PART IV

SPINE

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Prevention

1.1. PREVENTION: GENERAL PRINCIPLES

Authors: Steven Schmitt, Christopher Kepler

QUESTION 1: What can one do if an inadvertent contamination during instrumented spine surgery occurs?

RECOMMENDATION: There is no data to support a particular strategy in preventing infection after inadvertent contamination of spinal implants.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Left uncovered in the operating suite, spinal implants can become contaminated within 30 minutes [1]. There are no human data to support a particular algorithm for management of inadvertent contamination. In animal studies, tobramycin powder has been shown to reduce infection in contaminated spine surgery and vancomycin powder has been shown to reduce infection in contaminated knee surgery [2,3]. At least one suggests that management of inadvertent contamination should be individualized to the clinical situation and stage of surgery, and many surgeons are reluctant to proceed with implant surgery if contamination has occurred. Some experts recommend intraoperative irrigation with solutions containing antibiotics, without supporting data (personal communication).

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Author: Maja Babic

QUESTION 2: How should spine surgery patients with postoperative diarrhea be managed?

RECOMMENDATION: Diarrhea can be managed in a standard approach with careful attention to the surgical site.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Postoperative diarrhea poses a risk of contaminating the surgical incision. Maintaining a clean and dry surgical site is crucial. Postoperative diarrhea is generally self-limiting but infectious etiologies, especially *C. difficile*, are particularly concerning in the inpatient setting and should be ruled out. After infectious causes are ruled out, a standard approach should be implemented to address diarrhea including discontinuing potentially inciting medication (antibiotics), increasing fiber content and using antisecretory (i.e., bismuth subsalicylate) and antimotility (i.e., loperamide) agents. A balanced electrolyte rehydration should also be utilized. The use of probiotics and prebiotics can be used in cases of post-antibiotic-associated illness [1].

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1.2. PREVENTION: ANTIMICROBIALS

Authors: Alexander Montgomery, Rajesh Mangattil

QUESTION 1: Is there a role for oral antibiotics in the prevention of infection in patients with draining wounds following spinal surgery?

RECOMMENDATION: There is no reliable evidence for the use of prophylactic oral antibiotic therapy in patients with draining wounds after spine surgery.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

The incidence of spinal surgical site infection (SSI) has been reported to be from 0.7–16% [1–3]. Surgical drains are used in spine surgery to avoid the risk of a hematoma formation leading to potential neurological deficit [4]. Drains retained for a longer period have been shown to have a higher rate of bacterial contamination [5]. However, not using a drain has been found to be associated with the development of late-onset SSI [6,7]. Therefore, the use of drains decreases wound drainage and consequently decreases infection rates [8,9]. Prophylactic antibiotic cover for 24 hours has now become a standard of care following orthopaedic procedures [10].

Since the first systematic review on prophylactic measures against spinal SSI was published by Brown et al. in 2004 [11], there has been a considerable increase in the preventive strategies documented in the spine literature. However, many studies are of lower methodological quality with significant heterogeneity [12].

There was only one prospective randomized study showing no significant difference in the infection rates between patients receiving prophylactic antibiotic coverage for 24 hours or for the entire duration that the drain was in place. This study was on thoracolumbar fractures. It was not clear if the antibiotic cover was administered orally or parenterally [13]. In a review of 560 cases of closed suction drainage in single level lumbar decompressions, Kanayama et al. did not report on the use of prophylactic oral antibiotics [14]. Similarly, a 2018 systematic review by Yao et al. identified 11 randomized controlled trials (RCTs), 51 case-controlled studies (CCS) and 77 case series. They reported wide variations in the surgical indications, approaches and definitions of SSI. They found strong evidence that closed-suction drainage does not affect SSI rates, but had no mention of the use of prophylactic oral antibiotic therapy [15].

There were many studies that evaluated the risk factors for wound complications following spine surgery [16–18]. Past studies are archaic in nature with very little contribution or relevance to these authors. A staged treatment algorithm for spine infections did not specify or address the indication for oral antibiotics to prevent infection in draining wounds [19]. A recent retrospective study attributed the drain volume and time to the risk factors for SSI after lumbar surgery. There was no direct reference to the impact of oral or parenteral antibiotics in their study [13,20].

A systematic evidenced-based review included 36 observational studies involving 2,439 patients. However, these were non-interventional studies to evaluate the independent risk factors for patients developing SSIs following spine surgery [17]. In their systematic review and meta-analysis of wound drains in non-instrumented lumbar decompression surgery, Davidoff et al. included 5,327 cases who received drains. They found that the SSI rates were unaffected by the routine use of drains. However, none of these patients had prophylactic oral antibiotics [21]. Ho et al. reported a retrospective review of 70 patients who had undergone single-level lumbar discectomy. They suggested that surgical drains do not increase SSI risk and that drain tip cultures allow detection of postoperative infection at a very early stage. They found that this would lead to quicker initiation of antibiotic treatment [22].

Apart from a prospective randomized study that suggested no difference in the infection rates, there are no studies directly linking the role of oral antibiotics in the prevention of infection in patients with draining wounds following spine surgery [13]. Therefore, in the absence of reliable evidence, only a consensus recommendation can be made based on clinical opinion.

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Authors: Robert Sawyer, Joseph Weistroffer, Anna White

QUESTION 2: Is there a role for the addition of gentamicin to perioperative prophylactic antibiotics in spine surgery?

RECOMMENDATION: No, we recommend AGAINST the inclusion of gentamicin for perioperative prophylaxis in spine surgery. There is no data suggesting that the addition of gentamicin to systemic perioperative prophylactic antibiotic regimens decreases the rate of postoperative infections, and strong evidence showed that it is associated with harm (namely nephrotoxicity). The question of the use of local/topical gentamicin is unresolved.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 62%, Disagree: 15%, Abstain: 23% (Super Majority, Weak Consensus)

RATIONALE

The use of gentamicin to expand the gram-negative activity for perioperative antimicrobial prophylaxis in spine surgery has been considered for decades, yet positive outcomes data for this practice are lacking. Pons et al. reported on a randomized, blinded study of 826 patients undergoing neurosurgical procedures, including spine surgery, and found similar surgical site infection (SSI) rates for those assigned to ceftizoxime or vancomycin and gentamicin [1]. Ramo et al. reported on a multivariate analysis of 428 posterior spinal fusion patients and found that the addition of an aminoglycoside did not lower the SSI rate [2]. In a mixed population of more than 11,000 orthopaedic surgery patients treated over 5 years in the United Kingdom, Walker et al. noted no difference in SSI rates during a period when a combination of flucloxacillin and gentamicin was given for prophylaxis compared to one where co-amoxiclav was the prophylactic regimen of choice [3].

The association of aminoglycoside prophylaxis (even single-dose) for orthopaedic surgery and acute kidney injury (AKI) has now been well-documented. Dubrovskaya et al. reviewed more than 4,000 patients undergoing orthopaedic surgery, comparing those receiving a single dose of gentamicin combined with another antibiotic to those receiving non-aminoglycoside prophylaxis alone. Although for all patients the addition of gentamicin was not associated with AKI, gentamicin was associated with a statistically significantly higher rate of AKI for those undergoing spine surgery [4]. Bell et al. reported on a Scottish initiative where routine surgical prophylaxis was changed from cefuroxime to flucloxacillin and gentamicin (single-dose) between 2006 and 2010. Among 7,666 patients undergoing orthopaedic surgery, the gentamicin-containing regimen was associated with a 94% higher incidence of AKI [5]. Finally, in the previously-cited study by Walker et al., a change from routine prophylaxis with flucloxacillin and gentamicin to co-amoxiclav alone was associated with a 63% reduction in postoperative AKI [3].

Two meta-analyses on the association of gentamicin prophylaxis with nephrotoxicity have been published. Luo et al. compared the use of gentamicin and flucloxacillin to cefuroxime alone in studies of diverse surgery types. The risk of postoperative renal impairment was higher in the gentamicin group, especially for those undergoing orthopaedic surgery [6]. Srisung et al. analyzed 11 studies containing 18,354 patients comparing gentamicin versus non-gentamicin surgical prophylaxis regimens. Using random effects modeling, gentamicin prophylaxis in orthopaedic surgery was associated with a significantly higher risk of AKI (risk rate (RR) 2.99; 95% confidence interval (CI): 1.84, 4.88) [7].

Data regarding the use of topical or local wound gentamicin are limited. In a single-center study, van Herwijnen et al. reported a higher SSI rate for patients undergoing scoliosis surgery who received wound irrigation with gentamicin versus povidone-iodine [8]. On the other hand, Borkhuu et al. reported on 220 children undergoing spinal fusion and found a four-fold reduction in SSI for those treated with gentamicin-impregnated bone allograft [9]. Han et al. retrospectively analyzed data from 399 patients undergoing spine surgery. Among patients who had a gentamicin-impregnated collagen sponge applied to their wound, the SSI rate was 0.8%, versus 5% for those treated without the sponge [10]. At this time, however, given the variability in reported application methods for local gentamicin and the small number of patients studied, the routine use of topical gentamicin cannot be recommended.

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QUESTION 3: Should prophylactic antibiotic prophylaxis be repeated during spine surgery? If so, when?

RECOMMENDATION: In most uncomplicated spinal procedures, a single preoperative dose of prophylactic antibiotics is sufficient. Prophylactic antibiotics should be redosed intraoperatively for procedures lasting longer than twice the half-life of the antibiotic, or if there is excessive blood loss (blood loss > 1,500 mL) in order to ensure therapeutic levels.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

There are no randomized spine studies that compare the effectiveness of redosing prophylactic antibiotics during surgery to preoperative antibiotics alone. Therefore, this review was expanded to include other surgical subspecialties. Several major guidelines including those from the North American Spine Society (NASS), Infectious Disease Society of America (IDSA) and Surgical Infection Society (SIS) have made similar recommendations supported by pharmacokinetic data and retrospective studies [1,2]. Furthermore, the Centers for Disease Control and Prevention (CDC) recently noted that there is insufficient-quality evidence to make a recommendation regarding whether or not antibiotics should be redosed intraoperatively [3].

In a prospective study of 57 subjects undergoing elective surgery, an analysis of intraoperative serum cefazolin concentrations at approximately 3.5 hours after receiving a preoperative dose showed that antibiotic concentrations dropped below the minimum inhibitory concentration (MIC) for methicillin-susceptible *Staphylococcus aureus* (MSSA) and *Escherichia Coli* (*E. Coli*) [4]. Ohge and colleagues found that cefazolin concentrations had dropped below 80% of the MIC in the adipose tissue and peritoneum for multiple bacteria three hours after the preoperative dose was administered [5]. In a prospective study of 11 elective instrumented spinal procedures with a large expected blood loss, estimated blood loss (EBL) was found to have a strong negative correlation with cefazolin tissue concentrations (r = -0.66, p = 0.5). Based on the pharmacokinetic values, the authors recommended that procedures with an EBL greater than 1,500 mL should receive an additional dose of cefazolin [6].

In a retrospective study of 1,548 patients undergoing cardiac surgery, intraoperative redosing for procedures lasting greater than 400 minutes was shown to reduce the risk of surgical site infections (SSIs) (adjusted OR 0.44, 95% CI 0.23-0.86) [7]. Similarly, Scher et al. demonstrated that for surgeries longer than three hours, patients who were redosed with cefazolin intraoperatively had a lower SSI rate than those who only received preoperative cefazolin (6.1% vs. 1.3%, p < 0.01) [8]. In another retrospective review of 4,078 patients undergoing various general surgery procedures, cases with an EBL of greater than 500 mL or those that were not re-dosed intraoperatively during longer cases were associated with a higher rate of SSI [9].

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QUESTION 4: Should vancomycin powder be applied to the wound in patients undergoing spinal surgeries? Are there any potential harms associated with this practice?

RECOMMENDATION: Yes. Evidence suggests that vancomycin powder applied to the wound during spinal surgery reduces the risk of infection. However, the majority of studies lack a control arm and it is not known if vancomycin powder is better than antiseptic agents. There is insufficient evidence for or against the potential harm associated with this practice.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 79%, Disagree: 14%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Surgical site infection is a known risk of spine surgery with or without instrumentation, and gram-positive organisms are the most common pathogens in such infections. Many practitioners now apply vancomycin powder intraoperatively to reduce the risk of infection. Given concern for vancomycin's adverse effects and antimicrobial resistance, it is critical to consider a risk-benefit analysis of this practice.

A number of studies addressed the efficacy of vancomycin powder use in spine surgery. These have been the subject of several systematic reviews. Xie et al. reviewed 19 retrospective cohort studies and 1 prospective case study, with results suggesting benefit in all but 2 of these with an overall infection risk of 2.83-fold higher for patients not receiving vancomycin powder compared to those receiving it [1]. The authors pointed out study heterogeneity with regard to powder, drug dosage and exposure of bone graft and instrumentation to the drug, citing these as areas for future investigation. This trend toward benefit was confirmed in five other systematic reviews [2–6].

With regard to adverse effects, Ghobrial et al. performed a systematic review of 16 studies with 6,701 patients [7]. Of these, 1 patient developed nephropathy, 2 patients experienced hearing loss, 1 patient had an elevated vancomycin level and 19 patients developed culture-negative seroma. The authors highlighted the lack of in vivo evidence regarding vancomycin resistance. There was a trend toward gram-negative and polymicrobial infections among vancomycin powder recipients in one study [8].

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QUESTION 5: What is the optimal perioperative antibiotic prophylaxis for patients undergoing spine surgery? What considerations should be made in cases of drug allergies?

RECOMMENDATION: The optimal prophylactic antibiotic for an uncomplicated spine surgery is a first- or second-generation cephalosporin given intravenously within 60 minutes of initial incision.

In patients with a history of anaphylactic reaction after use of beta lactams or in countries with a high rate of methicillin-resistant *Staphylococcal* infections, vancomycin in a weight-adjusted dose (15 mg/kg) should be used. Clindamycin 600 mg intravenously is an alternative to vancomycin.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 79%, Disagree: 7%, Abstain: 14% (Super Majority, Strong Consensus)

RATIONALE

Current literature supports the use of prophylactic antibiotics for spinal procedures with or without instrumentation to decrease the risk of surgical site infections (SSI), with a first- or second-generation cephalosporin being the antibiotic of choice [1–6]. In addition, clinical guidelines set forth by the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS), the Society for Healthcare Epidemiology of America (SHEA) and the North American Spine Society support the use of first-generation cephalosporins [1,7,8]. Although comparative studies to evaluate the optimal timing for preoperative antibiotic have not been conducted for spine surgery, it is well-established that intravenous cephalosporins given within 60 minutes before initial incision is effective [9,10].

In a comparative study evaluating the addition of vancomycin powder for posterior thoracic and lumbar spine surgery, Sweet et al. found that vancomycin powder reduced the rate of SSI compared to intravenous cephalexin alone (0.2% vs. 2.6%, $p < 0.0001$).

Regarding prophylaxis regiments combining antibiotic agents, randomized clinical trials exist which show a reduced rate of postsurgical infections if a combination of a cephalosporin and gentamicin or vancomycin and gentamicin is used, compared to placebo [11,12]. However, there are no studies available which compare combination regimens with the standard prophylaxis with cefazolin. A study by Pons et al. comparing ceftizoxime versus the combination prophylaxis with vancomycin and gentamicin found no decreased infection rate, but higher toxicity with the combination regimen [13].

There is no specific recommendation for adapted prophylaxis in obese patients in spine surgery. However, in periprosthetic joint infections, adaptation is discussed in patients with a weight more than 100 kg since infection rate was twice that in other patients [13–15].

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Author: Dolors Rodriguez-Pardo

QUESTION 6: What are the optimal prophylactic antibiotics for patients with neurogenic bladder who are undergoing spine surgery?

RECOMMENDATION: The recommended standard perioperative antibiotic prophylaxis in spine surgery is cefazolin, but a broader-spectrum prophylaxis may be necessary in patient subpopulations more prone to acquiring surgical site infections (SSIs). In the case of neurogenic bladder, preoperative urine culture and individualized antibiotic prophylaxis are associated with a significant decrease in SSIs due to gram-negative bacilli (GNB).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 79%, Disagree: 14%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Prevention of SSI is of utmost importance in patients undergoing spine surgery, and perioperative antibiotic prophylaxis is a key measure to avoid this complication [1,2]. However, the superiority of one agent or schedule over any other has not been clearly demonstrated [1,2]. The recommended standard perioperative antibiotic prophylaxis in spinal surgery is cefazolin [1]. Isolated reports have shown that a broader-spectrum prophylaxis may be necessary in patient subpopulations more prone to acquiring poly-microbial SSI, such as those with neuromuscular deformities or spinal cord injury. In a retrospective observation study, Dessy et al. demonstrated that an enhanced antibiotic prophylaxis using intravenous (IV) cefuroxime for 24 hours plus vancomycin until drain removal in instrumented spinal surgery, and IV cefuroxime for 24 hours in non-instrumentation cases reduced the rate of SSIs in spine surgery [3].

There are no published data regarding the best antibiotic treatment to be used as prophylaxis in patients with neurogenic bladder. The North American Spine Society (NASS) evidence-based guidelines on antibiotic prophylaxis in spinal surgery have pointed out that potential subgroups of patients requiring effective prophylaxis against GNB may exist, although they have not been clearly defined [1]. In the case of patients with neurogenic bladder, they are more prone to urinary tract colorization and infection [4–5]. Although asymptomatic bacteriuria (AB) should not be routinely treated in these patients because of rising resistance patterns, in the case of symptomatic urinary tract infection (UTI) antibiotic treatment should be administered and antibiotic selection should be based on local and patient-based resistance patterns so that the spectrum can be as narrow as possible [5]. In this line, recent Clinical Guidelines for the Diagnosis and Treatment of UTI of the Spanish Society of Infectious Diseases state that screening for, and treatment of, AB prior to performing instrumental spinal surgery is recommended for patients with neurogenic bladders or urinary incontinence in order to reduce the risk of gram-negative SSIs [6].

It was reported that up to 61% of children with myelomeningocele have neurogenic bladders [7–9]. Hatlen et al. demonstrated that the presence of positive urinary cultures before elective spine surgery for children with myelomeningocele leads to an increased risk of perioperative spine infections [10]. Olsen et al. conducted a case-control study to determine independent risk factors for SSI following orthopaedic spinal operations [11]. Among the patient-level factors in the univariate analysis, any incontinence (bowel or bladder, or both and preoperative or postoperative) significantly increased the risk of SSIs.

Although gram-positive organisms (particularly *Staphylococcus aureus*) predominate as causative agents for SSIs in patients undergoing spine surgery, GNB accounted for a sizeable portion of SSIs, particularly among lower lumbar and sacral spine surgical procedures [2]. Patients with incontinence, neurogenic bladder or indwelling catheters are more prone to urinary tract colonization and infection and may therefore be at higher risk of SSIs by GNB [4]. Contamination by GNB should not occur during the operative procedure, as these microorganisms are not usually present among the patient's skin flora [12]. Previous studies have suggested that GNB contamination could be secondary to hematogenous seeding originating in the urinary tract or to local skin contamination in incontinent patients, especially those undergoing surgery at the lumbosacral level [12].

Nuñez-Pereira et al. hypothesized that detecting urinary tract colonization preoperatively and adjusting antibiotic prophylaxis according to urine culture results might lower the overall SSI rate by reducing the number of GNB infections [12]. They performed a retrospective cohort study comparing two consecutive groups of patients undergoing posterior spinal fusion and instrumentation at a single institution. Cohort A included 236 patients, operated on between January 2006 and March 2007, receiving standard preoperative antibiotic prophylaxis with cefazolin (clindamycin in allergic patients). Cohort B included 223 patients operated on between January and December 2009, receiving individualized antibiotic prophylaxis and treatment based on preoperative urine culture. The study demonstrated that preoperative urine culture and individualized antibiotic prophylaxis are associated with a significant decrease in SSI due to GNB in high-risk patients undergoing spinal surgery.

Measures aimed at preventing UTI in patients with neurogenic bladder such as closed catheter drainage in patients with an indwelling catheter and the use of clean intermittent catheterization could reduce the risk of perioperative spine infections [4]. Intravesical Botox, bacterial interference and sacral neuromodulation show significant promise for the prevention of UTIs in neurogenic bladder patients [5].

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1.3. PREVENTION: BONE GRAFT

Author: Dolors Rodriguez-Pardo

QUESTION 1: Does the use of allograft increase the risk of spinal infection?

RECOMMENDATION: The use of allograft seems to increase the risk for infection in pediatric and neuromuscular scoliosis, however there is no increased risk in the adult degenerative population.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 77%, Disagree 0%, Abstain: 23% (Super Majority, Strong Consensus)

RATIONALE

It has been postulated that infection risk from bone allograft may be caused by contamination or by the overwhelming of local host defenses [1,2]. Much of the data addressing this issue can be found in the pediatric literature. In a case-control study of 22 pediatric patients with infections after spine surgery, Croft et al. found that allograft use was strongly associated with surgical site infection (odds ratio (OR) = 10.7, $p < 0.0001$) [3]. Aleissa et al. showed similar results in 14 patients with SSI (risk rate (RR) 9.6, $p < 0.001$) [4]. Sponseller et al. were able to demonstrate a statistically significant increase in infection risk with the use of allograft versus autograft ($p = 0.010$) [5].

