Eur Spine J (2016) 25:4080–4087
DOI 10.1007/s00586-016-4641-y

ORIGINAL ARTICLE

Total en bloc spondylectomy for locally aggressive and primary malignant tumors of the lumbar spine

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Received: 18 December 2015 / Revised: 31 May 2016 / Accepted: 1 June 2016 / Published online: 4 June 2016

Abstract
Purpose To report outcomes after total en bloc spondylectomy (TES) for primary aggressive/malignant tumors of the lumbar spine.
Methods We performed a retrospective review of 23 neurosurgical patients operated between 2004 and 2014. Outcomes included perioperative complication rates and reoperation rates for instrumentation failure. The relationship between patient/operative parameters and complication development/instrumentation failure was investigated.
Results There were 15 men (65.2 %) and eight women (24.8 %), with a median of 47 years. The most common tumor was chordoma in 11 patients (47.8 %), followed by sarcoma in four (17.4 %), and giant cell tumor in three (13.0 %). All patients but one underwent a two-staged operation; median total estimated blood loss was 3200 mL and median total operative time was 18.5 h. Fifteen patients developed at least one perioperative complication (65.2 %), with the most common being wound infection and ileus (26.1 % each). There was one case of intraoperative iliac vein injury (4.4 %). Instrumentation failure occurred in 9 patients (39.1 %) at a median time of 23 months after index spondylectomy. Following logistic regression, there were no factors associated with complication development. On the other hand, postoperative radiation was significantly associated with instrumentation failure (OR 7.49; 95 % CI, 1.02–54.9). Local recurrence and 5-year survival was 8.7 and 84.4 %, respectively. Median follow-up time was 50 months.
Conclusions Although favorable oncological outcomes after en bloc resection of spinal tumors may be achieved in terms of recurrence and survival, TES in the lumbar spine remains a challenging procedure. Future investigation into complication avoidance and reconstruction techniques is encouraged.

Keywords Total en bloc spondylectomy · Spinal tumor · Lumbar spine · Chordoma · Sarcoma

Introduction

Total en bloc spondylectomy (TES) is an aggressive surgical technique that may be employed in the treatment of spinal neoplasms [1–6]. This procedure involves removal of an entire vertebral body and posterior elements, in an attempt to remove a tumor with negative margins. This procedure is indicated for primary malignant tumors, locally aggressive tumors (such as giant cell tumors), and sometimes for metastatic tumors. Although studies have reported favorable outcomes in terms of low recurrence rates and health-related quality of life measures [1, 3], the procedure carries major risks such as spinal cord injury, pleural effusion, postoperative cerebrospinal fluid leakage, and others [7, 8].

TES in the lumbar spine is particularly challenging, owing to the unique anatomy of this region. Contrary to TES in the thoracic spine, lumbar tumors are typically removed in staged posterior/anterior procedures, and there is potential risk of lumbar plexus, major vessel, and/or bowel injury. Additionally, late instrumentation failure

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may lead to severe back pain and/or neurological deterioration, and has been reported to occur in approximately 40 % of patients undergoing TES [9].

The aim of this study was to report our experience with TES in the lumbar spine, and examine complication rates, reoperation rates, and oncological outcomes for patients with primary aggressive/malignant spinal tumors.

Materials and methods

Study design and inclusion criteria

This study received local Institutional Review Board approval. A retrospective chart review of all adult neurosurgical patients who underwent surgery for a primary (locally) aggressive or primary malignant tumor of the spine between 2004 and 2014 was performed. Inclusion criteria for this study were: (1) patients with a tumor primarily located in the lumbar spine (L1–L5) and (2) patients undergoing TES. Patients undergoing anterior corpectomy alone or en bloc resection of only the posterior elements were excluded.

