

## Ventral fusion versus dorsal fusion: determining the optimal treatment for cervical spondylotic myelopathy

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Cervical spondylotic myelopathy (CSM) often can be surgically treated by either ventral or dorsal decompression and fusion. However, there is a lack of high-level evidence on the relative advantages and disadvantages for these treatments of CSM. The authors' goal was to provide a comprehensive review of the relative benefits of ventral versus dorsal fusion in terms of quality of life (QOL) outcomes, complications, and costs. They reviewed 7 studies on CSM published between 2003 and 2013 and summarized the findings for each category. Both procedures have been shown to lead to statistically significant improvement in clinical outcomes for patients. Ventral fusion surgery has been shown to yield better QOL outcomes than dorsal fusion surgery. Complication rates for ventral fusion surgery range from 11% to 13.6%, whereas those for dorsal fusion surgery range from 16.4% to 19%. Larger randomized controlled trials are needed, with particular emphasis on QOL and minimum clinically important differences. (<http://thejns.org/doi/abs/10.3171/2013.4.FOCUS13103>)

**KEY WORDS** • ventral fusion • dorsal fusion • cervical fusion •  
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CERVICAL spondylotic myelopathy can be surgically treated by a variety of techniques, including both ventral and dorsal decompression with fusion. The ventral approach refers to multilevel discectomy and/or corpectomy with instrumented fusion, whereas the dorsal approach refers to midline cervical laminectomy and fusion.<sup>8,18</sup> Each of these approaches has unique advantages and disadvantages. Although a dorsal approach is technically easier and avoids the morbidity associated with a ventral approach, it can cause significant postoperative muscular pain and is limited to patients who have either neutral or lordotic alignment. A ventral approach allows for direct decompression of ventral pathological entities in kyphotic, neutral, or lordotic spines, and avoids the pain associated with a posterior paraspinous musculature stripping approach, but is associated with its own complications including dysphagia, hoarseness, and cardiopulmonary events.<sup>1,4,5,10,21</sup>

*Abbreviations used in this paper:* CSM = cervical spondylotic myelopathy; EQ-5D = EuroQol-5 Dimensions health survey; MCID = minimum clinically important difference; mJOA = modified Japanese Orthopaedic Association; NDI = Neck Disability Index; NIS = Nationwide Inpatient Sample; QALY = quality-adjusted life year; QOL = quality of life; SF-36, SF-6D = 36-Item Short Form Health Survey, Short Form-6 Dimensions.

Traditional postoperative outcome measures such as complications, readmission rates, revision surgery rates, and return to work measures do not fully encompass the patient experience following surgery and the relative advantages and disadvantages of each of the approaches. Recent studies have increasingly investigated financial cost and QOL outcomes for these 2 surgeries.<sup>1,3,5,9,22</sup>

Despite the numerous studies on this topic, uncertainty remains about which of the 2 procedures is optimal for the treatment of CSM. Previous reviews on the topic, including one in this journal,<sup>13</sup> have attempted to address this uncertainty by using physiological parameters and other preoperative factors that may aid in the selection of the optimal surgical approach. Decision-making algorithms have also been suggested based on the location of the stenosis and alignment of the cervical spine.<sup>11</sup>

This review presents the state of the literature regarding the comparative effectiveness of ventral multilevel discectomy and fusion as opposed to dorsal fusion surgery for treating CSM. We summarize the recent studies comparing the 2 procedures based on QOL outcomes, postoperative complication profiles, and cost-effectiveness. This review seeks to provide a comprehensive guide to the published evidence comparing ventral multilevel discectomy and fusion to dorsal fusion for surgical treatment of CSM.

## Methods

A MEDLINE review of English-language literature was performed to identify studies comparing ventral multilevel discectomy and fusion with dorsal cervical fusion performed between 2003 and 2013. This time period was chosen to focus on only the most recent studies relevant to current clinical practice. The search terms included ventral cervical fusion, anterior cervical fusion, dorsal cervical fusion, posterior cervical fusion, cervical spondylotic myelopathy, and CSM. A total of 3512 results were retrieved from these searches. Furthermore, references from the identified studies as well as those from other review papers were used to ensure completeness. Studies were excluded if they did not pertain to ventral and dorsal fusion, involved single-level fusions, or if they were animal studies, single case reports, or clinical series with fewer than 10 patients reported, to ensure sufficient statistical power in study conclusions. Patients treated with laminectomy without fusion, and those who underwent laminoplasty procedures were not included because the primary focus of this review was on fusion. Studies were included only if they specifically pertained to clinical outcomes, complication profiles, or financial costs for ventral versus dorsal fusion surgery for CSM. Seven clinical studies were reviewed here.

