Neurological Outcomes After Surgical or Conservative Management of Spontaneous Spinal Epidural Abscesses

A Systematic Review and Meta-Analysis of Data From 1980 Through 2016

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Study Design: This is a meta-analysis.

Objective: Perform a systematic review and quantitative meta-analysis of neurological outcomes from all available spinal epidural abscess (SEA) literature published between 1980 and 2016.

Summary of Background Data: Current literature on SEAs lacks large-scale data characterizing prognostic factors and surgical indications.

Materials and Methods: PubMed was queried for studies reporting neurological outcomes from patients undergoing conservative or surgical management for spontaneous SEA. Inclusion criteria included outcomes data measured ≥ 6 months after presentation, ≥ 10 human subjects, and diagnosis by magnetic resonance imaging or Computed tomography-myelogram. Where available, demographic data, abscess location, comorbidities, pretreatment neurological deficits, treatment methods, bacterial speciation, and complications were extracted from each study. Potential outcome predictors represented by continuous variables were compared using student *t* test and categorical variables were compared using the Pearson χ^2 test. Variables identified as potentially associated with outcome ($P \leq 0.05$) were subjected to meta-analysis using Cochran-Mantel-Haenszel testing to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: In total, 808 patients were analyzed from 20 studies that met inclusion criteria. 456 (56.3%) patients were treated with surgery and antibiotics, and 353 (43.7%) patients were managed with antibiotics alone. Neither surgical intervention (OR = 1.01, 95% CI = 0.40–2.59), lumbosacral location (OR = 1.51, 95% CI = 0.23–9.79), nor neurological deficit on presentation (OR = 0.88, 95% CI = 0.40–1.92) were significantly associated with good (stable or improved) or bad (worsened) neurological outcome, whereas delayed surgery was significantly associated with bad outcome (OR = 0.01, 95% CI = 0.02–0.62) and cervicothoracic location approached significance for predicting bad outcome (OR = 0.41, 95% CI = 0.15–1.09).

Conclusions: Current literature does not definitively support or oppose surgical intervention in all SEA cases. Therefore, until better evidence exists, the decision to operate must be made on an individual case-by-case basis with the goals of preventing neurological decline, obtaining source control after failed conservative treatment, or restoring spinal stability.

Key Words: abscess, cervical, cervicothoracic, epidural, lumbosacral, neurological outcome, prognosis

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Spontaneous spinal epidural abscesses (SEA) are rare but morbid infections that develop between the spinal dura mater and bony vertebral elements.[1] In the 1970s, SEAs comprised ~0.2–1.2 per 10,000 hospital admissions and were diagnosed primarily by clinical suspicion and surgical exploration.[2] In the 1980s, increased intravenous (IV) drug use, implementation of prolonged IV medical therapies, and the development of magnetic resonance imaging resulted in a rise of SEA diagnoses. Today, it is responsible for between 2 and 12.5 cases per 10,000 hospital admissions.[3]

Depending on anatomic location and clinical presentation, SEAs can be treated conservatively with IV antibiotics or may require emergent neurosurgical intervention to avoid permanent neurological deficits, sepsis, or death.[4,5] In common practice, indications for neurosurgical intervention include an acutely or subacutely worsening neurological deficit due to mass effect from the abscess, failure of source control after completion of conservative therapy, or instability from associated osteomyelitis or discitis.[6] Accordingly, goals of treatment include decompression of neural

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elements, infection source control, and/or stabilization of the spine. Any neurosurgical intervention is almost always combined with prolonged IV antibiotics, which is considered standard of care.[7] Although neurosurgical consultation is always indicated, some studies suggest that patients with localized disease and minimal neurological deficits can be successfully managed with antibiotics alone.[8–11]

Unfortunately, the current body of literature on posttreatment neurological outcomes from SEAs is limited to small case series and qualitative reviews.[7,12] Results from these studies are often inconclusive or contradictory, and due to their small sample size, measured predictors of success or failure cannot be applied to the broader SEA population. To the best of our knowledge, there are no ongoing prospective trials assessing outcomes following treatment for spontaneous SEAs, and due to its low incidence, initiation of such a study would require many years of collaboration among multiple institutions. Two existing meta-analyses by Stratton et al[13] and Suppiah et al[14] have attempted to characterize outcomes following treatment of SEA; however, the first analysis only examined patients who were treated conservatively, whereas the second analysis included patients with iatrogenic SEAs. Therefore, the literature is currently without definitive data that might inform clinicians on when conservative versus surgical measures should be used to treat spontaneous SEAs. For this reason, our group performed a systematic review and the first quantitative meta-analysis of outcomes following conservative or neurosurgical intervention. By doing so, we provide the most up-to-date, large-scale collection of data regarding predictors of neurological outcomes in this patient population.

MATERIALS AND METHODS

Literature Search

PubMed was queried for peer-reviewed articles describing neurological outcomes following treatment for spontaneous SEAs. The following search criteria were used: (spine OR spinal) AND epidural AND (abscess OR infection) AND (surgery OR antibiotics OR evacuation). This search, performed on July 30, 2017 resulted in 1662 titles and abstracts that were examined for the following inclusion criteria: published between January 1, 1980 and December 31, 2016; available in English; and reported primary outcomes for ≥10 patients following treatment of SEAs. In total, 42 articles met these criteria and were reviewed in-full for the following exclusion criteria: iatrogenic SEA, mean follow-up <6 months, insufficiently disaggregated data, or previous spinal surgery with instrumentation. Ultimately, 808 patients from 20 eligible studies were identified and included for analysis (Fig. 1 for flowchart on study selection). This literature query and study design were guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15]

Data Collection

Neurological outcomes were categorized into 2 groups: good or poor. Good neurological outcomes were defined as

