Spinal Infections: Pathophysiology, Diagnosis, Prevention, And Management

Meera Madhav Dhodapkar

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Spinal Infections: Pathophysiology, Diagnosis, Prevention, and Management
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(Sponsored by: Dr. Jonathan Grauer, Dr. Daniel Rubio, Dr. Ehud Mendel)

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Prepared for partial fulfilment of requirements for Masters of Health Sciences (MHS)
and Doctor of Medicine Degree (MD)
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Abstract

Spine infections fall under one of two major categories, primary spinal infections as well as postoperative spine infections. Both of these events are rare but associated with significant morbidity and mortality, and the diagnosis as well as optimal intervention strategy utilized for management is not always clear. In particular, postoperative surgical site infection (SSI) is a rare but potentially devastating complication. Previous studies have assessed risk factors for postoperative spine SSI and one aimed to develop risk stratification tool to assess management options, but this tool has not been externally validated or regularly used.

The current thesis had two primary aims: 1) to review the literature and assess and describe the current consensus on strategies for the diagnosis of spinal infections, with a focus on imaging modalities and findings, and 2) to conduct an original single-institution retrospective research study investigating the rate of SSI following elective spine surgery, surgical management pursued, and success of traditionally utilized one-stage of irrigation and debridement (I&D) with closure over drains.

The work outlined in the current thesis seeks to provide an overview of the topic of spine infections with foci on both optimal use of imaging in the diagnosis as well as a focus on management strategies for postoperative SSI. We hope this data provides useful context and guidance to the practice of spine surgeons and other clinicians working up or managing patients with spinal infections.
Section 1: Imaging Diagnosis of Spinal Infections

Introduction
Spinal infections are increasingly prevalent in the general population, likely due to a combination of increased prevalence of predisposing conditions such as intravenous drug use and diabetes, as well as improved detection and diagnosis.\(^1\),\(^2\) They may be caused by direct inoculation following spinal procedures, but are more commonly a result of hematogenous seeding from a distant site.\(^3\) While certain clinical findings should increase suspicion for spinal infections, appropriate imaging findings are needed to confirm the diagnosis. In this review, relevant literature and evidence surrounding imaging modalities employed to aide in the diagnosis and evaluation of various spinal infections is discussed.

Statement of Purpose
This section of the current thesis aimed to review the literature and assess and describe the current consensus on strategies for the diagnosis of spinal infections, with a focus on imaging modalities and findings.

Methods
Student contributions
The below methods were carried out in their entirety by the student author of this dissertation, under the guidance of Dr. Jonathan Grauer, Dr. Daniel Rubio, Dr. Tamanna Patel, Mr. Scott Halperin, Dr. Comron Saifi, Dr. Peter Whang, Dr. Ehud Mendel, and Dr. Arya Varthi.

Ethics Statement and Human Subjects Research
As a narrative review and based on publicly available manuscripts, this study was exempt from IRB review.

**Literature Review**

This section was a narrative review of the literature seeking to describe the current status of diagnosis of spinal infections with a focus on imaging strategies. The search was conducted reviewing English language articles published in PubMed indexed journals over the course of 3/2023-4/2023.

Themes regarding imaging based diagnosis of spinal infections were synthesized based on current literature, and future directions of interest in the field were described.

**Results**

*Pyogenic spondylodiscitis*

Pyogenic spondylodiscitis (vertebral osteomyelitis-discitis) is estimated to account for <2%-4% of all cases of osteomyelitis.\(^4\)-\(^6\) It is thought to result from hematogenous spread from infectious bacterial microemboli. These microemboli most commonly originate in the arterial system, become lodged in one of the metaphyseal arteries, resulting in infarction and infection.\(^7\) The most common causative organism implicated in vertebral osteomyelitis is *Staphylococcus aureus* (*S. aureus*).\(^4\)-\(^6,\)\(^8\)-\(^10\) However, there is an increased incidence of *Pseudomonas* and *Salmonella* infection in intravenous drug users and sickle cell disease patients, respectively.\(^6\) Urinary tract infections are the most common infectious source.\(^4,\)\(^10,\)\(^11\) The lumbar spine is the most commonly affected site.\(^5,\)\(^6,\)\(^9,\)\(^10\) Infections usually begin in the anterior aspect of the
vertebral body along the endplates given the relatively greater number of blood flow to
the region. Infections originating within the disc spread to the two adjacent vertebral
endplates early in the course of the disease via anastomoses between adjacent
intermetaphyseal arteries, and therefore both the disc and two adjacent vertebral
endplates may involved in many of these cases.\textsuperscript{12}

Recognition of patients with pyogenic discitis/osteomyelitis based on clinical
findings may be difficult due to nonspecific symptoms and a highly variable time course.
Back pain is the most common presenting symptoms, seen in nearly 90\% of cases. Fever
is the second most common presenting symptom; however, it is only present in 60\% of
cases, which may lead to reduced suspicion for infection and delayed diagnosis.\textsuperscript{13}
Patients may also exhibit weight loss, malaise, and neurologic deficits on exam.\textsuperscript{11}
Although elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) may
be present and aide in the diagnosis, laboratory evaluation is not reliable in the evaluation
of suspected pyogenic discitis/osteomyelitis.\textsuperscript{14-16}

Obtaining plain radiographs are a common first step in imaging for patients with
nonspecific back pain, though their role is limited in the evaluation of infectious
etiologies. Radiographs have poor sensitivity to detect pyogenic discitis/osteomyelitis,
particularly early in the course of the disease.\textsuperscript{13} However, patients who present later in
the disease course, radiographs have been found to have abnormalities in nearly 90\% of
cases of pyogenic spondylodiscitis. The first radiographic sign of spine infection may be
as subtle as endplate irregularity.\textsuperscript{17} As the infection progresses, erosion of the endplate
and adjacent bone may become more prominent.\textsuperscript{11, 17} After a longer period of time (8-12
weeks), bone regeneration may result in visible sclerosis on radiographs and attempted
ankylosis of the infected disc space.\textsuperscript{18} While patients with severely degenerative disc diseases may manifest similar radiographic abnormalities to those mentioned above, degenerative etiologies may be distinguished from infectious etiologies by the presence of the vacuum disc effect, which is not found in spondylodiscitis.\textsuperscript{19}