Articles were further classified according to the level of evidence outlined by Resnick et al.,<sup>17</sup> in which studies are categorized into 3 classes. Class I evidence is the highest level, consisting of randomized controlled trials. Class II evidence includes most prospective studies other than randomized controlled trials. Class III studies consist of retrospectively collected data and case series. The level of evidence for the included studies was assessed by 2 independent reviewers (M.D.A. and D.L.), and any disagreement was resolved by reviewer consensus. Data collected from the included studies consisted of study type, patient sample size, specific complications and complication rate, health outcomes measured, types of questionnaires used, follow-up period, and costs.

## Results

Seven studies (1 prospective, 6 retrospective) consisting of 248,029 patients were identified and reviewed. Table 1 provides a summary of QOL outcomes assessed for the 2 procedures, Table 2 summarizes complications for each approach, and Table 3 summarizes the financial costs and cost-effectiveness studies associated with each approach.

### *Studies of QOL Outcomes*

Three studies (1 prospective, 2 retrospective) consisting of 192 patients undergoing ventral (n = 114), dorsal (n = 72), or ventral and dorsal (n = 6) fusion surgery for CSM were analyzed (Table 1). Outcome measures included the SF-36, SF-6D, EQ-5D, mJOA, and NDI. All 3 studies had a 1-year follow-up and reported significantly (p < 0.05) improved QOL outcomes for some or all of these questionnaires from the preoperative to postoperative period.

Of these studies, the highest level of evidence was in

the investigation by Ghogawala et al.,<sup>5</sup> who conducted a prospective study on patients (n = 50) with CSM undergoing either ventral (n = 28) or dorsal (n = 22) fusion. Both cohorts showed significant preoperative to postoperative improvement in mJOA (ventral: 2-point increase, p < 0.01; dorsal: 1.9-point increase, p < 0.01); EQ-5D (ventral: 0.16-point increase, p < 0.01; dorsal: 0.13-point increase, p = 0.04); and SF-36 scores (ventral: 9.9-point increase, p < 0.01; dorsal: 5.7-point increase, p = 0.03). In addition, the ventral cohort showed significant preoperative to postoperative improvement in the NDI score (18.4-point decrease, p < 0.01), and had significantly greater improvements only in the SF-36 score compared with the dorsal cohort. Although greater improvement for the SF-36 score was observed after ventral fusion, the dorsal cohort had a greater degree of myelopathy preoperatively than the ventral cohort, which may have confounded the results. In addition, the dorsal cohort on average had more levels surgically treated (3.1 vs 2.1 for ventral, p < 0.01) and was associated with a longer hospital stay (4 days vs 2.6 days) compared with the ventral cohort. Overall, both ventral and dorsal fusion surgery for CSM showed significant improvement in disease-specific symptoms and in QOL measures. The investigators concluded that a randomized controlled trial was needed to determine more accurately the optimal fusion approach for patients with CSM.

In 2012, Fehlings et al.<sup>3</sup> conducted a retrospective study of patients with CSM who were included in the AOSpine North America Cervical Spondylotic Myelopathy Study (n = 70 cases; 45 patients in the ventral fusion cohort and 19 in the dorsal fusion cohort; 6 patients had both). The QOL outcomes measured by the mJOA (3-point increase), NDI (11-point decrease), SF-36 (5-point increase), and SF-6D (0.07-point increase) all showed significant (p < 0.0001) improvement by 1 year postoperatively. Thus, in agreement with Ghogawala et al., they found that surgical management of CSM produced significantly improved QOL outcomes. However, this study did not make specific comparisons between ventral and dorsal fusion cohorts.

