International Journal of Infectious Diseases 99 (2020) 122–130

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Impact of the localization on disease course and clinical management in spondylodiscitis

Martin Stangenberg[a,1,*], Malte Mohme[b,1], Klaus Christian Mende[b], Darius Maximilian Thiesen[a], Theresa Krätzig[b], Benjamin Schoof[a], Sven Oliver Eicker[b], Marc Dreimann[a]

[a] Division of Spine Surgery, Department of Trauma and Orthopedic Surgery, University Medical Center Hamburg-Eppendorf, Germany
[b] Department of Neurosurgery, University Medical Center Hamburg-Eppendorf, Germany

ARTICLE INFO

Article history:
Received 24 April 2020
Received in revised form 9 July 2020
Accepted 19 July 2020

Keywords:
Spondylodiscitis
Vertebral osteomyelitis
Localization
Risk factors
Surgery

ABSTRACT

Objectives: Spondylodiscitis is a severe infection of the spine that can take a diverse number of disease courses depending on its localization, resulting in specific therapeutic strategies. This study aims to identify localization specific characteristics and clinical parameters for spondylodiscitis.
Methods: A retrospective review was performed of 211 patients from 2013–2018 with proven spondylodiscitis. In total, 33 were cervical, 48 thoracic and 112 lumbar. In 18 patients disseminated infestations of several localizations were found. The patient records were evaluated for clinical and outcome parameters and demographic characteristics.
Results: Patient age, Body Mass Index, inpatient and intensive care stay, and inpatient complications did not differ significantly between different infection localizations. C-reactive protein (CrP) levels showed a significantly reduced value in the thoracic area compared to other localizations. For comorbidities, there was a significantly higher prevalence of endocarditis in disseminated and lumbar infestations compared to thoracic and cervical cases. Epidural abscesses showed a highly increased incidence in cervical cases. With a 30-day mortality rate of 12.1% for cervical, 12.5% thoracic, 13.4% lumbar, and 22.2% in disseminated disease, no significant difference was observed.
Conclusions: The present study determined that, although the 30-day mortality rate does not differ according to the localization of the infection, specific clinical parameters, such as CrP values or comorbidities, showed localization-dependent differences.
© 2020 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

Pyogenic spinal infections include a broad range of clinical entities, including discitis, osteomyelitis, meningitis, epidural abscess, subdural empyema and spinal cord abscess. Pyogenic spondylodiscitis, defined as discitis with osteomyelitis, is responsible for 2–5% of all infectious bone diseases (Hadjipavlou et al., 2000; Grammatico et al., 2008; Sobottke et al., 2008). In most cases pyogenic spondylodiscitis occurs in chronically ill, immunodeficient and elderly people (Akiyama et al., 2013; Kehrer et al., 2015).

Whereas previous studies describe the incidence of pyogenic spondylodiscitis as ranging from 0.2 to 2.4 cases per 100,000 inhabitants per year in Europe (Sapico and Montgomerie, 1979; Krogsgaard et al., 1998; Grammatico et al., 2008), the incidence seems to be growing alarmingly over the past decades. This might be caused by the demographic changes of an ageing society and the increasing rate of accompanying risk factors, such as immunosuppressive treatments (Akiyama et al., 2013; Courjon et al., 2017). Recent reports from developed countries have shown an increasing annually incidence of pyogenic spondylodiscitis of 7.4 per 100,000 inhabitants in Japan, whilst in Denmark the incidence has risen from 2.2 to 5.8 per 100,000 inhabitants from 1995–2008, a comparable finding to Spain, and in England and Wales the incidence has increased by 150% from 1999–2011 (Lora-Tamayo et al., 2011; Akiyama et al., 2013; Kehrer et al., 2014; Sur et al., 2015).

Diagnosis of spondylodiscitis is often delayed because of rather unspecific symptoms such as lower back pain, fatigue and fever. Diagnostic measures include clinical examination, laboratory values (elevated C-reactive protein (CrP), procalcitonin levels

* Corresponding author at: University Medical Center Hamburg-Eppendorf, Martinistr. 52, D-20246 Hamburg, Germany.
E-mail address: m.stangenberg@uke.de (M. Stangenberg).
[1] These authors contributed equally.

https://doi.org/10.1016/j.ijid.2020.07.028
1201-9712/© 2020 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

and leucocyte counts, among others) and radiological imaging (i.e. magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET)). MRI plays the crucial role in diagnostics and therefore is the gold standard (Moritani et al., 2014; Herren et al., 2017). Nevertheless, clinical symptoms, radiographic and laboratory indicators may be lacking in the early stages of the disease when treatment would be the most effective (Butler et al., 2006; Akbar et al., 2011; Tsai et al., 2017).

Treatment strategies of patients with spondylodiscitis include conservative therapy with antibiotic therapy alone and immobilization with a rigid orthosis. The antibiotic regimen depends on the presence or absence of a pathogenic microorganism and should be chosen according to the resistogram. In cases where microbiological diagnosis is not possible, a broad-range antibiotic therapy should be chosen covering the most frequent gram-positive and gram-negative bacteria. Duration of antibiotic therapy is usually 12 weeks, even though recent studies seem to have shown non-inferiority of 6 weeks of antibiotic treatment in conservatively treated patients with positive microbial identification, in the absence of complicated courses (e.g. concomitant endocarditis) (Bernard et al., 2015).

Surgical techniques for spondylodiscitis include dorsal, ventral or one- or two-stage dorsoventral or ventrodorsal procedures depending on localization. In cervical cases, a ventral approach alone is often sufficient, whereas in the thoracic and lumbar spine a posterior or combined dorsoventral approach is mostly used (Duarte and Vaccaro, 2013; Rutges et al., 2016).

Even though therapeutic possibilities and diagnostic imaging have greatly improved during the past decades, successful treatment of spondylodiscitis remains a challenge. Little is known about how the different characteristics of pyogenic spondylodiscitis depend upon the infected spinal region. Understanding clinical features, such as the presence of epidural abscesses, complicating medical conditions, laboratory values, and revision and mortality rate, depending on the localization of the infection may help to further improve treatment of patients with spondylodiscitis. We have therefore performed a detailed analysis of a large cohort of patients with spondylodiscitis and analyzed the impact of the localization on disease course, clinical management and surgical approach.

Patients and methods

Study design and study population

We performed a retrospective data analysis of anonymized data sets from all patients who were treated for spondylodiscitis at our department between January 2014 and May 2018. Patients were identified by prospective registration of patients with spondylodiscitis treated at our department, combining information from discharge letters, as well as diagnostic and procedural codes, i.e. diagnostic related groups (DRG) codes. Clinical data was then retrospectively collected and analyzed. Overall 211 consecutive patients were identified. A detailed overview of the patient's characteristics can be found in Figure 1.