Recorded data

Patient data such as age, gender, smoking status, history of previous intralesional resection, previous chemotherapy, previous radiotherapy, and tumor histology were ascertained from clinical notes. Tumors were classified according to the Enneking classification system [10] and the Tomita scoring system [5]. The Enneking system classifies malignant tumors as Grade IA (low grade, intracompartmental), IB (low grade, extracompartmental), IIA (high grade, intracompartmental), IIB (high grade, extracompartmental), and III (metastatic disease). Benign tumors (such as giant cell tumor) are classified as grade I (latent; well-demarcated borders), grade II (active; indistinct borders), or grade III (aggressive; indistinct borders) [10]. On the other hand, the Tomita system classifies tumors based on their anatomic location as follows: (1) vertebral body, (2) pedicle, (3) posterior elements, (4) spinal canal, (5) paravertebral area, (6) adjacent vertebra, and (7) multiple, skip lesions. A Type 4 tumor, for example, involves areas 1–4 (vertebral body, pedicle, posterior elements, and epidural space) [5]. Surgical data such as number of resected levels, instrumented levels, use of cage, plate, estimated blood loss (EBL), operative time, and occurrence of any surgical complication were gathered from operative and follow-up clinical notes.

The primary outcome measures evaluated in this study were complication rates and reoperation rates for instrumentation failure/pseudoarthrosis. Follow-up protocol included a follow-up visit and X-rays, computed tomography (CT) scan and/or magnetic resonance imaging (MRI) every 3 months for the first year, every 6 months for the second year, and yearly thereafter. Secondary outcome measures included local recurrence and overall survival.

Statistical analysis

General descriptive statistics were performed for the study population. Data is presented as proportions or median values with interquartile ranges (IQR). A simple logistic regression analysis was done to investigate the relationship between specific patient and operative parameters and complication and instrumentation failure occurrence. Results are presented as odds ratios (OR) with 95 % confidence intervals (CI). Data was analyzed using Stata 12 SE (StataCorp LP, College Station, Texas). A probability value (p value) of less than 0.05 was considered statistically significant.

Results

Patient data

A total of 23 patients were included in this study and their characteristics are presented in Table 1. The median age at surgery was 47 years (IQR 29–70) and 15 patients were male (65.2 %). Three patients were active smokers at the time of operation (13.0 %). Seven patients (30.4 %) received previous radiotherapy, five previously underwent intralesional resection (21.7 %), and two received previous chemotherapy (8.7 %). Of the seven patients with history of previous radiotherapy, five received it as part of the treatment protocol at our institution. The two other patients had a history of previous intralesional resection at outside hospitals and received it as adjuvant therapy (one case of Ewing sarcoma and one case of chordoma).

The most common tumor was chordoma in 11 patients (47.8 %), followed by sarcoma in four cases (17.4 %), giant cell tumor in three cases (13.0 %), and aneurysmal bone cyst, hemangioepithelioma, neuroendocrine carcinoma, hemangiopericytoma, and desmoid fibroma in one case each (4.4 % each). Based on the Enneking classification, there was one grade IA tumor (low grade, intracompartmental), 13 grade IB tumors (low grade, extracompartmental), five grade IIB tumors (high grade, extracompartmental), and four grade III tumors (metastatic). Based on the Tomita system, three tumors were type 4, 13 tumors were type 5, and six tumors were type 6. The most common affected vertebrae were L4 and L5, each involving eight patients (34.8 %). Sixteen patients (69.6 %) underwent single-level TES, six patients (26.0 %) underwent two-level TES, and one patient (4.4 %)

Table 1 General characteristics of 23 patients who underwent total en bloc spondylectomy of the lumbar spine

Parameter	All patients (n = 23)
Age (median, IQR)	47 (29-70)
Male gender (%)	15 (65.2)
Smoker (%)	3 (13.0)
Previous intralesional resection (%)	5 (21.7)
Previous chemotherapy (%)	2 (8.7)
Previous radiotherapy (%)	7 (30.4)
Pathology	
Chordoma (%)	11 (47.8)
Sarcoma (%)	4 (17.4)
GCT (%)	3 (13.0)
ABC (%)	1 (4.4)
Hemangioepithelioma (%)	1 (4.4)
Neuroendocrine carcinoma (%)	1 (4.4)
Hemangiopericytoma (%)	1 (4.4)
Desmoid fibroma (%)	1 (4.4)
Enneking classification	
IA (%)	1 (4.4)
IB (%)	13 (56.5)
IIB (%)	5 (21.7)
III (%)	4 (17.4)
Tomita type	
4 (%)	3 (13.0)
5 (%)	13 (56.5)
6 (%)	7 (30.5)
Affected level	
L1 (%)	5 (21.7)
L2 (%)	4 (17.4)
L3 (%)	5 (21.7)
L4 (%)	8 (34.8)
L5 (%)	8 (34.8)
Number of resected levels	
1 (%)	16 (69.6)
2 (%)	6 (26.0)
3 (%)	1 (4.4)

ABC aneurysmal bone cyst, *GCT* giant cell tumor

underwent three-level TES. The median follow-up time for all patients was 50 months (IQR 24–75).