Also in 2012, Whitmore et al.<sup>22</sup> conducted a retrospective study on patients with CSM undergoing either ventral (n = 41) or dorsal (n = 31) fusion surgery. The ventral cohort had a greater, but statistically nonsignificant, improvement in both SF-36 (ventral fusion cohort: 8.5-point increase vs dorsal fusion cohort: 4.7-point increase) and NDI scores (ventral fusion cohort: 16.3-point decrease vs dorsal fusion cohort: 10.8-point decrease) compared with the dorsal cohort. No significant differences between the cohorts were identified for EQ-5D scores. Thus, in contrast to the study by Ghogawala et al., Whitmore and colleagues did not identify significant differences between ventral and dorsal cohorts. Further research is necessary to determine if true differences in QOL outcomes exist following ventral versus dorsal fusion surgery for patients with CSM.

### *Studies of Complications*

Four studies (1 prospective, 3 retrospective) consisting of 235,549 patients undergoing ventral (n = 46,766) or dorsal (n = 8241) fusion surgery for CSM were analyzed

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**TABLE 1: Studies of outcomes for ventral and dorsal fusion\***

Authors & Year	Study Design	Evidence Class†	Mean FU	Patient Sample	Outcome Measure	1-Yr Improvement, Ventral vs Dorsal
Ghogawala et al., 2011	prospective cohort	II	1 yr	50 overall	SF-36	9.9 vs 5.7 (p = 0.03)
				28 ventral	NDI	18.4 vs 5.9 (p = 0.07)
				22 dorsal	EQ-5D	0.16 vs 0.13 (p = 0.13)
					mJOA	2.0 vs 1.9 (p = 0.16)
Whitmore et al., 2012	retrospective cohort	III	1 yr	72 overall	SF-36	8.5 vs 4.7 (p = 0.12)
				41 ventral	NDI	16.3 vs 10.8 (p = 0.22)
				31 dorsal	EQ-5D	0.16 vs 0.13 (p = 0.56)
Fehlings et al., 2012 <sup>3</sup>	retrospective case series	III	1 yr	70 overall‡ 45 ventral 19 dorsal	SF-36 NDI mJOA SF-6D	ventral/dorsal comparisons not made

\* FU = follow-up.

† Level of evidence according to Resnick et al.

‡ Six patients had both ventral and dorsal fusion.

(Table 2). The overall complication rate ranged from 6.5% to 16.6%. Complication rates for ventral fusion surgery ranged from 11% to 13.6%, whereas those for dorsal fusion surgery ranged from 16.4% to 19%. Complications included hoarseness, cardiopulmonary dysfunction, dysphagia, wound infection, sensory loss, weakness, and death. Patients who underwent multilevel ventral decompression and fusion had a higher rate of hoarseness and dysphagia, whereas those who underwent dorsal fusions had a higher rate of neck pain or nerve palsies.

In 2007, Wang et al.<sup>21</sup> used the NIS to retrospectively review the medical records of 932,009 patients who underwent cervical spine surgery for degenerative disease (19% with CSM) between 1992 and 2001. Patients with CSM who underwent surgery had the highest complication rate (6.5%) and in-hospital mortality rate (0.39%) compared with the rates for other types of cervical spine surgery.

Boakye et al.<sup>1</sup> also used the NIS database to review

58,115 patients with CSM undergoing surgery between 1993 and 2002. These investigators reported an overall complication rate of 13.4% (16.4% for dorsal fusion, 11.9% for ventral fusion; no p value reported). Pulmonary (3.6%) and postoperative hemorrhages or hematomas (2.3%) were the most common complications for both ventral and dorsal fusion. Dysphagia (3%) and hoarseness (0.21%) were more prevalent in the ventral cohort. Pulmonary complications (4.6%) and hematomas (3.22%) were more prevalent in the dorsal cohort. Other complications for both cohorts included renal (1.45%), cardiac (1.2%), thromboembolic (0.73%), neurological (0.71%), and infection (0.43%).

Ghogawala et al.<sup>5</sup> showed that complication profiles did not significantly differ between ventral and dorsal cohorts (13.6% vs 17.9% for ventral and dorsal approach cohorts, respectively; p = 1.0). The overall complication rate was 16.6%. The dorsal cohort had greater rates of postoperative pain and disability compared with the ven-

