What's New in the Diagnosis and Prevention of Spine Surgical Site Infections.

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Review Article

What is new in the diagnosis and prevention of spine surgical site infections

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Abstract

BACKGROUND CONTEXT: Surgical site infection (SSI) after spinal surgery can result in several serious secondary complications, such as pseudoarthrosis, neurological injury, paralysis, sepsis, and death. There is an increasing body of literature on risk factors, diagnosis, and specific intraoperative interventions, including attention to sterility of instrumentation, application of minimally invasive fusion techniques, intraoperative irrigation, and application of topical antibiotics, that hold the most promise for reduction of SSI.

PURPOSE: The purpose of this review is to identify and summarize the recent literature on the incidence, risk factors, diagnosis, prevention, and treatment of SSIs after adult spine surgery.

STUDY DESIGN: The study design included systematic review and literature synthesis.

METHODS: For the systematic reviews, a search was performed in Medline and Scopus using keywords derived from a preliminary review of the literature and Medline MeSH terms. These studies were then manually filtered to meet the study criteria outlined in each section. Studies were excluded via predetermined criteria, and the majority of articles reviewed were excluded.

RESULTS: There are a number of patient- and procedure-specific risk factors for SSI. Surgical site infection appears to have significant implications from the patients' perspective on outcome of care. Diagnosis of SSI appears to rely primarily on clinical factors, while laboratory values such as C-reactive protein are not universally sensitive. Similarly, novel methods of perioperative infection prophylaxis such as local antibiotic administration appear to be modestly effective.

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CONCLUSIONS: Surgical site infections are a common multifactorial problem after spine surgery. There is compelling evidence that improved risk stratification, detection, and prevention will reduce SSIs.

Keywords: Spinal infection; Fusion; Topical antibiotics; Surgical wound infection; Spinal instrumentation; Inflammatory markers

Introduction

Surgical site infection (SSI) is a relatively common complication of spinal surgery with the potential of having devastating consequences such as pseudoarthrosis, neurological injury, paralysis, sepsis, and death. Management of SSI requires a multifactorial approach with a primary emphasis placed on prevention including preoperative risk stratification and conduct of the operation. Additionally, recent advances in early diagnosis and effective treatment of spinal SSI will hopefully serve to mitigate some of the potentially severe outcomes of this complication. Nearly all the literature presented in this review has been published within the past 5 years. Furthermore, two systematic reviews were conducted within this literature synthesis to more fully define the recent findings regarding biochemical markers of spinal SSI and intraoperative measures taken to prevent perioperative infection during spine surgery. Although the body of literature pertaining to SSI is quite large, those studies pertaining specifically to spinal surgery are somewhat limited. There is a particular lack of Level I evidence for any intervention. The pool of articles examined for the systematic reviews of laboratory markers to diagnose SSI and for SSI prevention are presented in the Figure, Top and Bottom.

Incidence

The reported incidence of spine SSI ranges from 1% to 14%. In a recent Medicare database subgroup analysis of lumbar fusions, infections were reported in 8.5% of index surgeries and 12% of revision surgeries [1]. However, prospectively collected sources have demonstrated an incidence of SSI as high as 14.9% in some populations [2].

Recent studies have provided benchmark rates of SSI after various types of spine procedures (Table 1). The overall incidence of infection in the Spine Patient Outcomes Research Trial study of lumbar degenerative conditions was 2% after disc herniation procedures [3], 2.5% after surgery for spinal stenosis [4], and 4% after surgery for degenerative spondylolisthesis [5]. The incidence of SSI after posterior cervical surgery was 2.3% for superficial SSI and 0.7% for deep SSI [6]. Based on a prospectively collected database of 108,419 cases, the overall infection rate for lumbar surgery was 2.1% (superficial=0.8%, deep=1.3%) [7]. These numbers may be useful to describe to patients as the data provides general benchmarks of infection rates. Other baseline data have been obtained from the investigational device exemption studies on artificial disc prostheses. The results of these studies are summarized in Table 2.

Although the incidence of SSI is relatively low in spine surgery, the effect of SSI is also perceived differently by

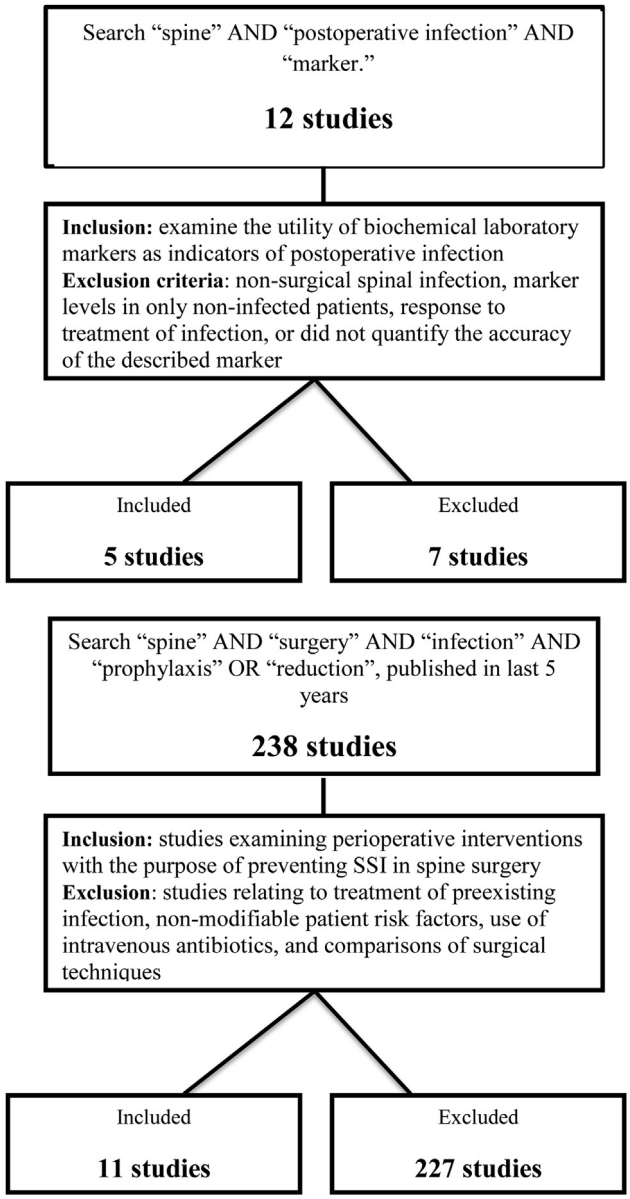

Figure. Flow diagram of articles screened and selected for systematic reviews of (Top) laboratory markers used to diagnose surgical site infection (SSI) and (Bottom) intraoperative SSI prevention.

Table 1
Summary of spine SSI infection rates

Population	Rate (%)	Reference
Medicare cervical	5.8	Wang [73]
Medicare lumbar	15–19	Wang [73]
SPORT IDH	2	Weinstein [74]
SPORT stenosis	2.5	Weinstein et al. [5]
SPORT degenerative spondylolisthesis	4	Weinstein et al. [5]
AO Spine CSM	2 superficial, 0.7 deep	Wilson et al. [22]
Prospective TJUH	16	Campbell [75]
Prospective trauma	3.5	Lonjon et al. [21]
STASCIS	3.4	Wilson et al. [22]

CSM, cervical spondylotic myleopathy; IDH, intervertebral disc herniation; SPORT, Spine Patient Outcomes Research Trial; SSI, surgical site infection; STASCIS, Surgical Timing in Acute Spinal Cord Injury Study; TJUH, Thomas Jefferson University Hospital.

surgeons and patients. Surgical site infection was more likely to be perceived as a serious event by patients than surgeons [8] and was likely to affect the perception of success of the surgery [9].

