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Risk factors for 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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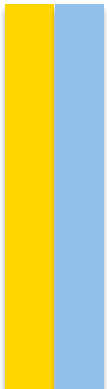

Risk factors for post-operative surgical-site infection after posterior thoracolumbar or lumbar surgery for degenerative spine conditions –
A Systematic Review with Meta-analysis

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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.

Estudante: Mariana Oliveira Ribeiro

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RESUMO

Fatores de risco para 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 a cirurgia da coluna vertebral. Trata-se de um problema de saúde de extrema importância, uma vez que se tem associado a uma morbilidade, mortalidade e encargos económicos significativos. Um dos primeiros passos fundamentais para reduzir a incidência da ILC é a identificação precisa dos fatores de risco para a sua ocorrência. Neste sentido, é importante identificar as variáveis relacionadas com o doente ou com o procedimento que aumentam o risco de ILC, de modo a que possam ser desenvolvidas estratégias para minimizar o risco para o doente.

Objetivos: O objetivo deste estudo foi realizar uma revisão sistemática dos fatores de risco para ILC após cirurgia toracolombar ou lombar posterior por patologia degenerativa da coluna vertebral.

Métodos: A pesquisa incluiu as bases de dados PubMed e EMBASE até 18 de novembro de 2023, tendo sido realizada uma revisão sistemática com meta-análise. Foram considerados elegíveis os estudos que consideraram a ocorrência de infeções pós-operatórias do local cirúrgico como resultado primário e que fizeram uma análise dos fatores de risco. Foram utilizados risk ratio, mean differences e intervalos de confiança de 95% para analisar os principais resultados.

Resultados: Dos 7443 estudos identificados, 24 cumpriam os critérios de inclusão. A taxa global de ILC foi de 2,39%. 42 variáveis foram significativamente associadas a um risco acrescido de ILC, nomeadamente obesidade, tabagismo, doença cardíaca crónica e ASA >2.

Conclusão: A presente revisão sistemática identificou a obesidade, o tabagismo, a doença cardíaca crónica e ASA >2 como os principais fatores de risco para ILC e muitas outras variáveis que poderão também, eventualmente, associar-se a um maior risco. O reconhecimento destes fatores de risco permitirá aos cirurgiões otimizar a condição pré-operatória dos doentes, bem como o procedimento cirúrgico, contribuindo para reduzir a incidência de ILC pós-operatória.

Palavras-chave: “coluna vertebral”, “toracolombar”, “lombar”, “torácica”, “lombossacral”, “infeção”, “posterior”.

ABSTRACT

Risk factors for 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. It is a major health problem since it has been associated with a significant morbidity, mortality and economical burdens. One of the most important first steps in reducing the incidence of SSIs is the accurate identification of risk factors for their occurrence. Therefore, it is important to identify patient-related or procedure-related variables that increase the risk of SSI so that strategies can be developed to minimize patient risk.

Objective: The aim of this study was to conduct a systematic review of risk factors for spine SSI after posterior thoracolumbar or lumbar surgery for degenerative spine conditions.

Methods: PubMed and EMBASE databases were searched up to November 18, 2023 and a systematic review with meta-analysis was performed. Studies assessing the occurrence of post-operative SSIs as the primary outcome with risk factors analysis were considered eligible. Risk ratios, mean differences and 95% confidence intervals were used to analyze the main outcomes.

Results: Of the 7443 studies identified, 24 met the inclusion criteria. The overall infection rate was 2.39%. 42 variables were significantly associated with an increased risk of SSI, particularly obesity, smoking, chronic heart disease and ASA >2.

Conclusions: This systematic review identified obesity, smoking, chronic heart disease and ASA >2 as the major risk factors for SSI and many other variables that can also potentially increase this risk. Awareness of these risk factors will help surgeons to optimize patient's preoperative condition and surgical procedure and help decrease the incidence of postoperative SSI.

Keywords: "spine", "thoracolumbar", "lumbar", "thoracic", "lumbosacral", "low back", "lower back", "infection", "posterior"

LIST OF ABBREVIATIONS

APTT	Activated Partial Thromboplastin Time
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CDC	Centers for Disease Control and prevention
CHD	Chronic Heart Disease
CRP	C-Reactive Protein
EBL	Estimated Blood Loss
ESR	Erythrocyte sedimentation rate
FPG-CV	Variation coefficient of fasting plasma glucose
GNRI	Geriatric Nutritional Risk Index
ICD-9	International Classification of Diseases, 9th revision system
ILC	Infeção do Local Cirúrgico
LEI	Lumbar Epidural Injection
MD	Mean Difference
MFBG	Mean Fasting Blood Glucose
mFI-5	Modified 5-Item Frailty Index
MIS	Minimally Invasive Surgery
MNA-SF	Mini Nutritional Assessment – Short form
PLIF	Posterior Lumbar Interbody Fusion
PT	Prothrombin Time
RBC	Red Blood Cells
RR	Relative Risk
SD	Standard Deviation
SSI	Surgical Site Infection
TLIF	Transforaminal Lumbar Interbody Fusion
TNFi	Tumor Necrosis Factor Inhibitor
WBC	White Blood Cells

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INTRODUCTION

Surgical site infection is the third most common complication after spinal surgery with its incidence ranging between 0.22%[1] and 16.1%[2], depending on the indication for surgery, the approach and several other conditions[3]. Infection places patients at a high risk for non-union, chronic pain, return to operating room, adverse neurological sequelae, worsened long-term outcomes and even death.[4] Undoubtedly, SSIs not only prolong hospital stay, but also increase medical, social and economic costs.[5] Treatment of SSIs often requires multiple readmissions, wound debridement or implant removal and prolonged antibiotic therapy.[6] Given the ongoing substantial clinical and economic impact of SSIs, efforts to reduce their occurrence are critically needed.[3]

One of the most important first steps in reducing the incidence of SSIs is the accurate identification of risk factors for their occurrence,[3] which relies on the definition of SSI. Currently, SSI can be defined using different methods and classifications, such as 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 of infection (Current Procedural Terminology). The frequency of SSI after spine surgery and the risk factors identified can vary according to the definition of infection used.[7]

There are a multitude of risk factors that increase the rates of infection, only some of which are modifiable.[4] Improved understanding of potentially modifiable risk factors, such as obesity[8] and tobacco use,[3] may help identify systematic changes that could markedly decrease SSIs. Patients should be counseled prior to undergoing elective spine surgery to optimize the modifiable risk factors present to reduce the rate of postoperative infection and other complications.[4] Improved understanding of risk factors, even those that are non-modifiable, including advanced age[9] and a high ASA score, could favorably impact surgical treatment and outcomes and even influence the selection process of patients for surgery or specific types of surgical procedures.[3]

Additionally, risk factors for SSIs after spinal surgery have also been classified in many studies as patient related, such as obesity, diabetes and tobacco use, or procedure related, including prolonged surgical time, the indication and the type of procedure, the location and the approach of the spinal operation.[3,9] Concerning these last two parameters, thoracolumbar surgeries in comparison with cervical surgery, as well as a posterior approach have been associated with an increased risk of SSI.[9] Therefore, the present study will focus on the risk factors for postoperative SSI after posterior thoracolumbar surgery.

The aim of this study was to conduct a systematic review of risk factors for spine SSI after posterior thoracolumbar or lumbar surgery for degenerative spine conditions.

METHODS

Search strategies and selection criteria

Databases searches were conducted in PubMed and EMBASE 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 and a third author decided any disagreements. Removal of duplicates was executed with the use of EndNote or manually when necessary.

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. For this systematic review, we only considered 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 included in the study. Studies including participants with other surgical indications, such as for the treatment of traumatic, oncological or infectious lesions, as well as with other conditions like inflammatory, neuromuscular, congenital spinal deformities or cerebral palsy were excluded. Only studies whose primary outcome was the occurrence of postoperative SSI with risk factors analysis were considered. In studies separating different types of SSIs (superficial, deep, organ-space), we have considered the total number of infections.

Data extraction

Two independent authors screened all titles and abstracts. Titles and 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, type of risk factor, incidence and percentage of infected participants, data on risk factor (continuous or categorical) and other characteristics related to the risk factor (if it is modifiable or not, patient-related or procedure-related). Continuous data was collected as mean and SD and categorical data as number and percentage. We have prioritized mean and SDs. In instances where mean and SD were not provided, it was sought to calculate these (when feasible) using the methods recommended by the Cochrane Handbook.[10] When data was present as median (range), the mean and SD were estimated accordingly to Hozo et al.[11] 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

Demographic data was reported using pooled means and SDs, weighted to the sample size. We computed the cumulative number and percentage of postoperative SSI divided by all participants included in the systematic review. We computed the mean difference (MD) for risk factors reported as continuous outcomes or the relative risk (RR) for risk factors reported as dichotomous data. These comparisons were computed with a meta-analysis procedure using a fixed-effects model. Heterogeneity was assessed using the I^2 statistics. Subgroup analysis was performed when feasible.

RESULTS

Search Results and Studies Characteristics

The initial database (n=7229) and hand searches (n=214) generated a total of 7443 records, of which 266 full texts were screened to assess their eligibility, after removal of duplicates and screening of titles and abstracts. Among these, a total of 24 studies[12–35] met the eligibility criteria and were included in this systematic review (Figure 1). The total number of patients included in this review was 66988, with a total 1598 SSIs (2.39%).

Patient-related modifiable risk factors

Obesity, defined as a BMI≥30 kg/m^2, was analysed by 5 studies[16,21,23,26,27] as a potential risk factor and was associated with a significantly higher risk of SSI (RR=2.13, 95% CI 1.61 to 2.83; I^2=0%). Within the obese population, Molina *et al.*[23] found no statistically significant difference in SSI rate in morbidly obese patients undergoing posterior lumbar MIS, compared to non-morbidly obese group (RR=1.50, 95% CI 0.14 to 16.32). BMI was reported in 7 studies,[14,18,25,26,29,32,35] suggesting that a higher BMI is a risk factor for SSI (MD=1.76, 95% CI 1.25 to 2.27). However, there was a high and significant heterogeneity (I^2=83%, P <.00001), which shows that the results are not consistent. Li et al.[18] found subcutaneous fat thickness to be associated with a higher rate of SSI (MD 7.51, 95% CI 5.56 to 9.46), but muscle thickness had no statistically significant association (MD=1.99, 95% CI -0.19, 4.17).

Nine studies[14,18,21,25,26,28,29,32,35] looked at the effect of diabetes mellitus, suggesting that it significantly increases the incidence of SSI (RR=4.50, 95% CI 3.59 to 5.63). Nevertheless, there was significant heterogeneity (I^2=78%, P <.0001), revealing some inconsistency between the results. Liu *et al*.[20] sought to determine risk factors associated with SSI, among patients with type 2 diabetes. Duration of diabetes >5 years, ≥2 fused vertebrae and a higher postoperative FPG-CV between diabetic patients, showed an increased risk of SSI. The effect of several other variables on diabetic patients was analysed and is described in table II, but no significant association was found with a higher rate of SSI.

Only one study[29] looked at the effect of preoperative HbA1c and found an association between a higher value and an increased risk of SSI (MD=2.20, 95% CI 1.65 to 2.75). Similarly, higher fasting blood glucose levels were associated with a greater rate of SSI (MD=1.30, 95% CI 0.49 to 2.11).[26] Smoking was assessed as a risk factor for SSI in ten studies[13,14,18,21,25,26,28,29,32,35] and was associated with a significantly higher risk of SSI (RR=1.81, 95% CI 1.40 to 2.34; I^2=0%).