Magnetic resonance imaging (MRI) is the gold standard in the evaluation of infectious discitis/osteomyelitis.\textsuperscript{20} Total spine MRI imaging is recommended in order to fully evaluate the extent of infection, including any adjacent or skip lesions.\textsuperscript{21} The earliest findings on MRI of infection of the disc space and vertebral body are caused by edema and inflammatory cell entry into the area.\textsuperscript{17} This results in hypo-intensity of the disc and adjacent vertebral bodies on T1 weighted images, and hyperintensity of the disc and adjacent vertebral bodies on T2 weighted images.\textsuperscript{12} Similar to radiographs, MRI changes in infection may display similarities to those observed in degenerative conditions of the spine. However, the major observed difference between these two etiologies is that while in degenerative disease the disc will appear hypointense on T2 due to losses of water content,\textsuperscript{22} in the infected disc the signal will be increased and the disc will be hyperintense on T2 weighted images. Decreased disc height is often described in patients with disc infections, however disc height is often normal, particularly in early infection. Disc height may even be increased or apparently increased, due to disc abscess or collapse of adjacent vertebral bodies. Presence of paraspinal or epidural inflammation, demonstrated by hyperintensity on T2 weighted images, is a valuable clue in ruling in the diagnosis, as spinal infections are nearly always associated with these findings.\textsuperscript{12, 23, 24} (Table 1)
While the cortical bone and therefore minor erosions of the endplate may be difficult to visualize on non-contrast MRI images, T1 weighted scans performed with gadolinium-diethylene triamine pervaacetic acid (Gd-DPTA) contrast demonstrate enhancement of the disc-endplate interface and/or the disc space itself.\textsuperscript{12} While non-contrast studies may provide sufficient evidence for diagnosis, contrast studies may help to distinguish degenerative findings,\textsuperscript{10} such as Modic endplate changes,\textsuperscript{25} from infectious findings. Furthermore, there may be accompanying abscesses in the paraspinal space which can further aide in the diagnosis\textsuperscript{26}. (Table 1)

**Table 1. Summary of Magnetic Resonance Imaging Findings In Common Pyogenic Spinal Infections, Stratified by Pre- and Post- Contrast Enhancement**

<table>
<thead>
<tr>
<th>MRI Imaging Findings</th>
<th>Pre-Gd</th>
<th>Post-Gd</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pyogenic spondyloendiscitis</strong></td>
<td>On T1-weighted images: Disc and adjacent vertebral body hypointensity On T2-weighted images: Disc and adjacent vertebral body hyperintensity</td>
<td>On T1-weighted images: Disc and disc-endplate interface hyperintensity</td>
</tr>
<tr>
<td><strong>Epidural abscess</strong></td>
<td>On T1-weighted images: Hypointense or isointense abscess compared to spinal cord On T2-weighted images: Hyperintense abscess compared to spinal cord</td>
<td>On T1-weighted images: Rim enhancing abscess, central fluid signal, alteration of thecal sac dimensions</td>
</tr>
</tbody>
</table>
CT scan may be performed in addition to MRI. CT scans can provide superior evaluation of bony abnormalities such as end plate and vertebral body erosion, as well as assessment of overall bone quality.\(^{27}\) Use of IV contrast may demonstrate enhancement of the epidural or paraspinal structures, and therefore is superior to non-contrast studies. However, CT with IV contrast, unlike CT myelogram and MRI, may fail to detect and/or accurately determine the extent of neurologic compression secondary to infectious intraspinal extension.\(^ {28}\)

Patients with certain implanted intracardiac devices or metallic foreign bodies may not be able to undergo MRI imaging. In these patients, computed tomography (CT) myelography can be performed to assess for involvement of the spinal canal with compression of neural structures.\(^ {29}\) Serious allergic reactions to iodinated contrast media are rare but possible. Additionally, there is risk of intra-dural inoculation from injection of iodinated contrast through potential infected epidural space, so CT with IV contrast is recommended prior to CT myelogram. However, given as the morbidity and mortality
associated with delay of diagnosis of spine infection and potential spinal cord compression can be severe, a corticosteroid premedication protocol should be seriously considered in these cases if other options for imaging are otherwise inaccessible.\textsuperscript{28}

Additionally, Technetium-99m diphosphonate bone scans have been described to demonstrate a high degree of sensitivity in the detection of spondylodiscitis, with some studies reporting greater than 90\% sensitivity.\textsuperscript{30} Bone scans will show focal hyperperfusion, hyperemia, and increased bony uptake in bone affected by osteomyelitis.\textsuperscript{31} However, such conditions which increase the rate of bone turnover such as fracture may produce some similar findings and so bone scan is less specific than some earlier described imaging modalities.

\textit{Spinal epidural abscess}

Spinal epidural abscess (SEA) is an infection of the space between the dura and the vertebral periosteum,\textsuperscript{32} most often caused by hematogenous spread of bacteria into the epidural space. Less commonly, SEA may occur due to secondary to extension from a pyogenic spondylodiscitis or facet joint infection or from iatrogenic inoculation from a spinal surgery.\textsuperscript{33, 34} SEA most commonly occurs at the thoracic spine, however, can occur anywhere along the spine and in certain cases may involve the entire spine. \textit{S. aureus} is the most common causative organism.\textsuperscript{2, 35, 36} Clinical non-specific signs of spinal infection (i.e, back pain, fever, limited range of motion, tenderness to palpation) with signs of neurologic compression (i.e, neurologic deficit) further increase the suspicion for SEA. SEA can occur either in the anterior or posterior epidural space,\textsuperscript{35} and the presenting neurologic deficits in these cases may be either due to direct compression
caused by the abscess or thrombophlebitis or thrombosis. Early diagnosis of SEA is difficult and as a result treatment is often delayed. The resulting morbidity and mortality associated with SEA is relatively high, with reports in the literature ranging from 18-30% in various studies. Risk factors for SEA include diabetes mellitus, IV drug use, chronic renal failure, alcohol use disorder, and immunodeficiency.

Gadolinium (Gd) contrast enhanced MRI is considered the gold standard for the imaging and diagnosis of SEA, with a reported sensitivity and specificity of greater than 90%. The abscess will appear hypointense or isointense compared to the spinal cord on T1-weighted images and hyperintense to the spinal cord on T2-weighted imaged. Following post-Gd T1-weighted imaging, the abscess will enhance peripherally in with a central fluid signal. In contrast, epidural plexus engorgement/phlegmon may enhance heterogeneously or homogenously on post-contrast T1 imaging. Distinguishing SEA from imaging findings in neoplasms, SEA more commonly violates the midline septum of the ventral epidural space. Diffusion weighted imaging may show restricted diffusion within the SEA. (Table 1)

In cases where patients cannot undergo MRI or MRI is inaccessible, CT with IV contrast may be obtained. While CT myelography may also be quite sensitive compared to MRI, it may increase the risk of spreading infection into the subarachnoid space. In patients with symptoms for at least 1 week prior to presentation, concomitant infection outside the spinal region, and with erythrocyte sedimentation rate (ESR) > 95 mm/h, imaging of the entire spine to exclude skip lesions may be warranted.
Primary pyogenic subdural abscess

Primary pyogenic subdural abscess of the spine is rare but presents with clinical features similar to epidural abscess. Similarly, the most commonly implicated causative organism is *S. aureus*, and risk factors for intradural abscess are similar to SEA. MRI is also the imaging technique of choice in these cases, and will reveal a crescentic collection. On T1-weighted images, the intradural abscess may appear isointense compared to dural contents, with hyperintense contents and hypointense capsular margins on T2 weighted images. Post-Gd T1-weighted imaging may reveal a thick, irregular enhancing wall.\(^5,48\) (Table 1) Compared to SEA, imaging findings suggestive of intradural abscess include preservation of the shape of the thecal sac\(^6\) and the epidural fat.\(^49\)