The incidence of SSI appears to be lower after certain minimally invasive spinal (MIS) surgeries. A review of 1,338 MIS surgeries from multiple institutions revealed an infection rate of 0.74% in fusion/fixations and 0.22% overall [10]. McGirt et al. [11] demonstrated that in a two-level spinal fusion, the minimally invasive technique was associated with a significantly lower incidence of infection (7% vs. 4.6%, p=.037). This was associated with an odds ratio of 1.469 (95% confidence interval 0.959–2.250). Additionally, a review by Parker et al. [12] compared postoperative infection after open and minimally invasive transforaminal lumbar interbody fusions. This analysis of 362 MIS and 1,333 open surgeries showed an infection rate of 4% in open spinal fusions versus 0.6% after MIS (p=.005). However, the benefits of minimally invasive techniques with regard to infection is not universally observed. In the study by Parker et al. [12] for single-level procedures, there was no significant difference between traditional and MIS procedures in terms of infection. Park and Ha [13] also described no difference in infection rate after single-level fusions. Kepler et al. [14] similarly showed no difference in infection rates between MIS and open techniques in patients undergoing posterior instrumentation after open anterior intervention. Hence, data are inadequate to make specific conclusions regarding the effect that a minimally invasive technique has on SSI risk. Yet, it appears that for multilevel instrumentation, MIS does provide some benefit.

Table 2
Infection rates from IDE studies of artificial disc prostheses

Device	Site	Fusion infection rate	TDA infection rate
Prodisc-L, 2012	Lumbar	2.7% (2/75)	0% (0/161)
Maverick, 2011	Lumbar	7.0% (12/72)	5.9% (24/405)
Charite, 2005	Lumbar	2% (2/99)	6.3% (13/205)
Kineflex, 2011	Cervical	4.4% (5/133)	3.4% (4/136)
Prodisc-C, 2009	Cervical	0.9% (1/106)	0% (0/103)
Bryan, 2007	Cervical	0% (0/59)	0% (0/56)

IDE, investigational device exemption; TDA, total disc arthroplasty.

Note: Coric (2011), Gornet (2011), Blumenthal (2005), Murrey (2009), Sasso (2007), and Zigler (2012) [76–81].

The recent literature has also provided insight that study methodology may confound the reported insight of SSI. A simultaneous comparative retrospective and prospective collection at the same institution identified significantly different rates of SSI between various methods. This study demonstrated a consistent underreporting of complication rates in retrospective studies utilizing database or diagnostic code search methodologies compared to those conducted prospectively [2]. Therefore, future studies of SSI should incorporate prospective data collection to obtain the most accurate data.

Risk factors for infection

Patient risk factors for infection have been well described in several studies. Findings from 19 studies are presented. Medical comorbidities, such as anemia, diabetes mellitus, coronary artery disease, diagnosis of coagulopathy, neoplasm, obesity, higher American Society of Anesthesiologist score, and malnutrition, have been implicated as SSI risk factors [2,15–17]. To relatively weigh these parameters and account for overlap between factors (such as obesity and diabetes), regression-based SSI prediction risk models have been developed. Statistically significant risk factors are summarized in Table 3 [18].

The understanding of the role of medical risk factors continues to evolve. Independent of associated disorders such as diabetes, obesity has been found to be a risk factor for SSI in some studies but not other studies. However, two recent studies found that distribution of body mass including skin fold thickness and L4 spinous process-skin thickness are spine-specific SSI risk factors independent

Table 3
Significant patient risk factors for spine SSI

Factor	OR (95% CI)
Cervical	
Neurological disorder	2.61 (2.43–2.8)
Cardiac disorder (other than HTN)	2.17 (2–2.36)
Drug or EtOH abuse	1.85 (1.6–2.14)
Pulmonary disorder	1.38 (1.31–1.47)
Diabetes	1.28 (1.2–1.36)
Psychiatric disorder	1.22 (1.14–1.31)
HTN	1.09 (1.04–1.14)
Thoracolumbar	
Neurological disorder	2.76 (2.55–3)
Drug or EtOH abuse	1.79 (1.64–1.95)
Cardiac disorder (other than HTN)	1.62 (1.53–1.71)
Pulmonary disorder	1.39 (1.31–1.48)
Cancer	1.31 (1.12–1.54)
Diabetes	1.12 (1.07–1.16)
Psychiatric disorder	1.1 (1.05–1.14)

Adapted from Chitale et al. [18].

CI, confidence interval; EtOH, ethyl alcohol; HTN, hypertension; OR, odds ratio; SSI, surgical site infection.

of body mass index [19]. The authors concluded that the distribution of adipose tissue and the depth of adipose tissue overlying the operative field increased the risk of SSI.

Additionally, the particular diagnosis for which the patient undergoes spinal fusion is an infection risk factor. Among elective procedures, patients undergoing surgery for degenerative disease have a lower infection rate compared to deformity (1.4% vs. 4.2%) [7]. Patients who undergo spinal procedures for trauma are known to have a higher risk for infection compared with patients undergoing spinal fusion for elective surgery (9.4% vs. 3.7%) [20,21]. Furthermore, the risk of infection is correlated with the severity of the trauma. In Wilson et al. [22], authors demonstrate that the rate of SSI rises commensurate to the level of neurologic impairment as quantified by the patient's Abbreviated Injury Scale score. Blam et al. [23] show an increased risk of SSI in patients with spinal cord injury versus those who undergo elective spinal surgery (9.4% vs. 3.3%, respectively).

Recent evidence has shown that case order may also contribute to the rate of SSI after spine surgery. In a study by Gruskay et al. [24], lumbar decompression performed later in the day (third case) led to three times higher incidence of SSI compared with those performed as the day's first case (odds ratio=1.88 [95% confidence interval 1.20–2.93], p=.005) although this did not hold consistent for spinal fusion surgery. Additionally, this group has also demonstrated a seasonal effect on the rate of postoperative effect. They find that SSI incidence peaks in the summer and fall with statistically significant drops in infection rate in the spring and winter [25].

Finally, there are procedure-specific risk factors that affect infection risk. Generally, complex procedures involving more extensive tissue dissection, increased blood loss, and longer operative time are considered to be more invasive and therefore may present a higher risk of perioperative complications. To quantify the spine procedural complexity, a surgical invasiveness index has been correlated with intraoperative blood loss [26] and infection risk [27] (Table 4). Durotomy has not been established as an infection risk factor [28,29]. Minimally invasive surgery has not been shown to reduce the incidence of infection after decompression [30] but has after fusion in some studies [7,12]. Future study is needed to evaluate the effects of bone graft choices, staged procedures, and minimally invasive surgery on infection risk.

