Spine

SPINE Volume 42, Number 8, pp E490–E495

SURGERY

Spinal Implants Can Be Inserted in Patients With Deep Spine Infection

Results From a Large Cohort Study

Hwee Weng Dennis Hey, MBBS, MRCS, MMed, MCI, FRCSEd, FAMS,* Li Wen Nathaniel Ng, MBBS (Sing),* Chuen Seng Tan, BSc (Hons), MSc, PhD,† Dale Fisher, MBBS, FRACP, DTM&H,‡ Anupama Vasudevan, BDS, MPH,‡ Ka-Po Gabriel Liu, MBBCh, MSc, FRCS, FRCSEd,* Joseph Shantakumar Thambiah, MBBS, MMed, FRCS, FAMS,* Naresh Kumar, MBBS, MS, DNB, FRCS, DM,* Leok-Lim Lau, MBBS, BA, MBBCh, MRCS, MMed, FRCS,* Hee-Kit Wong, MBBS, MMed, FRCS, MCh, FAMS,* and Paul Anantharajah Tambyah, MBBS, MD‡

Study Design. A retrospective, cohort study of 84 patients with deep spine infection managed at a major tertiary hospital over 14 years with a minimum follow up of 2 years.

Objective. To determine the role of instrumentation in spines with deep infection.

Summary of Background Data. It is often believed that implants should not be inserted in patients with deep spine infection because of the risk of persistent or recurrent infection. However, there are often concerns about spinal stability and a paucity of evidence to guide clinical practice in this field.

Methods. We compared the mortality, reoperation, and reinfection rates in patients with spine infection treated with antibiotics alone, antibiotics with debridement, and antibiotics with debridement and instrumentation. Significant outcome predictors were determined using multivariable logistic regression model.

Results. Forty-nine males and 35 females with a mean age was 62.0 years had spine infection affecting the lumbar spine predominantly. The most common form of infection was osteomyelitis and spondylodiscitis (69.4%). *Staphylococcus aureus* was the most common causative organism (61.2%). There was no difference in terms of reoperation or relapse for patients treated with antibiotics alone, antibiotics with debridement, or antibiotics with debridement and instrumentation. However, compared with antibiotics alone, the crude inhospital mortality was lower for patients treated with instrumentation (odds ratio, OR, 0.82; $P = 0.01$), and antibiotics with debridement (OR 0.80; $P = 0.02$).

Conclusion. Spinal instrumentation in an infected spine is safe and not associated with higher reoperation or relapse rates. Mortality is lower for patients treated with instrumentation.

Key words: debridement, deep spine infection, instrumentation, mortality, recurrence, relapse, reoperation.

Level of Evidence: 3

Spine 2017;42:E490–E495

Deep infection of the spine is not uncommon[1,2] and could result from hematogenous seeding,[3,4] adjacent spread,[5] or unintended inoculation of microorganism after procedures to the spine.[6] The treatment often involves a prolonged course of appropriate antibiotics,[7] surgical debridement with or without instrumentation of the affected spine.[8]

Bacteria that cause pyogenic infections are known to form a layer of biofilm on implants leading to difficulty in its eradication.[9] Although this is widely proven in arthroplasty surgery,[10] has not been shown as conclusively for the spine.[11] Instrumentation of the spine after judicious debridement of the infected bed bears this risk and has not been widely practiced. On the contrary, it may confer advantages when stability of the spine is of concern[12] despite the risk of biofilm infections.

We attempted to investigate the role of spinal instrumentation in deep spine infection. The objectives of this study were to compare the outcomes of patients in terms of mortality, relapse, and reoperation in patients who underwent three different management regimes, that is, antibiotic treatment, antibiotics and surgical debridement, and

From the *University Orthopedics, Hand and Reconstructive Microsurgery Cluster National University Health System, Singapore; †Saw Swee Hock School of Public Health, National University of Singapore, Singapore; and ‡Division of Infectious Diseases, University Medicine Cluster, National University Health System, Singapore.

Acknowledgment date: September 24, 2015. First revision date: February 16, 2016. Second revision date: March 5, 2016. Acceptance date: June 2, 2016.

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work.

No relevant financial activities outside the submitted work.