Septic facet arthritis is a rare infection of the facet joints, most commonly caused by *S. aureus*\(^50\) via hematogenous spread,\(^51\) with previous studies describing the clinical entity limited to case series of several patients.\(^51-53\) Elderly patients and immunocompromised patients are most commonly affected. Septic facet arthritis has been most frequently reported in the lumbar spine,\(^51\) however cases of cervical facet joint arthritis have also been published in the literature. Clinical signs suggestive of facet joint arthritis are nonspecific may include focal neurological deficit on exam, fever,\(^51-53\) however given the rarity of this diagnosis it is often not the most commonly considered etiology for such symptoms. Imaging evaluation is crucial to identify septic facet arthritis, with MRI with Gd contrast being the imaging modality of choice. Even in early disease (within 5 days of symptom onset),\(^50\) MRI with Gd enhancement has been
described to demonstrate isolated synovitis with T1 hypointensity and resultant enhancement on post-Gd imaging, and hyperintensity on T2.\textsuperscript{50} (Table 1) MRI may also show inflammatory changes of the joint with narrowing, erosion of the intervertebral space, as well as concomitant infections such as paraspinal or psoas abscess, or epiduritis.\textsuperscript{53} CT may demonstrate osteolysis of the corresponding side hemi-arch, or infiltration of the joint and of the paraspinal muscles.\textsuperscript{53} Technetium scintigraphy is highly sensitive and will demonstrate increased uptake at the suspected joint, however this finding may not be specific.\textsuperscript{50, 51, 53} Plain radiographs may demonstrate erosive arthritis late in the course of disease, however they may also may be unrevealing for any specific signs of infection early in the disease course.\textsuperscript{51}

**Discussion**

The above section presents findings from a narrative review examining the use of imaging in the diagnosis of spinal infections. Overall, imaging plays an important role in the diagnosis of spinal infections. Early diagnosis is paramount in the treatment of spinal infections and leads to improved outcomes. This article reviews the imaging and relevant clinical details of infections of the spine: pyogenic spondylodiscitis, tuberculous spondylodiscitis, septic facet arthritis, epidural abscess, and subdural abscess. Though radiographs can reveal subtle changes with infections, advanced imaging modalities have increased sensitivity to aid in early diagnosis. Magnetic resonance imaging (MRI) is emphasized given it is generally the most sensitive and specific advanced imaging modality. However, nuclear medicine imaging and computer tomography (CT) play a role diagnosis in cases where MRI is not available or contra-indicated. Additionally, CT is also important for image-guided biopsy to guide antimicrobial treatment.
Challenges and Limitations

This review has several limitations, some of which are inherent to study of spinal infections. First, we limited our search to English language and PubMed indexed articles published before 4/2023. While this may have limited our search, we still believe this review captures the relevant themes and strategies utilized in the imaging based diagnosis of spinal infections.

With regards to challenges of the current review, it is important to note that spinal infections are relatively rare clinical events. Thus, there is limited literature especially with regards to certain subtypes of spinal infections, nonetheless, we felt it crucial to summarize and describe what is present in the literature. Furthermore, this project was undertaken under the guidance of a spine surgeon and subject matter expert to ensure no landmark data or evidence or important themes were missed from the current review.

Conclusions

In summary, the present thesis presents findings of a narrative review summarizing diagnosis of spinal infections with a focus on imaging modalities in particular the role of advanced imaging modalities like MRI and CT with or without contrast and with or without biopsy which may help to guide antimicrobial treatment.
Section 2: Management of Postoperative Spine Surgical Site Infections

Introduction

Spine surgery may be considered for degenerative, deformity, traumatic, oncologic, or infectious pathologies.\textsuperscript{54-57} When performed for appropriate indications, outstanding functional results can be achieved,\textsuperscript{56, 58-60} but must be balanced against potential risks.\textsuperscript{61} Understanding how to best manage potential adverse outcomes, such as postoperative surgical site infections (SSIs), needs to be understood.

Postoperative spine SSIs are reported to occur in the range of <1\% to 3.1\% of cases.\textsuperscript{62,63,64,65} Risk factors for developing SSIs have been studied and include patient factors (such as age,\textsuperscript{66} smoking,\textsuperscript{67} obesity,\textsuperscript{66, 68} and diabetes mellitus\textsuperscript{67}) as well as surgical factors (such as instrumentation,\textsuperscript{64} number of levels fused,\textsuperscript{67} posterior approach,\textsuperscript{68} and longer duration of surgery\textsuperscript{68}). Most surgical site infections occur in the first month following surgery,\textsuperscript{64, 66, 69, 70} but can be further out as well.\textsuperscript{70}

Management of Spine Infections

If spine SSI is diagnosed, the most common management involves surgical irrigation and debridement (I& D) with closure over drains followed by a course of intravenous antibiotics.\textsuperscript{71} The advantage of primary closure over drains is that, if successful, this represents a one-stage solution to the issue at hand.\textsuperscript{72,73} Nonetheless, previous spine studies among relatively small samples of patients at single institutions have estimated the rates of failure of one-stage I&D to be variable, ranging from 18-35\%.\textsuperscript{74-76}
Alternatively, spine SSIs can be managed with serial procedures that are often associated with negative pressure systems at index or subsequent debridements. The advantage of initiation of negative pressure wound systems at the time of SSI presentation is that it initiates a linear course of serial procedures (in the operating room or at bedside) and primary closure can be considered in a delayed fashion (or the negative pressure wound system can be used as definitive treatment).

One study attempted to develop a tool to stratify patients presenting with spine SSI to an optimal treatment course based on their predicted risk for failure for one-stage I&D. That study reviewed 128 spine SSI patients and developed the Postoperative Infection Treatment Score for the Spine (PITSS) tool. Their algorithm evolved from several factors they associated with failure of one-stage I&D: diabetes mellitus, infection characteristics such as surgical culture MRSA-positivity, presence of distant/systemic site infection, and surgical characteristics such as instrumentation. Possibly due to the complexity of the model and lack of external validation, its utilization has not achieved broad clinical use.

The current study aimed to build on prior work by studying a population of postoperative spine SSIs to validate, refine, and/or simplify a systematic approach to the utilization of one stage I&D over drains versus serial procedures with negative pressure wound systems. If able to identify patients who may be at a high risk of failure of one-stage I&D, it was thought that this might support other treatment options for this subset of patients.
Statement of Purpose

The work outlined in this dissertation aimed to build on prior work by studying a population of postoperative spine SSIs to validate, refine, and/or simplify a systematic approach to the utilization of one stage I&D over drains versus serial procedures with negative pressure wound systems. If able to identify patients who may be at a high risk of failure of one-stage I&D, it was thought that this might support other treatment options for subsets of patents.

Methods

Student contributions

The below methods were carried out in their entirety by the student author of this dissertation, under the guidance of Dr. Jonathan Grauer, Dr. Daniel Rubio, Dr. Tamanna Patel, Mr. Scott Halperin, Dr. Comron Saifi, Dr. Peter Whang, Dr. Ehud Mendel, and Dr. Arya Varthi.

Ethics Statement and Human Subjects Research

As a retrospective review, our Institutional Review Board (IRB) exempted this study from further review.