Definitions

We defined a spondylodiscitis by characteristic radiological changes of the intervertebral disc and adjacent vertebrae in MRI and CT scans, and clinical findings such as back/neck pain, fever, elevated serum CrP levels and elevated white blood cells count (WBC). All patients underwent Gd-enhanced MRI of the whole spine after admission to our hospital and had CT scans of the affected region to better evaluate the presence and extent of bony destruction. The infection route in all cases was either hematogenous or *per continuitatem*. Postoperative spinal infections, open injuries of the spine with consecutive infections or patients suspected of having microcrystalline disease, such as gout, were excluded from our study. Immunosuppression was defined as the oral or intravenous regular use of cortisone (>10 mg of prednisolone per day or equivalent dosage for at least 4 weeks in a continuous fashion), antirheumatic drugs, other immunomodulatory drugs and ongoing chemotherapy. Obesity was defined as a body mass index (BMI) > 30 kg/m^2.

Localization of the infection was classified into four regions: cervical, thoracic, lumbar and disseminated. The last showed at least two affected regions of the spine, i.e. cervical *and* lumbar involvement. Infections of the cervicothoracic junction (C7/Th1) were counted as cervical spondylodiscitis, the thoracolumbar

a

Patient Cohort

Segments affected		
1	146	69.1%
2	32	15.2%
3	18	8.5%
4	6	2.8%
5	3	1.4%
6	4	1.9%
7	2	0.9%

Microbiology		
BC positive	97	46.0%
IOTA positive	134	63.5%
Both positive (overall)	64	30.3%
No Diagnosis (overall)	41	19.4%
- IOTA and BC present	31	14.7%
- Only IOTA or BC	10	4.7%

Immunosuppression		
	33	15.6%

Deceased		
	29	13.7%

Localization		
cervical	27	12.8%
cervico-thoracic	6	2.8%
thoracic	41	19.4%
thoracolumbar	7	3.3%
lumbar	92	43.6%
lumbosacral	20	9.5%

Disseminated localization		
Overall	18	8.5%
cervical-lumbar	6	2.8%
thoracic-lumbar	9	4.2%
cervical-thoracic	3	1.4%

Epidural abscess		
	98	46.4%

Psoas abscess		
	47	22.3%

b

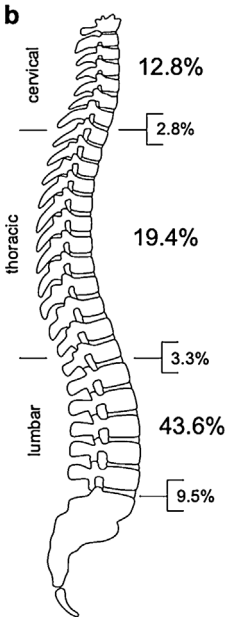


Figure 1. Overview of the patient cohort (a) and distribution of spondylodiscitis localizations (b).
BC = blood culture, IOTA = intraoperative tissue asservation.

junction (Th12/L1) accounted for thoracic and the lumbosacral junction for lumbar cases.

Microbiological diagnostic procedures

Microbiological diagnostic work-up included two sets of blood cultures (BD Bactec Plus aerobic and anaerobic medium) drawn before the start of antibiotic therapy, and analysis of three to four tissue specimens. Tissue specimens were homogenized upon arrival in the microbiological laboratory and plated onto Chocolate agar, Columbia blood agar and Sabouraud agar (all Thermo Fisher, Bremen, Germany). In addition, 2 ml Thioglycolate broth (Thermo Fisher, Bremen, Germany) were inoculated. Plates were incubated over 14 days at 37 °C in atmosphere containing 5% CO_2. Bacteria were identified by whole-cell MALDI-TOF mass spectrometry on a Biotyper instrument (Bruker Daltonics, Bremen, Germany). Low-pathogenic bacteria (e.g. *Staphylococcus epidermidis*) were considered clinically significant only when recovered from at least two independent intraoperative specimens.

Data analysis

Details about therapeutic management, pathology and bacteriology results, demographics, inflammatory laboratory parameters, preexisting medical conditions, complications, revision and mortality rates, and treatment and approach of surgical intervention were collected, analyzed and correlated to the localization of spondylodiscitis.

Statistics were computed using IBM SPSS v23.0 and Graphpad Prism 8. Results were deemed statistically significant at $p < 0.05$. Student's *t*-test, Chi^2 and Fisher's exact test were used for data comparison. Localization groups were analyzed for differences in variance and statistically significant differences using ANOVA and Tukey post-hoc test.

Results

Patient cohort and demographic characteristics

Overall, 211 adult patients with spondylodiscitis were included in this analysis; 139 were male (65.9%). Mean patient age was 64.6 ± 14.8 years, range 19–89 years. Mean patient stay was 27.2 days ± 20.7 days, of which 7.3 ± 15.1 days accounted for the patient's intensive care unit (ICU) treatment. Mean BMI was 26.9 ± 15.1 kg/m^2.

The median number of affected segments was one (range 1–7 segments). In total, 33 cases were localized in the cervical and cervicothoracic junction (15.6%), 48 in the thoracic and thoracolumbar junction (22.7%), and 112 were localized in the lumbar and lumbosacral junction (53.1%). In 18 patients, disseminated infections (8.5%) were observed: 6 were in a cervical and lumbar localization (2.8%), 9 in the thoracic and lumbar spine (4.3%), and 3 in a cervical and thoracic localization (1.4%). Epidural abscesses

a **Index values by localization**

	cervical	thoracic	lumbar	disseminated	P-value
age (y)	61.3 ±12.0	61.9 ±15.5	65.9 ±15.6	69.1 ±10.6	n.s.
BMI (kg/m2)	25.4 ±5.7	27.5 ±8.8	27.1 ±6.6	26.6 ±6.0	n.s.
hospital stay (d)	27.0 ±12.8	26.2 ±18.9	28.4 ±24.4	22.2 ±10.5	n.s.
ICU stay (d)	9.6 ±18.6	5.8 ±12.9	7.1 ±15.5	7.6 ±9.6	n.s.
segments affected*	1 ±1.1	1 ±1.5	1 ±0.5	3 ±1.7	n.s.
epidural Abscess	**26 (78.8%)**	**21 (43.8%)**	**47 (42.0%)**	**4 (22.2%)**	**<0.001**
psoas Abscess	-	-	38 (33.9%)	5 (27.8%)	**<0.001**
neurological deficit preop	**15 (45.5%)**	**12 (25.0%)**	**12 (10.7%)**	**4 (22.2%)**	**<0.001**
hemoglobin preop (g/dl)	10.7 ±1.5	11.2 ±2.0	10.9 ±1.8	10.4 ±1.9	n.s.
hemoglobin discharge (g/dl)	9.3 ±1.3	9.8 ±1.7	9.4 ±1.4	9.5 ±1.2	n.s.
leukocytes preop (/nl)	11.6 ±4.5	10.1 ±7.4	11.4 ±6.5	10.9 ±5.2	n.s.
leukocytes discharge (/nl)	7.6 ±2.6	8.0 ±6.7	9.0 ±7.6	7.9 ±4.1	n.s.
CrP preop (mg/l)	**122.7 ±104.0**	**79.0 ±73.3****	**130.2 ±99.8**	**166.8 ±131.0**	**<0.001 / n.s.**
CrP discharge (mg/l)	38.1 ±33.4	55.6 ±83.0	53.7 ±54.7	70.9 ±84.8	n.s.
creatinine preop (mg/dl)	1.3 ±1.3	1.2 ±1.4	1.4 ±1.3	1.5 ±1.3	n.s.
creatinine discharge (mg/dl)	1.2 ±1.2	1.2 ±1.4	1.3 ±0.9	1.1 ±0.5	n.s.

