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How to prevent post-operative surgical-site infection after posterior thoracolumbar or lumbar surgery for degenerative spine conditions?

A Systematic Review with Meta-Analysis

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STATEMENT OF INTEGRITY

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration.

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RESUMO

Como prevenir a infeção pós-operatória do local cirúrgico após cirurgia toracolombar ou lombar posterior por patologia degenerativa da coluna vertebral? Uma revisão sistemática com Meta-análise

Introdução: A infeção do local cirúrgico (ILC) é a terceira complicação mais comum após cirurgia da coluna vertebral, estando frequentemente associada a uma elevada morbilidade e mortalidade e a custos acrescidos. Neste sentido, as medidas profiláticas - pré, intra e pós-operatórias - são um foco importante para reduzir as taxas de infeção do local cirúrgico.

Objetivo: O principal objetivo foi avaliar sistematicamente a literatura para aferir a evidência atual sobre estratégias profiláticas contra a ILC após cirurgia, em adultos, por patologia degenerativa da coluna vertebral toracolombar, lombar ou lombossagrada, através de uma abordagem posterior.

Métodos: As pesquisas, realizadas por 2 autores, abrangeram as bases de dados PubMed e EMBASE até 18 de novembro de 2023. Foi efetuada uma revisão crítica de todos os títulos, resumos e artigos completos. Foram incluídos nesta revisão artigos cujos resultados primários foram a ocorrência de ILC pós-operatória, com ou sem estratégias preventivas, antes/após/durante cirurgia toracolombar realizada através de uma abordagem posterior para o tratamento de patologias degenerativas, tendo sido realizada uma meta-análise.

Resultados: Vinte e três estudos preencheram os critérios de inclusão. A taxa global de infeção foi de 2,94%. No período pré-operatório, a utilização de pensos anti-sépticos impregnados em iodopovidona diminuiu significativamente a taxa de ILC, bem como os esquemas de controlo da glicemia com insulina e com hipoglicemiantes orais. No período intra-operatório, vários métodos de prevenção registaram reduções estatisticamente significativas na taxa de ILC, com destaque para a vancomicina em pó, que apresenta a evidência mais forte. O uso de antibióticos por menos de 3 dias no período pós-operatório associou-se também a uma menor incidência de ILC.

Conclusões: Várias estratégias parecem promissoras na prevenção das ILC, no entanto, a utilização de vancomicina em pó é a mais estudada na literatura e com maior evidência de mitigação da infeção. São necessários mais estudos de elevada qualidade para determinar a sua quantidade ideal e chegar a conclusões fiáveis e definitivas sobre as restantes medidas preventivas.

Palavras-chave: Coluna vertebral; Toracolombar; Lombar; Torácica; Lombossagrada; Infeção; Posterior.

ABSTRACT

How to prevent post-operative surgical-site infection after posterior thoracolumbar or lumbar surgery for degenerative spine conditions? A Systematic Review with Meta-Analysis

Introduction: Surgical site infection (SSI) is the third most common complication after spinal surgery, often associated with significant morbidity and mortality, and increased costs. For this reason, prophylactic measures – preoperative, intraoperative and postoperative – are an important focus to reduce SSI rates.

Purpose: We aimed to systematically evaluate the literature to assess the current evidence on prophylactic strategies against SSI in thoracolumbar, lumbar or lumbosacral surgery in adults for degenerative spinal conditions through a posterior approach.

Methods: Database searches were conducted in PubMed and EMBASE databases by 2 reviewers up to November 18, 2023. A critical review of all titles, abstracts and full texts took place. Studies whose primary outcomes were occurrence for post-operative SSI with or without preventative strategies before/after/during thoracolumbar surgery through a posterior approach for degenerative conditions were included and meta-analysis was performed.

Results: Twenty-three studies met the inclusion criteria. The overall infection rate was 2,94%. Preoperatively, the use of povidone-iodine-impregnated antiseptic dressings significantly decreased the SSI rate, as well as blood glucose control schemes with insulin and oral hypoglycemic agents. Intraoperatively, several prevention methods had statistically meaningful reductions on SSI, in particular intrawound vancomycin powder with the strongest evidence. The use of antibiotics for less than 3 days postoperatively had lower rates of SSI.

Conclusions: Several strategies seem promising for preventing SSI, however the use of vancomycin powder is the most studied in the spine literature and with stronger evidence of infection mitigation. Further high-quality studies are necessary to determine its optimal amount and reach reliable and definitive conclusions about other preventative measures.

Keywords: Spine; Thoracolumbar; Lumbar; Thoracic; Lumbosacral; Low back; Lower back; Infection; Posterior.

LIST OF ABBREVIATIONS

CD	Closed drainage
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
ERAS	Enhanced Recovery After Surgery
ICD-9	International Classification of Diseases, 9th Revision system
IL	Iodine Lavage
ILC	Infeção do Local Cirúrgico
I&D	Irrigation and Debridement
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-sensitive *Staphylococcus aureus*
NAPD	Natural Pressure Wound Drainage
NEPD	Negative Pressure Wound Drainage
NPWT	Negative Pressure Wound Therapy
PL	Pulsed Lavage
RR	Risk Ratio
SL	Saline Lavage
SSI	Surgical-site infection

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INTRODUCTION

Surgical site infection (SSI) after spinal surgery is the third most common complication, after pneumonia and urinary tract infections.[1] The incidence of spinal SSI is reported to range between 0.22[2] and 16.1%[3]. Despite advances in surgical techniques and infection control measures to reduce its incidence, including improved operating room ventilation, sterilization methods, barriers, surgical technique and availability of antimicrobial prophylaxis, it remains a considerable concern for healthcare providers and patients alike.[3]

Many studies show that surgical site infections result in increased patient morbidity, mortality, and healthcare costs[4], with the costs of preventable SSIs being estimated to be $166 million to $345 million annually in the United States.[5] The main additional costs are related to reoperation, extra nursing care and interventions, as well as drug treatment costs. The indirect costs, due to loss of productivity, patient dissatisfaction and litigation, and reduced quality of life, have been studied less extensively.[3]