Several studies have analysed different comorbidities as potential risk factors for SSI. A significant increase in the postoperative rate of SSI was observed in patients with chronic heart disease[18,21,26,29,32] (RR=2.02, 95% CI 1.23 to 3.31; I^2=0%), rheumatic disease[18,21,29,32] (RR=2.45, 95% CI 1.33 to 4.52; I^2=58%), parkinson disease[21] (RR=8.22, 95% CI 1.45 to 46.61) and renal insufficiency[26] (RR=4.93, 95% CI 2.07 to 11.72). Liu *et al*.[21] documented a significant association between a Charlson Comorbidity Index ≥4 and a higher risk of SSI (RR=2.85, 95% CI 1.36 to 5.96). Similarly, Weaver *et al*.[30] looked at another comorbidity-based risk stratification tool - the Modified 5-Item Frailty Index (mFI-5) - and found that increasing mFI-5 versus mFI-5=0 (non-fragile patients) was significantly associated with a higher risk of SSI [(mFI-5=1 (mild to moderate frailty): RR=1.26, 95% CI 1.01 to 1.59; mFI-5≥2 (severe frailty): RR=2.14, 95% CI 1.68 to 2.72)].

The statistical analysis of other comorbidities, such as hypertension,[18,21,26,32] osteoporosis,[21,32] pulmonary disease,[21,26,29] cerebrovascular disease,[21,26,29] tumor,[21] tuberculosis,[21] thyroid disorders,[21] cauda equina injury,[21] neurogenic claudication,[21] chronic liver disease,[26] hemodialysis[25] and the presence of other perioperative infections[18] showed no significant association with higher risk of SSI (table II).

Preoperative albuminemia was reported in 5 studies,[18,21,26,29,32] suggesting that a lower level of albuminemia was associated with an increased risk of SSI (MD= -4.45, 95% CI -5.07 to -3.83). Additionally, two other studies[14,26] analysed the effect of preoperative hypoalbuminemia (≤35g/L) and found a significant association with a higher incidence of SSI (RR = 2.82, 95% CI 1.60 to 4.97). However, both findings revealed high heterogeneity (I^2=86%, P<.00001 and I^2=72%, P=0.06, respectively), showing some inconsistency between the results. Similarly, postoperative hypoalbuminemia (≤35g/L)[14,31] was associated with a higher rate of SSI (RR = 7.89, 95% CI 3.90 to 15.94), but revealed significant heterogeneity (I^2=61%, P=0.11) and therefore inconsistency in the results. There were two studies[21,26] on the correlation between the amount of total protein and postoperative SSI, which found a lower level of total protein to be associated with a significant increase in the infection rate (MD= -2.45, 95% CI -4.08 to -0.83).

Li *et al*.[19] analysed the effect of malnutrition using two nutritional screening tools - MNA-SF and GNRI. There were no significant differences in SSI among GNRI categories (table II). Regarding the MNA-SF score, there was no statistically significant difference between malnourished and at-risk patients (MNA-SF ≤11) compared with well-nourished patients (MNA-SF >11), however malnourished patients (GNRI <8) had a statistically significant increased prevalence of SSI, compared to at-risk patients (GNRI 8-11) (RR = 3.75, 95% CI 1.07 to 13.15).

Steroid use was assessed as a risk factor for SSI in 5 studies[14,18,21,25,29] and was associated with a significantly increased rate of SSI (RR=2.37, 95% CI 1.37 to 4.12). However, there was a high and significant heterogeneity (I^2=85%, P <.0001), showing some inconsistency in the results. Li *et al*.[17] sought to determine an association between preoperative lumbar epidural injections (LEIs), predominantly used to treat chronic low back pain, and the occurrence of SSI. The use of preoperative LEIs was associated to a higher rate of SSI compared to the control group in which no LEIs were used (RR=1.76, 95% CI 1.17 to 2.67). However, when comparing steroid vs non-steroid or time interval between LEIs and surgery (0-1 month vs >1 month), no significant association was found (table II).

Preoperative body temperature was reported in two studies,[18,21] suggesting that a lower preoperative body temperature was associated with a higher risk of SSI (MD=-0.13, 95% CI -0.20 to -0.06), although there was a significant heterogeneity, showing inconsistency between the results (I^2=69%, P=0.07). Preoperative RBC (x10^{12}/L),[21,26,29,32] preoperative hemoglobin (g/L),[18,21,26,32] preoperative hematocrit (%),[18,26] and postoperative hemoglobin (g/L)[18] were assessed by several studies, which have demonstrated lower levels to be associated with a higher incidence of SSI [(MD=-0.15, 95% CI -0.22 to -0.08; I^2=40%, P=0.17), (MD=-3.98, 95% CI -6.94 to -1.02; I^2=23%, P=0.27), (MD=-1.87, 95% CI -3.03 to -0.71; I^2=0%, P=0.37), (MD=-11.66, 95% CI -18.22 to -5.10), respectively]. A higher preoperative neutrophil count (x10^9/L) was also assessed by 2 studies[21,26] and associated with a higher rate of SSI (MD=0.67, 95% CI 0.01 to 1.32; I^2=0%, P=0.38). Several other preoperative parameters were reported in many studies, but statistical analysis of the data showed no significant difference in SSI rate: WBC,[18,21,26,29,32] platelets,[21,26,29,32] lymphocyte[18,21,26] and monocyte count,[21] serum natrium,[21] calcium[21,29] and potassium,[21,29] ESR,[21] CRP,[21] globulin,[21,29,32] fibrinogen,[29] triglyceride,[21] total cholesterol,[21] ALT,[21,32] AST,[21,32] creatinine,[21,32] BUN,[21] PT[29] and

APTT[29] (table II). Similarly, the association between alcohol consumption[18,21,29,32] and the development of SSI wasn't statistically significant (RR=1.31, 95% CI 0.86 to 1.99; I^2=0%).

Patient related non-modifiable risk factors

Several studies looked at the effect of ASA score. ASA >2 was assessed in 6 studies[21,24–26,29,32] as a potential risk factor for SSI and it was associated with a significantly higher rate of infection (RR=2.86, 95% CI 2.10 to 3.90; I^2=51%, P=0.07). Age was reported in 7 studies,[14,18,21,25,29,32,35] suggesting that a higher age was associated with an increased risk of SSI (MD= 5.93, 95% CI 4.50 to 7.36; I^2=35%, P=0.16). However, 2 studies[26,34] looked for a correlation between older patients (≥70 years) and an increased risk of SSI and found no statistically significant association (RR=1.63, 95% CI 0.84 to 3.16; I^2=0%, P=0.33). Eight studies[14,18,21,25,26,28,29,32] assessed male gender as a possible risk factor for SSI, but no significant association was identified (RR=1.04, 95% CI 0.80 to 1.34; I^2=66%, P=0.005).

Procedure-related modifiable risk factors

Seven studies[14,18,21,26,29,32,35] analysed the effect of operative time on the incidence of SSI and suggested that longer surgeries were associated with higher rates of infection (MD= 24.66, 95% CI 17.46 to 31.85). However, there was a high and significant heterogeneity, which shows that the results are not consistent. (I^2=67%, P=0.006). Ogihara *et al*.[25] used a 2-hour cut-off and found that an operative time over 2 hours was associated with a significantly higher rate of infection (RR=3.49, 95% CI 1.59 to 7.68). An increased preoperative stay[26] and total length of stay[14,21,26] were also associated with higher incidence of postoperative SSI [(MD= 1.60, 95% CI 0.60 to 2.60) and (MD= 10.19, 95% CI 7.60 to 12.78, I^2=0%, P=0.91), respectively].

Intraoperative blood loss[14,18,21,25,26,29,32,35] was analysed in eight studies, suggesting that greater blood loss was associated with a higher risk of SSI (MD= 64.94, 95% CI 48.22 to 81.66), although there was significant heterogeneity, showing inconsistency between the results (I^2=83%, P<.00001). Two studies[15,21] compared the effect of 2 or more fused levels with only 1 fused level on the incidence of SSI and suggested that 2 or more fused levels were associated with a greater risk of infection (RR=3.30, 95% CI 1.44 to 7.57; I^2=2%, P=0.31). Allogenic blood transfusion[18,21,26,33] and dural tear[12,18,25,32,33] were reviewed by several studies and were associated with an increased incidence of postoperative SSI [(RR=1.71, 95% CI 1.23 to 2.38, I^2=0%, P=0.45) and (RR=2.12, 95% CI 1.81 to 2.48), respectively], although dural tear's results were inconsistent (I^2=85%, P<.0001).

Longer drainage[18,21] and urinary catheter placement duration,[21] as well as an increased length of incision[21] were also associated with a higher risk of SSI [(MD= 0.77, 95% CI 0.39 to 1.16, I^2=66%, P=0.09), (MD= 0.61, 95% CI 0.01 to 1.21) and (MD= 1.46, 95% CI 0.38 to 2.54), respectively]. However, longer drainage showed significant heterogeneity (I^2=66%, P 0.09), showing inconsistency in the results. Hsiung *et al.*[35] found that a reduced irrigation is associated with a higher risk of SSI (MD= -358, 95% CI -660.78 to -55.22). Liu *et al*.[22] found no significant difference in the risk of SSI between PLIF and TLIF surgeries. Similarly, the number of screws,[21] allograft bone use,[18,26,32] perioperative invasive vascular catheterization,[18] duration of jugular vein catheterization[21] or the amount of postoperative drainage[14,18,26] weren't either associated with an increased risk of SSI. (Table IV).

Procedure-related non-modifiable risk factors

Three studies[14,29,32] focused on whether there was any association between preoperative diagnosis and an increased risk of SSI. Lumbar spinal stenosis was associated with a significantly higher risk of SSI compared to lumbar disc herniation (RR=1.69, 95% CI 1.01 to 2.83, I^2=0%, P=0.47). Lumbar instability/spondylolisthesis compared to lumbar disc herniation or with lumbar spinal stenosis wasn't associated with a statistically significant risk of SSI. Li *et al*.[18] found no significant difference in incidence of SSI between previous lumbar surgery or previous SSI. Similarly, Ogihara *et al.*[25] failed to associate revision or emergency surgery to a statistically significant risk of SSI.

DISCUSSION

SSI remains one of the most common complications after spinal surgery. The overall rate of SSI in this study was 2.39%, which is consistent with previously reported rates.[1,2] SSI has been associated with high incidence of morbidity and mortality. Therefore, it is important to identify variables patient-related or procedure-related that increase the risk of SSI so that strategies can be developed to minimize patient risk.

To the best of our knowledge, there are currently no systematic reviews aiming to identify risk factors for SSI after posterior thoracolumbar or lumbar surgery for degenerative spine conditions. 42 variables were significantly associated with an increased risk of SSI. The main finding of this systematic review is that obesity, smoking, chronic heart disease and ASA >2 were the major risk factors for SSI, being consistent among several studies and having a high and significant RR, which increases the certainty of these findings.

Patient-related modifiable risk factors

Obesity (BMI$\geq$30 kg/m^2) was considered an important risk factor for SSI.[16,21,23,26,27] Five other systematic reviews[36–40] corroborate these findings. Subgroup analysis of Molina *et al.*[23] found no significant difference in the morbid obese population. The association between obesity and SSI may be due to a greater subcutaneous fat thickness in the surgical region, since adipose tissue secretes numerous hormones and cytokines and this local inflammation may cause insulin resistance and systemic inflammation, contributing to an increased risk of SSI.[41] It also requires a longer incision, wider dissection and increased retraction, possibly creating a dead space with increased tissue necrosis, poor vascular perfusion and impaired bacterial oxidative killing, leading to a higher risk of SSI.[36,38,42–45] Several studies also reported a frequent association of other comorbidities in obese patients, like coronary artery disease, diabetes, hypertension and pulmonary disease,[16,23,27] as well as with other postoperative complications and other factors that potentially contribute to a greater infectious risk, such as a higher EBL, operative duration and length of stay.[43] Surgeons must recognize the increased morbidity risks in this population.