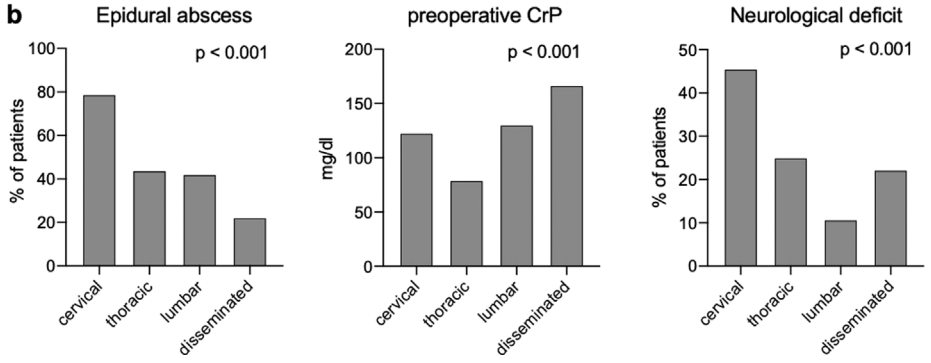


Figure 2. Index values by localization: (a) relevant collected values, (b) significant differences depending on the localization.
*cervical-lumbar $p = 0.006$, cervical-disseminated, $p < 0.001$, thoracic-lumbar $p = 0.001$, thoracic-disseminated $p < 0.001$, lumbar-disseminated $p < 0.001$; non-parametric group comparison with Mann-Whitney *U* test.
**thoracic-lumbar $p = 0.015$, thoracic-disseminated $p = 0.008$, thoracic-cervical $p = 0.203$; ANOVA, Post-HOC Analysis Tukey-HD.
BMI = body mass index, CrP = C-reactive protein, n.s. = not significant.

were found in 46.4% of cases (Figure 1). Median patient follow-up was 144 days.

Material asservation for microbiological diagnosis (blood cultures or intraoperative biopsy) was possible in all patients. In 11.4% ($n = 24/211$) patients, conservative treatment was performed with an antibiotic therapy regime alone. Out of these 24 patients, 15 received a transpedicular biopsy for histopathological and microbiological diagnosis, whilst 9 patients underwent no surgical intervention at all and therefore no intraoperative tissue asservation (IOTA) was available for diagnostic measures.

Microbiological diagnosis was successful in 170/211 cases (80.6%), either from IOTA or obtained blood cultures. In 46.0% ($n = 97/211$) of cases blood cultures were positive, whilst no blood cultures were obtained in 30 patients, thus, microbiological detection rate was 53.6% ($n = 97/181$). In 63.5% ($n = 134/211$) of cases, IOTA was able to detect the pathogenic microorganism. Nine patients were treated conservatively and had no IOTA (detection rate of 66.3%, $n = 134/202$). IOTA *and* blood culture results were positive in 30.3% ($n = 64/211$). Blood culture, IOTA *and* histopathology were positive in 21.8% ($n = 44/202$) of cases. There were no statistically significant differences concerning the efficacy of microbiological diagnostics between cervical/thoracic/lumbar or disseminated localizations. In cases without microbiological evidence, histopathology showed clear signs of spondylodiscitis in 61% ($n = 25/41$) of patients, the remaining 16 patients showed clear signs of spondylodiscitis in MRI and elevated inflammatory markers.

Index values by localization

Localization groups were analyzed for differences in variance and statistically significant differences relating to age, hospital and ICU stay, affected segments, BMI, hemoglobin, leucocyte count, creatinine, CrP, and the presence or absence of epidural and psoas abscesses. Results are shown in Figure 2. Significant differences were computed for preoperative CrP measurements, where thoracic spondylodiscitis scored significantly lower than lumbar and disseminated spondylodiscitis ($p < 0.001$); the difference to cervical spondylodiscitis was not significant. There was also a significant correlation ($p < 0.001$) between the presence of epidural abscesses in cervical cases (78.8%) in contrast to other localizations, in which only 43.8% (thoracic), 42% (lumbar) and 22.2% (disseminated) of epidural abscesses were detected. As one might expect, psoas abscesses were only found in lumbar and disseminated cases with involvement of lumbar infections. Neurological deficits occurred more frequently in cervical and thoracic localizations than in lumbar and disseminated cases ($p < 0.001$). All other differences were not statistically significant.

Comorbidities

The frequencies of comorbidities are listed in Table 1. Statistical significance was seen for the presence of endocarditis, which was more often found in lumbar ($n = 16/85$) patients who received a transesophageal echocardiography (TEE) (18.8%), and in disseminated spondylodiscitis ($n = 7/13$, 53.8%, Chi^2 $F = 7.957$, df3, $p = 0.002$). There was also a trend towards statistical significance in patients with preexisting 3MRGN ($n = 7/112$ lumbar cases 6.3% and 2/18 disseminated cases 11.1%; 3MRGN: multi-resistant gram-negative bacteria against 3 antibiotic groups. No preexisting 3MRGN patient developed cervical or thoracic spondylodiscitis, Chi^2 $F = 6.755$, df3, $p = 0.08$).

Complicating medical conditions

The frequencies of complications during the hospital stay, such as renal failure, sepsis, pneumonia, cardiac decompensation etc., were computed and are listed in Table 2. There were no significant differences relating to the different localizations.

Table 1
Pre-existing medical conditions by localization.