SSIs can worsen the patient's condition, prolong hospital stay, seriously affect patient's prognosis, leading to instrumentation failure, neurological dysfunction, neurologic injury and even death, causing catastrophic consequences for patients and additional physical, mental, and economical burdens.[1] This potentially devastating complication may require further revision surgeries or lead to chronic pain or deformity.[6]

There are variations in the definitions of SSI. For instance, SSI can be defined based on billing codes (International Classification of Diseases, 9th Revision system [ICD-9]), the Centers for Disease Control and Prevention (CDC) criteria for SSI, CDC criteria for deep SSI, and billing codes for irrigation and debridement (I&D) of infection (Current Procedural Terminology).[7]

Bacterial culture indicated that the most common causative microorganisms of SSI in spinal surgery are *Staphylococcus aureus*, and other members of *Staphylococcus* species, such as *Staphylococcus epidermidis*, and methicillin-resistant *Staphylococcus* species.[6]

Surgical site infection after spinal surgery has complex and multifactorial etiologies; therefore, there are numerous opportunities for prevention and risk mitigation.[6]

The type of surgery is perhaps the most notable variable affecting the incidence of SSIs in spinal surgery. Posterior surgical approach is associated with higher infection rates. In contrast, anterior spinal exposures are associated with a reduced risk of infection.[3] Given this difference, we limited our review to studies referring to surgical-site infections following posterior thoracolumbar spine surgeries.

The management of this surgical complications requires a multilevel comprehensive prevention strategy, including risk factor identification and mitigation and perioperative prevention.[1] Prophylaxis of SSI consists of three interconnected but distinct phases: preoperative, intraoperative, and postoperative.[8]

It has been estimated by the Society for Healthcare Epidemiology of America that up to 60% of SSIs are preventable if evidence-based guidelines are followed. For this reason, prophylactic measures – preoperative, intraoperative, and postoperative – are an important focus to reduce SSI rates.[9]

Preoperative period was considered from the decision to operate to entry into the theatre suite, intraoperative period from entry into the theatre suite to leaving the recovery room and postoperative following transfer from the recovery room.[10]

The current body of evidence suggests that a significant level of wound contamination occurs intraoperatively[11] with endogenous patient flora; therefore, much attention has been placed on the preoperative and intraoperative phases.[8]

Since the first systematic review on prophylactic strategies against SSI in spine surgery by Brown *et al.* in 2004, there has been an expansion of the number of preventative measures introduced and studied in the spine literature, most notably intrawound application of vancomycin powder.[9]

Some of the studied strategies to mitigate the SSI risk in the preoperative period to date are optimal preoperative management of chronic diseases, presurgical shaving, preoperative Methicillin-resistant *Staphylococcus aureus* (MRSA) and Methicillin-sensitive *Staphylococcus aureus* (MSSA) screening and treatment of colonization and chlorhexidine showers. Antimicrobial surgical preparation is also fundamental, and the surgical site can be prepared with either povidone-iodine or chlorhexidine.[6]

During surgery, the use of appropriate antibiotic prophylaxis perioperatively, intraoperative temperature regulation, wound irrigation, vancomycin powder, and incision closure with 2-octyl-cyanoacrylate are available to further prevent SSIs.[6]

Some of the postoperative interventions available are the use of intrawound drains, negative pressure wound therapy (NPWT), which is a promising approach for both, the prevention of SSI in high-risk populations and the management of SSI. Wound dressings can include silver-impregnated dressing or Aquaphor dressing that possess antimicrobial properties and promote wound healing. Prevena® is a promising NPWT surgical wound dressing.[6]

The purpose of the present study was to review the literature on surgical-site infection following posterior thoracolumbar or lumbar spine surgeries and investigate which measures can reduce the incidence of infection.

METHODS

Search Strategy and Study Eligibility Criteria

Database searches were conducted in PubMed and EMBASE up to November 18, 2023, using the search string detailed in *Table 1*. Searches were performed without publication date restrictions or filters applied. Manual searches were conducted by screening the reference lists of the included studies and other relevant reviews. Two authors independently screened all database records and performed the manual searches. A third author decided any disagreements. Removal of duplicates was executed with the use of EndNote, requiring manual removal when necessary. Errata/corrections/corrigenda and retractions of the included studies were sought. When available, pre-registered protocols were also retrieved.

We included clinical studies (regardless of randomization procedure), case-control studies and case series. Only studies published in English were considered. Letters, editorials, meeting abstracts, cadaveric studies, animal studies, case studies, commentaries and reviews were excluded. The population was adult patients (of any gender) that underwent thoracolumbar, lumbar or lumbosacral surgery through a posterior approach for the treatment of degenerative spinal conditions, excluding surgery of the cervical spine, as well as combined (anterior and posterior) approaches. Adult deformity cases were considered degenerative conditions and therefore were included in the study. Studies including participants with other surgical indications, such as treatment of traumatic, oncological or infectious lesions were excluded, as well as with other conditions like inflammatory, neuromuscular, congenital spinal deformities or cerebral palsy. The interventions included surgical procedures of thoracolumbar surgery through a posterior approach with or without instrumentation. Only studies whose primary outcomes were occurrence of post-operative surgical-site infection, with or without preventative strategies, before/after/during thoracolumbar surgery through a posterior approach were considered. In studies separating different types of SSI (superficial, deep, organ-space), we considered the total number of infections.

Data extraction

Two independent reviewers screened all titles and abstracts. Titles or abstracts that met inclusion criteria were included for full text review. Two authors collected the data for all outcomes (with a third author providing arbitrage). Collected data included study reference, year, sample size, preventative strategy, cumulative number and percentage of post-operative surgical-site infections.

Categorical data was collected as number and percentage. No continuous data was found in the included studies for SSI prevention. In cases of missing relevant data, the corresponding authors of the included studies were contacted. Otherwise, the methods suggested by Cochrane Handbook were employed.

Strategy for data synthesis

We computed the cumulative number and percentage of post-operative surgical-site infections divided by all participants included in this systematic review. Relative risk (RR) with 95% confidence intervals (CI) were computed for preventative measures reported as dichotomous data. These comparisons were computed with a meta-analysis procedure using a fixed-effects model. The level of statistical heterogeneity was assessed using the I^2 statistics. Subgroup analysis was performed when feasible.