Several systematic reviews have also addressed this subject. Fei et al. performed a meta-analysis of risk factors for surgical site infection after spine surgery in 12 high-quality studies [6]. They found a relative risk for infection of 2.72% with the use of bone allograft, though there was a broad confidence interval and they failed to reach statistical significance at $p = 0.244$. Meng et al. [2] performed a systematic review of 13 studies of infection risk in pediatric spine surgery. The use of allograft carried an odds ratio of 8.498 with a high statistical significance at $p < 0.001$, though the authors cautioned about possible bias due to study heterogeneity. Glotzbecker et al. found grade C evidence of an association between allograft use and surgical site infection [7].

On the other hand, multiple studies have demonstrated that even in the pediatric literature, there is conflicting evidence. Knapp et al. studied patients with Adolescent Idiopathic Scoliosis (AIS) and found that allograft did not increase the risk for infection [8]. In a case-control study of pediatric patients undergoing spinal fusion, Shen et al. also found that there was no increased risk with allograft [9]. In the adult population, several large studies have failed to find an association between allograft use and infection. Mark et al. looked at over 1,400 patients who underwent spinal fusion, and there was no difference in infection rate when using allograft or autograft [10]. Similarly, Saeedinia et al. looked at almost 1,000 patients undergoing spinal surgery and failed to find an association between allograft and infection [11].

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Authors: Steven Schmitt, Christopher Kepler, Wesley Bronson

QUESTION 2: Can allograft, synthetic bone substitute or autograft be used during revision spinal surgery in patients with prior spine infection?

RECOMMENDATION: Based on available data, it appears that allograft, autograft and synthetic cages may be used successfully along with posterior screw fixation and prolonged antibiotic therapy in the treatment of pyogenic spondylodiscitis. This data can probably be extrapolated to also confirm that allograft and autograft safe during revision spinal surgery with prior infection.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

There are several small studies suggesting that bone allograft and autograft may be used successfully with posterior screw fixation and antibiotics to treat spine infections. Dobran et al. reviewed 18 patients who underwent posterior screw fixation along with allograft and autograft for pyogenic spondylodiscitis [1]. All patients had successful fusion and normalization of C-reactive protein at a mean follow-up of 30 months. Likewise, Chung et al. reported a study of 20 patients who underwent anterior fibular allograft and posterior screw fixation for spondylodiscitis [2]. All patients had significant improvement in pain and satisfaction scores, with at least 36 months of follow-up. Only two patients had superficial wound complications. In a third study, An et al. reviewed 15 patients who underwent mixed allograft and autograft with posterior screw fusion [3]. All but one showed significant improvement in neurological deficit, functional outcome and pain, with a mean follow-up of 27 months.

Synthetic materials have also been used in the successful treatment of pyogenic spondylodiscitis. Shiban et al. reported 52 patients treated with polyetheretherketone (PEEK) cages in combination with posterior pedicle screw fixation [4]. Patients received two weeks of intravenous and three months of oral antibiotic therapy. Infection was cured in all and 16 of the 28 with some neurologic deficit improved at 12 months of follow-up. Similar results were reported with PEEK cages and posterior fixation by Schomacher et al. (51 patients, 20 months of follow-up) and Brase et al. (nine patients, mean follow-up 13 months) [5,6]. One study compared three different types of cages (titanium mesh, titanium and PEEK) versus autologous iliac bone strut [7]. All received posterior screw fixation. There were no significant differences in clinical or radiographic outcomes, and infections were judged cured in all at a mean of 36 months for follow-up. Multiple other studies report similar findings [8–10].

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1.4. PREVENTION: RISK FACTORS

Authors: Koji Yamada, Yoshihirio Uchida

QUESTION 1: Does prior or active tuberculosis (TB) preclude patients from undergoing spine surgery?

RECOMMENDATION: Prior or active TB does not preclude patients from undergoing spine surgery.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

The mainstay of treating spinal TB is chemotherapy [1]. Almost all antituberculous drugs penetrate well into tuberculous lesions [2], more than the desired minimum inhibitory concentrations (MIC) [3,4]. Abscesses usually resolve with medical therapy, as antituberculosis drugs penetrate very well [5,6].

There is controversy in the literature about the necessity of using surgical intervention in addition to spinal TB treatments. A Cochrane Database Review assessing the role of routine surgery in addition to chemotherapy in spinal TB including the studies from Medical Research Council (MRC) of the United Kingdom failed to reveal any statistically significant differences in various outcomes for additional surgery including: kyphosis angle, neurological deficit (none went on to develop this), bony fusion, absence of spinal TB, death from any cause, activity level regained, change of allocated treatment or bone loss [1]. Myelopathy with or without functional impairment most often responds to chemotherapy [7]. In two MRC studies conducted in Korea, more than 80% of patients had complete resolution of myelopathy or complete functional recovery when treated medically [8,9].

Though the review of the above trials was insufficient to say routine surgery early on was beneficial, several limitations exist [1]. First, two sets of trials reviewed in the literature were performed during the 1960s and 1970s, while in recent years new medications and better operative techniques have been developed. Second, the patients included in the MRC study were limited to two-vertebra disease with or without mild neural deficit [10,11]. The results for patients with moderate to severe motor weakness were not addressed. Moreover, the patients seen in developing countries often have a large number of vertebrae involved, accompanied with a greater chance of kyphosis progression [12] and late onset paraplegia [13,14]. Third, late onset paraplegia usually become present more than 15 years after initial spinal infection [15–17]. In MRC studies, increased progression of kyphosis was seen in the conservatively-treated group with a lower fusion rate during their follow-up period [18]. Considering the difficulties in treating severe late symptomatic post TB kyphosis, the follow-up period in these studies could be insufficient to detect the magnitude of late complications. Fourth, it is generally known that some patients do not respond well to conservative treatment and are considered nonresponders [19]. For these patients, surgery should be considered to procure adequate tissue to ascertain the diagnosis as well as to reduce the disease load.

Potential benefits of surgery include less kyphosis, immediate relief of compressed neural tissue, quicker relief of pain, a higher percentage of bony fusion, quicker bony fusion, less chance of relapse, earlier return to previous activities and less bone loss [1,2]. Early surgical intervention for prevention of deformity is relatively simple and may prevent late neurological problems due to kyphosis of the spine [15,20,21]. From a review of 124 articles, 17.1% of the procedures were performed with defined indications including: etiology, neurological deficit (severe or progressive), spinal instability with or without kyphosis (severe or progressive), multisegmental disease and paraplegia of greater than three months [19]. Surgical intervention for those without neurological recovery/improvement after chemotherapy for moderate motor weakness and surgical decompression of the cord under the cover of multi-drug chemotherapy for severe motor weakness irrespective to the duration of illness or cause, are also recommended [22].

Medical treatment is generally effective for those with or without mild neural deficit. Surgical intervention may be indicated in advanced cases with marked bony involvement, abscess formation or paraplegia, regardless of prior or active tuberculosis.

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Author: Carles Pigrau

QUESTION 2: Should routine methicillin-resistant *Staphylococcus aureus* (MRSA) screening be in place prior to spine surgery?

RECOMMENDATION: Routine MRSA screening should not be performed prior to spine surgery. However, in hospitals with a high incidence of *S. aureus* spinal surgical site infection (SSI) and particularly high rates of MRSA infections, MRSA screening might be useful.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 7%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

According to a recent review of 161 studies, the pooled average of SSI in spine surgery was 1.9% (range: 0.1 to 22.6%) [1]. Instrumented spinal fusion had the highest rate (3.8%), followed by spinal decompression (1.8%) and spinal fusion (1.6%). *S. aureus* contributed to almost 50% of spinal SSIs with a range of 0.02 to 10%. Among *S. aureus* spinal SSIs, the pooled rate of MRSA infections was 38% [1]. The 30-day mortality rate among patients with SSI was 1.06%, double that of those without SSI (0.5%), with mortality increasing with the complexity of spinal surgery or with the presence of underlying diseases [2]. Moreover, SSIs increased re-admission rates (from 20–100%), reoperation rates (with a pooled average of 67%) and doubled health-care costs [1].

Preoperative nasal carriage of *S. aureus* has been shown to be a risk factor for SSI, but rates have been variable between studies [3,4]. Nasal decolonization with the use of topical mupirocin is utilized in 90% of cases, however, the impact of using this strategy on the reduction of SSIs in orthopaedic surgery have reported conflicting results [5,6]. A recent meta-analysis of all published studies in cardiac and orthopaedic surgery suggested that decolonization was associated with a significant decrease in *S. aureus* SSIs when either the intervention was applied to all patients or only to those who were nasal carriers [7]. Another meta-analysis showed that an absolute reduction in SSIs of 1% may be cost-effective, however, universal decolonization may increase the risk of mupirocin resistance [8].

In a not-yet published retrospective study of 1,749 patients scheduled for elective instrumented neurosurgery, the MRSA colonization rate was 0.74%. After decontamination, all MRSA carriage was eliminated and none of the 13 MRSA carriers developed an SSI, while only 1 MRSA-negative case developed a MRSA SSI.

In a recent retrospective study of 4,973 consecutive spine patients who were given cefazolin as prophylactic antibiotic therapy rather than topical nasal antibiotics for decolonization, 49 (1.1%) were MRSA carriers, and 94 (2.1%) developed an SSI, 11 of which were caused by MRSA [9]. The SSI rates were similar in nasal carriers compared to non-MRSA carriers (3 of 49 vs. 91 or 4,433, $p = 0.13$) and nasal carriage was not a risk factor for spinal SSIs.

In conclusion, in patients undergoing spinal surgery, the low level of MRSA carriage and MRSA SSI are arguments against routine MRSA screening. In hospitals with a high incidence of *S. aureus* spinal SSI and high rates of MRSA infections, MRSA screening could be useful.

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QUESTION 3: Is there a role for routine decolonization of patients undergoing spine surgery? If so, what is the optimal agent(s)?

RECOMMENDATION: **There is evidence to support the use of institutionalized screening and decolonization programs in methicillin-resistant *Staphylococcus aureus* (MRSA) carriers to reduce the rate of surgical site infection (SSI), however the optimum agents for decolonization have not been determined.**

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 91%, Disagree: 0%, Abstain: 9% (Super Majority, Strong Consensus)

RATIONALE

There is evidence to support the use of institutionalized screening and decolonization programs to reduce the rate of SSI, however the optimum agents for decolonization have not been determined [1]. Preoperative nasal MRSA colonization is associated with increased risk postoperative spinal SSI. Thakkar et al. reported screening positive MRSA SSI rates of 12% compared with screening positive for MSSA (5.73%) and screening negative (1.82%) [2]. Furthermore, Ramos et al. found increased rates of SSI in hip and knee arthroplasty and spine fusions, reporting a 4.35% SSI rate in colonized (nasal MRSA and MSSA) patients versus a 2.39% rate in noncolonized patients [3].

While widely utilized preoperatively, there is minimal evidence specifically supporting the use of chlorhexidine gluconate (CHG) showers preoperatively. The 2015 Cochrane review written by Webster et al. reported minimal evidence supporting isolated use of CHG showers preoperatively. Four reviewed trials comparing CHG to placebo found no effect, and only one trial comparing CHG showers to controls reported an improvement in SSI rate [4].

The majority of reviewed literature bundles the use of nasal decolonization with other interventions (CHG wipes, CHG showers, etc.). Multiple reviews on the effectiveness of bundled interventions for decolonization in surgical patients (including orthopaedic surgery) report reduced SSI rates with nasal decolonization and CHG wipes [5,6]. Reported studies on nasal decolonization protocols have largely shown benefit in reducing SSIs. Mullen et al. used CHG wipes and alcohol-based nasal decolonization preoperatively and reported a mean reduction rate in SSI of 81% (1.76 per 100 to 0.33 per 100) [7].

Chen et al. reviewed 19 studies of decolonization protocols on orthopaedic procedures and found significant efficacy in reducing SSIs, reporting reduction of *S. aureus* SSIs ranging from 40–200% and reduction of MRSA SSI from 29–149% [8]. Bode et al. performed a randomized, double blinded trial to determine if decolonization would reduce the SSI rate. Of 6,771 general, orthopaedic and neurologic surgery patients, 18.5% tested positive for *Staphylococcus* and were decolonized with 5 days of CHG showers and mupirocin nasal ointment. SSI rates significantly reduced from 7.7 to 3.4% using eradication compared with the placebo control [9]. These interventions are likely cost-effective as well, as Slover determined that the cost-efficacy threshold for their institution's screening and decolonization protocol would be met with a spine SSI reduction of only 10% [10].

It is our recommendation that patients who screen positive for nasal MSSA and MRSA should be decolonized using 2% mupirocin ointment applied intranasally and 2% chlorhexidine gluconate (CHG) showers for five days preoperatively. Additionally, in patients positive for MRSA, intravenous vancomycin 15 mg/kg should be administered preoperatively prior to skin incision and for 24 hours postoperatively.

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QUESTION 4: How should patients currently using disease-modifying antirheumatic drugs (DMARDs) be managed in the perioperative period?

RECOMMENDATION: Spine surgeons caring for patients with rheumatic diseases must be aware that there are specific issues involved in their perioperative management. The optimal strategy for managing DMARD medications during the perioperative period of spine surgery is unknown due to the lack of evidence and it is largely based on low-quality evidence and expert opinion. A rheumatologist should be involved in the medication management around the time of surgery.

1. For nonbiologic DMARDs such as methotrexate (MTX), leflunomide, hydroxychloroquine and/or sulfasalazine, continuation of the current dose throughout the perioperative period is recommended.
2. For biologic DMARDs such as etanercept, we recommend that physicians withhold the biologic medication and plan elective surgery at the end of the dosing cycle for that specific medication. As an example, patients taking a weekly dose should schedule the surgery in the second week after the first withheld dose. These agents should not be restarted until external wound healing is complete, which is typically around two weeks. Exception: In patients taking tofacitinib (twice daily dose), withholding of tofacitinib for at least one week prior to surgery is recommended.
3. For medications typically used for systemic lupus erthematosus (SLE) patients, such as mycophenolate mofetil, azathioprine, cyclosporine and tacrolimus, the decision to withhold medications prior to surgery should be made on an individual basis.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Nonbiologic DMARDs

Although a reasonable concern exists about the potential of nonbiologic DMARDs to increase the risk of infection by affecting the immune response [1,2], stopping DMARDs prior to surgery may result in a flare-up of disease activity, which may adversely affect rehabilitation. Therefore, we suggest that patients continue the current dose of nonbiologic DMARDS throughout the perioperative period, including methotrexate (MTX), leflunomide, hydroxychloroquine and/or sulfasalazine. In clinical practice, the nonbiologic DMARD dose is often missed for one day and up to three days while the patient is hospitalized. Several studies of rheumatoid arthritis (RA) patients undergoing elective orthopaedic surgery have found that continued use of MTX through the perioperative period is safe [3,4]. A systematic review including four studies with RA patients undergoing elective orthopaedic surgery evaluated the effects of continuing MTX versus stopping MTX in the perioperative period [5]. Continued MTX therapy was safe perioperatively and was associated with a reduced risk of flares. There was no evidence to suggest that stopping MTX preoperatively reduced the incidence of infection or improved wound healing. However, in all of the studies, the mean dose of MTX was less than 15 mg per week.

The limited data on the use of leflunomide during the perioperative period is conflicting [6,7]. In one study, there were significantly more wound complications in patients taking leflunomide at the time of elective orthopaedic surgery compared with patients on MTX [7].

There are also limited data suggesting it is safe to continue hydroxychloroquine and sulfasalazine in the perioperative period. In a retrospective study of 367 orthopaedic surgeries among 204 RA patients, two-thirds of whom were receiving nonbiologic DMARDs including hydroxychloroquine and sulfasalazine, there was no increased infection associated with nonbiologic DMARD use [8].

Biologic DMARDs

We recommend that surgeons withhold biologic medication and plan the elective surgery at the end of the dosing cycle for that specific medication. As an example, patients taking weekly etanercept should aim to schedule the surgery in the second week after the first withheld dose. Patients taking adalimumab in two-week intervals should plan the surgery in the third week after the first withheld dose. In a similar manner, patients on monthly intravenous abatacept should schedule the surgery in the fifth week after the first withheld dose. Patients taking rituximab should wait until month seven after the last dose to schedule the surgery, presumably when B cells have returned to the circulation. However, nonelective procedures should not be delayed in patients who have been recently treated.

There is relatively little evidence available regarding the optimal timing for use of biologic DMARDs in the perioperative period, and our recommendation is largely based on indirect evidence suggesting an increased risk of infection associated with their use [9–11]. Many [12–16], but not all [17,18] retrospective studies suggest that use of tumor necrosis factor (TNF) inhibitors do not increase the risk of postoperative infections or impair wound healing.

The infectious risks of abatacept are similar to those of TNF inhibitors and other biologic agents, but there are no trials that have examined abatacept's safety perioperatively [9,19]. A case series described eight uncomplicated surgeries in seven RA patients on abatacept [20]. Similarly, there is no direct evidence regarding the safety of the interleukin (IL)-1 receptor inhibitor anakinra in the perioperative period. Conclusions regarding perioperative safety are largely based on trials in nonoperative patients showing that the infection rate was similar to that in patients receiving placebo [21].

These agents should not be restarted until external wound healing is complete, which is typically around two weeks. There is no evidence regarding the optimal time to restart biologic DMARDs in the perioperative setting and this approach is based on standard precautions used for biologic agents that warn against use in patients with active infection, such as an open wound.

Antirheumatic Kinase Inhibitor

In patients taking tofacitinib, we (Fang et al.) withhold the medication for at least one week prior to surgery. Tofacitinib is an orally-administered Janus kinase (JAK) inhibitor that is used in the management of patients with moderately to severely active RA. Our recommendation is based on indirect evidence from systematic reviews and meta-analyses of tofacitinib in nonsurgical patients showing there is an increased risk of infection with tofacitinib compared with placebo. Although the half-life is thought to be short for tofacitinib, there is uncertainty regarding the duration of immunosuppression after the drug is held [22].

Other SLE-specific Medications

There is uncertainty regarding the optimal perioperative medication management in patients with SLE given the lack of data. More data are needed to help guide perioperative medication management in lupus patients, including information on hydroxychloroquine, MTX, mycophenolate mofetil, azathioprine, cyclosporine and tacrolimus. Given the clinical spectrum of SLE disease severity and organ involvement, the decision to withhold medications prior to surgery should be made on an individual basis. Thus, for patients with severe SLE and multi-organ involvement in which discontinuation of the medication may result in a disease flare, it is reasonable to continue the medications through the surgical period. This is based on indirect evidence from organ transplant patients that supports continuing anti-rejection therapy during the time of surgery [23,24].

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QUESTION 5: Is postoperative hyperglycemia a risk factor for the development of infection following spinal surgery?

RECOMMENDATION: From the limited evidence, the association between postoperative hyperglycemia and surgical site infection (SSI) remains unclear and further study is needed.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

Postoperative hyperglycemia does not only occur in patients diagnosed with diabetes mellitus (DM). Only 41% of patients with serum glucose levels greater than 200 mg/dL were identified in the medical records with the diagnosis of diabetes [1]. Langlois et al. suggested that non-diabetic patients experienced a statistical increase in blood glucose levels in the first three days following spine surgery [2]. They also pointed out the possibility of blood glucose elevation in non-diabetic patients associated with postsurgical complications. After major surgery, perioperative blood glucose elevations may be associated with previously undiagnosed DM, or occur because of the activation of the hypothalamic-pituitary axis, a physical response to severe stress in individuals at risk [3].

DM is a disease of uncontrolled hyperglycemia, which impairs the immune system. The wound healing in patients with diabetes is impaired as a result of microangiopathic changes and ischemia, impaired granulocyte function and a lack of platelet-derived growth factor function in the wound [4]. Despite the lack of multiple randomized clinical trials, various retrospective studies have found that DM is strongly associated with SSI after spinal surgery [5–16]. Moreover, DM increases the risk of not only SSI but other postoperative complications such as urinary tract infection, unplanned readmission and prolonged length of stay [17–19].

From a retrospective case-control study of patients who underwent an orthopaedic spinal operation performed at a university-affiliated tertiary care hospital, the risk of SSI, the odds ratio for postoperative hyperglycemia (> 200 mg/dL), was 2.9 (95% confidence interval (CI): 1.2, 6.5) after univariate analyses. But, the risk did not remain significant after multivariate logistic regression analysis [11]. A retrospective case-control study evaluating 104 patients with SSI after spinal surgery matched with 104 randomly-selected control patients without SSI after spinal surgery, revealed that patients with postoperative glucose measurements greater than 126 mg/dL within 48 hours after surgery were significantly more likely to develop an SSI than patients without an elevated glucose measurement on univariate analysis (crude odds ratio: 3.2, 95% CI: 1.6, 6.3). But, it was not significant after adjusting for other variables [20]. A retrospective case-control study evaluating specific independent risk factors for SSI after laminectomy or spinal fusion at a tertiary care hospital affiliated with a university hospital, identified that high serum glucose (> 200 mg/dL) at any time during hospitalization was significantly associated with SSI in the univariate analysis (odds ratio: 3.0, 95% CI: 1.4, 6.3) [1].