	Cervical ($n = 33$)		Thoracic ($n = 48$)		Lumbar ($n = 112$)		Disseminated ($n = 18$)		Total ($n = 211$)		p-Value
Coronary heart disease	7	21.2%	10	20.8% %	22	19.6%	1	5.6%	40	19%	n.s.
Heart failure	7	21.2%	8	16.7%	13	11.6%	2	11.1%	30	14.2%	n.s.
Endocarditis*	**2**	**11.8%**	**1**	**3.7%**	**16**	**18.8%**	**7**	**53.8%**	**26**	**18.3%**	**0.002**
Chronic vesiculitis	1	3.0%	1	2.1%	8	7.1%	1	5.6%	11	5.2%	n.s.
Chronic renal failure	4	12.1%	6	12.5%	27	24.1%	4	22.2%	41	19.4%	n.s.
Dialysis	1	3.0%	1	2.1%	3	2.7%	1	5.6%	6	2.8%	n.s.
IDDM	8	24.2%	5	10.4%	18	16.1%	0	0.0%	31	14.7%	n.s.
NIDDM	1	3.0%	3	6.3%	5	4.5%	0	0.0%	9	4.3%	n.s.
Osteoporosis	3	9.1%	4	8.3%	3	2.7%	1	5.6%	11	5.2%	n.s.
Obesity	6	18.2%	13	27.1%	26	23.2%	4	22.2%	49	23.2%	n.s.
COPD	6	18.2%	6	12.5%	12	10.7%	2	11.1%	26	12.3%	n.s.
Alcohol abuse	5	15.2%	3	6.3%	11	9.8%	2	11.1%	21	10.0%	n.s.
i.v. drug abuse	3	9.1%	2	4.2%	5	4.5%	2	11.1%	12	5.7%	n.s.
HIV	0	0.0%	2	4.2%	1	0.9%	0	0.0%	3	1.4%	n.s.
Hepatitis (B or C)	3	9.1%	3	6.3%	7	6.3%	2	11.1%	15	7.1%	n.s.
3MRGN	**0**	**0.0%**	**0**	**0.0%**	**7**	**6.3%**	**2**	**11.1%**	**9**	**4.3%**	**0.08**
4MRGN	0	0.0%	1	2.1%	2	1.8%	0	0.0%	3	1.4%	n.s.
VRE	5	15.2%	6	12.5%	8	7.1%	2	11.1%	21	10.0%	n.s.
MRSA	1	3.0%	2	4.2%	2	1.8%	1	5.6%	6	2.8%	n.s.
Organ transplant	1	3.0%	2	4.2%	3	2.7%	1	5.6%	7	3.3%	n.s.
Malignoma	9	27.3%	9	18.8%	23	20.5%	5	27.8%	46	21.8%	n.s.
Liver cirrhosis	1	3.0%	4	8.3%	6	5.4%	0	0.0	11	5.2%	n.s.
Rheumatoid Disease	2	6.1%	3	6.3%	5	4.5%	3	16.7%	13	6.2%	n.s.
Stroke	1	3.0%	3	6.3%	7	6.3%	2	11.1%	13	6.2%	n.s.

* Of patients which received transesophageal echocardiography ($n = 142/211$), statistical testing using Chi^2-test.IDDM = insulin-dependent diabetes mellitus, NIDDM = non-insulin-dependent diabetes mellitus, COPD = chronic obstructive pulmonary disease, HIV = human immunodeficiency virus, 3MRGN = 3-multi-resistant-gram negative (resistant against 3 antibiotic groups), 4MRGN = 4-multi-resistant-gram negative (resistant against 4 antibiotic groups), VRE = vancomycin-resistant enterococci, n.s. = not significant.

Table 2
Complicating medical conditions by localization.

	Cervical ($n=33$)		Thoracic ($n=48$)		Lumbar ($n=112$)		Disseminated ($n=18$)		Total ($n=211$)		p-Value
Renal failure	7	21.2%%	11	22.9%	20	17.9%	2	11.1%	40	19.0%	n.s.
Sepsis	10	30.3%	16	33.3%	34	30.4%	4	22.2%	64	30.3%	n.s.
Shock	3	9.1%	6	12.5%	14	12.5%	2	11.1%	25	11.8%	n.s.
Liver failure	0	0.0%	1	2.1%	4	3.6%	2	11.1%	7	3.3%	n.s.
Pneumonia	2	6.1%	7	14.6%	8	7.1%	4	22.2%	21	10.0%	n.s.
Pulmonary embolism	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	n.s.
Myocardiac infarction	0	0.0%	0	0.0%	4	3.6%	0	0.0%	4	1.9%	n.s.
Cardiac decompensation	4	12.1%	6	12.5%	11	9.8%	1	5.6%	22	10.4%	n.s.
Stroke	0	0.0%	1	2.1%	1	0.9%	0	0.0%	2	0.9%	n.s.
Deep venous thrombosis	0	0.0%	0	0.0%	1	0.9%	0	0.0%	1	0.5%	n.s.
Delirium	2	6.1%	2	4.2%	11	9.8%	1	5.6%	16	7.6%	n.s.
Neurological deterioration	0	0.0%	1	2.1%	1	0.9%	2	11.1%	2	0.9%	n.s.

Statistical testing using Chi^2-test.
n.s. = not significant.

Treatment and surgical approach

Of the 211 patients, 9 were treated conservatively (4.3%), 97 (46.0%) were operated only from a posterior approach and 24 (11.4%) only from an anterior approach. A further 56 patients (26.5%) underwent dorsoventral surgery and 10 (4.7%) underwent ventrodorsal surgery. Analysis of surgical approaches based on the localization showed significant differences ($p<0.001$): in cervical cases, no patient was treated posteriorly alone whereas in thoracic and lumbar cases 54.2% and 56.3%, respectively, were treated from a posterior approach alone. A detailed list of surgical methods, depending on localization, can be found in Table 3.

In 187 cases, patients underwent surgical treatment, not including Jamshidi biopsy ($n=14$), such as debridement with spondylodesis, either from a posterior, anterior or combined posterior and anterior approach. Surgical treatment and approach were determined individually depending on the extent of bony destruction, localization, abscess formations and deformity, also taking into account patient specific parameters like age and comorbidities. If treated surgically, a biopsy from the infected disc

Table 3
Treatment and surgical approach by localization.

	Surgical approach						
	Conservative	Dorsal	Ventral	Dorsoventral	Ventrodorsal	Biopsy	Total
Cervical	1 3.0%	0 0.0%	15 45.5%	9 27.3%	8 24.2%	0 0.0%	33 100.0%
Thoracic	4 8.3%	26 54.2%	0 0.0%	10 20.8%	1 2.1%	7 14.6%	48 100.0%
Lumbar	3 2.7%	63 56.3%	1 0.9%	36 32.1%	1 0.9%	8 7.1%	112 100.0%
Disseminated	1 5.6%	7 38.9%	0 0.0%	2 11.1%	8 44.4%	0 0.0%	18 100.0%
Total	9 4.30%	97 46.0%	24 11.4%	56 26.5%	10 4.7%	15 7.1%	211 100.00%