Study cohort

All patients undergoing elective spine surgery at a single academic institution between 2013 and 2021 were identified. Exclusion criteria included index surgeries
performed for primary diagnoses of infection, polytrauma, or those performed for patients younger than 18 years of age. As a retrospective review, our Institutional Review Board (IRB) exempted this study from further review.

SSI was diagnosed based on the definition specified by the Center for Disease Control and Prevention (CDC) guidelines.79 Patient characteristics of those who did and did not develop SSI requiring return to the operating room for I&D were assessed. Patient characteristics included: age, sex, body mass index (BMI), American Society of Anesthesia (ASA) class, presence of specific comorbidities, and smoking status. The specific comorbidities included cardiovascular (CV)/pulmonary, insulin dependent diabetes mellitus (IDDM, on insulin), non-insulin dependent diabetes mellitus (NIDDM, not on insulin), chronic steroid use, and cancer at the time of surgery.

SSI and peri-operative characteristics & management

For those who developed SSI, index surgery characteristics were collected via manual chart review by one study author and included: patient’s spine primary diagnosis (degenerative, deformity, trauma, or oncologic), level (cervical, thoracic, lumbar, sacral), number of operated levels, surgical approach (anterior, posterior), instrumentation, dural tear / CSF leak, and bone graft type (allograft/graft supplement ± local bone, iliac crest ± supplement, none [non-fusion]).

Only SSI infection requiring return to the operating room for I&D or wound vacuum was assessed. Initial management of the SSIs was dichotomized into primary closure over drains versus initiation of series procedures with wound vacuum per the
treating physician. Patients were be considered to have failed the one-stage I&D and closure over drain approach if they required additional surgical debridement.

Of patients diagnosed with SSI, a number of additional parameters were assessed. The time from index surgery to I&D in days, laboratory data from within one week if infection management (white blood cell count [WBC], erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]), presence of distant/systemic infection (bacteremia as diagnosis by blood culture, and urinary tract infection [UTI] or pneumonia [PNA]). Finally, organisms identified at the time of I&D were determined (Methicillin sensitive Staphylococcus aureus [MSSA], Methicillin resistant Staphylococcus aureus [MRSA], Other).

Data analysis

Patients that underwent I&D with closure over drains were assessed as two distinct sub-cohorts- those that required further I&D procedures and those that did not. These comparisons were done for patient, procedural, and infection variables.

Univariable analyses were done with χ² tests, Fisher exact tests, or two sample t-tests, as appropriate. Multivariable logistic regression was used to assess association of factors associated with one-stage I&D failure. For multivariable analysis, continuous variables other than age were dichotomized. Lab values were dichotomized to assess odds of failure of one-stage I&D in patients with lab values above our institution’s reference ranges. Time to I&D was dichotomized to reflect odds of failure in patients who presented for I&D less than 30 days following their index procedures. All
multivariable analyses included or were controlled for age, sex, and ASA using methods previously described.\textsuperscript{80}

For an additional set of analyses, the primary study analysis was repeated grouping patients who were initially managed with wound vacuum with those who failed one-stage I&D to ensure that they were not drawing off a potentially higher risk group who would otherwise not have been detected in the primary analysis.

For yet one other set of additional analyses, the performance of the previously reports PITSS score\textsuperscript{75} was assessed for the current sample to determine sensitivity and specificity, positive predictive value (PPV), and negative predictive value (NPV) based on their cutoff for high risk of failing one-stage I&D.

P-value less than an alpha of 0.05 was considered significant for univariable analysis, a Bonferroni correction was applied for all multivariable analyses. Analyses were performed and graphics were made in Python version 3.8, STATA version 16, Excel version 16.16, and JMP version 15. This study was prepared in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for case-control studies.
Results

Study population

A total of 11,023 spine surgery patients were identified (Fig. 1). Of these, SSI requiring I&D was identified for 76 (0.69%, for which 86.8% were managed with I&D and closure over drains and 13.2% were managed with wound vacuum dressings from the outset). (Table 2)
Table 2. Pre-operative characteristics of patients undergoing primary spinal procedures performed at a single institution between 2013 and 2021 who did and did not develop SSI.

<table>
<thead>
<tr>
<th></th>
<th>Did not develop SSI (n=10,947)</th>
<th>Did not develop SSI (n=76)</th>
<th>Initial management with a wound vacuum (n=10)</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>60.2 (± 16.0)</td>
<td>62.3 (± 13.5)</td>
<td>55.1 (± 17.3)</td>
<td>62.8 (± 12.4)</td>
<td>67.7 (± 11.3)</td>
</tr>
<tr>
<td></td>
<td>(mean ± SD)</td>
<td></td>
<td></td>
<td>P value</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>= 0.220</td>
<td>= 0.97 (0.92,1.03)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>P = 0.270</td>
<td>P = 0.377</td>
</tr>
<tr>
<td>Male</td>
<td>5,650 (51.6%)</td>
<td>37 (48.7%)</td>
<td>4 (40%)</td>
<td>26 (54.2%)</td>
<td>7 (38.9%)</td>
</tr>
<tr>
<td>Female</td>
<td>5,297 (48.4%)</td>
<td>39 (51.3%)</td>
<td>6 (60%)</td>
<td>22 (45.8%)</td>
<td>11 (61.1%)</td>
</tr>
<tr>
<td>ASA class</td>
<td></td>
<td></td>
<td></td>
<td>P = 0.570</td>
<td>1.69 (0.45,6.31)</td>
</tr>
<tr>
<td>1</td>
<td>645 (5.9%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>4,838 (44.2%)</td>
<td>21 (21.6%)</td>
<td>4 (40%)</td>
<td>14 (29.2%)</td>
<td>3 (16.7%)</td>
</tr>
<tr>
<td>≥ 3</td>
<td>5,464 (49.9%)</td>
<td>55 (72.4%)</td>
<td>6 (60%)</td>
<td>34 (70.8%)</td>
<td>15 (83.3%)</td>
</tr>
<tr>
<td>Medical comorbidities</td>
<td></td>
<td></td>
<td></td>
<td>P = 0.617</td>
<td>1.49 (0.31,7.10)</td>
</tr>
<tr>
<td>CV/Pulmonary</td>
<td>6,137 (56.1%)</td>
<td>42 (55.3%)</td>
<td>5 (50%)</td>
<td>29 (60.4%)</td>
<td>8 (44.4%)</td>
</tr>
<tr>
<td></td>
<td>0.50(0.05,4.96)</td>
<td></td>
<td></td>
<td>P = 0.552</td>
<td>0.50(0.05,4.96)</td>
</tr>
<tr>
<td>IDDM</td>
<td>611 (5.6%)</td>
<td>11 (14.5%)</td>
<td>2 (20%)</td>
<td>5 (10.4%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td></td>
<td>1.32(0.08,22.36)</td>
<td></td>
<td></td>
<td>P = 0.847</td>
<td>1.32(0.08,22.36)</td>
</tr>
<tr>
<td>NIDDM</td>
<td>1,146 (10.5%)</td>
<td>13 (17.1%)</td>
<td>1 (10%)</td>
<td>10 (20.8%)</td>
<td>2 (11.1%)</td>
</tr>
<tr>
<td></td>
<td>0.20(0.01,3.11)</td>
<td></td>
<td></td>
<td>P = 0.249</td>
<td>0.20(0.01,3.11)</td>
</tr>
<tr>
<td>Chronic steroid use</td>
<td>511 (4.7%)</td>
<td>5 (6.6%)</td>
<td>0</td>
<td>1 (2.1%)</td>
<td>3 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>24.67(0.94,645.05)</td>
<td></td>
<td></td>
<td>P = 0.054</td>
<td>24.67(0.94,645.05)</td>
</tr>
<tr>
<td>Cancer at the</td>
<td>317 (2.9%)</td>
<td>5 (6.6%)</td>
<td>1 (10%)</td>
<td>3 (6.3%)</td>
<td>2 (11.1%)</td>
</tr>
<tr>
<td></td>
<td>0.65(0.04,10.93)</td>
<td></td>
<td></td>
<td>P = 0.764</td>
<td>0.65(0.04,10.93)</td>
</tr>
<tr>
<td>time of surgery</td>
<td>1,908 (17.4%)</td>
<td>13 (17.1%)</td>
<td>2 (20%)</td>
<td>10 (20.8%)</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>-------------</td>
<td>---------</td>
<td>------------</td>
<td>---------</td>
</tr>
</tbody>
</table>