**TABLE 2: Studies of complications for ventral and dorsal fusion\***

Authors & Year	Study Design	Evidence Class	Mean FU	Patient Sample	Complication(s)	Complication Rate
Wang et al., 2007	retrospective case series	III	10 yrs	932,009 overall (~177,082 CSM patients)	hoarseness, infection, systemic	6.5% overall
Boakye et al., 2008	retrospective case series	III	10 yrs	58,115 overall	pulmonary hemorrhages, hematomas	13.4% overall
				46,562 ventral		11.9% ventral
				8,112 dorsal		16.4% dorsal
Ghogawala et al., 2011	prospective cohort	II	1 yr	50 overall	dysphagia, C-5 palsies	16.6% overall
				28 ventral		13.6% ventral
				22 dorsal		17.9% dorsal
Fehlings et al., 2012 <sup>4</sup>	retrospective case series	III	2 yrs	302 overall	dysphagia, infection, minor CPEs, neck pain	15.6% overall
				176 ventral		11% ventral
				107 dorsal		19% dorsal

\* CPE = cardiopulmonary event.

**TABLE 3: Studies of costs and cost-effectiveness for ventral and dorsal fusion\***

Authors & Year	Study Design	Evidence Class	Mean FU	Patient Sample	QALYs	Mean Cost
Boakye et al., 2008	retrospective case series	III	10 yrs	58,115 overall 46,562 ventral 8,112 dorsal	NA	\$23,209 ventral \$30,927 dorsal
King et al., 2009	retrospective cohort	III	2.3 yrs	12,338 overall 10,449 ventral 181 dorsal	NA	\$14,300 ventral \$23,400 dorsal
Ghogawala et al., 2011	prospective cohort	II	1 yr	50 overall 28 ventral 22 dorsal	NA	\$19,245 ventral \$29,465 dorsal
Fehlings et al., 2012 <sup>3</sup>	retrospective case series	III	1 yr	70 overall 45 ventral 19 dorsal	0.07/yr, 0.64/10 yrs	\$21,066 overall†
Whitmore et al., 2012	retrospective cohort	III	1 yr	72 overall 41 ventral 31 dorsal	0.16/yr ventral 0.13/yr dorsal	\$21,563 ventral (CCR) \$27,942 dorsal (CCR) \$17,538 ventral (MED) \$16,579 dorsal (MED)

\* CCR = cost-to-charge ratio method; MED = Medicare reimbursement method; NA = not applicable.

† This amount is given in Canadian dollars (\$20,516 US); the rest of the costs are given in US dollars.

tral cohort. Of those patients in the ventral cohort who had complications, 80% had swallowing difficulties. The 3 patients (13.6%) in the dorsal cohort with complications each had C-5 palsy. Although the investigators did not define what was considered to be C-5 palsy (for example, loss of motor strength, sensory loss, pain in the C-5 distribution), this percentage is high compared with what has been reported in the literature.<sup>14</sup>

Fehlings et al.<sup>4</sup> analyzed 302 patients from the AOSpine North America Cervical Spondylotic Myelopathy Study who underwent surgical treatment for CSM. These investigators reported an overall perioperative complication (for example, infection, bleeding, dural tear, esophageal injury) rate of 15.6%, with an overall delayed complication (for example, pseudarthrosis, hardware breakage, graft dislodgement) rate of 4.4%. The ventral and dorsal cohorts had complication rates of 11% and 19%, respectively ( $p = 0.11$ ). The most common complications included cardiopulmonary (3%), dysphagia (3%), and wound infection (2.3%). Operative blood loss was significantly ( $p < 0.01$ ) greater in the dorsal cohort compared with the ventral cohort. The dorsal cohort also had a significantly ( $p = 0.03$ ) greater incidence of wound infection (4.7%) compared with the ventral cohort (0.6%).

#### Studies of Cost-Effectiveness

Five studies (1 prospective, 4 retrospective) consisting of 70,645 patients undergoing ventral ( $n = 57,125$ ) or dorsal ( $n = 8365$ ) fusion surgery for CSM were analyzed (Table 3). Of these 5 studies, the 4 that included cohorts of ventral versus dorsal fusion surgery all showed that costs were greater for dorsal when compared with ventral fusion surgery.

Fehlings et al.<sup>3</sup> calculated the financial costs and cost-effectiveness of both ventral and dorsal fusion surgery for

patients with CSM. Direct costs on average for both fusion surgeries were \$21,066 Canadian (\$20,516 US). The cost-utility ratio was \$32,916 Canadian/QALY gained, allowing the investigators to conclude that surgical management of CSM is cost-effective based on thresholds for cost-effectiveness in the literature.

