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Mortality and health-related quality of life in patients surgically treated for spondylodiscitis

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Abstract

Purpose: To assess mortality, disability, and health-related quality of life (HRQL) in patients surgically treated for spondylodiscitis. **Methods:** A retrospective longitudinal study was conducted on all patients surgically treated for spondylodiscitis over a 6-year period at a single tertiary spine center. Indications for surgery, pre- and postoperative neurological impairment, comorbidities, and mortality were recorded. A survey was conducted on all eligible patients with the EuroQol 5-dimension (EQ-5D) questionnaire and Oswestry Disability Index (ODI). **Results:** Sixty-five patients were diagnosed with spondylodiscitis not related to recent spine surgery. One-year mortality rate was 6%. In all, 36% and 27% had pre- and postoperative neurological impairment, respectively, with only one patient experiencing deterioration postoperatively. At final follow-up (median 2 years), mean ODI was 31% (SD = 22) and mean EQ-5D time trade-off score was 0.639 (SD = 0.262); this was significantly lower than that in the normal population ($p < 0.001$). Patients with neurological impairment prior to index surgery had lower EQ-5D scores ($p = 0.005$) and higher ODI ($p = 0.02$) at final follow-up compared with patients without neurological impairment. **Conclusions:** Several years after surgery, patients surgically treated for spondylodiscitis have significantly lower HRQL and more disability than the background population. Neurological impairment prior to index surgery predicts adverse outcome in terms of disability and lower HRQL.

Keywords

comorbidity, infection, mortality, outcome, spine, spondylodiscitis

Introduction

Although it still remains a rare condition, there has been an increasing incidence of spondylodiscitis over the past decades.[1,2] It is estimated that 20–40% of patients with spondylodiscitis will undergo surgical treatment.[3,4] The primary indication for surgery is progressive neurological impairment but indications also include epidural abscess, pain caused by spinal instability, progressive deformity, or failure to respond to conservative treatment.[5–9] Although several guidelines have been proposed,[7–9] there is no consensus regarding the indications for surgery. Correspondingly, various surgical methods have been described, all based on varying degrees of debridement of vertebral bodies and discs through anterior, posterior, or combined surgical approaches.[5–7,9–12] In most cases, stabilization with spinal implants is necessary, and in spite of the infectious nature of the condition, most studies report a low risk of recurring infection.[5,6,10,13,14]

The overall mortality of spondylodiscitis is 5–10%,[2–4,7,15] but studies reporting outcome after surgical treatment

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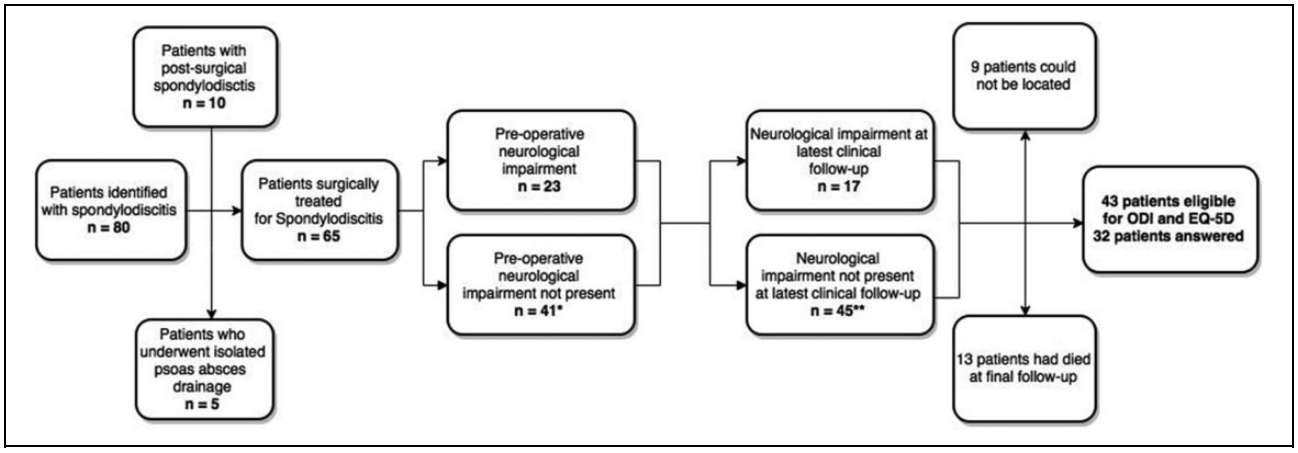

