

A systematic review: characteristics, complications and treatment of spondylodiscitis

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Abstract. – OBJECTIVE: This systematic review focuses on 5 key elements that may improve the decision-making process in spondylodiscitis: the infective agent, segmental instability, abscess development, neurological compromise and focus of infection.

MATERIALS AND METHODS: We included 64 studies published between May 2012 and May 2017, that reported both a description of the discitis and comparative data regarding the disease and its complications.

RESULTS: The majority of cases were caused by *Staphylococcus spp* (40.3%) and involved the lumbosacral region (52.3%). 27.8% of cases were associated to neurological compromise, 30.4% developed an abscess, 6.6% were associated to instability, and 54.7% underwent surgery. The abscesses mostly involved the lumbosacral region (60.4%) with paravertebral localization; 32.6% of cases involved the thoracic region, showing mostly epidural localization; a small number of cases (7%) involved the cervical region, mostly with epidural localization. 95% of paravertebral abscesses were treated percutaneously, while 85.7% of epidural cases underwent “open” surgery. Spinal cord compression mainly occurred in the cervical region (55.9%), neurological deficit was observed in over half of cases (65%), and surgery was required in most of the cases (83.9%). The majority of cases of instability involved the lumbosacral region (53.3%) and underwent surgery (87%). The focus of infection was mostly lumbosacral (61%) and almost all cases (95%) were treated surgically.

CONCLUSIONS: Spondylodiscitis is a complex and multifactorial disease, whose diagnosis and management are still challenging. Due to its potential morbidity, it is extremely important to investigate the 5 key elements discussed in this paper in order to provide an early diagnosis and initiate the most effective treatment.

Key Words

Spondylodiscitis, abscess, spine infection, neurological instability

Introduction

Spondylodiscitis is an inflammation of the vertebral bodies and the intervertebral disk space. It is a complex disease of multifactorial etiology and requires a multidisciplinary approach in order to determine the most appropriate surgical treatment¹⁻³. The annual incidence in western countries ranges widely from 0.4 to 2.4 per 100,000⁴. In many cases, injury of the motor segment may lead to instability, reduced mobility, and nervous structures compression, requiring surgical stabilization^{5,6}. The clinical practice guidelines of the Infectious Diseases Society of America (IDSA) identify 5 key elements that may help to improve the decision-making process in patients affected by spondylodiscitis: the infective agent, segmental instability, abscess development, neurological compromise and focus of infection⁷. These elements are widely connected to each other and they can exist together.

The severity of infection in a patient with spondylodiscitis is closely related to pathogenicity and virulence of the infectious agent, systemic involvement of the disease and whether the infection originated from visceral organs (cardiac, gastrointestinal or odontostomatological origin).

During the first phase of the disease, it is critical to isolate and correctly identify the causative pathogen, in order to initiate the most appropriate antibiotic therapy⁷⁻⁹.

Segmental instability refers to the degeneration of the motion segment, causing bone damage and altering the integrity of the ligamentous structures surrounding the disc. It can produce three effects: pain, direct dissemination of pathogens as consequence of the hypermobility and compression of neurological structures⁵⁻⁷.

An *abscess* is a collection of pus that can be localized either at the canal region compressing

the nervous structures (spinal epidural abscesses) or in the paravertebral region compressing the lumbar plexus (psoas abscess)^{7,10,11}.

Neurological compression can either be the consequence of instability or may be related to the persistence of epidural abscesses⁷⁻¹².

Finally, the *focus of infection* is the location of the disease, where the infected tissue often creates a sort of capsule that is difficult to eradicate with antibiotic therapy alone. In the case of a parasitic infection, this tissue can create a real mass effect⁷⁻¹³.

Materials and methods

Data Source

Studies were identified by searching electronic databases and scanning reference lists of articles. This search was applied to MEDLINE, EMBASE, and CINAHL using the following keywords: spondylodiscitis, abscess, spine infection, neurological instability, and neurological impairment.