On the other hand, a retrospective study evaluating perioperative variables to determine the risk factors for SSI in a total of 2,715 patients undergoing posterior lumbar spinal surgery revealed that high preoperative serum glucose (odds ratio: 1.169, 95% CI: 1.016, 1.345) and a history of DM (odds ratio: 2.227, 95% CI: 1.100, 4.506) were associated with SSI in multivariate logistic regression analysis, although postoperative serum glucose level showed no association [21]. In another retrospective study using the Nationwide Inpatient Sample (NIS) database, uncontrolled DM revealed a higher risk of postoperative infection (odds ratio: 4.90, 95% CI = 2.84, 8.46) than controlled DM (odds ratio: 1.91, 95% CI: 1.54, 2.37) [7]. But, there was no ICD-9-CM coding standard or parameter in the clinical setting that provides standardization of "uncontrolled" or "controlled" diabetic patients. Furthermore, the NIS does not provide quantitative data on blood glucose levels or hemoglobin A1c (HbA1c) percentage, making it impossible to further stratify cohorts based on overall control of a patient's diabetic condition.

Limited evidence supports the association between perioperative HbA1c and SSI [22,23]. The cut-off values for HbA1c differ among studies and the results were originated from small retrospective studies without multivariate analyses. Larger prospective studies are needed to confirm the association.

Though DM is strongly related to SSI in spinal surgery, no observational studies were able to reveal a significant association between postoperative hyperglycemia and SSI in multivariate analyses. From the limited evidence, the association between postoperative hyperglycemia and SSI remains unclear, and further study is needed on this issue.

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Authors: Steven Schmitt, Christopher Kepler

QUESTION 6: Is there an association between urinary tract infection (UTI) and surgical site infection (SSI) following spinal surgery?

RECOMMENDATION: Evidence regarding an association between UTI and SSI following spine surgery is conflicting and no convincing relationship has been proven. In a like fashion, no convincing relationship has been established between asymptomatic bacteriuria and SSI following spine surgery.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 71%, Disagree: 21%, Abstain: 8% (Super Majority, Strong Consensus)

RATIONALE

The treatment of organisms isolated from urine culture in the setting of orthopaedic surgery with hardware implantation is controversial and has been often driven by anecdote. The risk of seeding of hip and knee arthroplasties from asymptomatic bacteriuria has been studied and found to be small, with no cases in two studies [1,2]. A systematic review of the topic concluded that there was no evidence to support a direct causal relationship between perioperative asymptomatic bacteriuria and arthroplasty infection [3].

Data from the American College of Surgeons National Surgical Quality Improvement Program suggests that UTIs occur in nearly 1 of 50 patients undergoing posterior lumbar fusion procedures [4]. However, there are few studies that directly address a relationship between UTI and SSI in instrumented spine surgery. Nunez-Pereira et al. studied 466 patients, of whom 89 had UTIs and 54 had SSIs, with 22 patients having both [5]. Of these 22, the same organism was isolated from the surgical site and urine in nine patients. UTI conferred an odds ratio (OR) of 3.1 for SSI, though the statistical analysis recognized all UTIs and not just infections with the same organism. Tominaga et al. studied a cohort of 825 patients with 14 patients who developed SSIs and 20 patients who developed UTIs, and found no association between SSI and UTI [6].

It seems germane as well to address the relationship of asymptomatic bacteriuria and postoperative spine infection. Lee et al. studied 355 women > 65 years of age undergoing spine surgery [7]. Of these, 42 developed asymptomatic bacteriuria, with no association with SSI. A statistically significant association was found between asymptomatic bacteriuria with a Foley catheter in place and infection in patients who had undergone instrumentation of multiple levels. However, of 15 patients with postoperative infections, only 2 had the same organism (*Staphylococcus epidermidis* in both cases) isolated from cultures of surgical site and urine.

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Authors: Alexander Montgomery, Daniel Tarazona

QUESTION 7: What are the risk factors predisposing a patient to surgical site infections (SSI) after spine surgery?

RECOMMENDATION: Numerous risk factors for SSIs following spine surgery have been identified, including diabetes, obesity, prior SSI, smoking, longer operative times, posterior approach to spine and the number of levels fused.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

The relatively low incidence of postoperative SSIs after spine surgery makes it challenging for studies to evaluate the risk factors for SSI in a prospective manner [1]. Based on our literature search, a number of retrospective studies and a single prospective study were identified. The findings of prior studies have also been summarized by multiple systematic reviews. Pull ter Gunne et al. performed a systematic review of 24 studies that identified risk factors for SSI after spine surgery [2]. All 24 studies were case-control and case series. There was a total of 73 potential factors evaluated, 34 of which were found to be significant in at least 1 study. There were 11 risk factors that were found to be significant in at least 2 studies. Among all risk factors, diabetes, obesity and prior SSI were the only three that were confirmed as risk factors by a multitude of studies.

Similarly, there was another systematic review which analyzed 36 observational studies for which 46 independent factors were studied [3]. Only six risk factors had been consistently proven to show an association with SSI after spine surgery, including diabetes, obesity, longer operative time, smoking, history of SSI and type of surgical procedure (i.e. tumor resection).

More recently, a prospective multicenter surveillance study was performed which enrolled 2,736 patients who underwent posterior thoracic and/or lumbar spine surgery [4]. Of these patients, 24 (0.9%) developed postoperative deep SSI. Preoperative steroid therapy, spinal trauma, male gender and prolonged operating time (> three hours) were found to be independent risk factors for SSI after spine surgery. Several previous retrospective studies have not identified preoperative steroid use and male gender as risk factors for SSI after spine surgery [2,5,6].

An ongoing prospective study funded by Pfizer evaluating the potential role of vaccination against *Staphylococcus* is likely to provide valuable information regarding the most important risk factors for SSI after spine surgery.

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Authors: Claus Simpfendorfer, Pouya Alijanipour, Caroline J. Granger

QUESTION 8: Should all patients with psoas abscesses be screened for both spine and hip infections?

RECOMMENDATION: Cross-sectional imaging with computed tomography (CT) and magnetic resonance imaging (MRI) will identify the source of secondary psoas abscesses in the majority of cases. If no other source is identified, consider cross-sectional imaging with CT or MRI for both the hip and spine in the setting of psoas abscess.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain 0% (Unanimous, Strongest Consensus)

RATIONALE

The iliopsoas is formed by two distinct and separate muscles - the psoas major and iliacus muscles. Each muscle is covered by its respective fascia and is typically associated with different disease entities [1]. The psoas major arises from the transverse processes of the lumbar vertebrae, exiting the pelvis beneath the inguinal ligament where it joins the iliacus (forming the iliopsoas tendon) and inserts on the lesser trochanter of the femur [2]. The iliacus muscle originates from the superior portion of the iliac fossa, superior lateral aspect of the sacrum and ventral sacroiliac and iliolumbar ligaments [2]. The medial portion of the iliacus muscle joins the psoas major tendon (forming the iliopsoas tendon) and inserts on the lesser trochanter. The lateral portion of the muscle inserts directly on the anterior and anteromedial aspect of the femur below the lesser trochanter [3].

The literature often does not delineate between the two muscles, referring to the combined muscles as the iliopsoas or simply the psoas muscle. Making a distinction between these muscles can help determine the source of infection. With regards to musculoskeletal infections, the majority of psoas muscle abscesses reflect extension from an adjacent spondylodiskitis or septic facet [4–7]. In contrast, iliacus muscle abscesses are secondary to extension of an underlying hip infection through the iliopsoas bursa or infectious sacroiliitis.

The iliopsoas bursa is the largest bursa in the body and communicates with the hip joint in 14% of the population [8]. Communication of the joint capsule with the iliopsoas bursa is likely increased following hip arthroplasty [9]. With the majority of the bursa located deep in the iliacus muscle, hip joint infections typically involve the iliacus muscle alone or less often both the iliacus and psoas muscle [1,10]. When the psoas muscle is involved, there should be visible communication with a distended iliopsoas bursa. This is in contrast to the psoas abscess associated with spondylodiscitis, which does not involve the bursa.

Both lumbar spine osteodiscitis and septic hip arthritis can be associated with psoas abscess [11]. The spine as primary source of infection for secondary psoas abscess should always be included in the differential diagnosis [12]. Studies have reported that 10–36% of secondary psoas abscess is caused by disc infection [13,14]. The anatomical proximity and communication of the psoas muscle to the hip joint capsule creates a potential transit for bacterial spread from spine to the hip joint or vice versa [15]. Screening patients with a psoas abscess for both hip and spine infection can prevent this harmful infectious spread. However, it should also be considered that the infection may simultaneously result in multiple infection sites from the same original hematogenous source of psoas abscess or spinal infection.

A non-coincidental association exists between psoas abscess and hip infection, both in the virgin hip joint and in a prosthetic hip joint. There have been multiple reports regarding the progression of the extension of psoas abscesses into the virgin or prosthetic hip joints [16–19]. In one study, the percentage of prosthetic hip infections with associated psoas abscesses has been reported to be as high as 12% [19]. Hematogenous prosthetic infection and a medical history of neoplasm have been reported as risk factors of psoas abscess in patients with an infected hip replacement [19]. Psoas abscesses may also cause relapse of prosthetic hip infection.

It is recommended that practitioners screen patients with psoas abscesses for hip infection and spinal infection due to their anatomical communication, relationship in etiology and co-prevalence. Clinicians should be aware of the potential communication between the lumbar spine and hip joint via the psoas muscle and iliopsoas bursa. Successful treatment outcomes of psoas abscess are not only related to its early diagnosis, but also to the prompt detection of its spread to adjacent organs with potentially devastating outcomes, including the neural elements of spine and a prosthetic hip joint.

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1.5. PREVENTION: WOUND CARE

Author: Carles Pigrau

QUESTION 1: Is negative pressure wound therapy (NPWT) safe on spinal wounds in patients with a cerebrospinal fluid (CSF) leak?

RECOMMENDATION: NPWT may be harmful in patients with a CSF leak, leading to severe neurological sequelae.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

Intracranial hypotension may develop after dural puncture or spinal surgery by accidental intraoperative opening of the dura. As a complication to this, several cases of accidental drainage after spinal surgery and application of negative pressure suction devices (NPSDs) have been reported [1–4]. Secondarily, intracranial hypotension may develop leading to tonsillar herniation, subdural hemorrhage, severe neurological sequel and even death.

Recently, Sporns et al. reviewed the literature published in reference to patients diagnosed with postsurgical or post-traumatic intracranial hypotension [1,4]. In 24 relevant reports that included 27 cases, in 15 cases a NPSD (including NPWT or pleural drainage after thoracic surgery or traumatism) was applied, ten had no negative pressure devices and two could not be determined for application of a suction drain. All patients with NPSD had severe neurological symptoms, while only mild symptoms were observed in cases without such devices. They concluded that the increasing use of NPSDs causes the reported condition and that acute intracranial hypotension should be considered as an explanation of postoperative neurological symptoms or coma after cranial or spinal surgery. A precise radiological examination (preferably with magnetic resonance imaging) can help to rule out intracranial hypotension and dural laceration.

In conclusion, in patients with spinal wounds, NPSDs (including pleural drainages) may be harmful and lead to more severe neurological sequel than those cases with liquoral hypotension secondary to dural laceration without negative pressure devices.

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Author: Barrett Boody

QUESTION 2: What are the risks and benefits for the use of vacuum-assisted closure (VAC) devices/PICO dressings following spine surgery?

RECOMMENDATION: The use of incisional VAC therapy (such as PICO dressings) is limited, but available literature supports its use in the prevention of dehiscence and surgical site infection (SSI) in posterior thoracolumbar deformity surgery.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 14%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

Multiple case series and case reports have been published supporting the use of VAC therapy for staged treatment of deep/subfascial SSI in spine surgery, with the common use being at index or second debridement, followed by multiple VAC changes until the wound is suitable for closure [1–4]. The specific VAC techniques (such as fascia open or closed, number of suction devices, suction settings, etc.) is poorly described in available studies. Ploumis reported on 73 patients undergoing VAC therapy for deep SSI, noting an average of 1.4 procedures following VAC placement (including closure) and closure of wound at an average of 7 days. They noted that methicillin-resistant *Staphylococcus aureus* (MRSA) and polymicrobial wound infections were more likely to require subsequent debridement after index VAC placement prior to definitive closure [2]. Similarly, Mehbod described 20 similar patients with deep SSI following spine surgery treated with VAC therapy, with an average of 2.2 procedures (including closure) following index VAC placement and resolution of infection in all patients and closed wounds by 6 months [3]. Canavese described 33 pediatric patients treated with VAC therapy for deep SSI after thoracolumbar spine surgery, with only 1 case ultimately requiring partial removal of implants [5].

Complications for VAC therapy have also been widely described, including need for reoperation and/or revision of hardware, bleeding, flap closure or skin grafting, retention of foam sponge fragments and cerebrospinal fluid (CSF) leaks resulting in neurologic complications (coma, brain herniation and intracranial hemorrhage) [1,2, 6–8]. The use of VAC therapy in the setting of CSF leak should be avoided due to risks of tonsillar herniation [7]. While VAC therapy over dura has been described in cranial surgery, no publication specifically described the application of sponges over dura in spine surgery. Multiple cranial publications describe the technique for dural application as the use of the "white" sponge (polyvinyl foam), as it is hydrophilic and less adherent, with lower suction pressures (~ 50 mmHg) [9,10].

The only available paper on the application of incision VAC therapy (such as PICO dressings) for spine surgery was published by Adogwa et al., who reviewed 160 posterior thoracolumbar deformity surgeries, of which 46 used incisional negative pressure wound therapy for 3 days. The authors reported lower rates of wound dehiscence (6.38% vs. 12.28%) and lower SSI rates (10.63% vs. 14.91%) for the incisional negative pressure wound therapy group, both reaching statistical significance ($p < 0.05$) [11].

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Author: Jeffrey A. Rihn

QUESTION 3: What type of surgical dressing is most effective for lowering rates of surgical site infection (SSI) in patients undergoing spine surgery?

RECOMMENDATION: There are no randomized studies comparing the use of incisional negative pressure wound therapy (NPWT) to standard dry dressings in spine surgery. The World Health Organization (WHO) recommends the use of incisional NPWT for high risk surgical wounds to reduce the risk of SSI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 0%, Abstain: 14% (Super Majority, Strong Consensus)

RATIONALE

Incisional NPWT in the form of commercially available incisional suction dressings has recently gained popularity in the management of high-risk wounds in orthopaedic surgery.

These dressings are used at the time of index surgery primarily, with the aim of preventing wound complications such as SSI. Incisional NPWT protects the healing wound by preventing wound edge motion, improving of blood supply, removing of excess fluid and stimulating granulation tissue. A recent meta-analysis of all randomized and case-controlled trials comparing incisional NPWT to standard of care showed a reduction in SSI (50%), wound dehiscence and hospital length of stay [1]. In a pig spine model, Glaser showed improved early biomechanical properties as well as cosmesis in wounds dressed with incisional NPWT compared to standard dry dressings [2].

There are only two studies that have investigated incisional NPWT after spine surgery. A single-institution retrospective case-control study from Duke University showed a 50% decrease in wound dehiscence and a 30% decrease in SSI after a change to incisional NPWT dressing for thoracolumbar deformity wounds [3]. Similarly, a small randomized trial by Nordmeyer et al. showed a decrease in seroma and the need for nursing wound care intervention in patients who were treated with incisional NPWT [4]. The authors hypothesized that a decrease in seroma may lead to decreased SSI, but the study was underpowered to show this difference.

The 2016 WHO recommendations on intraoperative and postoperative measures for SSI prevention proposed prophylactic NPWT on primarily closed surgical incisions in high-risk wounds to reduce the incidence of SSI [5]. This recommendation drew on evidence from abdominal, thoracic and orthopaedic surgery.

In the absence of high-quality randomized trials and given the WHO recommendation, it would be reasonable to use incisional NPWT in settings where the surgeon believes the wound is at risk of infection or breakdown. Spine wounds at high risk of infection include those in patients with diabetes, increased BMI, extended operative times and chronic steroid use [6,7]. In the pediatric spine population, risk factors for SSI include high weight centile, neuromuscular scoliosis, greater comorbidities and prolonged operative time [8].

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Diagnosis

2.1. DIAGNOSIS: GENERAL PRINCIPLES

Authors: Robert Sawyer, Joseph K. Weistroffer, Anna White

QUESTION 1: What is the definition of surgical site infection (SSI) in spinal surgery?

RECOMMENDATION: **We recommend utilizing the definition provided by the Centers for Disease Control and Prevention (CDC), National Healthcare Safety Network (NHSN) Patient Safety Component Manual, Chapter 9: Surgical Site Infection (SSI) Event.**

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

The most persuasive argument for adopting the CDC's definition for an SSI lies in utilizing search protocols to map International Classification of Disease, 10th revision, Procedure Classification System (ICD-10-PCS) and Current Procedural Terminology (CPT) codes when querying databases.

The CDC definition is the accumulation of multiple years of planning/tracking and modifying this instrument via annual reviews and input from professionals worldwide. The description includes such categorical sub-elements as the definition of an operative procedure and the definition of an operating room. It includes criteria for the sub-classifications of a superficial incisional SSI, deep incisional SSI and organ/space SSI [1]. The CDC's definition delineates the exclusion of such events as cellulitis, stitch abscesses, as well as stab wound or pin site infections. It also defines such infections about primary or secondary wounds and the surveillance periods for SSI following operative procedures. Furthermore, numerous spine-related studies have utilized the same definition put forth by the CDC [2–5].

Adopting a thorough and uniform definition for SSI is imperative, as studies have shown that the rate of SSI following spine surgery varies based on the definition used [6]. In addition, having a standardized definition will improve surveillance, provide consistency among studies and improve overall patient care.

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Author: Claus Simpfendorfer

QUESTION 2: What defines delay in the diagnosis of a spine infection?

RECOMMENDATION: **There is no clear or established definition of delayed diagnosis for spine infection.**

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

The diagnosis of spinal infections is often delayed from one to three months from the onset of symptoms [1,2]. Delay in diagnosis is frequently secondary to nonspecific symptoms including back and neck pain. A couple of studies have used delayed diagnosis of greater than eight weeks as a predictor of lower recovery rates, neurologic deficits and long-term disability [2–4]. A recent study by Issa et al. demonstrated that the percent of positive cultures from blood and/or biopsy decreases as the delay in diagnosis increases [2–5].

Jean et al. looked at predictors of delayed diagnosis and found that X-rays resulted in an increased delay from 14 days to 34.7 days [6]. It is presumed that, although delaying diagnosis, X-ray findings (either normal or demonstrating degenerative changes) provide the physician with reassurance. Alternatively, Jean et al. found that fever at initial presentation, elevated C-reactive protein (CRP) and blood cultures shortened the time to diagnosis [6]. The most significant impact was the elevated CRP which shortened the diagnostic delay from 73 days to 17 days [6]. It is therefore suggested that CRP be routinely checked in cases of new onset or sudden increased back pain [6,7]. Furthermore, if CRP is elevated or if there is clinical suspicion for spine infection, MRI with gadolinium should be performed [8].

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Authors: John Koerner, David Kaye

QUESTION 3: Is there an optimal window for diagnosis of an early spine infection?

RECOMMENDATION: There is no defined window, but early diagnosis of a postoperative spine infection (up to three months from time of surgery) treated with surgical debridement and antibiotics often allows for retention of instrumentation.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

Although the evidence regarding this topic is from low-quality studies, the findings and recommendations are consistent. Most postoperative spinal infections in adults present early, typically within the first three months [1]. Early diagnosis and debridement typically allows for retention of implants when present [1]. Implant removal due to infection can result in satisfactory results and eradicate infection, but can lead to malalignment and pseudarthrosis [2].

Early spine infections (< three months after surgery) treated with irrigation and debridement have improved outcomes compared to before surgery, but cause increased back pain and a lower probability of achieving a minimal clinically important difference [3].

In a cohort study of 51 patients who developed a postoperative spinal implant infection, prompt treatment (< 3 months) with debridement allowed for implant preservation in 41 patients, versus 10 patients in which treatment was delayed and implants were removed [4]. Another case series identified 26 postoperative infections, of which 24 were able to be treated without removal of implants by aggressive debridement and secondary closure [5]. Early identification and treatment can often allow for implant retention compared to delayed presentation, when implants may need to be removed [6–8].

Late spine infections are, however, seen more commonly in idiopathic scoliosis cases [9]. In a case-controlled series of 236 patients, seven developed an infection [10]. One was early and the other six were diagnosed at an average of 34.2 months postoperatively.

It is typical for patients to have symptoms of low back pain for 4 to 10 weeks prior to diagnosis of spondylodiscitis [11,12]. Although most studies recommend early treatment, no specific timeframe could be identified that definitely leads to better outcomes.

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Author: Gregory Schroeder

QUESTION 4: How do early and late infectious complications differ following spine surgery?

RECOMMENDATION: Early infections, defined as occurring within 30 days of surgery, often present with local signs of infection such as increased surgical site pain, erythema, warmth and wound drainage. Conversely, late infections (> 90 days after surgery) commonly present with an insidious onset of chronic pain and implant failure/ pseudarthrosis if following a fusion.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 0%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

Postoperative spine infection occurs at a rate of 0.7–16% depending on the procedure; the lumbar spine is the site of 51% of infections [1].

