-procedure), formation of a new cortical bone shell was noted around the construct, and in some cases intervertebral osseous fusion was observed (Fig. 3), suggesting the achievement of stability. Clinical and imaging follow-up was limited by patient death or loss to follow-up, but is nevertheless representative in such a cohort with advanced metastatic disease.

In a complex case treated with bilateral VBSs and a unilateral-screw SAIF for lung cancer metastatic thoracic EO, mobilization of the non–screw-anchored VBS occurred. The ex post facto case analysis revealed a series of clinical and technical errors likely contributing to the occurrence of this unfortunate complication. The patient had unrecognized osteomyelitis at the metastatic vertebral level that worsened and evolved into an epidural abscess. Moreover, the presence of osteolysis involving one pedicle suggested unilateral screw fixation on the intact side, but a “kissing configuration” of the VBSs was made impossible by a sclerotic spur within the otherwise lytic VB, which eventually prevented the desired creation of a PMMA bridge between the two VBSs. Interestingly, evolving osteomyelitis likely caused mobilization of the nonanchored VBS, while the screw-anchored VBS remained in place.

The majority of patients with EO experience mechanical pain. While pain palliation is an indication for treatment, it did not represent a formal endpoint of the present study. Our rationale was straightforward. Thousands of studies, including randomized controlled trials in which patients were randomized against conservative therapy in both osteoporotic and neoplastic fractures, have demonstrated meaningful pain improvement with augmentation.[4,27,42] Even sham studies that fail to demonstrate the expected differential benefit have included augmentation patients whose pain dramatically improves after the procedure.[17] In our cohort with EO and diffuse metastatic disease, concomitant VA was deemed necessary at adjacent or distant levels in 22/35 patients (61 levels; Fig. 3), and these patients concurrently received different regimens of radiotherapy, chemotherapy, and supportive care (including steroids and analgesic drugs)[12] including for metastatic deposits outside of the skeleton, e.g., the viscera. Despite these confounding factors, in a retrospective review of the medical records, an experienced medical oncologist (V.E) assessed pain amelioration potentially attributable to the SAIF

procedure in 19/35 patients (with no new or changed therapeutic regimen). In 4/35 patients, pain amelioration was attributable to the procedure in combination with chemo- or radiotherapy, while in 7/35 patients no significant pain amelioration was noted after the procedure. In 1 case pain was not evaluable because the patient had died 2 days after the procedure because of a pulmonary embolism unrelated to PMMA migration. The remaining 4/35 patients had no definite pre-procedure pain clearly attributable to the vertebral target lesion. In this study we utilized a clinical oncological evaluation rather than a formal visual analog scale. The outcomes illustrated symptomatic improvement and are comparable to those previously reported with the use of VBS in extensive VB lytic lesions.[9]

The SAIF procedure allows patients to recover quickly as compared to their recovery following open surgery. Its less invasive nature facilitates the start or resumption of radiotherapy or chemotherapy soon after the procedure. Moreover, the proposed SAIF technique offers the advantage of immediate stabilization of the VB, while radiotherapy alone cannot ensure stabilization. Indeed, stand-alone radiotherapy can be followed by a phase of increased vertebral fragility and fracture risk.[23,37]

Furthermore, patients with mechanical pain attributable to metastatic destruction or collapse of the VB with resulting intervertebral instability are nonresponders to radiotherapy alone. These patients generally require some form of stabilization procedure to address their mechanical instability.[29] Thus, we believe SAIF to have a complementary role to treatment with radiation and/or chemotherapy to achieve immediate VB reconstruction and stabilization, rapid pain relief, and local disease control.[23]

The clinical protocol utilized by practitioners involved our multidisciplinary spine tumor board is to consider stabilization via SAIF when a patient has a VB affected by EO and would have difficulty recuperating in a timely fashion from more traditional operative approaches. In fact, EO lesions commonly demonstrate wide cortical boundary erosion, bone comminution, advanced vertebral collapse, and epidural mass, which all represent at least a relative contraindication to more standard VA procedures. In these patients SAIF could represent a minimally invasive option when anterior column reconstructive surgery is contraindicated or not desired. Finally, in the presence of lytic involvement of the posterior elements, signs of gross instability such as fracture-related kyphotic or scoliotic deformity, or the highest SINSs or when decompressive laminectomy is indicated, SAIF can be combined with a posterior surgical approach, as was done in 5/35 patients in this series.

Complications

The majority of complications were technical and asymptomatic. Two patients (5.7%) reported a clinical complication secondary to an epidural leak, including an L2 sensory and motor deficit necessitating surgical posterior decompression, with no permanent deficit, and transient self-limiting L5 radicular pain for which no treatment was required. Two previous studies have reported a similar rate of epidural cement leakage, either during VA of neoplastic lytic lesions with a dehiscent posterior wall (14.2%)[10] or during VBS augmentation in EO (12.2%).[9] No other patients experienced worsening of their neurological status postprocedure. One patient with metastatic lung cancer died on postoperative day 1 as the result of a non–PMMA-related pulmonary embolism, which can be considered a non–SAIF-specific perioperative complication.

One non-anchored VBS mobilized at the 1-month follow-up and required surgical correction. This situation was likely related to underlying osteomyelitis. We recommend bilateral screw fixation of the VBSs; whenever this is not possible, a “kissing configuration” of the VBSs should be obtained to ensure the creation of a PMMA bridge between the two VBSs. Similarly, we do not recommend the SAIF technique if both pedicles are involved by the osteolysis and do not ensure safe osseous anchoring via the screw(s).

This SAIF series, in which a total of 2/36 levels required repeat surgery, compares favorably to a recent large retrospective series of posterior instrumentation, separation surgery, and anterior column cement reconstruction,[2] which reported an 18% overall rate of multiple surgeries due to wound complications, CSF leakage, tumor recurrence, hardware failure, and other causes.

Study Limitations

The principal limitations of this study are attributable to its real-world design, relatively small sample size, and the absence of a systematic clinicoradiological follow-up. Moreover, this study lacked a control group; however, as previously mentioned, the multidisciplinary team considered the patients to be poor candidates either for VA because of their EO lesion features or for anterior column surgery because of their clinical conditions. The VB reconstruction scale that we utilized is qualitative but did have optimal interrater agreement between raters from two distinct disciplines.

The strength of this study relates to the prospectively established database utilized, with all treated cases managed and followed up based on an established multidisciplinary clinical practice. We believe that this study may represent a preliminary step to support SAIF, a promising new technique, and that a larger study may provide stronger information upon which to base this minimally invasive approach of stabilization in patients with extensive lytic VB lesions. In addition, FEM analysis data provide a supportive biomechanical rationale for use of the technique in EO cases.[31]

Conclusions

The SAIF technique allows 360° nonfusion internal fixation to stabilize the VB in patients with extensive lytic lesions. SAIF appears to be an effective stabilization procedure with durable results at follow-up, and while there were transient and permanent complications, the population targeted for this procedure is inherently challenging. Therefore, SAIF may represent an alternative option to a more invasive corpectomy, either as a stand-alone intervention or in combination with a posterior surgical approach of decompression and stabilization.

In Brief

The authors assessed whether a new minimally invasive procedure, stent screw–assisted internal fixation, is feasible, safe, and efficacious in stabilizing severe vertebral fractures caused by extensive neoplastic spinal lesions and whether the results are stable at follow-up. This study is important because it shows that this new technique can be used to stabilize severe spinal lesions, avoiding the invasiveness of a standard surgical approach in medically fragile patients affected by these tumors.

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Disclosures

Dr. Hirsch is a consultant for Medtronic, Relievent, and Cerenovus and holds positions with DMSB and DMC

Author Contributions

Conception and design: all authors. Acquisition of data: Distefano, Cianfoni, Scarone, Espeli. Analysis and interpretation of data: Distefano, Cianfoni, Scarone, Pesce, Espeli, La Barbera, Villa. Drafting the article: all authors. Critically revising the article: Pesce, Bonaldi, Hirsch. Statistical analysis: Distefano. Study supervision: Cianfoni, Villa, Bonaldi, Hirsch.

Supplemental Information

Previous Presentations
Portions of the data included in this study have been presented as an oral presentation at the Spine Interventional Neuroradiology Section at the 57th Annual Congress of the American Society of Neuroradiology held in Boston, Massachusetts, in May 2019.

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Figures and tables

Figure 1

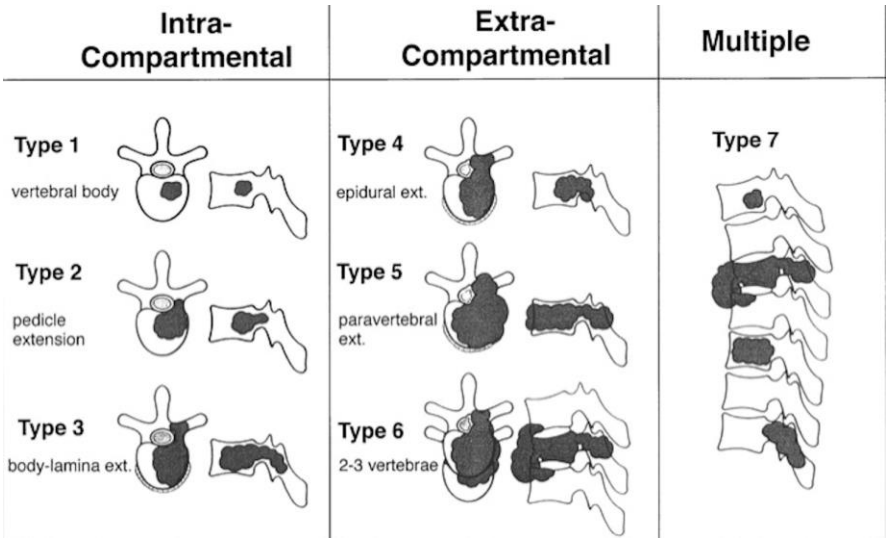

Figure 1. Schematic of Tomita's classification of spinal metastases. Lesions in the present study featured extensive osteolysis of the VB with wide cortical discontinuity, defined as "extreme osteolysis," corresponding to extra-compartmental type 4–6 lesions in the Tomita classification. Reprinted with permission from Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T: Surgical strategy for spinal metastases. *Spine 26 (3):*298–306, 2001. https://journals.lww.com/spinejournal/.

Figure 2

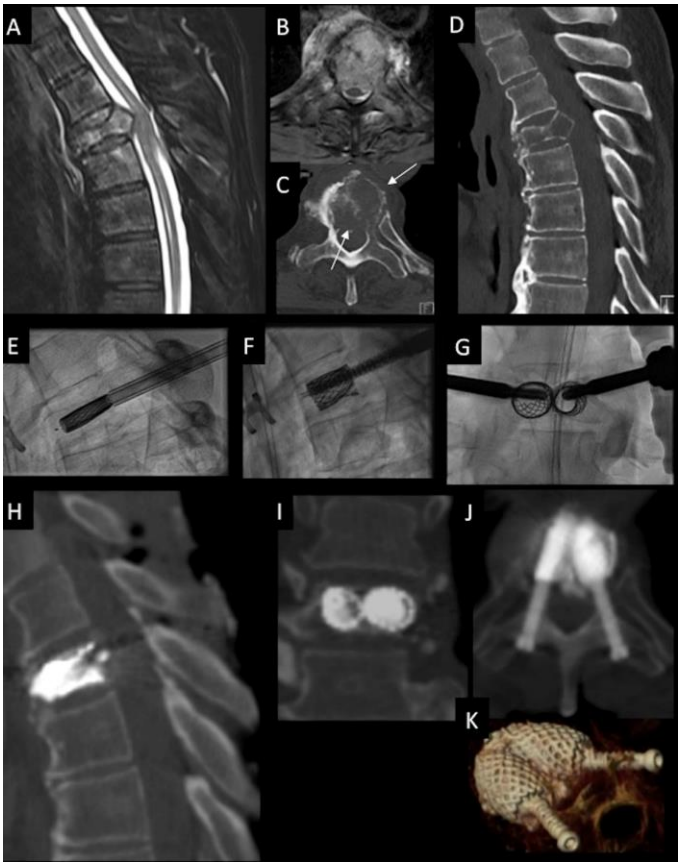

Figure. 2. Images obtained in the case of a lung cancer metastatic T4 fracture in a neurologically intact 72-year-old patient. Sagittal (**A**) and axial (**B**) fat-sat T2-weighted MRI showed VB collapse with central canal involvement and spinal cord compression, while CT (**C–D**) showed extensive osteolysis of trabecular and cortical VB components, namely posterior wall and left anterolateral wall dehiscence (*arrows* in C). The SAIF technique was performed with transpedicular stent placements (**E**) and expansion, followed by screw insertion (**F–G**) and cement augmentation. Postprocedure CT (**H–K**) showed fracture reduction, posterior wall retropulsion correction due to ligamentotaxis, and the stents/cement complex anchored by screws to the posterior elements, acting as a VB prosthesis. Figure is available in color online only.

Figure 3

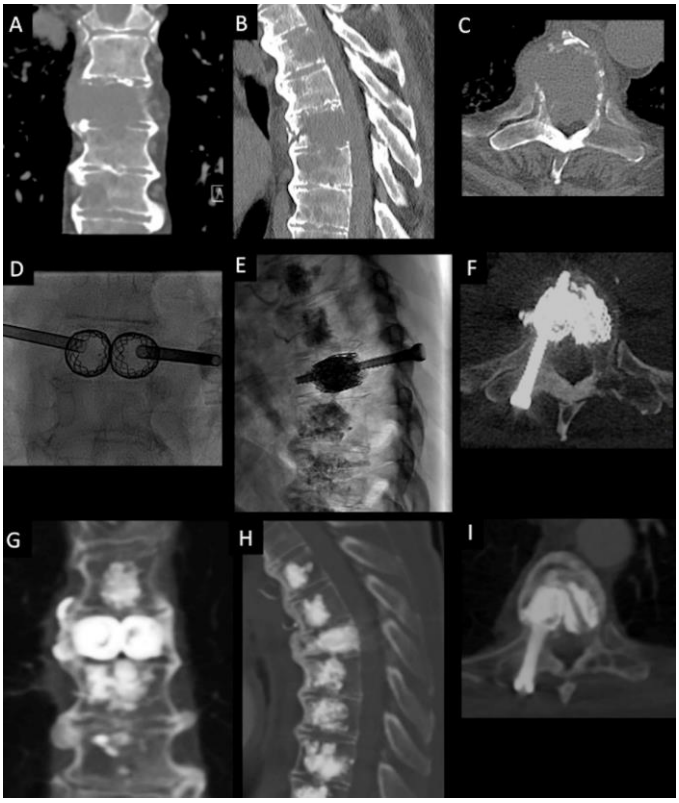

Figure 3. Images obtained in a 67-year-old patient with multiple myeloma and multilevel spine osteolysis. CT studies (**A–C**) showed EO of T7 with largely discontinuous VB cortical boundaries and a situation of impending collapse. The SAIF technique with bilateral stents and a unilateral screw was performed at T7 (**D–F**), along with cement-only VA at multiple other levels weakened by non-extreme lytic lesions. Follow-up CT at 24 months post-procedure (**G–I**) showed osseous re-apposition in formerly lytic lesions, embedding of the stents/cement complex, and intervertebral fusion suggesting stability.

Figure 4

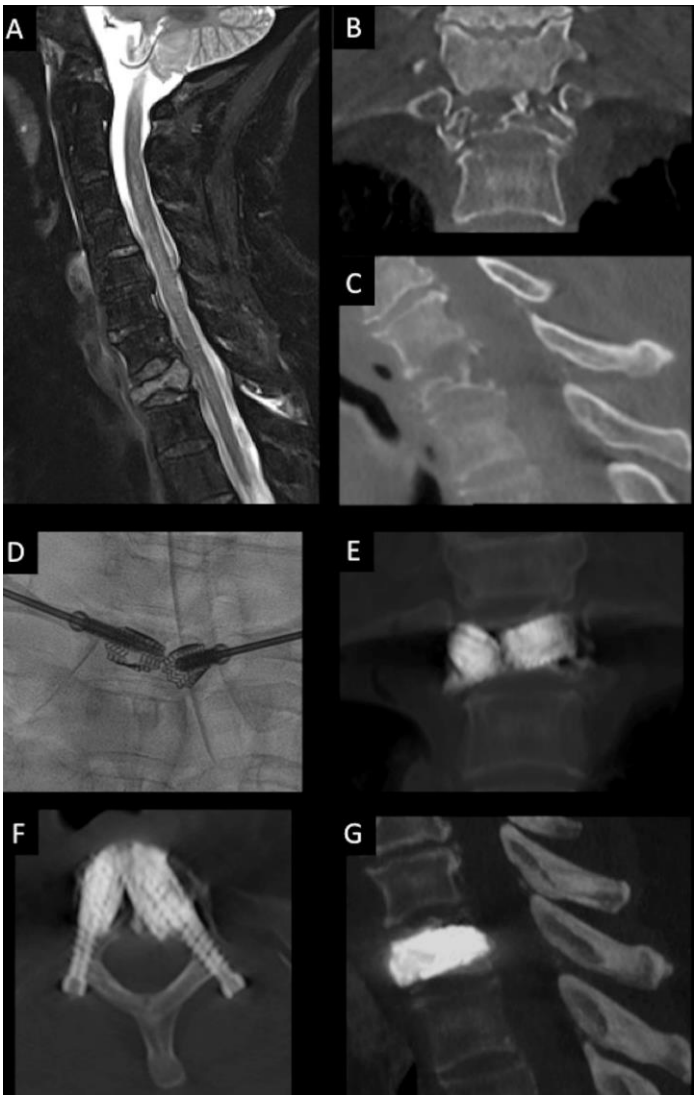

Figure 4. Images of a breast cancer metastatic T1 fracture in a 56-year-old patient. MRI (**A**) and CT (**B–C**) showed the severe VB lytic destruction and collapse. Long-segment posterior instrumentation would have limited the patient's mobility, and a T1 corpectomy would have posed significant surgical challenges. The patient could be treated with a percutaneous, minimally invasive, stand-alone SAIF approach (**D**). Postprocedure CT (**E–G**) displayed the optimal VB reconstruction by stents augmented with bone cement, anchored to the posterior elements by transpedicular fenestrated screws.

Figure 5

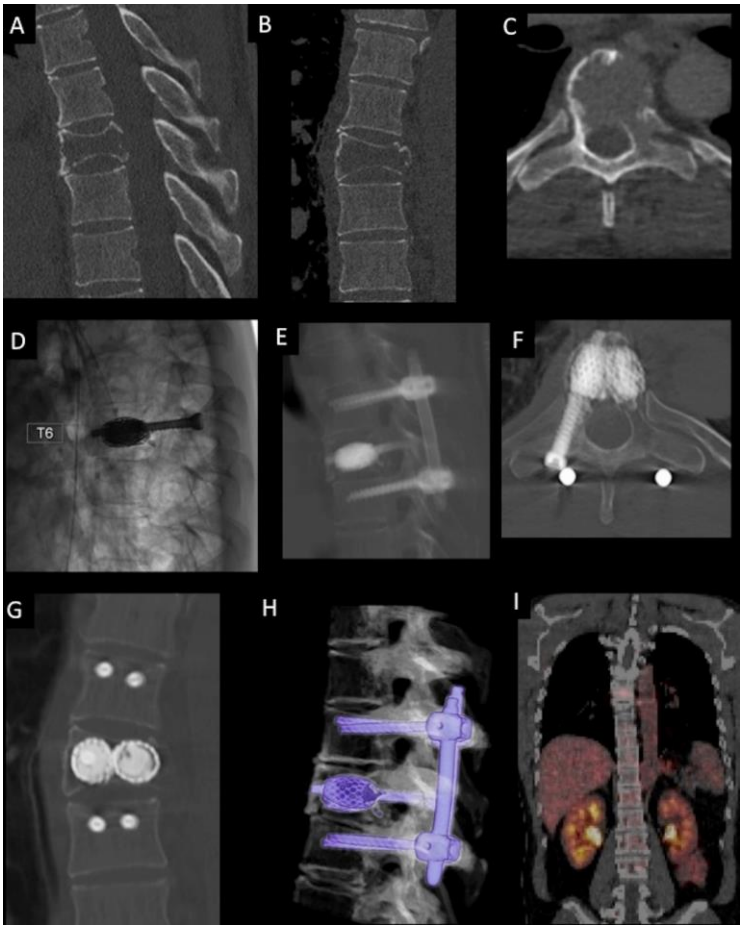

Figure 5. Images of a solitary plasmocytoma of T6 in a very tall and fit 52-year-old patient. Multiplanar CT images (**A–C**) showed EO of the VB also involving the left pedicle and the impending asymmetrical fracture causing scoliotic deformity in the frontal plane (B). The SAIF technique with bilateral stents and a unilateral screw was performed to reconstruct the VB (**D**) and avoid corpectomy. In the same anesthesia period, percutaneous short-segment dorsal instrumentation was added, as shown by postprocedure CT (**E–H**), to provide further stability given the patient's body habitus. PET-CT follow-up at 12 months (**I**), following chemotherapy, showed stable spinal alignment and no signs of residual or recurrent disease. Figure is available in color online only.

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Table 1

Characteristics of the study population and features of lytic lesions

Variable	Value
Total no. of patients	35
Sex: M/F	21/14
Mean age in yrs (range)	69.9 (43–87)
ECOG score Mean Median Range	 1.62 1 0–4
Treated levels Thoracic Lumbar	36 16/36 (44.4%) 20/36 (55.6%)
Primary cancer, no. of levels (%) Solid tumor metastases Multiple myeloma/plasmocytoma	 31 (86.1) 5 (13.9)
Epidural mass, no. of levels (%)	23/36 (63.9)
ESCC grade, no. of levels 0 1a 1b 1c 2 3	 8 5 9 5 5 4
VB collapse, no. of levels (%) ≤50% >50%	 14 (38.9) 22 (61.1)
SINS score Mean Median Range	 10.8 11 7–14

ECOG = Eastern Cooperative Oncology Group. ESCC: Epidural Spinal Cord Compression; SINS: Spinal Instability Neoplastic Score

Table 2

Summary of technical results and periprocedural complications

Variable	Value
Procedure, no. of levels (%)	
Stand-alone SAIF	31/36 (86.1)
SAIF + pPF	1/36 (2.8)
SAIF + L-PF	4/36 (11.1)
VBS, no. of levels (%)	
Bilat	33/36 (91.7)
Unilat	3/36 (8.3)
Screws, no. of levels (%)	
Bilat	18/36 (50.0)
Unilat	18/36 (50.0)
Cavity creation, no. of levels (%)	29/36 (80.6)
VA (cement only)	
No. of patients	22/35
No. of levels	61
VB reconstruction scale, no. of levels (%)	
Reader 1	
Excellent	27/36 (75.0)
Good	7/36 (19.4)
Fair	2/36 (5.6)
Poor	0/36 (0)
Reader 2	
Excellent	28/36 (77.8)
Good	6/36 (16.7)
Fair	2/36 (5.6)
Poor	0/36 (0)
Cement leak, no. of levels (%)	12/36 (33.3)
Epidural-foraminal space	7/36 (19.4)
Periprocedural complication, no. of levels	
-Cement leak requiring surgery w/ no permanent neurological deficit	1/36
-Self-limiting neurological symptom	1/36
-Death (day 2, PE)	1/36

L-PF = decompressive laminectomy and posterior fixation; PE = pulmonary embolism; pPF = percutaneous posterior fixation.

Table 3

Summary of follow-up results

Variable	No. of Levels (%)
FU, no. of levels 1 mo 3 mos ≥ 6 mos	 30/36 24/36 16/36
VBS mobilization (non-screw-anchored VBS)	1/30*
Asymptomatic subsidence	5/30* (17)
Local progression	2/30* (7)
Intervertebral fusion	4/16† (25)

FU = follow-up.
* Levels with available follow-up (range 1–30 months).
† Levels with available late follow-up (range 6–30 months).