Address correspondence and reprint requests to Hwee Weng Dennis Hey, MBBS, MRCS, MMed, MCI, FRCSEd, FAMS, University Orthopedics, Hand and Reconstructive Microsurgery Cluster, National University Health System, Singapore; E-mail: dennis_hey@nuhs.edu.sg

DOI: 10.1097/BRS.0000000000001747

antibiotics, surgical debridement, and instrumentation. We hypothesize that there will be no difference in any of the outcomes amongst the three treatment groups.

MATERIALS AND METHODS

This is a retrospective study of all patients with pyogenic deep spine infection treated at an academic medical center from 1999 to 2012 (14 years). The hospital is a tertiary healthcare center with seven spine specialists and eight active infectious disease specialists. In our institution, cefazolin is the empirical antibiotic of choice when a deep, spine infection is suspected. It will be started promptly after cultures have been taken from the patient and will be changed accordingly based on definitive culture results. Antibiotics will be discontinued after resolution of clinical signs of infection, normalized inflammatory markers, and negative interval MRI scans, which will be obtained 6 weeks to 3 month after start of treatment. Surgery for all deep spine infection was decided based on a clinical consensus made by spine specialists in consultation with the infectious disease team. Spinal instrumentation was deemed necessary if there was clinical or radiological suspicion of instability at the point of surgical decision making because of infection.

Isolation of microbial organisms often results in suboptimal yield and many patients with deep spine infection do not have positive culture results. To ensure all patients with deep spine infections are included in the study, we defined deep spine infection as patients with clinical- and radiological-apparent typical features; with or without the isolation of microbial organisms. In our inclusion criteria, patients had clinical features of back pain or constitutional symptoms (fever, loss of weight, and appetite) and radiological evidence on MRI scans, including (i) increased signal intensity on T2-weighted images in the vertebral body or disc space, or (ii) decreased signal intensity in the disc and adjacent endplates on T1-weighted images, with or without (iii) the presence of epidural and paraspinal abscesses. Patients with suspected or confirmed tuberculous infection that is endemic in the region were also excluded from the study.

The institution maintains an electronic database of all deep spine infection cases since 1999. All study patients were identified from this with further verification performed by two independent auditors not directly involved in the study to ensure all patients meet the inclusion criteria before enrolment into the study.

After Institutional Review Board approval, all electronic documentation and hardcopy medical case records were traced and pertinent data were collected. The three main outcome data collected include patient mortality, relapse of deep infection requiring only further antibiotics, and reoperations for deep spine infection. Patient characteristics and other predictors of poor outcome were also collected. They include demographics, clinical presentation, details of spine infection (radiological, laboratory, and microbiological findings), antibiotic treatment, and surgery (debridement and surgery).

All data were collected by a single investigator and audited by an independent spine specialist for accuracy. All radiological images inclusive of x-rays, computed tomograms (CT), and magnetic resonance imaging (MRI) were reviewed by two spine surgeons not directly involved in the study. If there were any discrepancy in the interpretation of these images, a musculoskeletal radiologist was consulted and a consensus was reached.

The outcome parameters of interest included mortality, reoperation for spine infection, and relapse of infection. Patient outcomes were tracked at least monthly up to 6 months and 3 monthly up to 2 years minimum. All patients whose medical records showed a loss to follow up were also contacted to ensure that they did not visit another hospital for a relapse of infection requiring treatment. All patients are followed up with a minimum of 2 years duration or if a positive outcome occurs whichever is shorter.

STATISTICAL ANALYSIS

All information collected was entered and tabulated into Microsoft Excel Spreadsheet 2011 [Version 14.0.4760.1000 (32-bit)] and analyzed using Statistical Package for the Social Sciences (version 16, SPSS Inc., Chicago, IL). Statistical significance is set as $P < 0.05$ for all computations.

For the purpose of statistical analysis, the patients were divided into three groups with each receiving a different treatment strategy. The first group received antibiotics alone, the second group received antibiotics and debridement, and the third group received antibiotics, debridement, and instrumentation.

Univariate analysis of baseline patient characteristics between comparison groups were performed using $\chi^2$and *t* test. Multivariable logistic regression modeling was subsequently used to determine the differences in each group in terms of outcome measures whereas adjusting for confounders. Odds ratios (OR) are represented and significant predictors of each outcome were also identified.