Additionally, manual searches of the reference lists of included studies, reviews, and guidelines on spondylodiscitis were performed. The PRISMA statement was consulted throughout this systematic review¹⁴.

Study Selection

The literature search was conducted independently and in duplicate by 2 investigators (GD and GF). The same authors independently selected potentially eligible studies for inclusion. Disagreements between the reviewers were resolved by consensus; if no agreement could be reached, it was planned that a third senior author (LG) would decide.

Data Extraction

The studies, screened according to the selection criteria reported above, were included if they met the following criteria: 1) A description of the discitis was reported; 2) Comparative data investigating the relationship between spondylodiscitis and abscess, neurological impairment, neurological instability and focus infection were provided; 3) They were published between May 2012 and May 2017. All selected studies were either case series, case report, cross-sectional, prospective, observational, case-control or cohort studies. However, our search was limited to articles written in English.

We developed a data extraction sheet, pilot-tested it on three randomly-selected included studies, and refined it accordingly. The data used for this

review were then extracted from selected studies and entered in a data extraction form by one investigator (FDR): author, study design, study year, participants, outcomes, and country. A second investigator (FC) checked the extracted data to ensure accurate reporting. Disagreements were resolved by discussion between the two investigators; if no agreement could be reached, it was planned that a third investigator would decide (MG).

Results

A total of 3583 articles were found in the databases and through additional searching. Out of these, 570 duplicates were removed. The flow chart of paper selection is reported in Figure 1.

A total of 64 articles are included in this review: 27 observational retrospective studies, 25 case reports, 8 case series (2 of which are retrospective), 1 case-cohort study, 1 clinical study, 1 case-control study, and 1 retrospective cohort study. 34 studies were conducted in Europe, 24 in Asia, 4 in the United States, 1 in Africa and 1 was multicenter (supplementary table I with complete data is available online).

The collected data was aggregated into 5 groups and analyzed according to the type of causative agent, site of abscess, site of spinal cord compression (with or without neurological compromise), site of instability, intervention strategy and focus of infection.

Starting from these data, we will provide a descriptive analysis of the studies included and investigate the different patterns of spondylodiscitis.

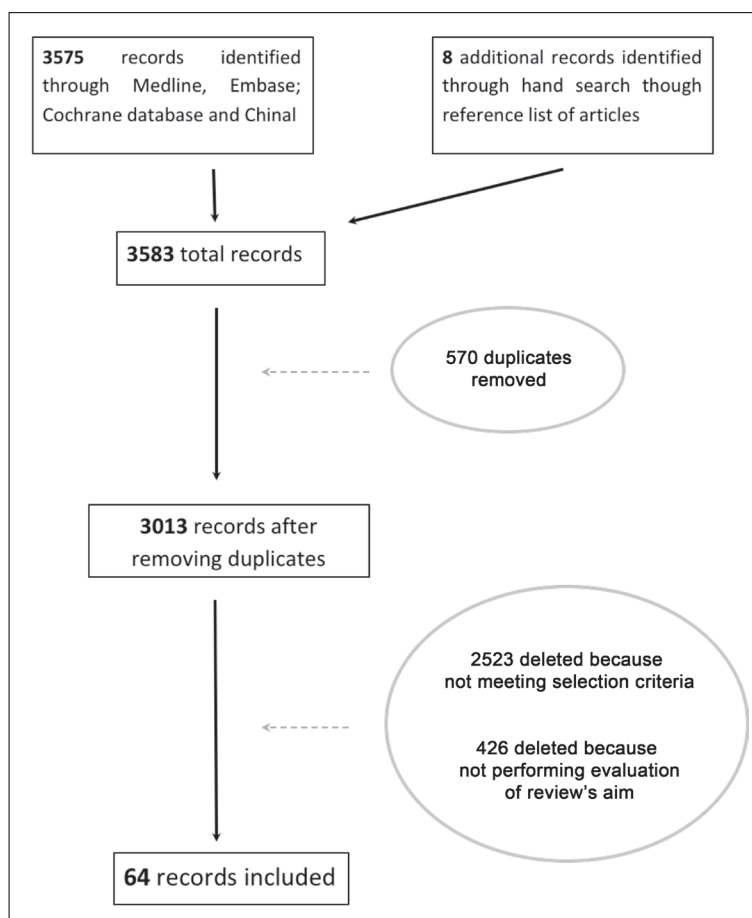
Characteristics of Infection and Complications