Chapter 6

Stent-screw Assisted Internal Fixation of Osteoporotic Vertebrae: a Comparative Finite Element Analysis on SAIF Technique

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Abstract

Vertebral compression fractures are one of the most relevant clinical consequences caused by osteoporosis: one of the most common treatment for such fractures is vertebral augmentation through minimally invasive approaches (vertebroplasty or balloon-kyphoplasty). Unfortunately, these techniques still present drawbacks, such as re-fractures of the treated vertebral body with subsidence of the non-augmented portions or re-fracture of the non-augmented middle column at the junction with the augmented anterior column. A novel minimally-invasive augmentation technique, called Stent-Screw Assisted Internal Fixation, has been recently proposed for the treatment of severe osteoporotic and neoplastic fractures: this technique uses two vertebral body stents and percutaneous cannulated and fenestrated pedicular screws, through which cement is injected inside the expanded stents to achieve optimal stents' and vertebral body's filling. The role of the pedicle screws is to anchor the stents-cement complex to the posterior column, acting as a bridge across the middle column and preserving its integrity from possible collapse. In order to evaluate the potential of the new technique in restoring the load bearing capacity of the anterior and middle spinal columns and in reducing bone strains, a Finite Element model of an osteoporotic lumbar spine has been developed. Both standard vertebroplasty and Stent-Screw Assisted Internal Fixation have been simulated: simulations have been run taking into account everyday activities (standing and flexion) and comparison between the two techniques, in terms of strain distribution on vertebral endplates and posterior and anterior wall, was performed. Results show that Stent-Screw Assisted Internal Fixation significantly decrease the strain distribution on the superior EP and the cortical wall compared to vertebroplasty, possibly reducing the re-fracture risk of the middle-column at the treated level.

Keywords: Osteoporosis; Vertebral Compression Fractures (VCF); Finite Element Model (FEM); Screw-Stent Assisted Internal Fixation (SAIF); spine biomechanics; vertebral augmentation

Introduction

Osteoporosis, defined as “a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a resultant increase in fragility and risk of fracture”, is a major clinical issue worldwide (Lippuner, 2003). Vertebral compression fractures (VCFs) is one of the most relevant clinical consequences, potentially causing acute and chronic pain, and reduced quality of life (Du et al., 2014), with an impact on mortality (Edidin et al., 2015). VCFs can occur spontaneously or due to trauma, generally a compressive load injury mechanism involving the vertebral body (VB) (Ensrud and Schousboe, 1983). The anterior and middle vertebral columns together support about 80% of the overall spinal load in standing, and those are most commonly involved (White and Panjabi, 1991). The spectrum of severity may range from mild and stable compression fractures, affecting the disc-endplate (EP) region and leading only to minor deformity, to unstable fractures with a high-degree of osseous fragmentation, collapse deformity, middle column involvement, pediculo-somatic junction fracture, and kyphotic deformity (Denis, 1983; Genant et al., 1993; Mc Cormack et al., 1994).

Vertebral augmentation (VA), performed with vertebroplasty or balloon-kyphoplasty, implies percutaneous image-guided injection of bone cement in the anterior two thirds of the VB (i.e. the anterior column), and it is widely used to treat fragility fractures, to arrest fracture progression, to palliate pain and to restore the load-bearing capability of the VB (Wardlaw et al., 2009; Klazen et al., 2010; Firanescu et al., 2011; Clark et al., 2016; Filippiadis et al., 2017). The injection of cement in the VB aims at a homogeneous trabecular filling, but it is stopped for safety reasons, when the cement approaches the posterior third of the VB, to avoid leakage in the central canal.

Re-fracture of the treated VB is a well-known and reported event following VA, although its timing and frequency are variable among published reports (Li et al., 2018; Lin et al., 2008). The re-fracture usually implies subsidence of the non-augmented portions of the VB around the cement cast (Nagaraja et al., 2015). This event may lead to minimal adjustment of the adjacent bony structures or it may lead to extensive collapse of the non-augmented portions of the vertebra.

A less frequent event is the re-fracture of the non-augmented middle column at the junction with the augmented anterior column (Gan et al., 2014). These fractures are often

characterized by collapse and retropulsion of the posterior wall, eventually associated with catastrophic splitting and separation between the augmented anterior portion of the VB and the middle column, accompanied by focal kyphotic deformity. Although largely under-reported in the literature, these dramatic events pose a real therapeutic challenge (Abudou et al, 2013; Gonschorek et al., 2017).

The importance of the mechanical stability of the middle column might be largely underestimated, since the load-bearing capacity of the vertebra is usually referred just addressing the anterior column. Furthermore, the middle column, with the posterior third of the VB, the posterior wall, and the pediculo-somatic junctions might represent a weak region even after satisfactory VA. In fact, it is expected that local strain gradients across the stiffer augmented and the weaker non-augmented regions, may lead to intensification effects, exposing to the risk of a secondary middle column re-collapse. This event may be particularly dramatic in severely osteoporotic patients or following a first severe “burst fracture” involving the anterior and middle columns.

A novel minimally-invasive augmentation technique, called Stent-Screw Assisted Internal Fixation (SAIF, Figure 1) has been recently proposed by Cianfoni et al. for the treatment of severe osteoporotic and neoplastic fractures (Cianfoni et al., 2019a; Cianfoni et al., 2019b). The SAIF technique includes insertion and balloon-expansion of two vertebral body stents (VBS), followed by the insertion of percutaneous cannulated and fenestrated pedicular screws. After the stents are expanded and the screws are in position, the cement is injected through the screws to achieve optimal stents’ and VB’s filling (endplate-to-endplate). The role of the stents is to help maintain the height restoration achieved by balloon inflation, avoiding deflation effect, and to act as a scaffold that allows homogeneous anterior column augmentation and prevents cement leakage (Cianfoni et al., 2019b; Diel et al., 2013; Rotter et al., 2010).

The potential role of the pedicle screws is to anchor the VBS-cement complex to the posterior elements, avoiding its displacement, and to act as a bridge across the middle column, preserving its integrity from possible collapse and splitting (Cianfoni et al., 2019a). As such, SAIF technique might reduce the risk of middle column collapse after a VA treatment in severe osteoporotic vertebral fractures.

Different studies investigated the relative importance of biomechanical factors playing a role in VA techniques. Rohlmann et al. (Rohlmann et al., 2010) performed a probabilistic numerical study reporting that in an augmented vertebra the cement volume and its elastic modulus have a dominant role compared to shape and symmetry of the cement plugs. Chevalier et al. (Chevalier et al., 2008) demonstrated that cement bridging both endplates (EPs) restores the load–bearing capacity of the treated vertebra (i.e. its vertebral stiffness and strength). Ottardi et al. (Ottardi et al., 2016a) demonstrated that a full height restoration is a key factor in reducing the stress on the surrounding structures.

A recent biomechanical study demonstrated the effectiveness of SAIF technique in restoring the load-bearing capacity of an extensively lytic vertebra, while reducing the strains (i.e. fracture risk) on surrounding bony structures (La Barbera et al., 2019). However, there are no studies investigating the SAIF technique in an osteoporotic model.

The aim of the current computational comparative study was to investigate whether SAIF technique is biomechanically advantageous compared to standard VA in restoring the load bearing capacity of the anterior and middle spinal columns and in reducing bone strains, in a lumbar spine osteoporotic model.

Materials and Methods

Intact OP model

An intact non-linear FEM describing the L1-S1 spine segment of a healthy 40 years-old human male without any spinal defect was initially considered (Ottardi et al., 2016b). The model (Figure 2), complete of vertebral bodies, intervertebral discs and 7 groups of lumbar ligaments, has already been validated by comparison with experimental measurements considering its kinematics, the compressive stiffness of the vertebrae and the strains reached on the cortical bone of the VB (Ottardi et al, 2016a).

Material properties were assumed from literature, as reported in a previous validation study [Ottardi et al., 2016b). To properly simulate an osteoporotic condition, the mechanical properties of the cancellous and cortical vertebral bone were reduced according to literature data for each VB (Chae et al., 2010). The model thus created was herein named “OP model”.

To prevent any artefact due to the application of the boundary conditions at cranial and caudal levels, the middle vertebra (L3) was selected as the level of interest to reproduce the different surgical techniques.

VA model

The vertebral augmentation (VA) technique was simulated by increasing the elastic modulus of anteriorly located elements from osteoporotic bone to cement. Such elements cover 2/3 of the whole L3 VB volume, according to post-operative imaging (Figures 1, 3). The cement volume (about 20 ml) resulted from the choice to reproduce optimal endplate bridging (Chevalier et al., 2008).

SAIF model

To describe SAIF technique on the OP model, the CAD model of the cannulated pedicle screw (2B1 SRL, Milan, Italy) was properly assembled in the two pedicles of the L3 vertebra using ICEM CFD (Ansys Inc), following boolean operations, the whole vertebra was finally remeshed using linear tetrahedral elements. Attention was paid in maintaining a good compromise between adequate mesh refinement and reasonable computational cost. For the same reason, the metallic stent was not included in the model, assuming it gives a negligible contribution to the overall compressive stiffness of the treated vertebra, since the injected bone cement

usually completely fills and surrounds the stents: however, the contribution of the cement confined into the stents was taken into account by creating two PMMA cylinders around the screws that simulate the stents filled with PMMA cement (Figures 1 and 3). To evaluate the full potential of SAIF technique, optimal endplate-to-endplate cement augmentation and maximal height restoration were assumed.

For all the materials linear elastic properties were assumed (Table 1), for the remaining properties (not modified from the original model) the reader is addressed to (Ottardi et al., 2016b).

Loading conditions

All models underwent two different loading scenarios (Figure 2). Standing was simulated applying a 500N follower load (Rohlmann et al., 2009; La Barbera et al., 2016c; La Barbera et al., 2017b). Flexion of the upper body, often associated to the event of VCF, was reproduced with a 1175N follower load and a 7.5 N/m moment on the L1 vertebra (Rohlmann et al., 2009; La Barbera et al., 2016c; La Barbera et al., 2017b). In both cases the inferior portion of S1 was considered fully constrained.

All the simulations were run on ABAQUS Standard 2017 (Dassault Systèmes Ri, Simulia Corp, Providence, RI, USA).

Comparative FE analyses

The load distribution in the L3 vertebra for the untreated osteoporotic (OP) condition, and for both techniques (VA, SAIF) was evaluated in terms of maximum and minimum principal strains on the cortical regions. Principal strains values, possibly related to bone fracture risk (Wang et al., 2018; Imai, 2015; Palanca et al, 2018), were evaluated at nodal values in specific regions located on the endplates, anterior and posterior walls. The endplates were divided in two regions of interest: the anterior and the middle column, corresponding to the cortical bone laying above the cement and the osteoporotic bone, respectively (specific elements were excluded to avoid strain intensification effects occurring at cement-bone interface). To highlight any statistical difference between the median values collected on each region of interest a paired Wilcoxon test with a 0.05 significance level was performed. Box plot representation, showing 25–75% interquartile ranges, median bar and whiskers indicating the 5–95% range (with a cross indicating the average value), was used to allow qualitative comparison.

To point out any mechanical issue related to the usage of the cannulated pedicle screw in all different scenarios, the maximum von Mises stresses was also considered.

Results

The median values obtained on the anterior column demonstrate that both SAIF and VA techniques reduced the principal strains in the treated vertebra compared to the OP case (Table 2).

Standing

The OP model demonstrates rather homogeneous strains across the whole VB, reaching relatively high values. Both EPs and the posterior wall undergo tensile strains due to transversal expansion (Poisson effect) of the trabecular bone which is compressed by the vertical load (Figure 4.a).

Following VA, the strains significantly decrease on the middle column, due to the higher load shared by the anterior column filled with stiff cement; in the middle column, the median strains significantly decrease of 15% ($p=0.03$, Figure 5) on the superior EP and of 48% ($p<0.01$, Figure 5) on the posterior wall, compared to OP condition. A not significant strain decrease is also observed on the inferior EP (-17% compared to OP model, Figure 7).

Following SAIF, the cannulated transpedicular screw constrains the transversal expansion of the trabecular bone within the middle column, where the remaining trabecular bone results to be loaded in compression similarly to OP case (Figure 4.a). Nevertheless, the median strain significantly decreases of 44% ($p<0.01$, Figure 5) on the superior EP, while of 72% ($p<0.01$, Figure 6) on the posterior wall compared to OP condition, with an overall significant decrease in strains also compared to VA (superior EP: -35%; posterior wall: -46%, $p<0.05$).

The maximum Von Mises stresses on the cannulated and fenestrated transpedicular screw in standing was relatively low (18 MPa).

Flexion

Due to the increased compressive load and the bending moment in flexion, the OP model demonstrates how the load shifts on the anterior column, where both the osteoporotic trabecular bone and the anterior cortical wall reach the highest compressive strains (Figure 4.b). In this condition the EPs undergoes tension (Poisson effect). Compared to standing,

the anterior column results to be more loaded than the middle one in upper body flexion, with an increase in median strain values of 230% on both EPs and up to 275% on the anterior cortex (Table 2); conversely strain increase are only of 30% up to 44% on the middle column.

Following VA, the load is shifted even more anteriorly, not only because of the increased load sharing on the augmented anterior spine (stiffer), but also due to the bending moment in flexion. Compared to standing, VA model demonstrates an increase in median strains on the anterior column of 150-178% on the EPs and of 400% on the anterior cortex during flexion (Table 2); the middle column was less affected (+22% on the superior EP, -10% on the inferior EPs and -15% on the cortex). Compared to OP condition, the median strains on the middle column of VA model were significantly reduced by 20% ($p=0.01$, Figure 5) on the superior EP, by 46% on the inferior EP ($p<0.05$, Figure 7), and by 69% ($p<0.01$, Figure 6) on the posterior wall.

The SAIF model demonstrated the highest strain increase in flexion compared to standing on the anterior column (+230% on the inferior EP, +300% on the superior, +450% on the anterior cortex), while the EPs of the middle column were less affected (+30% on the superior EP, +9% on the inferior) and the posterior wall saw a decrease in strain (-43%). This indicate the capability of SAIF technique in effectively transferring more load than VA on the anterior column, unloading the middle column.

The mechanical role of the cannulated transpedicular screw is to reduce the transversal expansion of the trabecular bone within the middle column compared to OP condition. The resulting strain significantly decreased by 43% ($p<0.01$, Figure 5) on the superior EP and by 89% ($p<0.05$, Figure 6) on the posterior wall compared to OP condition, but also compared to VA (-29% and -64%, respectively, $p<0.05$). Differences between SAIF and VA on the inferior EP were not significant (Figure 7).

The maximum Von Mises stresses on the transpedicular screw slightly increased in flexion, remaining quite low (32 MPa).

Discussion

Stent-Screw Assisted Internal Fixation (SAIF) technique has been recently introduced by Cianfoni et al. for the treatment of severe osteoporotic and neoplastic fractures (Cianfoni et al., 2019a; Cianfoni et al., 2019b).

SAIF technique couples the clinical advantages typical of VBS (cement augmentation, minimization of leakage and vertebral height restoration/maintenance) (Cianfoni et al., 2019b) with the percutaneous implantation of cannulated and fenestrated titanium pedicle screws, bridging the augmented VB with the posterior neural arch.

It is interesting to report that other transpedicular implants with or without bone-cement have already been described in the literature for the treatment of osteoporotic VCFs. Kettler and colleagues reported that BeadEx implant is superior over VA in restoring/maintaining the initial VB height and in providing stability after fracture even following complex dynamic loading in vitro (Kettler et al., 2006). Aebi and colleageus demonstrated that a PEEK V-Strut implant reinforce the VB strength similarly to VA (Aebi et al., 2018). Although purely speculative, the SAIF technique could offer some potential advantages over these techniques. As first, a more adequate reconstruction and scaffolding of the vertebra upon VBS implantation and cement filling, thus maximizing the footprint of the cement within the VB (Cianfoni et al., 2019a). As second, a high biocompatibility typical of titanium alloys of the cannulated screw that can promote bone-integration with the posterior structures.

Although a recent biomechanical study demonstrated the effectiveness of SAIF technique in restoring the load-bearing capacity of an extensively lytic vertebra, while reducing the strains (i.e. fracture risk) on the surrounding structures (La Barbera et al., 2019), no study ever investigated the advantages of SAIF technique in an osteoporotic model. The aim of the present computational study was, therefore, to investigate the advantages of SAIF technique in a lumbar spine osteoporotic model by comparison with standard VA and no treatment (OP). To demonstrate the full potential of the proposed technique, optimal endplate-to-endplate filling was assumed (Chevalier et al., 2008).

Considering standing, our results indicate that SAIF technique is significantly more effective than both no treatment (OP) and simple VA in reducing the median

strain distribution across the middle column (Figures 5, 6, 7), especially on the superior EP (-44% vs. OP, -35% vs. VA, $p<0.05$) and on the posterior wall (-72% vs. OP, -46% vs. VA, $p<0.05$). During upper body flexion, SAIF technique also promotes a higher load transfer on the anterior column compared to simple VA and to the untreated OP condition, while the middle column is less loaded (Table 2). This results in a significant reduction of the median strain across the middle column, especially on the superior EP (-43% vs. OP, -29% vs. VA, $p<0.05$) and on the posterior wall (-89% vs. OP, -64% vs. VA, $p<0.05$).

The qualitative strain distribution (Figure 4) supports the idea that the presence of convergent pedicle screws constrains the transversal expansion of the trabecular bone in the middle column, thus, reducing the fracture risk in this region compared to simple VA, where the weak not-augmented middle column is substantially “bare” (Cianfoni et al., 2019b). This concept is partially confirmed by post-operative CT images resulting from clinical practice (Figure 8), demonstrating that re-fracture often occurs in the middle column at the treated level following VA due to collapse and splitting. Although from the analysis of these images it is arguable that the weak regions not reinforced by cement are correlated to re-fractures involving the endplates and the posterior wall, it is still not possible to identify where the fracture initially started. Similarly, it is impossible to establish a clear correlation between our findings and the failure mechanisms reported in the published clinical literature (Li et al., 2018; Lin et al., 2008). The simulations performed within our study allowed to investigate one of the leading mechanical factors (i.e. strain distribution) involved in event and to highlight differences between simple vertebral augmentation (VA) and SAIF technique.

Considering the anterior column, SAIF technique is significantly superior to simple VA in decreasing the overall strain distribution, thus, reducing the risk for vertebral collapse (Figure 4, Table 2). This is particularly relevant during upper body flexion (worst-case loading condition) to reduce the fracture risk of the anterior cortex (about -80% vs. OP, about -45% vs. VA, $p<0.05$) and on both EPs (about -84% vs. OP, about -64% vs. VA, $p<0.05$). Recalling the assumption of optimal EP-to-EP filling (Chevalier et al., 2008, these results represent a superior limit. Although SAIF allows a more satisfactory reconstruction of the VB compared to VA, suboptimal cement filling of the anterior column may reduce the potential for strain reduction and fracture risk prevention.

Our study confirmed the mechanical reliability of the cannulated pedicle screw design also for applications in osteoporotic vertebrae. In line with the previous study on SAIF technique in an extensively lytic model (La Barbera et al., 2019), the maximum stress obtained on the cannulated pedicle screws is always much lower than the typical yield strength for titanium alloy (about 750 MPa). This was expected since the screw, as an internal fixation system, does not undergo any relevant loadings typical of standard pedicle screw connected to stiff rigid posterior instrumentation. (La Barbera et al., 2016a; La Barbera et al., 2016b; La Barbera et al. 2016c; La Barbera et al., 2017a; La Barbera et al., 2017b).

The present comparative study is surely affected by several limitations. The proposed approach does not describe failure phenomena related to vertebral body collapse. Moreover, the choice of adopting a principal strain criterion (Imai, 2015; Palanca et al., 2018) and of quantitatively analysing only the cortical structures should be read as a characteristic of the most severe osteoporotic fractures reported by the clinical literature (Wang et al., 2018; Genant et al., 1993). The principal strain values, never exceeding the typical failure strains for bone, confirm that the assumption of linear elastic strain is reasonable. In addition, it was assumed that the untreated OP vertebra was not fractured, nor collapsed (with a reduction in anterior height), therefore the results here reported could be considered, ideally, as a preventive cement augmentation, or as the result of a VA following an optimal vertebral height restoration. Moreover, the implementation of models correctly describing the peculiarity of a fractured scenario may increase the efforts needed for model validation with ad hoc experimental data, while increasing the complexity of the models. However, the current approach has the advantage to easily control specific parameters of interest (e.g. screw and cement usage), that may demonstrate a huge variability in clinical practice, adding a confounding effect on the results.

Despite vertebral augmentation techniques have been often related to an increased fracture risk on the vertebral adjacent levels (Ottardi et al., 2016a), such aspect was not analysed in the current paper. Moreover, despite in clinical practice the adjacent levels might undergo prophylactic vertebral augmentation (Cianfoni et al., 2019a; Cianfoni et al., 2019b), this aspect was not considered in our study and it could be part of future analyses, also evaluating the application of the SAIF technique at other spine levels.

Although the results here reported are promising, long-term clinical studies are required to fully demonstrate the safety end the clinical effectiveness of the new SAIF technique over other techniques.

Conclusions

SAIF technique is biomechanically advantageous over VA in significantly decreasing the strain distribution on the superior EP and the cortical wall, therefore reducing the re-fracture risk of the middle-column at the treated level. The present study provides a strong biomechanical rationale to support the usage of the SAIF technique for the treatment of osteoporotic vertebrae.

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Figures and tables

Figure 1

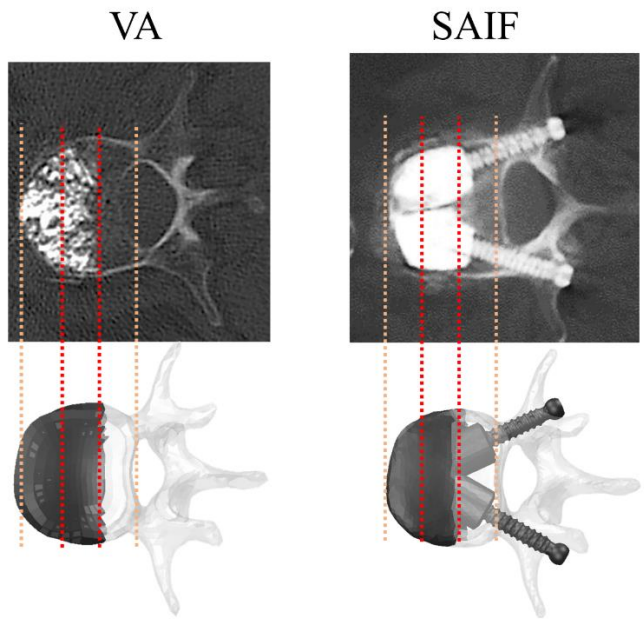

Figure 1: Post-operative CT images of vertebrae treated with VA and SAIF techniques compared with the simulated ones: in both cases, cement filling involves 2/3 of the vertebral body and it is anteriorly located. CT images are courtesy of A.C.

Figure 2

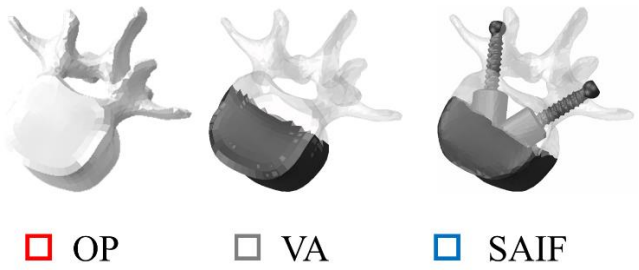

Figure 2: Representation of the intact model in standing, where an axial follower load (FL) was applied (a), and in upper body flexion, where an additional bending moment was applied on the superior EP of L1 (b). The lower part of S1 was constrained in both conditions.