In the present study, a higher BMI was associated with an increased risk of SSI, but the results were inconsistent.[14,18,25,26,29,32,35] However, 3 systematic reviews[36,38,42] found a strong association. Li *et al*.[18] showed that subcutaneous fat thickness at the surgical site was an independent and important risk factor for the development of SSI. Several studies suggest that local subcutaneous fat thickness is more predictive of SSI than the absolute BMI and deserves attention

in preoperative evaluation.[41,44,46–48] In fact, BMI can be influenced by muscular build and body habitus of a patient and may not correlate with fat content.[44]

Smoking was shown to be an important risk factor.[13,14,18,21,25,26,28,29,32,35] Five systematic reviews[36,38,40,42,49] support this finding and only one[39] found no significant association. Smoking has been shown to have an adverse effect on wound healing. In fact, smokers have poorer tissue perfusion and impaired immune response[50] and oxidative bacterial killing mechanisms, predisposing them to SSI.[36,49] Thomsen *et al.*[51] reported that patients undergoing different types of elective surgeries may benefit from intensive preoperative smoking cessation interventions, which must be initiated at least 4 weeks before surgery and include nicotine replacement therapy.[36]

Chronic heart disease was also found to be a significant risk factor for SSI.[18,21,26,29,32] Such as diabetes, CHD has poorer microcirculation around surgical tissues, having a negative impact on wound healing and inducing SSI occurrence.[26,52] It also has been associated with prolonged recovery, predisposing to postoperative complications. Furthermore, these patients may be prone to experience anemia with intraoperative blood loss and need for transfusion, which can potentially increase the risk of SSI.[53]

A definite conclusion that diabetes increases the risk of SSI could not be drawn, due to high heterogeneity.[14,18,21,25,26,28,29,32,35] Nevertheless, diabetes has been previously reported as an independent risk factor for SSI in six systematic reviews.[36–40,42] Diabetic patients' susceptibility to SSI is due to an immunocompromised state and microangiopathic changes that lead to local tissue ischemia with reduced wound healing potential and lower tissue concentrations of antibiotics.[36,54] Liu *et al.* found that higher postoperative FPG-CV, a glycemic variability indicator, increases the risk of SSI, as it leads to inflammation and oxidative stress, and showed that it is a better predictor of infection than MFBG or HbA1c, in diabetic patients.[20] An increased duration of diabetes (>5 years) was also considered a risk factor for SSI, due to a severely abnormal glucose metabolism, as well as 2 or more fused vertebrae.

High preoperative HbA1c[29] and fasting blood glucose[26] were also associated with an increased risk of SSI. In fact, the perioperative period may be associated with stress hyperglycemia, resulting from a transient decrease in insulin responsiveness. Therefore, tight glycemic control may be important to decrease the incidence of SSI following spinal surgery.[38]

Rheumatic disease was also found to be a significant risk factor for SSI.[18,21,29,32] A meta-analysis from Clay *et al*. including patients with rheumatic diseases treated with TNF inhibitor undergoing orthopaedic surgery, showed an increased risk of SSI and overall complications in patients under TNFi and a decreased risk in those who stopped treatment between 1 and 8 weeks before surgery. The authors suggest that inhibition of TNFα favors serious infections, since it has been recognized as the principal activator of the inflammatory cascade, playing a key role in the host's immune response.[55]

The effect of parkinson disease[21] and renal insufficiency[26] on SSI incidence was only investigated by one study. Despite having a significantly higher risk of SSI, further studies must be carried out to validate these findings.

Charlson Comorbidity Index ≥4[21] and an increasing mFI-5[30] were significantly associated with a higher risk of SSI. Similarly, a previous systematic review with meta-analysis[56] analysed 6 distinct frailty indices and found a significantly higher rate of SSI in frail patients (mFI-5≥2 or mFI-11≥0.27).

Given the heterogeneity of results, it's not possible to definitively determine the role that low preoperative albuminemia[18,21,26,29,32] and preoperative[14,26] and postoperative hypoalbuminemia

(≤35g/L)[14,31] play in the risk of SSI. However, a lower level of total protein[21,26] was associated with a significantly increased rate of infection. Hypoproteinemia can lead to immune suppression, local tissue edema and impaired microcirculation, which will affect normal wound healing and create conditions for bacterial colonization.[29] Li *et al*.[19] analysed the effect of malnutrition using two nutritional screening tools - MNA-SF and GNRI - and found that malnourished patients (GNRI <8) had a statistically significant increased prevalence of SSI, compared to at-risk patients (GNRI 8-11). Malnutrition (defined by low levels of albumin, prealbumin, transferrin or total lymphocyte count) has been reported as a significant risk factor for SSI by several systematic reviews.[37,40,57] Thus, it is advisable to assess nutritional status preoperatively and nutritional supplementation may be considered in malnourished patients undergoing complex surgeries.[40]

An association between the effect of steroid use[14,18,21,25,29] and the risk of SSI was not possible to identify, due to high heterogeneity of results. Similarly, three systematic reviews[38,39,42] found no significant association between steroid use and the incidence of SSI.

Li *et al*.[17] supported the association between the use of preoperative LEIs and a higher rate of SSI. When comparing steroid vs non-steroid or time interval between the LEIs and surgery (0-1 month vs >1 month), they found no significant difference. Yet, a recent meta-analysis[58] found a statistically significant association between preoperative corticosteroid spinal injections <1 month prior to lumbar spine surgery and an overall increased risk of infections.

Preoperative RBC,[21,26,29,32] hemoglobin,[18,21,26,32] hematocrit,[18,26] and postoperative hemoglobin[18] were assessed in several studies, which have demonstrated lower levels to be associated with a higher incidence of SSI. Tominaga *et al.*[59] also concluded that low preoperative hemoglobin level is a risk factor for SSI and that correction of hemoglobin may reduce postoperative SSI. In fact, low hemoglobin, RBC or hematocrit levels may request allogenic blood transfusion and result from intraoperative blood loss, two important known risk factors for SSI.[60]

Patient-related non-modifiable risk factors

ASA score >2 is one of the main risk factors in this study.[21,24–26,29,32] Three other systematic reviews[36–38] corroborate this finding. Patients with a higher ASA score are more likely to have comorbidities and poorer clinical conditions with an impaired immune system, being more susceptible to SSI.[21]

Meta-analysis on age[14,18,21,25,29,32,35] as risk factor suggested that those with SSI significantly tend to be on average 6 years older; however, being older (≥70 years)[26,34] did not seem to increase the risk of SSI. Although age, theoretically, may be a potential risk factor, since elderly patients have degenerated immune function and more comorbidities, turning them more vulnerable to surgical trauma,[29,38] this meta-analysis showed inconsistent results and, therefore, it cannot be considered a risk factor with a high degree of certainty. Indeed, other systematic reviews with meta-analysis[37–40,42] also found inconsistent and conflicting results on whether age is a risk factor for SSI after spine surgery. In fact, some studies have suggested that age should not be a major factor when deciding a surgery and that the attention should focus on a thorough evaluation and optimization of comorbidities.[26]

Procedure-related modifiable risk factors

Given the heterogeneity of results, it was not possible to definitively determine the impact of prolonged operative time[14,18,21,26,29,32,35] on the risk of SSI. However, Ogihara *et al*.[25] found a significant association between an operative time over 2 hours and a higher rate of SSI. Two systematic reviews[36,39] also considered a longer operative time an important risk factor. In fact, longer surgical procedures result in increased duration of tissue traction with ischemia and necrosis and can also increase the risk of direct wound contamination.[29,36]

Based on the results from one study,[26] increased preoperative stay was associated with a higher rate of infection, possibly as a reflection of a poor surgical medical condition, requiring preoperative optimization.

A definite conclusion that intraoperative blood loss increases the risk of infection could not be drawn, given the heterogeneity of results.[14,18,21,25,26,29,32,35] Similarly, other systematic reviews[36,38,40] have shown conflicting results. In fact, it is difficult to separate blood loss from other confounding variables such as surgical duration, invasiveness, as well as need for transfusion.[40]

Allogenic blood transfusion[18,21,26,33] was considered a significant risk factor for SSI. However, there is some conflicting evidence on this topic, with most studies also reporting a significant association between SSI and blood transfusion.[36–40,42,61] This association has been thought to be due to systemic immunomodulatory effects of the allogenic blood transfusions.[29,38,40,61–64]

Dural tear[12,18,25,32,33] could not be considered an important risk factor for SSI, due to inconsistent results. Similar controversial results have been found in spine literature.[38,40] However, this potential association may be due to the fact that a dural tear creates a communication between the epidural space and the cerebrospinal fluid, prolongs surgical time for repair and length of stay, as well as increases the risk of persistent cerebrospinal fluid leakage, delaying epithelialization and compromising wound healing.[38,40,65] Thus, careful intraoperative procedures to avoid dural tears may reduce the risk of SSI.[32]

Two or more fused levels were associated with a higher risk of SSI.[15,21] Two other systematic reviews support this finding.[36,40] Multilevel spinal fusion is associated with a higher risk possibly due to increased dead space by foreign bodies, inadequate vascular perfusion of the local wound and longer operative times.[20,36,60]

The effect of longer drainage on the infection risk was uncertain.[18,21] However, drains have been found to increase SSI rates in different types of surgeries, potentially by causing local tissue inflammation and by providing a route of entry for microorganisms from the skin surface.[66–69]

Hsiung *et al*.[35] found that a reduced irrigation was a risk factor for SSI. In fact, wound irrigation can reduce the microbial burden by removing tissue debris, metabolic waste and tissue exudate from the surgical field before wound closure.[70]

Limitations and future directions

The present study has some limitations. The strict inclusion criteria used enabled to reduce the heterogeneity of the included studies, leading to more reliable results in a specific population. Nevertheless, it also resulted in a smaller number of studies included, with smaller sample sizes. Additionally, some variables had a significant statistical heterogeneity and, subsequently, inconsistent results. Moreover, the definition of the SSI outcomes differed between studies and some risk factors mentioned in other systematic reviews were not assessed by the included studies.

Also, some data were presented in median (range) or median (interquartile range) format and needed to be converted into mean and SD for result comparisons, introducing a potential source of reduced reliability in the conclusions.

Therefore, the results of this study might overestimate the predicted effects and should be interpreted with the above limitations in mind. Future high-quality and high-powered studies are necessary to address these limitations and provide strong evidence on the risk of SSI after thoracolumbar spine surgery for degenerative diseases through a posterior approach.

CONCLUSIONS

SSI continues to be one of the most common complications after spinal surgery. It is imperative to recognize that the causes of postoperative SSI are multifactorial, including patient and procedure-related risks. This systematic review identified obesity, smoking, chronic heart disease and ASA >2 as the major risk factors for SSI and many other variables that can also potentially increase this risk. Awareness of these risk factors will help surgeons to optimize the patient's preoperative condition and surgical procedure and help decrease the incidence of postoperative SSI.

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 – Patient-related modifiable risk factors. **ALT**, Alanine Transaminase; **APTT**, Activated Partial Thromboplastin Time; **AST**, Aspartate Aminotransferase; **BMI**, Body Mass Index; **BUN**, Blood Urea Nitrogen; **CCI**, Charlson Comorbidity Index; **CRP**, C-Reactive Protein; **ESR**, Erythrocyte Sedimentation Rate; **FPG-CV**, Variation Coefficient of Fasting Plasma Glucose; **GNRI**, Geriatric Nutritional Risk Index; **Hb**, Hemoglobin; **Htc**, Hematocrit; **MD**, Mean Difference; **MFBG**, Mean Fasting Blood Glucose**; mFI-5**, Modified 5-Item Frailty Index; **MNA-SF**, Mini Nutritional Assessment Scale-Short Form; **N.A.**, not applicable; **PT**, Prothrombin Time; **RBC**, Red Blood Cells; **RR**, Risk Ratio; **WBC**, White Blood Cells; *****, median. **¥**, appendix figure.