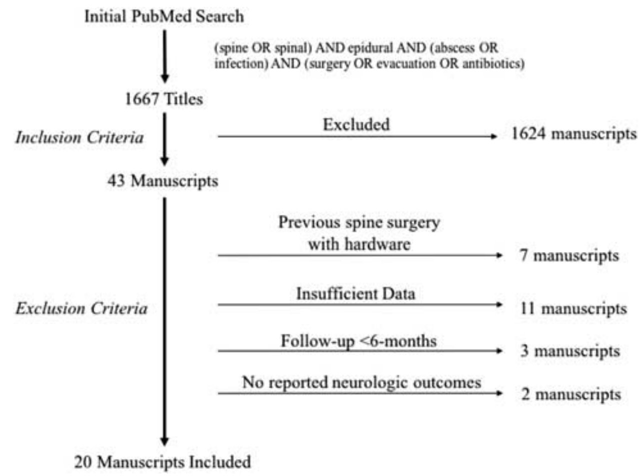

FIGURE 1. Literature search criteria as guided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[13]

neurological examinations that remained stable or improved at final follow-up, whereas poor outcomes were defined as examinations that worsened. Reporting of neurological outcome varied across studies and included the American Spinal Injury Association (ASIA) scale, Frankel Scale, Modified Barthel Index (MBI), Functional Independence Measure (FIM), Quadriplegia Index of Function (QIF), or Spinal Cord Independence Measure (SCIM). The original authors' reporting measure was used to classify patient outcomes into one of the above categories. In addition, neurological outcomes were compared by year of publication to examine for any trend over time (Fig. 2).

Demographic data (eg, age at initial presentation and sex) and comorbidities (eg, diabetes, sepsis at presentation, history of IV drug use, and malignancy) were included where available. Rostral-caudal (cervical, thoracic, or lumbosacral) and ventral-dorsal anatomic location (dorsal, ventral, both, or not otherwise specified) were also

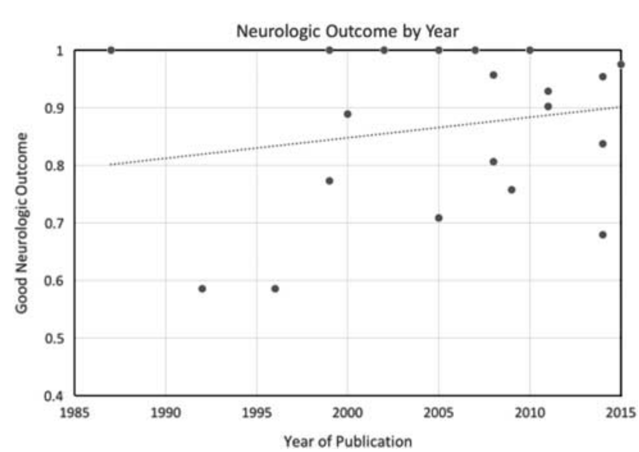

FIGURE 2. Neurological outcomes following treatment of spinal epidural abscess versus time. Linear regression revealed no significant trend ($r = 0.039$, $P > 0.05$).

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noted and compared. If the abscess spanned multiple areas, all affected areas were included in the analysis. Patients with any cervical involvement were included in an "any cervical" group, which was repeated for patients with thoracic, cervicothoracic, or lumbosacral involvement. All patients who underwent surgical management (immediate or delayed) with concurrent antibiotic treatment ("surgery" group) versus antibiotic treatment alone were also analyzed as were outcomes from patients who were treated with surgery >7 days after initial presentation ("delayed surgery" group). In the included manuscripts, patients with active neurological decline or overwhelming infectious disease burden tended to receive operative intervention within 7 days, even if they required medical optimization of other organ systems before surgery, whereas patients in the "delayed surgery" group underwent at least 7 days of conservative management before undergoing operative intervention. Therefore, 7 days was established as the cutoff between delayed and immediate intervention for the purposes of this study.

If identified, the infectious agent was categorized as methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *Staphylococcus aureus* (MSSA), other gram-positive bacteria, other gram-negative bacteria, or another agent. If >1 agent was isolated, both were included in the analysis. Patients' neurological statuses at presentation were also noted, as were signs and symptoms of persistent infection at follow-up (ie, radiographic progression, laboratory evidence, or clinical examination findings). Lastly, the presence of infectious and/or neurological complications included (but were not limited to) wound infection, wound breakdown, cerebrospinal fluid leak, or iatrogenic neurological injury.

Statistical Analyses

Preliminary univariate analysis was performed using unpaired 2-way student *t* tests for continuous variables and the Pearson χ^2 tests for categorical variables. Neurological outcomes following treatment for SEAs were stratified by each demographic, preoperative, perioperative, and postoperative variable of interest. The α cutoff was set at ≤ 0.05. Those variables that met statistical significance during this initial assessment were included in the formal meta-analysis.

Factors potentially predictive of neurological outcome were then included in a formal meta-analysis (Fig. 3) for all patients, and a similar evaluation was performed between surgically managed and nonoperatively managed groups. Factors included in the initial meta-analysis were repeated in the individual subset meta-analyses. It was not possible to include thoracic abscess location in the meta-analysis due to lack of studies with patients in both categories (thoracic location or nonthoracic location with good and poor neurological outcomes).