Diagnosis

There are no universally accepted clinical diagnostic criteria for SSI. Increased wound drainage at approximately 10 to 14 days postoperatively is the most common early sign of wound infection and is present in 67% of patients with SSI. Other infection-specific factors, such as increased pain, fever, or wound erythema, are present in less

Table 4
Surgical invasiveness index, validated to determine risk of blood transfusion

AD score	AF score	AI score	PD score	PF score	PI score
The number of vertebrae requiring partial or complete excision of the vertebral body (regardless of surgical approach or location of skin incision) or the disc caudal to that vertebra if the disc is excised from an anterior approach	The number of vertebrae that have graft material attached to or replacing the vertebral body, regardless of the surgical approach	The number of vertebrae that have screws, plate, cage, or structural graft attached to the vertebral body or replacing the vertebral body, regardless of the surgical approach	The number of vertebrae requiring laminectomy or foraminotomy at the foramens caudal to their pedicles and/or discectomy at the disc caudal to the vertebral body if the disc is excised from a posterior approach	The number of vertebrae that have graft material on their lamina, facets, or transverse processes	The number of vertebrae that have screws, hooks, or wires attached to their pedicles, facets, lamina, or transverse processes

AD, anterior decompression; AF, anterior fusion; AI, anterior instrumentation; PD, posterior decompression; PF, posterior fusion; PI, posterior instrumentation.
Note: Mirza et al. [26].

than 30% of cases. Of laboratory markers, C-reactive protein (CRP) is the most sensitive for the diagnosis of SSI and is elevated in more than 98% of cases [17]. Intraoperative cultures are often negative even in patients with established SSIs, and this may depend on when antibiotics are initiated.

A systematic review of the literature was performed to evaluate current science regarding biochemical markers of postoperative spine infection. A search was performed in Medline and Scopus using the search terms "spine" AND "postoperative infection" AND "marker." Search terms were derived from a preliminary review of literature and MeSH terms. Results were then screened for studies examining the utility of biochemical laboratory markers as indicators of postoperative infection. Articles were excluded if they examined nonsurgical spinal infection, studied marker levels in only noninfected patients, examined response to treatment of infection, or did not quantify the accuracy of the described marker. The majority of articles retrieved were excluded because of these criteria based on the information found in the abstracts. All levels of clinical study evidence were included.

Five articles were identified that met the inclusion criteria. Four of these were prospective observational cohort studies, and one a retrospective study. Whereas all five studies examined the CRP levels, four reported erythrocyte sedimentation rate (ESR), one studied amyloid-A, and one examined procalcitonin (PCT) levels. The standard kinetics of CRP levels in surgical patients has been well reported [31]. Given the reliability and historical use of CRP as a marker for infection, it is generally used as a benchmark for studies of other infection biomarkers. Accordingly, in each of these studies, it was noted that CRP rises and falls reliably in healthy noninfected patients during the postoperative period with a peak occurring at approximately postoperative Day 3. Mok et al. [32] showed that a number of variables regarding the operative procedure may contribute to the peak CRP value. These included operative duration, region, surgery type, preoperative CRP level, and number of levels [32]. Furthermore, a second peak or failure of CRP level to normalize was found to be a relatively accurate predictor of postoperative infection in each of these studies. These results are summarized in Table 5.

Lee et al. [33] also reported a significant increase in CRP in patients with postoperative spine infection; however, sensitivity and specificity were not calculated. With CRP as a benchmark, these studies examined other laboratory values as potential predictors of postoperative infection. One study [32] measured ESR along with CRP, which is currently the standard practice at many institutions. Similar to CRP, the kinetics of ESR after uncomplicated surgery have been well reported in the literature with a later peak than CRP, typically occurring around postoperative Day 4. However, in this study, less than half of the patients (48%) exhibited an ESR peak; in those who did exhibit a peak, sensitivity, specificity, positive predictive value, and positive predictive value were respectively 64%, 72%, 44%, and 85%. Given the similar sensitivity and specificity for these markers, the authors conclude that CRP is a significantly superior marker of infection because of the earlier and more reliable peak and more stable values.

Neutrophil count is also a frequently tested indicator of infection. One study investigated change in the absolute neutrophil count (ANC) after spine fusion. Whereas there was no significant difference in ANC values between the normal and infected groups up to 4 days postoperatively, there was a significant ($p<.0001$) rise in ANC in the periods 4 to 7 and 8 to 11 days postoperatively in the infected patients [33].

Serum amyloid-A (SAA) is an inflammatory protein that is produced in a very high quantity in situations of stress. Deguchi et al. [34] investigated SAA levels as a marker of postsurgical spine infection. This study recorded the correlation of SAA and CRP levels after spinal surgery in patients with and without SSI. Here, the authors showed a concomitant second peak in both CRP and SAA after surgery in three patients with SSI, with SAA levels demonstrating larger changes. Of note, many patients in this study who were thought to have developed early SSI were immediately treated with intravenous antibiotics and therefore marker levels were not reported. Furthermore, in the noninfected patients, there was a significant correlation between CRP and SAA levels through postoperative Day 7. However, by Day 13, the SAA level had dropped more quickly. Hence, the authors conclude that SAA is a superior marker for infection compared with CRP because of the more dramatic change in value and earlier return to baseline with similar kinetics [34].

Procalcitonin (PCT) is a precursor of calcitonin and has previously been described as an inflammatory marker in septic patients. As such, Nie et al. [35] examined the use of PCT measurement in predicting SSI after spinal surgery. In this study, biomarker values were measured 48 hours after surgery and analyzed for correlation with eventual SSI. Both PCT and CRP showed statistically significant correlations with the development of SSI with respective p values $<.001$ and .003. Additionally, receiver-operating characteristic curves of these two markers demonstrate superior sensitivity and specificity with PCT. The authors, therefore, conclude that PCT is superior to CRP in early prediction of SSI [35].

Table 5
Statistical metrics of postoperative CRP-level monitoring in predicting surgical site infection

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Mok et al. [32]	53	76	33	88
Kang et al. [82]	83.3	96.8	31.3	99.7
Nie et al. [35]	85	27	—	—

CRP, C-reactive protein; PPV, positive predictive value; NPV, negative predictive value.

Although they were not included in this review, a number of other inflammatory biomarkers have been examined in other fields of orthopedic surgery and may prove useful in predicting postoperative spine infections. In particular, interleukin-6 has been well studied in joint replacement surgery [36,37]. Leukocyte esterase is a recently reported marker in periprosthetic knee joint infection. Early studies have demonstrated that testing synovial fluid with a colorimetric strip test provides 80.6% sensitivity and 100% specificity in diagnosing joint infection in knees undergoing revision surgery [38].

The aforementioned studies all provide compelling evidence regarding the utility of these novel laboratory markers of SSI. However, each of these requires further investigation before being considered standard of care. In particular, few laboratory markers have been validated as a "gold standard" in association with culture-positive SSI. Yet, given the multitude of confounders affecting CRP and white blood cell levels in the postoperative patient, markers such as SAA, PCT, and leukocyte esterase may very well prove to be important diagnostic adjuncts. Nevertheless, it remains the practice of our institution not to test for these nonvalidated laboratory markers when evaluating a patient for potential SSI.

Intraoperative measures

There has been intense interest in intraoperative measures to reduce infections including skin preparation, intraoperative behaviors, wound irrigation, topical antibiotic application, wound closure, and postoperative drain use. Twenty-seven total studies are reviewed within this section.