	No. studies (Sample size)	Intervention group	Control group	I^2, p value	RR/MD (95% CI)	¥
Obese (BMI ≥30)	5 (4240)	113/1596	90/2644	0%, 0.63	2,13 [1.61,2.83]	2
BMI ≥ 40 vs 30-39,9	1 (423)	1/106	2/317	N.A.	1.50 [0.14,16.32]	
BMI	7 (8031)	187	7844	83%, <0.00001	1.76 [1.25, 2.27]	3
Subcutaneous fat thickness (mm)	1 (448)	32.26 ± 4.25 (n=20)	24.75 ± 6.25 (n=428)	N.A.	7.51 [5.56, 9.46]	
Muscle thickness (mm)	1 (448)	41.74 ± 4.75 (n=20)	39.75 ± 6.75 (n=428)	N.A.	1.99 [-0.19, 4.17]	
Diabetes mellitus	9 (9297)	110/1171	222/8126	78%, <0.0001	4.50 [3.59, 5.63]	4
Age	1 (238)	70* ± 11.85 (n=34)	67* ± 11.85 (n=204)	N.A.	3.00 [-1.30, 7.30]	
Male vs Female	1 (238)	15/104	19/134	N.A.	1.02 [0.54, 1.90]	
CV disease	1 (238)	23/157	11/81	N.A.	1.08 [0.55, 2.10]	
Operative time	1 (238)	180* ± 70.37 (n=34)	170* ± 48.15 (n=204)	N.A.	10.00 [-14.56, 34.56]	
Intraop. blood loss	1 (238)	300* ± 222.22 (n=34)	250* ± 148.15 (n=204)	N.A.	50.00 [-27.41, 127.41]	
Intraop. blood transfusion	1 (238)	250* ± 370.37 (n=34)	200* ± 185.19 (n=204)	N.A.	50.00 [-77.06, 177.06]	
BMI ≥ 25 vs < 25	1 (238)	16/124	18/114	N.A.	0.82 [0.44, 1.52]	
>5 years vs ≤5y DM2	1 (238)	27/137	7/101	N.A.	2.84 [1.29, 6.27]	

HbA1c	1 (238)	7.34* ± 0.64 (n=34)	7.34* ± 0.47 (n=204)	N.A.	0.00 [-0.22, 0.22]	
≥ 2 vs 1 fused vertebrae	1 (238)	31/157	3/81	N.A.	6.40 [1.89, 21.63]	
Length of incision	1 (238)	9.5* ± 2.96 (n=34)	9.0* ± 2.96 (n=204)	N.A.	0.50 [-0.57, 1.57]	
Drain placement	1 (238)	4.0* ± 0.93 (n=34)	4.0* ± 0.74 (n=204)	N.A.	0.00 [-0.33, 0.33]	
Preop MFBG	1 (238)	7.06* ± 1.53 (n=34)	7.23* ± 1.61 (n=204)	N.A.	-0.17 [-0.73, 0.39]	
Preop FPG-CV	1 (238)	9.39* ± 6.71 (n=34)	9.38* ± 6.73 (n=204)	N.A.	0.01 [-2.43, 2.45]	
Postop MFBG	1 (238)	7.73* ± 1.63 (n=34)	7.7* ± 1.52 (n=204)	N.A.	0.03 [-0.56, 0.62]	
Postop FPG-CV	1(238)	21.41* ±16.76 (n=34)	12.68* ± 6.46 (n=204)	N.A.	8.73 [3.03, 14.43]	
Preop HbA1c	1 (705)	7.5 ± 1.6 (n=33)	5.3 ± 0.8 (n=672)	N.A.	2.20 [1.65, 2.75]	
Fasting blood glucose	1 (1269)	7 ± 2.7 (n=43)	5.7 ± 1.4 (n=1226)	N.A.	1.30 [0.49, 2.11]	
Smoking	10 (9578)	81/1803	216/7775	0%, 0.54	1.81 [1.40, 2.34]	5
Chronic heart disease	5 (3964)	16/226	143/3738	0%, 0.41	2.02 [1.23, 3.31]	6
Rheumatic disease	4 (2695)	11/120	105/2575	58%, 0.07	2.45 [1.33, 4.52]	7
Parkinson disease	1 (958)	1/4	29/954	N.A.	8.22 [1.45, 46.61]	
Renal insufficiency	1 (1269)	5/33	38/1236	N.A.	4.93 [2.07, 11.72]	
CCI ≥ 4	1 (958)	10/143	20/815	N.A.	2.85 [1.36, 5.96]	
mFI-5 =1 vs =0	1 (19025)	179/10064	126/8961	N.A.	1.26 [1.01, 1.59]	
mFI-5≥2 vs =0	1 (13452)	135/4491	126/8961	N.A.	2.14 [1.68, 2.72]	
Hypertension	4 (3259)	45/974	81/2285	0%, 0.46	1.34 [0.94, 1.92]	8
Osteoporosis	2 (1542)	9/112	54/1430	72%, 0.06	1.58 [0.78, 3.23]	
Pulmonary disease	3 (2932)	6/87	100/2845	34%, 0.22	1.92 [0.87, 4.24]	9
Cerebrovascular disease	3 (2932)	10/191	96/2741	0%, 0.88	1.73 [0.92, 3.26]	10
Tumor	1 (958)	2/21	28/937	N.A.	3.19 [0.81, 12.51]	
Tuberculosis	1 (958)	0/4	30/954	N.A.	3.13 [0.22, 44.44]	

Thyroid disorders	1 (958)	1/22	29/936	N.A.	1.47 [0.21, 10.29]	
Cauda Equina Injury	1 (958)	2/23	28/935	N.A.	2.90 [0.74, 11.47]	
Neurogenic claudication	1 (958)	9/234	21/724	N.A.	1.33 [0.62, 2.85]	
Chronic liver disease	1 (1269)	4/57	39/1212	N.A.	2.18 [0.81, 5.89]	
Hemodialysis	1 (4027)	0/49	26/3978	N.A.	1.50 [0.09, 24.30]	
Other periop infections	1 (448)	1/29	19/419	N.A.	0.76 [0.11, 5.48]	
Preop albuminemia	5 (3964)	159	3805	86%, <0.00001	-4.45 [-5.07, -3.83]	11
Preop hypoalbuminemia (≤35g/L)	2 (1823)	15/190	47/1633	72%, 0.06	2.82 [1.60, 4.97]	
Postop hypoalbuminemia (≤35g/L)	2 (1020)	35/402	9/618	61%, 0.11	7.89 [3.90, 15.94]	
Total protein	2 (2227)	73	2154	0%, 0.43	-2.45 [-4.08, -0.83]	
MNA-SF≤11 vs>11	1 (252)	9/132	4/120	N.A.	2.05 [0.65, 6.47]	
<8 vs 8-11	1 (132)	5/33	4/99	N.A.	3.75 [1.07, 13.15]	
GNRI ≤ 98 vs >98	1 (252)	9/155	4/97	N.A.	1.41 [0.45, 4.45]	
<92 vs 92-98	1 (155)	3/70	6/85	N.A.	0.61 [0.16, 2.34]	
Steroid use	5 (6692)	13/176	115/6516	85%, <0.0001	2.37 [1.37, 4.12]	12
Lumbar Epidural Injection	1 (2781)	29/469	81/2312	N.A.	1.76 [1.17, 2.67]	
Steroid vs Non-steroid	1 (469)	19/245	10/224	N.A.	1.74 [0.83, 3.66]	
0-1M vs >1M	1 (469)	18/258	11/211	N.A.	1.34 [0.65, 2.77]	
Preoperative body temperature	2 (1406)	50	1356	69%, 0.07	-0.13 [-0.20, -0.06]	
Preop RBC (x10^{12}/L)	4 (3516)	139	3377	40%, 0.17	-0.15 [-0.22,-0.08]	13
Preop Hb (g/L)	4 (3259)	126	3133	23%,0.27	-3.98 [-6.94,-1.02]	14
Preop Htc (%)	2 (1717)	63	1654	0%, 0.37	-1.87 [-3.03,-0.71]	
Postop Hb (g/L)	1 (448)	20	428	N.A.	-11.66 [-18.22, -5.10]	
Preop Neutrophil count (x10^{9}/L)	2 (2227)	73	2154	0%, 0.38	0.67 [0.01,1.32]	
Preop WBC (x10^{9}/L)	5 (3964)	159	3805	72%, 0.006	0.18 [-0.06,0.42]	15
Preop Platelets (x10^{9})	4 (3516)	139	3377	0%, 0.73	3.24 [-6.87,13.35]	16

Preop Lymphocyte count (x10^9/L)	3 (2675)	93	2582	93%, <0.00001	-0.07 [-0.19,0.05]	17
Preop Monocyte count (x10^9/L)	1 (958)	30	928	N.A.	0.04 [-0.04,0.12]	
Preop Na+	1 (958)	30	928	N.A.	-0.27 [-1.04, 0.50]	
Preop Ca2+	2 (1663)	63	1600	81%, 0.02	-0.01 [-0.05, 0.02]	
Preop K+ (mmol/L)	1 (1663)	63	1600	0%, 0.43	-0.03 [-0.11,0.06]	
Preop ESR (mm/h)	1 (958)	30	928	N.A.	-1.31 [-3.89,1.27]	
Preop CRP (mg/L)	1 (958)	30	928	N.A.	-0.13 [-1.76,1.50]	
Preop Globulin	3 (2247)	96	2151	0%, 0.69	0.53 [-0.23,1.29]	18
Preop Fibrinogen (mg/dL)	1 (705)	33	672	N.A.	-0.40 [-0.57,-0.23]	
Triglyceride (mmol/L)	1 (958)	30	928	N.A.	0.24 [-0.11,0.59]	
Total cholesterol (mmol/L)	1 (958)	30	928	N.A.	-0.17 [-0.50,0.16]	
Preop ALT	2 (1542)	63	1479	50%, 0.16	-1.82 [-5.69,2.06]	
Preop AST	2 (1542)	63	1479	13%, 0.28	0.62 [-1.88,3.12]	
Pre creatinine (umol/L)	2 (1542)	63	1479	0%, 0.55	4.28 [-1.31,9.87]	
BUN (mmol/L)	1 (958)	30	928	N.A.	-0.27 [-1.81,1.27]	
Preop PT (s)	1 (705)	33	672	N.A.	0.20 [-0.22,0.62]	
Preop APTT (s)	1 (705)	33	672	N.A.	0.30 [-0.39,0.99]	
Alcohol	4 (2729)	28/501	88/2228	0%, 0.51	1.31 [0.86, 1.99]	19

Table III – Patient-related non-modifiable risk factors. **ASA**, American Society of Anesthesiologists Score; **MD**, Mean Difference; **N.A.**, not applicable; **RR**, Risk Ratio;. **¥**, appendix figure.

	No. studies (Sample size)	Intervention group	Control group	I^2, p value	RR/MD (95% CI)	¥
ASA >2	6 (8315)	92/3530	76/4785	51%, 0.07	2.86 [2.10, 3.90]	20
Age	7 (7720)	174	7546	35%, 0.16	5.93 [4.50, 7.36]	21
Age ≥70	2 (1454)	11/269	33/1185	0%, 0.33	1.63 [0.84, 3.16]	
Male	8 (8853)	119/5107	111/3746	66%, 0.005	1.04 [0.80, 1.34]	22

Table IV – Procedure-related modifiable risk factors. **MD**, Mean Difference; **N.A.**, not applicable; **PLIF**, Posterior Lumbar Interbody Fusion; **RR**, Risk Ratio; **TLIF**, Transforaminal Lumbar Interbody Fusion; **¥**, appendix figure.