Figure 1. Patient flowchart. *Information on neurological status was not available in one patient. **Information on neurological status was not available on three patients at the latest clinical follow-up.

are scarce, and few studies have reported the health-related quality of life (HRQL) after surgery.[16–20] A few studies have shown that a preoperative neurological deficit is a predictor of a negative outcome,[4,8,9] and neurological deficits are more often present when the spinal infection affects the cervical or thoracic regions.[8] No studies so far have examined HRQL in these groups. Such knowledge would be valuable as an element in establishing guidelines for the surgical treatment of spondylodiscitis.[7] The purpose of the present study was to assess the mortality, disability, and HRQL after surgical treatment of spondylodiscitis, compared to Danish population norm. The primary hypothesis of the study was that HRQL is reduced significantly 1 year after surgical treatment of spondylodiscitis when compared to the background population.

Material and methods

Study population

A retrospective cohort study was conducted on all patients undergoing surgical treatment of spondylodiscitis from January 1, 2005, through December 31, 2010, in a tertiary referral center serving 2.6 million people. Patients who had undergone spine surgery for other conditions within 3 months of admission were excluded (Figure 1).

Data analysis

Data collection and analysis were performed using Microsoft Excel® 2010 and the statistical software R version 3.3.2. The study was approved by the Danish Data Protection Agency (J.nr. 2014-41-2820). Data distribution was assessed with histograms, and continuous variables were compared using unpaired t test, Wilcoxon rank sum test, or Kruskal–Wallis analysis. A p value < 0.05 was considered statistically significant.

Clinical characteristics

Neurological status was assessed retrospectively based on the surgeon's preoperative clinical examination using Frankel's classification where grade A represents complete neurological injury and grade E represents normal motor function. Postsurgical neurological status was assessed at the latest clinical follow-up. Diagnosis was based on preoperative magnetic resonance imaging (MRI) findings, and in cases of positive microbiology, bacteriological diagnosis was made from positive blood cultures, needle biopsy, or surgical sampling. The level of spinal focus was defined as the level of surgical decompression. A Charlson Comorbidity Index (CCI) score was calculated for each patient,[21] indicating the severity of comorbidity, and patients were grouped into either low (0–1) or high ($\geq$2) CCI score in line with other studies.[22,23]

Surgical procedures

All types of surgical procedures were included (Table 2). Staged surgery was registered as one single procedure, and the first operation was recorded as the index surgery. The primary indication for index surgery was categorized as one of the following:

- neurological impairment (preoperative Frankel A–D with or without epidural abscess, deformity, or instability),
- epidural abscess (Frankel E and epidural abscess visualized on MRI), and
- instability/deformity (Frankel E and no epidural abscess, pain, and kyphosis/deformity and/or instability).

Patients with instability and/or deformity were further divided into those with ongoing infection and those who had completed a conservative treatment regime. Complications to surgery were defined as conditions requiring

unplanned reoperation within 48 h after the index procedure.

Mortality

Mortality was assessed on December 31, 2011, to allow for a minimum follow-up of 1 year for all patients. Patients lost to follow up were recorded as alive based on their last contact with our department. Patients' accumulated risk years from the date of index procedure and mortality were assessed for all patients at the 1-year mark and for all accumulated risk years.

Follow-up questionnaires

Patients who were alive and residing in Denmark on December 31, 2011, were sent two questionnaires by regular mail: the Danish version of the EuroQol 5-dimension (EQ-5D) questionnaire and the Oswestry Disability Index (ODI). HRQL and disability were examined in patients with and without neurological impairment prior to index procedure and for different levels of spinal focus. In order to compare groups, the "time trade-off" (TTO) method[24] was used to calculate an index value of the EQ-5D. A post hoc analysis was performed to further examine possible associations between EQ-5D/ODI scores and the indication for surgery, surgical strategy, comorbidity, or the presence of epidural abscess.