The current body of evidence suggests that a significant level of wound contamination occurs intraoperatively. In pediatric spinal deformity surgeries, 23% of patients had positive intraoperative cultures. Of those that cultured positive, 11.5% developed an early SSI [39]. In another study, 32.5% of patients undergoing spinal deformity correction had positive intraoperative cultures [40]. Implants exposed to the operating room environment are also a source of contamination. Bible et al. [41] show an overall 9.5% rate of implant contamination in instrumentation that had been opened since the beginning of a case. This rate was significantly reduced when the implants were covered during the case (2% vs. 16.7%). Furthermore, it is clear that the level of contamination increases directly with the amount of time it is open in the operating field. In vitro studies have demonstrated that the bacterial count on agar plates and surgical instruments left open in a standard surgical field increases steadily over time [42,43]. Indeed, a study by this institution provides evidence that preoperative time of greater than 1 hour is an independent risk factor for postoperative infection. An element of seasonality was also found as the longest in room times tends to occur in August, September, and October [44].

A variety of skin preparation agents are currently in use to facilitate preoperative decontamination of the wound. A recent prospective trial demonstrates similar levels of postoperative skin contamination in lumbar spine surgery after preparation with DuraPrep (3M Company, St. Paul, MN, USA) and ChloraPrep (CareFusion, Inc., San Diego, CA, USA) (32% vs. 34%, respectively) [45]. A systematic review of skin preparation in general surgical cases suggests a significant decrease in SSI rate with the use of chlorhexidine versus iodine skin prep [46].

Intraoperative techniques and behaviors involving the operative gown, sterile instrument draping, use of intraoperative fluoroscopy, and operative scrub cleanliness, may be conducive to minor violations of sterility that ultimately contribute to SSI. A cumulative effect of these multiple minor violations of sterility could result in a wound inoculation and ultimately an SSI [47]. The operative gown is most sterile in the region between the chest and the operative field. Therefore, elevating the table or touching the creases of the elbow, for example, may result in minor sterility violations [48]. Furthermore, the current procedure to detect operative instrument sterility violations relies on visual detection of breaches in the sterile instrument drape. A 2- to 3-mm puncture in a sterile instrument drape can be missed up to 50% of the time [49]. Additionally, the use of operative fluoroscopy may contribute to sterile field contamination. The top half and the back of the receiver are often colonized despite the use of a sterile drape [50]. If a surgeon grasps or manipulates the fluoroscope in this region, sterility can be breached. Additionally, the duration of scrub wear correlates with bacterial bioburden. Donning unworn scrubs before operating may decrease SSI rate [51]. Certainly, there are a multitude of potential sources of intraoperative contamination. The recent data are summarized in Table 6.

The only irrigation agent to have been demonstrated in systematic reviews to reduce SSI rate is povidone-iodine (PVP-I) [15]. In the reviewed studies by Chang et al. [52] and Cheng et al. [53], dilute solutions of PVP-I irrigation yielded SSI rates of 0%. This result was statistically significant in both studies. In both protocols, the surgical site was soaked with dilute PVP-I for 3 minutes and then copiously irrigated with normal saline before bone decortication.

Recently, the use of topical antibiotics has come into interest in adult spine surgery to reduce the risk of SSI based

Table 6
Sites of potential intraoperative contamination

Study	Source	Contamination rate (%)
Biswas et al. [50]	C-arm	56 (top) and 28 (upper front)
Krueger et al. [51]	Scrubs	41 (unworn) and 89 (post-call)
Bible et al. [48]	Gown	6–9 (chest to table) and 33–42 (above chest)
Bible [83]	Microscope	24 (eyepiece shaft and forehead) and 44 (overhead)
Bible et al. [41]	Implants	9.5 (2, covered and 16.7, uncovered)
Couture [84]	Cadaveric Allograft	9.4

on the belief that most wounds become inoculated and infected at the time of surgery. Topical antibiotics have been used in spine surgery in the past without any notable effect. Savitz et al. [54] demonstrated a significant reduction in intraoperative bacteria growth but no decrease in the incidence of SSI with polymyxin and bacitracin irrigation.

In addition to irrigation and standard antibiotic administration, a number of novel interventions to prevent SSI have been proposed, and a systematic review of the recent literature on this topic was conducted. A search of literature published in the last 5 years in Medline and Scopus was performed using search terms "spine" AND "surgery" AND "infection" AND ("prophylaxis" OR "reduction"). Search terms were derived from a preliminary review of the literature and Medline MeSH terms. These results were manually filtered for studies examining perioperative interventions with the purpose of preventing SSI in spine surgery. The only outcome of interest was rate of SSI after spine surgery. Exclusion criteria included studies relating to the treatment of preexisting infection, nonmodifiable patient risk factors, use of intravenous antibiotics, and comparisons of surgical techniques. As the objective of this review is to identify new and potentially novel interventions, experimental evidence of levels I to IV were included. Only case studies and reviews were excluded because of quality of evidence. Studies performed on animal subjects were also included. The majority of retrieved citations were excluded by information contained in the abstract such as subjects, therapies, and studied outcome.

The nature of this review does not lend itself to the performance of a meta-analysis. Each of the therapies investigated were supported by a limited number of heterogeneous studies of varied quality-of-evidence. As such, each intervention will be discussed individually. In total, 11 publications meeting the previous criteria were identified. With one exception, these studies examined different modalities and preparations of local intraoperative antibiotic delivery. This includes all nonintravenously administered intraoperative antibiosis.

Application of powdered vancomycin to the surgical site has been examined by multiple authors in recent years. To date, one case series and six retrospective reviews have been published on this subject. There have not been any randomized controlled trials examining the use of antibiotic powder as prophylaxis against SSI. These studies are summarized in Table 7. In each of these studies, all patients received standard perioperative intravenous antibiotics as per the protocols at the respective hospitals. Also, control and

Table 7
Summary of studies investigating use of local vancomycin as prophylaxis against SSI

Study	Study type	No. of patients enrolled	Vancomycin powder used	No. of control patients	Infection rate (%) (control)	No. of treatment patients	Infection rate (%) (vancomycin powder)	p Value	Comments
Sweet et al. [57]	Retrospective cohort (III)	1,732	2 g (1 g mixed with bone graft, 1 g applied as powder)	821	2.6 (n=21)	911	0.2 (n=2)	<.0001	Only recorded deep wound infection Only instrumented fusions
O'Neill et al. [55]	Retrospective cohort (III)	110	1 g	54	13 (n=7)	56	0	.02	Included both deep and superficial infections Treatment patients operated on by a different surgeon than control patients Operative time statistically longer in controls
Tofuku et al. [85]	Retrospective cohort (III)	384	500 mg (within fibrin sealant)	188	5.8 (n=11)	196	0	.0003	Used a novel vancomycin impregnated fibrin sealant Deep infection only Only instrumented fusions
Molinari et al. [56]	Case series (IV)	1,512	1 g	0	N/A	1,512	0.99 (n=15)	N/A	Deep infection only 56% noninstrumented
Godil et al. [58]	Retrospecitve cohort (III)	110	1 g	54	13 (n=7)	56	0	.02	Deep and superficial SSI
Caroom [86]	Retrospecitve cohort (III)	112	1 g	72	15 (n=11)	40	0	.007	Posterior C-Spine only Intervention group prepped with ChloraPrep vs. DuraPrep in control
Pahys et al. [59]	Retrospective cohort (III)	1,001	500 mg (plus alcohol foam prep and superficial drain placement)	483	1.86 (n=9)	195	0	.048	Also placed superficial drain and used alcohol foam prep in experimental group Significantly higher age and number of procedures ≥4 levels in experimental group

N/A, not applicable; SSI, surgical site infection.

treatment patient populations were statistically similar except where otherwise noted in Table 7 (ie, operative time in O'Neill et al. [55]).