25 different studies^{1,11,15-37} focused on the type of causative pathogen (Table I) and its complications. 1756 cases of spondylodiscitis were analyzed, 56% of cases were males and 38% females, with mean age 59.6 years.

Microbiology data was available for 1060 cases. Of these, 40.3% were found to be caused by *Staphylococcus spp*, 30.9% were caused by *Mycobacterium Tuberculosis*, 28.3% by other bacteria. Only a minority of cases had a fungal (0.5%) or viral (0.1%) etiology. No cases of parasitic infection were reported.

Regarding the site of infection, 52% of cases (919) involved the lumbosacral region, 22% the cervical region (384) and 26% the thoracic region (461).

As for the complications of spondylodiscitis, 27.8% of cases (488) were associated to neurolog-

Figure 1. Systematic selection of studies on spondylodiscitis

ical compromise, 30.4% (534 cases) developed an abscess, and 6.6% (116 cases) were associated to instability. 54.7% of cases (961) underwent surgery.

Spinal Abscesses

17 studies about spondylodiscitis complicated by abscess^{13,38-53} were analyzed (Table II), for a total of 43 cases with a similar proportion of males and females, and mean age of 65 years.

Concerning the site of spinal abscesses, the majority of them (60.4%, corresponding to 26 cases) involved the lumbosacral region, 32.6% (14 cases) the thoracic region and only a small number of abscesses (7%, 3 cases) involved the cervical region.

The characteristics of lumbosacral abscesses were analyzed, and they mostly showed a paravertebral localization (73%); only a minority (11%) were epidural, and two cases (8%) were both paravertebral and epidural. The majority of lumbosacral abscesses were treated percutaneously, 4 cases (15%) were treated with open surgery, and only one case (4%) didn't undergo surgery (this case had an epidural localization).

The characteristics of thoracic abscesses were not available for all cases, and the localization was not recorded in most of them (79%). All cases of thoracic abscess were treated surgically, mostly percutaneously (79%).

With regard to cervical abscesses, the localization was mostly epidural (66%) and the treatment was always surgical (all cases underwent "open" surgery).

As for the relationship between abscess localization (either epidural or paravertebral) and surgical treatment, 95% of paravertebral abscesses were treated with percutaneous surgery while 85.7% of epidural cases underwent "open" surgery.

Neurological Complications

5 studies about spondylodiscitis with neurological complications^{36,41,42,50,54} were analyzed (Table III) for a total of 143 patients, of which 49% were males (70) and 9.8% females (14), with mean age of 61.3 years. With regard to spinal cord compression, the majority of cases (55.9%, corresponding to

Table I. Descriptive analysis of the reviewed studies focused on the type of causative pathogen.