Heterogeneity among studies was determined using both Cochran Q and I^2 tests, which suggested the appropriateness of a fixed-effects model in all cases except for surgery, delayed surgery, and lumbosacral involvement, which required usage of a random effects model due to their heterogeneity. Lastly, Cochran-Mantel-Haenszel testing was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for each variable in question. Statistical analysis was performed using JMP 13.0 (SAS Institute, Cary, NC) and Review Manager version 5.3.[16]

RESULTS

Analysis of All Patients

Data from 808 patients across 20 case series were analyzed (Table 1).[3,4,18–34] No randomized-controlled trials were found. Overall, 670 (82.9%) patients experienced good neurological outcome following treatment for spontaneous SEA, which did not vary significantly across year published ($r=0.039$, $P>0.05$; Fig. 2). Demographic data including age ($P=0.77$) and sex ($P=0.69$) did not differ across outcome groups. Individual factors found to be potentially associated with worse neurological outcome included sepsis at presentation ($P<0.01$), thoracic location ($P<0.01$), and cervicothoracic involvement ($P<0.01$). Diabetes ($P<0.01$), dorsal lumbosacral involvement ($P=0.04$), any lumbosacral involvement ($P<0.01$), and those who were treated with surgery ($P<0.01$) were potentially associated with positive outcomes following SEA treatment. Postoperatively, neurological complications ($P=0.03$) and persistent infections ($P<0.01$) were found to be potentially associated with worse neurological outcomes (Table 2).

In a meta-analysis of all patients, greater odds of poor neurological outcome were identified for those who underwent delayed surgery (OR = 0.10, 95% CI = 0.02–0.62). Diabetes (OR = 3.46, 95% CI = 0.87–13.79), surgery (OR = 1.01, 95% CI = 0.40–2.59), and lumbosacral involvement (OR = 1.51, 95% CI = 0.23–9.79) were not independent predictors of either good or poor neurological outcome, but they did show nonsignificant trends toward better neurological outcomes. Cervicothoracic involvement (OR = 0.41, 95% CI = 0.15–1.09), and patients presenting with neurological deficits (OR = 0.88, 95% CI = 0.40–1.92) were also not independent predictors of either good or poor neurological outcome; however, they showed nonsignificant trends toward worse neurological outcomes. These findings are summarized in Figure 3.

Operatively Managed Patients

A total of 456 (56.4%) patients in this cohort received operative intervention for SEA. Univariate analysis determined that neurological deficit at presentation ($P=0.05$), thoracic location not otherwise specified ($P<0.01$), any thoracic involvement ($P=0.04$), and cervicothoracic involvement ($P=0.02$) were potentially associated with worse neurological outcomes. Lumbosacral involvement ($P=0.01$) was potentially associated with better neurological outcomes (Table 3).

A formal meta-analysis of patients undergoing surgical treatment revealed that lumbosacral involvement (OR = 3.13 95% CI = 1.11–8.87) was significantly associated with better neurological outcome. Cervicothoracic involvement (OR = 1.37, 95% CI = 0.27–6.91) showed nonsignificant trends toward better outcomes. Focal neurological deficit at presentation (OR = 0.45, 95% CI = 0.11–1.80) showed a nonsignificant trend toward worse neurological outcomes.

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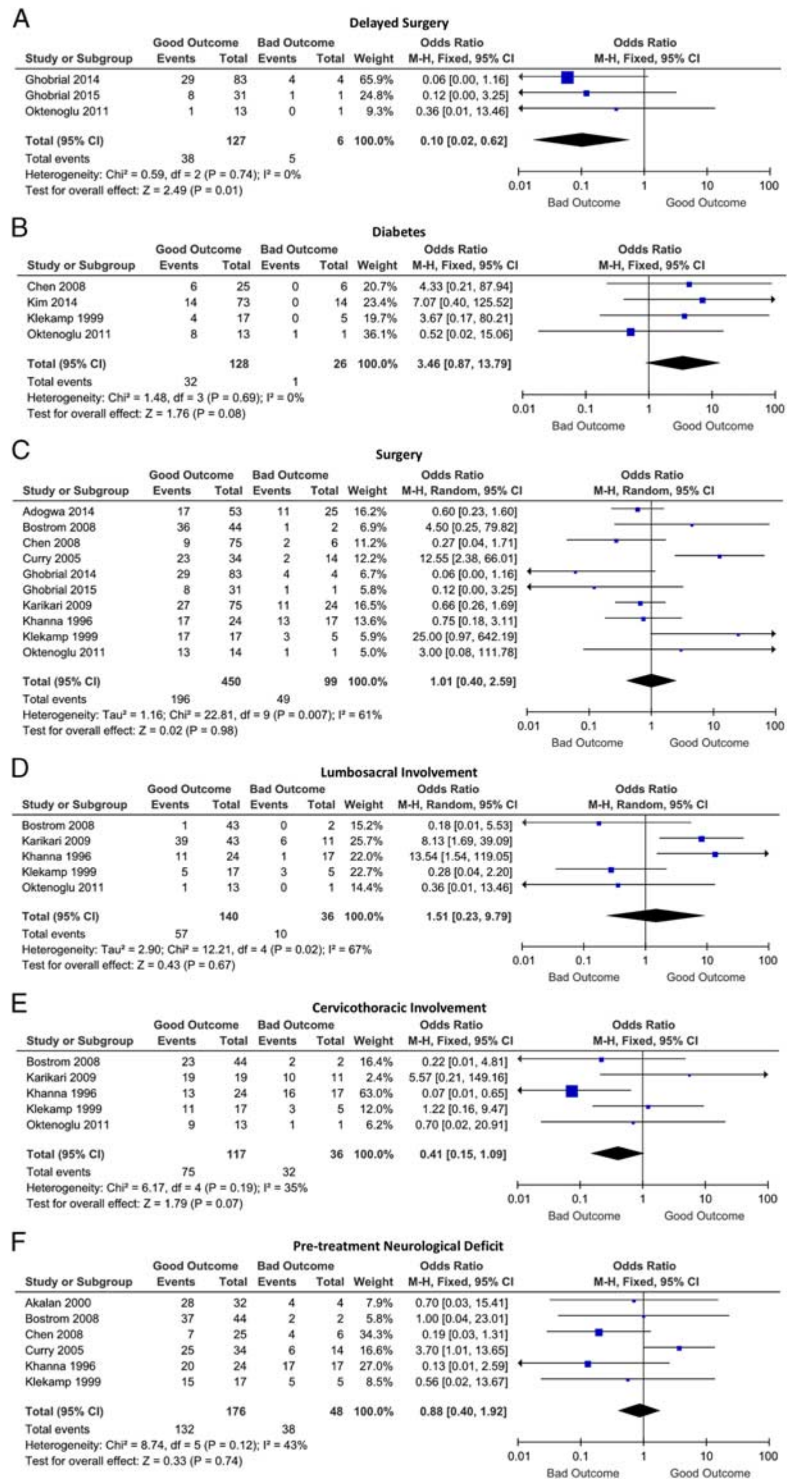