SSI= surgical site infection, I&D= Incision and drainage, CV = cardiovascular, IDDM = Insulin-dependent diabetes mellitus, NIDDM = Non insulin-dependent diabetes mellitus, ASA= American Society of Anesthesiologists

*p-values representative of analysis comparing patients who failed one-stage I&D versus those with resolution after one-stage I&D

*Odds ratios represent odds of failure of one-stage I&D given certain patient characteristics, p<0.003 significant given Bonferroni correction
Patients who did not develop surgical site infections

Of the patients who did not develop SSI, the average age was 60.2 +/- 16.0, 5,650 (51.6%) were male. The greatest fraction were >= ASA class 5,464 (49.9%), followed by ASA class 2 (n=4,838, 44.2%). Six thousand, one hundred and thirty seven patients had a history of cardiovascular or pulmonary comorbidities. Six hundred and eleven (5.6%) had a history of insulin dependent diabetes mellitus (IDDM) whereas 1,146 (10.5%) had a history of non-insulin dependent diabetes mellitus (NIDDM). Chronic steroid use was identified in 511 (4.7%) of patients and cancer at the time of surgery was present in 317 (2.9%) of patients. Smoking 1 year prior to surgery was identified in 1,908 (17.4%) of patients. (Table 2)

Patients who developed surgical site infections

Of the patients who did develop SSI, the average age was 62.3 +/- 13.5, 37 (48.7%) were male. The greatest fraction were >= ASA class (72.4%), followed by ASA class 2 (n=21, 21.6%). Forty-two patients (55.3%) had a history of cardiovascular or pulmonary comorbidities. 11 (14.5%) had a history of IDDM whereas 13(17.1%) had a history of NIDDM. Chronic steroid use was identified in 5 (6.6%) of patients and cancer at the time of surgery was present in 5 (6.6%) of patients. Smoking 1 year prior to surgery was identified in 13 (17.1%) of patients. (Table 2)

Patients managed with wound vacuums
Of the patients who did develop SSI, a minority (n=10, 13.2%) were managed initially with I&D and placement of a wound vacuum. The average +/- SD age of these patients was 55.1 +/- 17.3, 4 (40%) were male. The greatest fraction were >= ASA class 3 (n=6, 60%), followed by ASA class 2 (n=4, 40%). Five patients (50%) had a history of cardiovascular or pulmonary comorbidities. Two (20%) had a history of IDDM whereas 1 (10%) had a history of NIDDM. Chronic steroid use was identified in none of the patients and cancer at the time of surgery was present in 1 (10%) of patients. Smoking history prior to surgery was identified in 2 (20%) of patients. (Table 2) Eight (80%) of patients underwent their index procedures for degenerative diagnoses, one (10%) for deformity, one (10%) for oncology, none for traumatic diagnoses (0%). Two (20%) of the surgeries were in the cervical spine, eight (80%) were in the lumbrosacral spine. One patient underwent surgery with an anterior approach (10%), nine underwent surgery with a posterior approach (90%). Half (n=5, 50%) of the surgeries performed were with instrumentation. Two patients (20%) surgeries were complicated by dural tears or CSF leaks. Allografts/graft substitute with or without local bone was used in 5 (50%) of cases, whereas the other 5 (50%) did not use graft as they were non-fusion cases. (Table 3)
Table 3. Index procedure characteristics of patients undergoing primary spinal procedures performed at a single institution between 2013 and 2021 who developed SSI, univariable and multivariable analyses

<table>
<thead>
<tr>
<th>Initial management with a wound vacuum (n=10)</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I&amp;D, closure, no further intervention (n=48)</td>
<td>I&amp;D, closure, required further intervention (n=18)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spine Primary Diagnosis</th>
<th>[Spine Primary Diagnosis]</th>
<th>P value*</th>
<th>OR (95%CI)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenerative</td>
<td>8 (80%)</td>
<td>40 (83.3%)</td>
<td>11 (61.1%)</td>
<td>Reference</td>
</tr>
<tr>
<td>Deformity</td>
<td>1 (10%)</td>
<td>4 (8.3%)</td>
<td>3 (16.7%)</td>
<td>3.42 (0.34, 34.35)</td>
</tr>
<tr>
<td>Oncology</td>
<td>1 (10%)</td>
<td>3 (6.3%)</td>
<td>2 (11.1%)</td>
<td>1.06 (0.11, 9.91)</td>
</tr>
<tr>
<td>Trauma (Isolated)</td>
<td>0</td>
<td>1 (2.1%)</td>
<td>2 (11.1%)</td>
<td>1.83 (0.08, 39.69)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level</th>
<th>[Level]</th>
<th>P value*</th>
<th>OR (95%CI)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>2 (20%)</td>
<td>13 (27.1%)</td>
<td>1 (5.6 %)</td>
<td>Reference</td>
</tr>
<tr>
<td>Thoracolumbar</td>
<td>0</td>
<td>5 (10.5%)</td>
<td>8 (44.4%)</td>
<td>14.83 (0.96, 229.84)</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>8 (80%)</td>
<td>30 (62.5%)</td>
<td>9 (50%)</td>
<td>3.51 (0.28, 43.39)</td>
</tr>
</tbody>
</table>

Surgical Approach

| Anterior | 1 (10%) | 6 (12.5%) | 0 | - | - |

P=0.008
SSI = Surgical site infection, I&D = Incision and drainage, CSF = cerebrospinal fluid
*p-values representative of univariable analysis comparing patients who failed one-stage I&D versus those with resolution after one-stage I&D
 Odds ratios represent odds of failure of one-stage I&D given certain surgical characteristics, controlling for age, sex and ASA. p<0.003 significant given Bonferroni correction