RESULTS

Search results

The search algorithm returned a total of 7443 relevant articles, including the initial database and manual searching, of which 266 were selected for full text review after removal of duplicates and initial screening of titles and abstracts. Thus, a total of 23 articles[12–34] met the eligibility criteria and were included in this systematic review. Reasons for the 243 excluded articles are displayed in *Figure 1*.

The number of patients included in this systematic review was 14248, with an overall infection rate of 2,94%.

Preoperative Prevention Strategy

Tavanaei *et al*.[15] demonstrated a significant reduced rate of SSI with the use of povidone-iodine-impregnated antiseptic dressing applied to the anticipated incision site 12 hours preoperatively, comparing to the control group that merely received standard perioperative care with no additional intervention or placebo (RR=0.25, 95% CI 0.07 to 0.86). No other study included in this systematic review has studied this preventive method.

A retrospective study conducted by Liu *et al*.[24] analysed the incidence of SSI in patients with type 2 diabetes, comparing different preoperative blood glucose control schemes: subcutaneous injection of insulin, combined medication, oral hypoglycemic agent and diet therapy. Preoperative subcutaneous insulin injection scheme significantly reduced the risk of infection, when compared to diet therapy (RR=0.21, 95% CI 0.05 to 0.90) or combined medication schemes (RR=0.16, 95% CI 0.04 to 0.67), but not when compared to oral hypoglycemic agent (RR=0.40, 95% CI 0.09 to 1.85). Likewise, the preoperative use of oral hypoglycemic agent had a significantly lower incidence of SSI, compared to the use of combined medication (RR=0.39, 95% CI 0.16 to 0.93), but not in comparison with diet (RR=0.54, 95% CI 0.23 to 1.25). There were no differences comparing a diet regimen to combined medication (*Table II*).

Other preoperative interventions, such as the application of ERAS (Enhanced recovery after surgery) protocol in Wang *et al.* 2022[17] had no difference in postoperative SSI, comparing to the non-ERAS group (RR=0.76, 95% CI 0.40 to 1.44). Also, a study by Dobzyniak *et al.*[29] compared the use of a single preoperative dose of antibiotics with a multiple dose group, receiving one preoperative and at least three postoperative doses of antibiotics, but statistical analysis of the data showed no difference between the two groups for infection rate (RR= 0.77, 95% CI 0.18 to 3.17).

Intraoperative Prevention Strategy

Six studies looked at the effect of intrawound vancomycin powder in SSI rate.[13,16,18,21,30,32] Three of these studies[13,21,30] used 1 g of vancomycin, one used 2 g[16], and another applied 0.5 g and 1 g of vancomycin to patients with one/two segments and more than two segments, respectively.[32] The use of vancomycin significantly reduced the risk of infection (RR=0.46, 95% CI 0.28 to 0.76; I^2=23%). However, the subgroup analysis showed there is no clear consistency regarding the optimal amount of vancomycin powder that should be used (*Table III*).

Elmadag *et al.*[21] also aimed to determine the effect of local subfascial teicoplanin powder and compare it to vancomycin on infection outcomes. However, the use of 400 and 800 mg of teicoplanin in ≤2 and >2 spinal segment surgeries, respectively, did not lower the incidence of SSI (RR=0.39, 95% CI 0.08 to 1.87). In this study, the comparison between both intraoperative antibiotics also showed no significant difference in SSI prevention (RR=0.51, 95% CI 0.05 to 5.42).

Fei *et al*.[12] compared the effects of various lavage techniques – traditional saline lavage (SL), pulsed lavage (PL), closed drainage (CD), and iodine lavage (IL) – on preventing incision-related infection after posterior lumbar interbody fusion. In this study, we considered SSI as a positive bacterial culture in muscle layer. After analysis, PL, CD and IL groups exhibited a lower positive rate of bacteria in muscular tissues comparing to the SL group (RR=0.13, 95% CI 0.02 to 0.95; RR=0.06, 95% CI 0.00 to 0.99; RR=0.06, 95% CI 0.00 to 0.99], respectively).

Pulsed lavage was also studied in Hsiung *et al.*[25] Both studies[12,25] demonstrated a statistically meaningful reduction in SSI rate (RR=0.25, 95% CI 0.09 to 0.67; I^2=0%). Hsiung *et al*.

aimed to investigate the optimal amount of normal saline for irrigation to prevent postoperative SSI. However, there was no significant difference between a total irrigation of more than 6,000 mL or 2,000 mL (RR=0.34, 95% CI 0.11 to 1.09).

Two studies[19,33] have demonstrated a substantial and significant reduction in the SSI incidence with povidone-iodine wound irrigation as compared to regular saline irrigation (RR=0.12, 95% CI 0.02 to 0.92; I^2=0%). Subgroup analysis showed no significant difference between different concentrations used, 3% and 0.35% (RR=0.24, 95% CI 0.01 to 4.44; RR=0.08, 95% CI 0.00 to 1.40, respectively).

Two studies[26,34] provided information about rifampicin irrigation as a potential preventative measure, showing a significantly lower rate of SSI in those who were given rifampicin (RR=0.34, 95% CI 0.21 to 0.53; I^2=0). Yaldiz *et al.*[26] also looked at the effect of different wound closure techniques, reporting a significantly decreased rate of infection with staples (RR=0.48, 95% CI 0.27 to 0.85). It also demonstrated an association between the occurrence of SSI with the type of suture material used. Vicryl Plus® sutures significantly reduced its incidence, compared to those that did not use them (RR=0.32, 95% CI 0.19 to 0.55). Yet, the rate of wound infections was significantly higher in those who had Prolene® sutures (RR=3.87, 95% CI 2.28 to 6.56). There were no significant differences when Silk was used as a suture material (RR=0.85, 95% CI 0.13 to 5.57). When comparing SSI rates between the three materials, Vicryl® suture had significantly reduced risk of infection in comparison with Prolene® (RR= 0.26, 95% CI 0.15 to 0.44). There were no differences between the other possible comparisons of suture materials. (*Table III*)

Three studies[12,20,26] analysed the effect of closed drainage on infection outcomes, resulting in a lower rate, but without statistical significance and a high heterogeneity, showing some inconsistency between studies (RR=0.77, 95% CI 0.47 to 1.25; I^2=61%). Subgroup analysis of the different drains used (Hemovac drain[26] and Jackson-Pratt drain[20]) also showed no relevant differences (RR=1.11, 95% CI 0.63 to 1.94; RR=0.54, 95% CI 0.13 to 2.24, respectively).