Author	Year	Study Design	Participants	Country	Microbiology			
					<i>Staphylococcus Spp.</i>	<i>M. Tuberculosis</i>	<i>Other Bacteria</i>	<i>Viral Fungal Parasitic</i>
Chen et al ¹⁵	2013	CR	1	Taiwan				1
Lu et al ¹⁶	2015	OR	28	Germany	9	3	9	1
Suzuki et al ¹⁷	2013	OR	14	Japan			14	
Valancius et al ¹	2013	OR	196	Denmark	112		84	
Wang et al ¹⁸	2013	CS	183	China				
Fransen et al ¹⁹	2014	CO (R)	49	Netherlands	10	2	22	1
Lotte et al ²⁰	2014	CR	1	France			1	
Ozkan et al ¹¹	2014	OR	21	Germany	14		7	
Shiban et al ²¹	2014	OR	113	Germany	34		24	
Shousha et al ²²	2014	OR	50	Germany	29	1		
Batirel et al ²³	2015	OR	314	Multicentre		314		
Homagk et al ²⁴	2016	OR	296	Germany				
Huyskens et al ²⁵	2015	CS	13	Belgium	8			
Kehrer et al ²⁶	2015	CCO	298	Denmark	128		104	
Shah et al ²⁷	2015	CR	1	UK			1	
Comacle et al ²⁸	2016	CR	1	France				1
D'Souza et al ²⁹	2016	OR	4	USA			4	1
Muhamad Effendi et al ³⁰	2016	CR	1	Malaysia			1	
Giger et al ³¹	2016	CR	1	Switzerland			1	1
Hopkinson et al ³²	2016	CS (R)	23	UK	9		8	
Kang et al ³³	2016	OR	25	Korea	10	8		
Lu et al ³⁴	2017	CS	18	Taiwan	7		3	
Pizzol et al ³⁵	2016	CR	1	Italy				
Ghobrial et al ³⁶	2017	CS (R)	59	USA	46		13	
Ahuja et al ³⁷	2017	OR	45	UK	11		4	

OR = observational retrospective; CS = case series; CR = case report; CO = cohort study; CCO = case-cohort study; R = retrospective.

Table II. Descriptive analysis of the reviewed studies focused on the site of abscess.

Author	Year	Study Design	Participants	Country	Site Of Abscess		
					<i>Cervical</i>	<i>Thoracic</i>	<i>Lumbosacral</i>
Fu et al ³⁸	2012	CR	1	Taiwan			1
Lampropoulos et al ³⁹	2012	CR	1	Greece	1		
Sanmillán et al ⁴⁰	2013	CR	1	Spain			1
Shoakazemi et al ⁴¹	2013	CR	1	Ireland		1	
Akagawa et al ⁴²	2015	CR	1	Japan		1	
Chen et al ⁴³	2015	CLS	13	Taiwan		11	2
Dobson et al ⁴⁴	2015	CR	1	UK			1
Endo et al ⁴⁵	2015	CR	1	Japan			1
Farrar et al ⁴⁶	2015	CR	1	UK			1
He et al ⁴⁷	2015	CR	1	China			1
Kohlmann et al ¹³	2015	CR	1	Germany	1		
Suzuki et al ⁴⁸	2015	CS	15	Japan			15
Voelker et al ⁴⁹	2015	CR	1	Germany	1		
Yin et al ⁵⁰	2015	CR	1	China		1	
Bayraktutan et al ⁵¹	2016	CR	1	Turkey			1
Husainy et al ⁵²	2016	CR	1	UK			1
Mehdorn et al ⁵³	2016	CR	1	Germany			1

OR = observational retrospective; CS = case series; CR = case report; CLS = clinical study.

Table III. Descriptive analysis of the reviewed studies focused on site of spinal cord compression with or without neurological compromise and surgical treatment.

Author	Year	Study Design	Participants	Country	Site of Spinal Cord Compression			Neuro Deficit	Surgery
					<i>Cervical</i>	<i>Thoracic</i>	<i>Lumbosacral</i>		
Shoakazemi et al ⁴¹	2013	CR	1	Ireland		1		1	
Akagawa et al ⁴²	2015	CR	1	Japan		1	1	1	
Yin et al ⁵⁰	2015	CR	1	China		1		1	
Ghobrial et al ³⁶	2017	CS	59	USA	59		59	59	
Lemaignen et al ⁵⁴	2017	CC	81	France	21	41	19	33	58

CR = case report; case series; CC = case control

80 cases) involved the cervical region; 30.8% of cases (44) involved the thoracic region and a small part (13.3%, such as 19 cases) the lumbosacral region. Neurological deficit was observed in over half of cases (65%, such as 93 cases).

The vast majority of cases with neurological complications underwent surgery (83.9%, corresponding to 120 cases).