<table>
<thead>
<tr>
<th></th>
<th>9 (90%)</th>
<th>42 (87.5%)</th>
<th>18 (100%)</th>
<th>-</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Instrumentation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (50%)</td>
<td>26 (54.2%)</td>
<td>12 (66.7%)</td>
<td>1.50</td>
<td>0.32, 6.97</td>
</tr>
<tr>
<td>No</td>
<td>5 (50%)</td>
<td>22 (45.8%)</td>
<td>6 (33.3%)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td><strong>Dural tear or CSF leak</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (20%)</td>
<td>5 (10.4%)</td>
<td>3 (16.7%)</td>
<td>1.76</td>
<td>0.28, 10.95</td>
</tr>
<tr>
<td>No</td>
<td>8 (80%)</td>
<td>43 (89.6%)</td>
<td>15 (83.3%)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td><strong>Bone graft type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allograft/graft substitute ± local bone</td>
<td>5 (50%)</td>
<td>24 (50.0%)</td>
<td>10 (55.6%)</td>
<td>1.70</td>
<td>0.37, 7.92</td>
</tr>
<tr>
<td>Iliac crest ± supplement</td>
<td>0</td>
<td>4 (8.3%)</td>
<td>3 (16.7%)</td>
<td>2.71</td>
<td>0.31, 23.39</td>
</tr>
<tr>
<td>None (non-fusion)</td>
<td>5 (50%)</td>
<td>20 (41.7%)</td>
<td>5 (27.8%)</td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

Of the patients managed with initial wound vacuum, the average time to presentation with infection from index surgery was 22.8 +/- 4.98 days. With regards to labs, the average +/- SD WBC count was 10.9 +/- 6.5, ESR was 73.6 +/- 36.0, CRP was 118.4 +/- 106.6. None of the patients initially managed with wound vacuum were
diagnosed with any distant/systemic infection such as bacteremia, UTI or pneumonia.

The most common culprit organism identified was MSSA (n=5, 50%). (Table 4)
Table 4. Infection characteristics at time of I&D of patients undergoing primary spinal procedures performed at a single institution between 2013 and 2021 who developed SSI, univariable and multivariable analyses

<table>
<thead>
<tr>
<th>Time from index surgery [days] (mean ± SD)</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial management with a wound vacuum (n=10)</td>
<td>Univariable analysis</td>
</tr>
<tr>
<td></td>
<td>I&amp;D, closure, no further intervention (n=48)</td>
<td>I&amp;D, closure, required further intervention (n=18)</td>
</tr>
<tr>
<td></td>
<td>22.8 (± 4.98)</td>
<td>24.4 (± 22.3)</td>
</tr>
<tr>
<td>Labs</td>
<td>WBC (mean ± SD)</td>
<td>10.9 (± 6.5)</td>
</tr>
<tr>
<td></td>
<td>ESR (mean ± SD)</td>
<td>73.6 (± 36.0)</td>
</tr>
<tr>
<td></td>
<td>CRP (mean ± SD)</td>
<td>118.4 (± 106.6)</td>
</tr>
<tr>
<td>Distant/systemic Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacteremia</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>UTI or PNA alone</td>
<td>0</td>
</tr>
</tbody>
</table>
Compositions of those who did and did not fail initial I&D with closure over drains

Of the 66 patients who underwent I&D and closure over drains, 18 (27.3%) failed the attempted one-stage I&D and required subsequent I&D (Table 2, Table 3, Table 4).

Compared to patients who underwent initial I&D with primary closure without failure, those who required repeat intervention did not differ significantly in age (62.8 +/- 12.4 versus 67.7 +/- 11.3, p=0.220), sex distribution (n=26, 54.2% versus n=7, 38.9%, p=0.270), percent ASA class >=3 (n=34, 70.8% versus n=15, 83.3%, p=0.570), percent ASA class 2 (n=14, 29.2% versus n=3, 16.7%, p=0.570), percent with a history of CV/pulmonary comorbidities (n=29, 60.4% versus n=8, 44.5%, p=0.277), percent with a history of NIDDM (n=5, 10.4% versus n=4, 22.2%, p=0.242), percent with a history of chronic steroid use (n=1, 2.1% versus n=3, 16.7%, p=0.059), percent with a diagnosis of cancer at the time of surgery (n=3, 6.3% versus n=2, 11.1%, p=0.608), and percent with a history of smoking (n=10, 20.8% versus n=1, 5.6%, p=0.140). (Table 2)

<table>
<thead>
<tr>
<th>Organism identified</th>
<th>None</th>
<th>MSSA</th>
<th>MRSA</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9 (90%)</td>
<td>5 (50.0%)</td>
<td>1 (10.0%)</td>
<td>4 (40.0%)</td>
</tr>
<tr>
<td>WBC</td>
<td>44 (91.7%)</td>
<td>19 (39.6%)</td>
<td>5 (10.4%)</td>
<td>24 (50.0%)</td>
</tr>
<tr>
<td>ESR</td>
<td>8 (44.4%)</td>
<td>8 (44.4%)</td>
<td>1 (5.6%)</td>
<td>9 (50.0%)</td>
</tr>
<tr>
<td>CRP</td>
<td>Reference</td>
<td>-</td>
<td>P=0.470</td>
<td>-</td>
</tr>
<tr>
<td>PNA</td>
<td>-</td>
<td>-</td>
<td>0.30</td>
<td>P=0.368</td>
</tr>
</tbody>
</table>

SSI= Surgical site infection, I&D= Incision and drainage, UTI= Urinary tract infection, PNA= Pneumonia, WBC= white blood cell count, ESR= Erythrocyte sediment rate, CRP= C-reactive protein, MSSA= Methicillin sensitive Staph. Aureus, MRSA= Methicillin resistant Staph. Aureus
*p-values representative of analysis comparing patients who failed one-stage I&D versus those with resolution after one-stage I&D

Odds ratios represent odds of failure of one-stage I&D given certain infection characteristics, controlling for age, sex and ASA, p<0.003 significant given Bonferroni correction
Compared to patients who underwent initial I&D with primary closure without failure, those who required repeat intervention did not differ significantly in spine primary diagnosis related to index procedure (n=11, 61.7% degenerative versus n=40, 83.3%, p=0.150), approach (n=18, 100% posterior approach versus n=42, 87.5%, p=0.120), use of instrumentation (n=12, 66.7% versus n=26, 54.2%, p=0.360), procedure complicated by dural tear/CSF leak (n=3, 16.7% versus n=5, 10.4%, p=0.490), bone graft type utilized (n=10, 55.6% used allograft/graft substitute +/- local bone versus n=24, 50%, p=0.470) On the other hand, compared to patients who underwent initial I&D with primary closure without failure, those who required repeat intervention differed significantly in spinal level operated (n=1, 5.6% cervical level surgeries versus n=13, 27.1%, p=0.008). (Table 3)

Of the patient characteristics at the time of presenting with surgical site infection, only presence of bacteremia infection differed significantly between those who did and did not fail one-stage I&D (n=8, 44.4% presenting with bacteremia versus n=2, 4.2%, p<0.001) (Table 4). On the other hand, between those who did and did not fail one-stage I&D, time from index surgery to presentation with infection (24.4 +/- 22.3 versus 35.2 +/- 64.8, p=0.350), WBC (10.6 +/- 5.0 versus 10.6 +/-.47, p=0.980), ESR (60.4 +/- 36.0 versus 69.83 +/- 31.1, p=0.420), CRP (93.8 +/- 88.2 versus 99.5 +/- 79.5, p=0.830), and relative frequency of infection with MRSA (n=1, 5.6% versus n=5, 10.4%, p=0.470).