Figure 3

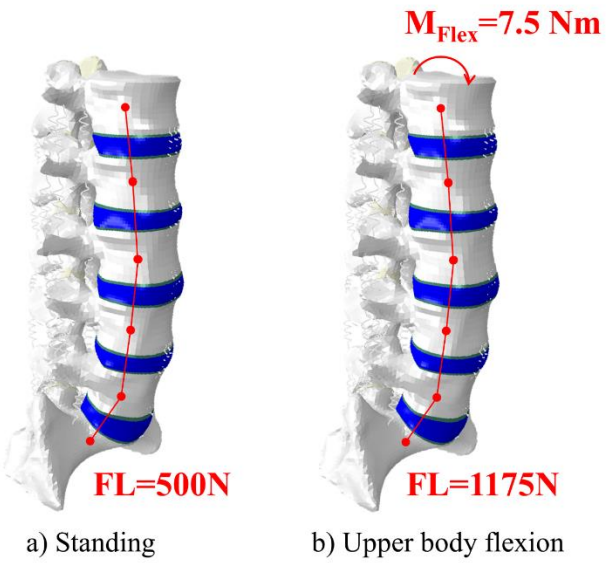

Figure 3. Representation of L3 vertebrae in all simulated conditions. From left to right: osteoporotic vertebra (OP) taken as a reference condition, vertebral augmentation (VA) and the new Stent-Screw Assisted Internal Fixation (SAIF). Bone is highlighted in shaded white, while screws and bone cement are in dark grey.

Figure 4

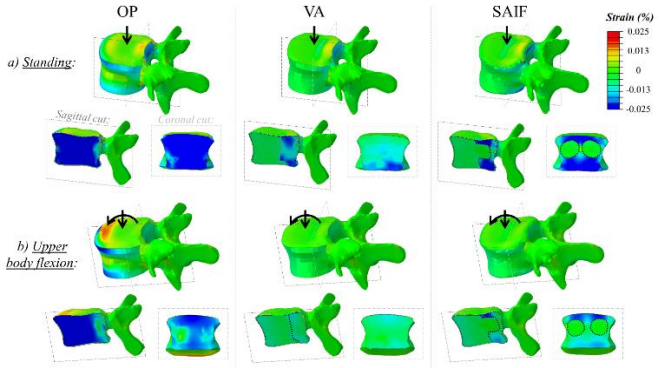

Figure 4: Principal strain maps on L3 vertebra in the untreated OP condition and in VA and SAIF models both in standing (a) and in upper body flexion (b). Sagittal cut through the entire vertebra and coronal cut through the middle column are also presented (the dotted lines cuts highlight the contour of the bone cement in VA, while cement it is also distributed around the fenestrated pedicle screw in SAIF to reproduce VBS shape).

Figure 5

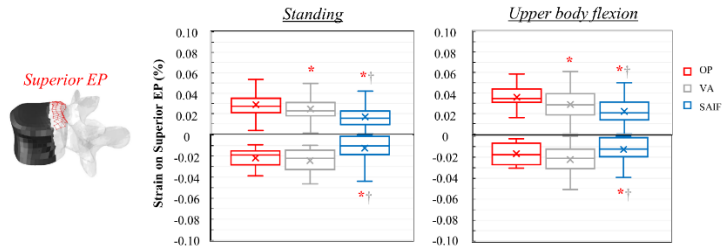

Figure 5: Box plots representing the strains on the superior EP of L3 for all the simulated configurations. The regions of the middle column where the strains were evaluated are highlighted in red on the L3 vertebra. *, †: indicate significant differences ($p<0.05$) in median values compared to OP and VA.

Figure 6

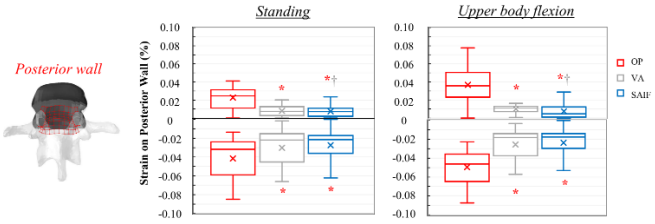

Figure 6: Box plots representing the strains on the posterior wall of L3 for all the simulated configurations. The regions of the middle column where the strains were evaluated are highlighted in red on the L3 vertebra. *, †: indicate significant differences ($p<0.05$) in median values compared to OP and VA.

Figure 7

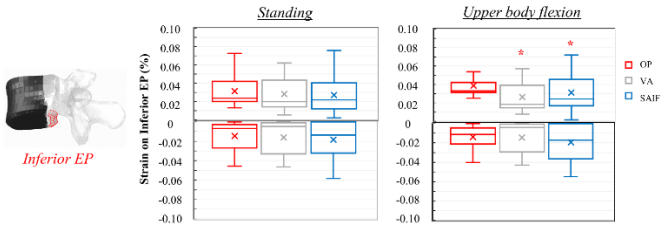

Figure 7: Box plots representing the strains on the inferior EP of L3 for all the simulated configurations. The regions of the middle column where the strains were evaluated are highlighted in red on the L3 vertebra. *, †: indicate significant differences ($p<0.05$) in median values compared to OP and VA.

Figure 8

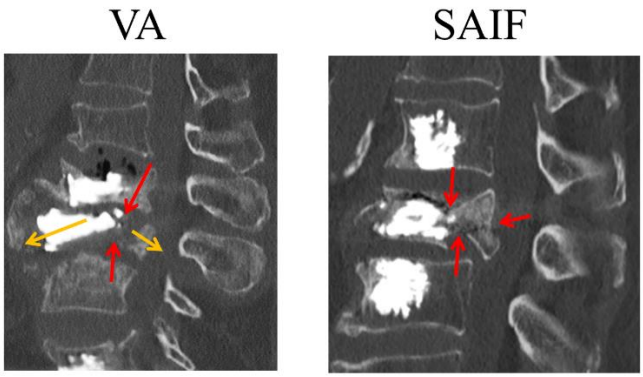

Figure 8: CT image (sagittal slices) taken on a lumbar vertebrae that re-fractured following VA (courtesy of A.C.). The L3 vertebra, previously treated with VA re-fractured with splitting of the anterior and middle column (yellow arrows); it can be noticed that a continuous fracture spreads from the superior to the inferior endplates (red arrows) with posterior wall retropulsion.

TABLE 1

MECHANICAL PROPERTIES OF THE MATERIALS USED IN THE SIMULATIONS. FOR OTHER MATERIAL PROPERTIES, PLEASE, REFER TO (14).

	Type of material	Elastic modulus (MPa)	Poisson ratio (-)	Literature reference
OSTEOPOROTIC CANCELLOUS BONE	Transversely isotropic	123.2 123.2 176	0.45 0.32 0.32	(Ottardi et al., 2016a; Chae 2010)
OSTEOPOROTIC CORTICAL BONE	Linear isotropic	4320	0.3	(Ottardi et al., 2016a)
BONE CEMENT (PMMA)	Linear isotropic	2500	0.438	(Hansen et al., 1992)
TITANIUM (PEDICLE SCREW)	Linear isotropic	110000	0.3	(La Barbera et al., 2015; La Barbera et al., 2016a; La Barbera et al., 2017a)

Table 2

Median principal strains values obtained in all regions of interest of the treated vertebra (L3) both for standing and upper body flexion on OP, VA and SAIF models.

Percentage differences for VA vs. OP and for SAIF vs. OP and vs. VA are highlighted in bold, whenever differences are significant.

To quantify variations in load sharing due to flexion, percentage strain increase compared to standing are also provided.

Region of interest			Standing						Upper body Flexion						*Flexion vs. Standing*		
			OP	VA	SAIF	*VA vs. OP*	*SAIF vs. OP*	*SAIF vs. VA*	OP	VA	SAIF	*VA vs. OP*	*SAIF vs. OP*	*SAIF vs. VA*	*OP*	*VA*	*SAIF*
Anterior Column	Superior EP	Max Princ. Strains (%)	0.018	0.010 (*)	0.002 (*, †)	***-44***	***-89***	***-80***	0.059	0.025 (*)	0.008 (*, †)	***-58***	***-86***	***-68***	*228*	*150*	*300*
		Min Princ. Strains (%)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	Anterior wall	Max Princ. Strains (%)	0.020	0.004 (*)	0.002 (*, †)	***-80***	***-90***	***-50***	0.075	0.020 (*)	0.011 (*, †)	***-73***	***-86***	***-45***	*275*	*400*	*450*
		Min Princ. Strains (%)	-0.036	-0.013 (*)	-0.008 (*, †)	***-64***	***-78***	***-39***	-0.155	-0.065 (*)	-0.036 (*, †)	***-58***	*-77*	***-45***	–	–	–

	Inferior EP	Max Princ. Strains (%)	0.016	0.009 (*)	0.003 (*, †)	*-44*	*-81*	*-67*	0.053	0.025 (*)	0.010 (*, †)	*-53*	*-81*	*-60*	*231*	*178*	*233*
		Min Princ. Strains (%)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Medial column	Superior EP	Max Princ. Strains (%)	0.027	0.023 (*)	0.015 (*, †)	*-15*	*-44*	*-35*	0.035	0.028 (*)	0.020 (*, †)	*-20*	*-43*	*-29*	*30*	*22*	*33*
		Min Princ. Strains (%)	-0.019	-0.022	-0.010 (*, †)	*+16*	*-48*	*-55*	-0.018	-0.021	-0.012 (*, †)	*+17*	*-33*	*-43*	–	–	–
	Posterior wall	Max Princ. Strains (%)	0.025	0.013 (*)	0.007 (*, †)	*-48*	*-72*	*-46*	0.036	0.011 (*)	0.004 (*, †)	*-69*	*-89*	*-64*	*44*	*-15*	*-43*
		Min Princ. Strains (%)	-0.032	-0.022 (*)	-0.021 (*)	*-31*	*-34*	*-5*	-0.046	-0.018 (*)	-0.017 (*)	*-61*	*-63*	*-6*	–	–	–
	Inferior EP	Max Princ. Strains (%)	0.024	0.020	0.022	*-17*	*-8*	*-4.5*	0.033	0.018 (*)	0.024 (*)	*-46*	*-27*	*+33*	*38*	*-10*	*9*
		Min Princ. Strains (%)	-0.007	-0.005	-0.014	*-29*	*+100*	*+180*	-0.011	-0.004	-0.017	*-64*	*-55*	*+325*	–	–	–

***, † indicate significant differences (p<0.05) in median values compared to OP and VA models, respectively.**

Negligible compressive strain values (with absolute value <0.001) are not reported and are here indicated with "–".

Chapter 7

The “Armed Concrete” Approach: Stent-Screw-Aassisted Internal fixation (SAIF) Reconstructs and Internally Fixates the Most Severe Osteoporotic Vertebral Fractures

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Abstract

Background

The treatment of severe osteoporotic vertebral fractures (VCFs) with middle-column (MC) involvement, high fragmentation, large cleft and/or pedicular fracture is challenging. The minimally invasive “Stent-Screw Assisted Internal Fixation” (SAIF) can reduce the fracture, reconstruct the vertebral body (VB) and fixate it to the posterior elements.

Objective

To assess feasibility, safety, technical and clinical outcome of SAIF technique in patients with severe osteoporotic VCFs.

Methods

We retrospectively analyzed 80 treated vertebrae. Severe VCFs were characterized by advanced collapse (Genant grade 3), high degree of osseous fragmentation (McCormack grade 2 and 3), burst morphology with MC injury, pediculo-somatic junction fracture and/or large osteonecrotic cleft. VB-reconstruction was evaluated on post-procedure radiographs and CT by two independent raters. Clinical and radiological follow-ups were performed at 1 and 6 months.

Results

SAIF was performed at 28 thoracic and 52 lumbar levels in 73 patients. One transient neurological complication occurred. VB-reconstruction was satisfactory in 98.7% of levels (interrater reliability 96%, K=1). One-month FUP was available for 78/80 levels and at 6 months or later (range 6-24, mean 7.9 months) for 73/80 levels. Significant VAS score improvement was noted at 1 and 6 months post-treatment ($p<0.05$). Patients reported global clinical benefit during follow-up (PGIC: 5.6+/-0.9 at 1 month and 6.1+/-0.9 at 6 months). Fourteen new painful VCFs occurred at different levels in 11 patients during follow-up, treated with VA or SAIF. Target-level stability was maintained in all cases.

Conclusions

SAIF represents a minimally-invasive, safe and effective option for patients with severe osteoporotic VCFs with MC involvement.

KEYWORDS: screw-stent assisted internal fixation (SAIF); vertebral body stents; pedicular screws; severe osteoporotic vertebral compression fractures (VCF); stabilization; internal-fixation; vertebral body reconstruction; middle column.

Introduction

Vertebral compression fractures (VCF) are well described clinical manifestations of osteoporosis[1]. The severity spectrum of VCF is broad. Many are mild and stable compression fractures affecting the anterior column (AC) with minor wedge or biconcave deformity usually treated with conservative therapy. Those more severely impacted may be treated with traditional augmentation techniques as VCFs are often associated with acute and chronic pain, physical impairment, disability and decreased quality of life with an impact on mortality[2].

At the other end of the spectrum, osteoporotic VCFs can take on a wide variety of troubling appearances. They can be unstable fractures with severe collapse and kyphotic deformity, burst morphology with middle column (MC) involvement and posterior wall retropulsion, pediculo-somatic junction fracture, high-degree of osseous fragmentation, advanced loss of integrity and quality of trabecular and cortical bone, and fractures with large osteonecrotic clefts. For purposes of this study, these types of fractures are aggregated together and referred to as "severe VCFs" [3-5] (online supplementary Figure 1S).

Vertebral augmentation (VA) is widely used to palliate painful VCFs resistant to conservative treatment[6]. For poor surgical candidates, these techniques are also an option to treat severe VCFs.

Ideally however, these severe VCFs would benefit from kyphosis reduction, supported with multi-compartmental stabilization to restore axial load-bearing capability of VB and arrest fracture progression[7-10]. Put differently, standard VA, either performed with vertebroplasty or balloon kyphoplasty, obtains cement augmentation of the AC, the anterior two thirds of the VB, while the MC is usually left non-reinforced, both for technical constraints and for safety measure to avoid risk of cement leak in the central canal. As such, the MC, after VA, is seen as a non-augmented "bare area" (Figure 1).

This bare area, commonly neglected with traditional percutaneous techniques, represents a weak point in an augmented vertebra[11], especially when already injured in these severe VCFs, and may play a key role in the re-fracture of treated level. These re-fractures may feature posterior wall retropulsion, cleavage and splitting between the augmented AC and the bare MC, focal kyphosis and instability, posing a real treatment challenge[12] (Figure 1).

Furthermore, in severely collapsed VBs, with high degree of fragmentation, pediculo-somatic fractures, and advanced loss of osseous integrity, standard VA might be unable to obtain significant height and kyphosis reduction, cement might disperse in uneven manner, and overall fail to achieve satisfactory stabilization.

These patients are complex and the challenge of treating these severe VCFs is bidirectional. While VA might represent an undertreatment for severe VCFs, the alternative of open surgical stabilization is invasive and carries risk of failure in patients with poor bone quality from osteoporosis[13].

Recently, a novel minimally-invasive augmentation technique, called stent-screw assisted internal Fixation (SAIF) has been proposed for the treatment of severe osteoporotic and neoplastic fractures[14,15]. This technique includes insertion and balloon-expansion of two vertebral body stents (VBS), followed by placement of percutaneous cannulated and fenestrated pedicular screws in the stents' lumen, and cement augmentation through the screws, representing an "armed concrete" approach.

The stents obtain and maintain fracture reduction while the pedicle screws anchor the VBS-cement complex to the posterior elements, avoiding its displacement, and act as a bridge across the MC, preserving its integrity from possible collapse and splitting[15]. Two biomechanical studies provide support for this approach in both neoplastic and osteoporotic models[11,16].

The purpose of this study was to assess the feasibility, safety, technical and clinical outcome of VB reconstruction and fixation through SAIF technique in a cohort of patients with osteoporotic severe VCFs.

Materials and methods

Patients

This is a retrospective analysis of a single-center, prospectively maintained database of a consecutive series of patients with severe thoraco-lumbar osteoporotic fractures treated with SAIF technique between August 2015 and October 2018. The VCFs were characterized by one or more of the following morphological features: advanced collapse (Genant grade 3) [5], burst morphology with MC injury, high degree of osseous fragmentation (McCormack comminution grade 2 and 3) [4], pediculo-somatic junction fracture and/or large osteonecrotic cleft. More than one of the above situations could exist in the same patient (online supplementary Figure 1S). The study was approved by the local Ethics Committee. Informed consent was obtained for all procedures. All patients underwent pre-procedural spinal CT and/or MRI at the target level, to accurately define the fracture morphology. Decision to treat with SAIF procedure was reached by a multidisciplinary team of clinical specialists involved in the care and treatment of spine patients including neurosurgeons, neuroradiologists, pain physicians and physical medicine and rehabilitation physicians.

SAIF procedure

SAIF procedural details have been previously described[15].

All procedures were performed percutaneously, under general anesthesia, with biplanar fluoroscopic guidance (Philips, Allura). Following bilateral trans-pedicular implant of VBS (DePuySynthes-Johnson&Johnson) and placement of uni- or bilateral screws (Injection pin, 2B1 S.R.L., Milan, Italy), cement augmentation was performed through the screw(s) with high viscosity polymethyl methacrylate (PMMA) (Vertaplex HV, Stryker, Kalamazoo, MI, USA) under real-time continuous fluoroscopic monitoring.

The stents-screws implant is not available for use in the United States lacking the FDA approval.

Further adjacent or distant vertebral levels were treated with VA during the same procedure, in case of multilevel osteoporotic VCFs, or with prophylactic intent, when deemed appropriate by the operator[17].

Patients were allowed to stand and walk without spinal braces as early as three hours after the procedure, and commonly discharged the same day, in a day-surgery setting.

Assessment of VB reconstruction, complications and follow-up

VB reconstruction was assessed with post-procedure radiographs and CT scan. CT data sets were reconstructed with a bone algorithm with 3 mm and 10 mm thick maximum intensity projection (MIP) images in the three orthogonal planes, and independently reviewed by a neuroradiologist (AC) and a neurosurgeon (PS). We adopted the same qualitative four grade scale (poor, fair, good, excellent) previously used in VBS and SAIF studies to assess VB reconstruction[14,18], based on overall assessment of correct placement and expansion of the implants, cement filling and VB height restoration.

Poor indicated failure to achieve sufficient augmentation of the AC, whereas excellent indicated appropriate stent expansion, cement filling and consequent satisfactory height restoration and correct screw(s) positioning. An excellent result would appear as an internal VB prosthesis of the affected VB. Good and excellent ratings were considered satisfactory results.

Intra-procedural complications, such as potentially significant cement leaks and misplacement of the screws were recorded.

Patients were followed-up at 1 month and 6 months, with a clinical exam and upright plain radiographs, and then at variable intervals, following clinical practice. For some patients late clinical follow-up was performed over the phone by a physician (DD). When clinically necessary further imaging with CT or MRI was performed during follow-up. The Visual Analog Scale (VAS) pain score (range: 0–10) was obtained before the procedure and 1 month and 6 months after treatment. Patient's Global Impression of Change scale (PGIC), featuring a 7 point response ((1) "extremely worse", (2) "much worse", (3) "a little worse", (4) "no change", (5) "a little better", (6) "much better", (7) "extremely better")[19] was obtained at 1 and 6 months after treatment.

Imaging follow-up was evaluated to assess re-fractures, new or worsening spinal deformity of the treated segment, mobilization of the VBS and screw implants, and new vertebral fractures at adjacent levels.

Statistical analyses

Analyses were conducted using SPSS version 20.0.0 (IBM Corp.). Descriptive statistics for demographic and clinical data were expressed as mean and range or median with interquartile range (IQR). Differences in VAS scores before and after treatment were tested by Wilcoxon test. A p value <0.05 was considered statistically significant.

VB reconstruction results were judged according to the following scale: poor, fair, good, or excellent. Excellent and good ratings were considered as satisfactory results[18]. Cohen's kappa coefficient (κ) was used to assess the proportion of agreement of the two independent raters beyond that expected by chance, and the classification by Landis and Koch[20] was used to define the agreement level: poor, < 0.00; slight, 0.00–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; substantial, 0.61–0.80; or almost perfect, 0.81–1.00.

Results

In 73 patients (21 men and 52 women; mean age 77.7 y, range 59-98 y), 76 levels with osteoporotic severe VCFs were treated in 73 procedures; then during follow-up, 4 subsequent severe VCFs at other levels were treated with SAIF, for a total of 80 levels treated with SAIF in 77 procedures. Treated levels were between T3 and L5, 28/80 thoracic (35%) and 52/80 lumbar (65%); more specifically 63/80 (79%) located at the thoraco-lumbar junction (T10-L2).

A summary of patient's demographic and clinical data and features of VCFs is provided in Table 1 whereas technical results and complications are summarized in online supplementary Table 1S, and follow-up results are summarized in online supplementary Table 2S.

Technical results

SAIF procedures were performed as a stand-alone intervention in 78/80 cases, in combination with a percutaneous posterior surgical fixation in 1 case, and after decompressive laminectomy and posterior surgical fixation in 1 case presenting with spinal cord compression and new neurological deficit.

VBS were positioned bilaterally in all cases. Bilateral screws were used in 67/80 (83.7%) levels and unilateral screws in 13/80 levels (16.3%).

Procedural and Periprocedural Safety

Cement leakage was detected at 8/80 levels (10%) on post-procedure CT, with an epidural or foraminal location in 3/80 levels (3.7%). These cases remained asymptomatic. One patient experienced hypoestesia and mild motor deficits in the lower limbs two days after the procedure. On CT examination there was no evidence of PMMA leaks. Post-procedure MRI demonstrated an intradural T2-hypointense tubular structure. This was hypothesized to represent a venous thrombosis. The symptoms resolved over the next few weeks and MRI performed 3 months post- procedure was normal. No other neurologic periprocedural clinical complications occurred.

VB reconstruction

VB reconstruction scores assigned by the two readers were respectively excellent at 73/80 (91.3%) and 74/80 (92.5%) levels, good at 6/80 (7.5%) and 5/80 (6.3%), fair at 1/80 (1.2%) for both readers and poor at none of treated levels, leading to satisfactory results (excellent or good rating) in 79/80 (98.7%) cases for both readers. The inter-rater reliability was 96% with a Cohen's kappa of 1 indicating perfect agreement among raters.

Follow-up results

Post-procedure clinical and radiological follow-up was available at 1 month for 78/80 treated levels (72/73 patients) and at 6 months or later (range 6-24 months, mean 7.9 months) for 73/80 levels (68/73 patients).

There was a statistically significant difference in VAS scores pre-procedure (median 8, IQR 8-9) vs. 1 month (median 3, IQR 1.7-5) and vs. 6 months (median 2, IQR 0-3) (Wilcoxon test, all $p < .00001$).

PGIC scale was 5.6±0.9 at 1 month and 6.1±0.9 at 6 months, indicating a very positive patient's subjective global clinical impact.

There were no cases of stent or screw dislocation until the last available follow-up.

Osseous subsidence of the treated VB around the VBS/cement complex was observed during follow-up in 16/80 levels (20%), with mild to moderate secondary VB height loss, without onset

of new symptoms, and no re-treatment or surgical intervention was necessary at the target level.

Eleven patients during follow-up required a new procedure for a total of 14 new painful VCFs at adjacent or distant levels. Ten levels were treated with vertebroplasty, while 4, with a new severe VCF, were treated with SAIF.