Results

A total of 65 patients were included (Table 1). *Staphylococcus aureus* was the predominant pathogen (38%) followed by *Mycobacterium tuberculosis* (14%). Eleven patients (15%) were culture negative. Of these, three patients were administered antituberculosis medical treatment. However, no positive culture or polymerase chain reaction was obtained from the blood or tissue sample.

The lumbar spine was the most frequent level of spinal focus (Table 1). Six patients had more than one focus in the spine, with the lumbar segments being primarily affected in all of them. Median time from diagnosis to index surgery was 4 days (interquartile range [IQR]: 4–34). Patients were clinically followed up for a median of 134 days (IQR: 25–455). Prior to the index procedure, 23/64 (36%) had neurological deficits, which were classified as Frankel D or lower. At the latest clinical follow-up, 17/62 (27%) had neurological deficits. Overall, 12/23 (52%) with preoperative neurological impairment improved by one or two Frankel categories during the study period (Figure 2). One patient experienced neurological deterioration, from Frankel category D to C due to a postoperative intraspinal hematoma. Neurological status was not assessed in one patient prior to index surgery and in three patients at the latest clinical follow-up due to the lack of information in the patient files.

Table 1. Baseline characteristics of patients surgically treated for spondylodiscitis.

Variable	No. (%)
Total number of patients	65 (100)
Sex	
Male	45 (69)
Female	20 (31)
Age at index surgery[a]	60 (51–70)
Comorbidities and risk factors	45/65 (69)
Alcohol abuse	17 (26)
Diabetes mellitus	16 (25)
Immunocompromised[b]	7 (11)
COPD[c]	7 (11)
IV drug abuse	6 (9)
Renal failure	5 (8)
Congestive heart failure	4 (6)
Liver cirrhosis	3 (5)
IBD	3 (5)
Disseminated cancer	2 (3)
Rheumatic disease	2 (3)
Chronic viral hepatitis	2 (3)
Cancer without metastasis	1 (2)
Endocarditis	1 (2)
Microbiological diagnosis	
Staphylococcus aureus	28 (38)
Mycobacterium tuberculosis	9 (14)
Enterobacteriae[d]	6 (9)
Coagulase neg. *Staphylococci*	4 (6)
Streptococci (*oralis* and *bovis*)	2 (3)
Atypical mycobacteriae	1 (2)
MRSA[e]	1 (2)
Haemophilus aphrophilus	1 (2)
Listeria monocytogenes	1 (2)
Pseudomonas aeruginosa	1 (2)
Polymicrobiel[f]	1 (2)
None	10 (15)
Level of spinal focus	
Cervical	3 (5)
Thoracic	15 (23)
Thoracolumbar	8 (12)
Lumbar	39 (60)
Multifocal involvement of the spine	6 (8)
Psoas abscess	23 (35)
Epidural abscess	46 (71)

IBD: inflammatory bowel disease.
[a]Median (interquartile range).
[b]Chemotherapy, steroid treatment, or immunodeficiency.
[c]Chronic obstructive pulmonary disease.
[d]*Escherichia coli* (3), *Enterococcus faecalis* (2), *Veillonella* (1).
[e]Methicillin-resistant *Staphylococcus aureus*.
[f]Citrobacter and *Enterococcus faecium*.

Surgery

A total of 79 surgical procedures for spondylodiscitis were performed in the 65 patients (Table 2). In 15 patients, indication for surgery was instability and/or deformity, and 5 (8%) of these had completed a conservative treatment regime and showed no sign of ongoing infection, and surgical biopsies were all culture negative. Median time from diagnosis to index surgery was 384 days (range:

