



## SYSTEMATIC REVIEW

# Severity and Outcomes of Neurologic Deficits Associated with Pyogenic Spondylodiscitis: A Systematic Review

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## Abstract

**Introduction:** Patients with advanced pyogenic spondylodiscitis can present with neurologic deficits, however, the prevalence, severity, and outcome of the neurologic deficits are not well known. A systematic review was performed to improve knowledge of this commonly encountered clinical scenario.

**Methods:** A comprehensive search of databases including PubMed, Science Direct and Google Scholar from 2000-2020 was performed. From 1478 articles, 75 were screened and 40 included. As the most commonly used classification for neurologic status was Frankel grading, we categorized the various neurologic findings corresponding to Frankel's descriptions. Results of treatment were expressed as complete recovery, partial recovery, unchanged, or deterioration.

**Results:** Among 3197 patients with pyogenic spondylodiscitis, 1314 cases showed a variety of neurologic manifestation: 415 (32%) presented with subjective symptoms including radicular pain, sciatica or numbness, 899 (28%) were diagnosed with a significant neurologic deficit on initial presentation. Patients with Frankel A/B deficits (N = 286, 22%) had the lowest proportion with complete recovery (16%) and the highest proportion to remain unchanged after treatment (34%). Patients with Frankel C deficits (N = 333, 25%) were more likely to have complete recovery (29%), although the majority had only partial recovery (53%), or remained unchanged (16%). Patients with Frankel D deficits (N = 280, 21%) were the most likely to experience complete recovery (53%) with a similar number of patients exhibited partial (25%) or no recovery (20%). A small percentage (2%) of patients in each Frankel group deteriorated after treatment. The comparison of neurologic outcome in the

non-surgically treated (n = 97) versus surgically treated (n = 449) patients revealed that surgical intervention was associated with improved neurologic recovery (R = - 0.205, p < 0.000).

**Conclusion:** The considerable number of neurologic deficits in addition to their poor recovery even after surgical intervention demonstrates that early diagnosis of pyogenic spondylodiscitis is crucial. Prompt surgical intervention is likely associated with improved neurologic recovery when compared to non-surgical treatment.

## Keywords

Osteodiscitis, Spondylodiscitis, Neurologic impairment, Neurologic deficit

## Introduction

Spondylodiscitis is the most common form of hematogenous osteomyelitis in patients aged > 50 years and represents 3%-5% of all cases of osteomyelitis [1]. Recently, the incidence of vertebral osteomyelitis has increased because of improved accuracy of diagnosis in addition to the rise in susceptible patients including diabetes mellitus, intravenous drug users, patients undergoing hemodialysis, and immune compromised hosts [2].

Neurological symptoms associated with spondylodiscitis have been reported with varying incidence, ranging from dyesthesia and radicular pain to complete paraplegia [3]. Previous studies have shown that neurological deficits develop because of epidural

abscesses or a pathological fracture. Furthermore, the severity of neurologic symptoms is correlated with delayed diagnosis, older age, virulence of the offending organism, and presence of co-morbidity. The purpose of this study is to report on the severity of neurologic impairment in spondylodiscitis patients and identify factors associated prognosis and neurologic recovery.

## Methods

A comprehensive search of different databases including PubMed, MEDLINE, Science Direct and Google Scholar from 2000 to 2020, was performed. The

searched keywords included “Vertebral Osteomyelitis” OR “Osteodiscitis” OR “Pyogenic Spondylodiscitis” AND “Neurologic Impairment” or “Neurologic Deficit”. Manual search of reference lists from relevant papers and guidelines was performed.

Initially 1478 articles were collected and their abstracts were screened. Seventy-five articles were selected based on inclusion and exclusion criteria. After comprehensive review of full texts, 40 studies which contained detailed neurologic exams and were eligible for systematic review (Table 1).