Discussion

In this series of patients with osteoporotic severe VCF, characterized by high degree collapse, osseous fragmentation, burst morphology with MC involvement, pedicular fracture, and/or large osteonecrotic cleft, SAIF proved to be a feasible and safe minimally-invasive procedure for VB reconstruction and stabilization (Figure 2 and 3), with good clinical outcome, and durable results at follow-up.

Most osteoporotic VCFs are stable lesions, with AC injury, and augmentation can reinforce the VB and prevent further collapse. Severe VCFs, however, almost invariably feature MC involvement. In these situations, VA, leaving the MC as a non-augmented “bare area” (Figure 1), might represent undertreatment, while surgical fixation is invasive, carries high rate of fixation failure in osteoporotic patients and might be contraindicated in fragile and elderly patients [12,13, 21].

Severe VCFs pose a treatment challenge not only regarding pain palliation, but also in terms of stabilization, kyphosis correction, and central canal encroachment.

This is the first reported series of osteoporotic severe VCFs treated with SAIF technique, with the intent to obtain a 360° non-fusion internal VB fixation, with an “armed concrete” approach. VBS is used to restore VB height and obtain kyphosis correction, scaffold the VB, help cement-containment and reinforce the AC. The addition of the screws guarantees the anchoring of the VBS-PMMA implant to the posterior elements, preventing their mobilization, and have the potential to reinforce and bridge the MC and the frequently associated pedículo-somatic junction fractures.

The structure offered by the metallic stents and the screws, along with the PMMA cement filling, appears as a VB prosthesis, in these vertebrae with very poor or highly destroyed bone stock (Figure 2 and Figure 3).

The procedure was safe in this series, with only one patient experiencing a transient self-resolving neurological complication, whose nature was not readily relatable to technical aspects of the procedure itself.

We observed a 3.7% rate of cement leaks in an epidural or foraminal location, but those patients remained asymptomatic. In light of the anatomic complexity of these fractures, this leakage rate seems reasonable when compared with more typical fracture patients.

The main purpose of SAIF procedure is vertebral reconstruction to restore axial load-bearing capabilities of the VB [15]. Technically, the construct was judged as satisfactory when appropriate placement of the devices, VBS expansion, and cement filling restored VB height and achieved reconstruction of the fragmented VB, appearing as a 360° non-fusion internal fixation of the affected VB. The reconstruction was judged satisfactory (good or excellent) in 98.7% of cases by the two raters, with perfect interrater agreement.

Follow-up was available for 78/80 levels at one month, and for 73/80 levels at six months and beyond, up to 24 months. The stability of the construct was maintained in all cases until the last available follow-up without VBS mobilization. Migration of stents in highly osteoporotic vertebral bodies is possible, with potential risk of lumbar plexus or great vessels damage[22]. In patients with extensive VB fragmentation (Figure 3) it is certainly conceivable that the stents might mobilize in absence of an intact VB cortical shell, as reported in a previous SAIF series in extreme neoplastic osteolysis[14].

The screw anchoring may represent a means of avoiding VBS mobilization in conjunction with other technical measures such as a PMMA bridge, cement interdigitation, and optimized implant(s) positioning (Figure 2).

In this series screws were positioned bilaterally in the majority of cases (67/80 levels). We recommend bilateral screw fixation to anchor the VBS-cement implant to the posterior elements thereby reducing the risk of VBS mobilization whenever possible. If this is not possible (i.e. pedicle fragmentation or small pedicular diameter) a “kissing configuration” of the VBSs should be obtained to ensure the creation of a PMMA bridge between the two VBSs.

All screws were correctly positioned within the pedicles and in the VBS under fluoroscopic guidance, with no screw loosening observed at follow-up. The screws implanted in the SAIF technique are not connected to posterior fixation rods; thus, there are no high loadings that could predispose to screw loosening or failure [11,16], differently from what occurs in posterior surgical instrumentation[23].

Following VA, refracture of the treated VB is a well-known event with an incidence ranging from 3.2% to 63% with a cumulative rate of 10.2% [24,25]. In cement-only VA, subsidence

may determine refractures of the non-augmented MC at the junction with the augmented AC[12], with collapse and retropulsion of the posterior wall, eventually associated with catastrophic splitting and separation between the augmented anterior portion of the VB and the MC, accompanied by focal kyphotic deformity (Figure 1).

Although largely under-reported in the literature, these dramatic events pose a real therapeutic challenge. This complication, as previously stated, could be biomechanically explained by the high strain gradient across the augmented AC and the weaker unprotected MC, leading to local intensification effects[11]; moreover, the higher load-transfer to the stiff AC[11], reduce the mechanical stimulus on the MC, leading to bone-resorption.

At imaging follow-up we observed phenomena of osseous remodeling around the VBS-PMMA cast, with features of mild re-fracture/subsidence in 16/80 treated levels (20%), with mild to moderate secondary VB height loss, and in a few cases, documented by CT, even mild increase in posterior wall retropulsion but without splitting nor increased kyphosis. One might consider subsidence of the endplates nearly physiological changes after SAIF, namely because the surrounding fractured and weakened bone of the VB, upon weight bearing loading, remodels and might undergo resorption phenomena against the new rigid internal scaffold, represented by VBS with PMMA, but usually this does not have clinical significance. In fact no patients in this series required re-intervention, nor surgical salvage at the target level.

These results seem to confirm recently published biomechanical data on a finite-element analysis (FEM) of the SAIF technique applied to a lumbar osteoporotic spinal model[11]. SAIF was significantly more effective than simple VA in reducing the median strain distribution across the MC, especially on the superior end-plate and on the posterior wall[11].

Clinical results revealed meaningful positive effect on back pain as revealed by significant reduction in VAS at one month after the procedure, that was sustained at the six-month follow-up. Moreover, the patients judged that the procedure had a very positive impact on their situation, as reflected by high PGIC scores at one and six months follow-up.

During follow-up 11 patients required a new procedure to treat new fractures, at adjacent or distant levels, because painful or causing local hyperkyphosis. Seven cases were treated with simple vertebroplasty, under local anesthesia, while in four cases, with a severe VCF, a new SAIF procedure was performed.

The causes of post-procedure fractures are debated: the stiffness of the SAIF construct is a possible cause, but it should be considered that all these patients presented with

extremely severe VCFs, suggesting advanced osteoporosis, many presented with multilevel VCFs, and 79% of the target level VCFs were at a thoraco-lumbar junctional level, characterized by significant focal kyphosis, therefore at particular biomechanical risk[26]. We strongly recommend an appropriate medical therapy to correct osteoporosis, which represents a major risk factor in the development of new VCFs.

In this series of severe VCF, pre-operative pedicular fractures were present in 31/80 levels (38.7%). Some authors have reported the cement augmentation of the pedicles and pediculo-somatic junction, the so-called pediculoplasty[27], but it should be considered that main loadings at the level of the pedicles and pediculo-somatic junction are in bending, thus involving local tensile loads on the bone, while PMMA is known to have optimal resistance to compressive loads rather than to tensile ones[28]. Pedicular screws offer the advantage of internally scaffolding the pedicles, while undergoing relatively low bending stresses[11], even when pedicular bone properties are totally compromised[16]. To confirm these concepts, pedicular or pediculo-somatic junction fracture have not shown dislocation or pseudoarthrosis in the current study at the latest follow-up.

The presence of intravertebral cleft is associated to significant VB height reduction and is an important risk factor that might prevent osseous healing and might promote the progression of collapse[29]. The dynamic instability, with subsequent hypermobility at the fractured level, may lead to gradual retropulsion of bony fragments into the spinal canal with the risk of possible neurological complications. In our series of severe VCFs a cleft was present in 56/80 levels (70%), in many cases associated with extremely poor bone stock remaining in the VB. In these cases the VBS recreate the internal structure of the VB, and favor a predictable and uniform cement distribution within the stents[15]. Furthermore, as demonstrated by Venier et al., “armed kyphoplasty” with rigid VB distraction devices, as VBS, safely address the posterior wall retropulsion, when present, by exploiting ligamentotaxis effect to achieve indirect central canal decompression[30].

Finally, in cases with signs of gross instability, or when a decompressive laminectomy is necessary, SAIF can be combined with a posterior surgical approach, as occurred in 2/80 cases in this series.

Study limitations

The study is retrospective but based on a prospectively maintained database. The patients included in this study were evaluated by a multidisciplinary team and considered poor candidate both for VA, because of the severity of their VCF, and for surgical stabilization, either for poor bone quality, and/or for their clinical conditions. In these conditions SAIF was actually a unique solution to a real world treatment challenge, which mitigates the limit of a lack of a control group.

Conclusion

Our results support the SAIF technique as a minimally-invasive procedure of internal stabilization to treat patients with severe osteoporotic VCFs with MC involvement. In our study SAIF proved to be feasible, safe, and effective treatment to stabilize the VB and to palliate pain, with durable results at follow-up. It might therefore be considered as a valuable option to a more invasive corpectomy, as a stand-alone intervention or in combination with a posterior surgical approach of stabilization. The use of this procedure in the clinical practice is supported by a strong biomechanical rationale. Further multicenter prospective data are necessary to confirm our results.

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31.

Figures and tables

Figure 1S

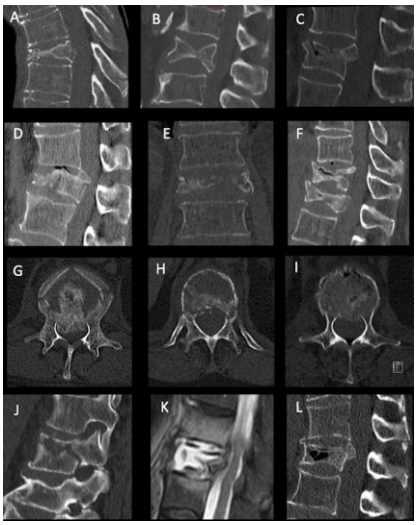

Figure 1S. Multiple examples of severe osteoporotic vertebral fractures included in this series, characterized by one or more features among: high degree of collapse, burst morphology with middle column injury, kyphosis, posterior wall retropulsion, high degree of fragmentation, pediculo-somatic junction fracture (G-J), and large osteonecrotic cleft (K-L).

Figure 1

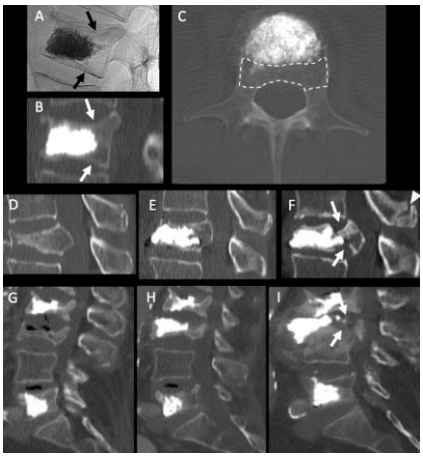

Figure 1. Parts A-C show the “bare area” concept: even after technically-satisfactory vertebral augmentation (VA) the middle column (MC) remains non-augmented, and well visible on axial CT, appears as a non-reinforced bare portion of the vertebral body (area outlined by dashed line on C). The junction between augmented and non-augmented vertebral body (arrows on A and B) might represent a weak point, subject to re-fracture, as in the two clinical examples (D-F and G-I). In both cases, after VA (E and H) of a fracture with MC involvement,

re-fracture occurs at the MC-“bare area” (arrows on F and I), ensuing in posterior wall retropulsion, splitting between augmented and non-augmented vertebral body, and focal hyperkyphosis. In F the arrowhead points at a spinous process fracture due to kyphotic deformity.

Figure 2

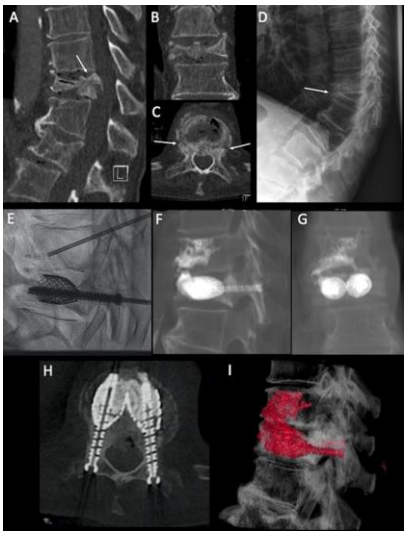

Figure 2. Osteoporotic severe fracture at a junctional level (T10), with burst morphology, high degree of fragmentation, middle column involvement (arrow on A), bilateral fracture at the pediculo-somatic junction (arrows on C), and severe collpase deformity with hyperkyphosis (arrow on D). E shows a fluoroscopic image after VBS expansion and fracture reduction, and pedicular screw insertion. F-I show the post-SAIF procedure reformatted CT, with cement filling of the stents, and vertebroplasty at the adjacent cranial level, that was also fractured, with a cleft along the inferior disc-endplate.

Figure 3

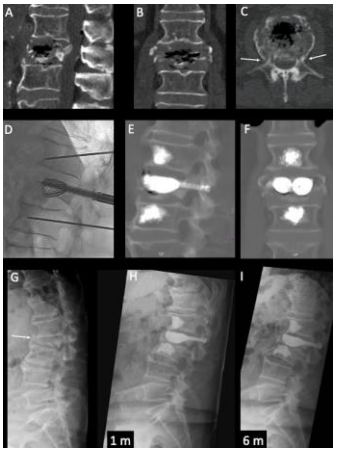

Figure 3. A-C show an extremely severe fragmentation of an L2 vertebral fracture, with middle column involvement, large air-filled cleft, and bilateral pedicular fracture (arrows on C). D shows fluoroscopic image of the SAIF set-up, with stents expanded, screws inserted and small caliber cannulae inserted at adjacent levels for prophylactic augmentation; E and show the post-SAIF CT, showing reconstruction of the vertebral body and the screws' internal fixation. G shows the standing plain film, pre-procedure, with severe collapse and focal kyphosis (arrow), which appears markedly reduced at 1 month follow-up, with stable results at the 6 month standing film (I).

Table 1

Characteristics of the study population and features of osteoporotic vertebral compression fractures

VARIABLE	VALUE
Tot no. of patients	73
Sex: M/F	21/52
Mean age (range)	77.7 (59-98)
Treated levels (%)	80
Thoracic	28/80 (35%)
Lumbar	52/80 (65%)
Thoraco-lumbar junction (Th10-L2)	63/80 (79%)
Fracture Morphology, no. of levels (%)	
VB collapse	
≤50%	21/80 (26.3)
>50%	59/80 (73.7)
Genant grade 3	51/80 (63.7)
Burst	56/80 (70)
Mc Cormack (grade 2 and 3)	80/80 (100)
Pediculo-somatic fractures	31/80 (38.7)
Osteonecrotic cleft	56/80 (70)

Table 1S

Summary of technical results and procedural complications

VARIABLE	VALUE
Procedure, no. of levels (%)	
Stand-alone SAIF	78/80 (98)
SAIF + PF	1/80 (1)
SAIF + L-PF	1/80 (1)
VBS, no. of levels (%)	
Bilateral	80/80 (100)
Unilateral	0/80 (0)
Screws, no. of levels (%)	
Bilateral	67/80 (83.7)
Unilateral	13/80 (16.3)
VB reconstruction, no. of levels (%)	
Reader 1	
• Excellent	73/80 (91.3)
• Good	6/80 (7.5)
• Fair	1/80 (1.2)
• Poor	0/80 (0)
Reader 2	
• Excellent	74/80 (92.5)
• Good	5/80 (6.3)
• Fair	1/80 (1.2)
• Poor	0/80 (0)
Procedural complications, no. of levels (%)	
Cement leak	8/80 (10)
Epidural-foraminal space	3/80 (3.7)
Neurological complication, no. of levels (%)	1/80 (1)

L-PF = decompressive laminectomy and posterior fixation; PF = percutaneous posterior fixation

Table 2S

Summary of clinical and radiological follow-up results

VARIABLE	VALUE
Follow-up, no. of levels (%) 1 month ≥6 months (range 6-24, mean 7.9)	 78/80 (97.5) 73/80 (91.2)
VAS, median (IQR) Before procedure 1 month post-procedure 6 months post-procedure	 8 (8-9) 3 (1.7-5) ***p<0.05*** 2 (0-3) ***p<0.05***
PGIC, mean (SD) 1 month follow-up 6 months follow-up	 5.6 (±0.9) 6.1 (±0.9)
Asymptomatic subsidence, no. of levels (%)	16/78* (20.5)
New VCFs, no. of levels (no. of patients) with worsening of pain requiring treatment (VPL or SAIF)	14 (11)

IQR= interquartile range; PGIC= Patients' Global Impression of Change scale; SD = standard deviation; VAS= Visual Analogue Scale; VCF= vertebral compression fracture; VPL= vertebro-plasty; * Levels with available follow-up (range 1-24 months).

Chapter 8 / a

“Armed Kyphoplasty”: An Indirect Central Canal Decompression Technique in Burst-Fractures

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Abstract

Background and purpose

Burst-fractures are characterized by middle column disruption and may feature posterior wall retropulsion (PWR). Indications for treatment remain controversial. Recently introduced vertebral augmentation techniques, using intra-vertebral distraction devices, such as vertebral-body-stents (VBS) and Spinejack (SJ), could be effective in fracture-reduction and fixation, and might obtain central canal clearance through ligamentotaxis. This study assesses the results of "armed kyphoplasty" (AKP) using VBS or SJ in traumatic, osteoporotic and neoplastic burst-fractures with respect to vertebral body height (VBH) restoration and correction of PWR.

Materials and methods

Retrospective assessment of 53 burst-fracture with PWR and no neurological deficit, in 51 consecutive patients, treated with AKP. PWR and VBH were measured on pre- and post-procedure CT. Clinical and radiological follow-up charts were reviewed.

Results

AKP was performed as a stand-alone treatment in 43 patients, combined to posterior instrumentation in 8, with laminectomy in 4. Pre-AKP and post-AKP mean PWR was 5.8 mm and 4.5 mm respectively ($p < 0.001$), and mean VBH was 10.8 mm and 16.7 mm respectively ($p < 0.001$). No significant clinical complications occurred. Clinical and radiological follow-up (1-36 months, mean 8 months) was available in 39 patients. Three treated levels showed a new fracture during follow-up, without neurological deterioration, and no re-treatment was deemed necessary.

Conclusions

In the treatment of burst-fractures with PWR and no neurological deficit AKP obtains fracture-reduction, internal fixation, and indirect central canal decompression. In selected cases, it might represent a suitable minimally-invasive treatment option, stand alone or in combination with posterior stabilization.

ABBREVIATIONS: AKP armed kyphoplasty, BKP balloon kyphoplasty, PLL posterior longitudinal ligament, PWR posterior wall retropulsion, SJ spinejack,, VBH vertebral body height, VBS vertebral body stenting, VPL vertebroplasty

Introduction

Thoraco-lumbar burst-fractures can result from axial-load high-energy trauma or occur even with minor trauma, if bone is weakened by osteoporosis or neoplasm. Burst-fractures are characterized by a high degree of osseous fragmentation, outward fragment dispersion, middle column disruption and may be associated with posterior wall retropulsion (PWR) in the central canal. Burst facture are considered unstable, carrying a risk for immediate or delayed neurologic compromise [1].

In practice, treatment of burst-fractures, especially without neurological injury, remains controversial, with indications ranging from conservative [2] to complex combined ventral and dorsal surgical approaches [3]. Conservative treatment may imply long periods of diminution of the activities of daily living. Moreover, burst fractures carry the risk of progressive focal kyphosis and neurological deterioration [4]. Conversely, surgical treatment should stabilize the vertebral body restoring vertebral body height (VBH) and alignment, correcting kyphosis, and decompressing the central canal [5, 6], thereby reducing pain and allowing early mobilization.

To address these goals, traditional pedicle-screw instrumentation allows indirect fracture- and kyphosis-reduction [7, 8], and via a dorsal approach the central canal can be decompressed by laminectomy and posterior wall fragments impaction [9, 10], or indirectly restored, through a posterior external cantilever and distraction maneuver, exploiting ligamentotaxis of the posterior longitudinal ligament [11]. Nevertheless, stabilization of the anterior column remains crucial in these fractures to avoid loss of correction and instrumentation failure [12]. Surgical anterior instrumentation with strut-grafting, mesh-cage and plates has proven effective to stabilize the anterior column [13, 14], but requires a more invasive approach that could be associated with increased morbidity [15].

A minimally-invasive approach would be desirable and might represent a balanced compromise. Cement augmentation, mainly with balloon-kyphoplasty (BKP) technique, as a standalone or in combination with posterior instrumentation, has been proposed as an option [16-19], but it might be not very effective in correcting kyphosis, due to the potential loss of height restoration at balloon deflation [20, 21]. Moreover, in the presence of PWR, BKP might be unable to clear the canal and is even considered relatively contraindicated, due to the risk of epidural cement leakage and further displacement of bony fragments in the central canal,

potentially leading to worsening of neurological condition [22, 23]. More recently introduced percutaneous intra-somatic distraction devices, such as Spinejack® (SJ) (Stryker, Kalamazoo, Michigan, USA) and vertebral body stents (VBS®) (DePuy-Synthes, Johnson&Jonhnson), allowing to perform an “armed kyphoplasty” (AKP) might be able to overcome the deflation effect of BKP and allow a minimally-invasive stabilization of the vertebral body [24, 25]. An effective internal vertebral body fracture-reduction and fixation might in turn allow ligamentotaxis-effect and canal-clearance.

In this study we retrospectively assess the results of AKP using VBS or SJ, with or without posterior instrumentation, in traumatic, osteoporotic and neoplastic burst-fractures with regard to correction of PWR and restoration of VBH.

Materials and methods

Patient population

All the patients who underwent AKP at a single Center between August 2013 and December 2017 were considered for the study. Inclusion criteria were: i) the presence of traumatic, osteoporotic (spontaneous or related to minor trauma), or neoplastic burst-fracture without neurological deficits, ii) the presence of a retropulsed bone fragment in the central canal documented on the pre-procedure CT, iii) a post-procedure CT scan obtained within 10 days from treatment. The local Ethics Committee approved this study.

Procedure

The AKP was performed under general anesthesia, using VBS (Fig. 1, 2, 4) or SJ (Fig. 3, 4), under biplane fluoroscopic guidance. The procedure was conducted utilizing standard techniques for either device [24, 25]. VBS AKP was performed stand-alone or with the additional insertion of pedicular screws anchoring the stents, in accordance with the recently reported Stent-Screw Assisted Internal Fixation (SAIF) technique [26] (Fig. 2, 4). Intra-operative myelography was used in selected cases of lumbar fractures to monitor the central canal stenosis during the procedure. When deemed necessary, AKP was performed in combination with a surgical posterior stabilization, either with percutaneous or open surgery, with or without decompressive laminectomy (Fig. 3), but without additional distraction or posterior wall fragment impaction. When deemed appropriate by the operator, in osteoporotic patients, prophylactic vertebral augmentation was performed at the adjacent level(s) [27]. The individual case treatment decision and approach was arrived at via a multidisciplinary spine board.

Measurements

PWR and VBH were measured on pre- and post-procedure CT scans by two readers, a neuroradiologist and a neurosurgeon, in consensus. Images were reformatted with orthogonal multiplanar reconstructions, with slice thickness 2 mm, interval 2 mm, bone algorithm, on a PACS system (iSite, Philips). A straight line was drawn on the mid-sagittal plane from the posterior-inferior corner of the cranial to the posterior-superior corner of the caudal adjacent vertebral bodies, ideally representing the original position of the normal pre-fracture posterior wall of the target level. This line intersected the retropulsed fractured posterior wall.

The PWR was then measured perpendicularly from this posterior wall line on the mid-sagittal image (Fig. 1). VBH measurement was obtained on the mid-sagittal image, from the superior to the inferior endplates, at the most collapsed point (Fig. 1).