Surgical technique

The detailed TES technique for lumbar tumors has been previously described [11, 12]. All patients but one in the present study underwent a two-staged posterior-anterior approach. Neuromonitoring was done via motor evoked potentials, somatosensory evoked potentials, and/or standard electromyography. Pediculotomies and osteotomies were done using Tomita saws. Posterior reconstruction was performed using a combination of pedicle screws, sacral screws, iliac screws, rods, transverse connectors, and/or cables. Posterior fibular strut autografts were used in four cases (17.4 %). Locally obtained autograft and demineralized bone matrix were used in all cases. The median EBL for the posterior stage was 2200 mL (IQR 1900–3000), and the median operative time was 13 h (IQR 12–13.5). The median number of instrumented levels was 4 (IQR 4–5).

The anterior retroperitoneal approach was performed with the aid of a general surgeon. Anterior reconstruction was performed using a distractible titanium cage in 15 patients (65.2 %) and distractible polyetheretherketone cage in eight (34.8 %) patients. An anterior plate and screws was used in 10 cases (43.5 %). Plastic surgery helped with wound closure in six cases (26.1 %) with the use of bilateral paraspinal muscle flaps. Median EBL for the anterior stage was 500 mL (IQR 250–1500), and the median operative time was 6.5 h (IQR 5–7.5).

Complications

The median length of stay for all patients was 16 days (IQR 11–19). Fifteen patients (65.2 %) developed at least one perioperative complication, with the most common being wound infection and ileus in 26.1 % of cases each (Table 2). Of the six cases of wound infection, five required reoperation for debridement and one was treated with antibiotics. The second most common complication was deep vein thrombosis with pulmonary embolism,

Table 2 General outcomes of 23 patients who underwent total en bloc spondylectomy of the lumbar spine

Parameter	All patients (n = 23)
Complication	
At least one complication (%)	15 (65.2)
Wound infection (%)	6 (26.1)
Ileus	6 (26.1)
DVT/PE (%)	4 (17.4)
Postoperative CSF leak (%)	3 (13.0)
Wound dehiscence (%)	2 (8.7)
Pneumonia (%)	1 (4.4)
Respiratory failure (%)	1 (4.4)
Delirium (%)	1 (4.4)
Vascular injury (%)	1 (4.4)
Postoperative radiotherapy (%)	7 (30.4)
Instrumentation failure/pseudoarthrosis (%)	9 (39.1)
Follow-up time (median months, IQR)	50 (24–75)

DVT deep vein thrombosis, *PE* pulmonary embolism, *CSF* cerebrospinal fluid which affected four patients (17.4 %); the third most common complication was postoperative cerebrospinal fluid leak, which occurred in three patients (13.0 %). There was one case of left iliac vein injury during anterior osteotomy (4.4 %). Bleeding was initially controlled with pressure and temporary clamps. After tumor delivery, the laceration was repaired using a bovine pericardial patch, which was sewed to the vein using 3-0 prolene suture; no further complications occurred in that patient. After logistic regression analysis, there were no significant factors associated with complication development (Table 3).

Instrumentation failure and long-term outcomes

Surgical margins were negative in 17 patients (73.9 %) and contaminated in six cases (26.1 %) due to significant tumor extension into the pedicles, strong dural attachment, and/or extensive invasion of the paraspinal soft tissue. Seven patients received postoperative radiotherapy (30.4 %). Nine patients (39.1 %) required reoperation due to instrumentation failure/pseudoarthrosis at a median time of 23 months (IQR 16–48) after index spondylectomy. The 12, 24, and 60-month reoperation-free survival rates were 91.3, 77.3, and 46 %, respectively (Figs. 1, 2). After logistic regression analysis, postoperative radiotherapy was significantly associated with instrumentation failure (OR 7.49, 95 % CI, 1.02–54.9) (Table 4). During the follow-up period, three patients (13.0 %) died from their disease, and two patients had local recurrence (8.7 %). Local recurrence occurred in one patient with initial negative margins and one patient with initial contaminated margins. The five-year overall survival rate was 84.4 %.