Spinal Instability

13 studies about spondylodiscitis complicated by instability^{5,6,23,55-64} were analyzed (Table IV) for a total of 799 patients, with mean age of 52.5 years.

With regard to the spinal level affected, over half (53.3%, for a total of 419 cases) of the cases of instability involved the lumbosacral region. The thoracic region was involved in 31.8% of cases (250) and the cervical region in 5.7% of cases (45). 3.5% of cases of instability were located at the thoracic and lumbar regions, while for 5.7% of cases (45) the level was not reported.

Only a small amount of cases (13%, corresponding to 103 patients) were treated without surgery, while 87% of cases (696) underwent surgical treatment. Of these, the vast majority (85.8%) of patients were treated with “open” surgery while 14.2% of cases (99) underwent minimally invasive surgery.

Focus Of Infection

To investigate the relationship between the focus of infection and treatment in spondylodiscitis,

18 studies^{5,13,15,16,22,56,59,60,65-73} were analyzed (Table V). A total of 553 cases were included, 43.9% male (243 cases) and 36.5% female (202 cases), with mean age of 48.8 years.

The focus of infection was lumbosacral in the majority of cases (61.2%), thoracic in 19.5% of cases and cervical in 11.3%. A minority of cases showed a thoracolumbar focus of infection, while 8% of cases did not report this information.

The majority of cases were treated surgically (94.9%, corresponding to 525 cases), while only a small number of cases did not require surgical treatment (5.1%, 28 cases).

Discussion

Spondylodiscitis is of considerable clinical interest in Europe, where many of studies analyzed (53%) were carried out.

As far as microbiology is concerned, in accordance with the literature⁷⁴, the most frequently

isolated organism is *Staphylococcus aureus*, a common pathogen that can become very virulent.

As for the site of infection, the majority of cases involve the lumbosacral region, likely because of its vascularization and its mobility, responsible for a “pump effect”. Regarding spondylodiscitis complicated by abscesses, the most frequently affected site is the lumbosacral region, where we can find a clear predominance of paravertebral abscesses. This can be explained by the presence of the retroperitoneum, that along with the psoas muscle represents a cavity where “masses” can grow, unlike the dorsal region where the thorax and the diaphragm act as a barrier that hinders the growth of masses. Regarding the other localization examined, we can state that epidural abscesses mostly involve the thoracic region. The rigidity of this area causes the disease to develop in a silent way, unlike the lumbar region where the clinical manifestations (pain and instability, due to damage to the motor segment) occur at an earlier stage. Moreover, we can observe that all cases of abscesses are treated with drainage (“ubi pus ibi vacuat”) and that there is a connection between localization and surgical treatment: almost all of the paravertebral abscesses undergo percutaneous surgery while the vast majority of epidural abscesses are treated with “open” surgery (the removal is always associated with decompression).

Concerning spondylodiscitis complicated by instability, it mainly involves the lumbosacral region and it is particularly evident in active people with high functional demands (mean age of patients examined = 52.5 years). In the elderly, on the other hand, the low functional demand in some way contributes to preserve spinal stability.

With respect to neurological complications, the results show that spinal cord compression mainly involves the cervical (55% of cases) and the thoracic region (almost 31% of cases), due to the anatomy of the spinal cord itself (presence of cauda equina below L1-L2). We can, therefore, conclude that cervical and thoracic abscesses are more likely to cause neurological damage, which is less frequent in case of lumbosacral involvement.

Regarding the focus of infection, we can state that the majority of cases involve the lumbosacral region, where the retroperitoneum allows substantial growth, and that almost all cases (96%) undergo surgical treatment. As a matter of fact, in the presence of a focus of infection, surgical excision represents the only way to ensure that the disease will respond to medical treatment.

Table IV. Descriptive analysis of the reviewed studies focused on site of instability with intervention strategy.