A few studies[14,22,23] found no difference in the incidence of postoperative wound infection between the use of negative versus natural pressure drainage (RR=0.91, 95% CI 0.27 to 3.11; I^2=0%).

Other potential intraoperative preventative measures were also investigated in different studies but with non-significant differences in SSI rate, such as 3% H_2O_2 irrigation[28] (RR=0.59, 95% CI 0.33 to 1.05), the use of fibrin tissue glue, Tisseel,[26] (RR=0.59, 95% CI 0.26 to 1.32), prophylactic intravenous administration of cefazolin[27] (RR=1.06, 95% CI 0.07 to 17.24), the use of an operative microscope or a bio-clean room [27] (RR= 1.66, 95% CI 0.39 to 6.95; RR= 0.76, 95% CI 0.31 to 1.88). Additionally, the use of drapes in Yaldiz *et al*.[26] did not have a significant effect on the infection rate (RR=0.93, 95% CI 0.44 to 1.93). The difference between using iodized drapes in comparison to noniodized ones was also not significant (RR=1.02, 95% CI 0.46 to 2.27).

Postoperative Prevention Strategy

Pei *et al.*[31] looked at the effect of postoperative antibiotic duration, using a 3-day cut-off. Statistically meaningful reduction in SSIs were documented when antibiotics were used for 3 days or less, in comparison to more than 3 days (RR=0.28, 95% CI 0.15 to 0.50).

DISCUSSION

Surgical site infection after spinal surgery is an important and common complication in spinal surgery, with a reported incidence between 0.22[1] and 16.1%.[3] The rate of overall SSI in the present study was 2,95%, which is comparable to that reported in the literature. Several strategies seem promising for preventing SSI, but the main finding of the present study is that the use of vancomycin powder is the most studied in the spine literature and with stronger evidence of infection mitigation. However, there is no clear consistency regarding the optimal amount of vancomycin powder that should be used.

To our knowledge, this is the first systematic review aiming to assess the current evidence on prophylactic strategies against SSI in thoracolumbar, lumbar or lumbosacral surgery in adults for degenerative spinal conditions through a posterior approach.

Preoperative Prevention Strategy

The use of 10% povidone-iodine-impregnated antiseptic dressing applied to the anticipated incision site 12 hours preoperatively may have a role in preventing SSI. However, these results should be read with caution since this preventative strategy was only investigated in one study (n=200) and may thus lack external validity.[15] Other studies [35,36] also support the use of antiseptic dressings for SSI prevention in patients admitted for a total joint hip and knee surgery. A systematic review conducted by Savage *et al*.[37] concluded that the use of a chlorhexidine bathing cloth before surgery may decrease the risk of SSI based on the results of three studies.[35,36,38]

Preoperative blood glucose control schemes in patients with type 2 diabetes can potentially be important preventative measures for surgical site infection, with subcutaneous insulin injection and oral hypoglycemic agent being the most effective, without significant difference between the two.[24] Literature on the correlation between preoperative blood glucose control scheme and postoperative SSI is scarce and controversial. A study in spine surgery, excluded from this systematic review for including other surgery indications than degenerative conditions, showed no statistical difference in SSI rate with insulin use in diabetic patients.[39] Umpierrez *et al.*[40] compared the efficacy of two different insulin regimens in different postoperative complications, including wound infection in patients with type 2 diabetes undergoing general surgery. Basal-bolus insulin regimen with glargine once daily and glulisine before meals improved glycemic control and reduced SSIs, comparing to a sliding scale regular insulin four times daily regimen.

Only one study[17] analysed the application of the ERAS protocol and found no significant difference in the incidence of postoperative SSI before or after its application. The ERAS protocol, initially created in colorectal surgery, is a program with multidisciplinary perioperative management approaches designed to reduce the surgical stress responses and accelerate recovery after surgery.[41] These findings are consistent with a meta-analysis of four studies from Tan *et al*.[42] concluding, with low quality evidence, that ERAS clinical pathways do not seem to reduce the rate of SSI in spine surgery. However, a systematic review by Blood *et al*.[43] found two studies[44,45] in pediatric population estimating that the implementation of different bundle protocols decreased the rate of SSI in both cases. A retrospective study by Chien[46] also analysed the effect of a standardized care bundle consisting of 4 components – perioperative antibiotics use, glycemic control, skin preparation and maintaining intraoperative body temperature -, showing a significantly lower rate in the post-bundle group. Even though these studies combine results of different protocols and procedures, may suggest the potential of some of these preventive measures and the need for more studies with higher quality to provide stronger evidence for spinal surgery.

A study by Dobzyniak *et al*.[29] showed no significant benefit in infection rate with the addition of postoperative antibiotics, when compared to a single preoperative dose of antibiotics. These results are consistent with the ones from a meta-analysis of five studies (n=3070) by Tan *et al*.[42]

Intraoperative Prevention Strategy

Intrawound vancomycin powder has shown to statistically reduce the incidence of SSI. However, there was no clear consistency regarding the optimal dosage.[13,16,18,21,30,32] Alemán-Villalón *et al*.[13] demonstrated that 1 g of local vancomycin powder provided significant protection against SSI, lidding to cost savings of around $75,460 USD per 100 spinal fusions performed, therefore, considering the application of local vancomycin powder a cost-effective option for the prophylaxis of SSI.

Several previous meta-analyses and systematic reviews support these findings.[11,37,47–52] Vancomycin is a glycopeptide antibiotic able to inhibit cell wall biosynthesis in gram-positive bacteria.[53] Its powder form, allowing for it to be spread evenly in the deep tissue, reaching extremely high levels required to treat bacterial biofilms while circumventing systemic toxicity, its low hospital cost, and its broad and effective spectrum against bacteria found in SSIs may justify the increasing popularity.[13]

In fact, in a systematic review by Ghobrial *et al*.[54] vancomycin powder appeared to be safe and effective, with a low rate of morbidity (0.3%). In 6701 patients, only 23 adverse events were registered: nefropathy (1 case), ototoxicity resulting in transient hearing loss (2 cases), systemic absorption resulting in supratherapeutic vancomycin exposure (1 case) and culture-negative seroma formation (19 cases). In terms of other possible concerns about the use of vancomycin, such as selective pressure on gram-negative SSIs or vancomycin resistance, none of the studies included in Ghobrial's systematic review supported these hypotheses.