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (IBM, Armonk, New York).
For non-normally distributed variables, we utilized the related samples Wilcoxon signed rank test to compare median pre-operative versus post-operative degree of PWR and to compare median pre-operative versus post-operative VBH. Visual analogue scale (VAS) scores for pain intensity at baseline, at 1 month, and at 6 months follow-up were also compared with the same non parametric test.

Follow-up

Every patient underwent plain-films and CT of the spine within 10 days from treatment to evaluate the procedure results. Clinical assessment after the procedure was mainly directed to assess for neurological deterioration. In a subgroup of patients, extended imaging and clinical follow-up was available, and was reviewed to evaluate long-term target-level stability results, new vertebral fractures, neurological status stability and other clinical conditions requiring a new treatment. The Visual Analog Scale (VAS) pain score (0-10) assessment pre-procedure, at 1- and 6-months post-procedure follow-up was available for a subgroup of patients.

Results

Patient population

Out of 193 patients, 94 patients were excluded because the fracture was not associated with a retropulsed bone fragment, 48 were excluded because either a pre- or a post-procedure CT scan was not available for analysis. Patient population, fulfilling all inclusion criteria, included therefore 51 patients (34/17 F/M, age range 46-90 years, mean 73 years), with thoracic (20/53) or lumbar (33/53) fractures. The most frequent treated levels were T12 and L1 (23/53). Two patients were treated at two levels. The fractures were traumatic in 32/53, osteoporotic in 12/53 and neoplastic in 9/53 cases.

Procedure

AKP was performed with VBS at 46/53 levels and with SJ at 7/53 levels. VBS AKP was performed with SAIF technique at 33/46 levels. Intra-operative lumbar myelography was performed in 4 cases (Fig. 1).

Concurrent posterior surgical stabilization with pedicular screws and rods was performed in 8/51 patients, along with decompressive laminectomy in 4/8.

In one case an epidural cement-leak occurred, causing L4 radicular pain, that promptly resolved after steroid nerve block. One patient experienced transient and completely reversible paraparesis, without evidence of worsening central canal compromise, and without epidural cement leaks on post-procedure CT and MR. No further intra-procedural clinical complications occurred. No other patient showed worsening neurological status after the procedure or at follow-up.

PWR and VBH

There was a statistically significant difference between the degree of PWR preoperatively (mean 5.8 mm; range 2-10 mm; SD +/- 2) and postoperatively (mean 4.5 mm; range 0 – 9.4 mm; SD+/- 1.9; $p < 0.001$) and there was a statistically significant difference between the VBH preoperatively (mean 10.7 mm; range 2-21 mm; SD +/- 4.4) and postoperatively (mean 16.5 range 7.7-23.6 mm; SD +/- 3.8 $p < 0.001$). When comparing pre- and postoperative CT scans, PWR difference ranged between +2 and -4 mm (mean -1.2 mm) and mean gain of VBH was 5.8 mm.,

Individual cases analysis showed that 41/53 levels had PWR correction, 6/53 had unchanged PWR and 6/53 had worsened PWR postoperatively, while 51/53 had some degree of VBH restoration and 2/53 showed reduced VBH at post-procedure CT.

Follow-up

Beyond the post-procedure clinical assessment, spine plain-films, and CT within 10 days, 39/51 patients (41/53 levels) had an extended clinical and imaging follow-up, at least with standing spine plain-films, at multiple and variable time-points, ranging from 1 to 36 months post-procedure (mean 8 months). In 19/41(46%) levels the post-procedure VBH was fully maintained, in 19/41 (46%) mild subsidence of the superior or inferior endplates was noted (Fig. 4),

with no significant impact on alignment and kyphosis, while in 3/41 (8%) a recurrent VBH collapse of the target-level was noted. In the follow-up group, 22/41 levels were studied with a cross-sectional imaging technique (8 with MRI and CT, 11 with CT and 3 with MRI), and PWR could be assessed: 14/22 showed stability of the PWR correction compared to the postoperative CT, while 8/22 showed a recurrence in PWR. Out of these 8 cases, 2 were associated to refracture of the target level, while 6 were associated to subsidence of the treated vertebra at follow-up. No retreatment was necessary at AKP-treated target levels. Clinical follow-up showed no neurological deterioration.

Pre-procedure and follow-up VAS pain score was available for 31/51 patients. Mean VAS score at baseline was 8.5 (range 6-10; Std. Deviation +/- 1.1), at 1 month follow up was 4.0 (range 0-9; Std. Deviation +/- 2.1), at 6 months follow up was 2.8 (range 0-7; Std. Deviation +/- 1.8). In this cohort the VAS scores at baseline versus 1 month and versus 6 months were significantly different ($p<0.0001$).

Discussion

In this study AKP, using recently introduced vertebral body fracture internal distraction devices, such as VBS and SJ, was safely able to obtain VBH restoration and PWR correction in traumatic (Fig. 3, 4), osteoporotic (Fig 1, 4) and neoplastic burst-fractures (Fig. 2). It was utilized as a stand-alone minimally-invasive procedure in the majority of the cases, or in combination with a posterior surgical approach (Fig. 3), but without the need to perform any direct form of PWR correction. This minimally-invasive approach carried only two peri-procedural complications, both with benign clinical resolution, showed durable results at follow-up, and required no re-intervention on the target level.

There is no definite consensus on management of burst-fractures with PWR. Some authors support conservative approach in neurologically intact patients, claiming the possible spontaneous remodeling and resorption of the posterior wall osseous fragment encroaching the central canal [28], while others suggest a variety of surgical approaches, including decompressive laminectomy, stabilization of the anterior column combined to a dorsal instrumentation [13, 15], and direct or indirect repositioning of retropulsed bone fragments [9, 10].

The goals of treatment are to obtain early patient mobilization and a painless, balanced, stable vertebral column with maximum spine mobility and optimal neurologic function. In neurologically-intact patients the different surgical techniques are not necessarily superior to a non-operative approach [6]. It is important to consider that these results might be influenced by the potentially significant morbidity and increased cost of an anterior column reconstructive surgery, and by the failure rate of a stand-alone posterior surgical fracture reduction and stabilization [11, 12]. A safe, effective, and durable minimally-invasive solution to reduce and stabilize the fracture might perform differently and better approach the ideal treatment goals.

BKP has been used to treat burst-fractures, especially in combined approach with dorsal instrumentation [17, 18], but its potential to effectively obtain VBH restoration has been questioned [20, 21]; and might even be relatively contraindicated [29]. Bearing all that in mind, in clinical practice BKP is likely used relatively frequently given the extreme pain and functional limitations patients can find themselves in for extended period of time. VBS and SJ have been reported as an alternative to BKP, to reduce the deflation effect and potentially guarantee more reliable height restoration in wedge shaped or incomplete burst compression fractures [30-32]. A recent randomized controlled trial showed better kyphosis correction, maintained at 12 months, for SJ versus BKP in osteoporotic compression fractures [33] . A cadaveric study [34] has shown SJ ability to reposition the retropulsed posterior wall of a burst fracture model, and substantially maintain this gain after cyclic re-compression, while posterior instrumentation alone did not maintain central canal clearance, but the potential of AKP to restore VBH and correct the PWR in burst fractures has not been investigated in vivo. In fact, most studies reporting the use of VBS and SJ have focused on wedge compression fractures of osteoporotic nature [25, 30, 31], and fewer have dealt with incomplete burst fractures [32] . Within these studies, pain outcome was typically the primary endpoint, while kyphosis or VBH correction were secondary endpoints. In general, repositioning of the posterior fragments is underrepresented in most evaluations [34].

The AKP is able to exert effective VBH restoration, avoiding height loss due to deflation effect, and is increasingly used as a stand-alone measure to reconstruct and restore axial load capability in traumatic, osteoporotic and malignant fractures [26, 35]. As a consequence of the internal fracture distraction and kyphosis reduction, AKP appears to allow ligamentotaxis correction of the PWR, without the need to perform external distraction through a posterior

instrumentation or even more invasive maneuvers of fragment repositioning through direct impaction. It is important to note that in this study we included 8 neoplastic fractures that had a retropulsed bone fragment (Fig. 2), while we did not include cases with epidural non-osseous soft-tissue mass. An epidural soft tissue mass might in-fact behave differently from an osseous PWR, and would have been more difficult to measure on post-operative CT. Intra-operative myelography, already described in the setting of vertebral augmentation procedures at risk for central canal encroachment [36], was used only in a minority of cases in this series but it seemed potentially useful, in selected patients, to have a visual control under fluoroscopy of the PWR and to directly demonstrate the effect of ligamentotaxis during fracture reduction (Fig. 1).

We found a statistically significant difference between the mean degree of PWR and VBH pre and postoperatively, which suggests the biomechanical effectiveness of the technique.

Beside the statistically-significant postoperative changes of PWR and VBH, we found 2 cases in which VBH was reduced postoperatively, 6 cases with worsened PWR, and 6 cases with unchanged PWR. Explanations for such technical failures are not clear. Worsening PWR can certainly be an undesired effect of the internal vertebral body distraction, as generally feared, if ligamentotaxis does not occur, but fracture, VBH, and PWR might have also negatively evolved in the time-lapse between preoperative imaging and the procedure. Unchanged PWR might have also be related to osseous healing and/or non-efficient ligamentotaxis, that might have not allowed fragment repositioning. In addition, the group of patients we analyzed was heterogeneous, having included traumatic, osteoporotic and malignant fractures, which theoretically may respond differently to AKP. While it is difficult to relate the technical efficacy in VBH restoration and PWR correction observed in this cohort to a definite measure of clinical benefit, PWR is still considered a relative contraindication to vertebral augmentation. Not infrequently, it represents an argument for open stabilization surgery. The results of this study might serve to mitigate the fear that AKP might worsen the status of neurologically intact patients with burst fractures. In the group of patients with available VAS pain score assessment there was significant and sustained pain reduction as expected when compared with previously published larger series utilizing similar treatment techniques [36]. In the 41 levels with available follow-up the results obtained with AKP confirmed to be stable at a mean follow-up period of 8 months (range 1-36 months), since in 38/41 the postoperative VBH was either stable or showed only minimal endplates subsidence (Fig. 4); only in 3 cases we encountered a re-fracture of

the vertebral body treated with AKP, with VBH loss. As far as PWR correction, 14/22 patients that had cross- sectional imaging follow-up available showed stable PWR at follow-up. Some degree of PWR recurrence was noted in 8/30, associated to recurrent collapse (2/8) or subsidence. Patients with re-fracture of the target level and/or PWR recurrence presented mild or no new symptoms at clinical follow-up, did not show neurologic deterioration and did not require any further invasive treatment.

One might consider subsidence of the endplates and minimal PWR recurrence nearly physiological changes after AKP, namely because the surrounding fractured and weakened bone of the vertebral body, upon weight bearing loading, remodels and might undergo resorption phenomena against the new rigid internal scaffold, represented by VBS and SJ with PMMA, but usually this does not have clinical significance. The 3 new collapses reported in this series occurred in elderly patients treated for traumatic (1/3) and osteoporotic (2/3) fractures, all in a context of non-treated osteopenia. The importance of a thorough management of frequently underlying osteopenia or osteoporosis in patients at risk remains critical so as to reduce new fracture risk or hardware failure [37].

AKP was performed using VBS in 46 levels and SJ in the remaining 7. We tend to use SJ for AKP when bone mass is preserved, especially in young patients, with traumatic mechanism of fracture, and impacted morphology of the fracture, which needs a powerful internal fracture distraction, while we rather use VBS in bone of poor quality, with high degree of vertebral body fragmentation, osteoporosis, lytic lesions, where the vertebral body rather needs an internal scaffold to restore its stability and axial load capability [35].

There are several limitations of the present study including it retrospective design, the small size and heterogeneity of the sample, and non-systematic follow-up. There might have been a selection bias in the studied patient series, but decision to treat with AKP versus standard surgical approach was reached for every individual patient in a multidisciplinary spine board. The inclusion in this series of patients treated in combination with a posterior surgical approach underscores the possibility to treat even severe burst-fractures with AKP, avoiding surgical stabilization of the anterior column, and more invasive maneuvers to clear the central canal.

Given the small number of patients and confounding factors, including concurrent surgical interventions, fracture etiology heterogeneity, and technical differences in performing the AKP procedure, the conclusions of our analysis need to be confirmed in larger prospective studies.

Conclusion

AKP appears to represent a viable technique to treat neuro-intact burst-fractures with PWR, in combination with posterior instrumentation, or in selected cases as a stand-alone procedure, being able to obtain VBH restoration and indirect central canal decompression through PWR correction. This minimally-invasive approach should offer durable results, and thus represents an alternative approach to avoid more invasive anterior column stabilization interventions and retropulsed bone fragment reposition techniques.

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Chapter 8 / b

Mechanical Cavity Creation with Curettage and Vacuum Suction (Q-VAC) in Lytic Vertebral Body Lesions with Posterior Wall Dehiscence and Epidural Mass before Cement Augmentation

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Abstract

Background and Objectives

We describe a novel technique for percutaneous tumor debulking and cavity creation in patients with extensive lytic lesions of the vertebral body including posterior wall dehiscence prior to vertebral augmentation (VA) procedures. The mechanical cavity is created with a combination of curettage and vacuum suction (Q-VAC). Balloon kyphoplasty and vertebral body stenting are used to treat neoplastic vertebral lesions and might reduce the rate of cement leakage, especially in presence of posterior wall dehiscence. However, these techniques could theoretically lead to increased intravertebral pressure during balloon inflation with possible mobilization of soft tissue tumor through the posterior wall, aggravation of spinal stenosis, and resultant complications. Creation of a void or cavity prior to balloon expansion and/or cement injection would potentially reduce these risks.

Materials and Methods

A curette is coaxially inserted in the vertebral body via transpedicular access trocars. The intravertebral neoplastic soft tissue is fragmented by multiple rotational and translational movements. Subsequently, vacuum aspiration is applied via one of two 10 G cannulas that had been introduced directly into the fragmented lesion, while saline is passively flushed via the contralateral cannula, with lavage of the fragmented solid and fluid-necrotic tumor parts. *Results:*
We applied the Q-VAC technique to 35 cases of thoracic and lumbar extreme osteolysis with epidural mass before vertebral body stenting (VBS) cement augmentation. We observed extravertebral cement leakage on postoperative CT in 34% of cases, but with no clinical consequences. No patients experienced periprocedural respiratory problems or new or worsening neurological deficit.

Conclusion

The Q-VAC technique, combining mechanical curettage and vacuum suction, is a safe, inexpensive, and reliable method for percutaneous intravertebral tumor debulking and cavitation prior to VA. We propose the Q-VAC technique for cases with extensive neoplastic osteolysis, especially if cortical boundaries of the posterior wall are dehiscent and an epidural soft tissue mass is present.

Keywords: vertebral augmentation; cavity creation; lytic vertebral body lesions; vertebral body stent

Introduction

Percutaneous vertebral augmentation (VA) with vertebroplasty (PVP), balloon kyphoplasty (BKP), or vertebral body stenting (VBS) is often performed in patients with painful, fractured, or at-risk-of-fracture neoplastic spinal lytic lesions. The main goals are reinforcement of the vertebral body, stabilization or prevention of a fracture, and pain relief [1–6]. However, complication rate of VA, including cement pulmonary embolism and epidural cement leakage, is higher in patients with neoplastic when compared with osteoporotic fractures [7,8]. In spinal neoplastic lesions, the trabecular and spongious components of the vertebral body are infiltrated by tumoral tissue and the cortical boundaries might be eroded by neoplastic osteolysis; therefore, upon injection, the cement often distributes unevenly and unpredictably and has increased tendency to leak outside of the vertebral body [7]. The rate of cement leakage in metastatic lesions can reach up to approximately 70% [8]. While leakage rate might be reduced by the use of high-viscosity cement [9] and/or by balloon kyphoplasty [10], especially in presence of posterior wall lytic dehiscence and soft tissue epidural mass, both balloon expansion and cement injection might instead extrude tumoral tissue outside of the vertebral body, worsening a central canal stenosis [11] or facilitating extraosseous disease spread [12]. Moreover, raised intravertebral pressure during balloon inflation and cement injection has been shown to favor bone marrow and tumor cell migration in the systemic circulation [11–14], with demonstrated temporary raise of pulmonary arterial pressure [15,16], very rarely symptomatic, but with unknown clinical effects and impact on oncological outcome [1,17].

Creation of a void or cavity prior to balloon expansion and/or cement injection seems to lower intravertebral pressure, thereby facilitating a more secure filing of the lytic defect [18], and has the potential of reducing risk of cement leakage, soft tissue mass dislodgement, and pulmonary fat and neoplastic cells embolism. It ultimately allows a greater amount of cement deposition in the vertebral body.

Radiofrequency ablation (RFA) [14,19], cryoablation [20,21], coblation [20,21], curettage [22], and bone marrow washout [23], each with its own potential advantages and limits, have been proposed to decompress the vertebral body prior to cement injection.

The aim of this study is to describe a new percutaneous image-guided minimally invasive technique for mechanical nonthermal intravertebral tumor debulking and cavity creation in

vertebral body lytic lesion. This technique, called “Q-VAC”, combines mechanical curettage and vacuum suction with lavage. We have applied this technique to cases with extensive osteolysis of the vertebral body, widely eroding cortical boundaries and posterior wall, often in the presence of an epidural mass, prior to VBS augmentation [24].

Materials and Methods

This is a technical note describing the procedural details and potential applications of this new technique, combining previously described and established procedures and devices [2,22,23,25]. We retrospectively evaluated all patients that underwent curettage and vacuum suction (Q-VAC) prior to cement augmentation at our institution between 01.03.2013 and 01.11.2018. Q-VAC technique was performed to aid in the cement augmentation of a spinal lytic metastatic lesion with extensive discontinuity of the cortical boundaries (“extreme osteolysis”). Since Q-VAC was performed with the intent to obtain satisfactory cement deposition in the vertebral body and to avoid undesired cement leakages and worsening of neurological status from tumoral soft tissue migration in the central canal, we considered the satisfactory stabilization of the lytic lesion as efficacy and any treatment-related clinical worsening due to cement leakage or tumor migration as complications. To assess the stability of the treated vertebral bodies, standing X-rays were obtained on the day following the procedure and 4 weeks after treatment.

The Institutional Review Board approved this investigation and the patients signed a required informed consent to undergo the procedure (Approval number: 2739 ID 14-136).

Procedural Details

All interventions were performed in a mono- or biplanar angiography suite (Allura Xper, Philips, Best, The Netherlands). The patients were placed under general anesthesia while in the supine position and then turned into the prone position. Intravenous antibiotic prophylaxis was administered at the beginning of the procedure. After percutaneous fluoroscopically guided insertion of two 4.5 mm (7G) caliber trocars via transpedicular access (Access kit VBS, DePuySynthes-Johnson & Johnson, New Brunswick, NJ, USA), a Kyphon Latitude II Curette T-Tip 7 or 8 mm (Medtronic, Memphis, TN, USA) was coaxially inserted in the vertebral body via transpedicular access trocars. Subsequently, the curette tip was locked at 30, 60, or 90 degrees off-axis and the tissue present in the vertebral body was fragmented or “mashed-up” by multiple

tational (as a windshield wiper) and anteroposterior translational movements of the curette, while respecting the bony boundary of the vertebral body, under fluoroscopic control, until soft tissue consistency decreased due to tissue fragmentation. After retraction of the curette, a 10 G cannula was introduced into the now fragmented lesion via each access trocar. One cannula was connected to a 60-cc syringe filled with saline via a short luer-lock connection tubing and the second to a vacuum pump with a Penumbra Hi-Flow Aspiration Tubing (Penumbra, Alameda, CA, USA) producing aspiration force of 242 Mbar. The aspiration was then activated and the saline solution was passively flushed from the contralateral cannula through the fragmented lesion with lavage of the fragmented solid and fluid-necrotic tumor parts. Depending on the amount of tumor extraction or suspected residual tumor, repetition of the procedure was possible and performed at operator's discretion. After cavity creation, insertion and expansion of the VBS, followed by cement augmentation, was performed as previously described [24]. Patients underwent postoperative plain films and CT and clinical follow-up, as reported in the clinical study [24]. Figure 1 shows an illustration of the technique.

Results

We applied the Q-VAC technique to 35 cases (19/16 M/F) (age 44–84, mean 67.9 y) of thoracic and lumbar (from T1 to L5) extreme osteolysis before VBS cement augmentation. Lytic lesions were related to solid tumor metastases in 27 cases and multiple myeloma in 8. In 21/35 cases, an extraosseous epidural mass was present on preprocedural imaging. We observed extravertebral cement leakage on postoperative CT in 34% of cases, but with no clinical consequences. No patients experienced periprocedural respiratory problems nor new or worsening neurological deficit. All treated vertebral bodies were stable at follow-up imaging, without secondary height loss.

Discussion

In patients with neoplastic lytic vertebral lesions, reducing pain, stabilizing fractures or lesions at risk of fracture, and ultimately improving quality of life are key elements of treatment. VA, with its technical variants, has an established role in achieving these goals [1,2,5]. However, not all procedures are applicable to extensive lytic lesions. VA of an extensive lesion with erosion of the posterior wall or epidural tumor spread bears the risk for spinal cord

compression, either from cement leakage or from further central canal encroachment by the epidural mass, and risk of pulmonary cement embolism or tumor spread locally or hematogenously [8,11,13].

Creation of a cavity prior to cement injection or intravertebral device expansion, such as balloons and VBS, might help increase safety and avoid severe adverse events. There are alternatives which have been proposed to reduce the cement migration from vertebrae like BKP [2], RFA and cryoablation [26], and bone marrow lavage [23].

Specific limits of BKP concern the raise of intravertebral pressure provoked during balloons inflation that might displace tumoral tissue through a dehiscent posterior wall and cause further central canal stenosis, or mobilize bone marrow fat cells and neoplastic cellular aggregates into the systemic circulation. In addition, due to balloon deflation and its removal before cement injection, the intravertebral neoplastic tissue may re-expand elastically again, obliterating the previously created cavity.

RFA and cryoablation prior to cement injection result in reduction of tumor mass due to induction of necrosis [14,19–21]. These techniques can also cause thrombosis of the vertebral and paravertebral veins, reducing the PMMA embolization risk. Regarding the potential use to obtain an intravertebral cavity though, in both techniques, the induction of tumor cell necrosis does not correspond to an immediate void creation. Subsequent cement injection simply pushes residual tumor cells and necrosis aside. As additional drawbacks, RFA and cryoablation require a safety margin with vital and nervous structures, imply adjunctive time and cost increase [26].

Another described technique for cavity creation, the percutaneous controlled ablation (coblation), utilizes a plasma field to evaporate tumor cells at low temperatures, in theory allowing subsequent low-pressure cement injection with a reduced risk of cement leaks and epidural tumor displacement [3,27,28]. This technology, characterized by technical limitations in addressing large soft tissue lesions [24] and high costs, is no longer commercially available.

Although not truly a cavity creation technique, the bone marrow “washout” or lavage has been described firstly in a cadaveric spine model [29] and then in an animal model [30,31] to reduce cement injection forces, reducing cement extravasation, and fat embolic load to a degree below the threshold for eliciting a cardiovascular response. Jet lavage has also been reported in a clinical setting in a series of osteoporotic vertebral compression fractures [32] to potentially reduce the risk of cement leakage and prevent pulmonary embolism. Finally,

bone marrow washout has been reported in a small series of patients treated with multilevel vertebroplasty for multiple myeloma spine lesions [23].

Nevertheless, we found simple aspiration or washout attempts only able to partially remove the fluid, necrotic, or bloody parts of vertebral neoplastic lesions, as in multiple myeloma, but solid vertebral lesions commonly occur in metastatic breast and lung cancer cannot be removed with simple aspiration and lavage through transpedicular cannulas. For this reason, in the Q-VAC technique, before vacuum suction and lavage, we implemented a purely mechanical cavity creation using intravertebral soft tissue mass fragmentation through a curette. The use of a coaxial curette has been described in case of sclerotic changes after vertebral body fractures to maximize height restoration during balloon kyphoplasty [22], but it has not been employed to fragment neoplastic intravertebral soft tissue, nor combined to consequent aspiration.