FIGURE 3. Forest plots showing meta-analysis results for all patients. CI indicates confidence interval; *df*, degrees of freedom; I^2, heterogeneity; M-H, Mantel-Haenszel. full color online

Conservatively Managed Patients

A total of 352 (43.6%) patients in this study received conservative management for SEAs. Univariate analysis determined that male sex ($P=0.04$), IV drug use ($P<0.01$), and MRSA ($P=0.02$) were potentially associated with worse neurological outcomes, while younger age ($P=0.03$) was potentially associated with better neurological outcome (Table 4).

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TABLE 1. Included Studies

References	Patients Included in Analysis
Chen et al[17]	31
Kim et al[3]	87
Ghobrial et al[18]	87
Curry et al[4]	48
Akalan and Ozgen[19]	36
Tacconi et al[20]	10
Wu et al[21]	41
Ghobrial et al[22]	40
Oktenoglu et al[23]	14
Uchida et al[24]	37
Chuo et al[25]	3
Nussbaum et al[26]	40
Tang et al[27]	33
Danner and Hartman[28]	3
Ugarriza et al[29]	11
Klekamp and Samii[30]	22
Karikari et al[31]	100
Adogwa et al[32]	78
Bostrom et al[33]	46
Khanna et al[34]	41
Total	808

Formal meta-analysis of patients undergoing conservative treatment showed that cervicothoracic involvement (OR = 1.82, 95% CI = 0.22–15.30) and diabetes (OR = 5.83, 95% CI = 0.70–48.59) showed nonsignificant trends toward better neurological outcomes. However, data from only 2 studies could be aggregated into the meta-analysis for this cohort and due to the lack of eligible studies, these were not included in the meta-analysis or conclusions.

DISCUSSION

Spontaneous SEAs can be morbid and potentially deadly conditions. Although some neurosurgical pathologies have well-described and evidence-based treatment guidelines, the current literature on SEAs is limited to case reports and small case series that are filled with equipoise.[12] As a result, existing data on SEA management are often contradictory and difficult to interpret and apply. Therefore, here, we provide the first quantitative meta-analysis of all available data from the past 30 years of conservative and surgical treatment of spontaneous SEAs. In doing so, we have generated the most up-to-date, large-scale analysis of all available data regarding the surgical and nonsurgical treatment of spontaneous SEAs.

Surgical Versus Conservative Management

Proper management of SEAs has proven highly controversial with no clear consensus on which method to use. To date, 3 options have been put forth—immediate surgery, medical or conservative therapy, and delayed surgery. For many years, immediate surgical decompression has been considered standard clinical practice.[31,32,35] However, advancements in antibiotic therapy and percutaneous drainage techniques have revitalized conservative management as a possible alternative. Medical or conservative therapy typically begins with aggressive hemodynamic resuscitation, maintenance of arterial blood pressures, and initiation of broad spectrum IV antibiotics.[36] Cultures from blood, urine, and/or Computed tomography-guided aspiration are typically obtained to aid in bacterial speciation and antibiotic selection.[37,38] Patients can then be closely followed for signs of neurological improvement and resolution of infection. For patients who fail conservative therapy, a third therapeutic option exists, namely "delayed" surgery to reduce the infectious burden. Multiple studies have examined the efficacy and safety of these various treatment modalities with no consensus to date.

As noted above, surgical therapy was the standard of practice for many years and thus multiple studies support its efficacy. For example, in a 2013 retrospective analysis of 77 patients undergoing prompt surgical or conservative treatment, Connor et al[2] demonstrated immediate surgical decompression to be a strong independent predictor of better neurological outcome at discharge. In another case series by Patel et al[39] in 2014, early surgery resulted in far better neurological outcomes when compared with those treated by medical therapy or delayed surgery. Furthermore, in a study of 127 patients by Kim and colleagues, only 57.5% of patients with SEA were successfully treated conservatively with IV antibiotics alone, which is inferior to surgical outcomes demonstrated by Nussbaum et al,[26] Danner and Hartman.[28] In contrast to these results, a 2004 series of 57 SEA cases treated with IV antibiotics and/or percutaneous drainage by Siddiq et al[9] demonstrated neurological outcomes similar to those of surgery regardless of comorbid illnesses, disease onset, or presenting neurological examination. A 2005 study of 24 conservatively managed SEA patients by Pereira and Lynch demonstrated that patients' initial neurological examination, not the treatment method, was the main predictor of neurological outcome.[5] Additional studies in 2005, 2006, and 2009 have also demonstrated comparable results between surgery and conservative therapies.[31,40,41] In short, the data are highly divided regarding which treatment modality is best.