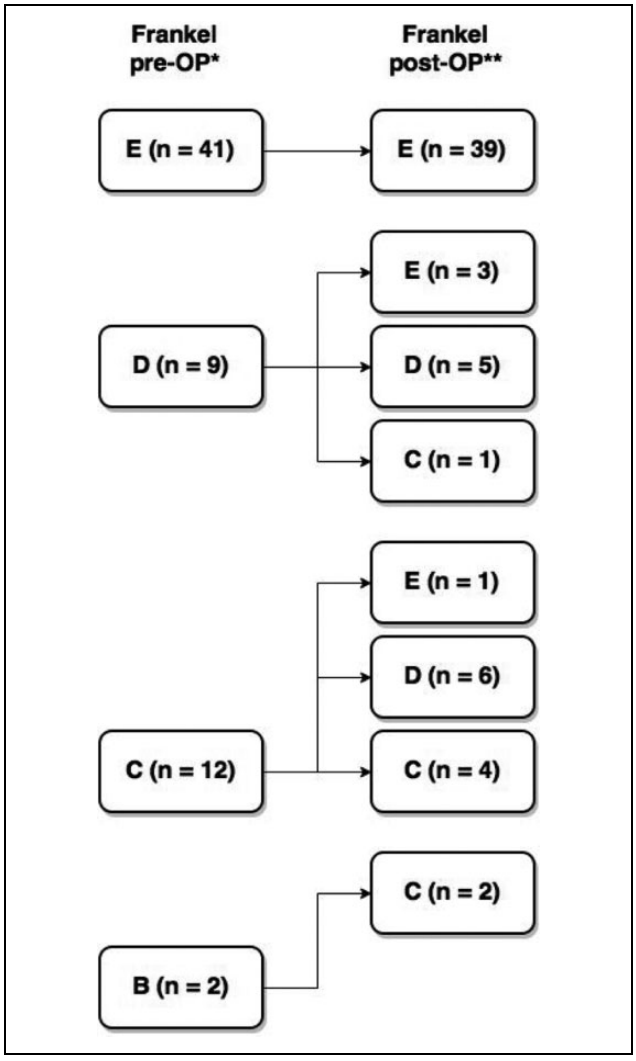

Figure 2. Neurological status prior to index surgery (preop) and at the latest clinical follow-up (postop) according to the Frankel classification. *Information on neurological status was not available for one patient. **Information on neurological status was not available for three patients at latest clinical follow-up.

Table 2. Surgical approach of the 79 spinal procedures for spondylodiscitis performed in 65 patients.

Total number of patients	No. = 65
Total number of spinal procedures	79
Complications to spinal procedures	5 (6%)
Index procedure surgical approach	
Anterior decompression	3 (4%)
Anterior decompression and instrumentation	9 (13%)
Posterior decompression	29 (41%)
Posterior decompression and instrumentation	11 (16%)
Combined two-stage anterior and posterior instrumentation	13 (19%)
Indications for index surgery	
Neurological impairment	23 (35%)
Epidural abscess	27 (42%)
Deformity/instability	15 (23%)

145–1438) in this group. Six patients had surgical drainage of psoas abscess performed in an isolated procedure at some point of their disease. Five patients developed postoperative complications requiring revision surgery. All five patients were primarily operated with posterior decompression. The indication for revision surgery was neurological deterioration and intraspinal hematomas diagnosed on MRI within 48 h of surgery. Of the 65 patients, 13 (20%) underwent reoperation, not including the 5 revision procedures due to complications. Four of these 13 patients had posterior decompression performed as index surgery and underwent an additional spinal procedure with posterior instrumentation.

Mortality and follow-up

The 1-year crude mortality rate was 6.5%. Patients accumulated a total of 185 person-years of observation for mortality (median 2 years). Overall mortality was 12/65 (18%) in this period. At final follow-up, a total of 13 patients had died (1 patient died after assessing mortality but before receiving follow-up questionnaires), and 9 patients could not be located, primarily due to emigration. The remaining 43 patients received the EQ-5D questionnaire and ODI median 2 years after their index procedure (IQR: 1.2–4.9 years) of which 32 (74%) answered both questionnaires. On the EQ-5D visual analog scale, the mean health status was 59 (SD = 21) on a scale from 0 to 100, where 0 is the worst possible health. The mean TTO score of the patients in our study (0.639, SD = 0.262) was significantly lower than that of a Danish age- and sex-matched normal population ($p < 0.0001$).[24] The median ODI score was 29 (IQR: 18–44), where a score of 0 corresponds to no disability at all. Only preoperative neurological impairment was a predictor of adverse outcome, with significantly lower EQ-5D and higher ODI scores at follow-up in this group (Table 3). Additionally, we found significant differences in ODI and EQ-5D scores between the three indication categories ($p = 0.027$ and $p = 0.036$, respectively; Figure 3).