Each of the experimental studies reviewed demonstrated a statistically significant decrease in SSI after local administration of vancomycin powder. In the case series out of the University of Rochester [56], the infection rate among patients treated with vancomycin powder was at or below the generally accepted range for SSI after spine surgery [1]. Also of note, Sweet et al. [57] measured the wound and serum levels of vancomycin in 178 consecutive patients. In 80% of those subjects, serum vancomycin was never detectable. Only 6% of patients had a detectable serum drug level after postoperative Day 1. A potential weakness of these studies is the failure to include superficial wound infections in their analysis. Although deep infections are certainly more concerning, it stands to reason that superficial infection rate would be affected less by intrawound application of vancomycin powder, and as such, one would expect a less significant drop in infection if these infections were included.

Godil et al. [58] examined the use of local application of vancomycin powder with end point of any SSI, including deep and superficial infections. The authors again found a significant reduction in SSI after the use of vancomycin powder (13% vs. 0%, $p=.02$). In addition, this study examined the cost-effectiveness of this intervention. In this regard, they determined that the cost of treating postoperative infection was approximately $33,705 per patient. As such, at a cost of $4,400 per 100 patients, use of vancomycin powder has the potential to save approximately $433,765 per 100 spinal fusion patients.

Pahys et al. [59] examined the use of local vancomycin powder in addition to the preparation of the surgical site with drapes and alcohol foam and the placement of a superficial drain. The two treatment groups in this study were patients with alcohol prep and drain placement (AD) and those with local vancomycin in addition to the previous measures. There was no group in whom only local vancomycin was used. Nevertheless, these interventions significantly decreased postoperative infection rate with vancomycin powder causing a further reduction. Whereas the control group had a 1.86% infection rate, the alcohol prep and drain placement group had a 0.3% SSI rate ($p=.047$) and the local vancomycin in addition to the previous measures group had a 0% SSI rate ($p=.048$).

Local application of gentamicin for SSI prevention has been successfully studied in other surgical fields and proposed for use in spine surgery [60]. A study performed in rabbits examines the use of gentamicin-impregnated poly(lactide-co-glycolide) microspheres for the prevention of postoperative infection. In this well-designed study, spinal instrumentation was placed at three sites in a rabbit and then contaminated with standardized *Staphylococcus aureus*. Gentamicin microspheres were placed on two noncontiguous sites, whereas a control microsphere was placed at the third. The study demonstrated a 75% infection rate at control sites compared with 38% at therapy sites ($p<.01$) [61].

Local antibiotic delivery may also be achieved by incorporating the antibiotic into the bone allograft. Studies by two separate authors have examined this therapy in spine surgery patients. The publication from Borkhuu et al. [62] examined the use of gentamicin-soaked allograft in children with cerebral palsy. In a subgroup of patients, freeze-dried corticocancellous allograft was soaked in 8- to 10-mg/kg gentamicin and applied on top of instrumentation before closure. The authors demonstrated a statistically significant decrease in deep SSI in the group receiving antibiotic-loaded allograft (3.9% vs. 15.2%) [62]. The study by Gruenberg et al. [63] is unfortunately not published in English, and a full review could not be performed. However in this study the authors used vancomycin-supplemented cancellous graft and demonstrated a reduced albeit not statistically significant decrease in SSI rate [63].

Only the nonpharmacologic therapy included in this literature search examined the use of capacitive coupling devices. These devices are similar to the bone stimulators currently used for nonhealing fractures. The device is placed on the patient's skin and delivers a standardized electromagnetic current to the bone and implant. In a pilot study performed in a rabbit model, use of this technology significantly reduced infection rate of the implant ($p=.0011$). However, no change in bacterial load was noted at any of the other studied sites that included bone, fascia, and hematoma [64]. Use of local antibiotic administration is an attractive option for the prevention of SSI as it provides an apparent protection from deep wound infection while avoiding the systemic consequences of administering high doses of antibiotics orally or intravenously.

Postoperative protocols also affect infection risk. A retrospective study by Rao et al. [65] found an increased mean number of days of closed suction wound drainage in patients with infection versus patients without infection (5.1 vs. 3.4 days). Additionally, it has been suggested that use of 2-octyl-cyanoacrylate (Dermabond, Ethicon Inc., Somerville, NJ, USA) for skin closure may decrease the rate of infection, perhaps due to the fact that a bandage is not required. A prospective analysis of 235 patients undergoing spine surgery with Dermabond closure demonstrated a very low 0.43% postoperative infection rate [66].

Treatment

Treatment of SSI relies on early identification, diagnosis, and evacuation of gross purulent material. Treatment options include primary closure, closed vacuum system, hardware retention, and intravenous antibiotics. A recent retrospective review of 20 patients demonstrated a good success rate of delayed primary closure after 5 to 14 days of vacuum-assisted wound closure (VAC) therapy in patients with infected instrumented lumbar spine fusions

[67]. Use of a wound vacuum system may facilitate retention of hardware [68].

Plastic surgery reconstruction is also occasionally used in the reconstruction of infected spine wounds. The gold standard plastic surgical procedure has been rotational flaps such as a trapezius muscle flap [69]. Recently paraspinous muscle flaps have also been shown to facilitate wound healing and hardware retention [70,71].

There is little literature to guide surgeons regarding which patients would most benefit from two-stage (irrigation and debridement with delayed primary closure) reconstruction and which patients can achieve a successful result with a single-stage (primary closure) procedure. A recent retrospective study identified predictors of repeat irrigation and debridement (I&D) and failure of single-stage primary closure [72]. These factors were then used to create a Postoperative Infection Treatment Score for the Spine (PITSS). Spine location, comorbidities, microbiology, distant site infection, use of instrumentation, and use of bone graft were each identified as significant predictors of infection complexity. These components and the associated scoring are presented in Table 8. A high PITSS score predicts a higher likelihood of a patient requiring multiple cleansing procedures. This score was correlated with the probability of multiple I&D requirements to establish an objective stratification scheme. Scores of 7 to 14 indicate low risk (<0.24), 15 to 20 indeterminate risk (0.24–0.52), and 21–33 high risk (>0.52). Patients who are considered higher risk may benefit from two-stage reconstruction.

Table 8
PITSS to predict likelihood of requiring two-stage reconstruction after postoperative infection

Predictors	PITSS score
Spine location	
Cervical	1
Thoracolumbar	2
Lumbar/sacral	4
Comorbidities	
None/other	0
Cardiovascular/pulmonary	1
Diabetes	4
Microbiology	
Gram positive	2
Gram negative or polymicrobial without MRSA	4
Polymicrobial with MRSA or MRSA alone	6
Distant site infection	
None	1
UTI/PNA	3
Bacteremia alone	5
Bacteremia+PNA/UTI	6
Instrumentation	
Yes	6
No	2
Bone graft	
None	1
Autograft	3
Other (allograft, BMP, and synthetic)	6

Adapted from Dipaola et al. [72].

BMP, bone morphogenetic protein; MRSA, methicillin-resistant *Staphylococcus aureus*; PITSS, Postoperative Infection Treatment Score for the Spine; PNA, pneumonia; UTI, urinary tract infection.