Consistent with these previous studies, our analysis did not identify surgical intervention as an independent predictor of neurological outcome, suggesting an overestimated efficacy of surgery as a primary treatment for patients with SEAs. In this meta-analysis, surgical intervention resulted in good neurological outcome in 85.5% of patients who underwent surgery, which is similar to the success rate found by other studies[42–44]; however, surgery was only utilized as the treatment modality in 61.9% of all patients with good neurological outcome. These discoveries are contrary to the longstanding belief that operative intervention is associated with higher probability of good neurological outcome, and they suggest that a more careful case-by-case evaluation be utilized. A large, randomized-controlled trial with age and comorbidity-matched controls is undoubtedly necessary to help resolve this controversy.

Predictors of Good Neurological Outcome

Overall, 82.9% of patients included in this meta-analysis experienced good neurological outcome, defined as a ≥ 6 months postoperative neurological examination that was unchanged or improved compared with that at time of presentation. This percentage is similar to several previous case

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TABLE 2. All Patients

Category	Variables		N (%)		*P*
			Good Neurological Outcome	Poor Neurological Outcome	
	Total		670 (82.9)	138 (17.1)	—
Demographics	Age at presentation (mean ± SD) (N)		54.7 ± 16.7 (44)	57.0 ± 17.2 (6)	0.77
	Sex	Male	124 (76.1)	37 (80.4)	0.69
		Female	39 (23.9)	9 (19.6)	—
Comorbidities	Diabetes	Yes	57 (28.8)	1 (3.8)	**< 0.01**
		No	141 (71.2)	25 (96.2)	—
	IV drug abuse	Yes	4 (5.0)	0 (0)	1.00
		No	76 (95.0)	18 (100)	—
	Sepsis	Yes	7 (7.7)	10 (41.7)	**< 0.001**
		No	84 (92.3)	14 (58.3)	—
	Malignancy	Yes	25 (15.2)	4 (14.8)	1.00
		No	140 (84.8)	23 (84.2)	—
	Neurological deficit at presentation	Yes	161 (75.9)	39 (79.6)	0.71
		No	51 (24.1)	10 (20.4)	—
Cervical	Dorsal	Yes	5 (3.6)	0 (0)	0.59
		No	136 (96.4)	37 (100)	—
	Ventral	Yes	9 (6.4)	0 (0)	0.21
		No	132 (93.6)	37 (100)	—
	Both	Yes	1 (0.71)	1 (2.7)	0.37
		No	140 (99.3)	36 (97.3)	—
	Not otherwise specified	Yes	37 (26.2)	15 (40.5)	0.11
		No	104 (73.8)	22 (59.5)	—
	Any cervical involvement	Yes	52 (36.9)	16 (43.2)	0.57
		No	89 (63.1)	21 (56.8)	—
Thoracic	Dorsal	Yes	12 (8.5)	0 (0)	0.07
		No	129 (91.5)	37 (100)	—
	Ventral	Yes	6 (4.3)	2 (5.4)	0.67
		No	135 (95.7)	35 (94.6)	—
	Both	Yes	6 (4.3)	0 (0)	0.35
		No	135 (95.7)	37 (100)	—
	Not otherwise specified	Yes	34 (24.1)	19 (51.4)	**< 0.01**
		No	107 (75.9)	18 (48.6)	—
	Any thoracic involvement	Yes	58 (41.1)	21 (56.8)	0.10
		No	83 (58.9)	16 (43.2)	—
	Any cervicothoracic involvement	Yes	93 (66.0)	33 (89.2)	**< 0.01**
		No	48 (34.0)	4 (10.8)	—
Lumbosacral	Dorsal	Yes	15 (8.9)	0 (0)	**0.04**
		No	153 (91.1)	37 (100)	—
	Ventral	Yes	9 (5.4)	0 (0)	0.37
		No	159 (94.6)	37 (100)	—
	Both	Yes	7 (4.2)	0 (0)	0.36
		No	161 (95.8)	137 (100)	—
	Not otherwise specified	Yes	58 (34.5)	10 (27.0)	0.44
		No	110 (65.5)	27 (73.0)	—
	Any lumbosacral involvement	Yes	89 (53.6)	10 (27.0)	**< 0.01**
		No	78 (46.4)	27 (73.0)	—
	Surgery	Yes	390 (61.6)	66 (49.3)	**< 0.01**
		No	243 (38.4)	68 (50.7)	—
	Delayed surgery	Yes	54 (18.2)	5 (21.7)	0.78
		No	242 (82.8)	18 (78.3)	—
	Hardware placed during surgery	Yes	4 (25.0)	1 (100)	0.29
		No	12 (75.0)	0 (0)	—
Infectious agent	MSSA	Yes	42 (40.4)	4 (33.3)	0.76
		No	62 (59.6)	8 (66.7)	—
	MRSA	Yes	20 (19.2)	5 (41.7)	0.13
		No	84 (80.8)	7 (58.3)	—
	Other gram-positive bacteria	Yes	13 (12.5)	1 (8.3)	1.00
		No	91 (87.5)	11 (91.7)	—
	Any gram-positive bacteria	Yes	75 (72.1)	10 (83.3)	0.51
		No	29 (27.9)	2 (16.7)	—
	Any gram-negative bacteria	Yes	20 (19.2)	3 (25.0)	0.70
		No	84 (80.8)	9 (75.0)	—

(*Continued*)

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TABLE 2. All Patients (*continued*)

Category	Variables		N (%) Good Neurological Outcome	Poor Neurological Outcome	*P*
Postoperative complication	Neurological	Yes	1 (0.4)	2 (6.4)	**0.03**
		No	241 (99.6)	29 (93.6)	—
	Infectious	Yes	2 (0.8)	16 (51.6)	**< 0.001**
		No	240 (99.2)	15 (48.4)	—
	Other	Yes	5 (2.1)	2 (6.4)	0.18
		No	237 (97.9)	29 (93.6)	—

IV indicates intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.
Bold value indicates statistically significant result where $P < 0.05$.

series and reviews.[4,32,45,46] On univariate analysis, the authors found these outcomes to be positively correlated with diabetes, lumbosacral involvement, and operative management, but negatively correlated with thoracic abscess location and cervicothoracic location. However, none of these factors reached statistical significance in meta-analysis.