Detailed treatment by localization

	conservative	dorsal	dorsal with interbody fusion (cage)	dorsal plus ventral iliac crest	dorsal plus ventral vertebra replacement	dorsal plus VCR	ventral with iliac crest and plate	ventral with cage und plating	ventral with vertebra replacement and plate	decompression or biopsy alone	ACDF with dorsal instrumentation	Total
Cervical	1 3.0%	0 0.0%	0 0.0%	5 15.2%	7 21.2%	0 0.0%	3 9.1%	9 27.3%	5 15.2%	0 0.0%	3 9.1%	33 100.0%
Thoracic	4 8.3%	13 27.1%	4 8.3%	6 12.5%	3 6.3%	11 22.9%	0 0.0%	0 0.0%	0 0.0%	7 14.6%	0 0.0%	48 100.0%
Lumbar	3 2.7%	18 16.1%	40 35.7%	38 33.9%	2 1.8%	0 0.0%	0 0.0%	0 0.0%	1 0.9%	10 9.8%	0 0.0%	112 100.0%
Disseminated	1 5.6%	2 11.1%	0 0.0%	5 27.8%	0 0.0%	0 0.0%	3 16.7%	4 22.2%	1 5.6%	2 11.1%	0 0.0%	18 100.0%
Total	9 4.3%	33 15.6%	44 20.9%	54 25.6%	12 5.7%	11 5.2%	6 2.8%	13 6.2%	7 3.3%	19 9.0%	3 1.4%	211 100.0%

VCR = vertebral column resection.
ACDF = anterior cervical discectomy and fusion

and the adjacent vertebra was taken and examined microbiologically and histopathologically. In cases receiving a transpedicular biopsy only, a Jamshidi needle (10 gauge) was used.

Revision rate and 30-day mortality

The revision rate for all cases was 17.5% (37/211); there was no significant difference in the different localizations. Revision was defined as an unplanned re-operation. Overall, 29 patients (13.7%) died from complications of spondylodiscitis within the first 30 days (in hospital) after diagnosis of spondylodiscitis. Different localizations showed no statistically different mortality rates (cervical: 12.1%, thoracic: 12.5%, lumbar: 13.4%) except for disseminated cases, where 22.2% died within 30 days (Table 4). The number of affected segments also had no influence on the mortality rate: monosegmental spondylodiscitis cases constituted 69.1% of all cases (Figure 1) and 68.9% of deceased patients had monosegmental involvement.

Histopathology, antibiotics and bacterial species

An overview of microbiological and histopathology data is presented in Figure 3. Methicillin-susceptible *S. aureus* (MSSA) was the most common bacterial specimen in this cohort. Histopathology was positive in 68% of cases ($n = 117/172$). No intraoperative histopathology was obtained in 14.9% of surgically treated patients ($n = 30/202$). Detection rates based on localization of spondylodiscitis showed no significance and were 87.5% in cervical, 65.8% in thoracic, 62.8% in lumbar and 75.0% in disseminated cases. Antibiotics were administered for a mean duration of 69 ± 35 days overall, of which 27 ± 22 days were intravenous antibiotics. Antibiotic regimens were individually calculated with the in-house antibiotic stewardship team and reevaluated after successful microbiological diagnosis.

Discussion

With regard to the pre-existing diseases, there was no dependency of the localization except for endocarditis. This is more of a comorbidity than a pre-existing disease and occurs in the literature in about 5.9–10% of cases simultaneously with spondylodiscitis. It is most likely explained by microemboli and bacteremia (Ninet et al., 1984; Morelli et al., 2001; Le Moal et al., 2002). Spondylodiscitis and endocarditis can cause each other and it often remains unclear which pathology existed first. In our study, 12.3% of patients had concomitant endocarditis, with a detection rate of 18.3% in patients undergoing TEE. A TEE has only been used as a standard in every patient in our clinic since 2016, so only 142/211 patients received TEE. Prior to 2016, only patients with a clinical suspicion of endocarditis were studied. In 2019, Behmanesh described 10 cervical, 5 thoracic and 21 lumbar spondylodiscitis in 36 cases of endocarditis but no association between multifocal and unifocal involvement. In contrast, we found an increased occurrence of endocarditis with disseminated involvement of the spine (Behmanesh et al., 2019). This is most likely explained by bacteremia with increased bacterial load in disseminated cases at least if one suggests the disseminated infestation of the spine as the focus of the infection and not vice versa. Due to the heterogeneity and small size of the disseminated spondylodiscitis group further investigation in a larger cohort is required to confirm these results.

Preoperative neurological deficits in our study occurred in a total of 20.4%, whereas Gentile found a rate of 27.8% in a meta-analysis of 1756 cases (Gentile et al., 2019). Interestingly, cervical spondylodiscitis showed a significantly more frequent occurrence of neurological deficits compared to other localizations of the spinal column, which also matches the more frequent occurrence of epidural abscesses we found in this area as a possible explanation.

The laboratory inflammatory values showed significantly lower values for the CrP at hospital admission in the thoracic spine (mean 79.0 mg/l) than in cervical (122.7 mg/l) and lumbar cases (130.2 mg/l) as well as the expected increased values in disseminated infestation (166.8 mg/l). The CrP is considered the best monitor for treatment response in spondylodiscitis and is elevated in more than 90% of spondylodiscitis cases (Kapsalaki et al., 2009; Duarte and Vaccaro, 2013). However, no correlation between localization and the absolute level of the CrP value has been described before. It remains unclear why the thoracic cases showed significantly lower CrP levels on admission, especially as the value at discharge did not show any significant difference.

The distribution of localizations in our study (15.6% cervical, 22.7% thoracic, 53.1% lumbar, disseminated 8.5%) showed a similar distribution to a recent meta-analysis that found 21.8% cervical, 26.2% thoracic and 52.3% lumbar manifestations in a total of 1764 cases (Gentile et al., 2019). Data on the number of disseminated cases are not available in the meta-analysis, whereas Kehrer et al. reported 11.7%, Shiban et al., 5% and Sur et al., 12.7% multifocal involvement (Shiban et al., 2014; Kehrer et al., 2015; Sur et al., 2015).

In our study, we observed a high prevalence of epidural abscesses (78%) in the cervical patient group. This is in line with previous studies describing epidural abscess formation in up to 80% of patients (Shousha and Boehm, 2012). Interestingly, despite a total of 42 cases with cervical infection, there was no involvement of the upper cervical spine C0-C2. This coincides with the observations of Pola et al., who also did not report any infestations of this region in 250 cases (Pola et al., 2017). The reason for this lies in the fact that no intervertebral discs exist above the segment C2/C3; therefore, the spread of the infection is not favored as usual. The incidence of cervical involvement in spondylodiscitis varies between 6% and 22% in the literature (Heyde et al., 2006; Kehrer et al., 2014; Gentile et al., 2019). Although cervical spondylodiscitis is still rare, the overall rising incidence of spondylodiscitis and the increasing availability of MRI diagnostics might contribute to the increasing relevance in clinical practice. In addition, improvements in diffusion weighed imaging techniques might contribute to the sensitive detection of epidural abscesses in this location (Moritani et al., 2014). In relation to the thoracic and lumbar region, the cervical spine might be predisposed for epidural abscesses, as an infection of the disc can spread quicker from the cervical vertebrae, which are also smaller in size, to the epidural layers, which are

Table 4
Surgical revision rate and 30-day-mortality by localization statistical testing using Chi^2-test.