**Table 1:** Contributing studies.

Study	Sample size	Age, year, mean (SD)	Male, N	Multi-level, N	Delayed treatment, days, mean (SD)	Epidural abscess, N
Asamoto [4]	27	56	15	2	-	17
Ascione [5]	30	64	13	0	48	-
Bernard [6]	359	61	250	39	34	-
Bettini [7]	56	47.8	21	6	50	3
Cervan [8]	23	67	15	2	49	14
ChinPea [9]	48	66.8	19	0	120	35
Hoh [10]	24	59	13	-	-	-
Dimar [11]	42	60	29	2	14.4	1
Dragsted [12]	65	60	45	3	6	384
Kim [13]	355	60	211	83	-	355
Elsaid [14]	19	43.8	12	0	11.7	15
Erick [15]	110	60	67	12	39	-
Gupta [3]	260	67	163	0	32	158
Hadj- pavlou [16]	101	46	76	0	-	39
Heyde [17]	20	59.7	9	3	90	12
Karadimas [18]	163	56	101	141	48	-
Lee [19]	51	60	32	17	-	28
Livorsi [20]	35	53	30	13	-	26
Martin Mc. [21]	253	60	160	20	54	43
Masuda [22]	5	63.8	2	0	62	2
Matsubara [23]	52	70	31	0	-	30
Mavro-genis [24]	153	57	93	3	-	-
Nolla [25]	64	59	36	3	48	39
Ozkan [26]	21	65	12	1	-	-
Robach [27]	135	59	85	0	-	46
Rosinsky [28]	16	68	9	2	10	2
Schinkel [29]	32	61	18	5	44	19
Schuster [30]	47	49	33	12	-	33
Shiban 1 [31]	113	65	78	28	-	33
Shiban 2 [32]	25	66	14	0	-	11
Shousha [33]	30	64.5	19	11	-	24
Siddiq [34]	57	56	33	27	-	57
Sobottke [35]	32	74.9	21	12	65	12
Curry [36]	48	61	30	1	7	48
Urrutia [37]	102	65	74	34	-	11

<b>Valacius [38]</b>	196	59	106	12	52	60
<b>Woergen [39]</b>	62	64	35	14	-	8
<b>Yoshimoto [40]</b>	45	65	-	2	-	-
<b>Zarrouk [41]</b>	29	58	-	4	29	19
<b>Dennis [42]</b>	84	62	49	47	-	-

**Table 2:** International Standards for Neurological Classification of Spinal Cord Injury ASIA (ISNCSCI)\*\*.

#### **A = Complete**

There is no motor function or sensation preserved in sacral segments S4-5.

#### **B = Sensory Incomplete**

Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-5 (light touch or pin prick at S4-5 or deep anal pressure) AND no motor function is preserved more than three levels below the motor level on either side of the body.

#### **C = Motor Incomplete**

Motor function is preserved below the neurological level and more than half of the key muscles below the NLI have a muscle grade less than 3\*.

#### **D = Motor Incomplete**

Motor function is preserved below the neurological level and at least half of the key muscle functions below the NLI have a muscle grade of at least 3 or higher\*.

#### **E = Normal**

Once sensation and motor function are graded as normal in all segments in a person with prior deficits, they are given an AISA of E. A person without an initial SCI does not receive an AISA grade.

\*It is important to recognize that for a patient with a grade of C or D, they must either have voluntary anal contraction or sacral sensory sparing with sparing of motor function more than three levels below the motor level for that side of the body;

\*\*Certain clinical pearls when using ISNCSCI include the followings:

- Both key and non-key muscle functions can be used to determine motor incomplete status (differentiation between AISA B from C).
- When distinguishing between a sensory incomplete versus a motor incomplete (AISA B from C) injury, the MOTOR LEVEL on each side is used. When distinguishing between motor incomplete injuries (AISA C from D), the SINGLE NEUROLOGICAL LEVEL is used. (Reference for the ASIA score)

### **Study selection criteria**

The inclusion criteria were: 1) Studies on pyogenic spondylodiscitis; 2) Adult patients with confirmed spondylodiscitis who had been treated conservatively or surgically; 3) The series with objective neurologic exam before and after an appropriate treatment; and 4) Studies published in English. Non-pyogenic spondylodiscitis, animal studies, iatrogenic infections and the articles lacking specific description of neurologic findings were excluded.