RESULTS

This study included 84 patients who satisfied the inclusion criteria. There were 49 males (58.3%) and 35 females (41.7%). The mean age was 62.0 (SD 14.4) years. Table 1 shows the baseline characteristics of the patients. The most commonly involved level of the spine was the lumbar region, specifically at L4 and L5, which was involved in 48.0% and 47.1% of the patients, respectively. The majority had two levels of involvement, and this was observed in 47 patients (or 55.3%) of the cohort.

The most common form of infection was osteomyelitis/spondylodiscitis, and this was observed in 59 patients (69.4%). *Staphylococcus aureus* was the most common causative organism isolated (61.2%), followed by *Klebsiella pneumoniae* (18.8%). In terms of antibiotic treatment, none of our patients had beta-lactam allergy. Empirical antibiotics administered includes cefazolin in 52 patients (61.9%) amoxicillin-clavulanic acid in 16 patients, ceftriaxone in 12 patients and meropenem in four patients. Patients

TABLE 1. Baseline Characteristics of Study Population

N=84		
Demographics		
Age mean (SD)	62.0 (SD 14.4)	
Gender	49 males	58.3
	35 females	41.7
Ethnicity	Chinese	64.4
Comorbidities		
ASA 1-2	57	67.9
ASA 3-4	27	32.1
Charlson 0	8	9.5
Charlson 1	8	9.5
Charlson 2	29	34.5
Charlson 3	18	21.4
Charlson 4	15	17.9
Charlson >4	6	7.1
Clinical Presentation		
Back Pain	68	80.0
Fever	20	23.5
LOW/LOA	16	18.8
Neurological symptoms	20	23.5
Neurological deficits	19	22.4
Skin changes / cellulitis	5	5.9
Autonomic involvement	7	8.2

N=84		
Involvement of spine		
C1	1	1.2
C2	3	3.5
C3	4	4.7
C4	4	4.7
C5	7	8.2
C6	6	7.1
C7	4	4.7
T1	4	4.7
T2	4	4.7
T3	7	8.2
T4	7	8.2
T5	6	7.1
T6	6	7.1
T7	6	7.1
T8	9	10.6
T9	9	10.6
T10	8	9.4
T11	7	8.2
T12	6	7.1
L1	9	10.6
L2	20	23.5
L3	30	35.3
L4	41	48.0
L5	40	47.1
S	16	18.8
1 Level	1	1.2
2 Levels	47	55.3
3 Levels	19	22.4
>3 Levels	16	18.8

N=84		
Site of infection		
Osteomyelitis/ Spondylodiscitis	59	69.4
Epidural abscess	34	40.0
Paravetebral/ Psoas	37	43.5
Laboratory values (at admission)		
TW (x10^9/L)	13.7 (SD 7.5)	
ESR (mm/hr)	74 (SD 33.9)	
CRP (mg/L)	88.8 (SD 85.2)	
Laboratory values (highest point)		
TW (x10^9/L)	20.3 (SD 21.2)	
ESR (mm/hr)	103.1 (SD 76.3)	
CRP (mg/L)	127.4 (SD 105.8)	
Microbiology		
Staphylococcus aureus	52	61.2
Klebsiella pneunomia	16	18.8
Pseudomonas aeruginosa	11	12.9
Escherichia coli	14	16.5
Coagulase negative Staphylococci	7	8.2
No organism growth	14	16.5

Legend:

ASA = American Society of Anaesthesiologist grading

LOW = Loss Of Weight

LOA = Loss of Appetite

TW = Total white

ESR = Erythrocyte sedimentation rate

CRP = C-reactive protein

who did not receive cefazolin as the first-line empirical antibiotic treatment also had suspected infection elsewhere in the body.

On admission, patients had a mean total white count (TW) of 13.7 x 10^9/L, erythrocyte sedimentation rate (ESR) of 74 mm/hr, and C-reactive protein (CRP) of 88.8 mg/L. This increased to a maximum value of TW 20.3 x 10^9/L, ESR of 103.1 mm/hr, and CRP of 127.4 mg/L preoperatively. No patients presented with pathological fractures in our cohort.