Boakye et al.<sup>1</sup> used data from the NIS database to estimate an average total cost of both ventral and dorsal fusion surgery for CSM to be \$25,419. Dorsal fusion surgery had significantly greater costs (\$30,927) than ventral fusion surgery (\$23,209). King et al.<sup>9</sup> performed a retrospective review of the Washington State Inpatient Database (1998–2002) that used a published algorithm for identifying cervical spine surgery admissions related to cervical spine degenerative disease (not CSM specific). Hospital charges were significantly ( $p < 0.01$ ) greater for dorsal (\$23,400) compared with ventral (\$14,300) fusion surgery (2.3-year mean follow-up).

Similarly, Ghogawala et al.<sup>5</sup> showed that dorsal fusion surgery was associated with significantly greater costs (\$29,465) than ventral fusion surgery (\$19,245) in a 1-year follow-up. Costs were derived by combining Medicare reimbursements or cost-to-charge ratios with actual hospital charges.

Whitmore et al.<sup>22</sup> also conducted a cost analysis by using 2 different cost calculation methodologies: cost-to-charge ratios and Medicare reimbursement. Using the former, the investigators found that dorsal fusion surgery had significantly ( $p = 0.02$ ) greater costs (\$27,942) compared with ventral fusion surgery (\$21,563). Because the costs of ventral fusion were less than those of dorsal fusion, the calculated incremental cost-effectiveness ratio for ventral fusion was negative and, thus, was said to be “dominated” by ventral fusion. In contrast, when using the Medicare reimbursement calculations the costs

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were not significantly different (dorsal: \$16,579, ventral: \$17,538), and the incremental cost-effectiveness ratio for ventral fusion was \$34,533/QALY gained. This study highlighted how different conclusions can be reached relative to cost-effectiveness or significant differences in cost depending on which cost methodology is used. Notably, there is much heterogeneity in the literature regarding methods by which both “costs” and “cost-effectiveness” have been measured to date.

### Discussion

Patients with CSM commonly present with varying patterns of trunk or extremity numbness, neck pain, loss of hand dexterity, motor weakness in the upper extremities, and gait disturbances.<sup>11,16</sup> Although the first-line treatment in the majority of patients is conservative management (including cervical immobilization via a neck collar or brace and physical therapy<sup>11,16</sup>), surgical decompression and/or fusion is often indicated in patients with progressive neurological demise with correlative spinal cord compression. There are various surgical techniques that are commonly used. The choice of surgical procedure will vary based on the individual patients, the region of pathology, number of levels involved, cervical alignment, presence or absence of neck pain, and surgeon preference. In all patients, however, the goal of the surgery is to decompress the spinal cord, preserve alignment and stability of the spinal column, and prevent further injury.<sup>11</sup> Regardless of the approach, early operative intervention can lead to superior outcomes. Suri et al.<sup>19</sup> showed in a prospective study of 146 patients that those with less than a 1-year duration of symptoms had significantly superior outcomes postoperatively (that is, motor/sensory/autonomic/disability improvement) compared with those who had a longer duration of symptoms.

The present review demonstrated that both ventral and dorsal fusion result in significantly improved postoperative QOL compared with preoperatively. The 2 studies<sup>5,22</sup> that compared QOL outcomes for ventral versus dorsal fusion surgery demonstrated that ventral fusion leads to superior results, although in only one of these studies were these findings statistically significant.<sup>5</sup> Limitations of the studies included retrospective study design, small patient samples, and short follow-up time (1 year). More prospective, well-designed studies are needed for better clarification of the QOL outcomes of these surgeries.

In addition, the included studies suggest that the complication rates and costs are significantly greater for dorsal fusion compared with ventral fusion. However, the complication rates for ventral fusion are also high and must be considered when consulting patients. To explain the cost differences between the 2 procedures, Whitmore et al.<sup>22</sup> showed that there were significantly higher in-hospital charges for dorsal fusion. The Boakye et al.,<sup>1</sup> King et al.,<sup>9</sup> and Ghogawala et al.<sup>5</sup> studies do not provide detailed descriptions of their cost data or explanations for this difference, and this makes it difficult to accurately assess and make comparisons between the groups in these studies regarding “costs.” The costs of some of the studies reviewed here did not include all relevant direct

costs, including outpatient imaging technician fees or physical therapy and rehabilitation fees, or indirect costs to patients, such as loss of productivity and caregiver costs. Future cost-effectiveness analyses should include detailed descriptions of the cost differences for a better explanation of the true cost-effectiveness differences between ventral and dorsal fusion for CSM.