Discussion

In the present study, the HRQL was significantly reduced in patients surgically treated for spondylodiscitis compared with the population norm. Preoperative neurological impairment was identified as a negative predictor of HRQL, despite neurology improvement in most patients.

The primary strength of the present study is that it is a one-center study with a high number of patients compared with other studies of surgical treatment of spondylodiscitis. Baseline characteristics did not differ significantly from other studies of patients with spondylodiscitis undergoing surgical as well as conservative treatment.[3,5,6,10,12,16,19,25] A considerable number of patients had comorbidities consistent with the literature.[3,4,8,15] The predominant pathogen was *S. aureus*, but in a large number of patients no

Table 3. EQ-5D "TTO" and ODI scores at minimum 1-year follow-up.

		EQ-5D TTO-score		ODI	
Group	*n*	Median (IQR)	Difference	Median (IQR)	Difference
Level of spinal focus					
Thoracic/cervical	18	0.682 (0.584–0.734)	$p = 0.338$	26 (19–53)	$p = 0.845$
Lumbar/thoracolumbar	47	0.723 (0.520–0.783)		28 (18–41)	
Neurological impairment preoperative					
Yes (Frankel A–D)	23	0.592 (0.367–0.660)	$\boldsymbol{p = 0.011}$[b]	38 (30–63)	$\boldsymbol{p = 0.034}$[b]
No (Frankel E)	41[a]	0.742 (0.658–0.805)		24 (14–33)	
Index surgical approach					
Instrumentation[1]	33	0.723 (0.609–0.774)	$p = 0.791$	30 (22–44)	$p = 0.458$
No instrumentation[2]	32	0.660 (0.367–0.776)		22 (18–37)	
Comorbidity					
Low Charlson score (0–1)	50	0.723 (0.592–0.776)	$p = 0.599$	29 (18–42)	$p = 0.826$
High Charlson score ($\geq$2)	15	0.660 (0.463–0.774)		22 (20–48)	
Epidural abscess					
Present	46	0.660 (0.367–0.776)	$p = 0.606$	24 (18–54)	$p = 0.371$
Not present	19	0.723 (0.684–0.776)		30 (24–38)	
Psoas abscess					
Present	23	0.689 (0.333–0.783)	$p = 0.760$	18 (17–49)	$p = 0.528$
Not present	42	0.716 (0.609–0.775)		30 (19–42)	

IQR: interquartile range; 1: Anterior, posterior or combined decompression and instrumentation; 2: Isolated anterior or posterior decompression only; TTO: time trade-off; ODI: Oswestry Disability Index; EQ-5D: EuroQol 5-dimension

[a]Information on neurological status was not available in one patient.

[b]$p < 0.05$ was considered statistically significant using Wilcoxon rank sum test.

microbiological diagnosis could be established in accordance with the literature.[3,4]

Most studies report overall mortality, even though this strongly correlates to the length of follow-up.[15] The 1-year crude mortality rate in our study was comparable with the 4.8% reported by Woertgen et al.,[16] but less than a recent large-scale registry study on a Danish population.[15] The high mortality rate (20%) in the latter study was possibly due to an older study population and inclusion of patients who were too critically ill to be referred to a tertiary hospital. A nationwide study of spondylodiscitis by Aagaard et al. showed a 1-year crude mortality rate of 5.6%.[22] By including only patients with *S. aureus* bacteremia, the increased mortality compared with a background population was shown to be mainly due to comorbidities. Overall, there is no evidence of increased mortality in surgically treated spondylodiscitis patients compared with those treated conservatively.[4,8,15,16]

The high rate of mortality and morbidity seen in spondylodiscitis patients is likely multifactorial. Our study did not find an association between CCI score and adverse morbidity outcome (Table 3). This may be due to a type 2 error since the high CCI group included only 15 patients; however, the CCI represents only 1-year mortality and not necessarily HRQL and disability. Additionally, the small number of patients limited our subgroup analysis to include only EQ-5D and ODI scores rather than mortality as outcome measure.