	No. studies (Sample size)	Intervention group	Control group	I^2, p value	RR/MD (95% CI)	¥
Operative time	7 (4962)	191	4771	67%, 0.006	24.66 [17.46, 31.85]	23
Operative time >2h	1 (4027)	16/1265	10/2762	N.A.	3.49 [1.59, 7.68]	
Preop stay	1 (1269)	5 ± 3.3 (n=43)	3.4 ± 2.6 (n=1226)	N.A.	1.60 [0.60, 2.60]	
Lenght of stay	3 (2781)	92	2689	0%, 0.91	10.19 [7.60, 12.78]	24
Intraoperative blood loss	8 (8989)	217	8772	83%, <0.00001	64.94 [48.22, 81.66]	25
≥2 vs 1 fused levels	2 (1161)	27/600	8/561	2%, 0.31	3.30 [1.44, 7.57]	
Allogenic blood transfusion	4 (3215)	61/746	95/2469	0%, 0.45	1.71 [1.23, 2.38]	26
Dural tear	5 (31977)	303/9501	346/22476	85%, <0.0001	2.12 [1.81, 2.48]	27
Drainage time	2 (1406)	50	1356	66%, 0.09	0.77 [0.39, 1.16]	
Duration of urinary catheter	1 (958)	30	928	N.A.	0.61 [0.01, 1.21]	
Lenght of incision	1 (958)	30	928	N.A.	1.46 [0.38, 2.54]	
PLIF vs TLIF	1 (226)	9/125	5/101	N.A.	1.45 [0.50, 4.20]	
Retaining screws	1 (958)	1.83 ± 0.83 (n=30)	1.78 ± 0.85 (n=928)	N.A.	0.05 [-0.25, 0.35]	
Allograft bone	3 (2301)	22/414	74/1887	0%, 0.52	1.52 [0.95, 2.44]	28
Periop invasive vascular catheterization	1 (448)	11/193	9/255	N.A.	1.61 [0.68, 3.82]	
Jugular vein catheterization time	1 (958)	30	928	N.A.	0.41 [-1.10, 1.92]	
Postop drainage	3 (2271)	82	2189	94%, <0.00001	-21.54 [-46.27, 3.18]	29
Irrigation amount (ml/h)	1 (444)	13	431	N.A.	-358 [-660.78, -55.22]	

Table V – Procedure-related non-modifiable risk factors. **LDH**, Lumbar Disc Herniation; **LI/S**, Lumbar Instability/Spondylolisthesis; **LSS**, Lumbar spinal stenosis; **N.A.**, not applicable; **RR**, Risk Ratio; **¥**, appendix figure.

	No. studies (Sample size)	Intervention group	Control group	I^2, p value	RR (95% CI)	¥
Diagnosis						
LSS vs LDH	3 (1097)	26/367	29/730	0%, 0.47	1.69 [1.01, 2.83]	30
LI/S vs LDH	3 (1260)	22/530	29/730	0%, 0.69	1.06 [0.62, 1.84]	31
LSS vs LI/S	3 (897)	26/367	22/530	0%, 0.92	1.67 [0.96, 2.91]	32
Previous lumbar surgery	1 (448)	4/56	16/392	N.A.	1.75 [0.61, 5.05]	
Previous SSI	1 448)	2/45	18/403	N.A.	1.00 [0.24, 4.15]	
Revision surgery	1 (4027)	0/376	26/3651	N.A.	0.18 [0.01, 2.99]	
Emergency surgery	1 (4027)	1/53	25/3974	N.A.	3.00 [0.41, 21.73]	

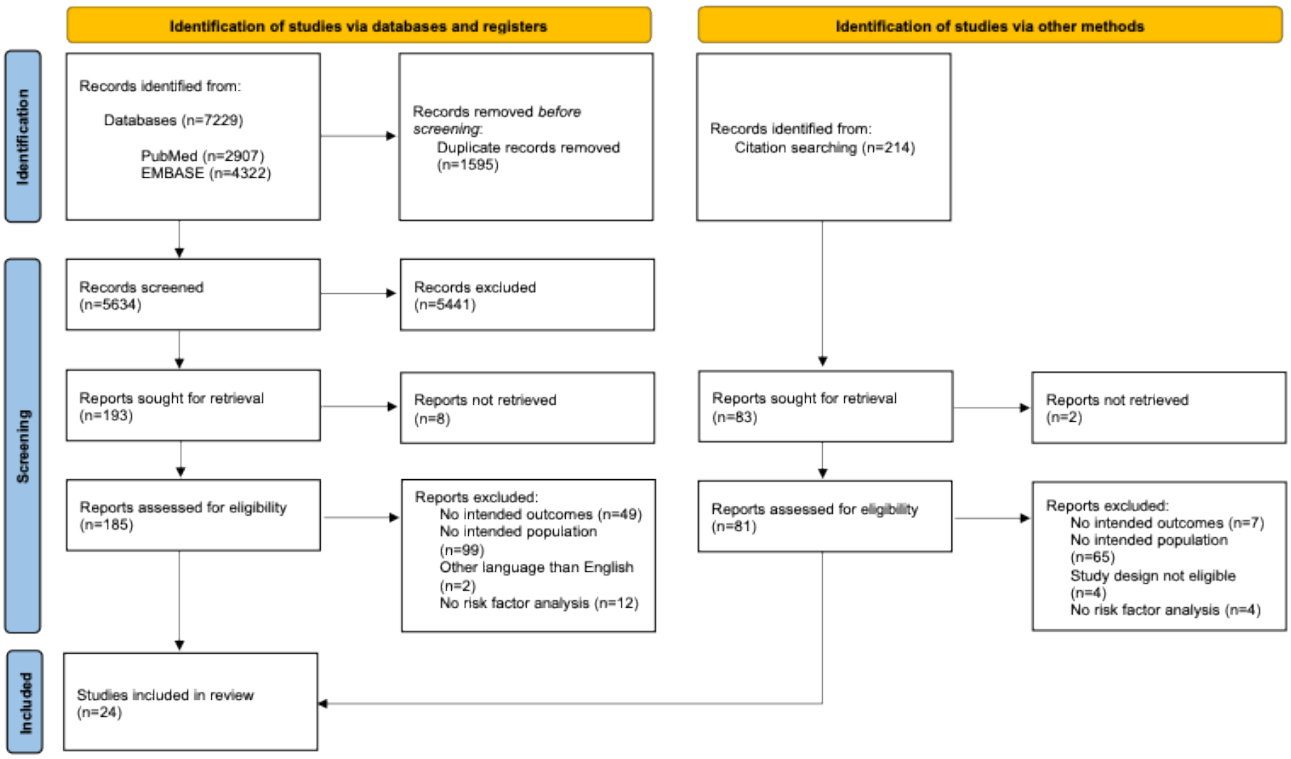

Figure 1 - PRISMA 2020 flow diagram.

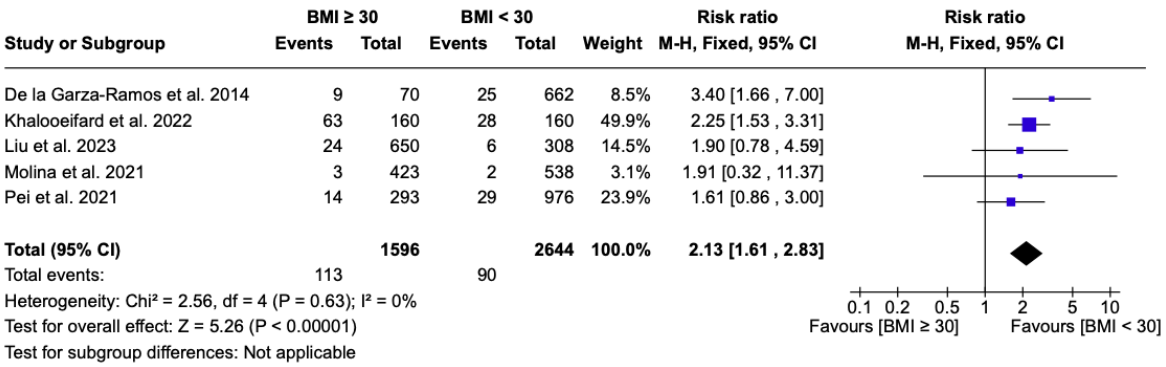

Figure 2 – Forest plot for obesity (BMI ≥30).

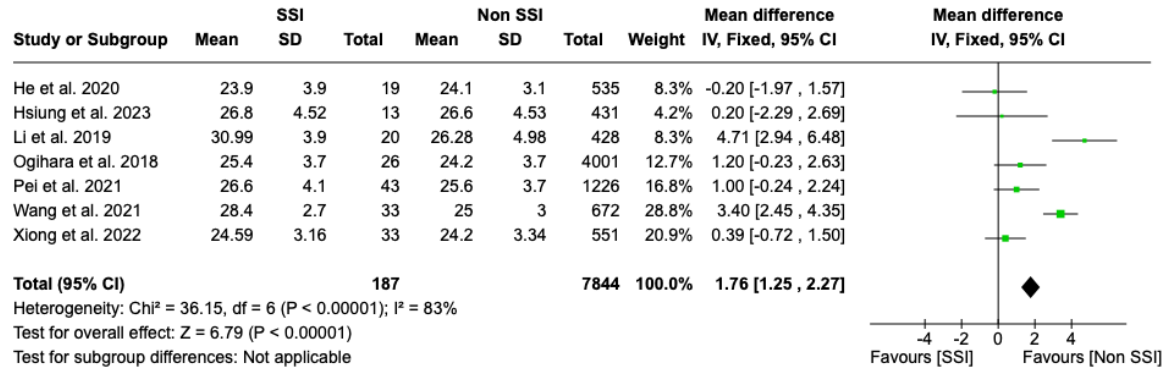

Figure 3 – Forest plot for BMI.

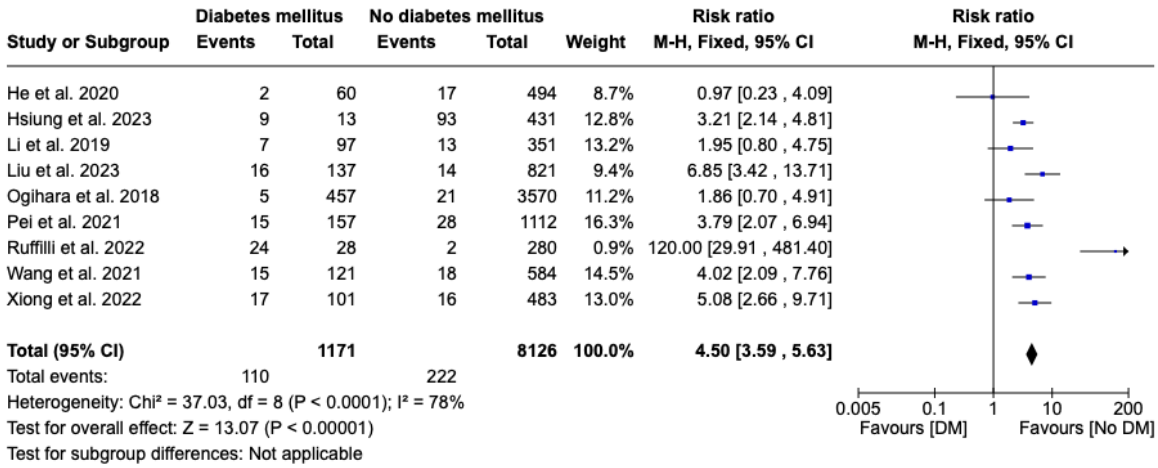

Figure 4 – Forest plot for diabetes mellitus.

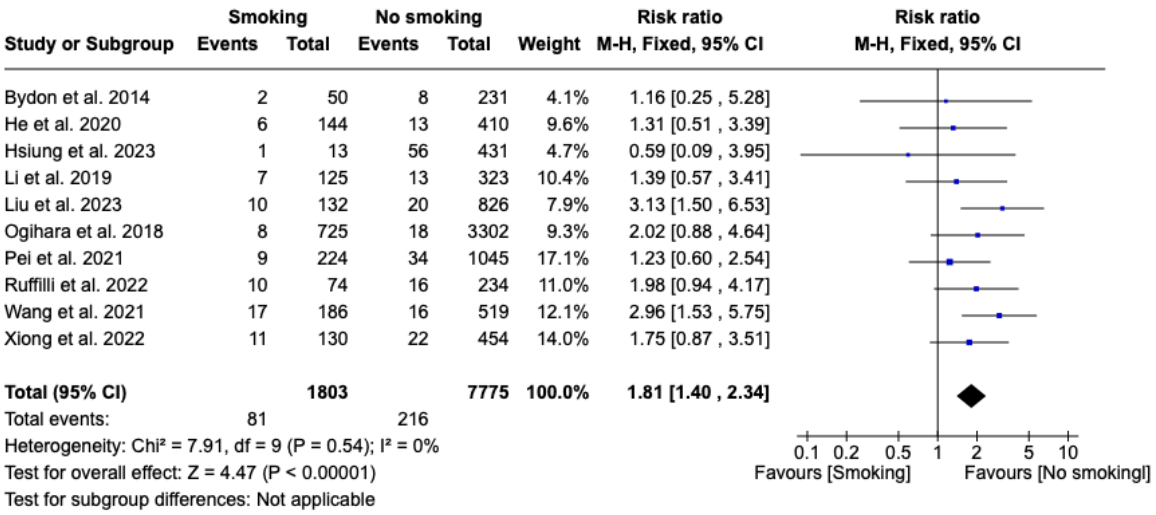

Figure 5 – Forest plot for smoking.