Discussion

Lièvre (France) and Stener (Sweden) were among the first to describe spondylectomy for oncological purposes [13, 14], a technique that was later popularized by Roy-Camille (France) in the 1980 s and early 1990 s [15, 16]. These techniques however, were based on intracapsular curettage or piecemeal resection, and carried the risk of tumor cell contamination. The term "total en bloc spondylectomy (TES)" was later devised by Tomita (Japan) in the 1990 s and differed from the previous techniques in that this newer procedure involved cutting the vertebra at the level of the pedicle (potentially minimizing tumor cell contamination), and then delivering the posterior and anterior elements in an en bloc fashion; the procedure was regarded as an "oncological subcompartmental resection" [17].

Although en bloc resection is considered a fairly aggressive surgical approach, it has become the treatment of choice for spinal tumors such as chordoma, bone/soft tissue sarcoma, giant cell tumor, adamantinoma, and others, given the growing body of evidence supporting good local control and longer overall survival rates [4–6, 15, 18–20]. In the present study, 23 patients underwent TES in the lumbar spine, a particularly challenging region for several reasons: close relationship between the vertebrae and greater vessels, importance of the lumbar plexus for lower extremity function, close relationship to abdominal structures, and large insertion area of the iliopsoas muscles. Furthermore, unlike TES of the thoracic spine or total en bloc sacrectomies, which can often be done from a sole posterior approach, TES in the lumbar generally requires a two-staged combined approach because of limitations imposed by the lumbar roots. Specifically, the diseased vertebral body cannot be removed safely from a posterior alone approach due to limited room between bridging lumbar roots, and lumbar roots cannot be sacrificed to accommodate such delivery, as is the case in the thoracic spine or sacrum. For these reasons, the majority of descriptions of TES in the lumbar spine for non-metastatic tumors are case reports and small case series [11, 21–26].

Kawahara et al. reported outcomes of ten patients who underwent TES for tumors involving L4 or L5 [12]. Six patients were treated for aggressive benign tumors and four patients for solitary metastasis. All cases involved combined approaches; posterior stabilization was achieved via pedicle screws and rods, and anterior reconstruction was done with a titanium mesh cage in eight patients and with autogenous iliac bone strut graft in two cases. There was

Table 3 Factors associated with complication development after total en bloc spondylectomy of the lumbar spine

Parameter	Odds ratio (95 % confidence interval)	*p* value
Increasing age	1.01 (0.96–1.06)	0.622
Male gender	1.20 (0.20–7.18)	0.842
Smoker	0.21 (0.02–2.83)	0.243
Previous chemotherapy	1	–
Previous radiotherapy	0.60 (0.09–3.78)	0.592
Multilevel spondylectomy	1.50 (0.22–10.3)	0.680
Number of instrumented vertebrae (>4)	1.11 (0.19–6.49)	0.907