Conclusions and recommendations

Postoperative spinal SSIs can be devastating complications for both the patient and the surgeon. Fortunately, as demonstrated in this review, the body of literature regarding diagnosis, prevention, and treatment of these infections is expanding rapidly. Yet there is very little Level I evidence to guide surgeons in their management of the potentially infected spinal surgery patient. Diagnosis of a SSI after surgery on the spine is still very much a clinical diagnosis. Although the risk factors and diagnostic studies described here provide intriguing directions for future study, none of the results provide strong enough evidence to recommend changing current clinical practice. Rather, a thorough knowledge of the risk factors associated with infection and the utility of common laboratory values may serve as valuable adjuncts to obtaining a diagnosis.

Certainly, a multifaceted approach to prevention is the key to managing infection risk. The importance of strict sterile conduct during the operation is reemphasized by the data demonstrating multiple sources of micro-contaminations. In addition, efforts should be made to minimize time spent in the operating suite. Although operative time is generally not a modifiable variable, preoperative operating room time can often be streamlined and appears to contribute to postoperative infection risk [44]. Additionally, data in favor of applying local vancomycin to the surgical site are quite compelling. Given the apparent reproducibility of these results, it may be advisable to consider regular use of antibiosis in high risk patients. As such, we recommend that institutions discuss implementing protocols regarding the use of topical vancomycin powder or other similar antibiotic therapy. Of course, further research leading to Level I evidence would be beneficial in establishing such guidelines. Furthermore, there is little research regarding the effect of preoperative conduct before the operation on SSI risk, and this will be another important avenue of investigation.

Management of the SSI patient is at once straightforward and remarkably challenging. The PITSS system provides a useful guide for predicting the success of a primary closure after wound washout. The availability of VAC systems has revolutionized open wound management in numerous surgical fields including but not limited to spinal surgery. Indeed, experience with VAC is somewhat more limited in the spine as opposed to other areas. However, the evidence provided in this review suggests an improvement in hardware retention with the use of these systems. As such, this should be strongly considered when planning a delayed primary closure because of grossly purulent material or a high PITSS score. Additionally, when wound closure is difficult, consultation with colleagues in

plastic surgery for flap coverage may serve to improve outcomes.

This review is limited primarily by the nature of the literature selected. There is a vast body of knowledge published regarding SSI; however, we have chosen to focus primarily on those that pertain specifically to spinal surgery. The use of prophylactic systemic antibiotics is also not addressed although this is a traditional cornerstone of SSI prevention. Nevertheless, the scope of this review is exceptionally broad and as such precludes a detailed presentation of all the data reviewed. Furthermore, as previously noted, the data presented in the systematic reviews does not lend itself to meta-analyses as there we no common quantitative end points. Therefore, no strong conclusions can be made regarding these data.

In summary, infection after spinal surgery is a highly morbid and costly complication worthy of significant research and discussion. Patients should be advised about infection risk because of patient- and procedure-specific factors. Certainly, no single intervention will eradicate infection; however, the data provided in this review offer a number of promising prospects for infection prevention, diagnosis, and treatment. The addition of prospective investigations in this field will serve to greatly benefit all spinal surgeons and their patients.

References

[1] Kurtz SM, Lau E, Ong KL, Carreon L, Watson H, Albert T, et al. Infection risk for primary and revision instrumented lumbar spine fusion in the Medicare population. J Neurosurg Spine 2012;17:342–7.

[2] Campbell PG, Yadla S, Malone J, Maltenfort MG, Harrop JS, Sharan AD, et al. Complications related to instrumentation in spine surgery: a prospective analysis. Neurosurg Focus 2011;31:E10.

[3] Weinstein JN, Lurie JD, Tosteson TD, Tosteson AN, Blood EA, Abdu WA, et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the spine patient outcomes research trial (SPORT). Spine 2008;33:2789–800.

[4] Weinstein JN, Lurie JD, Tosteson TD, Zhao W, Blood EA, Tosteson AN, et al. Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis. Four-year results in the spine patient outcomes research trial (SPORT) randomized and observational cohorts. J Bone Joint Surg Am 2009;91:1295–304.

[5] Weinstein JN, Tosteson TD, Lurie JD, Tosteson A, Blood E, Herkowitz H, et al. Surgical versus nonoperative treatment for lumbar spinal stenosis four-year results of the spine patient outcomes research trial. Spine 2010;35:1329–38.

[6] Fehlings MG, Smith JS, Kopjar B, Arnold PM, Yoon ST, Vaccaro AR, et al. Perioperative and delayed complications associated with the surgical treatment of cervical spondylotic myelopathy based on 302 patients from the AOSpine North America Cervical Spondylotic Myelopathy Study. J Neurosurg Spine 2012;16:425–32.

[7] Smith JS, Shaffrey CI, Sansur CA, Berven SH, Fu KM, Broadstone PA, et al. Rates of infection after spine surgery based on 108,419 procedures: a report from the scoliosis research society morbidity and mortality committee. Spine 2011;36:556–63.

[8] Hart R, Cabalo A, Bess S, Akbarnia B, Boachie-Adjei O, Burton D, et al. Comparison of patient and surgeon perceptions of adverse events following adult spinal deformity surgery. Spine 2013;38:732–6.

[9] Bono CM, Harris MB, Warholic N, Katz JN, Carreras E, White A, et al. Pain intensity and patients' acceptance of surgical complication risks with lumbar fusion. Spine 2013;38:140–7.

[10] O'Toole JE, Eichholz KM, Fessler RG. Surgical site infection rates after minimally invasive spinal surgery. J Neurosurg Spine 2009;11:471–6.

[11] McGirt MJ, Parker SL, Lerner J, Engelhart L, Knight T, Wang MY. Comparative analysis of perioperative surgical site infection after minimally invasive versus open posterior/transforaminal lumbar interbody fusion: analysis of hospital billing and discharge data from 5170 patients. J Neurosurg Spine 2011;14:771–8.

[12] Parker SL, Adogwa O, Witham TF, Aaronson OS, Cheng J, McGirt MJ. Post-operative infection after minimally invasive versus open transforaminal lumbar interbody fusion (TLIF): literature review and cost analysis. Minim Invasive Neurosurg 2011;54:33–7.

[13] Park Y, Ha JW. Comparison of one-level posterior lumbar interbody fusion performed with a minimally invasive approach or a traditional open approach. Spine 2007;32:537–43.

[14] Kepler CK, Yu AL, Gruskay JA, Delasotta LA, Radcliff KE, Rihn JA, et al. Comparison of open and minimally invasive techniques for posterior lumbar instrumentation and fusion after open anterior lumbar interbody fusion. Spine J 2013;13:489–97.

[15] Schuster JM, Rechtine G, Norvell DC, Dettori JR. The influence of perioperative risk factors and therapeutic interventions on infection rates after spine surgery: a systematic review. Spine 2010;35(9 Suppl):S125–37.

[16] Abdul-Jabbar A, Takemoto S, Weber MH, Hu SS, Mummaneni PV, Deviren V, et al. Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data. Spine 2012;37:1340–5.

[17] Pull ter Gunne AF, Hosman AJ, Cohen DB, Schuetz M, Habil D, van Laarhoven CJ, et al. A methodological systematic review on surgical site infections following spinal surgery: part 1: risk factors. Spine 2012;37:2017–33.

[18] Chitale R, Campbell PG, Yadla S, Whitmore RG, Maltenfort MG, Ratliff JK. International classification of disease clinical modification 9 modeling of a patient comorbidity score predicts incidence of perioperative complications in a nationwide inpatient sample assessment of complications in spine surgery. J Spinal Disord Tech; Epub ahead of print 2012 Sep 6.