In the present study, neurological status was assessed retrospectively based on the latest clinical follow-up, with significant variation in the length of this period. In all, 36% of patients had neurological impairment at the time of their index procedure (Figure 1). This is comparable to the results reported in the literature, ranging from 27 to 56% in studies of surgically treated patients[5,6,12,25,26] and 17–27% in conservatively treated patients.[3,4,8] Overall 52% of patients with preoperative neurological impairment improved by one or two Frankel grades (Figure 2). Although this number might have increased with longer clinical follow-up for some patients, it is slightly higher compared to another Danish study[12] where only 45% improved in neurological status, whereas other studies have shown improvement in neurological impairment in 80–87% of cases.[5,6] However, these studies differed from our study as all patients underwent a combined anterior–posterior procedure. Obviously, patient selection affects the preoperative neurological status, and comparison of studies with different surgical strategies can therefore be challenging.

To evaluate HRQL and disability, the EQ-5D and the ODI questionnaires were chosen. EQ-5D is a general health questionnaire with a limited number of questions, and the possibility to compare an overall score with results from various other populations, as well as the background population.[24,27] Since no disease-specific questionnaire exists regarding spondylodiscitis, we chose the ODI, a disease-specific questionnaire for patients with chronic low back pain (CLBP), which has been widely used in the evaluation of surgical outcome in other spondylodiscitis studies.[27]