One potentially positive factor that warrants further discussion is lumbosacral involvement. The lumbosacral location is the most common location for SEA[47] owing to its larger epidural space and greater volume of infection-prone fat.[19,28,48] Because of the lumbosacral spine's larger canal diameter and presence of nerve roots instead of spinal cord, it has been postulated that there is longer time from abscess presentation to irreversible neurological damage.[34,49] In addition, the vascular supply provided by Batson plexus facilitates antibiotic delivery to the infectious focus.[50] When compared with abscesses located in the cervical or thoracic regions, which have a smaller canal diameter and contain the spinal cord, lumbosacral abscess location has been associated with better neurological outcome.[51,52] However, data supporting a potentially positive predictive value for lumbosacral location come from mostly small case series or reviews. In addition, there are other studies that have shown no correlation between abscess location and neurological outcome.[18,39,53] Although the authors of this manuscript believe cervical and thoracic abscesses are more dangerous and should warrant consideration for earlier surgery, this meta-analysis suggests an indeterminate impact of abscess location on neurological outcomes.

Predictors of Poor Neurological Outcome

Univariate analysis showed that pretreatment neurological deficits, cervicothoracic abscess location, and pretreatment sepsis was found to be likely associated with poor neurological outcome. However, meta-analysis did not show these factors to be significant predictors of outcome. Delayed surgery, however, reached statistical significance in meta-analysis as an independent predictor of poor neurological outcome, although the strength of this conclusion is limited because only 3 studies were eligible for inclusion. Although the impact of the delayed surgery meta-analysis result is limited due to a relative paucity of eligible studies, it is perhaps intuitive that patients who are deemed to need surgery and then experience a delay in surgical treatment would have worse neurological outcome. The findings thus support the established belief that patients who would benefit from surgical management should undergo prompt intervention.[54]

Although only trending toward significance in predicting poor neurological outcomes in this meta-analysis, cervicothoracic abscess location has been shown in previous small case series to be associated of worse neurological outcomes.[34,44] Oftentimes, patients with cervicothoracic SEA have atypical presentations and poorer baseline health status, which delay and complicate appropriate treatment.[55] However, as previously mentioned, our analysis suggests that the overall body of literature does not support a definitive link between location and neurological outcomes.[4,17]

Indications and Goals for Surgery

Although there is no consensus on operative candidates in SEAs, it is generally accepted that patients with acute or subacute neurological decline, failed medical management, and/or evidence of mechanical instability require surgical intervention.[54,56] Correspondingly, goals of surgery include neural decompression, abscess drainage, and/or mechanical stabilization of the spine.[7,57]

Removal of a compressive abscess is thought to improve vascular perfusion of the spinal cord and prevent ischemic damage.[58] This is typically achieved through posterior access surgery involving total laminectomy of affected levels, drainage of pus, debridement of all infected tissue, and copious irrigation with antibiotic-infused solution.[59] Some surgeons; however, suggest that hemilaminectomy with debridement can sufficiently decompress the neural elements.[60] More recently, Tan et al[61] and Safavi-Abbasi et al[56] successfully demonstrated minimally invasive transpedicular decompression as a viable alternative to open posterior decompression. Percutaneous abscess drainage with Computed tomography-guidance has also been shown as an effective method of abscess drainage and infection control.[37,62]

SEAs can also compromise spinal stability, which is typically evaluated using the Denis 3-column model.[63] In cases of spinal instability, instrumented fusion with allograft or autograft and bracing have shown some degree of success at restoring stability; however, most surgeons hesitate to place instrumentation near a demonstrated infectious process and only do so in cases of high preoperative infectious burden, preoperative malalignment, and/or a neurological deficit.[40,64–66] This meta-analysis did not show any