When comparing patients who received three different types of intervention (24 patients with antibiotics alone, 33 patients with combined antibiotics and surgical debridement, 27 patients with antibiotics, surgical debridement, and instrumentation) (see Figure 1). The mortality rate was significantly lower for patients who underwent surgical

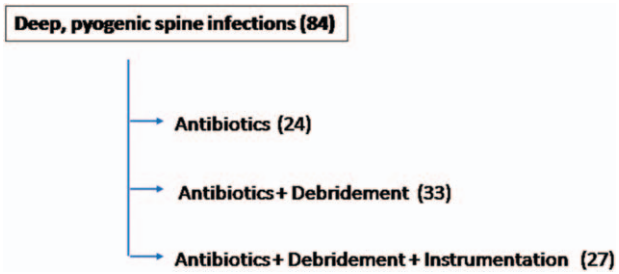

Figure 1. The numbers of patients in each cohort of the study.

debridement (OR = 0.80, 95% CI = 0.70–1.00, $P = 0.02$) and for those who underwent debridement with instrumentation (OR = 0.82, 95% CI = 0.70–0.96, $P = 0.01$). In this analysis, starting empirical antibiotics was the only parameter found to be associated with lower mortality (OR = 0.68, 95% CI = 1.00–1.01, $P = 0.01$).

There was no difference found among the three groups in terms of relapse of deep spine infection and reoperation rates. Table 2 shows the results for the three different outcomes.

DISCUSSION

Deep infection is common in the native spine. The prevalence rates reported in the literature ranged from 0.2 to 2 cases per 10,000 hospital admissions.[13,14] The mainstay of treatment for this potentially serious condition lies in its early diagnosis and prompt treatment.[15] However, there is a paucity of evidence to suggest what might be the best treatment for this condition once it is diagnosed.[16] Current modalities include antibiotics alone,[17–20] antibiotics with surgical debridement[21,22] or antibiotics with surgical debridement and instrumentation.[23] Till date, a few studies have compared the effectiveness of these treatment

TABLE 2. Mortality, Relapse, and Reoperation Rates After Antibiotics Alone, Antibiotics Plus Debridement, and Antibiotics Plus Debridement With Instrumentation

Mortality			
Treatment	**OR**	**95% (CI)**	***P***
Antibiotics	1.00	—	—
Antibiotics + debridement	0.80	0.70–1.00	0.02
Antibiotics + debridement + instrumentation	0.82	0.70–0.96	0.01
Parameter	**OR**	**95% (CI)**	***P***
Age	1.38	1.03–1.85	0.07
ASA	1.07	0.98–1.16	0.13
Charlson Comorbidity Index	1.05	0.84–1.04	0.14
Given appropriate empirical antibiotics	0.68	1.00–1.01	0.01
Relapse			
Treatment	**OR**	**95% (CI)**	***P***
Antibiotics	1.00	—	—
Antibiotics + debridement	1.08	0.88–1.31	0.46
Antibiotics + debridement + instrumentation	0.99	0.82–1.20	0.95
Parameter	**OR**	**95% (CI)**	***P***
Age	1.05	0.88–1.27	0.54
ASA	0.99	0.81–1.26	0.16
Charlson Comorbidity Index	0.99	0.83–1.15	0.38
Reoperation			
Treatment	**OR**	**95% (CI)**	***P***
Antibiotics	1.00	—	—
Antibiotics + debridement	0.93	0.84–1.02	0.13
Antibiotics + debridement + instrumentation	0.91	0.83–1.01	0.07
Parameter	**OR**	**95% (CI)**	***P***
Age	0.98	0.94–1.03	0.48
ASA	1.15	0.97–1.20	0.25
Charlson Comorbidity Index	1.13	0.95–1.15	0.22

ASA indicates American Society of Anesthesiologists; CI, confidence interval; OR, odds ratio.

options.[16] Instrumentation in a potentially infected surgical bed may lead to persistence or recurrence of infection. This can influence spine surgeons, who may then defer instrumentation to a later date even if it is clinically indicated.[24] The other available treatment options in patients who require stabilization of the spine may include spinal nursing and bed rest,[25] application of external orthotics,[26] or delayed instrumentation after multiple debridements[27] aiming at achieving eradication of infection before inserting a foreign body into an infected bed.