A postoperative infection is classified as early when it occurs within 30 days of the initial surgery. Early infections typically present with increasing back pain (83–100%) as the primary symptom [2,3]. Fever, weight loss, erythema, swelling, warmth, tenderness and elevated white blood cell (WBC) count may also be present, with fever having an incidence of 16–65% [2–4]. One of the most reliable and specific signs of early infection is increased wound drainage (67%) as it can occur in both deep and superficial infections [4].

A postoperative infection occurring three to nine months following surgery can be classified as a late infection. As opposed to early infections, late infections typically present with delayed symptoms such as lack of adequate fusion, chronic pain or implant failure months after surgery [5]. Local symptoms may also occur, including increased pain and tenderness at the incision site. Wound drainage may occur but is less common than in early infections [5].

Complications of postoperative spine infection include impairment of function, significant morbidity and increased health care costs approximating up to $200,000 per patient [1,3]. Increase in hospital stay and increased rates of repeat surgery have also been observed.

Gram-positive bacteria, specifically *Staphylococcus aureus,* are responsible for approximately 45% of spine infections [6]. Other gram-positives such as *Staphylococcus epidermis* and *Enterococcus* as well as gram-negatives *Pseudomonas aeruginosa* and *Escheria coli* have been observed at lower incidences [1,2,6]. There is no clear association between type of surgical procedure and bacteria strain. However, gram-negatives tend to present more commonly in sacral and lumbar regions [6]. Fungal infections may occur in immunocompromised patients. *C. acnes* has recently been identified as another potential causative organism [2]. No significant difference has been observed in the type of organism present in early and late infections.

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Author: Bryan Alexander

QUESTION 5: Are there patients with degenerative pathology, such as disc herniations, who are actually infected with a low-grade infection (e.g., *Propionibacterium acnes*)?

RECOMMENDATION: The association between the *Cutibacterium acnes (C. acnes)* (formerly *P. acnes*) and degenerative spinal disease is inconclusive.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 14%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

The initial connection between potential low-level infection and degenerative spinal pathology was drawn when a group identified over half of discectomies performed for disc herniation as culture positive for *C. acnes* or coagulase-negative *Staphylococcus spp* [1]. A large number of predominantly small studies have since come to opposite conclusions on the connection between these bacteria and degenerative spinal disease, most commonly evaluated radiographically by the presence of Modic changes (examples of those finding no relationship [2–7] versus those finding a correlation [8–12]). One controversial placebo-controlled, double-blinded trial administered extended-duration antibiotic therapy to those patients with Modic type 1 changes and demonstrated better pain resolution in those receiving antibiotics [8].

Recent systematic reviews, each published in 2015, independently concluded that while there was strong evidence from multiple studies that patients undergoing spinal surgery have increased rates of bacteria at the site of degenerative disease of spine, causation between that finding and the pathologic changes resulting in back pain were unclear [1,13,14].

One important cause for heterogeneity in the data is the possibility that microbiologic sampling could be more readily contaminated with bacteria based on differences in surgical and collection technique [3,15]. However, this does not fully explain the fact that in clinical studies, *C. acnes* is consistently the most common, if not only, organism isolated. Recent studies, including control groups of patients not anticipated to have infectious etiologies for their spinal condition, have also noted increased rates of bacterial presence in degenerative disease compared to patients without degenerative disease [2,16]. Methods attempting to disrupt biofilm-encapsulated bacteria have attempted to explain negative culture results from earlier studies [10,17]. Similarly, molecular subtyping of *C. acnes* allows for better characterization of these isolates into those more likely to be routine skin contamination from those more likely to be pathogenic [2,17–19]. These studies have demonstrated a mixture of these subtypes present, with those generally not representing skin flora predominating. Recent studies have additionally investigated histologic methods [20], inflammatory cytokine responses [16,21] and proteomic analysis [22] in addition to bacterial presence as a marker for true infection. Finally, some groups have recently used animal models to attempt to support a connection between bacterial inoculation and symptomatic spinal pathology [23,24].

Though still unverified, there is an enlarging body of evidence using modern techniques and accounting for technical limitations in earlier studies for the role of infection in at least some types of degenerative spinal pathology. A well-designed, multicenter trial effort, which successfully confirms this connection would allow for reasonable consideration of further studies utilizing antibiotic therapy as a non-invasive therapy option for degenerative disc disease.

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Authors: Barrett Woods, Maja Babic

QUESTION 6: What is the diagnostic algorithm of patients with suspected hematogenous vertebral osteomyelitis? Is the algorithm different for patients with tuberculosis (TB)?

RECOMMENDATION: We support the diagnostic algorithm for suspected hematogenous vertebral osteomyelitis per Infectious Disease Society of America (IDSA) Clinical Practice Guidelines, 2015. Diagnostic algorithm is not different for patients with TB.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 6%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Vertebral osteomyelitis typically occurs due to hematogenous seeding of the adjacent avascular disc from a distant foci [1]. Appropriate management is contingent upon timely diagnosis. Patients with vertebral osteomyelitis are commonly misdiagnosed and treated for degenerative pathology [2]. This often leads to a delay in treatment on average from two to four months [3]. The diagnosis of vertebral osteomyelitis is not challenging in patients with acute onset low back pain and fever. In this circumstance the diagnosis can be confirmed with a serologic test and imaging studies. However, fever and leukocytosis occur in approximately 45% of patients with bacterial vertebral osteomyelitis and very rarely in those with fungal, brucellar or mycobacterial infections [4,5]. Vertebral osteomyelitis should be suspected in patients who have recalcitrant back pain in the setting of elevated inflammatory markers. In 2015, the IDSA published Clinical Guidelines for the diagnosis and treatment of native vertebral osteomyelitis (NVO) in adults [6,7]. These guidelines provide an algorithmic approach to the diagnosis of NVO based on a systematic review of the literature.

Obtaining a detailed history is a critical portion of the diagnostic algorithm and should include any recent travel, infections, open wounds, recent antibiotic treatment and intravenous drug use. Patients who have back pain and a history of bacteremia, particularly *Staphylococcus aureus,* should be suspected of having vertebral osteomyelitis; therefore, further work up is warranted in these scenarios [8–10]. Patients with vertebral osteomyelitis typically present with back pain exacerbated by physical activity. Pain may not be isolated to the affected area and can radiate to the abdomen, hip, leg, scrotum, groin or perineum [11]. A full physical examination should be performed and include assessment of motor and sensory function. It takes three to six weeks after the onset of symptoms for bone destruction to be evident on plain radiographs. Thus, normal images do not exclude diagnosis.

Magnetic resonance imaging (MRI) should be obtained in patients with suspected vertebral osteomyelitis, as it has a sensitivity of 97%, specificity of 93% and an accuracy of 94% in diagnosing vertebral osteomyelitis [12,13]. Gadolinium enhancement is critical to appreciate paravertebral or epidural involvement [14]. A repeat MRI should be considered in two to four weeks in a patient suspected of vertebral osteomyelitis whose initial imaging study failed to show features consist with the diagnosis [15]. Imaging features consistent with TB infections include destruction of two or more contiguous vertebrae, extension along the anterior longitudinal ligament and disc infection, with or without a paraspinal mass or mixed soft tissue fluid collection [16]. In patients for whom MRI is not possible, a spine gallium/Tc99 bone scan is an alternative with a sensitivity and specificity of around 90% for diagnosing vertebral osteomyelitis [17,18]. Positron emission tomographic scanning is also highly sensitive for detecting osteomyelitis [19].

Serologic testing is important in the diagnostic algorithm of vertebral osteomyelitis. A minimum of two blood cultures should be obtained for patients with suspected vertebral osteomyelitis [20]. Blood cultures should be incubated for up to two weeks and should include aerobic, anaerobic and fungal. Leukocytosis has low sensitivity and specificity in the diagnosis with approximately 40% of patients with osteomyelitis having a normal white blood cell (WBC) count [21]. However, an elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) in patients with back pain, though not specific, has a sensitivity that can range from 94% to 100% [22].

In patients with suspected vertebral osteomyelitis who reside in or have traveled to areas endemic for TB, a purified protein derivative (PPD) skin test can be performed; however, this test has a low sensitivity and specificity for diagnosis. An interferon-γ release assay has been shown to have a higher sensitivity than PPD, especially in immunocompromised patients with immune compromise [23]. Enzyme-linked immunospot assay has some diagnostic utility for TB and has been proven superior to PPD alone (sensitivity 82.8% vs. 58.6% and specificity, 81.3% vs. 59.4%, respectively) [24].

Empiric antibiotic therapy should not be initiated in aseptic patients without neurologic deficit until an image-guided biopsy can be obtained, especially if microbiologic diagnosis for a known associated organism has not been established by blood cultures or serologic tests [6]. Biopsy increases the likelihood of microbiologic diagnosis, improving the chance of successful medical management through targeted antibiotic therapy [25]. *S. aureus* bacteremia eliminates the need for biopsy, and antibiotics should not be delayed [8,22]. If biopsy is non-diagnostic, a repeat biopsy, image-guided or open biopsy, should be considered.

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Author: Taolin Fang

QUESTION 7: Should antibiotics be held prior to image-guided biopsy/aspiration for a suspected spine infection?

RECOMMENDATION: **We recommend that prior to image-guided biopsy/aspiration for a suspected spine infection, all antibiotics should be withheld until after appropriate culture samples are obtained. Antibiotic administration, without aspiration/biopsy may be justified in patients who are critically ill and cannot withstand intervention or in patients with deteriorating neurological conditions.**

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

The definitive diagnosis of spinal osteomyelitis can be made only with isolation of the organism from a positive blood culture or biopsy and culture of the tissues from the region of the infection. Spinal biopsies may be performed using computed tomography (CT) or fluoroscopy for guidance in localizing the site of the suspected infection. The identification of the infecting organism is useful in directing antibiotic therapy. In suspected infection of the spine, biopsy and culture of the tissues from the affected site has been reported to be successful in the identification of the infecting organism in 46–91% of cases [1–5].

In real practice, there are some instances where antibiotic treatment is empirically instituted before the patient has been biopsied. Such cases may include patients who have been on antibiotics for other infections such as pneumonia or patients with surgical implants and prior deep wound infections who are on chronic antibiotic therapy. Theoretically, retrieval of a pathogen from the disc space or vertebral body may be compromised by previous or ongoing antibiotic treatment. However, we were unable to identify any high-quality randomized clinical trial comparing the culture results of the image-guided biopsy between patients who received empirical antibiotic treatment versus those who did not have any antibiotic treatment prior to biopsy.

There has been a general consensus of opinion that antibiotics should be withheld prior to biopsy of the site of suspected infection in an effort to improve the yield of culture [6,7]. A study by Rankine et al. found that the yield of biopsy in isolating the infecting organism was lower at 25% in patients who had received antibiotics compared to 50% yield in patients who had not received antibiotics [8]. It is important to note that not all studies agree with the notion of withholding antibiotics prior to biopsy of the infected site. A recent study by Sehn et al. [9] reported that four of 14 patients with a high suspicion for infection, who were confirmed to have been treated with antibiotics within 3 days of their biopsy, had positive cultures. The yield of culture was not different from the cohort of 92 patients who had not received antibiotics (28.6% vs. 30.4%, $p = 0.86$). Both of the reports were retrospective non-randomized studies with a relatively small sample size.

In the absence of randomized prospective data, and using the logic drawn from other fields of orthopaedic study related to this issue, we recommend that empirical treatment with antibiotics be withheld in patients with suspected infection of the spine until biopsy of site of suspected infection can be carried out. There are, however, circumstances (such as situations involving critically ill patients and those with deteriorating neurological status) in whom antibiotics may be started prior to the performance of biopsy.

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Authors: Koji Yamada, Alexander Montgomery, Yoshihiro Uchida, Mangattil Rajesh

QUESTION 8: What is the incidence of infectious bacterial meningitis (PBM) following spinal surgery? Does the use of instrumentation affect this?

RECOMMENDATION: The incidence of PBM following spinal surgery varies from 0.1–0.4%. There is insufficient evidence to make any observations as to whether the use of instrumentation affects the incidence of PBM following spinal surgery.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

PBM is a potentially devastating complication following spinal surgery. It could occur after any primary elective spinal surgery with or without instrumentation, traumatic fracture-dislocation or surgical site infection after spinal instrumented surgery [1–3]. This also presents as a delayed complication after scoliosis surgery and through a dural tear with cerebrospinal fluid (CSF) leakage [4,5].

The early diagnostic differentiation from PBM and postoperative aseptic meningitis (PAM) is difficult and depends on CSF culture results [6–7]. The success in the treatment of patients with PBM depends on the stage of diagnosis, speed of diagnostic evaluation and appropriate anti-microbial and adjunctive therapy [8–9].

PBM is a potentially life-threatening infection with higher rates of mortality and significant disabling morbidity [9]. Pneumococcal meningitis is the most prevalent and is associated with a mortality of 30% [10]. PBM can also be caused by staphylococci [11], aerobic gram-negative bacilli (including *P. aeruginosa*) [12] and methicillin-resistant *Staphylococcus aureus* (MRSA) [13].

The incidence of PBM is rare after spinal surgery and is considered to be related to incidental durotomy [14]. Patients who have the triad of fever, neck stiffness and consciousness disturbance during postoperative period should be suspected and subjected to further evaluations [14]. In a large retrospective study, Lin et al. reviewed 20,178 lumbar spinal surgeries and reported a PBM rate of 0.10% [14]. Another retrospective study by Twyman et al. reported the incidence of PBM to be 0.18% after spinal operations with and without instrumentation [15]. The incidence could be as high as 0.4% after spinal surgery, when epidural abscess, subdural empyema, brain abscess, bone-flap infections and wound infections are combined [16].

In their sub-analysis, Lin et al. found that dural tears, pseudomeningocele and poor wound healing contributed to the majority of the complications [14]. The optimal management of PBM required reoperation to repair dural tears and administration of parenteral antibiotics [17]. The occurrence of pseudomeningocele is a sequela of dural tear, imperfect suture of the dura or fascia and inappropriate administration of antibiotics [14,18,19]. Zhang et al. reported surgical intervention to be an effective method of treating PBM where initial conservative measures failed. They proposed the idea that it is important to consider the possibility of PBM in any patient with CSF leakage after spinal surgery. They recommended early diagnostic imaging and CSF cultures to ensure prompt diagnosis and treatment [20].

Spinal instrumentation surgery usually involves longer operative time, greater blood loss and a higher incidence of subsequent SSI compared to decompression surgery alone. These features of spinal instrumentation surgery could influence the incidence of PBM. There is little literature examining the potential association of instrumentation with PBM with no supporting evidence linking the use of instrumentation to the incidence of infectious meningitis after spinal surgery [14,15,20]. Therefore, based on available evidence, it is not possible to link the use of instrumentation during spine surgery with PBM.

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Author: Taolin Fang

QUESTION 9: What are the early infectious complications after operations on the spine following the use of instrumentation?

RECOMMENDATION: Early infections are traditionally defined as those occurring within a month after surgery, typically becoming evident within two to three weeks of surgery. Recently, the definition has been broadened to include infection within 90 days of surgery.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 60%, Disagree: 20%, Abstain: 20% (Super Majority, Weak Consensus)

RATIONALE

Early infections are traditionally defined as those occurring within a month of surgery, typically becoming evident within two to three weeks of surgery. Recently the definition of early infection has been broadened to include infection within 90 days of surgery [1]. Surgical site infections (SSIs) and wound dehiscence are among the most common complications following spine surgery. It has been reported that the incidence of SSIs after adult spine surgery varies from 2–20% following instrumented procedures [2].

A study based on the American College of Surgeons' National Surgical Quality Improvement Program database reported that in a total of 99,152 spine surgery cases between 2012 and 2014, the overall wound complication rate was 2.2% with superficial SSI, 0.9% with deep SSI, 0.8% organ space SSI and 0.4% dehiscence: 0.3%. Of all the patients who experienced wound dehiscence, 46% had concomitant SSI. The average postoperative day of occurrence was 14 days with a standard deviation of 9 days (superficial SSI: 16 ± 8, deep SSI: 13 ± 10, organ/space SSI: 11 ± 10, dehiscence: 17 ± 8) [3].

Similar to other SSIs, early infections after spine surgery may present as pain, fever, erythema, swelling, warmth, tenderness and wound drainage. Local pain may herald the development of infection, particularly when it is escalating in nature. Wound drainage is common for both superficial or deep SSIs and may be present in up to 90% of patients [4].

Early postoperative spinal infections are most frequently due to relatively virulent pathogens such as *Staphylococcus aureus*, beta-hemolytic streptococci and aerobic gram-negative bacilli. *Staphylococcus aureus* is the most common bacteria responsible for early postoperative infection after spinal surgery [5–7]. The majority of the cases are due to methicillin-sensitive *Staphylococcus aureus* (MSSA), however the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) is escalating [8]. The majority of early infections are due to a single pathogen [9]. There has been an increase in the frequency of infections caused by gram-negative bacteria and other organisms such as *Pseudomonas aeruginosa*, *Escherichia coli*, Enterobacter and Acinetobacter [10–12].

Utilization of posterior instrumentation is well-recognized as a risk factor for the development of postoperative spinal wound infections. However, this finding is largely based on suboptimal retrospective analyses. Multiple factors increase the rates of infection following instrumented spinal surgery, such as increased wound exposure to air due to longer surgical time, greater soft tissue dissection, increased muscle/skin retraction, greater blood loss and potentially larger dead spaces [13–15].

However, anterior spinal exposures were reportedly correlated with a reduced risk of infection as they typically traverse relatively avascular tissue planes and avoid significant muscle dissection [16–19]. It is yet to be determined whether minimally invasive spine surgery is associated with lower infection rates versus open surgery following the use instrumentation [20–21], although a recent study involving 108,419 procedures reported that the use of a minimally invasive approach was associated with a lower rate of infection for lumbar discectomy (0.4% vs. 1.1%, $p < 0.001$) and for transforaminal lumbar interbody fusion (1.3% vs. 2.9%, $p = 0.005$) [22].

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2.2. DIAGNOSIS: BIOMARKERS

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QUESTION 1: Are there any diagnostic tools that are useful for early surgical site infection (SSI) detection following spinal surgery? Does this differ whether or not there was instrumentation?

RECOMMENDATION: C-reactive protein (CRP) can be used to diagnose early SSI following spinal surgery.

A failure of CRP to decline or a second rise on postoperative days four to seven is a sensitive marker for infection following spine surgery, including both instrumented and non-instrumented spine surgery.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 86%, Disagree: 7%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

In a prospective study of 73 consecutive patients undergoing spinal decompression with and without instrumentation, inflammatory markers were assessed. They showed that following uncomplicated spinal surgery, CRP levels rise sharply, peaking on the second postoperative day [1]. Peak CRP values after instrumented lumbar surgery are significantly higher than those after non-instrumented spine surgery, but decline with the same half-life [1]. CRP was superior to erythrocyte sedimentation rate (ESR) in early detection of infections after cervical spine surgery, as shown in a prospective study of 51 cases [2]. In another large, prospective trial including 400 elective discectomy cases, CRP was shown to be a reliable, simple and economical screening test for infectious complications after lumbar microdiscectomy, superior to classical laboratory parameters. The sensitivity of serial CRP testing was calculated to be 100% with 95.8% specificity. ESR and white blood cell measurements fail to reach distinctive significance in diagnosing early SSI [3].

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QUESTION 2: When do common blood biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) or Procalcitonin normalize after spine surgery?

RECOMMENDATION: Following spinal surgery with or without instrumentation, CRP values peak on days 2-3 postoperatively and normalize within 14 days. ESR also normalizes within 14 days.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 50%, Disagree: 29%, Abstain: 21% (NO Consensus)

RATIONALE

Multiple prospective studies suggest that CRP values peak within 2-3 days postoperatively (peak levels depend on extent of surgery, levels involved, etc.) and decrease back to baseline within 14 days. A rapid decline of CRP postoperatively is interrupted if postoperative infection sets in and a secondary rise occurs [1,2]. Prospective studies have shown that ESR peaks by day four following spinal surgery and in the majority of cases normalizes by two weeks postoperatively [3]. However, monitoring of CRP level was found to be superior to that of ESR for early detection of infections after cervical spine surgery in a series of 51 cases of anterior cervical fusion [4]. A second rise of CRP and ESR or failure to decline is an indicator of potential surgical site infection [5,6]. Limited data is available on the value of Procalcitonin [7].

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Author: Maja Babic

QUESTION 3: Is there a role for the use of serum biomarker for the diagnosis of spinal surgical site infection (SSI)?

RECOMMENDATION: Yes, C-reactive protein (CRP) is a predictable, reliable and economical screening tool for early infectious complications following spine surgery. Erythrocyte sedimentation rate and white blood cell count have nonspecific kinetics that are less helpful in identifying early SSI.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 67%, Disagree: 25%, Abstain: 8% (Super Majority, Weak Consensus)

RATIONALE

In a prospective study involving 348 patients who underwent decompression laminectomy, postoperative CRP was helpful in detecting early infectious complications following surgery. As a predictor for early wound infection, the sensitivity, specificity, positive predictive value and negative predictive value for abnormal CRP responses were calculated as 100%, 96.8%, 31.3% and 100%, respectively. Close observation of the surgical site is recommended in patients with abnormal CRP values at day five or seven postoperatively, namely for failure to decline or a secondary rise [1].