The effect of vancomycin on osteogenesis is also a concern of many researchers and clinicians, in particular with protocols that involve the admixture of vancomycin powder within the bone graft, considering the possible risk of pseudarthrosis. The existing literature is quite limited and unclear, with some studies[55–57] with osteoblast cell cultures showing a decrease in osteoblast activity when higher concentrations of vancomycin were used. However, a systematic review by Kang *et al*. found no increase in pseudoarthrosis rate based on three studies.[58–60] Hence, this reenforces the necessity of further in vivo studies to determine the optimum concentration of intrawound vancomycin. [54]

Other systematic literature review examined the use of vancomycin in clean orthopaedic surgery, showing no benefit of parenteral administration of vancomycin comparing to standard prophylaxis, but finding that local vancomycin, in the form of intrawound powder in spine surgery or antibiotic cement in the case of adult reconstruction, is effective. Vancomycin in both local and parenteral forms in prophylactic doses appeared to be safe, with few adverse effects, most of them involving infusion reactions of parenteral administration.[61]

In this study, there was not enough data to categorize the interventions into instrumented and non-instrumented, but Molinari *et al*.[62] in their study reported a lower rate of infection with the application of 1 g of powdered vancomycin before wound closure for both instrumented and uninstrumented cases.

Elmadag *et al*.[21] tried to find an alternative antibiotic to vancomycin: teicoplanin powder. In this study, teicoplanin powder was not able to significantly reduce SSI. However, had a significantly higher fusion mass compared to the vancomycin and control group, which is consistent with findings from Göçer *et al*.[63].

It has been widely acknowledged that bacteria originating from patient's skin and airborne dust particles in the operating room may contaminate surgical wounds, and that wound irrigation is an important method to control this contamination.[64] Fei *et al*.[12] compared the effectiveness of 3 wound irrigation techniques (PL, CD and IL) with conventional SL, concluding that PL, CD and IL are good solutions for preventing postoperative bacterial infections within muscle layers.

Pulsed lavage, investigated in two different studies[12,25] in this systematic review, seems to be a promising preventative method. In fact, pulsed irrigation with a higher pressure than bulb syringe irrigation seems to be more effective in destroying the bacteria's biofilm.[65] Other studies in literature [65,66] confirm this efficacy, however there were a few reports that high-pressure pulsed irrigation could render deep penetration of bacteria.[67]

The optimal amount of normal saline intrawound irrigation was also investigated, showing no significant difference between a total irrigation of more than 6,000 mL or 2,000 mL. However, retrospectively, the optimum cut-off point for the amount of saline irrigation per hour during surgery to prevent infection was 1400mL/h. In comparison, a systematic review by Blood *et al*.[43] concluded that a volume of irrigation greater than 2000mL/h was protective against SSI.

In this review, the risk of SSI was not significantly influenced by closed drainage.[12,20,26] These findings support prior studies that also questioned the necessity for the routine use of a drain.[37,42,68–72] In fact, surgical drains are used in a variety of procedures and ultimately serve to decrease the risk of blood accumulation, which, in theory, helps to prevent epidural hematomas, SSIs and neurologic deficits.[68] However, the use of drains did not provide a significant benefit or better surgical results in several systematic reviews and meta-analyses in different orthopaedic surgeries, [37,68–72] with one finding no significant difference in rate of SSI in lumbosacral spine surgery with high-quality evidence.[42] This suggests that a reconsideration of routine insertion of drains is necessary, although the decision to place a drain is complex and other important factors should be considered in terms of risk-benefit scale, such as anticoagulant use, surgeon's impression of intraoperative bleeding, hemostasis, and increased morbidity, such as blood transfusion requirements.[20]

Three studies[14,22,23] compared the effect of natural pressure drainage (NAPD) to negative pressure drainage (NEPD), showing no significant difference between the two. This discussion arises because, in theory, NEPD can produce more force, which could reduce the size of the hematoma more powerfully. However, it may result in excessive external drainage and blood loss. Conversely, NAPD can cause some blood and fluid collections in the wound maintaining a certain tension, achieving a better hemostatic effect, with less drainage volume and drain indwelling time.[14]

Povidone-iodine wound irrigation may have a role in preventing SSI.[19,33] Although only 2 studies met the inclusion criteria, other systematic reviews and meta-analyses corroborate these findings.[11,37,47,72,73] In fact, a network meta-analysis in spinal surgery concluded that povidone-iodine irrigation was the best intervention, among other intrawound treatments like vancomycin, gentamycin and hydrogen peroxide.[47] Povidone iodine solution is a broad-spectrum antiseptic agent, with bactericidal activity against most pathogens including MRSA, able to avoid bacterial resistance.[33]

Rifampicin irrigation of the wound also demonstrated to significantly reduce the rate of SSI.[26,34] In fact, rifampicin is a cheap and accessible antibiotic with anti-staphylococcal biofilm activity, that may have a role is SSI prevention. However, further studies with larger series must be carried out to verify these results.[34]

Other intrawound therapy investigated was irrigation with hydrogen peroxide, a powerful oxidizing reagent with broad-spectrum antibiotic activity, with a local hemostatic effect.[28] However, no significant effect in preventing SSI was found,[28] which was validated by other systematic review. [47]

The use of staples was associated with significantly lower rates of infection. However, these results should be read with caution, since they derive from only one retrospective study, with small and very different sample sizes between the two groups (n=485 in staples group vs. n=55 in control group).[26] Two meta-analyses[74,75] comparing the effects of sutures and staples for skin closure across different specialties showed uncertainty whether there is a difference between the two. However, with low-quality evidence, sutures reduced postoperative pain and improved satisfaction with cosmetic results.[74]

The type of suture material was also associated with the occurrence of SSI. Vicryl Plus® sutures significantly decreased the rate of infection, being superior to Prolene® sutures.[26] In fact, other meta-analyses[37,76–78] showed similar benefits in using triclosan-coated sutures, compared with non-antibacterial coated sutures.