[19] Mehta AI, Babu R, Karikari IO, Grunch B, Agarwal VJ, Owens TR, et al. 2012 Young investigator award winner: the distribution of body mass as a significant risk factor for lumbar spinal fusion postoperative infections. Spine 2012;37:1652–6.

[20] Rechtine GR, Bono PL, Cahill D, Bolesta MJ, Chrin AM. Postoperative wound infection after instrumentation of thoracic and lumbar fractures. J Orthop Trauma 2001;15:566–9.

[21] Lonjon G, Dauzac C, Fourniols E, Guigui P, Bonnomet F, Bonnevialle P, et al. Early surgical site infections in adult spinal trauma: a prospective, multicentre study of infection rates and risk factors. Orthop Traumatol Surg Res 2012;98:788–94.

[22] Wilson JR, Arnold PM, Singh A, Kalsi-Ryan S, Fehlings MG. Clinical prediction model for acute inpatient complications after traumatic cervical spinal cord injury: a subanalysis from the surgical timing in acute spinal cord injury study. J Neurosurg Spine 2012;17(1 Suppl):46–51.

[23] Blam OG, Vaccaro AR, Vanichkachorn JS, Albert TJ, Hilibrand AS, Minnich JM, et al. Risk factors for surgical site infection in the patient with spinal injury. Spine 2003;28:1475–80.

[24] Gruskay J, Kepler C, Smith J, Radcliff K, Vaccaro A. Is surgical case order associated with increased infection rate after spine surgery? Spine 2012;37:1170–4.

[25] Gruskay J, Smith J, Kepler CK, Radcliff K, Harrop J, Albert T, et al. The seasonality of postoperative infection in spine surgery. J Neurosurg Spine 2013;18:57–62.

[26] Mirza SK, Deyo RA, Heagerty PJ, Konodi MA, Lee LA, Turner JA, et al. Development of an index to characterize the "invasiveness" of spine surgery: validation by comparison to blood loss and operative time. Spine 2008;33:2651–61; discussion 2662.

[27] Cizik AM, Lee MJ, Martin BI, Bransford RJ, Bellabarba C, Chapman JR, et al. Using the spine surgical invasiveness index to identify risk of surgical site infection: a multivariate analysis. J Bone Joint Surg Am 2012;94:335–42.

[28] Desai A, Ball PA, Bekelis K, Lurie J, Mirza SK, Tosteson TD, et al. SPORT: does incidental durotomy affect long-term outcomes in cases of spinal stenosis? Neurosurgery 2011;69:38–44; discussion 44.

[29] Desai A, Ball PA, Bekelis K, Lurie JD, Mirza SK, Tosteson TD, et al. Outcomes after incidental durotomy during first-time lumbar discectomy. J Neurosurg Spine 2011;14:647–53.

[30] Fourney DR, Dettori JR, Norvell DC, Dekutoski MB. Does minimal access tubular assisted spine surgery increase or decrease complications in spinal decompression or fusion? Spine 2010;35(9 Suppl):S57–65.

[31] Larsson S, Thelander U, Friberg S. C-reactive protein (CRP) levels after elective orthopedic surgery. Clin Orthop Relat Res 1992;237–42.

[32] Mok JM, Pekmezci M, Piper SL, Boyd E, Berven SH, Burch S, et al. Use of C-reactive protein after spinal surgery: comparison with erythrocyte sedimentation rate as predictor of early postoperative infectious complications. Spine 2008;33:415–21.

[33] Lee JH, Lee JH, Kim JB, Lee HS, Lee DY, Lee DO. Normal range of the inflammation related laboratory findings and predictors of the postoperative infection in spinal posterior fusion surgery. Clin Orthop Surg 2012;4:269–77.

[34] Deguchi M, Shinjo R, Yoshioka Y, Seki H. The usefulness of serum amyloid A as a postoperative inflammatory marker after posterior lumbar interbody fusion. J Bone Joint Surg Br 2010;92:555–9.

[35] Nie H, Jiang D, Ou Y, Quan Z, Hao J, Bai C, et al. Procalcitonin as an early predictor of postoperative infectious complications in patients with acute traumatic spinal cord injury. Spinal Cord 2011;49:715–20.

[36] Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am 2010;92:2102–9.

[37] Honsawek S, Deepaisarnsakul B, Tanavalee A, Sakdinakiattikoon M, Ngarmukos S, Preativatanyou K, et al. Erratum to: relationship of serum IL-6, C-reactive protein, erythrocyte sedimentation rate, and knee skin temperature after total knee arthroplasty: a prospective study. Int Orthop 2011;35:1749.

[38] Parvizi J, Jacovides C, Antoci V, Ghanem E. Diagnosis of periprosthetic joint infection: the utility of a simple yet unappreciated enzyme. J Bone Joint Surg Am 2011;93:2242–8.

[39] Nandyala SV, Schwend RM. Prevalence of intraoperative tissue bacterial contamination in posterior pediatric spinal deformity surgery. Spine 2013;38:E482–6.

[40] Shiono Y, Watanabe K, Hosogane N, Tsuji T, Ishii K, Nakamura M, et al. Sterility of posterior elements of the spine in posterior correction surgery. Spine 2012;37:523–6.

[41] Bible JE, O'Neill KR, Crosby CG, Schoenecker JG, McGirt MJ, Devin CJ. Implant contamination during spine surgery. Spine J 2013;13:637–40.

[42] Ahn DK, Park HS, Kim TW, Yang JH, Boo KH, Kim IJ, et al. The degree of bacterial contamination while performing spine surgery. Asian Spine J 2013;7:8–13.

[43] Dalstrom DJ, Venkatarayappa I, Manternach AL, Palcic MS, Heyse BA, Prayson MJ. Time-dependent contamination of opened sterile operating-room trays. J Bone Joint Surg Am 2008;90:1022–5.

[44] Radcliff KE, Rasouli MR, Neusner A, Kepler CK, Albert TJ, Rihn JA, et al. Preoperative delay of more than 1 hour increases the risk of surgical site infection. Spine 2013;38:1318–23.

[45] Savage JW, Weatherford BM, Sugrue PA, Nolden MT, Liu JC, Song JK, et al. Efficacy of surgical preparation solutions in lumbar spine surgery. J Bone Joint Surg Am 2012;94:490–4.

[46] Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol 2010;31:1219–29.

[47] Beldi G, Bisch-Knaden S, Banz V, Muhlemann K, Candinas D. Impact of intraoperative behavior on surgical site infections. Am J Surg 2009;198:157–62.

[48] Bible JE, Biswas D, Whang PG, Simpson AK, Grauer JN. Which regions of the operating gown should be considered most sterile? Clin Orthop Relat Res 2009;467:825–30.

[49] Waked WR, Simpson AK, Miller CP, Magit DP, Grauer JN. Sterilization wrap inspections do not adequately evaluate instrument sterility. Clin Orthop Relat Res 2007;462:207–11.

[50] Biswas D, Bible JE, Whang PG, Simpson AK, Grauer JN. Sterility of C-arm fluoroscopy during spinal surgery. Spine 2008;33:1913–7.

[51] Krueger CA, Murray CK, Mende K, Guymon CH, Gerlinger TL. The bacterial contamination of surgical scrubs. Am J Orthop (Belle Mead NJ) 2012;41:E69–73.

[52] Chang FY, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Can povidone-iodine solution be used safely in a spinal surgery? Eur Spine J 2006;15:1005–14.