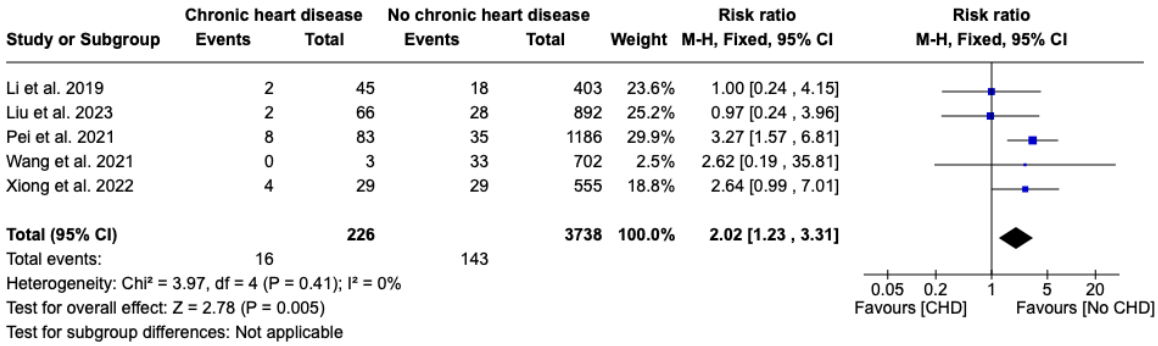

Figure 6 – Forest plot for chronic heart disease.

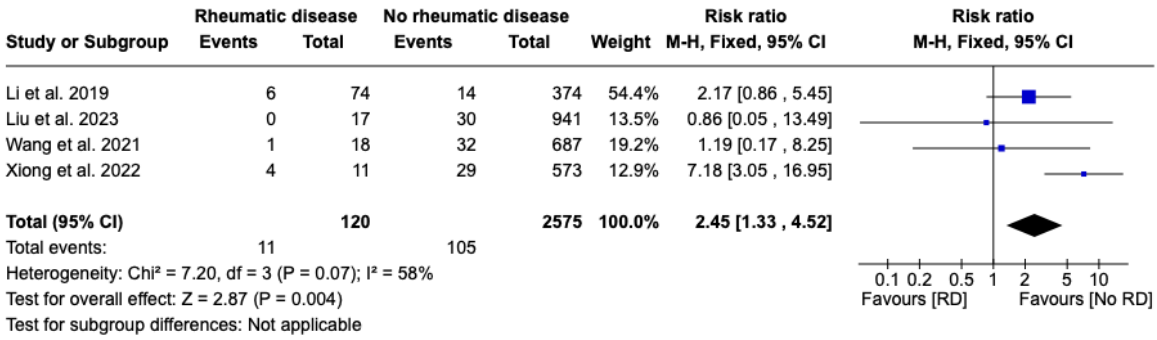

Figure 7 – Forest plot for rheumatic disease.

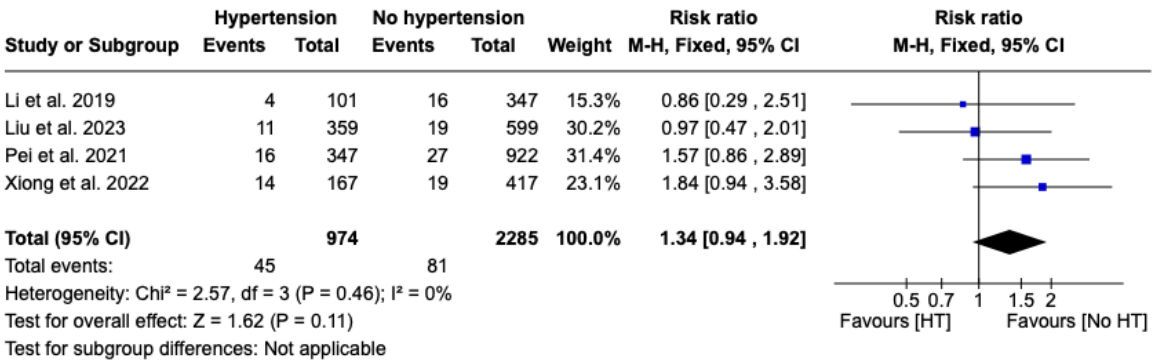

Figure 8 – Forest plot for hypertension.

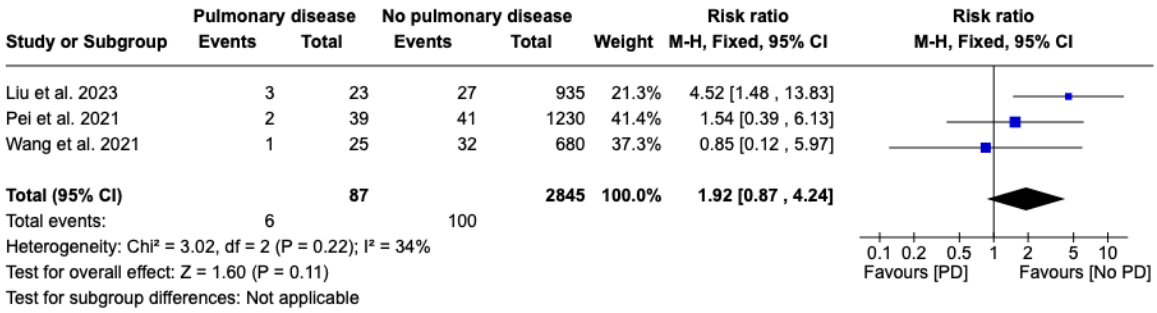

Figure 9 – Forest plot for pulmonary disease.

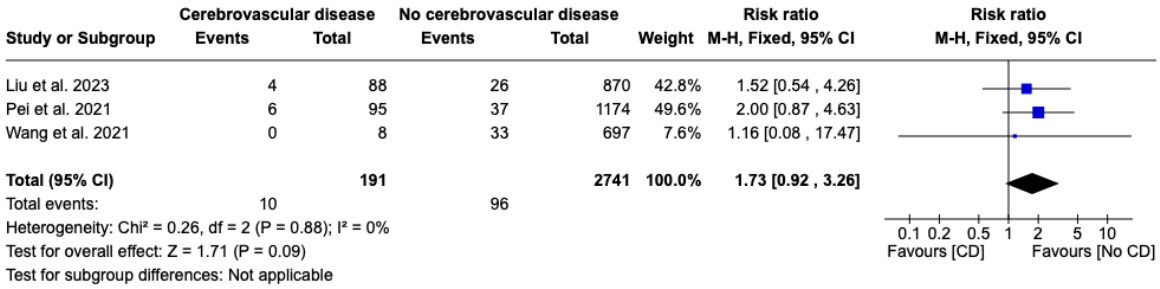

Figure 10 – Forest plot for cerebrovascular disease.

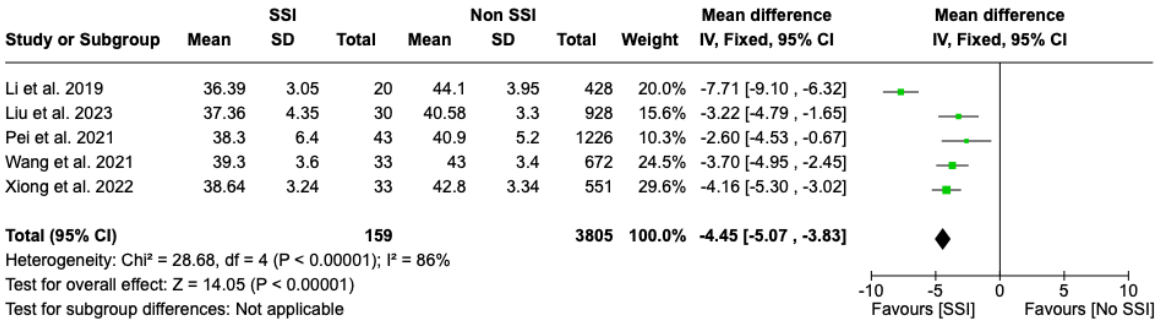

Figure 11 – Forest plot for preoperative albuminemia.

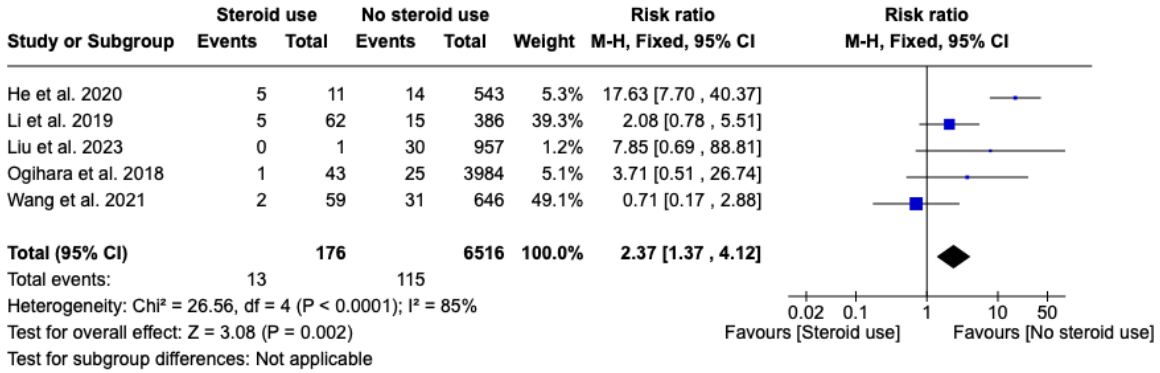

Figure 12 – Forest plot for steroid use.

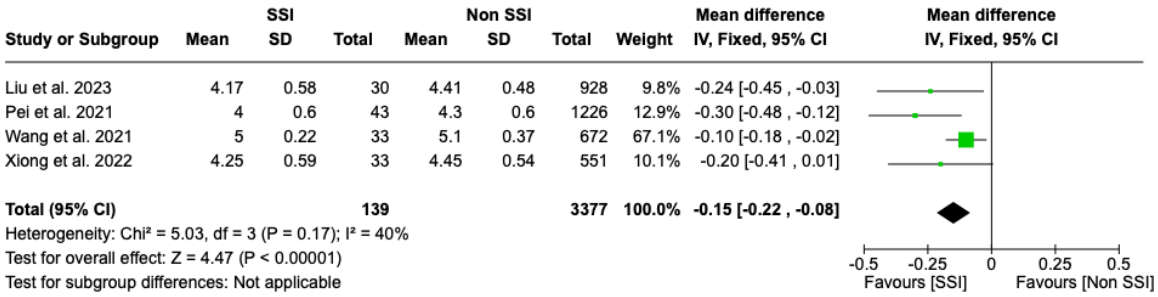

Figure 13 – Forest plot for preoperative red blood cell ($x10^{12}$/L).

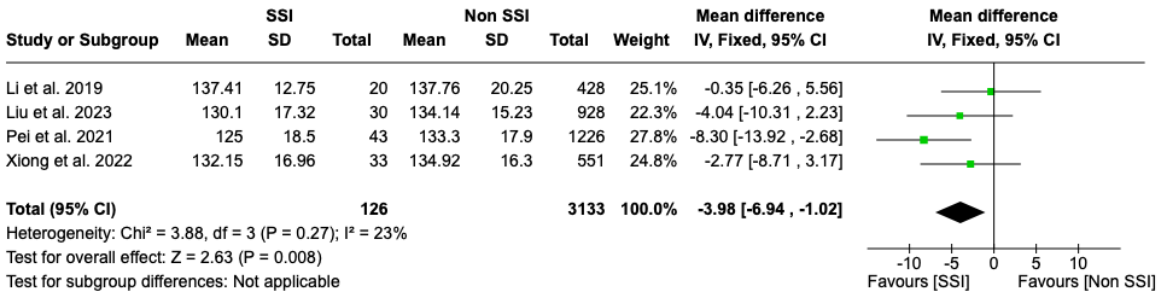

Figure 14 – Forest plot for preoperative hemoglobin (g/L).