### **Data extraction**

The extracted data from each study consisted of number of patients, mean age, gender distribution, location of involved levels, period before appropriate treatment was instituted, presence of epidural abscess, neurologic status at presentation and at final follow up.

### **Data analysis**

Data collection and analysis were performed using Microsoft Excel® 2010 and the statistical software was used. Data distribution was assessed and continuous

variables were compared using unpaired t test, Wilcoxon rank sum test. A p value < 0.05 was considered statistically significant. To assess the correlations, the Fischer exact test was used. The neurologic outcome of the medically treated patients was compared with surgical group. Pooling of data within the subgroups was done using weighted averages based on the sample size.

### **Classification of neurologic manifestations and sequelae**

The neurologic status and sequelae was expressed by various statements in the different articles. However, the most common applied classification for neurologic deficits was Frankel grading, which is similar to international standards for neurological classification of spinal cord injury (ISNCSCI) designed by the American Spinal Injury Association (ASIA) (Table 2).

We proposed certain equivalents for the Frankel grading in order to classify the reported neurologic status. Conditions described as “severe or marked”, “paraplegic or tetraplegic or quadriplegic”, “paralysis”,

“complete cord”, “myelopathy” and “cauda equina” were considered equivalent to Frankel grade A and B. The reported physical exams did not allow to easily distinguish between Grade A and Grade B. The neurologic manifestation described as “moderate”, “paresis”, “foot drop” and “incomplete cord” were considered equal to Frankel grade C. Reported symptoms such as “mild”, “minimal” and “weakness” were considered equal to Frankel grade D. The “pure sensory problems”, “only numbness”, “radicular pain” and “sciatalgia” were classified as equal to Frankel grade E. The neurologic results of treatment, medically or surgically, were classified as complete recovery (regain normal sensory and motor functions), partial recovery (one or two grade improvement in the motor functions), unchanged or deterioration (worsening of neurologic status).

## Results

### Study characteristics and limitation

As almost all the articles assessed neurologic outcomes retrospectively, the bias and limitation associated with retrospective analysis are also present in this study.

### Demographic data

3236 patients with pyogenic spondylodiscitis were included with a mean age 60.3 years. There were 1,966 males (62%) out of 3,162 reporting gender data. There was a mean treatment delay of 56.24 days in 1828 cases with onset of symptoms prior to treatment initiation.

In addition, there was multi-level involvement in 513 (16%) of 3212 patients. The most common location of vertebral infection was lumbar and thoracolumbar spine (60%), followed by thoracic spine (27%), and then cervical spine (13%). The incidence of concomitant epidural abscess in the patients with neurologic deficit was 53% (1228 in 2331). The articles studying only cervical spondylodiscitis demonstrated higher risk of neurologic symptoms (52%, 37 of 71 cases) and a higher frequency of epidural abscess formation (72%, 36 of 50 cases) in comparison to the non-cervical involvement.

### Neurologic manifestations and sequelae (Table 3)

Among 3236 spondylodiscitis cases, 1314 patients had a variety of neurologic manifestation: 415 (32%) presented with subjective symptoms including radicular pain, sciatica or numbness, whereas 899 cases (68%) had a significant neurologic deficit defined as Frankel A,B,C or D.

Although the Frankel A & B, the most severe subtypes of neurologic deficits, constituted a smaller group (22%) of patients, they showed the lowest possibility for complete recovery (16%,  $p < 0.001$ ) in addition to the highest risk to remain unchanged after treatment (34%).