Postoperative Prevention Strategy

A postoperative antibiotic duration of 3 days or less seemed protective in comparison to more than 3 days.[31] Another meta-analysis[42] used a different cut-off of 48 hours, concluding, with low quality of evidence, that prolonging antibiotic administration for more than 48 hours postoperatively did not reduce SSI rate.

Limitations and future directions

This study has several limitations. First, most of the conclusions derived are from retrospectively obtained clinical data and not well-designed prospective studies. Secondly, some of the studies had inconsistent definitions of SSI. Thirdly, by implementing these strict inclusion criteria, the present systematic review provides a more precise and accurate assessment of the effect of different preventative measures on the target population. However, this decreases the total number of studies and sample sizes, which may overestimate effects, reducing statistical power. Also, no studies were found for some other prophylactic strategies mentioned in other systematic reviews, that may be important in degenerative spine surgery. This points toward the knowledge and research gap that currently exists for postoperative measures for SSI prophylaxis in spine surgery.

It is important to acknowledge these limitations when interpreting the results of the present study. Additionally, to address these limitations, further well-designed prospective high-powered and high-quality studies are warranted to provide more robust evidence of the effectiveness and optimal parameters of different measures to reduce SSI following spinal surgery in adult degenerative conditions.

CONCLUSION

SSI is an important and common complication after spine surgery, often associated with significant morbidity, mortality and increased costs, that should be always acknowledged by spine surgeons. There is strong evidence in the literature that optimizing specific preoperative, intraoperative and postoperative variables can significantly lower the risk of developing SSI. Based on this systematic review, vancomycin powder is the most studied and with stronger evidence of infection mitigation. However, there is still no clear consistency on the optimal dosage that should be used. Some other strategies seem promising for preventing SSI, yet further high-quality studies are required to reach reliable and definitive conclusions.

TABLES AND FIGURES

Table I – Search Strategy

Databases	Results	Search strategy	Date
Pubmed	2907	((((spine OR thoracolumbar OR lumbar OR thoracic OR lumbosacral OR "low back" OR "lower back") AND (infection)) AND (posterior))) NOT (trauma[Title/Abstract] OR cervical[Title/Abstract] OR tumor[Title/Abstract] OR neoplasia[Title/Abstract] OR pediatric[Title/Abstract] OR peadiatric[Title/Abstract] OR children[Title/Abstract] OR adolescent*[Title/Abstract] OR Spondylodiscitis[Title/Abstract])	18/11/2023
EMBASE	4322	'(spine OR thoracolumbar OR lumbar OR thoracic OR lumbosacral OR 'low back' OR 'lower back') AND infection AND posterior NOT (trauma:ab,ti OR cervical:ab,ti OR tumor:ab,ti OR neoplasia:ab,ti OR pediatric:ab,ti OR peadiatric:ab,ti OR children:ab,ti OR adolescent*:ab,ti OR spondylodiscitis:ab,ti)	18/11/2023
Total	7229		

Table II – Summary of the preoperative preventative measures for SSI. **ATB**, antibiotics; **OHA**, Oral hypoglycemic agent; **N.A.**, not applicable; *****, appendix figure.

	No. studies (sample size)	Intervention group	Control group	I^2, p value	Risk Ratio (95% CI)	*
Povidone-iodine-Impregnated Dressing	1 (200)	3/100	12/100	N.A.	0.25 [0.07,0.86]	
Blood glucose control	1 (238)					
Insulin vs OHA	1 (120)	2/50	7/70	N.A.	0.40 [0.09,1.85]	
Insulin vs Diet	1 (125)	2/50	14/75	N.A.	0.21 [0.05,0.90]	
Insulin vs Combined medication	1 (93)	2/50	11/43	N.A.	0.16 [0.04,0.67]	
OHA vs Diet	1 (145)	7/70	14/75	N.A.	0.54 [0.23,1.25]	
OHA vs Combined medication	1 (113)	7/70	11/43	N.A.	0.39 [0.16,0.93]	
Diet vs Combined medication	1 (118)	14/75	11/43	N.A.	0.73 [0.36,1.46]	
ERAS protocol	1 (1060)	16/530	21/530	N.A.	0.76 [0.40,1.44]	
Combined ATB vs. Single ATB	1 (610)	5/418	3/192	N.A.	0.77 [0.18,3.17]	
Single preop ATB	1 (217)	3/192	0/25	N.A.	0.94 [0.05,17.74]	
Combined ATB	1 (443)	5/418	0/25	N.A.	0.68 [0.04,12.01]	

Table III – Summary of the intraoperative preventative measures for SSI. **N.A.**, not applicable; **NAPD**, Natural Pressure Drainage; **N.E.**, not estimable; **NEPD**, Negative Pressure Drainage; **500mg/ 1g**, 500mg with ≤ 2 fused levels; 1g with >2 fused levels; *****, appendix figure.