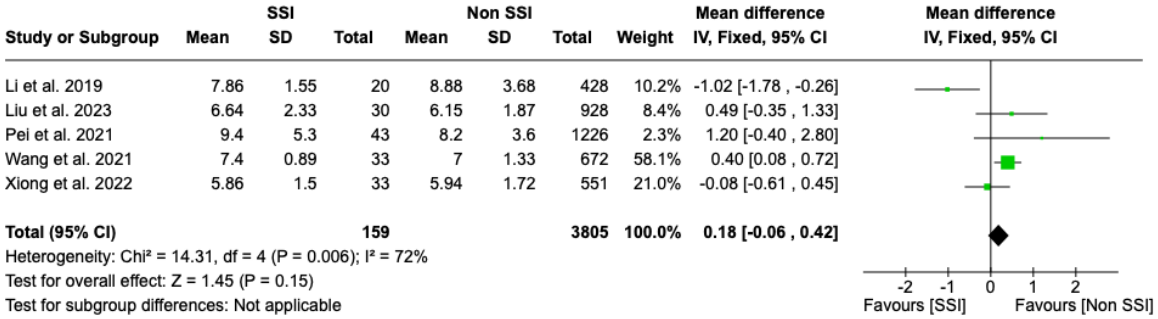

Figure 15 – Forest plot for white blood cell (x10^9/L).

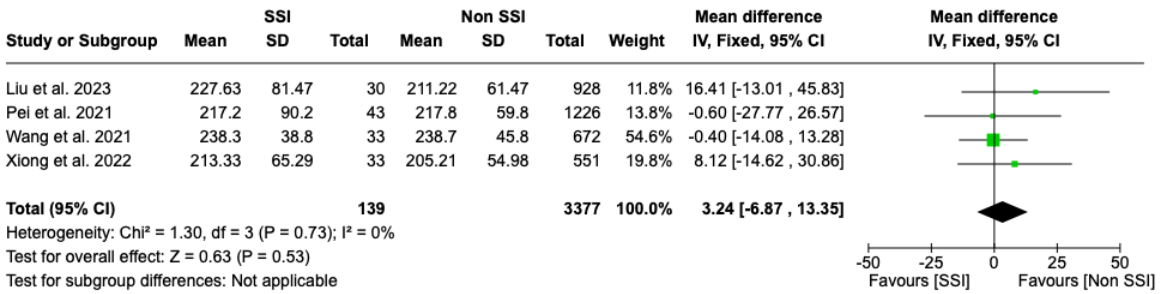

Figure 16 – Forest plot for preoperative platelet count (x10^9/L).

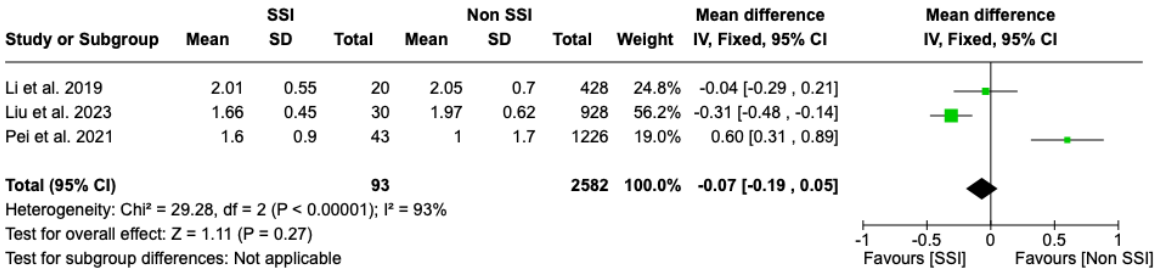

Figure 17 – Forest plot for preoperative lymphocyte count (x10^9/L).

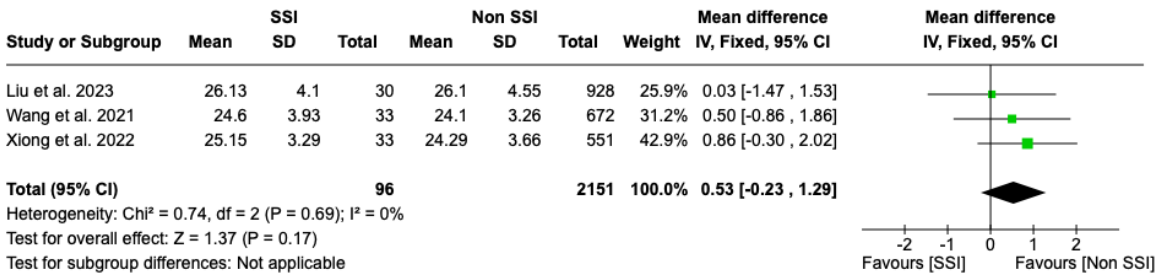

Figure 18 – Forest plot for preoperative globulin.

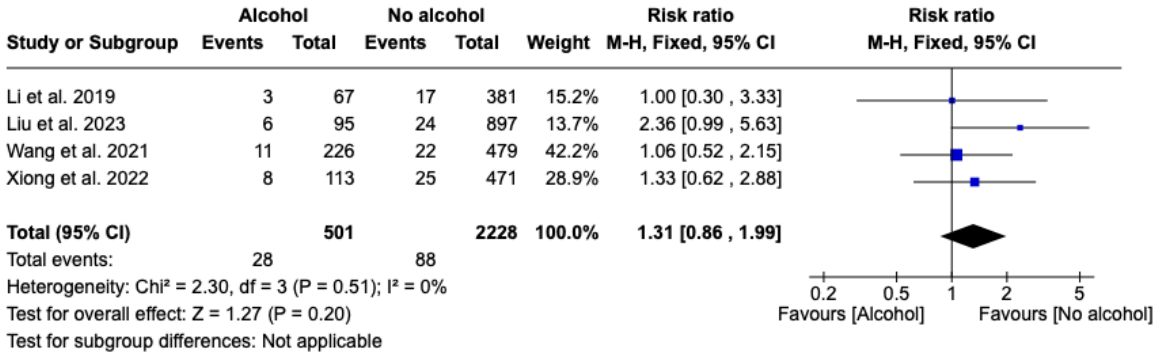

Figure 19 – Forest plot for alcohol consumption.

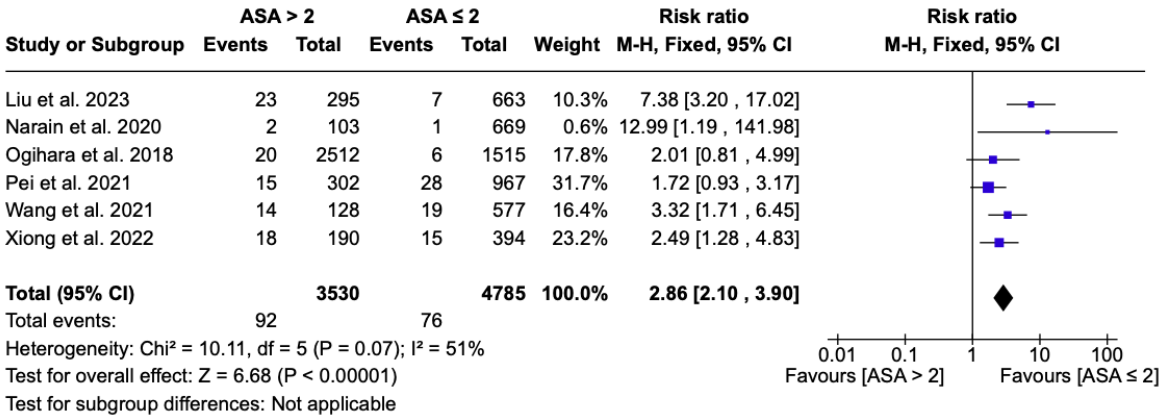

Figure 20 – Forest plot for ASA > 2.

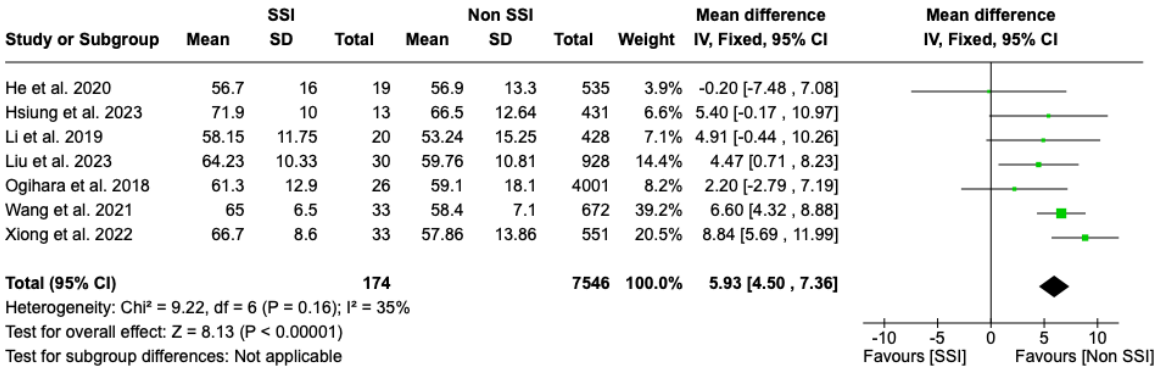

Figure 21 – Forest plot for age.

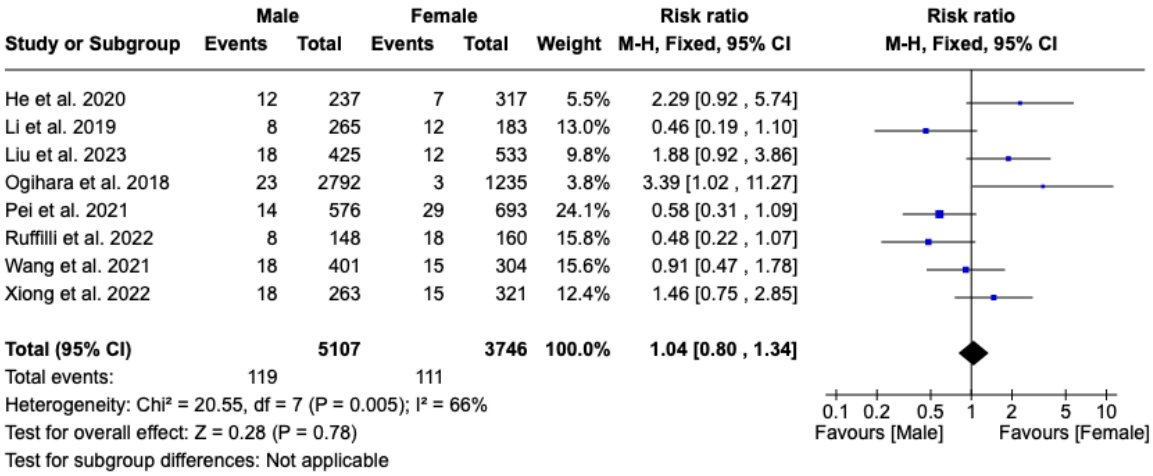

Figure 22 – Forest plot for male gender.