Advantages of the Q-VAC are the creation of a true intravertebral cavity without increasing intraosseous pressure and without risk of thermal injuries to adjacent vital and nervous structures. The cavity creation adds no more than ten minutes to the procedure and does not require expensive devices. Nevertheless, the Q-VAC technique is only intended for creating a cavity in the vertebral body prior to VA, and by no means has the intent of local tumor control. Standardized oncological therapy should be considered as clinically indicated. Another limitation of this study is that it is single arm; Q-VAC has not been compared with any other debulking procedure.

Application: We propose the Q-VAC technique for cases with extensive neoplastic osteolysis of the vertebral body, especially if cortical boundaries of the posterior wall are dehiscent and an epidural soft tissue mass is present. In these cases, the Q-VAC allows a minimally invasive percutaneous debulking of the soft-tissue tumor component centrally located in the vertebral body, resulting in the creation of a cavity that in turn allows safer expansion of balloons if a BKP is to be performed or if VBS or stent-screw-assisted internal fixation (SAIF procedure) [24,25] is planned, and in general a potentially safer and more predictable deposition of larger amount of cement. In fact, in this severe lytic lesions, VBS and SAIF techniques offer a vertebral body reconstruction, with the stents acting as an internal scaffold representing a vertebral body prosthesis and helping contain the cement. Through these techniques, large volume implants are deployed and consequently large volume of cement can be deposited in the vertebral body, to the potential advantage of greater local stability. Preliminary cavity creation seems to be a desirable technical adjunct in such cases.

Conclusions

In our cohort, the Q-VAC technique, combining mechanical curettage and vacuum suction with lavage, is a safe, inexpensive, and reliable method for percutaneous intravertebral tumor debulking and cavitation prior to VA and its technical variants as VBS and SAIF, in extensive lytic vertebral neoplastic lesions.

Author Contributions: conceptualization, A.C.; data curation, M.I.; methodology, A.C.; supervision, J.A.H. and A.C.; visualization, E.I.P.; writing – original draft, E.I.P.; writing – review & editing, M.I, M.P., D.D., J.A.H. and A.C.

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Conflicts of Interest: The authors declare no conflict of interest.

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Figures and Tables

Figure 1

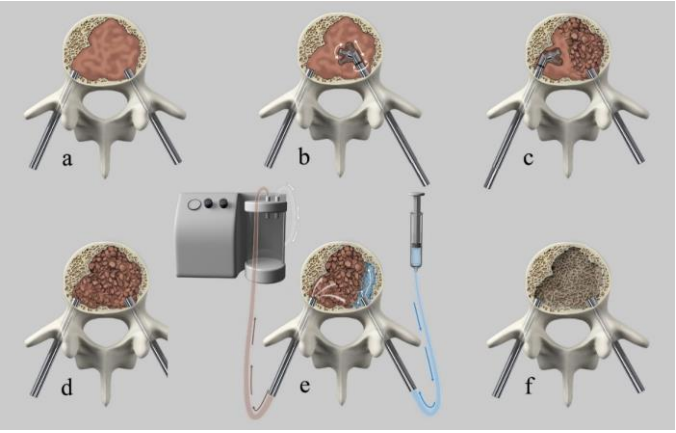

Figure 1. Illustration of the curettage and vacuum suction (Q-VAC) technique. (**a**), transpedicular introduction of the cannulas into the vertebral body. (**b**), coaxially inserted curette in the vertebral body via transpedicular access trocars with subsequent angulation of the curette and fragmentation of the solid lesion by multiple rotational and anteroposterior translational movements. (**c**), contralateral tumor fragmentation. (**d**), Illustration of the completely fragmented vertebral lesion. (**e**), connection of one cannula to a syringe filled with saline and the second to a vacuum pump. Activation of aspiration with subsequent passive flushing of saline through the fragmented lesion, with lavage of the fragmented solid and fluid-necrotic tumor parts. (**f**), created cavity after tumor debulking before subsequent vertebral augmentation.

Two illustrative cases present typical patients and treatments (Figures 2 and 3):

Figure 2

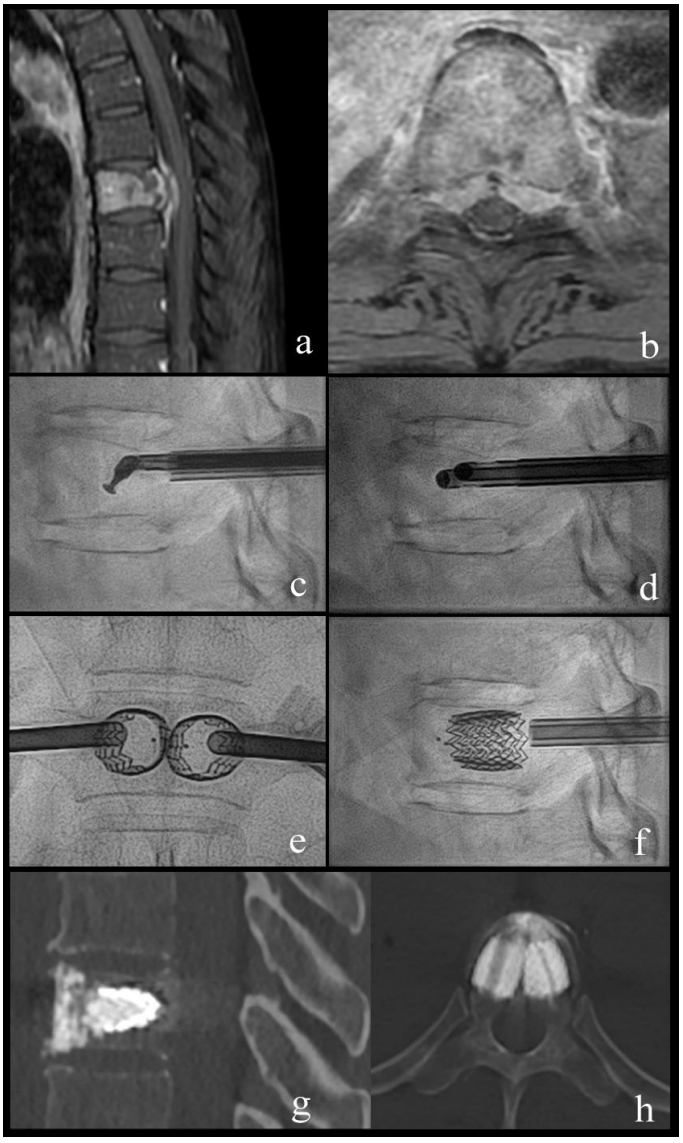

Figure 2. Case 1; a 63-year-old woman with breast cancer and newly diagnosed bone metastases. (**a**,**b**), sagittal and axial T1-weighted fat-suppressed enhanced MR images show vertebral lesion with involvement of the posterior wall and an epidural mass. (**c**), lateral fluoroscopy view with angulated coaxial curette in the vertebral body for lesion fragmentation and cavity creation. (**d**), lateral fluoroscopy view after introduction of two 10 G cannulas into the fragmented lesion for tumor flush and aspiration. (**e**,**f**), lateral and anteroposterior fluoroscopy views after vertebral body stenting (VBS) deployment with height restoration of the fractured vertebral body. (**g**,**h**), sagittal and axial CT after VBS and cement augmentation.

Figure 3

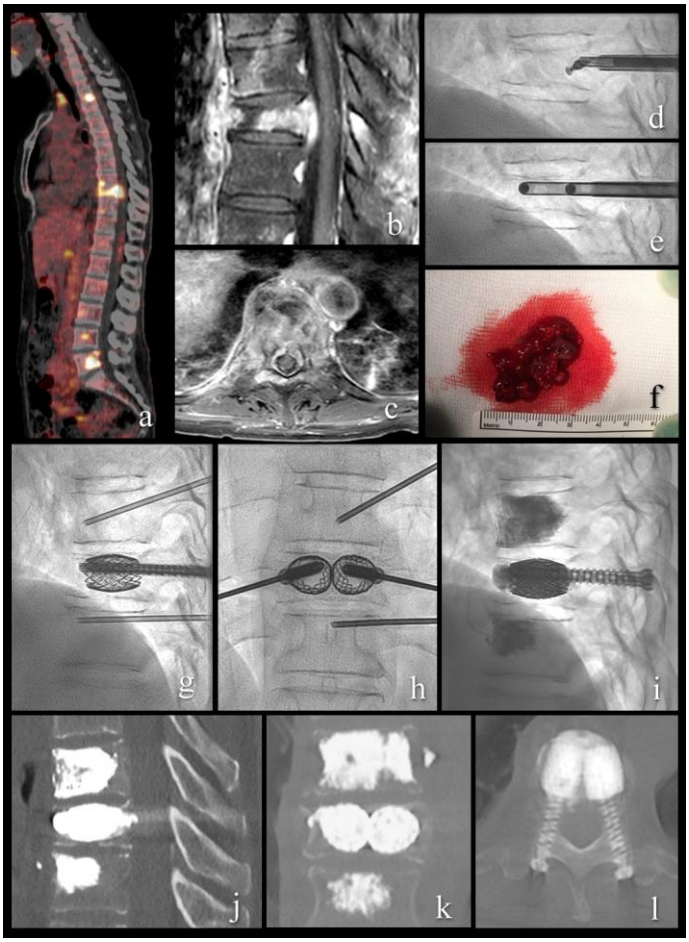

Figure 3. A 54-year-old patient with metastatic renal cell cancer and acute onset back pain. (**a**), FDG PET-CT with multiple spinal lesions with increased FDG uptake. (**b**,**c**), sagittal and axial T1-weighted fat-suppressed enhanced MR images show the vertebral lesion with involvement of the posterior wall, an epidural mass, and pathologic fracture. (**d**), lateral fluoroscopy view with angulated curette in the vertebral body for lesion fragmentation. (**e**), lateral fluoroscopy view after introduction of two 10 G cannulas into the fragmented lesion for tumor flush and aspiration. (**f**), aspirated tumor soft tissue, histologically compatible with renal cell cancer metastasis. (**g**–**i**), lateral and anteroposterior fluoroscopy views with stent-screw assisted internal fixation (SAIF) and cement augmentation. (**j**–**l**), sagittal, coronal, and axial CT after SAIF.

Chapter 9

A Multicenter Prospective Randomized Controlled Non-Inferiority Trial on the Efficacy and Safety of Minimally Invasive SAIF Vertebral Reconstruction Technique versus Spinal Fixation in Unstable Osteoporotic Vertebral Compression Fractures

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Abstract

Introduction

Osteoporotic vertebral fractures (OVF) represent a significant cause of morbidity, mortality, decreased level of function and quality of life. Stable fractures with controllable pain can be managed conservatively or with minimally-invasive techniques of vertebral augmentation (VA) in case of persistent pain. At the other end of the spectrum, the most severe OVFs are unstable and can lead to further collapse, progressive kyphosis and neurological injury. Regarding these unstable fractures, the standard vertebral augmentation techniques are generally considered an under-treatment and instead surgical stabilization is frequently necessary to restore the physiological loading capacity of the spine allowing a fast and painless mobilization. Unfortunately, the elderly, osteoporotic patient population poses serious challenges to spinal surgery, due to tissue frailty and frequent comorbidities.

A novel minimally-invasive interventional technique, called Stent-screw Assisted Internal Fixation (SAIF), reconstructs, stabilizes and restores axial load capability of the vertebral body, without a multi-level rigid construct and could represent a less invasive alternative to surgical stabilization in the treatment of unstable OVF.

Methods and analysis

This is a multicenter prospective randomized controlled parallel-group non-inferiority trial to evaluate the effectiveness and safety of the SAIF intervention in comparison with multilevel surgical stabilization in participants with unstable OVFs.

At least 140 patients will be randomized with 1:1 allocation.

The primary objective is to determine whether the effect of SAIF intervention on improvement in quality of life is not inferior to multilevel traditional surgical stabilization at one year follow-up. The principal secondary objective is to evaluate whether the effect of the SAIF intervention on the radiological outcome is not inferior to multilevel traditional surgical stabilization. Other secondary objectives are to compare both treatments in terms of length of operation, blood loss, days of hospitalization postoperatively, pain, the intake of analgesics, disability, and cost-effectiveness.

Ethics and dissemination

Ethics approval was obtained from the Ethics Committee of the Canton Ticino, Switzerland. All patients that agree to participate will be asked to sign an informed consent form. Results will be disseminated through international publications in peer-reviewed journals, in addition to international conference presentations.

Article summary

Strengths and limitations of this study

- This is the first multicenter prospective randomized controlled study comparing a novel interventional minimally invasive procedure called SAIF to standard surgical treatment of unstable osteoporotic vertebral fractures
- The study aims to assess non-inferiority of SAIF compared to surgical fixation in terms of specific quality of life metrics and in terms of radiological outcomes as vertebral height restoration and kyphotic correction in patients suffering from unstable osteoporotic vertebral fractures
- The study can provide high-level evidence for a less invasive method to treat unstable osteoporotic fractures than current care (i.e. surgical fixation), which might be a significant advantage in an elderly and frail population
- The study might face difficulty in recruiting patients due to randomization between two treatments with different invasiveness profiles
- The surgical control treatment does not have a standardized technique and is left to the operator’s choice because there is no clear consensus on the surgical technique to be considered gold standard

Introduction

Background and rationale

Osteoporosis is an increasing health problem worldwide with an enormous economic burden for society.[1–5] Osteoporotic vertebral fractures (OVF) represent a significant cause of morbidity, mortality, decreased level of function and quality of life.[6–12] Stable fractures with controllable pain can be managed conservatively, and only those that remain painful despite conservative treatment can be treated with minimally-invasive measures of vertebral augmentation (VA).[6,13] At the other end of the spectrum, the most severe OVFs are unstable, and can lead to further collapse, progressive kyphosis and neurological injury.[14,15]

Standard vertebral augmentation techniques are generally considered an under-treatment of these unstable fractures, and surgical stabilization, with various techniques, is considered necessary to restore the physiological loading capacity of the spine, and allow fast and painless mobilization.[16–18] Unfortunately, the elderly, osteoporotic patient population poses serious challenges to spinal surgery, due to tissue frailty and frequent comorbidities. More specifically, all the surgical stabilization techniques include rigid posterior fixation of multiple spinal segments, but the reduced bone mechanical properties of osteoporotic patients can lead to hardware implant failure, new fractures, complications, and need of re-intervention.[19–21] In addition, treatment and reinforcement of the anterior spinal column, which is necessary to enhance posterior stabilization, requires a more invasive surgical approach, which carries a significant rate of complications and prolonged recovery time in this elderly population.[22]

A novel minimally-invasive interventional technique, called Stent-screw Assisted Internal Fixation (SAIF), reconstructs, stabilizes and restores axial load capability of the vertebral body, including anterior and middle column, without a multi-level rigid construct.[23] SAIF has been tested in simulations with finite elements analysis when applied to severe neoplastic and osteoporotic fractures, showing favorable biomechanical results, even in comparison with surgical stabilization models.[24,25] Furthermore, the first case series have been recently published, demonstrating it to be a safe and effective treatment in severe osteoporotic and neoplastic fractures.[26,27] There is, however, a need to compare this new promising technique with the traditional surgical approach in a randomized, controlled, multicenter study.

SAIF could represent a less invasive alternative to surgical stabilization in the treatment of unstable OVF, with at least equal quality of life outcomes and possibly reducing

peri-procedural and long-term complications, and length of hospital stay. If successful, this study has the potential to change the way unstable OVFs are treated.

Objectives

The purpose of this study is to evaluate effectiveness and safety of the SAIF intervention in comparison with multilevel surgical stabilization in participants with unstable OVFs. The primary objective is to determine whether the effect of SAIF intervention on improvement in quality of life is not inferior to multilevel traditional surgical stabilization at one year follow-up. The principal secondary objective is to evaluate whether the effect of the SAIF intervention on the radiological outcome is not inferior to multilevel traditional surgical stabilization. Other secondary objectives are to compare both treatments in terms of length of operation, blood loss, days of hospitalization postoperatively, pain, the intake of analgesics, disability, and cost-effectiveness. Additionally, the study aims to assess short and long-term safety of the SAIF intervention in patients with OVFs.

Trial design

This is a multicenter prospective randomized controlled parallel-group non-inferiority trial, with 1:1 allocation, comparing quality of life and radiological outcomes at 12 months follow-up between two cohorts of patients with unstable OVFs, one that receives the SAIF intervention and one that receives spinal fixation with cement augmented pedicle screws bridging the fractured vertebra, with or without (percutaneous) cement augmentation of the fractured vertebra, with or without reconstruction of the anterior column via anterior or lateral approach.

Simultaneously, we will pursue an observational study in which we will include patients that fulfill the inclusion criteria but are not fit for major invasive surgery yet can undergo the less invasive SAIF intervention. The observational cohort is not part of the randomized control trial, but outcomes will be assessed during one year of follow-up, in order to assess if the SAIF intervention can offer an effective treatment to a wider population which cannot be treated by surgery.

Figure 1 provides a flow diagram of study design, timing of pre- and postoperative sessions and follow-up evaluations.

Methods and analysis

Participants

This protocol has been written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist [28] The study will be conducted in European public health system hospitals.

Participants fulfilling the following inclusion criteria are eligible for the study:

- patients aged 50 years or older
- one to two unstable OVFs*, as assessed on CT scan, type OF 3-5**, located between T2 and L5, of age <3 months or with persistent edema on STIR, or with unhealed pseudoarthrosis
- patients reporting pain upon mobilization
- a diagnosis of osteoporosis, based on a DEXA T-score ≤ -2.5, or on a spontaneous thoracolumbar vertebral fracture or a vertebral fracture caused by minor trauma
- able to read and speak the official language of the region of the site
- able to provide informed consent and have signed the informed subject consent form

**additional OVF without unstable features (OF 1-2) allowed*

*** OF-Classification*[17]

The presence of any one of the following criteria will lead to exclusion of the participant:

- compressive neurologic symptoms such as myelopathy or radiculopathy with motor deficit
- acute infection
- spinal malignancy
- comorbid severe psychiatric conditions
- known or suspected non-compliance, drug or alcohol abuse
- known hypersensitivity or allergy to the investigational product
- inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant

Interventions

The SAIF intervention

Under general anesthesia or conscious sedation, under fluoroscopic guidance, vertebral body stents (VBS) are positioned via trans-pedicular access bilaterally in the vertebral body.[15] The stents are expanded by balloon inflation with a manual hydraulic pump, using saline or contrast dye, trying to obtain fracture reduction and height restoration. The balloons are deflated and removed, while the expanded stents remain in place. At this point the trocars are removed leaving a k-wire (1.4x350 mm, blunt tip) in place. The tract is not dilated. Over the k-wire, through the same 6-8 mm skin stab incision, a low-profile manual screw-driver is used to place percutaneous transpedicular fenestrated cannulated screw of desired length (34-55 mm) and caliber (5 or 6 mm), as planned on the basis of the pre-procedure CT axial images. The screw is inserted into the lumen of the stent, until the bulbous head reaches the dorsal cortex of the posterior elements. Via a k-wire exchange a cannula is inserted in the fenestrated screw to inject polymethyl methacrylate (PMMA) cement through the screws into the VBS. PMMA injection is monitored with real time fluoroscopy in lateral view with intermittent antero-posterior checks. Cement injection is halted if extravertebral leaks occur or if cement approaches the posterior wall. When cement injection is deemed complete the injection cannula is retracted and the screw left in place. At operator's discretion simple vertebral augmentation can be performed via a unipedicular approach at adjacent levels with prophylactic intent or in case of less severe fractures (OF 2) thought to be symptomatic, at adjacent or distant levels. The patients are allowed to stand and walk as early as three hours after the procedure and, if clinically conditions allow, may be discharged the same day.

Control Intervention

Spinal fixation with cement augmented pedicle screws bridging the fractured vertebra, with or without (percutaneous) cement augmentation of the fractured vertebra, with or without reconstruction of the anterior column via anterior or lateral approach.

In case of an open posterior procedure a posterior median incision is made and the spinous process and laminae of the affected spinal segment exposed by retraction of the spinal muscles. Fenestrated pedicle screws (minimum 8 screws) are inserted transpedicularly into one or more vertebrae above and below the fractured vertebra. In case of percutaneous fixation,

the screws are inserted under fluoroscopy or under 3D navigation by a stab incision through the skin and subcutaneous tissue. Because of osteoporosis with decreased bone strength, PMMA cement is injected through the screws for better fixation. When deemed necessary a balloon kyphoplasty or a simple cement augmentation of the fractured vertebra can be performed. Then the screw heads are connected to rods in order to provide primary stability of the segment involved. In case of adjacent fractures, a cement augmentation is allowed, based on surgeon's choice. When deemed necessary, a second operation via an anterior approach of the spine (either thoracotomy or lumbotomy) can be performed to remove the fractured vertebral body and replace it by a metal vertebral cage for extra stabilization of the anterior column of the spine.

Outcome measures

The primary endpoint will be the change in the Quality of Life questionnaire of the European Foundation of Osteoporosis (QUALEFFO) score at 12 months from baseline. The Working Party of the European Foundation for Osteoporosis has developed this questionnaire for patients with vertebral fractures and it has good face and content validity in assessing quality of life in osteoporotic patients.[29] The questionnaire covers the domains pain, physical function, social function, general health perception and mental function. QUALEFFO is repeatable, coherent and discriminates well between patients with vertebral fractures and control subjects.[29]

The QUALEFFO-41 is based on 41 questions and is calculated as the sum of all answers, which are then linearly transformed on the scale 0-100. A high score indicates a poor quality of life. The anchors vary between domains as well as between items within a domain. An example of an anchor for the domain pain is "no back pain" to "unbearable" (5 point response scale). Another example of the response scale for the domain activities of daily living is "no difficulty" to "impossible without help" (5 point response scale). The QUALEFFO score will be assessed at baseline, 1, 3, 6, and 12 months follow-up.

The principle secondary objective of this study is to evaluate whether the effect of the SAIF intervention on the radiological outcome is not inferior to surgical stabilization in participants with unstable osteoporotic vertebral fractures (OVFs). We choose this outcome as a principle secondary objective as for the inclusion of the patients in the SAIF study, the instability of the fracture is the main indication for surgical stabilization.