Of 149 patients undergoing elective spine surgery, 20 developed infectious SSI complications. Postoperative CRP kinetics were predictable and indicative of early infection where a secondary rise or lack of CRP decrease had a sensitivity, specificity, positive predictive value and negative predictive value of 82%, 48%, 41%, and 86% for infectious complications, respectively [2].

Out of 400 patients undergoing lumbar micro-discectomy over a 15-month period, 9 developed infectious complications related to surgery. CRP values were shown to be a reliable and economic screening tool in identifying the patients at risk with a sensitivity for serial CRP testing (day one and five postoperatively) calculated as 100% with a specificity of 95.8% [3].

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QUESTION 4: Is there a role for molecular techniques such as polymerase chain reaction (PCR) or next-generation sequencing (NGS) for the diagnosis of spinal surgery infection? If so, in which group of patients should this be done?

RECOMMENDATION: It is reasonable to selectively incorporate these diagnostic modalities as an adjunct to standard methodologies where there is a history or high pre-test probability for culture negative infection.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 71%, Disagree: 14%, Abstain: 15% (Super Majority, Strong Consensus)

RATIONALE

Successful management of periprosthetic joint infections (PJI) is significantly enhanced with a prompt and accurate microbiological diagnosis. Conventional culture methods for diagnosis of PJI can be compromised and complicated by early antibiotic treatment, heterogeneity of surgical sampling, fastidious microorganisms difficult to grow in culture and non-planktonic pathogens utilizing biofilms. Therefore, modern molecular microbiologic methods have naturally been seen as very promising for increasing diagnostic yield in these circumstances. Technologies that have more recently been applied to PJI generally include ribosomal RNA sequencing, species-specific and multiplex PCR and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).

Specifically, with respect to spinal and vertebral infections, these varied technologies have demonstrated success in leading to an etiologic diagnosis. These methods have been used to identify a variety of pathogens, including *Staphylococcus spp.* [1–3], *Streptococcus spp* [3,4], *Enterococcus spp.* [4], Enterobacteriaceae [3–5], *Brucella spp.* [6], *Mycobacterium spp.* [2], atypical bacteria (*T. whipplei*) [7], *Mycoplasma spp.*) [8], anaerobes (*Clostridium spp.*) [3], *Fusobacterium spp.*) [4,9] and fungi (*Aspergillus spp.*) [10].

By far, the most experience with these techniques for spinal infections is in the diagnosis of Pott's disease (*Mycobacterium tuberculosis*) [2,6,11–15]. These reports generally demonstrate a high sensitivity and specificity of PCR modalities, though many of these studies have been completed in tuberculosis endemic geographic areas with likely higher inoculum infections and a well-defined pre-test probability.

False positive results from dead or colonizing/contaminating bacteria is a concern with these tests, and studies evaluating the appropriate number of samples to optimize sensitivity and specificity specific to these molecular methods are limited and not specific to spinal infections [16]. Another important concern with molecular techniques for PJI diagnostics is that they do not commonly allow for susceptibility testing to appropriately target antimicrobial therapy. Certain resistance mechanisms, such as methicillin resistance in *S. aureus* [1,17,18] or rifampin resistance in *M. tuberculosis* [12], are reliably expressed if genetically detected. This is not the norm, however, as resistance expression is generally a complex phenotype determined by multiple factors. Care should be taken not to overly rely on non-susceptibility-generating techniques, as they can just as easily lead to long courses of overly-broad therapy, as can no etiologic diagnosis at all, undermining patient safety and important principles of antimicrobial stewardship. In addition, it has been noted that utilizing molecular methods as an adjunct to and in combination with standard culture methodologies often serves to improve overall diagnostic yield [3].

A few studies have attempted to establish test sensitivity and specificity data when compared to routine culture for bone and joint specimens in general [4,15,19–23], however these efforts are limited by lack of a true gold standard diagnostic method for comparison, the variety of testing methodologies clinically employed and non-standardized clinical criteria for utilization of these methods. Predictably, results vary widely, with sensitivities reported between 50–92% and specificities between 65–94% [20]. No studies investigating sensitivity and specificity of these techniques specific only to spinal post-surgical infections have yet been reported. Therefore, an evidence-based evaluation of the appropriate clinical criteria for utilization of these techniques in spinal surgery patients is not currently possible. One study proposed a strategy for routine collection and potential use of molecular diagnostics in PJI [24]. There is no data investigating the cost effectiveness for any diagnostic schema incorporating molecular methods, however given their positive proof-of-concept and the significant clinical impact of spinal post-surgical infections, it seems reasonable to selectively incorporate the use of molecular methods into situations where there is a high pre-test probability for indolent or culture-negative infection as further studies are done to standardize their use.

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QUESTION 5: For which investigations should samples obtained by image-guided biopsy be sent?

RECOMMENDATION: A priority should be placed on obtaining bacterial cultures and pathohistology. In the appropriate epidemiological setting, mycobacterial, fungal and brucellar cultures can be considered.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RESPONSE

There is limited data available in the literature to help establish clear evidence-based parameters for treatment. However, there are society-based clinical guidelines such as the 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults, which provide assistance in decision-making. Highlights from this statement recommend the acquisition of image-guided aspiration biopsy in patients with suspected vertebral osteomyelitis when a microbiologic diagnosis for a known associated organism has not been established by blood cultures or serologic tests. Further, they recommend for the addition of fungal, mycobacterial or brucellar cultures on image-guided biopsy and aspiration specimens in patients with suspected vertebral osteomyelitis if epidemiologic, host risk factors or characteristic radiologic clues are present, or if testing to appropriately stored bacterial specimens reveal no growth [1].

There is some data to suggest that standard samples should be sent for both microbiology and pathohistology. Pathologic evaluation is meaningful, particularly in culture negative cases where the presence of leukocytes can indicate pyogenic osteomyelitis, or visualization of granulomas can suggest mycobacterial infection or brucellosis [2]. Pathology can also support ruling out diagnoses like ankylosing spondylitis, hemodialysis-associated spondyloarthropathy or neuropathic Charcot joint deformities [3]. Furthermore, crystal deposits can aid in the diagnosis of pseudogout [4].

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Authors: Chad Craig, Michael Steinhaus

QUESTION 6: How many intraoperative tissue samples should be sent for culture in suspected spinal surgery infection?

RECOMMENDATION: With the currently-available evidence, it is recommended that at least three to five tissue samples be sent for culture in cases of suspected spinal infection. In the setting of instrumentation, we recommend additional techniques, such as vortexing and sonification, to increase the yield of culture samples.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 80%, Disagree: 13%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Turnbull described surgical site infections (SSIs) in spinal surgery in 1953, noting three cases of deep infection of the disc after discectomy as well as significant morbidity that followed [1]. While clinically these cases presented as infection, Turnbull reported them as "presumed" infection because culture of the causative organism was not obtained. Since his work, the incidence of SSI following spine surgery has been studied extensively, with reported incidences ranging from 0.2–15%, varying widely based on underlying pathology and procedure type, with revision procedure, fusion, implantation, and traumatic injury carrying the greatest risk [2–6]. The most common causative culprits are *Staphylococcus* species, including methicillin-resistant *S. aureus* (MRSA) [3,6–9], although less virulent organisms such as *Propionibacterium acnes* can also occur, particularly in revision cases without a definitive preoperative diagnosis of infection [10–12]. Prior to obtaining intraoperative cultures, some suggest computed tomography-guided aspiration, although this practice has been shown to have low sensitivity [13,14].

The evidence for the optimal number of specimens to obtain in cases of suspected spinal infection is sparse. In their study of patients undergoing Cotrel-Dubousset instrumentation, Bemer et al. evaluated cases of *Cutibacterium acnes (C. acnes)* infection, noting that in earlier years of the study one to two samples for culture were obtained, whereas later in their series they had increased that number to four to six samples. Based on their experience and the difficulty in diagnosis of *C. acnes*, these studies recommend that at least four deep tissue samples be taken to facilitate interpretation of the cultures [11].

In the setting of implantation, one major challenge is that peri-implant cultures may not be accurate and it can be difficult for biofilm cultures to grow [15]. In their study of removed spinal implants in the setting of infection, Sampedro et al. report using a technique of vortexing and sonification followed by culturing, which resulted in significantly increased sensitivity compared to simply taking two to nine peri-implant tissue samples [12]. Finally, in a study assessing specimens taken from orthopaedic device revision surgery (5.1% spine cases), the standard procedure was to obtain three to six (mean: four) samples per case, including specimens from the inflammatory membrane around the implant, joint capsule (as applicable) and any macroscopically suspect tissues [16]. In this study, a threshold of at least three positive samples with identical microorganisms was used for diagnosis. The authors note that this definition is strict compared to other studies that use two identical culture-positive specimens for diagnosis and report that their findings would not have differed had they used a lower threshold of two.

It is important to remember that positive cultures may not represent true infection and should be interpreted in the overall context of the individual patient and clinical picture. Gelalis et al. studied bacterial contamination during simple and complex spinal procedures in 40 patients, taking culture swabs during each case, first from the sterile transparent sheet over the operative site at the start of the case, followed by hourly samples from the surgical wound. The authors reported that none of the patients with positive cultures developed clinical signs of infection or required antibiotics, whereas three patients with negative cultures developed postoperative infection [17].

Though there is little guidance in the spine literature, the data in arthroplasty may help to guide future practices. In a study looking at revision hip and knee arthroplasty, Atkins et al. found that the presence of three or more culture-positive specimens was highly predictive of infection (likelihood ratio, 169; sensitivity, 66%; specificity, 99.6%), whereas a single culture-positive specimen was found to have low diagnostic value (likelihood ratio, 0.7; post-test probability of infection, 10.6%) [15]. In their study, the authors determined that five or six samples are required to produce excellent sensitivity and specificity. Similarly, in a study of periprosthetic joint infection caused by MRSA, Parvizi et al. took five cultures in each case [18]. In accordance with the evidence, the Workgroup of the Musculoskeletal Infection Society recommends that three to five culture samples be taken and incubated in an aerobic and anaerobic environment [19].

There is little evidence regarding the optimal number of samples to obtain in the setting of suspected spinal surgery infection. Given the limited data that is available in the spine literature, we conclude that taking at least three to five tissue samples represents current best practice. In the setting of instrumentation, we recommend additional techniques, such as vortexing and sonification, to increase the yield of culture samples.

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2.3. DIAGNOSIS: IMAGING

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QUESTION 1: What is the optimal mode of imaging in the diagnosis of spine infections? If magnetic resonance imaging (MRI) is contraindicated, what imaging modality should be used?

RECOMMENDATION: MRI remains the gold standard for the diagnosis of spinal infection, with sensitivity and specificity above 90%. In the presence of MRI contraindications, consider a combination of modalities, such as computed tomography (CT), positron emission tomography-CT (PET-CT), and single photon emission CT (SPECT)+67Gallium or Gallium-67.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Plain radiography should be the initial exam performed for all patients with non-specific spine or back complaints. In patients with spinal infections, early radiographic findings will occur two weeks to three months after the onset of symptoms. Plain radiographic findings characteristic of a spinal infection include disc space narrowing, end plate irregularity, loss of end plate contour, subchondral defects and/or hypertrophic or sclerotic bone formation. Disc space narrowing has been reported as the most consistent plain radiographic finding occurring in 74% of cases [1]. Late plain radiographic findings include vertebral body collapse, pathologic fractures, segmental kyphotic collapse and/or bony ankylosis. Plain radiography has reported sensitivity of 82% and specificity of 57 to 59% in subjects with pyogenic spondylodiscitis [2,3]. While this modality may not provide the highest level of diagnostic quality, it can give clinicians an understanding of global and focal alignment, deformities associated with infectious processes and mechanical stability [4]. Plain radiographs may also be used for post-treatment surveillance and/or monitoring for potential late deformity or instability associated with these diseases.

CT is an advanced imaging technique that can be utilized for diagnosing spinal infections. It provides higher resolution and multiplanar imaging of the bony architecture. CT findings characteristic of spinal infections can include cystic bony changes, gas within vertebral discs, endplate osteolysis surrounding the vertebral disc and/or paravertebral soft tissue swelling or abscess formation [5–7]. The addition of contrast media during computed tomography can help better delineate the edges of paravertebral abscesses and edematous musculature [5–7]. In cases with neurological deficits or new onset radiculopathy, post-myelogram CT scan can provide excellent detail of the spinal canal and potential epidural and/or subdural abscesses [8]. In cases where myelogram is performed, it is recommended to analyze the cerebral spinal fluid to rule out meningitis [9]. SPECT is a scintigraphic CT modality that has increased bone contrast resolution, and when combined with technetium or gallium, has high sensitivity and diagnostic accuracy for spinal infections. SPECT with gallium has been shown to be superior to SPECT + technetium and is now the recommended imaging modality for patients with MRI contraindications [10].

MRI remains the gold standard for early and accurate diagnosis of spinal infections [11–20]. MRI has a reported sensitivity of 96%, specificity of 93% and diagnostic accuracy of 94% [18]. MRI has higher accuracy for differentiating degenerative and neoplastic conditions from infections in patients presenting with severe back pain of unknown etiology [11]. While MRI may provide the most detailed information for diagnosing possible infections, it does not reduce the need for tissue biopsy for histological analysis. T1-weighted and T2-weighted sequences should be obtained. The most common MRI findings consistent with spinal infections show decreased vertebral body intensity with poor differentiation between the disc and body on T1-weighted images and increased disc space intensity with marked decreased vertebral body intensity on T2-weighted images [16,18,20]. Utilizing gadolinium contrast can enhance MRI ability to detect and delineate epidural abscesses [21]. All publications consider MRI the gold standard imaging modality for spinal infections and recommend it should be used in all patients without MRI-specific contraindications.

Radionucleotide studies are another modality that is useful for diagnosing spinal infections. These include technetium-99m bone scans, gallium-67 scans, and indium-111 labeled leukocyte scans. Pathologic changes have been shown to appear sooner on radionucleotide studies compared to plain radiography [22–27]. Gallium scans have demonstrated earlier diagnosis of disc-space infections compared to technetium scans and have a reported sensitivity of 89%, specificity of 85% and accuracy of 86% [22,23,28]. Technetium-99m scans have a reported sensitivity of 90%, specificity of 78% and accuracy of 86%.18 When both gallium and technetium scans are performed together, the sensitivity is increased to 90%, specificity 100% and accuracy is 94%.18

Indium-111 scans are known to be sensitive for appendicular skeletal infections, however sensitivity is low in the spine [29–32]. In patients with low-virulence chronic infections, indium-111 scans can provide false-negative results due to white blood cell pooling with any inflammatory process [31]. Indium scans may also result in false-positive results in neoplastic conditions. One important advantage of indium-111 scans is the ability to differentiate non-infectious conditions such as hematoma or seroma in patients with unclear soft tissue etiology. This may be a valuable diagnostic step when investigating possible postoperative infections. Overall, most publications endorsed less utility for radionucleotide studies versus MRI. However, in patients with MRI contraindications, technetium-99m combined with gallium-67 studies is another method that has high sensitivity, specificity and diagnostic accuracy similar to MRI.

There is no single diagnostic test with 100% accuracy for these devastating diseases. A full diagnostic workup includes laboratory studies, blood cultures, imaging and tissue histological analyses. It is generally accepted that plain radiography should be the first imaging study obtained, however, diagnostic sensitivity is low. MRI remains the gold standard with the highest sensitivity, specificity and accuracy compared to other modalities. In the presence of MRI contraindications, clinicians should utilize SPECT+gallium-67 or gallium-67 and technetium-99 combined scans to achieve similar diagnostic accuracy as MRI.

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QUESTION 2: Is there a role for computed tomography (CT) scan with contrast in the diagnosis of spinal infections in patients who cannot undergo magnetic resonance imaging (MRI)?

RECOMMENDATION: **Although evidence is limited for the routine use of CT scan with contrast, there is a role for it to be used in the presence of spine infection where MRI is contraindicated or when other advanced imaging is not available**

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Although there is growing evidence of the safety of MRI in the presence of implanted metallic devices [1], obtaining such a study may not always be possible. CT with either extradural or intravenous contrast can be used to identify spine infections.

Prior to the wide adoption of MRI, CT myelography was commonly used to diagnose extradural compressive pathology such as epidural abscesses [2]. The use of this invasive investigation in the setting of postoperative spine epidural abscess has not been studied. However, it can be assumed that the accuracy will be lower due to metal artefact [3].

The role of CT with intravenous contrast in the postoperative setting is unclear and has not been directly studied. CT is most useful in identifying implant and bony related complications such as implant loosening, endplate erosion and destruction. The addition of contrast provides information on paraspinal soft tissue involvement, phlegmon or abscesses albeit with lower sensitivity and specificity when compared to MRI [4].

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Author: Glenn S. Russo

QUESTION 3: Is there a role for nuclear imaging (e.g., positron emission tomography scan (PET)) in the diagnosis of spinal infections?

RECOMMENDATION: **PET scan, preferably PET-computed tomography (PET-CT), can be used as an adjunct to magnetic resonance imaging (MRI) to diagnose spinal infections when an MRI cannot be performed or is inconclusive.**

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

At the present time, MRI is the imaging test of choice for diagnosing spondylodiscitis (SD). This study should be performed when SD is suspected to avoid the morbidity and mortality associated with a delay in diagnosis. MRI is a favored choice as part of an infectious work up due to its lack of ionizing radiation, multi-planar capability, superior soft tissue contrast and ability to evaluate the neural structures. It has a sensitivity and specificity of 97% and 93% respectively. Ultimately, its accuracy in diagnosing SD is 94% [1–3]. A typical protocol should include T1- and T2-weighted sequences with gadolinium. T2 and post-gadolinium T1-weighted sequences should also be performed with fat suppression to increase the sensitivity of identifying pathology [4,5]. Furthermore, MRI allows for the evaluation of bone marrow edema and disc space inflammation, as well as paraspinal and epidural soft tissue involvement. Gadolinium is helpful in differentiating phlegmonous changes versus abscess formation.

Fluorine-18-fluorodeoxyglucose (18F-FDG) is the radionuclide-imaging test that can be a useful compliment to MRI. The role of 18F-FDG in the diagnosis of SD has been extensively investigated [6–13]. It has shown acceptable levels of sensitivity and specificity and is useful when MRI cannot be performed or is inconclusive. In addition to its value for diagnosing spondylodiscitis, 18F-FDG can be utilized to monitor response to treatment. Gallium-67-SPECT/CT is an acceptable alternative when 18F-FDG is not available [14].

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QUESTION 4: How can postoperative infections be distinguished from normal postoperative changes on magnetic resonance imaging (MRI)?

RECOMMENDATION: The presence of an abscess in the back muscles or posterior site, confirmed by gadolinium enhancement, is the most frequently-reported change on MRI of patients with surgical site infection (SSI). The presence of a collection of fluid outside the head of the pedicle screws is another sign of SSI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 71%, Disagree: 8%, Abstain: 21% (Super Majority, Strong Consensus)

RATIONALE

A search was conducted using the MeSH terms “spine AND MRI AND surgical site infection.” The initial search yielded 149 references, and after screening, 13 abstracts remained. However, only three studies assessed the use of MRI for postoperative spine infections and were found eligible.

Kanayama et al. retrospectively used MRI in 20 patients with surgical site infections after instrumented spinal surgery [1]. In their series they considered two markers for diagnosing SSI: (1) the presence or absence of osteomyelitis at the instrumented vertebra and (2) the presence or absence of intervertebral abscess. All 20 patients had a confirmed SSI, but in 7 MRIs it was considered negative. The study mainly aimed to assess the utility of MRI to confirm the severity of the infection. Using the above-mentioned criteria, they tried to predict the need for implant removal. However, MRI was not evaluated as a diagnostic tool for assessing the presence or absence of infection.

Kim et al. reviewed 43 patients with MRI after SSI [2]. First, they divided their infections on an anatomical basis, assessing if it affected only the posterior region (31 cases), only the anterior area or both posterior and anterior regions [2]. In addition, they looked for abscess in different spinal locations (posterior epidural space, laminectomy site, back muscles, subcutaneous fat layer, paravertebral space, psoas muscle and anterior epidural space). They also evaluated the presence of osteomyelitis of the vertebral body and discitis. The most frequent findings were abscesses in the back muscles in 40 patients (93%), abscesses in the laminectomy site in 29 (67.4%) and in the subcutaneous fat layer in 27 (62.8%). All abscesses were identified by the presence of peripheral rim or diffused enhancement of adjacent soft tissue after administration of intravenous gadolinium.

They did not compare their findings with those of patients without confirmed SSI. The authors concluded that for diagnosing infection, the posterior surgical field was more important than the vertebral body or the disc area. This conclusion supports the findings of the previous study by Kanayama, in which seven patients with SSIs did not show involvement of the vertebral body or the disc area.

Finally, Kimura et al. published a comparative study on postoperative MRI including 17 patients with a deep SSI and 64 non-SSI controls who had an MRI examination within 4 weeks after surgery [3]. Their investigation focused on the “pedicle screw fluid sign” (PS fluid sign) and did not search for other signs of infection. The PS fluid sign refers to the collection of fluid outside the head of a pedicle screw, suggesting the presence of an abscess on axial MRI scans. The authors observed that fluid collections medial to the pedicle screw head are not infrequent. They considered that when the collection expands outside the head of the screw into the paravertebral muscles, it is likely to be an abscess. In their view, artifacts have little effect on the area outside the screw head, compared with the inside. In their study, this sign was positive in 15 of 17 deep SSI infections and only in 7 of 64 patients without infection. Sensitivity was 88.2%, specificity 89.1%, positive predictive value 68.1% and negative predictive value 96.6%.