Multivariable analysis confirmed the presence of bacteremia resulted in high odds of failing one-stage I&D (OR 38.3, 95% CI [confidence interval] [4.67, 314.31], P=0.0007) (Table 3). On the other hand, with regards to pre-operative characteristics, notably age (OR= 0.97 per unit increase, p=0.377), female sex (OR 1.69, p=0.433), ASA
class $\geq 3$ (OR 1.49, $p=0.617$), presence of any CV/pulmonary comorbidities (OR 0.50, $p=0.552$), presence of any IDDM (OR 1.32, $p=0.847$), presence of NIDDM (OR 0.20, $p=0.249$), presence of chronic steroid use pre-operatively (OR 24.67, $p=0.054$), diagnosis of cancer at the time of surgery (OR 0.65, $p=0.764$), smoking history prior to surgery (OR 0.62, $p=0.698$) were not associated with increased odds of failure of one-stage I&D. (Table 2)

With regards to operative characteristics, spine primary diagnosis (relative to degenerative, deformity OR 3.42, $p=0.296$, oncology OR 1.06, $p=0.959$, trauma OR 1.83, $p=0.701$), level operated (relative to cervical, thoracolumbar OR 14.83, $p=0.054$, lumbosacral OR 3.51, $p=0.327$), instrumentation (OR 1.50, $p=0.608$), dural tear or CSF leak (OR 1.76, $p=0.543$), bone graft type (relative to non fusion cases, allograft/graft substitute +/- local bone OR 1.70, $p=0.498$, iliac crest autograft +/- supplement OR 2.71, $p=0.366$) were not associated with increased odds of failure of one stage I&D. (Table 3)

Finally, with regards to infection characteristics, time from index procedure to presentation with infection (OR 2.82, $p=0.568$), WBC count (OR 5.17 per unit increase, $p=0.053$), ESR (OR 0.44 per unit increase, $p=0.503$), CRP (OR 2.57, $p=0.468$), presence of UTI/pneumonia (OR 6.65 relative to no distant infection or bacteremia, $p=0.211$), and MRSA identified as causative organism (OR 0.30, $p=0.368$) were not associated with an increased odds of failure of one-stage I&D. (Table 4)

Of note, the failure rate of one-stage I&D among patients who presented with bacteremia was 80% (n=8), compared to 18% (n=10) among patients who did not present with bacteremia. (Figure 2)
**Secondary analyses**

Of the 76 patients who underwent I&D for SSI, 10 (13.2%) were managed with I&D and placement of wound vacuum as their initial management of SSI. There were not included in the primary analysis for factors associated with failure of one stage I&D and closure over drain, but secondary analyses were performed grouping them with the failure of attempted one staged I&D and closure over drains. Factors identified as significant in univariable and multivariable analysis were unchanged from the primary method of analysis.

Then, further was done to assess how the results of the current study would have been predicted by the earlier referenced PITSS score.\(^{75}\) In considering the PITTS score prediction of patients at high risk for failure of one stage I&D, the sensitivity of the model was 12.5%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 71.2%.
Discussion

*Primary and secondary infections of the spine*

Spinal infections are increasingly prevalent in the general population, likely due to a combination of increased prevalence of predisposing conditions such as intravenous drug use and diabetes, as well as improved detection and diagnosis. They may be caused secondary to direct inoculation following spinal procedures, but are also commonly a result of hematogenous seeding from a distant site. Therefore, an understanding of the etiology, diagnosis, and management strategies for both primary and secondary infections of the spine is of the utmost importance.

*Risk factors associated with spinal infections*

There are a number of risk factors that have been identified as associated with primary spinal infections such as SEA and vertebral osteomyelitis, in particular diabetes mellitus, IV drug use, chronic renal failure, alcohol use disorder, and immunodeficiency. These infections are complex but may require a multidisciplinary approach integrating the expertise of radiologist, with imaging (in particular MRI) providing a key role in the diagnosis, musculoskeletal infectious disease providing important insight into the most likely causative organism and optimal antibiotic/antifungal agent, and spine surgeons managing any further interventions such as irrigation and debridement which may be required to clear the infection.

In the postoperative setting following elective spine surgery, superficial surgical site or deep surgical site infection of the spine are a rare but serious complication. Risk
factors for developing SSIs include patient factors such as age, smoking, obesity, and diabetes mellitus. Additionally, surgical factors such as instrumentation, number of levels fused, posterior approach, and longer duration of surgery have been associated with increased risk of development of surgical site infection. While patient risk factors such as smoking status, obesity and diabetes may be optimized in the preoperative setting, and optimizing surgical planning in order to select the optimal approach, minimal required numbers of levels fused, and minimal required duration of surgery may help to prevent surgical site infections, certain factors may be immutable.

Reducing risk of postoperative spine SSIs

There are a number of preoperative strategies utilized to mitigate the risk of postoperative spine infection. These include utilization of sterile technique, optimization of preoperative patient health and functional status, and perioperative antibiotics. While the standard of care at most centers is a single dose of cefazolin perioperatively, the addition of gram negative coverage in the form of aminoglycosides is being increasingly considered in certain cases which may be at higher risk for these types of infections. While these antibiotics have been suggested to decrease postoperative infection rates in other orthopaedic surgeries such as femoral neck fracture fixation and neuromuscular scoliosis fusion, they are also associated with significant toxicity such as renal complications. Furthermore, as our data suggests, many postoperative spine surgical site infections are not as a result of a gram negative culprit organism and therefore additional gram negative coverage may not reduce rates of infection and may inadvertently lead to increased antibiotic resistance. Further research into this question.
not only in scoliosis patients, but also in adult fusion cases and non-fusion adult spinal surgeries will be required to better understand the risks and benefits associated with additional antibiotic coverage.

Management of postoperative spine SSIs

In the case that a SSI does occur, understanding how to best manage patients returning with SSI following spine surgery is important to optimize outcomes following this adverse event. The mainstays of therapy in these patients are one of two options, one-stage I&D with primary closure over drains or placement of a wound vaccum with planned repeat interventions for wound vaccum removal, repeat I&D, and exchange.

While ideally, all patients could be managed with the least invasive intervention strategy possible, one-stage I&D with primary closure, some patients’ infections may not clear with this level of intervention. In such cases, repeat intervention would be required with unplanned repeat I&D. In patients at a high risk of requiring repeat I&D, planning multistage interventions in the form of placement of a wound vacuum as an initial intervention may be more appropriate. Further understanding of patients at a high risk for failure of one-stage I&D may not only help with risk stratification of these patients and direction to an appropriate intervention strategy but also may help to set patient expectations appropriately. Thus, the current study thus sought to assess the rate and factors associated with success of managing spine SSI with I&D and closure over drains, the most commonly utilized approach.