Author	Year	Study Design	Participants	Country	Site of Instability			Surgery		
					<i>Cervical</i>	<i>Thoracic</i>	<i>Lumbosacral</i>	<i>No</i>	<i>Open</i>	<i>Mini-inv</i>
Lin et al ⁵⁵	2012	OR	48	Taiwan		16	32		48	
Lin et al ⁵⁶	2013	OR	77	China			77		77	
Nasto et al ⁵⁷	2013	OR	27	Italy		27	27		27	
Bydon et al ⁵⁸	2014	OR	118	USA	35	40	43		118	
Lin et al ⁵⁹	2014	OR	45	Taiwan					45	
Madhavan et al ⁶⁰	2014	OR	10	USA			10		10	
Mohamed et al ⁶¹	2014	OR	15	USA	2	7	6		15	
Srinivasan et al ⁶	2014	OR	48	USA					48	
Včelák et al ⁵	2014	OR	31	Czech Republic			31		31	
Batirel et al ²³	2015	OR	314	Multicenter	8	154	176	103	112	99
Lin et al ⁶²	2015	OR	22	China			22		22	
Hassan et al ⁶³	2016	OR	42	Egypt		33	20		42	
Funao et al ⁶⁴	2017	CS	2	Japan			2		2	

OR= observational retrospective; CS= case series; mini-inv.= mini-invasive surgery

Table V. Descriptive analysis of the reviewed studies focused on the site of abscess.

Author	Year	Study Design	Participants	Country	Focus of Infection		
					<i>Cervical</i>	<i>Thoracic</i>	<i>Lumbosacral</i>
Chen et al ¹⁵	2013	CR	Taiwan	1		1	
Lin et al ⁵⁶	2013	OR	China	77			77
Calvert et al ⁶⁵	2014	OR	England	15		8	7
Chung et al ⁶⁶	2014	OR	Taiwan	20		10	10
Lin et al ⁵⁹	2014	OR	Taiwan	45			
Madhavan et al ⁶⁰	2014	OR	USA	10			10
Shepard et al ⁶⁷	2014	CR	USA	1			1
Shousha et al ²²	2014	OR	Germany	50	50		
Včelák et al ⁵	2014	OR	Czech Republic	31			31
Dreimann et al ⁶⁸	2015	OR	Austria	10		10	
Kohlmann et al ¹³	2015	CR	Germany	1	1		
Lu et al ¹⁶	2015	OR	Germany	28			28
Patel et al ⁶⁹	2015	CS	USA	6			6
Yaldız et al ⁷⁰	2015	OR	Turkey	39		19	24
Yoon et al ⁷¹	2015	CR	Korea	1			1
Agarwal et al ⁷²	2016	OR	USA	124	1	26	97
Hassan et al ⁶³	2016	OR	Egypt	42		33	20
Shiban et al ⁷³	2016	OR	Germany	52	11	3	29

OR = observational retrospective; CR = case report; CS = case series

The main strength of this review is the coverage of a wide variety of studies from different countries, a lot of which were assessed at the first stage of screening. Therefore, we were able to detect even small but clinically relevant studies. Unfortunately, this work also has some limitations: many selected studies are case reports or case series with a small sample size and thus a low potential representativeness of the population, considering the heterogeneous nature of subjects in the different studies. Moreover, not all studies provide adequate and consistent data, required for inclusion in the analysis that we carried out. Further researches will be necessary in order to refine our understanding of the underlying mechanisms of spondylodiscitis.

Conclusions

The incidence of spondylodiscitis has considerably grown over the years. It could be due to the increasing number of the susceptible patients, and to the growing sensibility and specificity of modern imaging technologies. In spite of this, the early diagnosis of spondylodiscitis and therefore its management are still challenging, due to the insidious onset of the disease and the misleading clinical aspects.

The 5 elements discussed in this review could be useful to address the multidisciplinary team (radiologist, infectious disease specialist, spinal surgeon and rehabilitation staff) toward the most appropriate medical or surgical treatment. Despite the limitations previously described, this paper highlights the importance of spondylodiscitis assessment in a wide, but heterogeneous population. Further research is necessary to provide higher levels of evidence for the management of patients with spondylodiscitis.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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