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TABLE 3. Surgical Patients

Category	Variables		n (%) Good Neurological Outcome	Poor Neurological Outcome	*P*
	Total		390 (85.5)	66 (14.5)	—
Demographics	Age at presentation (mean ± SD) (N)		55.7 ± 16.7 (35)	52.5 ± 20.3 (4)	0.78
	Sex	Male	80 (75.5)	23 (71.9)	0.65
		Female	26 (24.5)	9 (28.1)	—
Comorbidities	Diabetes	Yes	33 (40.2)	1 (16.7)	0.40
		No	49 (59.8)	5 (83.3)	—
	IV drug abuse	Yes	3 (5.1)	0 (0)	1.00
		No	56 (94.9)	14 (100)	—
	Sepsis	Yes	7 (9.6)	3 (17.6)	0.39
		No	66 (90.4)	14 (82.4)	—
	Malignancy	Yes	6 (9.2)	0 (0)	1.00
		No	59 (90.8)	6 (100)	—
	Neurological deficit at presentation	Yes	141 (88.1)	26 (100)	**0.05**
		No	19 (11.9)	0 (0)	—
Cervical	Dorsal	Yes	5 (4.8)	0 (0)	0.58
		No	99 (95.2)	25 (100)	—
	Ventral	Yes	6 (5.8)	0 (0)	0.60
		No	98 (94.2)	25 (100)	—
	Both	Yes	0 (0)	1 (4.0)	0.19
		No	104 (100)	24 (96.0)	—
	Not otherwise specified	Yes	16 (15.4)	6 (24.0)	0.37
		No	88 (84.6)	19 (76.0)	—
	Any cervical involvement	Yes	27 (26.0)	7 (28.0)	0.81
		No	77 (74.0)	18 (72.0)	—
Thoracic	Dorsal	Yes	12 (11.5)	0 (0)	0.12
		No	92 (88.5)	25 (100)	—
	Ventral	Yes	4 (3.8)	1 (4.0)	1.00
		No	100 (96.2)	24 (96.0)	—
	Both	Yes	4 (3.8)	0 (0)	1.00
		No	100 (96.2)	25 (100)	—
	Not otherwise specified	Yes	26 (25.0)	16 (64)	**< 0.01**
		No	78 (75.0)	9 (36.0)	—
	Any thoracic involvement	Yes	46 (44.2)	17 (68.0)	**0.04**
		No	58 (87.9)	8 (32.0)	—
	Any cervicothoracic involvement	Yes	64 (61.5)	22 (88.0)	**0.02**
		No	40 (38.5)	3 (12.0)	—
Lumbosacral	Dorsal	Yes	11 (10.3)	0 (0)	0.12
		No	96 (89.7)	25 (100)	—
	Ventral	Yes	6 (5.6)	0 (0)	0.59
		No	101 (94.4)	25 (100)	—
	Both	Yes	7 (6.5)	0 (0)	0.35
		No	100 (93.5)	25 (100)	—
	Not otherwise specified	Yes	27 (25.2)	5 (20.0)	0.80
		No	80 (74.8)	20 (80.0)	—
	Any lumbosacral involvement	Yes	51 (47.7)	5 (20.0)	**0.01**
		No	56 (52.3)	20 (80.0)	—
	Hardware placed during surgery	Yes	4 (26.7)	1 (100)	0.31
		No	11 (73.3)	0 (0)	—
Infectious agent	MSSA	Yes	18 (26.5)	0 (0)	0.33
		No	50 (73.5)	6 (100)	—
	MRSA	Yes	20 (29.4)	3 (50.0)	0.37
		No	48 (70.6)	3 (50.0)	—
	Other gram-positive bacteria	Yes	8 (11.8)	1 (16.7)	0.55
		No	60 (88.2)	5 (83.3)	—
	Any gram-positive bacteria	Yes	46 (67.6)	4 (66.7)	1.00
		No	22 (32.4)	2 (33.3)	—
	Any gram-negative bacteria	Yes	13 (19.1)	2 (33.3)	0.60
		No	55 (80.9)	4 (66.7)	—
Postoperative complication	Neurological	Yes	0 (0)	0 (0)	—
		No	145 (100)	10 (100)	—
	Infectious	Yes	2 (1.4)	3 (30.0)	**< 0.01**
		No	143 (98.6)	7 (70)	—
	Other	Yes	5 (2.8)	0 (0)	1.00
		No	141 (97.2)	10 (100)	—

IV indicates intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.
Bold value indicates statistically significant result where $P < 0.05$.

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TABLE 4. Conservatively Managed Patients

Category	Variables		n (%) Good Neurological Outcome	Poor Neurological Outcome	*P*
	Total		243 (69.0)	109 (31.0)	—
Demographics	Age at presentation (mean ± SD) (N)		50.9 ± 16.9 (9)	66.0 ± 1.4 (2)	**0.03**
	Sex	Male	44 (77.2)	14 (100)	**0.04**
		Female	13 (22.8)	0 (0)	—
Comorbidities	Diabetes	Yes	1 (4.8)	0 (0)	1.00
		No	20 (95.2)	4 (100)	—
	IV drug abuse	Yes	0 (0)	7 (100)	**< 0.01**
		No	18 (100)	0 (0)	—
	Sepsis	Yes	19 (19)	5 (23.8)	0.56
		No	81 (81)	16 (76.2)	—
	Malignancy	Yes	19 (19)	4 (20.0)	1.00
		No	81 (81)	16 (80.0)	—
	Neurological deficit at presentation	Yes	20 (38.5)	13 (56.5)	0.21
		No	32 (61.5)	10 (42.5)	—
Cervical	Dorsal	Yes	0 (0)	0 (0)	—
		No	37 (100)	12 (100)	—
	Ventral	Yes	3 (8.1)	0 (0)	0.57
		No	34 (91.9)	12 (100)	—
	Both	Yes	1 (2.7)	0 (0)	1.00
		No	36 (97.3)	12 (100)	—
	Not otherwise specified	Yes	21 (56.8)	9 (75.0)	0.32
		No	16 (43.2)	3 (25.0)	—
	Any cervical involvement	Yes	25 (65.6)	9 (75.0)	1.00
		No	12 (32.4)	3 (25.0)	—
Thoracic	Dorsal	Yes	0 (0)	0 (0)	—
		No	37 (100)	12 (100)	—
	Ventral	Yes	2 (5.4)	1 (8.3)	1.00
		No	35 (94.6)	11 (91.7)	—
	Both	Yes	2 (5.4)	0 (0)	1.00
		No	35 (94.6)	12 (100)	—
	Not otherwise specified	Yes	8 (21.6)	3 (25.0)	1.00
		No	29 (78.4)	9 (75.0)	—
	Any thoracic involvement	Yes	12 (32.4)	4 (33.3)	1.00
		No	25 (67.6)	8 (66.7)	—
	Any cervicothoracic involvement	Yes	29 (78.4)	11 (91.7)	0.42
		No	8 (21.6)	1 (8.3)	—
Lumbosacral	Dorsal	Yes	4 (6.6)	0 (0)	1.00
		No	57 (93.4)	12 (100)	—
	Ventral	Yes	3 (4.9)	0 (0)	1.00
		No	58 (95.1)	12 (100)	—
	Both	Yes	0 (0)	0 (0)	—
		No	161 (100)	12 (100)	—
	Not otherwise specified	Yes	31 (50.8)	5 (41.7)	0.75
		No	30 (49.2)	7 (58.3)	—
	Any lumbosacral involvement	Yes	39 (63.9)	5 (41.7)	0.20
		No	22 (36.1)	7 (58.3)	—
Infectious agent	MSSA	Yes	24 (66.7)	4 (66.7)	1.00
		No	12 (33.3)	2 (33.3)	—
	MRSA	Yes	0 (0)	2 (33.3)	**0.02**
		No	36 (100)	4 (66.7)	—
	Other gram-positive bacteria	Yes	5 (13.9)	0 (0)	1.00
		No	31 (86.1)	6 (100)	—
	Any gram-positive bacteria	Yes	29 (80.6)	6 (100)	0.57
		No	7 (19.4)	0 (0)	—
	Any gram-negative bacteria	Yes	7 (19.4)	1 (16.7)	1.00
		No	29 (80.6)	5 (83.3)	—
Postoperative complication	Neurological	Yes	1 (1)	2 (9.5)	0.08
		No	96 (99.0)	19 (90.5)	—
	Infectious	Yes	0 (0)	13 (61.9)	**< 0.001**
		No	97 (100)	8 (38.1)	—
	Other	Yes	1 (1)	2 (9.5)	0.11
		No	96 (99.0)	19 (90.5)	—