In conclusion, abscesses in the back muscles, laminectomy site and subcutaneous fat layer, after administration of gadolinium were the most common findings related with surgical site infection. In addition, the PS fluid sign had a sensitivity of 88.2% and specificity of 89.1%.

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Treatment

3.1. TREATMENT: GENERAL PRINCIPLES

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QUESTION 1: Can a non-surgical approach be used to treat postoperative spine infections? If so, what factors predict a successful outcome?

RECOMMENDATION: Postoperative spine infections should be treated with irrigation and debridement (with or without implant removal) followed by appropriate antibiotic therapy. Antibiotic suppression without surgical intervention should be attempted in cases where the patient is not a surgical candidate, or in attempt to achieve spinal fusion prior to implant removal.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 80%, Disagree: 7%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

Postoperative surgical site infections are a major complication that occur between 1 and 12% of all spinal surgeries [1–3]. Treatment varies based on general location in relation to superficial, or deep to the muscular fascia, and the time from initial surgery, with early infections occurring before 90 days and late infections occurring after 90 days.

In the case of superficial wound infections, local debridement, healing by secondary intention and a short course of antibiotics is usually sufficient [4]. Deep surgical site infections, on the other hand, require aggressive irrigation and debridement with or without implant removal. The retention of hardware predominantly depends on if the infection is early or late. Several studies have demonstrated that hardware can be retained successfully following aggressive irrigation and debridement in the setting of early infection, except in cases where the implants are loose or there is bony involvement [5–9]. Optimal treatment of delayed infections is aggressive irrigation and debridement with implant removal [10–12]. In the cases where spinal fusion has been achieved, implant removal is routinely performed. However, in cases of fusion failure or pseudoarthrosis, surgical options include aggressive debridement and irrigation with attempted implant retention, implant removal with primary or delayed reimplantation or implant removal without reimplantation [6,13–16].

Antibiotic suppression without surgical intervention is attempted in cases where the patient is not a surgical candidate, or in an attempt to achieve spinal fusion prior to implant removal.

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QUESTION 2: When should patients with suspected infections of the spine be referred to an infectious disease department?

RECOMMENDATION: There is no data on the timing or need for a referral to an infectious disease department. We support a multidisciplinary approach to managing clinical spine infections.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Only one paper has addressed the collaboration with an infectious disease-specialized team in order to improve outcomes for patients with spinal surgical site infections (SSIs). The paper is a retrospective study reporting on 40 patients, none of whom needed implant removal [1]. The paper didn't report on the exact timing when collaboration started, but reported three main advantages related with this collaboration:

1. Efficient detection of auxiliary bacteria (reached 88%)
2. Early treatment with antibiotics
3. Appropriate duration of administration of antibiotics

There were no other papers which discussed this issue, and all subsequent searches on related articles yielded no more information on the matter.

From a theoretical point of view, referral, or at least counselling by an infectious diseases specialist, might have some advantages. Antibiotic treatments are more complex today and only specialists are adequately up-to-date on the issue. The appropriate treatment choice might be difficult in patients with allergies, multi-resistant smears or simply a low tolerance for the medication. Adjusting the choice of antibiotic, taking into account side effects and tolerance, will very likely improve compliance, which is paramount in reaching a successful treatment outcome.

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QUESTION 3: Which patients with vertebral osteomyelitis (VO) are suitable for outpatient management? Does any criteria exist to aid in this decision-making?

RECOMMENDATION: There are no studies aiming to identify which patients diagnosed with VO can be treated on an outpatient basis.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

VO, also known as spondylodiscitis, describes an infection of the vertebrae and intervertebral disc. By comparison, discitis describes infection limited to the intervertebral disc, however there are many who consider discitis and VO to be different stages of the same disease process. VO can arise from hematogenous seeding, contiguous spread from infection in adjacent soft tissues or direct inoculation during spinal surgery or procedures (i.e., epidural). Management of native vertebral osteomyelitis (NVO) depends on the location of the infection, disease progression and the patient's general condition including age and comorbidities.

Conservative treatment is reasonable in the early stages with no or minor neurologic deficits or in the case of severe comorbidities. However, in cases of doubt, surgical treatment should be considered. Both options require a concomitant antimicrobial therapy, initially applied intravenously and administered orally thereafter [1]. To date, there is no consistent data from randomized controlled trials to guide the optimal duration and appropriate route of antibiotic therapy. Although the optimal duration of antibiotic therapy remains controversial, it should never undercut six weeks [2]. Recent Infectious Diseases Society of America (IDSA) guidelines for the diagnosis and treatment of NVO in adults include evidence and opinion-based recommendations for the management of patients with NVO treated with antimicrobial therapy, with or without surgical intervention, but do not address the issue of which patients affected by NVO can be treated on an outpatient basis [3,4]. The extent of pursuing spinal biopsies to determine etiology, antimicrobial therapy, response to treatment and preference for surgical techniques and timing all vary widely in clinical practice with heterogeneous studies limiting comparisons. Surgery, rather than conservative approaches, is being proposed as the default management choice because in carefully-selected patients it can offer faster reduction in pain scores and improved quality of life [5–9]. Due to a heterogeneous and often comorbid patient population and the wide variety of treatment options, no generally applicable guidelines for VO exist and management remains a challenge.

The goals of treatment include establishing a diagnosis and identifying the pathogen, eradicating the infection, preventing or minimizing neurologic involvement, maintaining spinal stability and providing an adequate nutritional state to combat infection. Often, this can be accomplished with non-operative approaches.

The mainstay treatment of pyogenic infections of the spine remains antibiotic therapy and immobilization with a proper orthosis. If nonsurgical treatment fails, however, surgical intervention may be required. Surgery is indicated in the following circumstances: to obtain a bacteriologic diagnosis when closed biopsy is negative or deemed unsafe, when a clinically significant abscess is present (spiking temperatures and evidence of sepsis), in cases of refractory to prolonged non-operative treatment where the sedimentation rate remains high or pain persists, in cases of spinal cord compression causing a neurologic deficit and in cases of substantial deformity or vertebral body destruction, especially in the cervical spine. Alton et al. reported that 75% of patients with an epidural abscess in the cervical spine who underwent medical management failed and that medical management failure was associated with a significantly increased risk of neurologic injury [10]. Patel et al. reported on 128 patients with an epidural abscess and found that 41% failed medical management. However, there were significant predictors of medical failure [11]. Four key predictors were identified, including diabetes mellitus, C-reactive protein (CRP) greater than 115, white blood cell count greater than 12.5 and positive blood culture. Patients with none of the aforementioned parameters only failed 8.3% of the time. Those with one parameter failed 35.4% of the time, those with two parameters failed 40.2% of the time and patients with three or more parameters failed 76.9% of the time.

Once the antibiotic is prescribed by oral route, if the patient is stable, the treatment could be administered in an outpatient setting. Several studies described a successful switch to oral antibiotics after 10 days, using oral agents with a high bio-availability and tissue penetration (i.e., fluorquinolones, rifampin, fusidic acid and clindamycin) [12–15]. A retrospective analysis of all patients diagnosed with NVO, at the University Hospital of Basel, Switzerland, concluded that switching to an oral antibiotic regimen after two weeks of intravenous treatment may be safe, if CRP has decreased compared to baseline CRP and epidural or paravertebral abscesses of significant size have been drained [16]. Importantly, these results do not extend to patients with endocarditis, surgical site infection, and/or vertebral implants. Also, positive blood cultures, neurological abnormalities and staphylococcal infections (compared with negative microbiology) are associated with longer intravenous courses [17].

Outpatient parenteral antibiotic therapy (OPAT) has become an option allowing for early discharge of hospitalized patients who have infections without a reliable oral alternative and requires lengthy antibiotic therapy. It provides numerous benefits, some of the most remarkable being that OPAT permits early discharge and reduces costs, avoids hospitalization trauma in children or immobilization syndrome in the elderly and reduces nosocomial infections by multidrug resistant organisms [17]. OPAT also allows for self-administration of antibiotics using elastomeric pumps [18,19]. Different retrospective studies and case series have reviewed the experience with OPAT in several countries [17,19–27]. β-Lactam antibiotics are commonly used in OPAT with higher treatment success among those treated with ceftriaxone and ertapenem, while oxacillin was associated with a higher rate of antimicrobial discontinuation because of antimicrobial-related complications [17,20,26]. Other alternatives are teicoplanin, telavancin or daptomycin in the case of gram-positive infections [17,25,28]. All this data regarding OPAT confirms that infection management in an outpatient setting is safe, clinically efficacious, and acceptable for treating a wide range of infections with high levels of patient satisfaction and substantial cost savings. Therefore, OPAT could be considered an effective alternative for appropriately selected elderly patients with vertebral osteomyelitis.

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Authors: Chad Craig, Dolors Rodriguez-Pardo, Evan Sheha

QUESTION 4: What is the optimal treatment of spinal infections caused by *Propionibacterium acnes* (*P. acnes*)?

RECOMMENDATION: When possible, patients should undergo complete removal of implants after *Cutibacterium acnes* (*C. acnes*) (formerly *P. acnes*) infection, especially in the setting of latent infection. Antibiotic regimens typically involve specific parenteral antibiotics for a period of greater than two weeks, with the most common antibiotic duration being six weeks of multiple parenteral and/or oral agents. However, the duration of antibiotic treatment is highly variable. It is unclear in which setting patients may be successfully treated with antibiotic therapy alone and instrumentation may be retained. Penicillin is currently the standard of care, but other non beta-lactam antibiotics should be considered based on the susceptibility profile.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 73%, Disagree: 7%, Abstain: 20% (Super Majority, Strong Consensus)

RATIONALE

P. acnes is an anaerobic, gram-positive bacillus existing as normal flora of the skin and sebaceous glands and was originally considered a common contaminant of blood cultures as well as an uncommon cause of brain, pulmonary and dental infections [1]. *C. acnes* infections are commonly thought to originate from patient skin approximation with surgical sites, are frequently poly-microbial, require an extended incubation period in culture media for diagnosis and form a resistant biofilm, making treatment with antibiotics alone difficult [2–4].

P. acnes infection of the spine was first reported as an etiology of spine infection by Serushan et al. in 1982 [5]. The patient presented with osteomyelitis of the cervical spine and was treated with 40 days of intravenous penicillin with resolution of his fever and neck pain. *C. acnes* has subsequently been implicated in vertebral osteomyelitis and discitis and may present with insidious onset of back pain, fever and/or neurologic symptoms, with treatment typically involving administration of parenteral antibiotics. Additional debridement or percutaneous drainage of abscesses occurs in rare cases [6–8]. Duration of antibiotics ranged from 2-28 weeks in one series, and typically involved multiple agents due to the frequency of co-infection with other pathogens including *Staphylococcus,* Lactobacillus and Enterococcus species [9].

Tsai et al. reported on successful treatment of two cases of *C. acnes* osteomyelitis of the cervical spine with anterior debridement, decompression and fusion with autograft and treatment with a combination of oral and parenteral antibiotics for 6-16 weeks [10]. Overall, the decision to treat *C. acnes* vertebral osteomyelitis and discitis with surgery, antibiotics or a combination of these approaches has been made on a case-by-case basis. No well-defined, widely-applicable treatment regimen was identified in the literature.

C. acnes also frequently presents as a delayed infection after spinal instrumentation, which has been attributed to its low virulence and slow growth rate, and is common in instrumented pediatric scoliosis surgery [4,11–17]. Viola et al. reported a series of eight patients with delayed infection, one of which had *C. acnes* infection and was treated with irrigation and debridement, removal of instrumentation and six weeks of cefotetan with good results and no loss of balance or alignment at midterm follow-up. Of 23 patients with delayed infections after posterior TSRH instrumentation, Richards and Emara found that the causative agent in delayed infections was *C. acnes* in 12 (52.1%). Patients underwent removal of instrumentation with either primary or delayed closure and parenteral antibiotics (two to five days) followed by a course of oral antibiotics for an additional two to four weeks [18]. Tribus reported on a delayed infection with *Staphylococcus epidermidis* and *C. acnes* resulting in laminar erosions seven years after TSRH instrumentation. The patient was treated with removal of instrumentation and seven weeks of intravenous vancomycin and oral rifampin with resolution of pain and infection [12]. In cases of late implant infections, successful treatment typically involved implant removal and greater than two weeks of a combination of parenteral and oral antibiotics.

In the largest single study evaluating treatment of *C. acnes* infection after Cotrel-Dubousset instrumentation, Bemer et al. conducted a retrospective study investigating various treatment regimens including complete or partial implant removal, implant replacement and maintenance of implants with irrigation and debridement, both with and without antibiotics. Patients who underwent partial removal with antibiotic monotherapy or absence of antibiotic therapy were more likely to develop a secondary infection. Ultimately, wide variation in treatment regimens prevented more meaningful analysis of the results, though the authors concluded that complete removal of implants should be performed when possible and antibiotics should be tailored to the sensitivities of the specific organism and given for a duration of three to six months or less than three months when following total implant removal [19]. In another large case series of surgical site infection (SSI) after spine surgery, Maruo and Berven listed *C. acnes* infection as an independent risk factor for treatment failure (p = 0.042) [4]. Though they did not comment on the specific treatment strategies utilized for patients with *C. acnes* SSI, they note that 7 of 12 patients (58%) with late infection treated with implant retention and antibiotics required subsequent implant removal.

Due to the variation in treatment strategies for *Propionibacterium acnes* infections of the spine and the lack of prospective trials evaluating optimal antibiotic regimen, the optimal treatment of spinal infections with *C. acnes* is indeterminate. However, given reports of numerous successful treatment strategies in the literature, complete removal of implants when applicable followed by an extended course of parenteral antibiotics results in overall high cure rates for *C. acnes* infections of the spine.

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3.2. TREATMENT: ANTIBIOTICS

Authors: John Koerner, Katherine Belden

QUESTION 1: Is there a role for oral antibiotics in the treatment of early postoperative spine infections?

RECOMMENDATION: There may be a role for highly bioavailable oral antibiotics in the treatment of early postoperative spine infection in select circumstances.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Broad-spectrum intravenous (IV) antibiotics may be indicated prior to identification of the infecting organism in patients with early postoperative infections while waiting for surgical intervention, or for patients who are medically unstable and cannot undergo surgery [1]. Other than the latter cases, there is no role for oral antibiotics alone in the treatment of patients with acute postoperative spine infections. Patients with established postoperative infections of the spine require surgical intervention.

The administration of antibiotics may potentially adversely affect the outcome of treatment of these patients by interfering with isolation of the infecting organism. Antibiotic therapy should be withheld in patients with suspected spine infection, as the yield for biopsy to isolate the infecting organism is reduced when the antibiotic is administered. In a study by Cornett et al., the yield for biopsy culture dropped from 80% for those who did not receive antibiotics to 48% for those who did [1]. Another study of 87 patients, however, demonstrated that the yield for biopsy of spondylodiscitis did not significantly decrease with prior treatment of antibiotics [2]. Despite this, it is still recommended that antibiotics be withheld when possible. If antibiotics are to be administered, biopsy is still indicated to isolate the infecting organism and allow for optimal treatment of the patient.

In a large case series of 1,980 patients, 74 infections were diagnosed [3]. The treatment algorithm consisted of six weeks of IV antibiotics if the patient was not fused. If the patient was fused, *Staphylococcus aureus* and gram-negative infections were treated with six weeks of IV antibiotics followed by six weeks of oral antibiotics with implant removal. In patients with propionibacteria and coagulase-negative *Staphylococcus*, four weeks of oral antibiotics were given. Oral antibiotics were not recommended as an initial treatment. Other studies have demonstrated the benefit of oral antibiotics as suppression therapy after treatment with surgical debridement and a course of IV antibiotics [4,5].

Multiple other studies have demonstrated the benefit of surgical debridement and IV antibiotics for infection [6]. In a consecutive case series of 2,391 patients, 46 cases of wound infection were identified and all treated with surgical debridement [7]. One series of 111 patients identified eight patients with postoperative infections after posterior lumbar interbody fusion [8]. All were treated with irrigation and debridement followed by four to six weeks of intravenous antibiotics followed by another six to nine weeks of oral antibiotics.

Multiple case series and expert opinion studies recommend avoiding oral antibiotics in suspected postoperative infection until culture samples are taken for better diagnosis and accurate treatment of these patients [9]. The majority of patients with established postoperative infection require surgical debridement.

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Author: Yvonne Achermann

QUESTION 2: Is there a role for the use of oral antibiotic in treatment of acute and chronic spinal infections?

RECOMMENDATION: There may be a role for highly bioavailable oral antibiotics in the treatment of acute and chronic spine infection in select circumstances.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Vertebral osteomyelitis

In vertebral osteomyelitis (spondylodiscitis) without an implant, experts recommend a treatment duration of 6 to 12 weeks [1]. However, a retrospective study over 10 years by Roblot et al. found no difference in relapse rate comparing 6 and 12 weeks of treatment [2]. An open label, non-inferiority, randomized, controlled trial by Bernard et al. firstly showed that 6 weeks was not inferior to 12 weeks. In both groups, intravenous treatment was only given for a median time of 14 to 15 days and was followed by an oral fluoroquinolone and rifampin combination or aminopenicillin (both regimens with high oral bioavailability) [3]. The authors could not see a difference in the proportion of treatment failure between patients given intravenous treatment for more than one week and those for less than one week.

Postsurgical infection with an implant

There are many studies in this field regarding optimal treatment duration and agents in spinal implant-associated infections, but they are all retrospective with low levels of evidence. There are no up-to-date prospective and/or randomized studies published investigating the optimal duration of antibiotic treatment and the role of oral antibiotics in implant-associated spinal infections.

Most studies demonstrated successful treatment of spinal implant-associated infections with a total duration of six weeks [4–6]. If implants are not removed, reported durations of treatment are up to 12 weeks with intravenous treatment for 6 weeks, followed by oral antibiotic treatment for another 6 weeks [7,8].

Yet, regarding duration of intravenous treatment, there are no clear recommendations. Some studies treat intravenously for a prolonged time for up to four [8–10] or six weeks [4,11–13]. But there are also retrospective studies in which intravenous treatment was given for two weeks or less followed by oral antibiotics with good oral bioavailability [14]. Billieres et al. did a multivariate analysis on risk factors for relapse of infection and did not find an association with duration of total or intravenous antibiotic treatment [14]. Another study by Kowalsky et al. also concluded that duration of intravenous treatment is no risk factor for neither acute nor chronic infections [15].

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QUESTION 3: Is there a role for chronic antibiotic suppression after treating patients with retained infected spinal hardware?

RECOMMENDATION: The use of chronic antibiotic suppression (CAS) has not been clearly investigated until now. However, it can be an option for patients whose implants cannot be removed or who refuse further surgeries because of comorbidities.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Only one study has compared patients receiving CAS [1]. They found that 5 out of 22 patients with CAS had treatment failure, compared with 5 out of 6 in the control group. The definition they used for treatment failure was described as the need for an unanticipated debridement or a clinician's decision to give a second course of antibiotics. Suppressive antibiotics were given for a median time of 303 days (IQR 147 to 672) to patients with early onset infection and 410 days (IQR 61 to 667) to patients with late onset infection. Data on treatment failure was reported only for early onset infection patients. It could be argued that patients already under CAS would not have been eligible for a second course of antibiotic treatment and this could partly increase the rates of treatment failure on the group without CAS, biasing the study results.

Other studies reporting on antibiotic treatments show large variations in the duration of treatment. Miyazaki et al. reported a mean duration of oral treatment of 336 days, ranging from 89 to 1,673 days [2]. Their study focused on multi-resistant surgical site infection treated with implant retention. Maruo et al. reported an average duration of antibiotic treatment of 255.8 days with a standard deviation of 283.4 days [3]. All these reports show a huge variation in the length of antibiotic treatment, with a select group of patients in each study receiving CAS. Decision for prolonged CAS was made at the clinician's discretion and based on the patient's symptoms, so there is no particular setting in which it would be possible to offer a sound recommendation. Besides the mentioned paper by Kowalski, there are no reports comparing CAS with other treatment regimes.

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Authors: Alexander Vaccaro, Anand Segar

QUESTION 4: Is there a role for combination antibiotics (i.e., dual or triple) in treating patients with surgical site infection (SSI) following spinal surgery?

RECOMMENDATION: There is insufficient evidence to recommend the routine use of combination antibiotics in the setting of postoperative spine infections. However, there may be a role for combination antibiotics in certain circumstances related to specific pathogens.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 87%, Disagree: 13%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

The incidence of postoperative spine infection has been reported as between 0.7 and 16%, with higher rates noted in procedures with hardware implantation [1,2]. The most common organisms isolated are *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *S. aureus* and *Enterococcus*. Up to 20 to 30% of infections are noted to be poly-microbial [3,4].

Antibiotic treatment is directed at the isolated micro-organism/s and usually only a single anti-microbial agent is used. There are a few reports of dual antibiotic therapy with rifampin, the most common additive agent [3,5]. Rifampin is chosen due to its ability to penetrate biofilms associated with implant-related infections [6]. Evidence from a mouse model has shown that the addition of rifampin to vancomycin led to an increase in bacterial death, but no change in the final outcome from the SSI [7]. There are no clinical studies comparing the use of single to multi-agent antibiotic therapy for postoperative spine infections.