Several studies have suggested that instrumentation in patients with deep spine infection after surgical debridement is not as risky as previously believed.[24] The benefits of spinal stabilization in certain patients may outweigh the potential risks of infection relapse, reoperations, or mortality.[27] Complications from immobilization or the use of external orthotics have also been cited as reasons for instrumentation in the surgical management of these patients.[28]

In this study, we found that patients treated surgically have a significantly lower mortality rate compared with those treated with antibiotics alone. This could be because of better reduction of pathogenic microorganism load compared with relying solely on systemic antibiotics. It has been documented in numerous studies that penetration of infective foci by systemic antibiotics may be impeded because of a relatively impervious and a vascular reactive zone of tissue surrounding abscesses.[29–31] In this instance, surgical debridement serves as a good adjunct not only to reduce the bacterial load but also to allow penetration of antibiotics into the infected bed.[32] Our study also showed similar results between those who underwent surgical debridement and those who had surgical debridement with instrumentation. As all our patients were operated based on a clinical decision made by a panel of spine surgeons, it is reasonable to conclude that instrumentation in an infected native spine can be performed as long as there is a clinical indication. This has also been shown in other studies.[23] However, this finding may be confounded by the fact that ours is a retrospective study in which the younger and fitter patients were more likely to have surgery rather than a conservative approach although the ASA score and Charlson Comorbidity Index in the multivariable analysis just failed to reach statistical significance.

Many pyogenic organisms form biofilms rapidly on implants. These biofilms are self-sustaining and hard to eradicate.[10] Although this phenomenon is well known in arthroplasty surgery, it has not been as well documented in spine surgery.[16] The theoretical risk of biofilm formation if instrumentation was performed may be offset by the good blood supply of the axial skeleton when compared with the appendicular skeleton.[32] Larger and longer follow-up studies are required to confirm this. We believe that as long as a thorough debridement is performed with reduction of infection load, instrumentation can be performed if clinically warranted. Proper assessment of the purpose and functionality of the implants at the point of debridement is crucial.

This study showed that effective empirical antibiotics was a predictor of lower mortality rates during the treatment of an infected native spine. Deep spine infections may be difficult to diagnose[33] as they may present with nonspecific symptoms such as isolated spinal pain or fever.[34,35] When there is a high index of suspicion for these infections, empirical antibiotics can then be started to allow better prognosis as shown by Nussbaum *et al*.[6] However, in circumstances when surgery or a biopsy is planned, it may be helpful to defer starting antibiotics until the procedure is performed to avoid false negative culture results.

There are several strengths to this study. It is one of the larger clinical studies evaluating clinical outcomes in the management of spinal infection available in the literature. The data collected was maintained judiciously by two departments *via* a database over the past 14 years. A minimum 2-year follow up is also available for all patients who did not have a positive event to allow meaningful statistical calculation. The limitation of this study lies in its retrospective nature, which may be subjected to bias. Although our institution has a guideline in terms of the choice of empirical antibiotic, some patients did not receive cefazolin because of suspected concurrent infections. Differences in antibiotic treatment may confound results and have to be interpreted with caution. The findings in our study showing appropriate empirical antibiotics, as positive predictor of good outcome should be specifically evaluated in future studies. Lastly, the study subjects are managed over a 14-year period. This may lead to inevitable time-dependent factors that can also potentially bias the results.

CONCLUSION

Spinal instrumentation in an infected native spine is safe and associated with a lower mortality rate. There were no differences in relapse and reoperation rates. In this study, administration of early, appropriate, empirical antibiotics was also found to be a significant predictor of good outcome. We believe that deep infection of the spine may not preclude instrumentation. Large prospective studies should be conducted to validate this observation.

➢ Key Points

- ❑ Spinal instrumentation in an infected spine is safe and associated with a lower mortality rate.
- ❑ There is no difference with respect to relapse and reoperation rates when comparing antibiotics alone, antibiotics with debridement, or antibiotics with debridement and instrumentation.
- ❑ Effective empirical antibiotics are shown to decrease mortality rates in an infective native spine.

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