Surgical revision needed				
Localization	*n*	Revision	%	*p*-Value
Cervical	33	8	24.2	n.s.
Thoracic	48	7	14.6	n.s.
Lumbar	112	18	16.1	n.s.
Disseminated	18	4	22.2	n.s.
Total	211	37	17.5	
Mortality by localization				
Localization	*n*	Mortality	%	*p*-Value
Cervical	33	4	12.1	n.s.
Thoracic	48	6	12.5	n.s.
Lumbar	112	15	13.4	n.s.
Disseminated	18	4	22.2	n.s.
Total	211	29	13.7	

n.s. = not significant.

a

Intraoperative tissue	n	%
MSSA	55	36.7%
MRSA	4	2.7%
Staphylococcus spp	27	18.0%
Enterobacteriaceae	14	9.3%
Streptococcus spp	5	3.3%
Myc. tuberculosis	8	5.3%
Candida	5	3.3%
Other	32	21.3%
Total	*150*	

Bloodcultures	n	%
MSSA	35	31.0%
MRSA	6	5.3%
Staphylococcus spp	27	23.9%
Enterobacteriaceae	19	16.8%
Streptococcus spp	3	2.7%
Myc. tuberculosis	1	0.9%
Candida	4	3.5%
Other	18	15.9%
Total	113	

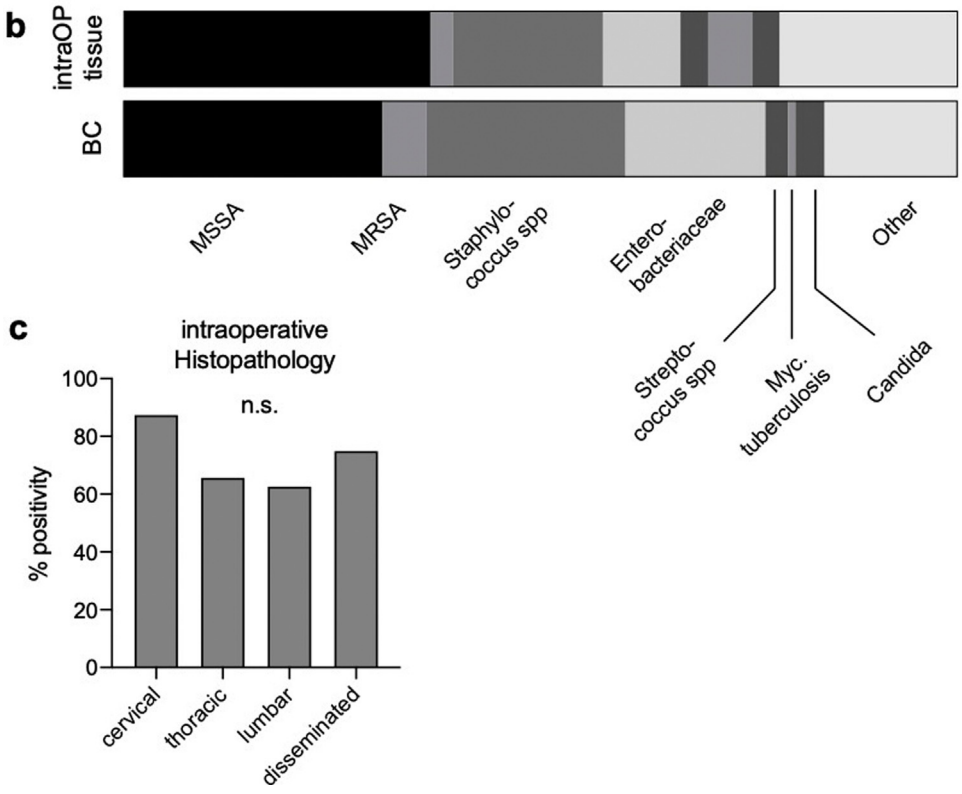


Figure 3. Microbiological and histopathological diagnosis: (a) and (b) intraoperative tissue and blood culture results, (c) histopathological diagnosis depending on the localization.
MSSA = methicillin-susceptible *S. aureus*, MRSA = methicillin-resistant *S. aureus*, Myc. tuberculosis = *M. tuberculosis*, n.s. = not significant

potentially less tightly connected due to the high mobility and greater range of motion of the cervical spine.

Current anatomical views hypothesize that the larger volume and better vascularization of the thoracic and lumbar vertebrae forms the basis for the preferential occurrence of spondylodiscitis in this location. Thoracic vertebral bodies are approximately 4–5x, and lumbar vertebrae 6x the volume of a cervical vertebrae, which thereby pass significantly less blood per minute compared to the larger thoracic and lumbar region. A similar pathophysiological basis of distribution is suspected for metastatic manifestation in the spine, as cervical spinal metastases are only observed in approximately 10% of cases with spinal metastasis (Maccauro et al., 2011). Studies investigating the distribution of cancer cells highlighted the preferential venous drainage of thoracic and lumbar organs into their corresponding vertebral bodies, especially in the context of increased intra-thoracic/-abdominal pressure (Batson, 1995; Maccauro et al., 2011). Taken together, the better vascularization, increased blood flow due to their size and number, as well as the interdependence on intrathoracic/abdominal pressure, presumably results in a higher incidence of thoracic and lumbar spondylodiscitis. The role of the lymphatic system is not well defined. Future imaging studies, incorporating dynamic contrast enhancement techniques, will certainly provide further insights to explain the vascularization differences between the cervical and lumbar spine, especially in the affected elderly population.

Therapeutic decision-making of surgical or conservative treatment should not be primarily dependent on localization or the skills of the surgeon, but on the extent of instability and the presence of sepsis, neurological deficits and epidural abscesses. Likewise, persistence or progression of infection under conservative therapy, the development of segmental kyphosis, or immobilizing pain should influence the therapeutic decision in favor of surgery (Duarte and Vaccaro, 2013; Berbari et al., 2015; Herren et al., 2017; Lener et al., 2018). All therapy decisions and surgeries in our case series have been performed by experienced spine surgeons so that any impact of surgical skills on the treatment decision can be ruled out.

Surgical approaches differed considerably depending on the localization. As known from the literature, surgical strategies and treatment options for spondylodiscitis are very heterogeneous. The decision on the type of surgical treatment is based not only on the localization but also on the existence of epidural abscesses, the extent of bony destruction, secondary deformity and other patient-specific parameters (Eysel et al., 1997; Akbar et al., 2011; Duarte and Vaccaro, 2013; Shiban et al., 2014; Homagk et al., 2016; Herren et al., 2017; Appalanaidu et al., 2018). Due to the difficult posterior accessibility of the intervertebral disc in the cervical spine and the need for resection and debridement of the disc space, the less invasive ventral approach was chosen in all of the cases and, in 51.5%, an additional dorsal approach was also necessary (either dorsoventral or ventrodorsal). Thoracic and lumbar cases were treated with combined approaches in 22.9% and 33.0% respectively.