[53] Cheng MT, Chang MC, Wang ST, Yu WK, Liu CL, Chen TH. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. Spine 2005;30:1689–93.

[54] Savitz SI, Savitz MH, Goldstein HB, Mouracade CT, Malangone S. Topical irrigation with polymyxin and bacitracin for spinal surgery. Surg Neurol 1998;50:208–12.

[55] O'Neill KR, Smith JG, Abtahi AM, Archer KR, Spengler DM, McGirt MJ, et al. Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. Spine J 2011;11:641–6.

[56] Molinari RW, Khera OA, Molinari WJ III. Prophylactic intraoperative powdered vancomycin and postoperative deep spinal wound infection: 1,512 consecutive surgical cases over a 6-year period. Eur Spine J 2012;21(4 Suppl):S476–82.

[57] Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. Spine 2011;36:2084–8.

[58] Godil SS, Parker SL, O'Neill KR, Devin CJ, McGirt MJ. Comparative effectiveness and cost-benefit analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma. J Neurosurg Spine 2013;19:331–5.

[59] Pahys JM, Pahys JR, Cho SK, Kang MM, Zebala LP, Hawasli AH, et al. Methods to decrease postoperative infections following posterior cervical spine surgery. J Bone Joint Surg Am 2013;95:549–54.

[60] Knaepler H. Local application of gentamicin-containing collagen implant in the prophylaxis and treatment of surgical site infection in orthopaedic surgery. Int J Surg 2012;10(1 Suppl):S15–20.

[61] Stall AC, Becker E, Ludwig SC, Gelb D, Poelstra KA. Reduction of postoperative spinal implant infection using gentamicin microspheres. Spine 2009;34:479–83.

[62] Borkhuu B, Borowski A, Shah SA, Littleton AG, Dabney KW, Miller F. Antibiotic-loaded allograft decreases the rate of acute deep wound infection after spinal fusion in cerebral palsy. Spine 2008;33:2300–4.

[63] Gruenberg MF, Petracchi M, Valacco M, Solá C. Use of vancomycin in bone grafts as prophylaxis of acute infection in spine surgery. Coluna/Columna 2008;7:251–6.

[64] Gilotra M, Griffith C, Schiavone J, Nimmagadda N, Noveau J, Ludwig SC. Capacitive coupling reduces instrumentation-related infection in rabbit spines: a pilot study. Clin Orthop 2012;470:1646–51.

[65] Rao SB, Vasquez G, Harrop J, Maltenfort M, Stein N, Kaliyadan G, et al. Risk factors for surgical site infections following spinal fusion procedures: a case-control study. Clin Infect Dis 2011;53:686–92.

[66] Wachter D, Bruckel A, Stein M, Oertel MF, Christophis P, Boker DK. 2-Octyl-cyanoacrylate for wound closure in cervical and lumbar spinal surgery. Neurosurg Rev 2010;33:483–9.
[67] Mehbod AA, Ogilvie JW, Pinto MR, Schwender JD, Transfeldt EE, Wood KB, et al. Postoperative deep wound infections in adults after spinal fusion: management with vacuum-assisted wound closure. J Spinal Disord Tech 2005;18:14–7.
[68] Ahmed R, Greenlee JD, Traynelis VC. Preservation of spinal instrumentation after development of postoperative bacterial infections in patients undergoing spinal arthrodesis. J Spinal Disord Tech 2012;25:299–302.
[69] Mitra A, Mitra A, Harlin S. Treatment of massive thoracolumbar wounds and vertebral osteomyelitis following scoliosis surgery. Plast Reconstr Surg 2004;113:206–13.
[70] Mericli AF, Tarola NA, Moore JH Jr, Copit SE, Fox JW IV, Tuma GA. Paraspinous muscle flap reconstruction of complex midline back wounds: risk factors and postreconstruction complications. Ann Plast Surg 2010;65:219–24.
[71] Mericli AF, Mirzabeigi MN, Moore JH Jr, Fox JW IV, Copit SE, Tuma GA. Reconstruction of complex posterior cervical spine wounds using the paraspinous muscle flap. Plast Reconstr Surg 2011;128:148–53.
[72] Dipaola CP, Saravanja DD, Boriani L, Zhang H, Boyd MC, Kwon BK, et al. Postoperative infection treatment score for the spine (PITSS): construction and validation of a predictive model to define need for single versus multiple irrigation and debridement for spinal surgical site infection. Spine J 2012;12:218–30.
[73] Wang MC, Shivakoti M, Sparapani RA, Guo C, Laud PW, Nattinger AB. Thirty-day readmissions after elective spine surgery for degenerative conditions among US Medicare beneficiaries. Spine J 2012;12:902–11.
[74] Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Hanscom B, Skinner JS, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. JAMA 2006;296:2441–50.
[75] Campbell PG, Yadla S, Nasser R, Malone J, Maltenfort MG, Ratliff JK. Patient comorbidity score predicting the incidence of perioperative complications: assessing the impact of comorbidities on complications in spine surgery. J Neurosurg Spine 2012;16:37–43.
[76] Coric D, Nunley PD, Guyer RD, Musante D, Carmody CN, Gordon CR, et al. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the Kineflex|C artificial disc investigational device exemption study with a minimum 2-year follow-up: clinical article. J Neurosurg Spine 2011;15:348–58.
[77] Gornet MF, Burkus JK, Dryer RF, Peloza JH. Lumbar disc arthroplasty with Maverick disc versus stand-alone interbody fusion: a prospective, randomized, controlled, multicenter investigational device exemption trial. Spine 2011;36:E1600–11.
[78] Blumenthal S, McAfee PC, Guyer RD, Hochschuler SH, Geisler FH, Holt RT, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemptions study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: part I: evaluation of clinical outcomes. Spine 2005;30:1565–75; discussion E387–91.
[79] Murrey D, Janssen M, Delamarter R, Goldstein J, Zigler J, Tay B, et al. Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. Spine J 2009;9:275–86.
[80] Sasso RC, Smucker JD, Hacker RJ, Heller JG. Artificial disc versus fusion: a prospective, randomized study with 2-year follow-up on 99 patients. Spine 2007;32:2933–40; discussion 2941–2.
[81] Zigler JE, Delamarter RB. Five-year results of the prospective, randomized, multicenter, Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential arthrodesis for the treatment of single-level degenerative disc disease. J Neurosurg Spine 2012;17:493–501.
[82] Kang BU, Lee SH, Ahn Y, Choi WC, Choi YG. Surgical site infection in spinal surgery: detection and management based on serial C-reactive protein measurements. J Neurosurg Spine 2010;13:158–64.
[83] Bible JE, O'Neill KR, Crosby CG, Schoenecker JG, McGirt MJ, Devin CJ. Microscope sterility during spine surgery. Spine 2012;37:623–7.
[84] Couture J, Cabana F. Irradiated allograft bone in spine surgery: to culture or not? A single center retrospective study. Spine 2013;38:558–63.
[85] Tofuku K, Koga H, Yanase M, Komiya S. The use of antibiotic-impregnated fibrin sealant for the prevention of surgical site infection associated with spinal instrumentation. Eur Spine J 2012;21:2027–33.
[86] Caroom C, Tullar JM, Benton EG Jr, Jones JR, Chaput CD. Intrawound vancomycin powder reduces surgical site infections in posterior cervical fusion. Spine 2013;38:1183–7.