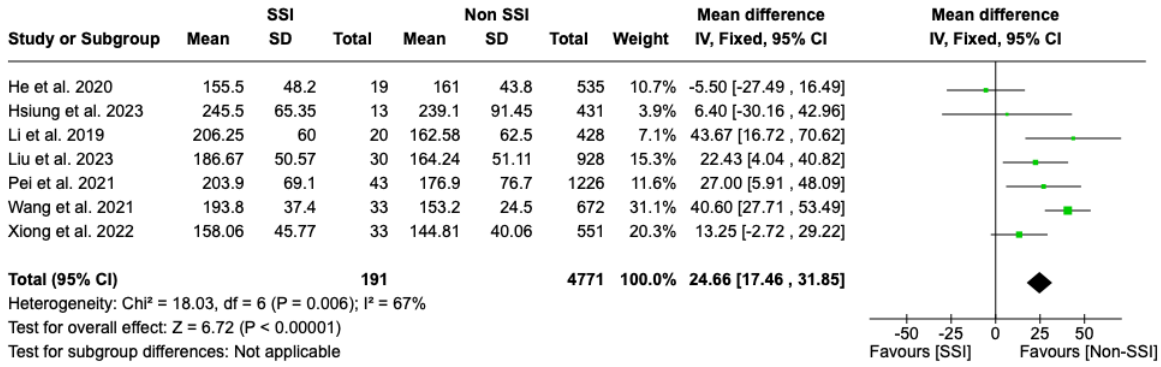

Figure 23 – Forest plot for operative time (min).

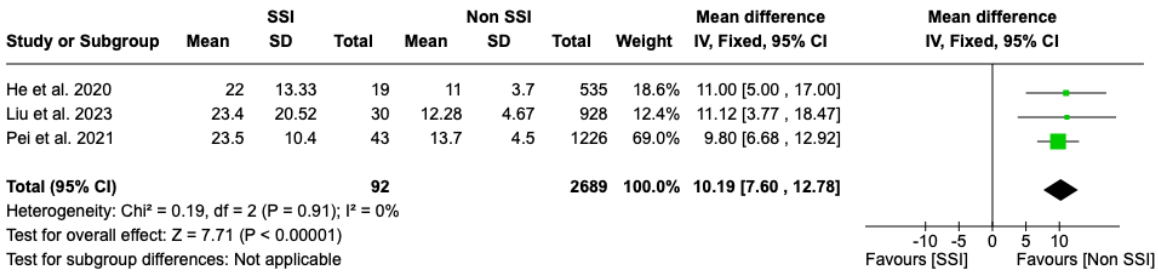

Figure 24 – Forest plot for length of stay.

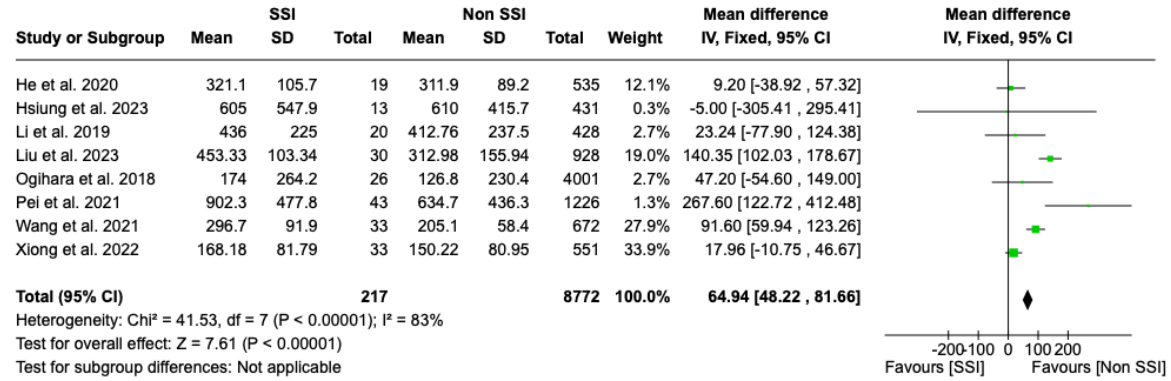

Figure 25 – Forest plot for intraoperative blood loss (ml).

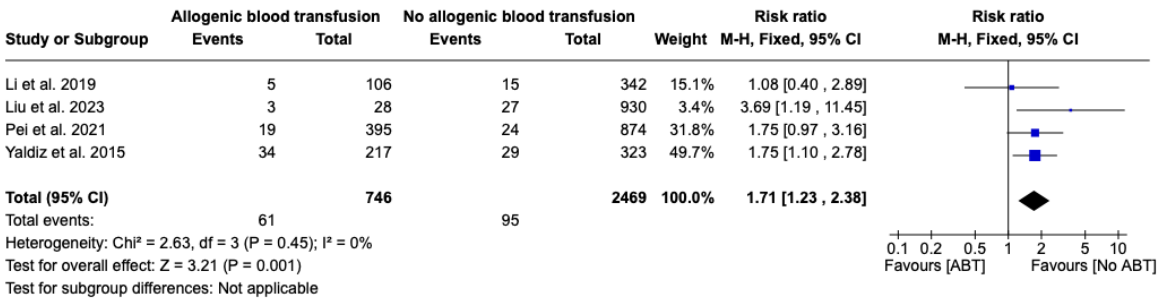

Figure 26 – Forest plot for allogenic blood transfusion.

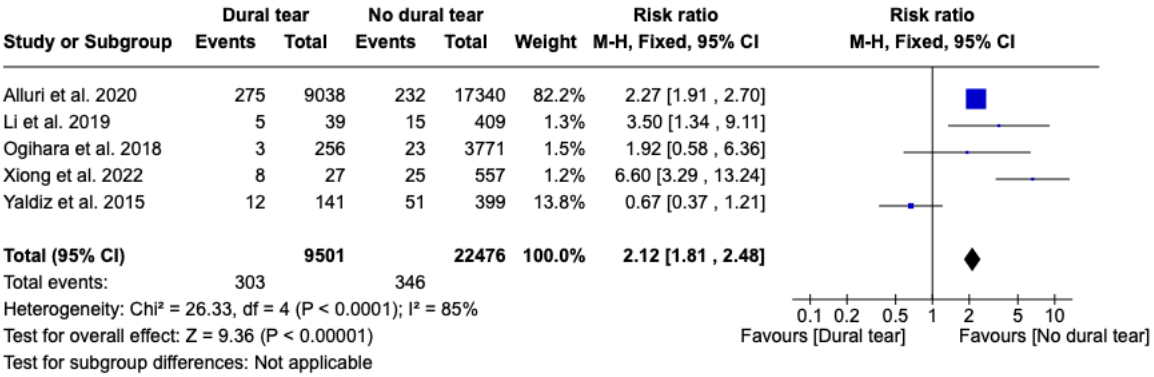

Figure 27 – Forest plot for dural tear.

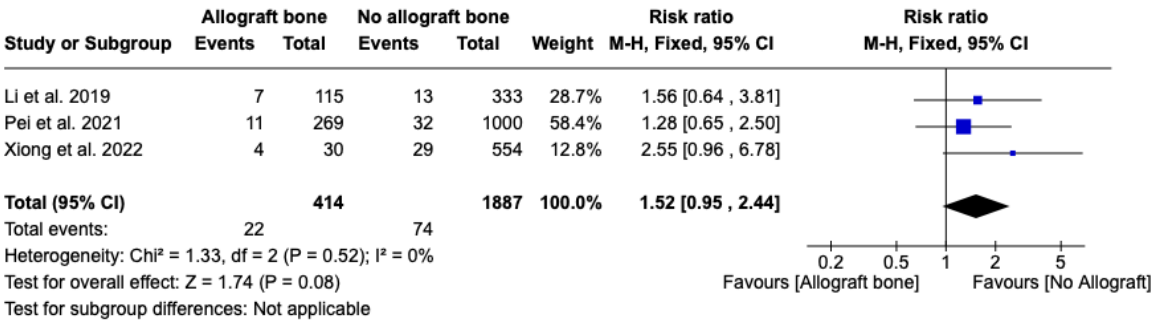

Figure 28 – Forest plot for allograft bone.

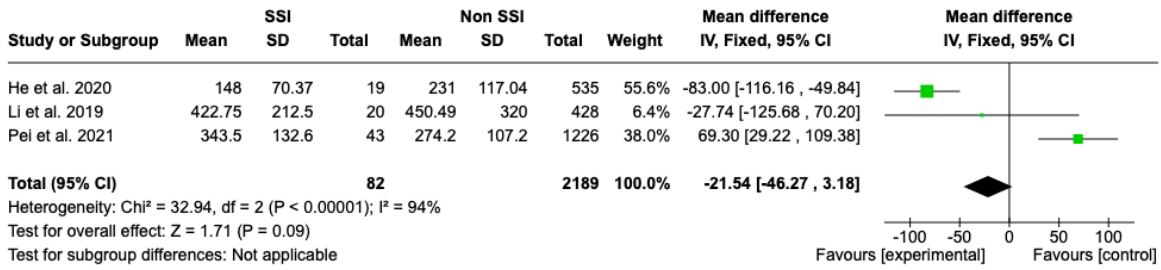

Figure 29 – Forest plot for postoperative drainage (ml).

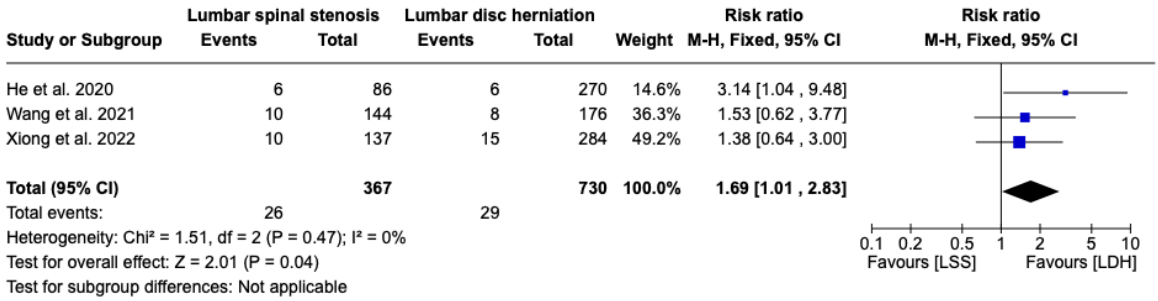

Figure 30 – Forest plot for lumbar spinal stenosis vs lumbar disc herniation.

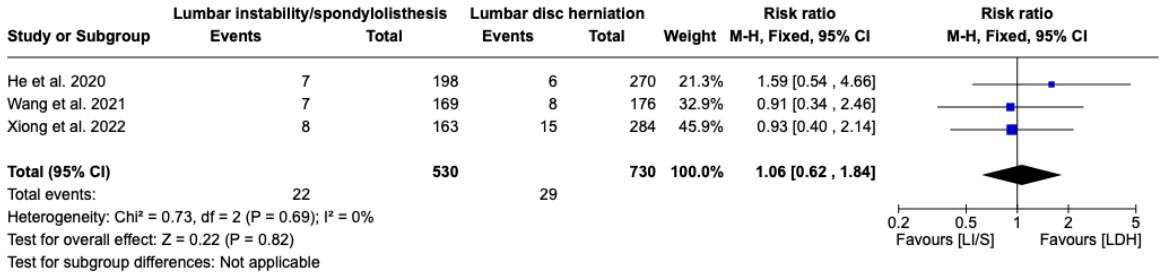

Figure 31 – Forest plot for lumbar instability/spondylolisthesis vs lumbar disc herniation.

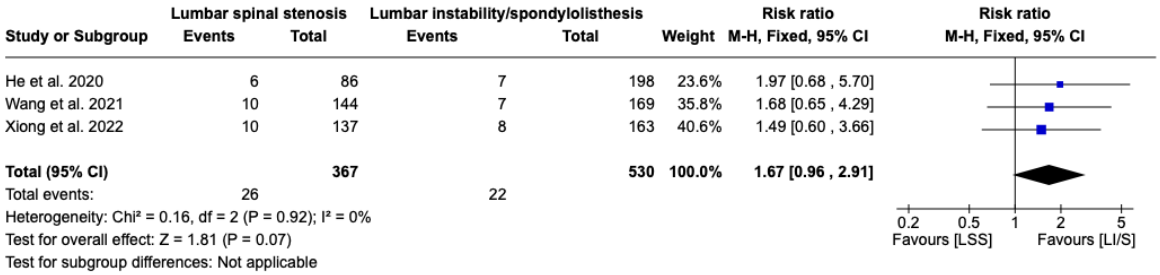

Figure 32 – Forest plot for lumbar spinal stenosis vs lumbar instability/spondylolisthesis.

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