Despite the expected differences in the type of surgical treatment for cervical, thoracic and lumbar infections, the surgical revision rate in our study showed no dependence on localization. Rates were higher in cervical (24.2%) and disseminated cases (22.2%) than in thoracic (14.9%) or lumbar cases (16.1%), but differences were not significant. In previous studies, the revision rate for surgically treated spondylodiscitis was between 1.9% and 32.3% (Karadimas et al., 2008; Akbar et al., 2011; Madert et al., 2013). Bydon and colleagues found a revision rate of 17.8% and could also find no connection to the localization of the infection (Bydon et al., 2014). Thus, we can conclude that surgical treatment of spondylodiscitis on all spinal segments works to the same extent and is associated with similar revision rates.

In our study, a total mortality rate of 13.7% was found within the first 30 days. Other recent large studies mostly reported similar short-term mortality rates in hematogenous spondylodiscitis (Rutges et al., 2016). Kehrer et al. found a mortality rate of 13.4% in the first 90 days after diagnosis of spondylodiscitis, Loibl found an infection-related mortality of 12.4%, Karadimas found 12.3% and Valancius reported 8.7% mortality for conservatively treated and 1.9% for surgically treated patients (Karadimas et al., 2008; Valancius et al., 2013; Kehrer et al., 2014; Loibl et al., 2014). In contrast, Pola was able to demonstrate a very low mortality of 4.8% in 250 patients with two years of follow-up (Pola et al., 2017). It is important to note that our study population consisted of haematogenous *and* per continuitatem spondylodiscitis (e.g. via infected foreign material like aortic prostheses, vicryl meshes etc. or esophago-tracheal fistulas). The latter were associated with an increased mortality rate, thereby increasing overall mortality. The relatively high mortality rate in our study could also be due to the fact that, as a tertiary care center, we have a high proportion of inpatient transfers (19%) from other hospitals where therapy had failed or where no care was possible in the referring hospital due to the severity of the disease.

Nevertheless, there was no significant correlation between localization of the infection and mortality rate, even if the rate was almost twice as high in disseminated cases. The connection between the extent of spondylodiscitis and outcome appears logical at first, since a higher microorganism load is to be expected for the organism in disseminated infestation. Thus, a higher microorganism load would be expected to result in increased morbidity and mortality. However, no influence of the number of infected segments on mortality and complication rates existed, so that this hypothesis appears questionable. Rather, the – although not significantly – increased mortality rate in disseminated spondylodiscitis cases seems to be due to the more invasive approach and the increased number of surgical procedures. Surprisingly, in our case series, cervical and thoracic infections showed similar outcome compared to lumbar cases, although cervical and thoracic manifestations can be seen as a prognostic factor for poor outcome in spinal infections (Govender, 2005; Duarte and Vaccaro, 2013).

Limitations of our study are certainly the conception as a retrospective single-center study as well as the relatively short follow-up and the fact that no outcome scores were recorded. Findings from our single-center study, which is biased due to a high prevalence of complex supraregional cases, including a high prevalence of patients requiring surgical intervention, should not be generalized to other institutions and always consider differences in regional patient characteristics. In addition, the descriptive design of our study, a vast number of potential confounding variables and the small group size in certain localizations in combination with an overall small number of events causing larger error margins in some statistical test significantly limits the conclusive value of the multivariate analysis.

Conclusion

Our study correlates disease course, clinical management, and surgical approach with the localization of the spinal infection in one of the largest patient cohorts examined so far. In the course of our investigations we find evidence that the localization of spondylodiscitis is likely not affecting the occurrence of complications, the revision rate and in particular the 30-day mortality. However, we observed notable differences in the incidence of epidural abscesses, concomitant endocarditis, preoperative neurological deficits and initial CrP in thoracic infections. Prospective studies with a longer follow-up in particular are necessary to detect further differences and to be able to tailor the therapy depending on the localization. At the present time there is no clear evidence that the localization of the infection decisively influences the course of the disease.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

The study was conducted according to the local ethical standards (ethics committee of the Hamburg Medical Chamber) and the Declaration of Helsinki.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgements

The authors thank Holger Rohde, MD, PhD from the Institute of Medical Microbiology, Virology and Hygiene, University Medical Center Hamburg-Eppendorf, Germany for input regarding the microbiological methods and materials used. We thank Eik Vettorazzi from the Institute of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf, Germany for support concerning statistical testing and interpretation.

References

Akbar M, Lehner B, Doustdar S, Fürstenberg CH, Hemmer S, Bruckner T, et al. Pyogene Spondylodiszitis der Brust- und Lendenwirbelsäule: Eine neue Klassifikation zur Entscheidungsfindung bei der Wahl der operativen Therapie. Orthopade 2011;40(7):614–23.

Akiyama T, Chikuda H, Yasunaga H, Horiguchi H, Fushimi K, Saita K. Incidence and risk factors for mortality of vertebral osteomyelitis: a retrospective analysis