	No. studies (sample size)	Intervention group	Control group	I^2, p value	Risk Ratio (95% CI)	*
Vancomycin Powder	6 (1720)	23/938	45/782	23%, 0.26	0.46 [0.28,0.76]	2
1g	3 (315)	4/147	21/168	0%, 0.96	0.21 [0.08,0.61]	3
2g	1 (86)	2/43	1/43	N.A.	2.00 [0.19,21.24]	
500mg/ 1g	1 (891)	7/527	13/364	N.A.	0.37 [0.15,0.92]	
Teicoplanin Powder	1 (69)	2/35	5/34	N.A.	0.39 [0.08,1.87]	
Vancomycin vs Teicoplanin Powder	1 (69)	1/34	2/35	N.A.	0.51 [0.05,5.42]	
Lavage techniques	1 (160)					
CD vs. PL	1 (80)	0/40	1/40	N.A.	0.33 [0.01,7.95]	
IL vs. PL	1 (80)	0/40	1/40	N.A.	0.33 [0.01,7.95]	
PL vs. SL	1 (80)	1/40	8/40	N.A.	0.13 [0.02,0.95]	
CD vs. IL	1 (80)	0/40	0/40	N.A.	N.E.	
CD vs. SL	1 (80)	0/40	8/40	N.A.	0.06 [0.00,0.99]	
IL vs. SL	1 (80)	0/40	8/40	N.A.	0.06 [0.00,0.99]	
Pulsed lavage	2 (524)	5/291	17/233	0%, 0.39	0.25[0.09,0.67]	
≥6000 mL vs 2000 mL normal saline irrigation	1 (444)	4/251	9/193	N.A.	0.34 [0.11,1.09]	
Povidone-iodine irrigation	2 (264)	0/129	8/135	0%, 0.59	0.12 [0.02,0.92]	
3% solution	1 (20)	0/9	2/11	N.A.	0.24 [0.01,4.44]	
0.35% solution	1 (244)	0/120	6/124	N.A.	0.08 [0.00,1.40]	
Rifampicin Irrigation	2 (706)	39/529	27/177	0%, 0.76	0.34 [0.21,0.53]	
Staples	1 (540)	51/485	12/55	N.A.	0.48 [0.27,0.85]	
Vicryl Suture	1 (540)	51/502	12/38	N.A.	0.32 [0.19,0.55]	
Silk Suture	1 (540)	1/10	62/530	N.A.	0.85 [0.13,5.57]	
Prolene Suture	1 (540)	11/28	52/512	N.A.	3.87 [2.28,6.56]	
Silk vs Vicryl	1 (512)	1/10	51/502	N.A.	0.98 [0.15,6.43]	
Vicryl vs Prolene	1 (530)	51/502	11/28	N.A.	0.26 [0.15,0.44]	
Silk vs Prolene	1 (38)	1/10	11/28	N.A.	0.25 [0.04,1.73]	

Closed drainage	3 (967)	52/632	27/335	61%, 0.08	0.77 [0.47,1.25]	4
Hemovac	1 (540)	49/410	14/130	N.A.	1.11 [0.63,1.94]	
Jackson-Pratt	1 (347)	3/182	5/165	N.A.	0.54 [0.13,2.24]	
NAPD vs. NEPD	3 (397)	5/209	5/188	0%, 0.81	0.91 [0.27,3.11]	5
3% H_2O_2 Irrigation	1 (2626)	18/1281	32/1345	N.A.	0.59 [0.33,1.05]	
Fibrin tissue glue	1 (540)	6/82	57/458	N.A.	0.59 [0.26,1.32]	
Cefazolin IV	1 (4027)	26/3949	0/78	N.A.	1.06 [0.07,17.24]	
Use of an operative microscope	1 (4027)	2/193	24/3834	N.A.	1.66 [0.39,6.95]	
Use of a bio-clean room	1(4027)	6/1142	20/2885	N.A.	0.76 [0.31,1.88]	
Drape	1 (540)	56/484	7/56	N.A.	0.93 [0.44,1.93]	
Iodized drape vs Noniodized drape	1 (484)	50/431	6/53	N.A.	1.02 [0.46,2.27]	

Table IV – Summary of the postoperative preventative measures for SSI. **ATB**, antibiotics; **N.A.**, not applicable; *****, appendix figure.

	No. studies (sample size)	Intervention group	Control group	I^2, p value	Risk Ratio (95% CI)	*
Duration of postop use of ATB (≤ 3d)	1 (1269)	22/1004	21/265	N.A.	0.28 [0.15,0.50]	

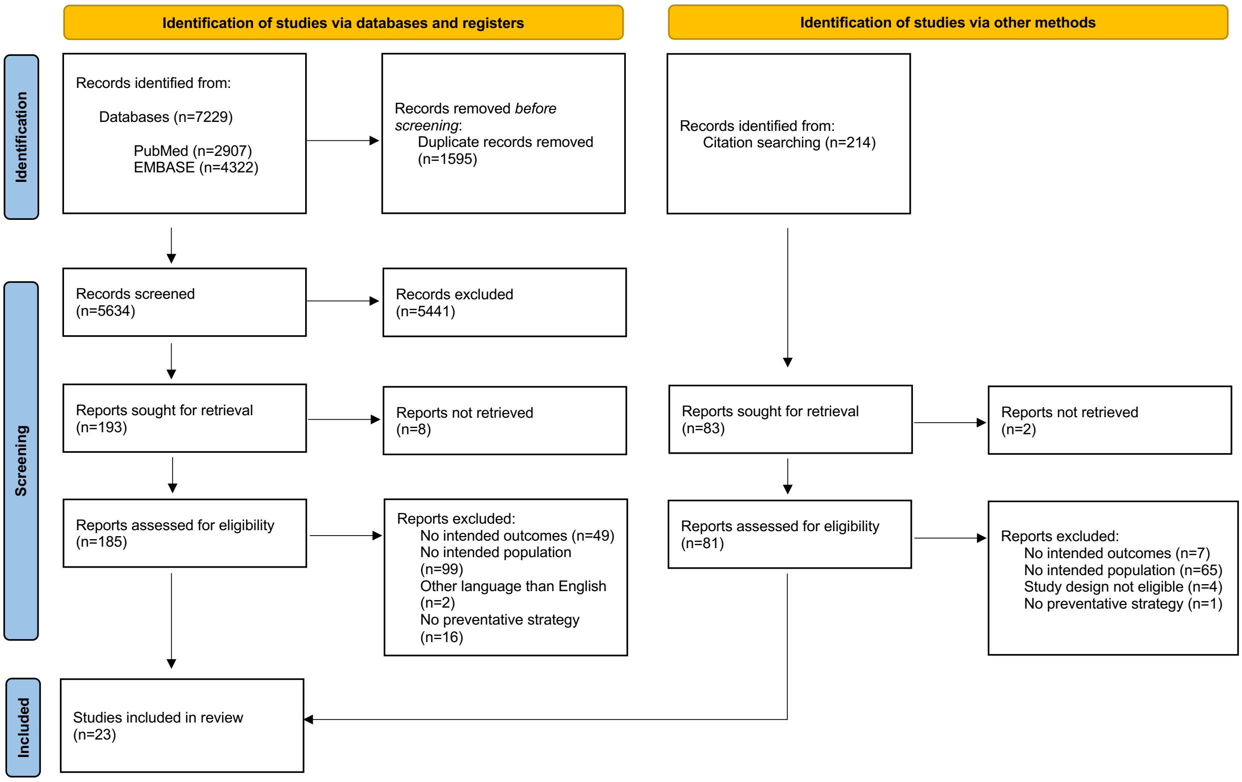

Figure 1 – PRISMA 2020 flow diagram.