The majority of Frankel C (N = 333) had partial recovery (53%) whereas 29% had complete recovery. A remarkable number of Frankel D (N = 280) exhibited complete recovery (53%) with almost an equal number of patients had partial (25%) or no recovery (20%). Approximately 34% of patients with neurologic symptoms (n = 449) promptly underwent surgery after confirmation of diagnosis. Whereas, 353 patients (27%) sustained surgical intervention between 1-14 months after diagnosis.

We compared the outcome of neurologic impairment in the patients who were treated non-surgically (n = 97) with the patients who underwent surgical procedure initially (n = 449). Surgical intervention was associated with a higher rate of neurologic recovery (R = -0.205,  $p < 0.000$ ).

## Discussion

The current study highlights the relatively poor prognosis of neurologic deficits associated with pyogenic spondylodiscitis. Delays in diagnosis and treatment can lead to progressive infection that spreads into the spinal canal resulting in epidural abscess formation [43,44]. The compressive effects of epidural abscesses cause severe pain in addition to myelopathy and radiculopathy [45]. In addition, associated ischemia and infarction of the spinal cord can aggravate the neurological status. Furthermore, vertebral bone destruction and secondary spinal instability potentially exacerbates canal compromise beside neurologic compression [46].

The rate of neurologic compromise has been reported from 7% by Hadjipavlou up to 57% by Curry Jr, et al. At least a simple extremity weakness manifests in 79% of patients with neurologic impairment, according to Butler study [8,16,36,47]. Aneta, et al. reported neurological symptoms in 1/3 of the cases and ranged from radicular pain to radicu lopathy (29%) to paresis (2-13%) and cauda equina syndrome. (10%) [48]. Current systematic review demonstrated radicular pain and absence of motor deficit in 32% of patients with neurologic findings. However, significant motor deficits occurred in 68% of patients consisted of 22% Frankel A & B, 25% Frankel C and 21% Frankel D.

**Table 3:** Neurologic recovery stratified by Frankel Grade.

	Complete recovery	Partial recovery	Unchanged	Deteriorated	Total
Frankel A&B	45 (16%)	137 (48%)	98 (34%)	6 (2%)	286 (22%)
Frankel C	97 (29%)	178 (53%)	53 (16%)	5 (2%)	333 (25%)
Frankel D	149 (53%)	71 (25%)	55 (20%)	5 (2%)	280 (21%)
Total	291 (32%)	386 (43%)	206 (23%)	16 (2%)	899

The relatively high percentage of Frankel A & B case that were paraplegic or had a cauda equina syndrome might be attributed to the age, delayed diagnosis, epidural abscess formation, multi-level involvement, or cord level involvement. The roles of these factors in development of neurologic impairment were assessed:

- 1) **Age:** In the past decades, the most frequently affected people were elderly patients who more often experience multiple co-morbidities and are subject to drug-resistant organisms, particularly MRSA [45]. However, the current study demonstrated a drift of neurologic symptoms to the younger ages (range: 43-70 years, median: 60.3 years), that is high likely attributed to the increased number of IV drug user patients
- 2) **Delayed diagnosis:** The delayed diagnosis of spondylodiscitis, reported between 1 and 6 months, has significant impact on the natural history and the neurological outcome. This systematic review confirmed the high possibility of delayed diagnosis in the spondylodiscitis patients with neurologic deficit, roughly 56.2 days (from 10 to 120 days). The diffuse and non-specific back pain, commonly absence of constitutional symptoms, inconclusive or late responding lab tests, late appearance of radiographic features, and general tendency to attribute the back pain to the degenerative changes particularly in older patients, all lead to delayed diagnosis. Delayed treatment often facilitates the “break out” of the infection into the adjacent tissues planes including the epidural space, the psoas muscles, paraaortic/retroperitoneally in the abdomen, retropharyngeally in the neck, and paravertebral and retroplural in the chest along with the development of sepsis. The infection spreads from the disc space into any available space which explains the frequency of epidural abscess formation in the patients with spondylodiscitis. Another important consequence of the delay in diagnosis of spondylodiscitis is the progression of bony destruction that leads to progressive destruction of the endplates, the trabecular bone of the vertebra and progressive collapse and segmental kyphosis leading to instability [47,48].
- 3) **Epidural abscesses formation:** It has been commonly reported in the patients with significant neurologic deficits, leading to myelopathy, radiculopathy or back pain. In this systematic review, the epidural abscess was found in 56% of spondylodiscitis cases with neurologic symptoms. The frequency of the development of epidural abscesses may in fact be the primary cause of the frequently encountered neurologic symptoms encountered with spondylodiscitis [16].