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Author: Yvonne Achermann

QUESTION 5: How long should antibiotics be administered after surgical debridement for an acute postsurgical spinal infection?

RECOMMENDATION: For vertebral osteomyelitis: Initial intravenous treatment for one to two weeks, followed by an oral treatment of four to five weeks to reach a total treatment duration of six weeks.

For deep surgical site infections: There is limited knowledge about the ideal duration of antibiotic treatment and which intravenous and/or oral agents should be given. As extrapolated from studies in periprosthetic joint infections (PJIs) and retrospective studies in spine infections, 12 weeks of antibiotic treatment can be recommended in cases with early infection and implant retention, six weeks if the implant is removed and prolonged suppressive treatment in delayed infections without removal of the implant.

LEVEL OF EVIDENCE: Moderate for vertebral osteomyelitis. Limited for surgical site infections after spine surgery

DELEGATE VOTE: Agree: 80%, Disagree: 13%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Vertebral Osteomyelitis

In vertebral osteomyelitis (spondylodiscitis) without an implant, experts recommend a treatment duration of 6 to 12 weeks [1]. However, a retrospective study over 10 years by Roblot et al. [2] found no difference in relapse rate between 6 and 12 weeks of treatment [2]. An open label, non-inferiority, randomized, controlled trial by Bernard et al. first showed that 6 weeks was not inferior to 12 weeks. In both groups, intravenous treatment was only given for a median time of 14 to 15 days followed by an oral fluoroquinolone and rifampin combination or aminopenicillin (both regimens with high oral bioavailability) [3]. The authors could not see a difference in the proportion of treatment failure between patients given intravenous treatment for more than one week and those for less than one week.

Postsurgical infection with an implant

There are many studies in this field regarding optimal treatment duration and agents in spinal implant-associated infections, but they are all retrospective with low levels of evidence. There are no up-to-date prospective and/or randomized studies published investigating the optimal duration of antibiotic treatment and the role of oral antibiotics in implant-associated spinal infections.

Most studies demonstrated successful treatment of spinal implant-associated infections with a total duration of six weeks [4–6]. If implants are not removed, reported durations of treatment are up to 12 weeks with intravenous treatment for six weeks, followed by oral antibiotic treatment for another six weeks [7,8].

Yet, regarding duration of intravenous treatment, there are no clear recommendations. Some studies treat intravenously for a prolonged time for up to four [8–10] or six weeks [4,11–13]. But there are also retrospective studies in which intravenous treatment was given for two weeks or less followed by oral antibiotics with good oral bioavailability [14]. Billieres et al. did a multivariate analysis on risk factors for relapse of infection and did not find an association with duration of total or intravenous antibiotic treatment [14]. Another study by Kowalsky et al. also concluded that duration of intravenous treatment is not a risk factor for acute chronic infections [15].

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QUESTION 6: How long should antibiotics be continued when spinal wounds are left to heal by secondary intention?

RECOMMENDATION: Only standard perioperative antibiotic prophylaxis is recommended.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Following spine surgery, surgical wounds are normally closed via primary intention where all tissue is fastened closed with sutures, staples, glue or some other form of closure material. In rare cases, however, wounds are left to close naturally via secondary intention. Normally, this is done in cases where the risk of persistence of infection is high or when a large gap in soft tissue exists as a result of tissue loss.

Antibiotic prophylaxis has been shown to be useful in preventing infection following spine surgery. However, no specific agent or schedule has been identified as superior over any other [1].

In a randomized, blinded, controlled study, Gupta et al. found that topical antibiotics, specifically sucralfate, increased wound healing in patients at four weeks following hemorrhoidectomy left to heal via secondary intention when compared to placebo (78% compared to 52%) [2]. In contrast, Doung et al. found that the use of trimethoprim-sulfamethoxazole in pediatric skin abscess treatment compared to placebo did not significantly affect the recurrence of new lesions in the long term [3].

A systematic review by Norman et al. found that no robust evidence exists on the relative effectiveness of any antibiotic preparation in cases where surgical wounds have been left to heal by secondary intention [4]. There is no high-level evidence directly related to spine surgery for this topic. In general, if there is hardware present, patients often should receive at least six weeks of intravenous antibiotics and continued suppressive antibiotics until the wound heals.

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QUESTION 7: What is the optimal duration of antibiotic treatment following spine infection in patients within whom hardware is retained? Is the antibiotic treatment different for those with spine infection without hardware?

RECOMMENDATION: There are no case-control studies allowing for an evidence-based recommendation on the optimal length of antibiotic treatment following spine infections in the presence of retained hardware. The most commonly implemented antibiotic regime is three months. However, duration of treatment was highly variable among all studies. Patients with non-instrumented surgeries did well with a shorter course of antibiotics.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

After searching PubMed, CINAHL and Embase (with MeSH terms "surgical site infection," "spine" and "antibiotic") and reviewing 381 abstracts, a final 14 studies included treatment of spinal surgical site infection (SSI) with retained implants (including data on antibiotic treatment regimens) [1–14]. There were no studies analyzing or comparing different antibiotic regimes. Most of these studies were retrospective in nature, however one study was a prospective observational study. There were no studies comparing different antibiotic treatment regimens. There was also a wide variation in the duration of treatment among the studies ranging from 42 to 597 days in 1 study, and ranging between 89 and 1,673 days in a separate study [9,11]. These variations were usually related to treatment failure or poor control of the infection. Of 14 studies, 7 reported mean antibiotic treatments of 12 weeks or 3 months [3–6,10,13,14]. All but three studies reported on time of intravenous (IV) and oral antibiotics. The most reported mean time for IV antibiotic administration was an average of four to eight weeks in eight studies. One study reported on 81 SSIs, of which 39 were treated with suppressive antimicrobial therapy [2]. At final two-year follow-up, seven patients were still under antibiotic treatment.

Three studies reported data on patients with early and late infection [2,5,10]. Also, there were significant variations regarding the onset of infection. Some studies only reported ranges and gave no mean or median values. Of the nine studies with available mean data, mean time to onset of infection was 103.2 days. Removing an outlier with 778 days for late infection, mean time to onset of infection was 18.98 days (range of mean values was 2.9 to 54)

There was only one retrospective study analyzing the antibiotic treatment regimen in a series of 74 patients, all with implant removal (IR) [15]. Patients had a median duration of IV antibiotics of four weeks and an additional five weeks of oral antibiotic treatment. There were no comparative studies regarding different antibiotic regimen.

Regarding IR, there were two very different settings in which implants had to be removed. Of 729 SSI cases recorded in the 15 studies, implants were removed in 195 patients (26.74%). In 114 cases (15.6%), IR was performed as part of SSI treatment during the first debridement procedure. In the remaining 81 cases (11.11%), IR was performed because of treatment failure after several debridement procedures. The fact that IR can be split into two differentiated groups makes it more difficult to compare treatment regimes. Usually, when IR was performed as the initial treatment, antibiotic regimens tended to be shorter [15]. On the other hand, when IR was performed because of treatment failure, antibiotic treatments were longer.

With regards to non-instrumented spine surgeries, Maruo et al. compared 59 non-instrumented infections with 166 instrumented cases [8]. They reported longer antibiotic treatment for instrumented cases (mean 40 days IV vs. 25.4 in non-instrumented and mean 255 days oral vs. 42). Only 10% of the non-instrumented cases needed more than one debridement compared to 28% for instrumented spine procedures. Of the non-instrumented spine surgeries, 20% were successfully treated without surgical debridement compared to only 6% of instrumented spine procedures.

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Author: Maja Babic

QUESTION 8: What tests should be used to monitor response to antibiotic treatment in patients with spine infection?

RECOMMENDATION: Serum C-reactive protein (CRP) levels are closely related to clinical response in spine infections and are therefore the preferred marker in monitoring the therapeutic course.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

In two large retrospective studies including 363 patients, criteria for discontinuation of treatment included CRP normalization in addition to resolution of clinical symptoms [1,2]. A weekly decrease of CRP by 50% has been suggested as a therapeutic response in the retrospective study population [3].

Lack of normalization of serum CRP levels is a predictor of treatment failure and warrants additional evaluation, as demonstrated both by a retrospective cohort including 79 patients and a prospective study including 21 patients followed for postsurgical wound infections of the spine [4–5].

Moreover, in a retrospective analysis of 61 patients treated for bacterial spondylodiscitis, the only predictor for de-escalating intravenous therapy to highly bioavailable oral agents was a CRP decrease by week 2 of therapy [6].

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QUESTION 9: Which is the best alternative antimicrobial therapy for fluoroquinolone-resistant gram-negative acute post-surgical infection in spinal surgery?

RECOMMENDATION: The choice of antimicrobial therapy should be based on the pathogen and the susceptibility profile.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

Currently, over 30% of all spinal surgical site infections (SSIs) are secondary to gram-negative bacteria (GNB). Focusing on acute post-surgical infection of spinal surgery, there is no published experience regarding the best therapeutic strategies in case infection by GNB resistant to quinolones. Thus, the treatment criteria used in these cases are the same as those used in the case of fluoroquinolone-resistant GNB periprosthetic join infections (PJIs). The importance of using fluoroquinolones in acute PJIs due to gram-negative bacilli has been demonstrated, but limited antimicrobial agents are available in the case of implant-associated infections caused by fluoroquinolone-resistant GNB [1–3].

The most commonly used antibiotics in the event of fluoroquinolone resistance are β-lactams and carbapenems with or without anti-pseudomonal activity [4]. Grossi et al. described the outcome of 76 GNB-PJIs managed with a curative intent and in their experience, intravenous β-lactams throughout treatment duration (median 90 days) results in an effective alternative to fluoroquinolones [5].

Therapeutic alternatives to β-lactams have been poorly assessed. Cotrimoxazole, which can be switched to oral therapy, has been successfully used in some of these cases [1–6]. Other possible alternatives are the "recovery" of the use of less conventional antibiotics, such as colistin and fosfomycin [7–9]. Colistin shows good spread in bacterial biofilm and a synergistic effect when combined with other antibiotics, especially β-lactams, and has been demonstrated to be effective in vitro against *P. aeruginosa* and enterobacteria [7]. Corvec et al. compared the activities of fosfomycin, tigecycline, colistin and gentamicin (alone and in combination), against a CTX-M15-producing strain of *Escherichia coli* in vitro and in a foreign-body infection model [10]. Fosfomycin was the only single agent, which was able to eradicate *E. coli* biofilms (cure rate, 17% of implanted, infected cages). In combination, colistin plus tigecycline (50%) and fosfomycin plus gentamicin (42%) cured significantly more infected cages than colistin plus gentamicin (33%) or fosfomycin plus tigecycline (25%) ($p < 0.05$). The combination of fosfomycin plus colistin showed the highest cure rate (67%), which was significantly better than that of fosfomycin alone ($p < 0.05$). Therefore, the authors conclude that the combination of fosfomycin plus colistin is a promising treatment option for implant-associated infections caused by fluoroquinolone-resistant GNB, but the effectiveness of this combination should be assessed in vivo.

Other potential therapeutic alternatives are combinations that include tigecycline or rifampin for their demonstrated in vitro synergism with several drugs. Tigecycline has been used for carbapenemase-producing gram-negative PJIs, although bone concentrations of the drug are usually lower than the minimum inhibitory concentrations of these bacteria [11]. Drapeau et al. recently described a literature review of 19 clinical studies on the use of rifampin in treatments for multidrug resistant gram-negative (MDRGN) bacterial infection [12]. Nonetheless, the real clinical benefit of using rifampin-containing therapies for MDRGN bacteria in terms of clinical outcome and survival rates remains to be defined.

The development of new agents (ceftazidime/avibactam, aztreonam/avibactam, cefiderocol, ceftolozane/tazobactam) with activity against MDRGN bacteria will provide important therapeutic options for clinicians, but definitive data showing clinical efficacy is currently lacking [13].

The efficacy of intrawound tobramycin powder in terms of eradicating a known bacterial contamination in an *Escherichia coli*-infected rabbit spinal implantation model was assessed, with the researchers concluding that intrawound tobramycin eliminated *Escherichia coli* surgical site contamination [14].

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Authors: Steven Schmitt, Christopher Kepler

QUESTION 10: Is there a difference in the efficacy of vancomycin beads versus vancomycin powder for spinal implant infections?

RECOMMENDATION: It is unclear whether there is a difference in the efficacy of vancomycin beads versus vancomycin powder for spinal implants infections.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Currently, there are no studies comparing or individually evaluating the efficacy of vancomycin powder and vancomycin beads for the treatment of infections following spinal instrumentation.

3.3. TREATMENT: IMPLANTS

Authors: Pouya Alijanipour, Caroline Granger

QUESTION 1: Should a cage be removed in patients with postoperative spine infection?

RECOMMENDATION: No. The interbody cage can be maintained in the absence of clinical and radiographic signs of loosening or displacement of the cage or compression on neural and vascular structures. However, the cage should be removed if the infection persists despite salvage attempts consisting of irrigation and debridement procedures combined with intravenous antibiotic treatment.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 73%, Disagree: 0%, Abstain: 27% (Super Majority, Strong Consensus)

RATIONALE

The incidence of surgical site infection in the presence of an interbody cage depends on various factors including the type of approach (anterior, posterior or lateral) and whether the cage is stand-alone or associated with posterolateral instrumentation fusion. Series with stand-alone posterior lumbar interbody fusion (PLIF) or anterior lumbar interbody fusion (ALIF) have lower infection rates (up to 3%) compared to those with long constructs in degenerative adult scoliosis (up to 11%) [1]. On the other hand, adding interbody fusion to posterolateral spinal fusion can be a risk factor for infection and a series of posterolateral fusion with interbody fusion reported higher incidence of surgical site infection compared to those without interbody fusion, most probably due to prolonged surgical procedure, increased blood loss and tissue damage associated with interbody fusion (0.3% versus 1.4%) [2].

Spondylodiscitis at the site of an interbody fusion can present with or without signs of superficial wound infection. If superficial infection does not exist, deep infection can be underestimated or ignored initially due to late presentation. In one report, the average time to diagnosis for spondylitis in patients with PLIF was 164.5 days (range 10–410 days) and time to diagnosis longer than three months was the only predictive factor of failure of intravenous antibiotic treatment and need for implant removal [3]. Moreover, the intervertebral disc tissue is a naturally avascular tissue, limiting the efficiency of immune response as well as efficiency of antibiotics for eradication of infection. Delayed treatment of cage infection can be associated with the risk of extension of infection to the neural elements as well as to the vital retroperitoneal organs and major vessels with disastrous consequences [4].

Cage removal is associated with a risk of interbody space collapse, foraminal narrowing, loss of alignment, progression of deformity, loss of fixation, instability and pseudoarthrosis [5]. On the other hand, inappropriate cage retention can establish bacterial colonization and biofilm formation on the surface of the implants, and diminishes the efficacy of antibiotic treatment [6]. Time of presentation (early versus late postoperative infection), chronicity and severity of symptoms are other considerable factors [7,8].

According to the published case series, in most cases of interbody cage infection, the cage can successfully be retained with an initial salvage attempt consisting of irrigation and debridement procedures combined with antibiotic treatment [1,9–15]. Although, there is no agreed definition criteria for failure of salvage treatment, the following conditions have been considered as indication of cage removal: presence of discitis, osteomyelitis, signs of cage loosening, epidural abscess, extension of infection to soft tissues and presence of bone loss [1,4,8]. Most of these criteria are based on the findings of advanced imaging such as computed tomography and magnetic resonance imaging. One study presented 10 cases with uncontrolled infection of interbody cage, all of which were placed via posterior approaches. In 9 out of 10 cases, solid bone fusion was achieved via an anterior procedure consisting of cage removal and the use of autogenous iliac bone graft to fill the interbody space [16]. An anterior approach for removal of a posteriorly-placed interbody cage prevents complications associated with epidural scar tissue and fibrosis due to the inflammatory response to the original surgery and infection process [16].

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QUESTION 2: Is there a length of time of infection beyond which instrumentation should be removed?

RECOMMENDATION: The data suggests that early infection can commonly be treated with implant retention and debridement followed by intravenous (IV) antibiotics and common oral antibiotic treatment. If the patient has achieved spinal fusion, the implants can be safely removed. In the setting of pseudarthrosis, thought should be given to removal of implants to eradicate infection followed by re-instrumentation.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

The primary goals of treating postoperative spinal surgical site infections (SSIs) are to eradicate the infection, maintain stability and achieve fusion (when warranted). While the decision to retain existing instrumentation in the setting of an acute infection may be necessary for maintaining stability or promoting fusion, this may jeopardize the surgeon's ability to completely eradicate the SSI. The preponderance of available evidence suggests the ability to both retain hardware and successfully eradicate the infection depends on the acuity of the presentation, with early diagnoses of SSI (within 30 to 90 days after index procedure) having higher rates of successful retention after debridement and IV antibiotics, while deep infections over one year commonly require removal.

Several studies have demonstrated successful eradication of infection with debridement and hardware retention for early-onset SSI. Patel et al. reviewed surgical debridement and retention of instrumentation in 17 patients with SSI after spinal arthrodesis ranging from 1 to 6 weeks after the index procedure, noting eradication of infection in all patients and successful fusion in 15 of 17 (88.2%) [1]. Sierra-Hoffman et al. reported successful instrumentation retention with early onset (< 30 days) SSIs with debridement and long-term antibiotics alone, noting eradication of infection in 17 out of 19 (89.5%) patients. However, six of the seven late infections (> 30 days) ultimately required instrumentation removal for eradication of the infection [2].

Pull ter Gunne et al. noted that their management of SSI involved aggressive debridement (89.3%) with hardware retention (if stable) and revision of hardware (if unstable), followed by an average of 40 days of antibiotics. With this protocol, 76% of their deep infections were eradicated with a single debridement, although no comment was made about the chronicity of the SSI prior to reoperation [3]. Kowalski et al. reported on 30 acute SSIs (< 30 days) with 80% successfully retaining implants with surgical debridement and IV antibiotics followed by oral suppressive antibiotics [4]. Tominaga et al. reviewed risk factors for unavoidable removal of instrumentation after SSI < 90 days, finding that 12 of 16 cases successfully retained implants after debridement and IV antibiotics, but noted that 3 of 4 failures grew methicillin-resistant *Staphylococcus aureus* (MRSA) on operative cultures, compared with only 1 of 12 successfully-treated cases diagnosed with MRSA [5]. Nunez-Pereira et al. reported 43 patients with acute SSI after posterior spinal fusion requiring debridement and IV antibiotics for at least 8 weeks, finding 90.7% survival (survival to follow-up timepoint with avoidance of implant removal) at 6 months, 85.4% at 12 months, and 73.2% out to 4 years [6]. Multivariate analysis revealed a significant risk of treatment failure in patients who developed sepsis (hazard ratio 12.5 [95% confidence interval 2.6 to 59.9]; p < 0.001) or who had more than three fused segments (hazard ratio 4.5 [95% confidence interval 1.25 to 24.05]; p = 0.03) [1].

Accurately predicting the number of required debridements to eradicate the SSI can be challenging. Thalgott et al. identified that initial debridement culture results and the patient's comorbidities, including systemic disease, immunocompromise and malnourishment, are prognostic for the number of debridements required. Healthy patients with less virulent bacteria commonly required a single debridement, while immunocompromised hosts, multiple and/or more virulent organisms, and polymicrobial infections often require multiple debridements [7]. DiPaola et al. evaluated risk factors predicting multiple debridements, identifying MRSA and distant site infection as the strongest predictors, and diabetes mellitis, the presence of instrumentation, use of allograft and posterior lumbar spine location also displaying significant associations [8].

Conversely, delayed diagnoses of SSI commonly require implant removal for successful infection eradication. Hedequist et al. found all 26 cases with SSIs presenting greater than 3 months postoperatively required implant removal to definitively clear the infection [9]. Similarly, Kowalski et al. reported 7 out of 13 late diagnoses of SSI (> 30 days) failed debridement and initial implant retention, requiring secondary surgery for implant removal [4]. Tsubouchi et al. noted that although 29 out of 43 patients successfully retained spinal implants for SSI < 30 days postoperatively, only 4 of 12 patients diagnosed later than 30 days and 0 of 4 patients diagnosed later than 90 days successfully retained implants [10]. Garg et al. reported on 42 patients with deep infection more than 1 year postoperatively after spinal fusion, noting that 41 required implant removal and retention attempted in 1 patient failed. Additionally, 27 of the 42 patients showed *C. acnes* on intraoperative cultures [11].

Ho et al. reviewed their experience with pediatric SSI after instrumented fusion for scoliosis, noting that 43 out of 53 (81%) patients had retained implants at their first irrigation and debridement. They found a significant increase in secondary debridement required with implant retention (47%) in comparison to implant removal at the first irrigation and debridement (20%). However, implant removal was associated with a 10-degree or greater curve progression in 60% of patients [12]. Balancing the need for spinal stability and prevention of deformity progression or pseudarthrosis against a more complete eradication of infection remains a case-by-case decision guided by surgeon experience.