using the Japanese diagnosis procedure combination database. BMJ Open 2013;3:.
Appalanaidu N, Shafafy R, Gee C, Brogan K, Karmani S, Morassi G, et al. Predicting the need for surgical intervention in patients with spondylodiscitis: the Brighton Spondylodiscitis Score (BSDS). Eur Spine J 2018;28(4):751–61.
Batson O. The function of the vertebral veins and their role in the spread of metastases, 1940. Clin Orthop Relat Res 1995;312:4–9.
Behmanesh B, Gessler F, Schnoes K, Dubinski D, Won SY, Konczalla J, et al. Infective endocarditis in patients with pyogenic spondylodiscitis: implications for diagnosis and therapy. Neurosurg Focus 2019;46(1):1–5.
Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF, Schmitt SK, et al. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis 2015;61:859–63.
Bernard L, Dinh A, Ghout I, Simo D, Zeller V, Issartel B, et al. Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial. Lancet 2015;385:875–82.
Butler JS, Timlin M, O'Byrne JM, Shelly MJ, Powderly WG. Nontuberculous Pyogenic Spinal Infection in Adults: a 12-year experience from a tertiary referral center. Spine (Phila Pa 1976) 2006;31(23):2695–700.
Bydon M, De La Garza-Ramos R, Macki M, Naumann M, Sciubba DM, Wolinsky JP, et al. Spinal instrumentation in patients with primary spinal infections does not lead to greater recurrent infection rates: an analysis of 118 cases. World Neurosurg 2014;82(6):e807–14.
Courjon J, Lemaignen A, Ghout I, Therby A, Belmatoug N, Dinh A, Pyogenic vertebral osteomyelitis of the elderly: characteristics and outcomes on behalf of the DTS (Duration of Treatment for Spondylodiscitis) study group 2017;12(12).
Duarte RM, Vaccaro AR. Spinal infection: state of the art and management algorithm. Eur Spine J 2013;22(12):2787–99.
Eysel P, Hopf C, Vogel I, Rompe JD. Primary stable anterior instrumentation or dorsoventral spondylodesis in spondylodiscitis?: results of a comparative study. Eur Spine J 1997;6(3):152–7.
Gentile L, Benazzo F, De Rosa F, Boriani S, Dallagiacoma G, Franceschetti G, et al. A systematic review: characteristics, complications and treatment of spondylodiscitis. Eur Rev Med Pharmacol Sci 2019;23(2):117–28.
Govender S. Spinal infections. J Bone Jt Surg 2005;87-B:1454–8.
Grammatico L, Baron S, Rusch E, Lepage B, Surer N, Desenclos JC, et al. Epidemiology of vertebral osteomyelitis (VO) in France: analysis of hospital-discharge data 2002–2003. Epidemiol Infect 2008;136(5):653–60.
Hadjipavlou AG, Mader JT, Necessary JT, Muffoletto AJ. Hematogenous pyogenic spinal infections and their surgical management. Spine (Phila Pa 1976) 2000;25 (13):1668–79.
Herren C, Jung N, Pishnamaz M, Breuninger M, Siewe J, Sobottke R. Spondylodiscitis: diagnosis and treatment options – a systematic review. Dtsch Arztebl Int 2017;114(51–52):875–82.
Heyde CE, Boehm H, El Saghir H, Tschöke SK, Kayser R. Surgical treatment of spondylodiscitis in the cervical spine: a minimum 2-year follow-up. Eur Spine J 2006;15(9):1380–7.
Homagk L, Roehl K, Hofmann GO, Klauss JR, Marmelstein D, Homagk N. Spondylodiscitis severity code: scoring system for the classification and treatment of non-specific spondylodiscitis. Eur Spine J 2016;25(4):1012–20.
Kapsalaki E, Gatselis N, Stefos A, Makaritsis K, Vassiou A, Fezoulidis I, et al. Spontaneous spondylodiscitis: presentation, risk factors, diagnosis, management, and outcome. Int J Infect Dis 2009;13(5):564–9.
Karadimas EJ, Bunger C, Lindblad BE, Hansen ES, Høy K, Helmig P, et al. Spondylodiscitis. A retrospective study of 163 patients. Acta Orthop 2008;79 (5):650–9.
Kehrer M, Pedersen C, Jensen TG, Hallas J, Lassen AT. Increased short- and long-term mortality among patients with infectious spondylodiscitis compared with a reference population. Spine J 2015;15(6):1233–40.
Kehrer M, Pedersen C, Jensen TG, Lassen AT. Increasing incidence of pyogenic spondylodiscitis: a 14-year population-based study. J Infect 2014;68(4):313–20.
Krogsgaard MR, Wagn P, Bengtsson J. Epidemiology of acute vertebral osteomyelitis in Denmark. Acta Orthop Scand 1998;69(5):513–7.
Lener S, Hartmann S, Barbagallo GMV, Certo F, Thomé C, Tschugg A. Management of spinal infection: a review of the literature. Acta Neurochir (Wien) 2018;160 (3):487–96.
Loibl M, Stoyanov L, Doenitz C, Brawanski A, Wiggermann P, Krutsch W, et al. Outcome-related co-factors in 105 cases of vertebral osteomyelitis in a tertiary care hospital. Infection 2014;42:503–10.
Lora-Tamayo J, Murillo O, Verdaguer R, Narváez JA, Ariza J, Euba G, et al. Changing trends in the epidemiology of pyogenic vertebral osteomyelitis: the impact of cases with no microbiologic diagnosis. Semin Arthritis Rheum 2011;41 (2):247–55.
Maccauro G, Spinelli MS, Mauro S, Perisano C, Graci C, Rosa MA. Physiopathology of spine metastasis. Int J Surg Oncol 2011;1–8.
Madert J, Liem M, Frosch KH, Niemeyer T. Dorsolateraler Zugang und interkorporelle Spondylodese bei Spondylodiszitis der Brust- und Lendenwirbelsäule (TLIF-Technik). Oper Orthop Traumatol 2013;25(3):262–72.
Le Moal G, Roblot F, Paccalin M, Sosner P, Burucoa C, Roblot P, et al. Clinical and laboratory characteristics of infective endocarditis when associated with spondylodiscitis. Eur J Clin Microbiol Infect Dis 2002;21(9):671–5.
Morelli S, Carmenini E, Caporossi AP, Aguglia G, Bernardo ML, Gurgo AM. Spondylodiscitis and infective endocarditis: case studies and review of the literature. Spine (Phila Pa 1976) 2001;26(5):499–500.
Moritani T, Kim J, Capizzano AA, Kirby P, Kademian J, Sato Y. Pyogenic and non-pyogenic spinal infections: emphasis on diffusion-weighted imaging for the detection of abscesses and pus collections. Br J Radiol 2014;87(1041):20140011.
Ninet J, Gayet JL, Etienne J, Bonvoisin B, Vignon E, Berthou JD, et al. Bacterial endocarditis presenting as acute vertebral osteomyelitis: 14 cases. Eur Heart J 1984;5(Suppl C):101–5.
Pola E, Autore G, Formica VM, Pambianco V, Colangelo D, Cauda R, et al. New classification for the treatment of pyogenic spondylodiscitis: validation study on a population of 250 patients with a follow-up of 2 years. Eur Spine J 2017;26 (Suppl 4):479–88.
Rutges JPHJ, Kempen DH, van Dijk M, Oner FC. Outcome of conservative and surgical treatment of pyogenic spondylodiscitis: a systematic literature review. Eur Spine J 2016;25(4):983–99.
Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. Rev Infect Dis 1979;1(5):754–76.
Shiban E, Janssen I, Wostrack M, Krieg SM, Ringel F, Meyer B, et al. A retrospective study of 113 consecutive cases of surgically treated spondylodiscitis patients. A single-center experience. Acta Neurochir (Wien) 2014;156(6):1189–96.
Shousha M, Boehm H. Surgical treatment of cervical spondylodiscitis: a review of 30 consecutive patients. Spine (Phila Pa 1976) 2012;37(1):1–7.
Sobottke R, Seifert H, Fatkenheuer G, Schmidt M, Goßmann A, Eysel P. Current diagnosis and treatment of spondylodiscitis: differential diagnosis. Dtsch Aerzteblatt Online 2008;105(10):181–8.
Sur A, Tsang K, Brown M, Tzerakis N. Management of adult spontaneous spondylodiscitis and its rising incidence. Ann R Coll Surg Engl 2015;97 (6):451–5.
Tsai TT, Yang SC, Niu CC, Lai PL, Lee MH, Chen LH, et al. Early surgery with antibiotics treatment had better clinical outcomes than antibiotics treatment alone in patients with pyogenic spondylodiscitis: a retrospective cohort study. BMC Musculoskelet Disord 2017;18(1):1–7.
Valancius K, Hansen ES, Høy K, Helmig P, Niedermann B, Bünger C. Failure modes in conservative and surgical management of infectious spondylodiscitis. Eur Spine J 2013;22(8):1837–44.