**4) Multi-level involvement:** The most common location of vertebral osteomyelitis has been reported in the lumbar, then thoracic, and then cervical area, respectively. Multi-level involvement has been reported in 3-13% of patients [16,49]. We found the distribution of spinal infection resembling the previous studies and the likelihood of multilevel involvement was approximately 16%. Presumably, multiple episodes of sepsis particularly in IV drug users can explain the frequency of multilevel spondylodiscitis associated with neurologic involvement.

**5) Cord level involvement:** This review supports a higher level of risk of a neurological deficit when the spondylodiscitis involves the cervical or thoracic spine. The presence of a spondylodiscitis infection in the cervical spine is relatively uncommon but the severity of neurologic compromise and the incidence of concomitant epidural abscess is higher than thoracic or lumbar involvement [33]. This study also confirmed neurologic deficit in 52% and epidural abscess in 72% of cervical spondylodiscitis cases.

Conventional treatment of spondylodiscitis is consisted of administration of appropriate antibiotics for 6-12 weeks and surgical intervention in the circumstances with failure of conservative treatment [43,47,50]. However, great diligence must be maintained during conservative treatment since rapid progression of bony destruction, instability, segmental kyphosis, and a neurological deficit will demand abandoning antibiotic therapy alone and require surgical debridement. Neurologic compromise has led to several authors suggesting different treatments. Yoshimoto, et al. evaluated the result of conservative treatment in paralysed patients who were not able to undergo surgery due to poor general condition. He discovered that paralysis improved in 73% of these patients with nonoperative treatment [40]. Cheung, et al. believe that only 10-20% of patients suffering from pyogenic spondylitis require open surgery. He also expressed that surgical decompression can improve the prognosis for neurological recovery much better than non-operative management [51]. Graeff, et al. pointed out that epidural abscess, multilevel osteomyelitis, or diabetes escalate the risk of conservative treatment failure [52]. McHenry MC, concluded that in the patients with neurologic compromise, the outcome of surgery was favorable in nearly 70%; even better results was achieved in the absence of diagnostic delay [21]. Zarghooni, et al. reported persisted motor deficit in 30% and hypaesthesia in 90% after surgical intervention but the quality of life and patients' satisfaction was higher in the surgical treated group of patients. Lerner, et al. identified an improvement of neurological deficits

for 76% after surgery while 20% showed no change [53]. Hadjipavlou, et al. demonstrated that only 23% of patients with paralysis on admission recovered completely after surgical decompression [16].

In contrast to the previous authors, we compared the frequency and outcome of different Frankel's grades. Approximately 27% of conservatively treated deficits experienced failure of treatment and underwent surgical approach from 1 to 14 months after diagnosis. Furthermore, 34% of patients with neurologic symptoms required prompt surgery because of severe (Frankel A or B) or progressive neurologic impairment.

## Conclusion

Due to remarkable number of severe neurologic deficits in addition to their poor recovery even after surgical intervention, it is crucial to establish diagnosis of pyogenic spondylodiscitis in a timely manner. Surgical treatment, performed in an appropriate time, high likely is associated with a higher neurologic recovery rate in pyogenic spondylodiscitis.

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