IV indicates intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.
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relationship between surgical fusion and outcomes, which reflects the literature's current ambiguity regarding intraoperative decision making and neurological outcomes.

Study Limitations

The usage of retrospective studies in a meta-analysis contains multiple inherent limitations.[67] Although this 808 patient meta-analysis is the largest known data set describing outcomes following treatment for SEA, not all variables were reported for each patient. Accordingly, the analysis of each variable consisted of only a subset of the entire study group, and lack of published information regarding certain variables prevented analysis of certain subgroups at all. For example, in this manuscript, agents not identified as MSSA, MRSA, or other gram-positive or gram-negative agents were placed into the "another agent" category for analysis. It is likely that, given the statistical nonsignificance of infectious agent on clinical outcome, further delineation between pyogenic and nonpyogenic sources (ie, tuberculosis) would also not reach statistical significance due to inadequate power.

Another limitation of this type of analysis comes from the binary division of outcomes into "good" and "poor." In this study, a "good" outcome is defined as a stable or improved postoperative neurological examination, whereas a "poor" outcome is defined as a worsened examination. Unfortunately, this means that some patients who present neurologically devastated are still considered to have "good" outcomes if they remain the same postoperatively. Although it may seem counterintuitive to think that potentially paralyzed patients who remain paralyzed experienced a "good" outcome, it is important to recognize that oftentimes it is impossible to reverse neurological injury that has already occurred (ie, if the infection has already caused a spinal infarction, or if the injury is not acute upon presentation). Although the ideal outcome (conservative or operative) for anyone with a SEA is resolution of disease, mechanical stability, and complete recovery of any neurological deficit, the realistic expectation is that neurological status is stabilized and disease burden is eliminated. The authors thus believe that patients who are stabilized from a neurological and infectious perspective are most appropriately categorized as "good" neurological outcomes. By changing the definition of neurological outcomes to include functional status (ie, activities of daily living or Karnofsky Performance Scores), it becomes increasingly difficult to incorporate individual studies that otherwise do not include these data in their reported results (ie, ASIA scales), thus reducing the power of the meta-analysis. This is further evidence for the need for a well-powered, prospective study that could potentially examine the difference between improved, stabilized, and/or worsened neurological examinations, as well as functional status, as primary outcome measures.

These limitations are not novel to this manuscript, as all meta-analyses relying on previously published data suffer from similar constraints.[68] In addition, relying only on published data makes this analysis susceptible to positive skew from publication bias, as important but negative relationships or lack of associations are less likely to have been published.[69] In the absence of large prospective, randomized, controlled trials, our methodology allows us to capture the largest available data set for analysis of neurological outcomes and prognostic factors after treatment of spontaneous SEAs.

Another limitation of this study comes from the query of only 1 database; however, PubMed is one of the largest and most comprehensive literature repositories and was able to yield over 1660 relevant titles before the application of study-specific inclusion and exclusion criteria. Future work can consider inclusion of other databases. Moreover, this study excluded iatrogenic SEAs, as these are often treated differently. It would be worthwhile for future studies to determine whether similar prognostic indicators exist for this subset of patients.

Furthermore, this manuscript also draws from literature published by multiple surgeons and neurointensivists from multiple hospitals and countries. Although the overall treatment methods and surgical techniques are similar, small differences in treatment timing, empiric antibiotic coverage, patient comorbidities, diagnostic modalities, and surgical technique may all have varying levels of impact on neurological outcomes. Moreover, this study utilized manuscripts published over 35 years during which time the evolution of SEA pathophysiology and standard-of-care practice has changed dramatically; however, as shown in Figure 2, neurological outcomes have remained statistically similar across all years of data inclusion.

CONCLUSIONS

Contrary to common belief, our study shows that the cumulative literature published over the past 35 years does not definitively support or oppose surgical intervention in all cases of spontaneous SEA. Therefore, the decision to operate must be made on an individual case-by-case basis with the goals of preventing neurological decline, obtaining source control after failed conservative treatment, or restoring spinal stability. Delaying surgery seems to be an independent predictor of poor neurological outcome, especially in the setting of a neurological deficit, and the decision to operate should not be delayed in cases of active neurological decline. Furthermore, while cervicothoracic location likely portends a worse outcome that should prompt strong consideration for early surgical intervention, there is a paucity of data to support this conclusion. Therefore, a large, prospective, randomized, controlled trial comparing surgical and conservative treatment for SEAs is indicated to properly assess for factors that might affect surgical decision making and/or improve neurological outcomes in these patients.

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