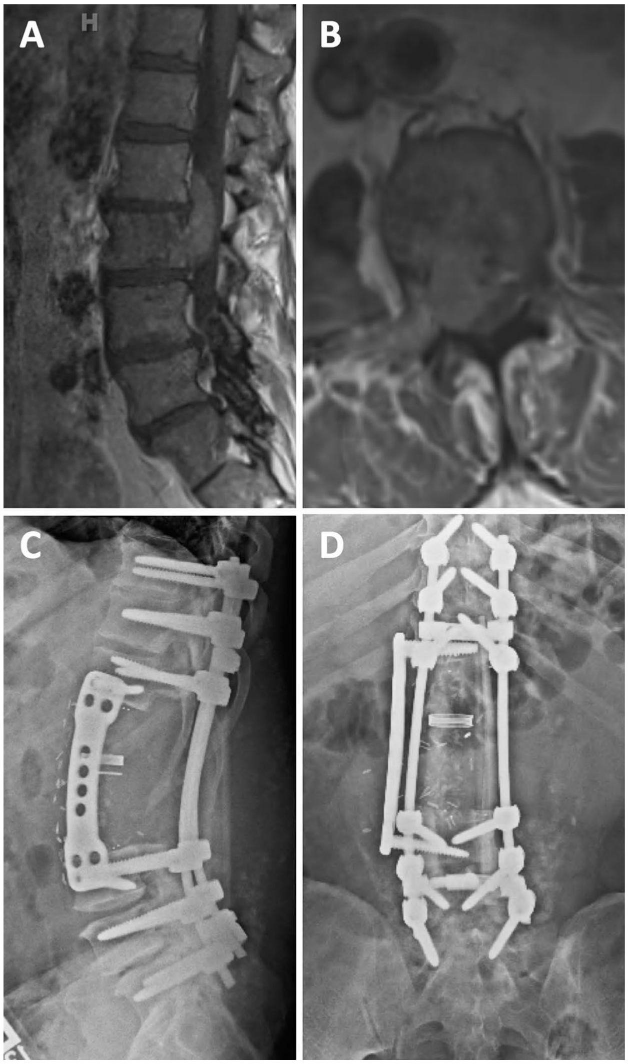

Fig. 1 A 70-year-old male presented with a 4-month history of low back and right thigh pain. MRI revealed a lesion originating from the L2 vertebral body (**a**) and extending rostrally behind the L1 vertebral body; the tumor also extended into the spinal canal, causing significant neural compression (**b**). The patient underwent CT-guided biopsy, which was consistent with chordoma. Preoperatively, he received stereotactic body radiotherapy (1800 cGy to the 67 % isodose line given in three fractions). A TES was performed at the L1 and L2 levels, and anterior reconstruction was made using a distractible PEEK cage and plate (**c** and **d**). The patient is currently disease-free at 33 months of follow-up (Department of Neurosurgery, Johns Hopkins University School of Medicine)

one case of wound infection (10 %), one case of ileus (10 %), three cases of transient weakness (30 %), and two cases of instrumentation failure requiring revision surgery (20 %) [12].

The perioperative complication rate in our series was 65.2 %, a considerably high rate. The most common complications were wound infection and ileus, seen in 26.1 % of cases each. Wound healing is an important issue in patients undergoing en bloc spondylectomy for several

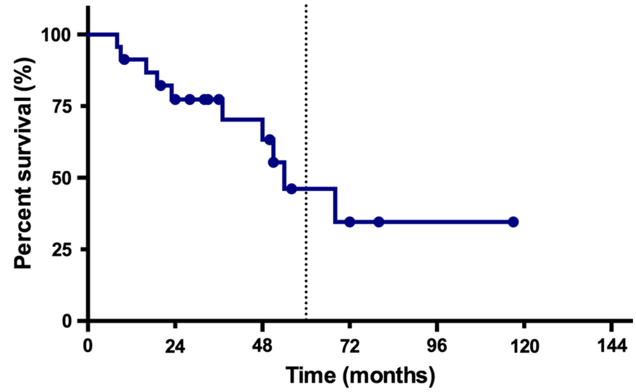

Fig. 2 Kaplan–Meier survivorship curves showing instrumentation failure rates for all patients

reasons. First, some patients have a history of previous chemotherapy and/or radiotherapy, both of which have been shown to impair wound healing [8, 27]. Second, wound healing may be compromised due to the large skin incision, soft tissue devitalization, and incomplete obliteration of dead space [28]. In a recent study by Hayashi et al., the authors found that independent risk factors for surgical site infection following TES included combined approaches and the nonuse of iodine-supported spinal instruments [29]. Although iodine-supported instruments were not used in our series, it may be a potential way to reduce the rate of wound infection following these procedures. Long operative time has also been associated with wound infection after TES [29]. Median total operative time in our study was around 18 h, and some of the factors that may have contributed to this include multi-level spondylectomies (30.4 % of patients), history of previous surgery (21.7 %), history of previous radiation (30.4 %), and involvement of plastic surgery for closure (26.1 %). Although some have suggested a posterior-only approach as a means to reduce operative time [30, 31], a combined approach is needed for tumors below L1 or L2. Although the TES technique has certainly evolved since its original description, performing this procedure in the lumbar spine remains challenging, and further investigation into ways to reduce operative time and perioperative complications are needed.