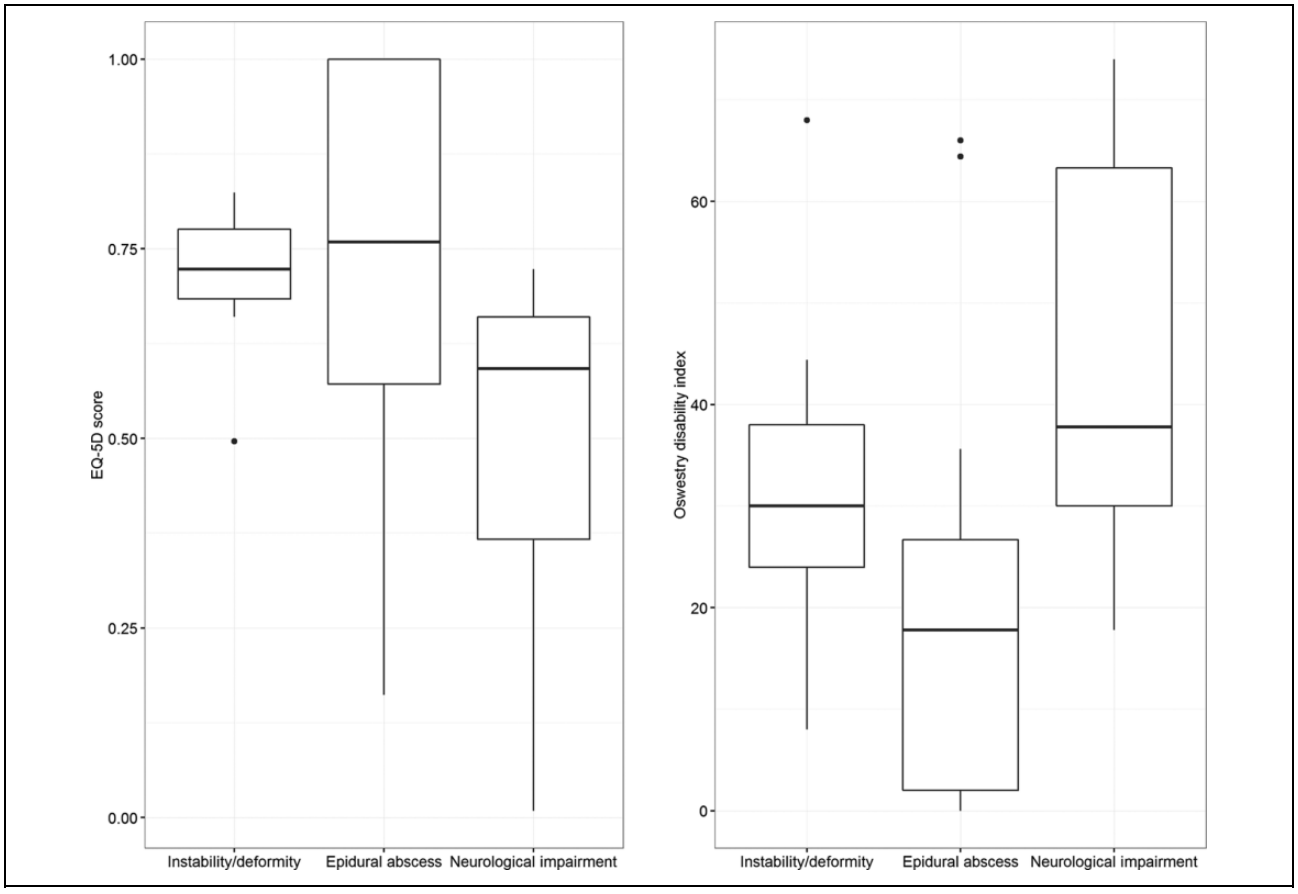

Figure 3. Box plot of the association between EuroQol 5-dimension (EQ-5D) and Oswestry Disability Index (ODI) scores at follow-up and primary indication for index surgery. Kruskal–Wallis analysis with significant differences in ODI score ($p = 0.027$) and EQ-5D score ($p = 0.036$) between the three indication categories.

Based on the mean EQ-5D TTO scores, the HRQL was significantly lower in spondylodiscitis patients compared with a normal Danish population of similar age and gender[24] (Table 3). This is in line with the results shown by Woertgen et al.[16] using the Short-Form 36 (SF-36) health survey. They also suggested a slightly better outcome in patients treated surgically than those treated conservatively. We identified only one prospective randomized trial by Linhardt et al., assessing HRQL and disability in 22 patients by comparing anterior surgery with a combined anterior–posterior procedure.[19] Overall, better outcome was found in the group with an anterior-only approach, using the SF-36 and ODI, 2 and 5 years after surgery. ODI scores for the group with a combined anterior–posterior procedure were comparable with the average score in our study; but in the group undergoing anterior surgery, the ODI score was much lower and the SF-36 scores even better than that in a healthy population.

Overall, the ODI score in our study was comparable to other studies with scores ranging from 23 to 30.[11,19,20,25] It has previously been shown that neurological impairment is a risk factor for adverse outcome in terms of recurrent infection and increased short-term mortality.[9,15] Our study confirmed that preoperative neurological impairment is a predictor of adverse outcome in terms of higher disability and lower HRQL (Table 3). Some studies suggest that neurologic deficits are more common when the disease involves cervical and thoracic levels of the spine.[4,8] However, no difference was found with regard to the level of spinal focus in the current study. We identified two former studies assessing EQ-5D in selected spondylodiscitis patients treated surgically; however, these studies examined selected surgical strategies and included only eight and 27 patients, respectively.[18,20]

The literature on surgical treatment of spondylodiscitis generally supports stabilization of the infected levels with spinal instrumentation.[5,7,9,12,13,16] Four patients in our study underwent an isolated posterior decompression as index surgery but later underwent reoperation with instrumentation. Moreover, all five patients with complications underwent posterior decompression as index surgery. A post hoc analysis however showed no difference in HRQL and disability between instrumented and uninstrumented cases (Table 3), although this result could be biased by patient selection as the decompression group possibly had less extensive disease at baseline.

The primary limitation of the present study is its retrospective design. This could especially affect the classification of neurological impairment. However, the primary focus of the study was the comparison of HRQL with the normal population and not the detailed neurologic outcome. Since the majority of variables of the patient population correspond to results in the literature, we find that the results regarding HRQL are representative of patients with surgically treated spondylodiscitis and not related to a specific procedure. Although a higher response rate would be desirable, we find that the 74% response rate is acceptable for this heterogenic population and in line with previous studies with a similar design.[16,17]

Conclusion

To our knowledge, this is the largest study assessing HRQL with EQ-5D after surgical treatment of spondylodiscitis. The HRQL was significantly lower than that in a normal population of similar age and gender. Finally, preoperative neurological impairment predicted adverse outcome despite neurological improvements after surgery. Our findings may aid future studies in determining which patients would benefit from surgery when compared with conservative treatment.

Declaration of conflicting interests

Casper Dragsted has received a research scholarship from The Lundbeck Foundation, funding was paid to the institution.Theis Aagaard has no conflicts of interest. Søren Ohrt-Nissen has received research funding paid to the institution from K2M. Martin Gehrchen and Benny Dahl have received research funding paid to the institution from Globus Medical Inc., Medtronic International and K2M.

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