The radiological outcome will be based on:

- restoration of angular kyphosis at index level (local kyphotic angle LKA and vertebral kyphotic angle VKA) comparing pre-operative with postoperative standing radiographs (local) and full spine standing radiographs at follow-up
    - This will be quantified as kyphosis correction at the index level in degrees. The non-inferiority margin is determined at 4 degrees
- vertebral body height restoration (anterior VB, mid VB, post VB, or ratio of these) comparing pre- and post-operative computed tomography (CT) scan
- global kyphosis/lordosis and balance (Sagittal Vertical Axis, SVA) assessed with full spine standing radiographs

Other secondary objectives are to compare both treatments in terms of:

- length of operation (minutes from skin insertion to skin closure)
- blood loss measured by:
    - intraoperative blood loss (ml) (aspirated blood collected in the suction bottle)
    - number of units of transfusion during hospitalization
    - proportion of patients receiving blood transfusion from the beginning of the intervention to discharge
- days of hospitalization postoperatively
    - we will record hospitalized rehabilitation separately
    - if outpatient (day surgery), the days of hospitalization are zero
- back pain measured with the numeric rating score (NRS): 11-point NRS ranging from 0 (no pain at all) to 10 (the worst imaginable pain). A score of zero (0) will indicate that the patient is pain free, while a score of ten (10) will indicate that they are experiencing the worst pain imaginable.
    - back pain will be assessed at baseline and at discharge, and at 1, 3, 6 and 12 months follow up in comparison to baseline
- the intake of analgesics
    - the Medication Quantification Scale (MQS): The MQS is an instrument to quantify medication regimen use in pain populations. The score is calculated for each medication by taking a consensus-based detriment weight for a given pharmacologic

    - class and multiplying it by a score for dosage. The calculated values for each medication are then summed for a total MQS score. The score can provide a useful point measure of medication usage for any pain medication regimen.[30,31]
    - intake will be assessed at baseline and at 1, 3, 6 and 12 months follow up in comparison to baseline
- disability: Roland-Morris disability questionnaire (RMDQ)
    - 24 items that assess functional status over the past 24 hours in patients with back pain
    - a change in 2–3 points on the RDQ is considered the minimum clinically important change[32]
    - will be assessed at 1, 3, 6 and 12 months follow up.
- Cost-effectiveness
    - Parallel to the trial an economic evaluation, with a time horizon of one year, will be performed to assess the cost-effectiveness of the SAIF intervention compared to the spinal fixation, expressed in an incremental cost effectiveness ratio (ICER): the cost per quality-adjusted life year (QALY) gained. The QALY takes into account the quantity (longevity/mortality) and the health-related quality of life (HRQoL) benefits of the treatments. The EuroQol 5 dimensions 5 levels (EQ-5D-5L) is used to assess HRQoL[33] and is assessed at baseline 3, 6 and 12 months.
    - Individual-level resource use in- and outside the hospital is collected using the hospital information system and patient-reported cost surveys assessed at baseline, 3, 6 and 12 months.

Sample size

The sample size has been calculated to test the hypothesis that SAIF is not inferior to surgical stabilization in improving quality of life in participants with unstable OVFs at one year follow-up. The expected standard deviation in QUALEFFO scores is 16, as was observed in the recently published VAPOUR study.[34] We set the non-inferiority margin at 8, meaning that we would consider SAIF to be inferior in case we would not be able to exclude a difference between groups of over 8 points in favor of surgical stabilization. We need to include at least 63 patients per group, or 126 on total, to be able to have sufficient statistical power (i.e., 80%) to

show that SAIF is not inferior to surgical stabilization by more than 8 points using a 95% confidence interval. To allow for up to 10% loss to follow-up, we will include a total of 140 patients. The non-inferiority margin for the principal secondary outcome, kyphosis correction, is 4 degrees. With the abovementioned sample size, we would have over 90% power to exclude that margin, given a standard deviation of 6.6 degrees. The latter has been estimated using preliminary data (not yet published).
We expect to be able to finalize inclusion within 60 months.

Randomization

A computer-generated randomization will be used to allocate the participant to either the SAIF arm or the surgical stabilization arm with a 1:1 allocation. We will use concealed block randomization stratified by center, with block sizes of 6. The randomization is performed by the Principal Investigator or a Co-investigator per site, who is not blinded for group assignment.

Data collection and management

All study related data will be collected on a case report form by the research team and will be entered in a research electronic data capture (REDCap) database.[35] After data-entry is completed and data have been checked and corrected as appropriate, the anonymized data from the REDCap database will be imported automatically in R, version 3.5.1, for statistical analysis. Data access is limited to the investigators of this trial for data-entry and to the designated authorities for data monitoring purposes. The trial data and analysis outputs will be archived for 15 years at the study site.

Statistical methods

Baseline characteristics of all included patients will be reported as mean and standard deviation (SD) or median and first and third quartile for continuous variables, depending on their distribution, and as count and percentage for categorical variables. In case of over 10% missing outcome data, we will use multiple imputation with fully conditional specification to impute incomplete patient records.
The analyses of the primary outcome and principle secondary outcome will be performed per protocol, as suggested for testing non-inferiority hypotheses. Additional intention

to treat results will be presented also. All other analyses will be performed according to the intention to treat principle.
The non-inferiority hypotheses of the primary outcome and principle secondary outcome will be tested by computing the 95% confidence interval (CI) of the difference between groups at one year and comparing the upper bound of the 95% CI to their respective non-inferiority margins (i.e., 8 points on the QUALEFFO, 4 degrees kyphosis correction). In case the confidence bound does not cross the non-inferiority margin, non-inferiority may be concluded.

Intra- and perioperative blood loss, the length of operation, postoperative hemoglobin decline, disability (RMDQ), medication use (MQS), and intensity of back pain will be compared between groups at one year follow up using the independent-samples t-test. The number of postoperative hospitalization days will be compared using the independent-samples t-test or Poisson regression, depending on the nature of the distribution. In addition to cross-sectional analyses of continuous outcomes at the primary endpoint at one year follow-up, we will use (generalized) linear mixed-effects regression to model change over the course of follow-up time and the interaction between group and time. The proportion of patients receiving blood transfusion from the beginning of the intervention to discharge will be compared between groups using Pearson's chi-square test or Fisher's exact test.

The cost-effectiveness analysis will be conducted with an intention-to-treat approach and cost-effectiveness is expressed using the ICER.[36,37] Non-parametric bootstrapping with 5000 replicates of the joint distribution of costs and QALYs will estimate the probability of the SAIF intervention being cost-effective for various willingness to pay thresholds for the ICER, presented in a cost-effectiveness acceptability curve (CEAC). Several one-way sensitivity analyses will be performed to assess the robustness of results. To assess safety, the percentage of patients that experience different AE's and SAE's, need additional spinal surgery, report any complication, and report a complication scoring 3 or 4 on the Clavien-Dindo classification, will be described including 95% binomial CI and will be compared between groups using Pearson's chi-square test or Fisher's exact test.

Monitoring

A certified clinical monitor will monitor the research project. The monitor will review the data quality and will ensure that study activities are carried out in accordance with good clinical practice, the study protocol, and applicable regulatory requirements.

Patient involvement

Patients and members of the public were involved at several stages of the trial, including the design, management, and conduct of the trial. We received input and endorsement from the regional subspecialty medical association caring for patients with osteoporosis (Associazione dei Reumatologi della Svizzera Italiana) and from the regional patients' association (Lega Ticinese contro il Reumatismo). We carefully assessed the burden of the trial interventions on patients. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Limitations of the study

The limitations are those inherent to a prospective, randomized, non-blinded controlled study, including difficulty in recruiting patients due to potential patient refusal due to significantly different invasiveness profile of the two treatments.

An additional aspect that could be regarded as a limitation is the non-standardized control surgical treatment, whose technique is left to the operator's choice, since there is no consensus on the standard surgical treatment of the fractures under study.

Ethics and dissemination

Research ethics approval and consent to participate

The Research Ethics Committee of the Canton Ticino, Switzerland has approved this trial. Patients that agree to participate will sign an informed consent form provided by an independent observer. Any amendment to the protocol must as well be approved by this institution.

Confidentiality

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject identification code numbers will

further ensure subject confidentiality. Direct access to source documents will be permitted for purposes of data review by authorized personnel involved in the trial and inspections. Patients' identity will not be disclosed to the person in charge of the statistical analysis and will not appear in any publication or public presentation of the study results. Coded data will be transferred to The Netherlands for statistical analysis and this EU Country has data protection regulations equivalent to the Swiss ones. Results of this trial will be published in a peer reviewed journal and communicated to a wider scientific audience at scientific meetings, and professional formation events.

Declaration of interest

This study doesn't concern any conflict of interest.

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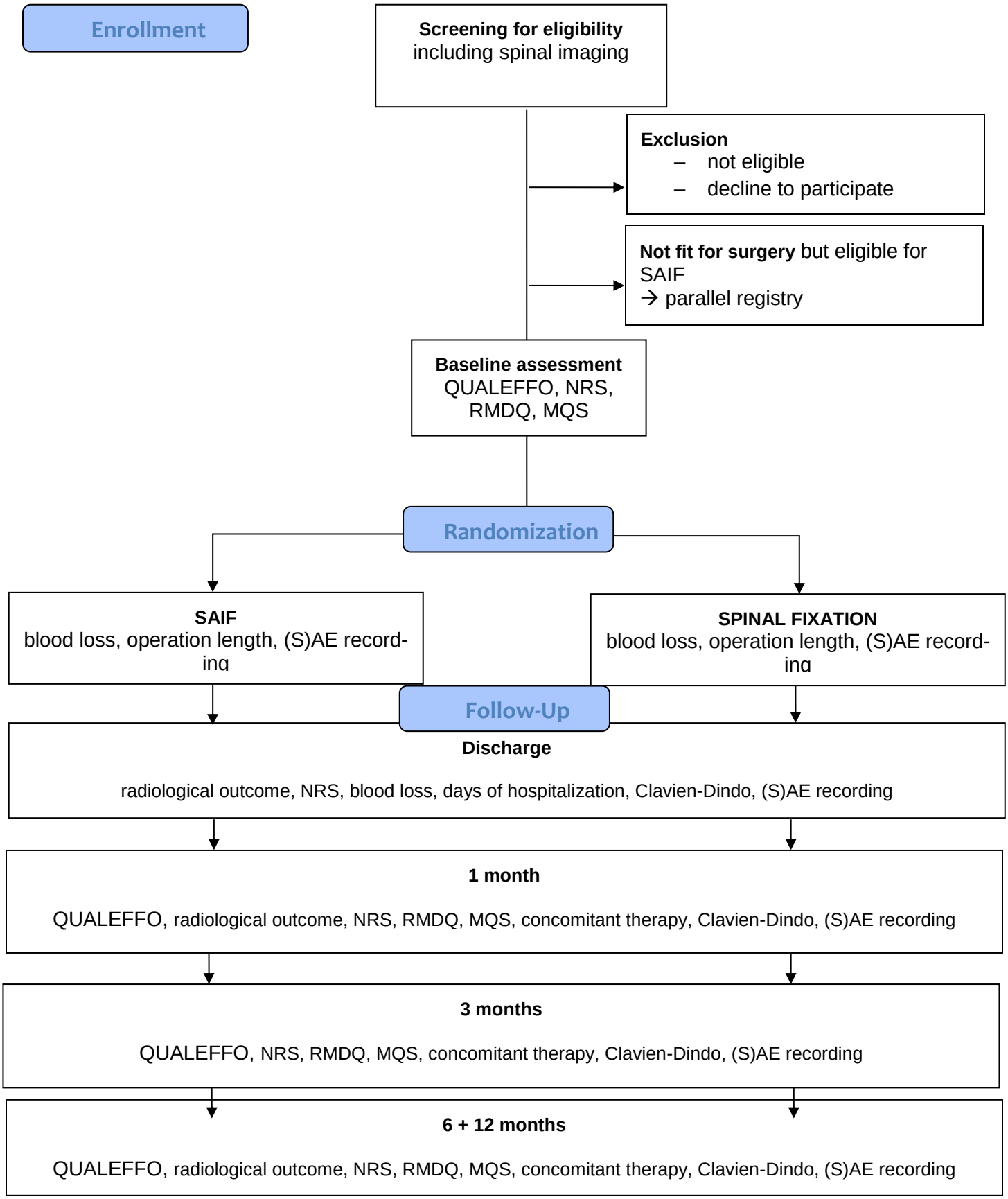
Figure 1: flow diagram of the study design, timing of pre- and post-operative sessions and follow-up evaluations.



Chapter 10

Summary and Discussion

Vertebral fractures, caused by underlying osteoporosis or cancer, present across a wide range of severity, with stable or unstable features, and relative preservation or loss of vertebral body osseous integrity. [1–3]

These fractures pose the clinical problems of pain, bed bounding or reduced function, spinal deformity, and neurological compromise. Their treatment varies from conservative non-invasive approaches, to minimally invasive cement vertebral augmentation techniques, and to surgical interventions for anterior and posterior column stabilization. [4] In most severe fractures vertebral augmentation might not be feasible and is generally regarded as an undertreatment, and surgical stabilization is then advocated. [5] Nevertheless, surgery is a rather invasive therapeutic measure, that carries significant morbidity, especially in fragile patients, such as elderly or metastatic cancer patients. A therapeutic alternative filling the gap between standard vertebral augmentation techniques and surgical stabilization, with a less invasive profile, yet able to offer effective stabilization and pain palliation, with a favorable safety profile, would be desirable.

The overall research aim of this thesis was to assess whether a recently developed minimally invasive image-guided interventional technique, based on a reinforced or “armed” vertebral augmentation technique, called stent-screw assisted internal fixation (SAIF), could fill that gap and represent a viable therapeutic option in severe neoplastic and osteoporotic vertebral fractures without neurological impairment.

In **chapter 2**, **research question 1**, whether vertebral body stenting (VBS) could be used to reconstruct the anterior column in extreme osteolysis (EO) of the vertebral body, was addressed.

The study included 41 vertebrae (in 29 patients) with EO, featuring high degree of collapse in 22/41 and epidural mass in 21/41. VBS augmentation was performed as a stand-alone procedure in 26/29 patients (36 vertebral levels), or it was added to posterior surgical fixation, with decompressive laminectomy when deemed necessary, in the remaining cases, thereby avoiding corpectomy and grafting. The study results showed excellent feasibility, with VBS-augmentation being performed in all cases; despite some degree of cement leakage was present in 34% of treated levels, no clinically relevant intra-procedural complications occurred. Vertebral reconstruction was rated by a neuroradiologist and a neurosurgeon as satisfactory (grade 3-4 good-excellent in 90% of cases). These results were maintained throughout a mean follow-up of 15 months, and only one patient underwent new surgical stabilization due to an

adjacent vertebral fracture. The VBS seemed particularly appropriate in the treatment of these EO lesions, in fact, with their large support-surface, filled with PMMA, VBS could provide primary reinforcement of the anterior column, and their tight mesh may help achieve cement containment. This approach has then been replicated, in its version combined with surgical decompression and posterior stabilization, by Mohammed et al., in their study published in 2020, on a series of 14 patients with neoplastic spinal cord compression, thereby providing anterior column support and avoiding a more invasive corpectomy. [6] Another series, recently published, described the successful results of VBS augmentation in 78 thoraco-lumbar compression fractures of different etiologies. [7]

Nevertheless, in most severe EO, given the fact that PMMA-bone cement has no adhesive properties, in lack of containment by osseous cortical margins, the VBS-cement complex might dislodge under axial load. In fact, in one case, a ventral shift of the VBS-cement complex was noted at radiological follow-up in our study. This particular case induced us to consider a technical solution to this limitation. Stability of the construct could be further enhanced by an anchor from the VBS-cement complex in the vertebral body to the posterior elements, more rarely involved in lytic destruction than the vertebral body.

In **chapter 3**, **research question 2**, whether the VBS-cement complex could be integrated by transpedicular screws, and which applications could be addressed by this new technique, called SAIF, was addressed by a technical explanation of the procedural steps of SAIF, its rationale, and its potential clinical applications.

The issue of anchoring the cement after vertebroplasty or kyphoplasty had already been investigated in the past in patients with fractures with higher risk of cement displacement, such as those characterized by a high degree of fragmentation or avascular necrosis of the vertebral body. [8–10] However, in the absence of a definitive solution, it was suggested that a better interdigitation of cement in the trabecular bone could help, but this may be unpredictable or difficult to achieve. [11]

The pediculoplasty, which is injection of cement in the pedicles, along the needle tract, was first described in 2002 [12] as a possible solution for that purpose. However, it is somehow limited, because the PMMA bone cement is highly resistant to axial load but poorly resistant to bending forces, as those acting on the pedicles; moreover, the pediculoplasty is a technique with higher risk of cement leakage in the central canal and neuroforamina, with the risk of injury to

the adjacent nervous structures. To obviate these limitations Amoretti et al. in 2014, [13] and Pusceddu et al. in 2017 [14] have proposed a vertebroplasty technique performed through a previously inserted pedicular fenestrated screw. This technique has been presented again, in combination with balloon kyphoplasty this time, by Yonezawa et al. in 2021. [15]

Inspired by surgical techniques, the optimal anchorage to the posterior elements can be provided by cannulated surgical screws in order to obtain the highest resistance to loading and bending forces, and at the same time the safest technique due to absence of risk of cement leakage. Nevertheless, this new technique does not address the issue of vertebral body height restoration, mechanical support and cement containment faced by a standard vertebroplasty or balloon kyphoplasty in challenging fractures.

Chapter 3 describes a new technique, combining VBS kyphoplasty and pedicular screw fixation, named Stent-screw-Assisted Internal Fixation – SAIF. The VBS, besides its features that allow anterior column reconstruction, represents an ideal device for fixation to posterior elements, as it may accommodate the screw to reach the anterior third of the vertebral body within its own lumen; the other devices developed for implant-based kyphoplasty obstruct instead the central portion of the vertebral body compelling the use of shorter, and consequentially less stable and effective, pedicular screws.

From a procedural point of view, the SAIF technique presents additional advantages beyond the anchorage of the stents to the posterior elements, namely the treatment of pedicular fractures and improved support for the middle column, and is useful in multiple clinical scenarios. Generally speaking, it might be useful for comminuted fractures, fractures with loss of cortical bone integrity and for fractures with damage of the middle column and/or posterior wall involvement. For neoplastic lesions, the use of SAIF might be considered to augment extensive osteolytic lesions with dehiscent cortical boundaries (**Tomita** extra-compartmental lesions type 4–6) [16] that are fractured or at risk of impending collapse, but it could be also used to perform vertebral augmentation in severe osteoporotic fractures with crush deformity, advanced collapse (**Genant** grade 3), [17] high degree of fragmentation (**McCormack** grade 2 and 3) [18] and large osteonecrotic clefts.

The whole construct of stents, screws and cement is fully contained inside the vertebra, acting as an internal vertebral body prosthesis fixed to the neural arch and, unlike surgical

corpectomy and posterior instrumentation, do not require fixation of adjacent vertebral levels, thereby preserving the role of adjacent disc spaces and of the spinal functional units. To this regard SAIF can be regarded as a non-fusion vertebral reconstruction technique, that obtains fixation within the vertebra itself, therefore called internal fixation, as opposed to the bridging fixation of the adjacent vertebrae operated by standard surgical stabilization. SAIF can also be combined with posterior surgical stabilization, thereby at least replacing a more invasive corpectomy. Its limited invasiveness compared to surgical stabilization, makes it an interesting option, especially for fragile patients.

In **Chapter 4**, **research question 3**, whether SAIF has a biomechanical rationale in the stabilization of extreme osteolytic lesions of the vertebral body, and how SAIF compares mechanically to surgical posterior fixation, was addressed by a biomechanical simulation, on a finite element analysis (FEM) of a lytic vertebra model.

The effect of SAIF on the lytic vertebra model was analyzed biomechanically in terms of restoration of the load-bearing capacity of the vertebral body (i.e.: axial stiffness) and in terms of reduction of re-fracture risk (i.e.: principal strains).

The study revealed that SAIF effectively restored the load-bearing capability of the vertebral body to values comparable of an intact spine, while significantly reducing the strains on the superior endplate and the posterior wall (beyond 90%), and on the anterior wall (about 40%) compared with an untreated vertebra. Of even greater interest, the surgical fixation was significantly less effective than SAIF in reducing the strains, both on anterior and posterior walls, potentially indicating a greater fracture risk.

However, a further scenario which was analyzed in our model was the supplementation of the SAIF technique with posterior fixation, to understand whether the techniques could work synergistically. This model showed only a marginal decrease of the strains on the bony structures (about 5% on the superior endplate and posterior wall, 16% on the anterior wall), with such a relatively small advantage that it should be weighed against the greater invasiveness of a surgical posterior fixation technique and a potential interference with initiation of radiation treatment.

Neoplastic fractures, especially those characterized by EO, pose several treatment challenges. These fractures are unstable, cause pain and pose a risk of neurological compromise. [5,19] Moreover, radiation therapy, used to obtain local disease control in spine metastases, carries an additional significant risk of transient weakening of the bone and increased risk of collapse. Such complex fractures have been rarely managed by minimally invasive interventional procedures, as the primary goal is to treat the potential instability of the spine, a process that is thought to require surgical stabilization. Standard augmentation techniques are usually considered either unsafe, contraindicated, impossible or at least an undertreatment in these fractures [20,21].

The SAIF technique aims at treating both pain and biomechanical instability, with posterior surgical fixation being the standard treatment for comparison . In this clinical scenario the FEM study attributed a theoretical biomechanical rationale to SAIF in the stabilization of extreme osteolytic lesions, as an alternative treatment to surgical fixation.

In **chapter 5**, **research question 4**, whether SAIF is clinically safe and efficient to treat extreme osteolytic lesions of the vertebral body, is addressed by a study reporting on a clinical series of patients affected by neoplastic EO of a vertebra, fractured or at risk of fracture, deemed unstable or potentially unstable according to the Spinal Instability Neoplastic Score (**SINS**), [22] treated with SAIF.

In 36 SAIF procedures performed in 35 patients, the SAIF technique proved to be feasible and safe for vertebral body reconstruction and stabilization, confirming the biomechanical data on finite-element analysis (FEM) models, with satisfactory clinical and radiological results. Cement leakage was in fact observed in 12/36 cases, but only one was symptomatic and required surgical decompression, with no permanent sequelae. No other intra-procedural complications occurred, and despite the fact that 23/36 of the treated levels showed an epidural mass on pre-procedure MRI, no post-procedure worsening of neurological status was observed. The vertebral body reconstruction, judged independently by an interventional neuroradiologist and a neurosurgeon, was deemed good/excellent in 94.5% of cases by the two raters, with high interrater agreement. At follow-up the results were stable in all cases but one, that developed osteomyelitis, mobilization of the SAIF construct, and required surgical intervention.

The main focus of this study was on mechanical stability, through assessment of vertebral body reconstruction and spinal stability at follow-up. Although most patients with EO report some form of mechanical pain, pain palliation was not a primary endpoint of this study, as multiple studies, including a randomized controlled trial, have demonstrated meaningful pain improvement with cement augmentation in neoplastic vertebral fractures. [10] Certainly, SAIF has also a role in pain palliation, as a form of vertebral augmentation, when necessary.

SAIF procedures were performed as a stand-alone intervention and in conjunction with posterior surgical fixation, with or without laminectomy, showing the compatibility of SAIF with posterior surgical open or percutaneous stabilization techniques.

Altogether with the low invasiveness profile, SAIF appeared particularly advantageous in patients with spinal metastases, since it could be performed in day-surgery or a very short hospitalization setting. Patients receiving SAIF can in fact return promptly to daily activities, and there is no interference with chemotherapy and radiation treatment regimen. It should be underscored that these oncological patients require individualized clinical decisions for the planning of comprehensive treatment strategies. In our clinical setting this effort was undertaken by a multidisciplinary spine tumor board composed of medical and radiation oncologists, spine surgeons, neurologists and neuroradiologists with extensive experience in the treatment of oncological disease, who defined indications for and the timing of medical, radiation or invasive treatments. [23–27]

In **chapter 6**, **research question 5**, whether there is a biomechanical rationale to explain the re-fractures of the middle column after cement augmentation in osteoporotic vertebrae, is addressed by a FEM study on an osteoporotic spine model. The “bare area” concept, the lack of augmentation of the middle column after standard vertebral augmentation, as vertebroplasty and balloon kyphoplasty, is investigated biomechanically, and SAIF is compared to standard vertebral augmentation in its efficacy to stabilize the middle column.

The conventional augmentation model was effective in reducing strain both in the anterior and to a lesser extent in the middle column. The SAIF technique, however, proved superior to conventional augmentation techniques improving the results by a significant margin

and further reducing the strains both at the anterior and middle column. The improvements where particularly relevant at the superior endplate of the anterior column and at the posterior wall (-68% and -64% in upper body flexion compared to vertebral augmentation).

The distribution of the loads was also remarkably improved by promoting a higher load transfer on the anterior column compared to simple augmentation and to the untreated osteoporotic condition, while the middle column resulted to be relatively unloaded.