Mok et al. reviewed the functional impact of infection after posterior spinal fusion with 12 early (< 90 days) and 4 late (> 90 days) SSIs undergoing debridement with retention of instrumentation, and reported no significant difference in long-term SF-36 outcomes compared with non-infected controls at an average follow-up of 56.7 months [13]. Kuhns et al. similarly compared quality of life (QOL) scores between infected posterior cervical fusions requiring reoperation to noninfected matched controls. While the total projected costs were increased ($21,778 vs. $9,159) and 6-month QOLs were significantly lower for the infected cohort, no significant differences were found in QOL outcomes at the 12-month follow-up [14].

Recent literature has questioned the significance of time-based decision-making for implant removal following SSI and instead has turned to advanced imaging to understand the causes of implant retention failures. Kanavama et al. evaluated preoperative magnetic resonance imaging (MRIs) in SSIs, noting that once vertebral osteomyelitis and/or intervertebral abscess were evident in MR images, all the hardware should be removed [15]. Six of seven patients without osteomyelitis or intervertebral abscess successfully retained implants, while 9 of 13 patients with osteomyelitis or intervertebral abscess ultimately required implant removal and three of four patients who retained implants resulted in loss of fixation stability [15].

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Author: Wesley Bronson

QUESTION 3: Should bone graft be removed in patients with postoperative spine infection? If yes, should a distinction be made between allograft and autograft?

RECOMMENDATION: Bone graft need not be routinely removed following irrigation and debridement, especially if partially incorporated. However, loose or purulent graft should be considered for removal. Retained allograft may increase the risk for requiring repeat debridement compared to autograft.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 87%, Disagree: 0%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

No literature could be found that directly stratified patients who had bone graft retained versus removed. Weinstein et al. studied 46 postoperative infections in 2,391 patents [1]. In their regimen, bone graft material that appeared viable was left in place and instrumentation was retained as well. After six weeks of antibiotics, all of the wounds healed. Massie et al. similarly reported that bone graft may be retained and rarely is it necessary to remove all bone graft [2]. Ahmed et al. also showed in their retrospective review that debridement and antibiotics with implant and bone graft retention (allograft and autograft) can result in complete eradication of infection [3].

Nonetheless, bone graft loosened by irrigation may be removed. It seems rational that unincorporated bone graft and loose, dead bone serves as a continued nidus for infection and as such should be removed [4]. Multiple authors thus recommend thorough irrigation and debridement with removal of nonviable, purulent and loose graft material. However, this appears largely based upon intuition and not strict evidence.

There is limited evidence that perhaps autograft is better tolerated in the setting of an infection. Dipola et al. created a predictive model to differentiate patients requiring one versus multiple debridements [5]. The use of bone graft rather than autograft was shown to be predictive of requiring multiple debridements. Perhaps, therefore, closer attention ought to be given to the viability and infection burden in patients with allograft. However, no specific recommendations can be given and this should be considered on a case-by-case basis, with considerations of host status, infectious organism and infection burden.

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Author: Yvonne Achermann

QUESTION 4: What are the indications for implant retention or removal of hardware in spinal infections?

RECOMMENDATION: In early or acute infections, debridement with retention of the implant might be possible and should always be favored, as removal of the implant carries a great risk for non-fusion despite the risk of chronic low-grade infections with possible implant loosening. In late infections, removal is recommended if feasible.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 87%, Disagree: 7%, Abstain: 6% (Super Majority, Strong Consensus)

RATIONALE

Similar to periprosthetic joint infections (PJI), several authors recommend that in early spinal implant-associated infections (within one month after surgical treatment or symptom duration less than three weeks), a debridement with retention of the implant constitutes a sufficient treatment strategy [1–5]. However, their recommendation is based on a retrospective, small case series of patients. There are also reports describing continuous irrigation in early infections [6,7], but no controlled studies with non-continuous irrigation are published.

In chronic infections, which are often caused by low-grade pathogens, such as coagulase-negative staphylococci or *Cutibacterium acnes*, removal of implants is regarded as the treatment of choice [3,8–10]. Infections with low-grade pathogens often present in a delayed fashion so that the implant-associated biofilm is mature and bacteria in the biofilm cannot be killed by antibiotics only or debridement with retention of the implant. In addition, patients with chronic infections often present with pseudarthrosis [11]. Hedequist et al. retrospectively reported on 26 chronic infections in which curing was only achieved after removal of the implants with prior unsuccessful treatment attempts with implant retention [12]. In six patients, hardware reimplantation was needed due to progression of the underlying deformity (curve progression). Implant removal carries the risk of disc collapse, lack of fusion, loss of normal lordosis and pseudarthrosis [3,13], which have to be considered.

There are no recommendations as to whether only the dorsal instrumentation or the interdiscal cage should be removed as well for successful treatment. In addition, no prospective clinical trials comparing removal versus retention of the implant in chronic infections exist. Lall et al. nicely summarized treatment regimens of deep wound infections after spinal instrumentation [14].

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Authors: Barrett Woods, Maja Babic

QUESTION 5: Is there a role for one-stage exchange of hardware in the presence of spinal infections?

RECOMMENDATION: There is insufficient data on one-stage exchange of hardware in the presence of spine infection.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Evidence supports debridement and implant retention in early implant-associated infections. In delayed implant-associated spine infections, evidence favors hardware removal followed by a course of antibiotics. Even if solid fusion is present, significant loss of correction can occur, posing the question of whether one-stage exchange of hardware would be adequate [1]. It is established that placing spinal instrumentation into an infected spine is safe when necessary for spinal stability and eradication infection, with low recurrence and reoperation rates [2]. Data on hardware one-stage exchange in deep infections with instrumentation is lacking.

Infection following instrumented spinal fusion can result in significant morbidity to the patient, resulting in prolonged hospitalization, chronic pain and need for revision surgery. In addition to the morbidity, the economic impact of this type of infection to the healthcare system and patient cannot be overstated. Several risk factors associated with the development of surgical site infection (SSI) following instrumented spinal fusion have been identified [2–4]. Management of superficial infection typically consists of oral or intravenous (IV) antibiotics, with surgical intervention reserved for failure of medical management, symptomatic deep infections or draining wounds with soft tissue compromise. Treatment of deep infections surgically is complicated by the presence of spinal instrumentation. Eradication of infection is the primary goal of surgery, however premature removal of instrumentation can result in pain, pseudoarthrosis and deformity [5–7].

Several series have been published illustrating successful treatment of deep wound infection with irrigation debridement and retention of original instrumentation [8–14]. Picada et al. published on a series of 26 patients with infection following instrumented spinal procedures, with 24 (92.3%) successfully treated with surgical debridement, intravenous antibiotics, nutrition optimization and primary or delayed secondary closure [13].

Kowalski et al. retrospectively reviewed the management of 81 patients with infections following spinal instrumentation. The cohorts were defined by early and late onset infection [9]. Of the patients with early onset infection, 28 of 30 were treated with irrigated debridement and retention of hardware with predicted probability of treatment success at two years being 71%, while patients with late onset infections required removal of hardware to achieve an 84% probability of treatment success at two years. Maruo et al. retrospectively reviewed a series of 225 consecutive patients with SSIs following spinal surgery [10]. Of those, 126 or 76% were successfully treated with surgical debridement, IV antibiotic therapy and retention of hardware. Failure of this treatment strategy was associated with late infection, long constructs with pelvic fixation, *Propionibacterium acnes* speciation and poly-microbial infection.

Nunez-Pereira et al. published on a series of 43 consecutive patients with SSI treated with surgical debridement and targeted antibiotic therapy with retention of original instrumentation [11]. At a 26-month follow-up, 10 patients (23.3%) failed, requiring removal of hardware, or died. Multivariate analysis found treatment failure associated with sepsis and long constructs (> three levels fused). Tominaga et al. published a retrospective series of 16 consecutive patients who developed SSI following spine instrumentation over an eight-year span [15]. Twelve of the 16 cases (75%) were successfully treated with retention of hardware, with failure associated with long instrumented constructs, previous spinal surgery, low preoperative hemoglobin, high preoperative creatinine and methicillin-resistant *Staphylococcus aureus* (MRSA) speciation. DiPaola et al. developed a predictive model determining the need for single versus multiple irrigation and debridement procedures to successfully eradicate postsurgical spinal infection [8]. The authors identified MRSA-positive cultures, bacteremia, non-autogenous bone graft and diabetics as predictive for requiring multiple debridement procedures. Vacuum-assisted closure (VAC) can be used to help facilitate wound healing following irrigation and debridement with hardware retention for spinal infection [16].

There are several studies illustrating the successful management of SSI following spinal instrumentation with surgical debridement, IV antibiotic therapy and primary or delayed secondary closure. Factors consistently associated with treatment failure included late infection, long constructs with pelvic fixation, *C. acnes*/MRSA speciation and bacteremia. Patients with these characteristics should likely have removal of hardware in addition to surgical debridement. Multiple debridement procedures may be required to successfully treat the infection, which can be assisted by the use of a wound VAC.

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3.4. TREATMENT: WOUND CARE

Authors: Carles Pigrau, Gregory Schroeder

QUESTION 1: Should infected wounds undergo primary closure or a two-stage closure?

RECOMMENDATION: The current recommended practice for spine wounds remains primary closure in the majority of postoperative infections. However, there may be circumstances when primary closure of the wound may not be possible or preferred. This may include patients with grossly contaminated traumatic wounds, patients with persistent wound drainage when attempts to address drainage have failed or patients with severe soft tissue loss when primary closure is not possible.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Following surgery, wounds are typically closed in a primary fashion. Alternative methods of wound closure include secondary closure and delayed primary closure. Secondary closure is when wounds are left to close naturally on their own. Delayed primary closure (DPC), a combination of secondary and primary closure, is when a wound is cleaned and left open until infection is controlled, followed by surgical closure of the wound. Delayed primary closure is only used on occasion, typically involving contaminated traumatic injuries.

In their prospective randomized study, Singh et al. found that patients undergoing delayed primary closure of contaminated abdominal wounds related to hollow viscus perforation had lower infection rates (17.5%) and shorter hospital stays (18.1 days) when compared to patients undergoing primary closure (42.5% infection and 20.7 days) [1]. Chiang et al. found a similar result for treatment of perforated appendicitis. Patients randomized to primary closure had an infection rate of 38.9% and an 8.4-day length of stay, while patients randomized to delayed primary closure had an infection rate of 2.9% and a 6.3-day length of stay [2].

DPC has also been shown to result in no long-term issues and not be associated with a higher incidence of complications in pediatric liver transplant recipients [3]. Orthopaedic surgeons are familiar with DPC in the context of fasciotomy wounds in patients with compartment syndrome when delayed primary closure is utilized [4,5].

There are, however, no high-level studies related to the role of DPC in spine surgery. In the absence of concrete evidence, and in borrowing from general surgery and other fields of orthopaedics, we feel that primary closure of a wound is the most preferred method of dealing with wound issues in spine patients. However, there may be circumstances when primary closure of the wound may not be possible or preferred. This may include patients with grossly contaminated traumatic wounds, patients with persistent wound drainage when attempts to address drainage have failed and in patients with severe soft tissue loss when primary closure is not possible.

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Author: Wesley Bronson

QUESTION 2: What is the indication for muscle advancement flaps in patients with spinal infections?

RECOMMENDATION: **Muscle advancement flaps are useful to help close wounds with exposed hardware as well as those which fail local treatment/vacuum-assisted closure (VAC) therapy and to help improve infection eradication.**

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Multiple risk factors exist for wound complications following spinal surgery, including diabetes, chronic obstructive pulmonary disease, resection of neoplasm with excision of significant soft tissue and prior radiation. Additionally, infection is often complicated by loss of soft tissue and poor tissue viability, which leads to an inability to close the wound overall, resulting in exposed hardware [1,2].

Even if the wound is able to be closed primarily or following VAC therapy, it is important to recognize that the same factors that led to the infection and wound breakdown in the first place still exist [3]. To that end, local or vascularized muscle flaps provide multiple advantages over simple wound closure or delayed primary closure. Muscle flaps have been shown to increase blood flow and oxygen delivery, and decrease bacterial load [4–6].

It seems rational that wounds that are completely unable to be closed due to large soft tissue defects with exposed hardware or wounds that fail to close following VAC therapy are reasonable indications for flap coverage. But, the absolute indication for flap coverage following wound debridement in an otherwise closeable wound remains unclear. Multiple authors argue that it remains a reasonable option versus irrigation and debridement with immediate or delayed primary closure.

Dumanian et al. reviewed their experience with flap coverage for spinal wounds [7]. Fifteen patients in their group had postoperative wound dehiscence or infection, with 12 patients having exposed hardware. They were treated with either immediate local flap coverage or two to three days of dressing changes followed by flap coverage. Of the surviving 14 patients, 13 had healed wounds at final follow-up, and none required hardware removal. One patient on chronic steroids/immunosuppression had persistent infection treated with chronic suppressive antibiotics.

Chieng et al. performed a systematic review on the use of flaps for management of wound complications [8]. While several case reports and retrospective series present supportive data, the authors note that relying on the data is difficult as no level 1 or level

2 evidence exists. Additionally, there is a lack of comparative studies directly looking at flap coverage versus traditional wound closure techniques.

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Authors: Koji Yamada, Kazuhiro Kohata

QUESTION 3: What is the optimal irrigation solution (volume, type and frequency) during clean or infected spinal surgery cases?

RECOMMENDATION:

1. There is insufficient evidence to recommend for or against normal saline irrigation before closure for the purpose of preventing surgical site infection (SSI) in clean spinal surgery.
2. There is insufficient evidence to support recommendations for optimal volume, type and frequency of irrigation to prevent SSI in clean spinal surgery.
3. Consider the use of irrigation with an aqueous povidone-iodine solution before closure for the purpose of preventing SSI in clean spinal surgery.
4. There is insufficient evidence to recommend for or against chlorhexidine and antibiotic solution irrigation of incisional wounds for the purpose of preventing SSI in clean spinal surgery.
5. There is insufficient evidence to recommend a specific solution (volume, type and frequency) for irrigation in infected spinal surgery.

LEVEL OF EVIDENCE:

1. Consensus
2. Limited
3. Moderate
4. Consensus
5. Consensus

DELEGATE VOTE: Agree: 73%, Disagree: 7%, Abstain: 20% (Super Majority, Strong Consensus)

RATIONALE

1: Irrigation versus no irrigation

No randomized controlled trials (RCTs) or observational studies have compared incisional wound irrigation with normal saline versus no irrigation in clean spinal surgery.

One retrospective observational study evaluating 1,831 posterior lumbar interbody fusion (PLIF) procedures demonstrated a significantly higher risk of SSI with no local bone irrigation compared to those with local bone irrigation in multivariate analysis (odds ratio (OR): 5.248, $p = 0.001$) [1]. Two retrospective observational studies demonstrated no significant association between interbody irrigation with SSI compared with no interbody irrigation in those undergoing PLIF and lumbar microdiscectomy [1,2].

2: Optimal volume, type and frequency of irrigation for clean spinal surgery

No RCT has compared the amount of normal saline for irrigation to prevent SSI in spinal surgery. One observational study including 223 consecutive spinal operations in a single university hospital demonstrated a significant association with prevention of SSI (OR 0.08, 95%, confidence interval (CI) 0.01 to 0.61) with sufficient amount of saline (mean > 2,000 ml per hour compared with < 1,000 ml per hour) in a multivariate analysis [3].

No RCT or observational study has compared the frequency of irrigation to prevent SSI in spinal surgery.

A very low quality of evidence from two observational studies demonstrated a benefit of pulse pressure irrigation compared to bulb syringe irrigation with normal saline [4,5]. One study showed an advantage of decreasing wound contamination rate in PLIF surgical procedures (OR:6.35, $p = 0.046$) [4]. Another study showed significant decrease of postoperative infection by ten-fold (11% [28/261] vs. 0.7% [2/263], $p < 0.001$) by using pulsatile irrigation with vancomycin and ceftazidime prophylaxis for posterior spinal fusion surgeries in adolescent idiopathic scoliosis patients [5].

3 and 4: Optimal solution for clean spinal surgery

There is moderate-quality evidence from two RCTs and two observational studies that povidone iodine irrigation has a significant benefit in reducing SSI risk in patients with primarily closed surgical incisions when compared to conventional normal saline wound irrigation [6–9]. In one RCT focusing on primary instrumented lumbosacral posterolateral fusion performed by the same surgeon, SSI was significantly lower in those who underwent 0.35% povidone-iodine irrigation compared with normal saline irrigation (0% [0/120] vs. 4.8% [6/124], p = 0.029), with no significant difference in fusion rate, wound healing, improvement of pain score, function score and ambulatory capacity [6].

In another RCT focusing on spinal surgery, SSI was significantly lower in those who underwent 0.35% povidone-iodine irrigation compared with normal saline irrigation (0% [0/208] vs. 3.4% [7/206], p = 0.0072) [7]. In one observational study comparing before and after the application of combination of 0.3% betadine irrigation with intra-wound vancomycin (VCM) powder (1 gm), the incidence of SSI significantly decreased after intervention (1.3% [15/1173] vs. 2.4% [30/1,252], p = 0.042) with a protective effect in multivariate analysis (OR 0.23, 95% CI: 0.06-0.86; p = 0.0287) [8]. In another observational study involving 950 spinal surgeries comparing before and after application of povidone-iodine and hydrogen peroxide solution irrigation, those irrigated with povidone-iodine and hydrogen peroxide solution were less likely to develop SSI compared with pre-intervention period (0% [0/490] vs. 1.5% [7/460]) [9].

No RCT or observational study has compared chlorhexidine or antibiotic solution irrigation to normal saline irrigation to prevent SSI in spinal surgery.

5: Optimal irrigation for infected spinal surgery

No RCT or observational study has compared incisional wound irrigation with no irrigation in infected spinal surgery.

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Author: Carles Pigrau

QUESTION 4: Is negative pressure wound therapy (NPWT) effective in the treatment of wounds that are left to heal by secondary intention?

RECOMMENDATION: **There is no evidence that NPWT is superior to conventional standard dressing changes in the treatment of wounds that are left to heal by secondary intention.**

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 60%, Disagree: 20%, Abstain: 20% (Super Majority, Weak Consensus)

RATIONALE

Animal studies have shown that sub-atmospheric pressure improves the local wound environment through both direct and indirect effects. Sub-atmospheric pressure accelerates healing and reduces the time to wound closure and the incidence of wound infections [1,2]. NPWT removes interstitial fluid and improves lymphatic drainage and microvascular blood flow. It increases oxygen and nutrient delivery in the wound, facilitates removal of metabolic byproducts, increases granulation tissue formation and ultimately accelerates wound healing. Moreover, by isolating the wound from the surrounding environment, NPWT may reduce the colonization of the wound by bacteria and avoid superinfections, particularly in areas with high skin contamination rates such as the perineal and lower back spine area.

Predominantly observational studies, but also small trials (low quality of evidence), have suggested that rates of surgical site infection (SSI) may be lower if NPWT is used instead of conventional wound dressings [3]. In a meta-analysis of six randomized control trials including a systematic review, it was observed that the risk of SSI was reduced when NPWT was used (odds ratio 0.56, 95% CI 0.32 to 0.96) in both clean and clean-contaminated procedures. However, results were no longer significant for orthopaedic/trauma surgery [3]. In a Cochrane meta-analysis that compared NPWT with other types of wound dressing for persistently-draining wounds in skin graft patients, in orthopaedic patients undergoing arthroplasty and general/trauma surgery patients it was concluded that there is no evidence for the effectiveness of NPWT on the complete healing of wounds expected to heal by primary intention [4]. An up-to date systematic review in trauma patients concluded that, based on available observational studies, NPWT [5] was safe and showed an efficacy comparable to standard dressings [6]. The primary clinical advantages of NPWT in the trauma population are its ease of application, decreased number of dressing changes and reduction in the complexity of subsequent reconstructive procedures [7–11].

In a 2013 systematic review of NPWT for spinal wounds, no randomized clinical trials were found that addressed the use of NPWT to treat wound healing or spine SSIs, nor as prophylactic wound treatment to prevent wound breakdown and infection [12]. The duration of NPWT therapy and the number of debridement and irrigation procedures performed before the definitive wound closure operation were variable. After this review, an additional non-comparative study [12] showed the benefits of this therapy among only 6 of 317 infections after surgery for spinal stenosis. An average of 5.1 debridement and irrigation procedures were performed before the definitive wound closure operation. Vacuum-assisted closure dressings were changed at 3-day intervals and the median duration was 15 days (range 9-24).

After the revision published in 2013, only one longitudinal cohort study addressed NWPT use as a prophylactic therapy for spinal wounds. It is a well-designed, retrospective longitudinal study, which includes 160 adult patients with thoraco-lumbar spine deformity undergoing multi-level thoraco-lumbar fusion [13]. A 50% decrease in the incidence of wound dehiscence was observed in the NPWT cohort (46 cases) compared to the non-NPWT cohort (114 patients) and the incidence of postoperative SSI was significantly lower (10.6% vs 14.9%, $p = 0.04$).

In conclusion, prophylactic use of NWPT may significantly reduce wound dehiscence and wound infection after long-segment thoraco-lumbar spine fusion. There is no further evidence addressing the superiority of NWPT therapy compared to standard dressings. NPWT is safe in cases without dural leaks, easy to apply, and it decreases the number of dressing changes and reduces the complexity of wound closure. All these factors favor its use in selected cases.

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