Postoperative ileus had the same incidence and wound infection, and is not uncommon after abdominal surgery. Preventive strategies include avoidance of salt and water overload, alvimopan (peripheral opioid receptor antagonist), and gum chewing [32]. Although there were no cases of nerve root or bowel injury, there was one case of vascular injury, which fortunately did not result in any sequela. Mesfin et al. also reported one case of aortic and vena cava tear in a patient who underwent TES for epithelioid hemangioendothelioma [33]. The patient had a history of previous unsuccessful tumor resection, resulting

Table 4 Factors associated with instrumentation failure after total en bloc spondylectomy of the lumbar spine

Parameter	Odds ratio (95 % confidence interval)	*p* value
Increasing age	1.02 (0.98–1.08)	0.269
Male gender	1.11 (0.19–6.49)	0.907
Smoker	0.75 (0.06–9.71)	0.826
Previous chemotherapy	1.62 (0.08–29.8)	0.744
Previous radiotherapy	1.25 (0.21–7.61)	0.809
Multilevel spondylectomy	2.93 (0.47–18.3)	0.250
Number of instrumented vertebrae (>4)	1.44 (0.26–7.96)	0.676
Expandable titanium cage	0.5 (0.09–2.88)	0.438
Expandable PEEK cage	2.0 (0.35–11.5)	0.438
Anterior plate	0.5 (0.09–2.84)	0.434
Posterior fibular strut graft	1	–
Postoperative radiotherapy	7.49 (1.02–54.9)	0.047*

* Indicates statistical significance

in "substantial scarring" that may have contributed to the occurrence of vessel tear [33]. Fortunately, these lesions were managed with the aid of vascular surgeons without further complications [33].

The risk of instrumentation failure requiring reoperation was 39.1 % in this study, with postoperative radiotherapy identified as a significant predictor for this, increasing the odds by a factor of 7.5. Similar to our findings, Matsumoto et al. reported an instrumentation failure rate of 40 % after TES and also identified irradiation as an important predictive factor [9]. Despite radiotherapy being associated with instrumentation failure, the use of this treatment modality may not always be avoided, given that it serves as adjuvant therapy for treatment of tumors such as chordoma and certain sarcomas. However, future research into the optimal dosage and fractionation therapy is warranted, as preclinical data has suggested that hypofractionation may preserve normalized vertebral body bone volume, as compared to single high-dose therapy [34] Interestingly, multilevel spondylectomy did not significantly increase the odds for instrumentation failure. Nonetheless, the failure rate after multilevel resection was almost twice as high (57.1 vs. 31.3 %), and not reaching statistical significance was most likely due to the relatively small sample. The implementation of more robust strategies, such as vascularized structural autograft, could be researched in the future in an attempt to obtain fusion in patients with these large bony resections.

Ultimately, it is important to remember that the objective of performing a TES, when feasible, is to decrease local recurrence and prolong survival. As mentioned previously, en bloc resection has shown a significant oncological advantage over contaminated/intralesional resection [5, 6, 15, 18–20], but the benefits/risks of such an "aggressive" procedure must be acknowledged by both the surgeon and patient. Furthermore, two recent case reports from Japan have suggested that reconstruction after TES using nitrogen-frozen vertebral bone may further decrease disease progression in patients with metastatic lesions [35, 36]. These studies have suggested that re-implantation of frozen diseased bone (for arthrodesis) stimulates an anti-tumor immunologic response, potentially serving as adjuvant therapy; this has proven successful after TES for metastatic thyroid and lung adenocarcinoma in two separate patients, decreasing the systemic metastatic disease burden [35, 36]. Additionally, this same principle has also been applied to primary malignant extremity tumors such as Ewing's sarcoma and osteosarcoma [37], and the exciting results warrant further investigation in patients with spinal neoplasms.

Limitations

This study has several limitations. The retrospective nature of this study carries the risk of information bias, and the relatively small sample size could have resulted in study underpowerment and inability to detect statistical significance in some of the analyzes. Additionally, patient reported health-related quality of life outcome measures were not available for review. Despite the recognized limitations, this study showed that TES may result in a relatively low local recurrence rate and favorable overall survival, albeit with a high risk for complication occurrence and instrumentation failure.

Conclusion

Total en bloc spondylectomy in the lumbar spine represents a unique challenge given the unique anatomy of this region. This is a feasible procedure in carefully selected patients, but the risk for perioperative complication development and late instrumentation failure should be acknowledged.

Acknowledgments No funds were received in support of this work. Daniel M. Sciubba (DMS) has consulting relationships with Medtronic, Depuy-Synthes, Orthofix and Globus.

Compliance with ethical standards

Conflicts of interest The authors have no conflicts of interest.

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