Rate of development of SSI
Adult, elective spine surgeries performed at a single academic institution between 2013 and 2021 were evaluated. Patients who developed SSI requiring surgical intervention were identified. In our cohort of 11,023 spine surgeries, the infection rate was found to be 0.7%. This statistic highlights the relatively rarity of this adverse event. Furthermore, this rate aligns well with the literature which reports rates between <1 and roughly 3% for various spine surgeries. This substantiates this population for further study of spine SSI, as well as highlights the need to leverage large populations of spinal surgery patients to obtain a sufficient number of SSI patients to study.

Management of postoperative SSI

We next sought to examine the relative utilization of the various mainstays of management of postoperative SSI, in particular one-stage I&D with primary closure versus placement of a wound vacuum and a planned multistage intervention. The vast majority of spine SSIs identified for this study were managed with I&D and closure over drains (86.8% of spine SSIs). However, the failure rate of such one-stage I&D in our sample was 27% (n=18). While this failure rate is consistent with rates reported in the literature, this data highlights that a significant number of patients may fail this intervention strategy. In these cases, planning a multistage intervention with initial placement of wound vacuum may be more ideal. Regardless, this data is helpful for appropriate patient counseling of the expected rate of failure is prior to attempted one-stage I&D. Additionally, this high failure rate supported the desire within our study to understand if there were factors that predicted failures that should be considered.
Factors predictive of failure of one-stage I&D

Several factors were significantly different between patients who did and did not fail one stage I&D on univariable analysis, specifically spinal level operated (n=1, 5.6% cervical level surgeries versus n=13, 27.1%, p=0.008) and presence of bacteremia (n=8, 44.4% presenting with bacteremia versus n=2, 4.2%, p<0.001). Despite this however, only one factor emerged as significant on multivariate analysis – presence of bacteremia on initial presentation with surgical site infection (OR 38.3).

In the presence of bacteremia, those managed with attempted one-stage I&D and closure over drain failed this management in 80% of cases. This was interpreted to suggest that one-stage I&D and closure over drains should probably be avoided when possible in the setting of bacteremia as these patients may require inevitably require multiple interventions.

It is notable that several variables that might have been expected to correlate based on previous studies of this topic with failure of attempted on-stage I&D and closure over drains were not found to be significant in the current study, specifically WBC count, CRP levels, causative bacteria (i.e., S. Aureus or MRSA), as well as time between index surgery and presentation with infection.

Initial management with I&D and wound vacuum

It is acknowledged that 13.2% of spine SSI identified in the study population were managed initially by I&D and wound vacuum dressings. It was because of this that a secondary analysis was done grouping spine SSIs managed with wound vacuum dressing from out outset with the patients who failed attempted one-stage I&D over drains. This
was undertaken to determine if surgeon selection and thus selection bias in our study, which may have accounted for the 13.2% managed with wound vacuums, affected the study results. With no difference in what significant variables associated with either initial application of wound vacuum or failure of one-stage I&D detected, this was determined not to be the case.

*Validation of the PITSS tool*

The study results were also assessed from the perspective of the previously published (and earlier referenced) PITSS study. We thus calculated the PITTS score and risk stratified our study patients based on this model. When this was one, considering the PITTS score prediction of those at high risk for failure of one stage I&D, specificity was 100%, meaning that all of those who did not fail one stage I&D were predicted not to fail. Positive predictive value was also 100%, meaning that all of the patients who were predicted to fail did so. However, negative predictive value was lower at 71.2%, meaning that not all of the patients predicted not to fail one-stage I&D did not fail (roughly 28.8% ended up failing). More notably the sensitivity of the model was only 12.5%, meaning that only 12.5% of the patients who failed one-stage I&D were predicted to do so. Of note, presence of distant site infection was incorporated as a variable in the PITSS risk stratification tool, further supporting the external validity of this finding.
Challenges and Limitations

The main challenge associated with completion of this project was collecting data captured within the EHR. In particular, several pre-operative, intraoperative, and infection characteristics were required to be obtained per manual review, for example surgical approach (anterior versus posterior, etc.) and graft type utilized (which needed to be obtained from surgeon operative notes). Thus, charts for a relatively large number of patients needed to be parsed by the author of this thesis to collect certain data points. However, these data points were crucial and this work was imperative to the success of the project.

The present study has several limitations. First, the study was performed at a single institution and therefore may lack external validity. Second, because of the rarity of development of SSI, the sample size is relatively small as is inherent to studies on this topic. Additionally, this study was performed retrospectively and therefore was limited by the data recorded and potentially effect of clinical judgments that were not identified. Additionally, as with all retrospective studies only description of observed associations and not an inference of causality can be made. Finally, in order to attempt to capture a homogenous cohort of patients undergoing elective spine surgery, we excluded from the analysis polytrauma patients. Further studies should seek to understand the nature and course of postoperative SSIs in this patient population. Regardless, we feel that our study nonetheless provides a meaningful contribution to the literature.
**Conclusion**

In conclusion, the current dissertation summarizes data from a retrospective case-control study of patients who developed postoperative SSIs following spine surgery is presented, where it was found that significantly higher odds of failing one-stage I&D exist among those patients who presented with bacteremia.

Although decisions to manage an SSI with one strategy versus another are multifactorial, the current study highlights a subgroup of those presenting with postoperative spine I&D for which consideration of wound vacuum or delay of primary closure might be considered.
Dissemination

The current thesis is a combination of three projects which have been submitted and published in several spine journals. Also, this project has been prepared and presented at several national meetings, in particular the Orthopaedic Research Society Annual Meeting (poster), as well as the Association of Bone and Joint Surgeons Annual Meeting.

Citations from this Thesis

Articles/chapters in this thesis were published in:


Figure 1. Flow chart of identification of patients with postoperative surgical site infections following spine surgeries performed for non-infectious diagnoses at a single institution between 2013 and 2021

Identification of patients

Spine surgeries performed for non-infectious diagnoses at a single academic institution between 2013 and 2021

n= 11,023

Did not develop SSI

10,947 (99.3%)

Developed SSI

76 (0.7%)

Initial management with I&D and closure over drains

66 (86.8% of SSI)

Required no further intervention

48 (72.7% of I&D and closure over drains)

Failed one stage I&D and required further I&D

18 (27.3% of I&D and closure over drains)

Initial management with I&D and placement of wound vacuum

10 (13.2% of SSI)
Figure 2. Failure rate of one-stage I&D in patients overall, and with and without any distant/systemic infection

Overall (n=66)

- Failed: 27%
- Did not fail: 73%

Bacteremia (n=10)

- Failed: 18%
- Did not fail: 82%

No Bacteremia (n=56)

- Failed: 80%
- Did not fail: 20%
References


80. Galivanche AR, Mercier MR, Adrados M, et al. Admission NarxCare Narcotics Scores are not Associated With Adverse Surgical Outcomes or Self-reported Patient