Standard augmentation techniques, in fact, aim at anterior column reinforcement. [28–32] The fracture of the middle column is indeed frequently cited as a contraindication to traditional vertebroplasty and kyphoplasty, because the concomitant fracture of the anterior and middle column, as in burst fractures, is considered a sign of instability. These fractures are frequently characterized by collapse and retropulsion of the posterior wall and if treated with anterior column-only cement augmentation, might undergo catastrophic splitting between the augmented anterior portion of the vertebral body and the middle column. [20,33]

Moreover, the vertebral body accesses generally used for any kind of vertebral augmentation are strongly limited in approaching a triangular-shaped area located immediately ventral to the posterior wall, and that could be named “bare area”. [34] This area is normally inaccessible to needles, and cement distribution in this area is difficult, unpredictable, or undesired because of the higher risk of leakage in the contiguous epidural space. Acting as a reinforcement of the posterior third of the vertebral body, the screws utilized in the SAIF technique were proven effective in stabilizing and protecting the middle column, despite the biomechanical simulation of the “bare area”. This biomechanical advantage of SAIF technique, compared to conventional augmentation in restoring the load bearing capacity of the anterior and middle spinal columns might lead to favor SAIF in osteoporotic fractures with crush deformity, advanced body collapse, pediculo-somatic junction fracture and large osteonecrotic clefts, since many of these fractures present with middle column involvement.

In **chapter 7**, **research question 6**, whether SAIF is clinically safe and efficient to treat severe osteoporotic fractures of the vertebral body, is addressed via a study on a series of patients affected by severe osteoporotic fractures treated with SAIF.

Eighty severe thoraco-lumbar osteoporotic vertebral compression fractures, with the majority (79%) at the thoracolumbar junction (T10–L2) were treated with SAIF. There were no intra-procedural complications and no symptomatic cement leakages. One patient experienced un-explained transient self-resolving hypoesthesia and mild motor deficits in the lower limbs. The vertebral reconstruction score was good or excellent in 98.8% of cases, with perfect inter-rater agreement. There was a statistically significant difference in VAS pain scores before the pro-cedure versus 1 and 6 months after. The patient's global impression of change (PGIC) scale indicated a very positive patient's subjective global clinical impact.

No cases of stent or screw dislocation were seen until the last available follow-up, highlighting the great reliability of the technique in obtaining a stable and durable vertebral reconstruction. Despite the presumably scarce bone quality in this elderly osteoporotic population, no screw mobilization was noted during follow-up, probably due to the minimal forces acting on the ped-icle screws in the SAIF construct, differently from the pull-out strains acting on screws of a surgical stabilization construct.

After the SAIF procedure, patients were allowed to stand and walk without spinal braces as soon as 3 hours after the procedure and commonly discharged the same day, in a day-surgery setting.

Treatment of severe osteoporotic vertebral fractures with middle column injury should aim at fracture reduction, correction of pathological kyphosis, restoration of axial load-bearing capa-bility with arrest of fracture progression and early mobilization. [21] In many clinics surgical stabi-lization is considered the gold standard, but it is invasive, carries a significant risk of morbidity in the elderly population, and carries a high risk of mechanical failure in patients with poor bone quality. [35] In this clinical scenario SAIF seemed to offer a valid minimally invasive alternative, able to fulfill the treatment requirements.

In **chapters 8a** and **8b**, **research question 7**, whether the frequently associated posterior wall retropulsion might represent a contraindication to the SAIF procedure, was addressed

by two different studies. One study (**8b**) represents a description of a technique to create a true cavity in the vertebral body, in those vertebrae with extreme osteolysis and posterior wall de-hiscence, before performing SAIF. We developed and described

a technique (“Q-VAC”) to create a cavity using intravertebral soft tissue mass fragmentation by means of a mechanical curette before vacuum suction and lavage. Associated to the SAIF technique, Q-VAC might lead to debulking of the centrally located soft-tissue tumor component in the vertebral body, resulting in the creation of a cavity that allows safer expansion of VBS and to a potentially safer and more predictable deposition of larger amount of cement, ultimately reducing the risk of central canal compromise in presence of posterior wall retropulsion or erosion.

The bone marrow “washout” or lavage has been reported in a clinical setting in a series of osteoporotic vertebral compression fractures, potentially reducing the risk of cement leakage and prevent pulmonary embolism, and in a small series of patients treated with multilevel vertebroplasty for multiple myeloma spine lesions. [36] Nevertheless, we found simple aspiration or washout attempts are only able to partially remove the fluid, necrotic, or bloody parts of vertebral neoplastic lesions, as in multiple myeloma, but cannot remove solid vertebral lesions commonly occurring in metastatic breast and lung cancer.

The use of a coaxial curettes has been previously described in case of sclerotic changes after vertebral body fractures to maximize height restoration during balloon kyphoplasty, but it has not been employed to fragment neoplastic intravertebral soft tissue in lytic lesions.

Creation of a cavity prior to cement injection or intravertebral device expansion, such as balloons or VBS, might help increase safety and avoid severe adverse events. Proposed solutions to reduce the cement migration include radiofrequency ablation and cryoablation prior to cement injection, which may result in reduction of tumor mass due to induction of necrosis, and can cause thrombosis of the vertebral and paravertebral veins therefore reducing the PMMA embolization risk. [37–41]

However, the induction of tumor cell necrosis does not correspond to an immediate void creation and their use to obtain an intravertebral cavity remains questionable, as subsequent cement injection would simply push residual tumor cells and necrosis aside. As additional drawbacks, radiofrequency and cryoablation require a safety margin with vital and nervous structures and imply adjunctive time and cost increase.

The other study (**8a**) assessed a series of 53 fractures of mixed etiology, with posterior wall retropulsion, that were treated with an armed kyphoplasty technique (AKP) using vertebral

body fracture internal distraction devices such as VBS and SpineJack®. AKP was able to obtain posterior wall retropulsion correction in traumatic, osteoporotic and neoplastic burst fractures. It was used as a stand-alone minimally invasive procedure in most cases or in combination with a posterior surgical approach, but without the need to perform any direct form of posterior wall retropulsion correction. The SAIF technique was performed in 33/53 levels.

A statistically significant difference between pre- and postoperative posterior wall retropulsion and vertebral body height was found, suggesting the biomechanical effectiveness of the technique, and showed durable results: no re-intervention was required on the target level at the end of the follow-up. Two patients presented transient new neurological symptoms, with spontaneous clinical resolution, and their imaging did not show any sign of worsening of central canal compromise No patients presented onset of new permanent neurological deficits. In two cases worsening of posterior wall retropulsion was noted, which remained uneventful.

Posterior wall retropulsion has been considered a relative contraindication for vertebral augmentation (and in particular for traditional balloon kyphoplasty) because it is unable to clear the canal and might lead to worsening of the neurological condition through epidural cement leakage or further displacement of bony fragments or neoplastic soft tissue epidural component in the central canal. [37] The inflation of balloons during balloon kyphoplasty might in fact potentially worsen a posterior wall retropulsion, while the subsequent deflation effect, [10] with loss of vertebral height restoration, does not guarantee a reliable fracture reduction and kyphosis correction. Even simple injection of cement can exert a mass effect, with displacement of soft tissue tumor mass in the central canal, as demonstrated with post-balloon kyphoplasty CT-myelograms by the study of Lis et al. [42]

Traditionally, open surgery is considered the best treatment to obtain indirect fracture reduction, kyphosis correction, central canal decompression by laminectomy and posterior wall fragment impaction, accomplished by ligamentotaxis of the posterior longitudinal ligament. Nevertheless, stabilization of the anterior column is crucial in burst fractures with severe fragmentation to avoid loss of correction and instrumentation failure, [43] and although surgical anterior instrumentation has proved effective in stabilizing the anterior column, it requires a more invasive approach which could be associated with increased morbidity. Some authors, on the contrary, support a conservative approach in patients without neurological deficits, claiming that spontaneous remodeling and resorption of the posterior wall fragment could eventually

occur. [35,43] The risk of spinal cord compression after vertebral augmentation is higher for fractures caused by extensive lytic lesions with erosion of the posterior wall or epidural tumor spread, either from cement leakage or from further central canal encroachment by the epidural mass**.** [44]

In recent years kyphoplasty with metallic implants like VBS and SpineJack® ("armed kyphoplasty" or "AKP") has been reported as an alternative to balloon kyphoplasty that potentially guarantee better height restoration in compression fractures by avoiding height loss due to deflation effect, and is increasingly used as a stand-alone measure to reconstruct and restore axial-load capability in burst fractures, even with posterior wall retropulsion. A cadaveric study has shown the ability of SpineJack® to reposition a retropulsed posterior wall of a burst fracture model and substantially maintain this gain after cyclic recompression. This ability rests on fracture distraction and kyphosis correction allowing reduction of posterior wall retropulsion through ligamentotaxis. In the same experimental setting posterior instrumentation alone did not maintain central canal clearance. However, the potential of armed kyphoplasty to correct the posterior wall retropulsion in burst fractures had not been investigated in vivo.

In this study the SAIF technique confirmed its potential in being a minimally invasive approach that might represent a balanced compromise between invasive surgical treatment and conservative approach for the treatment of burst fractures even with significant posterior wall deformation and retropulsion. This series gives preliminary indication that posterior wall retropulsion does not seem to be a contraindication to SAIF, which to the opposite exploits the ligamentotaxis to obtain posterior wall retropulsion correction along with vertebral body fracture reduction.

In **chapter 9**, **research question 8**, whether SAIF is non-inferior in terms of clinical efficacy and cost-effectiveness to multilevel posterior spinal fusion in patients with severe unstable osteoporotic fractures, is addressed by a randomized controlled study design. Despite promising results for SAIF in terms of safety, clinical and radiological outcomes as reported in Chapter 2 through Chapter 8, a higher level of evidence, through prospective and controlled data, is necessary to make a change for clinical practice on a larger scale. In fact, the most severe osteoporotic fractures, following the recent classification system and treatment recommendations of the German Society of Orthopedics and Trauma (DGUS), [45,46] represent an almost exclusive surgical indication for a 360° stabilization approach. Such interventions pose a risk of

morbidity in the fragile, elderly population, with high costs, prolonged hospitalizations, and the risk of delayed failures, such as pull out of implants and adjacent fractures, in case of poor bone quality. In addition, due to the fact that these fractures occur frequently in elderly patients, often with co-morbidities, a major surgical intervention might be contraindicated, resulting in patients that are left untreated, often bed-bound, or with progressively worsening kyphosis, risk of falling, pulmonary problems, chronic pain, opiate over-use, and overall increased mortality risk. [47] In case the trial should show non-inferiority of the SAIF procedure, the shorter duration of the SAIF procedure, the negligible blood loss, the shorter hospital stays and prompt return to normal activities, compared to the multilevel surgical option, should also make this procedure more suitable than the traditional multilevel surgical stabilization, even in the elderly population, allowing a safe and efficient treatment in a larger portion of those patients.

The study is designed as a multicenter prospective randomized controlled study, aiming at assessing non-inferiority of SAIF compared to multilevel surgical fixation in terms of QUALEFFO, a specific quality of life metrics in osteoporotic patients, and in terms of radiological vertebral height restoration and kyphotic correction in patients suffering from unstable osteoporotic vertebral fractures. Study follow-up duration will be 12 months. Additionally, complications, blood loss, length of hospital stay, and cost-effectiveness will be measured. The control group, undergoing control surgical stabilization, comprises multilevel posterior fixation, with or without cement screw augmentation, with or without index level augmentation with vertebroplasty of kyphoplasty, with or without index level corpectomy and grafting, based on the treating physician's decision and individualization of approach.

While this multiple technique control group may be regarded as a methodological weakness, it takes in consideration the lack of consensus on the most appropriate surgical technique to treat these fractures, and thus closely adheres to clinical practice. The study might face difficulty in recruiting patients due to randomization between two treatments with different invasiveness profiles; to minimize this risk SAIF procedure will not be offered to eligible patients as a standard procedure outside the trial. The trial aims at enrollment of 140 patients and will be preceded by a 12 months feasibility trial supposed to enroll 20 patients.

Simultaneously, we will pursue an observational study in which we will include patients that fulfill the inclusion criteria but are not eligible as they are considered not fit enough for major invasive surgery, but still can undergo the less invasive SAIF intervention.

The observational cohort is not part of the randomized controlled trial, but outcomes will be assessed during one year of follow-up, in order to assess if the SAIF intervention can offer an effective treatment to a fragile population that cannot be treated by multilevel fixation surgery.

The study protocol has been examined and accepted by the Ethical committee of Canton Ticino (Switzerland).

Conclusions

This thesis investigated a novel minimally invasive percutaneous image-guided technique to treat severe thoraco-lumbar vertebral fractures of neoplastic or osteoporotic nature. This technique, called Stent-screw assisted internal fixation (SAIF) was tested by biomechanical simulations and clinically by assessment of large patient series. The SAIF technique seemed to be able to fill the gap between standard vertebral augmentation, that can be considered an undertreatment in severe fractures, and multilevel spinal fusion techniques with posterior and anterior approaches, that are invasive and carry a high risk of morbidity in fragile patients.

SAIF seems to offer safe, effective, and durable treatment of severe neoplastic and osteoporotic vertebral fractures with no neurological deficit. The technique can be performed in an outpatient day-surgery setting or with a short hospital stay, and when deemed necessary, SAIF can be combined with posterior spinal fusion, thereby avoiding a more invasive anterior approach with corpectomy. In neoplastic patients the SAIF technique does not interfere with chemo- or radiation-therapy regimen. However, more robust, prospective data need to be acquired through a randomized controlled trial to gather high level evidence for clinical efficacy and cost effectiveness of SAIF in order to improve current clinical practice on a larger scale.

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Chapter 11

Valorisation

Impact Paragraph: Valorization of Research

In this chapter, we will translate the findings of this thesis in terms of 'knowledge valorization'. Knowledge valorization of research refers to the process of creating value from knowledge, by making it available for social and or societal utilization.

Spinal disorders are common and have a substantial impact on both patients and society, affecting more than 1.7 billion people worldwide. With aging of our population, the burden of spinal disorders on society, in terms of decreased quality of life and an increase in costs, is expected to further rise.

Low bone mass by osteoporosis affects a steadily growing number of people in the economically developed countries.[1] The number of older adults with osteoporosis is expected to increase by about 30% from 2010 to 2030.[2] Fragility fractures present major medical and socio-economic challenges and it has been estimated that approximately 76,000 new fragility fractures occurred in the Netherlands in 2010, of which 12,000 were vertebral fractures.[3]

New vertebral fragility fractures occur in approximately 500,000 patients per year in Europe. Fragility fractures can be life-changing and bring pain, isolation and dependence. Vertebral fragility fractures can lead to a downward spiral of symptoms and morbidity, from pain and disability to impaired pulmonary and respiratory function. There are also associated mortality risks, with up to 72% mortality rate at 5 years and 90% at 7 years.[4–6] The economic burden of fragility fractures is huge (approximately 37 billion euros in 2010 for Europe) and the costs are expected to increase by 25% in 2025.

Another rising healthcare problem related to the spine is spinal metastases. Spinal metastases affect more than 70% of terminal cancer patients.[7] Advances in medical treatment for systemic disease have improved survival rates among patients with cancer, which has contributed to an increased incidence of spinal bone metastases. Spinal metastases can cause skeletal-related events such as a pathologic fracture or spinal cord compression, with necessity for radiation therapy or surgery (for pain or impending fracture), with potential adverse impact on quality of life. The occurrence of a skeletal-related event contributes significantly to the cost of care.[8] Data from a large study across four major European countries showed that all types of skeletal-related events are associated with considerable health resource utilization and costs of up to €12,082 per event.[9]

Narcotic analgesics, back braces, and immobilization are common non-surgical means for treatment of vertebral fragility fractures, but may be poorly tolerated in elderly patients with side effects, such as constipation and increased risk of falls.[10,11] In most severe cases patients are bed bound and might require hospitalization, thereby increasing risks of complications, comorbidities, and healthcare costs.

Even after best conservative medical management, these fractures not infrequently lead to poor recovery of health condition, spinal deformity, sagittal imbalance, poor balance and gait, increased risk of falls. In such cases, surgical vertebral augmentation intervention with vertebroplasty or balloon kyphoplasty can provide improved pain relief, functional recovery, and health-related quality of life.[12–15] Furthermore, lower mortality risk and a higher probability of being discharged to home instead of a nursing facility have been reported for augmentation over non-surgically managed patients in the majority of claims-based studies.[6,16–20] Additionally, a randomized trial on more acute and more painful vertebral fragility fractures reported earlier discharge from hospital and less tendency to progressive kyphotic deformity in patients treated with vertebral augmentation compared to those in the sham placebo group.[11] A recent meta-analysis[21] reported that invasive treatment of osteoporotic vertebral fragility fracture is superior to non-surgical management with regard to pain palliation, without affecting quality of life nor causing more subsequent vertebral fractures.

Although these are encouraging data regarding vertebral augmentation techniques in the treatment of patients with painful osteoporotic vertebral fractures, in severe, unstable fractures, such as those classified OF 3 to OF 5, patients will need to be treated not only to palliate pain, but also to regain spinal stability and axial load capacity. In these situations, standard vertebral augmentation techniques may be regarded as unsafe, not feasible or at least as an undertreatment. In such severe cases, surgical fixation is considered.[22] However, operative treatment can be complex in these often fragile patients because of physical deconditioning, medical comorbidities, balance and gait problems with subsequent risk of falling, and poor bone quality with concomitant risk of poor operative fixation and new fractures. Spinal fusion in such cages carries in fact high rates of mechanical failure and proximal junctional failure, for which low bone mineral density because of osteoporosis is an important determinant.

When the vertebral body has lost its structure and ability to bear the axial load, vertebral body resection and cage grafting might be considered, with a 360° surgical approach,[23,24]

which, despite its biomechanical efficacy, is highly invasive surgery, carrying high rates of complications, high costs, and long hospitalization and recovery times, especially in fragile and elderly patients.[25,26]

The need to balance potential risks and benefits in clinical practice requires a patient-tailored assessment and decision making. Moving between the hurdles of this delicate balance causes some patients to be undertreated with conservative treatment or a standard cement augmentation where a more powerful stabilizing technique would have been required, while other patients will be treated with an invasiveness that their clinical condition cannot withstand, and thus a large portion of patients may be left untreated because there is no suitable treatment that can be offered to them.

The percutaneous surgical technique Stent-screw-assisted internal fixation (SAIF), subject of this thesis, could fill this treatment gap, offering a minimally invasive yet efficient tool in case of severe osteoporotic and neoplastic vertebral fractures, to palliate pain and restore axial load capability.

Biomechanical studies in this thesis showed how SAIF can be used to reconstruct the anterior column on simulation models of osteoporotic and neoplastic vertebral body lesions, favorably comparing to surgical posterior stabilization and to standard vertebral augmentation. The biomechanical simulations showed that the vertebral bodies treated with SAIF recovered their axial load biomechanical capabilities. In addition, the middle vertebral column, generally left untreated by standard vertebral augmentation techniques was reinforced by the SAIF construct. This may expand the list of indications for SAIF treatment to unstable fractures with middle column involvement. Very satisfactory results were then confirmed clinically in patients with neoplastic extensive osteolytic destruction of the vertebral body, where SAIF was shown to offer an alternative to more invasive corpectomy. By providing an internal scaffold of the destroyed vertebral body, filled with bone cement and anchored to the posterior osseous vertebral elements, SAIF could be considered as an internal non-fusion means of 360° vertebral stabilization. Such an “armed concrete” approach proved to be efficient and safe also in complex unstable osteoporotic vertebral fractures. Exploiting the ligamentotaxis mechanism, the fracture reduction achieved with SAIF can also lead to indirect central canal decompression in those challenging fractures presenting with posterior wall retropulsion. Combining percutaneous curettage, lavage and vacuum suction of the vertebral body, even extensive neoplastic

vertebral lesions with central canal involvement, in neurologically intact patients, can be treated with SAIF. All these biomechanical, technical, and clinical results, pose the basis for the application of SAIF in vertebral fractures traditionally representing exclusive indications for surgical fusion. In the clinical series of both osteoporotic and neoplastic cases, SAIF was combined with posterior surgical stabilization, as a means of vertebral body reconstruction, thereby avoiding at least the most invasive surgical part of vertebral body resection and grafting in selected cases.

Technically, the SAIF procedure can be performed in an angiography suite and does not necessarily require an operating room. It can be performed in day-surgery setting, with hardly any blood loss, and with greatly reduced operating times as compared to spinal fusion. Early yet unpublished results of SAIF across centers have shown its reproducibility and consistency. Obviously, training of operators is crucial to endure a standard level of performance. SAIF is likely to speed up recovery and discharge, minimizing days of hospitalization, and also minimizing the post-intervention interval for radiation treatment in patients with neoplastic lesions. The costs of this procedure are in between those for standard vertebral augmentation (vertebroplasty or balloon-kyphoplasty) and those for standard surgical fixation. Dedicated appropriate reimbursement policies are at present lacking, but should be considered and should take into account all the potential benefits of this procedure.

Patients with severe vertebral fragility fractures or extreme neoplastic osteolytic vertebral lesions, who could benefit from SAIF, are typically fragile, because of age, comorbidities, and oncological treatment. Management of these patients cannot be limited to the surgical treatment of their vertebral lesion, but should consider a multidisciplinary approach for their multidimensional problem, including pharmacological treatment for low bone mass, a comprehensive pain treatment, physical therapy, fall prevention, and rehabilitation. In case of metastatic spinal lesions, SAIF has to be considered solely as a means for stabilization of the vertebral injury, while the local and systemic disease control strategy has to be left to the oncologist.

As a next step, we designed a protocol for a prospective randomized controlled trial with the aim to gather level I evidence to ascertain whether SAIF is not inferior to surgery in treatment of severe unstable osteoporotic fractures, and to better ascertain its cost-effectiveness. The same level of evidence should be pursued for complex extensive lytic neoplastic lesions of the spine, causing fracture or posing the risk of impending collapse.

Such level of evidence might lead to an additional option in the treatment paradigm of severe pathologic and osteoporotic vertebral fractures, that should be accompanied of course, by training of surgical operators toward this new technique, and by parallel development of health policies for reimbursement.

These factors may ultimately lead to the possibility to offer patients a minimally-invasive effective treatment for severe osteoporotic and neoplastic spinal fractures, with a positive impact on their quality of life, and a potential to save healthcare resources when compared to standard surgical treatment.

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He worked as a neuroradiologist the Radiology Dept. of Policlinico “A. Gemelli” Catholic University of Rome from 2002 to 2004 and from 2006 to 2008. He passed the United State Medical License Examination in 2004 and completed a Neuroradiology clinical fellowship at University of California San Diego during the year 2004-2005. He worked as an Assistant and then as an Associate Professor in Neuroradiology at Medical University of South Carolina in Charleston, SC-USA from 2008 to 2012. Since 2012 he is the Head of Diagnostic and Interventional Neuroradiology, at the Neurocenter of Southern Switzerland in the Ente Ospedaliero Cantonale, in Lugano – Switzerland. He is Professor of Neuroradiology at Medical University of Bern – Switzerland. His skills reside in diagnostic neuroimaging, interventional endovascular neurointerventions and in particular in minimally invasive image-guided spinal interventions. He is member of European and American medical specialty associations; he is reviewer for international specialty journals, speaker and faculty at multiple international scientific meetings, and he is author and co-author of numerous neuroradiology book chapters and scientific publications in international peer-reviewed jounals..
He is married to Lucia Casolari, and has three children, Benedetta (2006), Emma (2008), and Lorenzo (2011).
Alessandro Cianfoni has a passion for competitive sport that is a relevant part of his life. He has competed at an international level in wheelchair basketball, where he has been part of the Italian national team, wheelchair tennis, where he has attained the swiss championships, and freediving, where he holds two world records.

List of Publications

Publications related to this thesis in peer-reviewed journals

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