Study or Subgroup	Vancomycin Events	Vancomycin Total	No vancomycin Events	No vancomycin Total	Weight	Risk ratio M-H, Fixed, 95% CI
Alemán-Villalón et al. 2021	2	82	10	102	19.2%	0.25 [0.06 , 1.10]
Elmadag et al. 2023	1	34	5	34	10.7%	0.20 [0.02 , 1.62]
Kar et al. 2021	1	31	6	32	12.7%	0.17 [0.02 , 1.35]
Li et al. 2019	10	221	10	207	22.2%	0.94 [0.40 , 2.20]
Suh et al. 2015	2	43	1	43	2.1%	2.00 [0.19 , 21.24]
Wang et al. 2022 (a)	7	527	13	364	33.1%	0.37 [0.15 , 0.92]
Total (95% CI)		**938**		**782**	**100.0%**	**0.46 [0.28 , 0.76]**
Total events:	23		45			

Heterogeneity: $Chi^2 = 6.47$, $df = 5$ ($P = 0.26$); $I^2 = 23\%$
Test for overall effect: $Z = 3.02$ ($P = 0.003$)
Test for subgroup differences: Not applicable

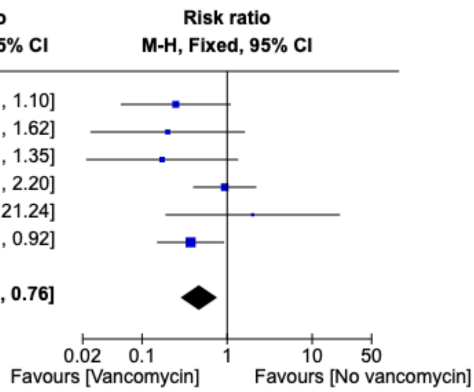

Figure 2 - Forest plot for Vancomycin Powder use. (a)[32]

Study or Subgroup	Vancomycin Powder 1g Events	Vancomycin Powder 1g Total	No vancomycin Events	No vancomycin Total	Weight	Risk ratio M-H, Fixed, 95% CI
Alemán-Villalón et al. 2021	2	82	10	102	45.0%	0.25 [0.06 , 1.10]
Elmadag et al. 2023	1	34	5	34	25.2%	0.20 [0.02 , 1.62]
Kar et al. 2021	1	31	6	32	29.8%	0.17 [0.02 , 1.35]
Total (95% CI)		**147**		**168**	**100.0%**	**0.21 [0.08 , 0.61]**
Total events:	4		21			

Heterogeneity: Chi² = 0.09, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 2.90 (P = 0.004)
Test for subgroup differences: Not applicable

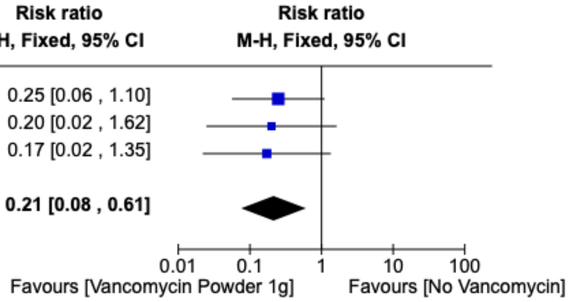

Figure 3 – Forest plot for 1 g of Vancomycin Powder use.

Study or Subgroup	Closed Drainage Events	Closed Drainage Total	No-drain Events	No-drain Total	Weight	Risk ratio M-H, Fixed, 95% CI
Fei et al. 2017	0	40	8	40	24.3%	0.06 [0.00 , 0.99]
Jang et al. 2021	3	182	5	165	15.0%	0.54 [0.13 , 2.24]
Yaldiz et al. 2015	49	410	14	130	60.7%	1.11 [0.63 , 1.94]
Total (95% CI)		**632**		**335**	**100.0%**	**0.77 [0.47 , 1.25]**
Total events:	52		27			

Heterogeneity: Chi² = 5.07, df = 2 (P = 0.08); I² = 61%
Test for overall effect: Z = 1.06 (P = 0.29)
Test for subgroup differences: Not applicable

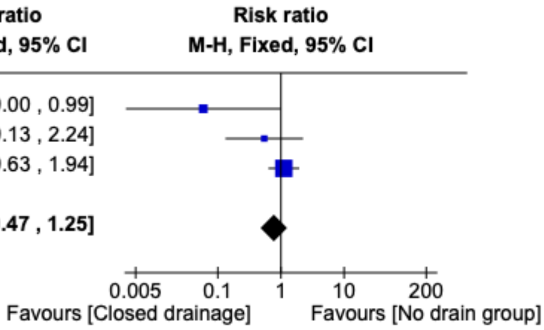

Figure 4 – Forest plot for Closed Drainage.

	Natural Pressure Drainage		Negative Pressure Drainage			Risk ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Chen et al. 2020 (a)	1	68	2	64	39.6%	0.47 [0.04 , 5.06]
Elfiky et al. 2023	1	29	1	33	18.0%	1.14 [0.07 , 17.39]
Jiang et al. 2023	3	112	2	91	42.4%	1.22 [0.21 , 7.14]
Total (95% CI)		**209**		**188**	**100.0%**	**0.91 [0.27 , 3.11]**
Total events:	5		5			

Heterogeneity: Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable

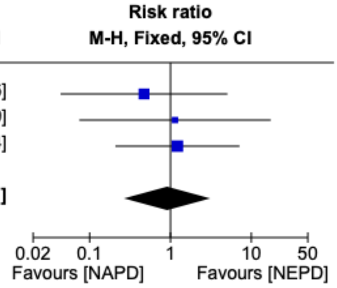

Figure 5 – Forest Plot for Natural vs Negative Pressure Drainage. (a)[14]

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