Many of the studies reviewed here focused exclusively on statistically significant differences and did not ascertain clinical relevance. Clinically significant meaning has become increasingly important in assessing treatment options. The MCID for anterior cervical discectomy and fusion (ventral fusion) has recently been investigated by Parker et al.<sup>15</sup> The MCID represents the critical threshold necessary to achieve treatment effectiveness and be beneficial to the patient. Many studies have evaluated the MCID for the questionnaires used in the studies discussed herein, including the visual analog scale, NDI, and EQ-5D.<sup>2,6,23,24</sup> The reported MCID will be different depending on the type of procedure (for example, ventral and dorsal fusion). By identifying the clinically meaningful improvements for each of these surgeries (that is, based on patient reports of QOL), investigators will be better able to ascertain cost-effectiveness and to comparative the effectiveness of the 2 procedures.

We acknowledge certain limitations that must be considered when interpreting the results of the present review. First, as in any systematic review, we include data from multiple studies and multiple surgeons with differing techniques and data collection and reporting methods. These differences, including differences in the reporting of major and minor complications, may somewhat confound the overall results. Second, nearly all of these studies represent Class III evidence, which is mainly retrospective. Studies of this design type may not account for differences in the patient sample with regard to comorbidities or the number of levels that were surgically treated. Wang et al.<sup>21</sup> and Boakye et al.<sup>1</sup> in particular used the NIS, which is the largest publicly available inpatient care database in the US, updated annually, with approximately 8 million hospital stays. Databases of this nature may be associated with significant sampling bias and coding errors that can confound results. The clinical data reviewed represent the low quality of evidence currently available and indicate the need for more well-designed prospective studies of this commonly encountered disease process.

In 2009, Mummaneni et al.<sup>12</sup> performed a systematic review to compare the efficacy of different surgical techniques, including ventral and dorsal fusion, for the treatment of CSM. The investigators found insufficient evidence to recommend ventral fusion over dorsal fusion because both produced comparable improvement in patients with CSM. Notably, this conclusion was based on Class III evidence, most of which was published more than 10 years ago, none of which incorporated cost or QOL data. Their study further supports the need for studies with better levels of evidence that include cost and QOL outcomes.

Finally, studies focusing solely on ventral corpectomy and fusion or laminoplasty were not included. Compared with multilevel discectomy and fusion, ventral corpec-

tomy has been shown to have higher complication rates, including graft dislodgements and fusion failure.<sup>7,18,20</sup> However, ventral corpectomy has been shown to yield similar QOL outcomes to ventral multilevel discectomy and fusion and, thus, should be investigated further in the future.<sup>12</sup> In addition to ventral and dorsal fusion, laminoplasty is also commonly used in the surgical treatment of patients with CSM. This approach leads to comparable postoperative improvement in CSM symptoms and has a complication rate of approximately 12%, which is within the same range as ventral and slightly below that of dorsal fusion.<sup>4,12</sup> Despite these limitations, the present review summarizes the current state of the literature published over the past decade and offers guidance to future research on the topic.

### Conclusions

We have summarized the studies from the past decade and have found that both ventral and dorsal fusion surgeries lead to significantly improved QOL outcomes in patients with CSM. Controversy remains regarding the preferred surgery for this patient population. Recent studies have shown that dorsal fusion has both a higher complication rate and costs significantly more than ventral fusion. Most of the studies we reviewed, however, were Class III evidence, and therefore prospective studies are needed for a better comparison of the outcomes of the 2 surgical procedures. Furthermore, a greater focus on MCID values and clinically relevant findings is needed, to supplement the traditional use of statistical significance. Finally, cost-effectiveness analyses need to be more comprehensive (including more of the indirect costs) to understand better the true costs, cost-effectiveness, and comparative effectiveness of ventral versus dorsal fusion for CSM.

### Disclosure

Dr. Mroz owns stock in PearlDiver, Inc., he is a consultant for Globus, and he receives fellowship support and speaking honoraria from AOSpine. No grant, technical, or corporate support was received in conducting this study or writing this manuscript.

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