

Risk factors for surgical site infection following lumbar spinal surgery: a meta-analysis

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Objective: To identify risk factors for surgical site infection (SSI) in patients who had undergone lumbar spinal surgery.

Methods: Studies published in PubMed, Web of Science, and Embase were systematically reviewed to determine risk factors for SSI following lumbar spinal surgery. Results are expressed as risk ratios (RRs) with 95% CIs and weighted mean difference (WMD) with 95% CI. A fixed-effect or random-effect model was used to pool the estimates according to heterogeneity among the studies included.

Results: Sixteen studies involving 13,393 patients were included in this meta-analysis. Pooled estimates suggested that diabetes (RR 2.19, 95% CI 1.43–3.36; $P < 0.001$), obesity (RR 2.87, 95% CI 1.62–5.09; $P < 0.001$), BMI (WMD 1.32 kg/m², 95% CI 0.39–2.25; $P = 0.006$), prolonged operating time (WMD 24.96 minutes, 95% CI 14.77–35.15; $P < 0.001$), prolonged hospital stay (WMD 2.07 days, 95% CI 0.28–3.87; $P = 0.024$), hypertension (RR 1.28, 95% CI 1.08–1.52; $P = 0.005$), and previous surgery (RR 2.06, 95% CI 1.39–3.06; $P < 0.001$) were independent risk factors for SSI in patients who had undergone lumbar spine surgery. Current smoking (RR 0.89, 95% CI 0.75–1.06; $P = 0.178$), American Society of Anesthesiologists grade > 2 (RR 2.63, 95% CI 0.84–8.27; $P = 0.098$), increased age (WMD 1.43 years, 95% CI –1.15 to 4.02; $P = 0.278$), COPD (RR 1.21, 95% CI 0.68–2.17; $P = 0.521$), cardiovascular disease (RR 1.63, 95% CI 0.40–6.70; $P = 0.495$), rheumatoid arthritis (RR 1.76, 95% CI 0.53–5.90; $P = 0.359$), and osteoporosis (RR 1.91, 95% CI 0.79–4.63; $P = 0.152$) were not risk factors for postoperative SSI.

Conclusion: Our results identified several important factors that increased the risk of postoperative SSI. Knowing these risk factors, surgeons could adequately analyze and evaluate risk factors in patients and then develop prevention measurements to reduce the rate of SSI.

Keywords: lumbar spinal surgery, surgical site infection, risk factors, meta-analysis

Introduction

Surgical site infection (SSI) is one of the most serious complications following lumbar spine surgery during the early postoperative stage. SSI rates have been reported to be 0.7%–12.0%.^{1,2} Despite several interventions in clinical practice, including the use of prophylactic antibiotics, improvements in surgical techniques, and postoperative care, SSI continues to affect patients after lumbar surgery.^{3,4} SSI usually requires surgical debridement, which leads to higher postoperative morbidity and mortality.^{5–7} This would increase the duration of hospital stay, reoperation rates, and additional treatment costs.^{5–7} Therefore, determining risk factors for postoperative SSI and seeking methods to reduce SSI rates are very necessary.

There have been several studies to investigate postoperative SSI risk factors, such as increased age,⁸ obesity,^{9,10} diabetes,^{8,10} smoking,¹⁰ previous infection,¹¹ prolonged operating time,¹² prolonged hospital stay,¹³ and admission from a health care facility.¹⁴

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However, the results of these studies were inconsistent. In order to systematically assess the most important risk factors for SSI following lumbar spinal surgery, we conducted this meta-analysis. Based upon identified risk factors, we can deduce preventive strategies to reduce the risk for SSI, thereby decreasing the morbidity, mortality, and health care costs.

Methods

Search strategy

This meta-analysis was performed according to the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statement.¹⁵ We did a comprehensive search on PubMed, Embase, and Web of Science from their inception to May 11, 2018. Search items were ((“lumbosacral region” [MeSH terms] OR (“lumbosacral” [all fields] AND “region” [all fields]) OR “lumbosacral region” [all fields] OR “lumbar” [all fields]) AND (“surgery” [subheading] OR “surgery” [all fields] OR “surgical procedures, operative” [MeSH terms] OR (“surgical” [all fields] AND “procedures” [all fields] AND “operative” [all fields]) OR “operative surgical procedures” [all fields] OR “surgery” [all fields] OR “general surgery” [MeSH terms] OR (“general” [all fields] AND “surgery” [all fields]) OR “general surgery” [all fields])) AND (“surgical wound infection” [MeSH terms] OR (“surgical” [all fields] AND “wound” [all fields] AND “infection” [all fields]) OR “surgical wound infection” [all fields] OR (“surgical” [all fields] AND “site” [all fields] AND “infection” [all fields]) OR “surgical site infection” [all fields] AND (“risk factors” [MeSH terms] OR (“risk” [all fields] AND “factors” [all fields]) OR “risk factors” [all fields] OR (“risk” [all fields] AND “factor” [all fields]) OR “risk factor” [all fields])). There was no limitation on language or publication type. Moreover, we also manually searched the references of the studies and reviews included to identify other potentially eligible studies.

Inclusion criteria

Two independent investigators performed the literature search, literature review (title/abstract review, full-text review, and included eligible studies). Any disagreement between them was resolved by discussion and consensus. All studies that investigated risk factors for postoperative SSI after lumbar spinal surgery were considered eligible for data analysis. We included the studies that met inclusion criteria of randomized controlled trial, cohort study, or case-control study, adult patients who had undergone lumbar spinal surgery, and presence of risk factors for postoperative SSI.

Data extraction and quality assessment

Two independent investigators performed the data extraction. Data extracted included country of study, number of patients in SSI group and non-SSI group, baseline characteristics, and outcomes. We used the modified Newcastle–Ottawa Scale (NOS)¹⁶ to evaluate the quality of observational studies (cohort study, case-control study). This method consists of three items: patient selection, comparability of experimental and control groups, and assessment of outcomes of interest.¹⁶ The total score is 9, and higher scores indicate better quality. Any study is considered of high quality if the NOS score is >5 points.¹⁶

Statistical analysis

Dichotomous variables are expressed as RRs with 95% CIs and continuous variables weighted mean difference (WMD) with 95% CIs. We used a fixed-effect model (Mantel–Haenszel method)¹⁷ or random-effect model (DerSimonian–Laird method)¹⁸ to pool all data according to heterogeneity across the included studies. Heterogeneity among the studies was assessed using the I^2 statistic,¹⁹ where $I^2 > 50\%$ was considered substantial heterogeneity.¹⁹ When significant heterogeneity was identified, sensitivity analysis was performed to explore the potential source of heterogeneity. Publication bias was evaluated by Begg’s²⁰ and Egger’s²¹ test. We considered $P < 0.05$ statistically significant, except where otherwise specified. All statistical analyses were performed using Stata version 12.0 (StataCorp, College Station, TX, USA).

Results

Study identification and selection

Figure 1 shows the article-screening and -selection process for inclusion in this study. The initial search yielded 896 studies. Of these, 512 were excluded for duplicate records and 362 excluded after the review of title/abstract. Then, 22 studies were left for full-text review. Among these, six were excluded: four for not providing eligible data,^{22–25} and two that were unrelated to our topic.^{26,27} Finally, 16 studies^{28–43} met the inclusion criteria and were included in this meta-analysis.

Study characteristics and quality assessment

The main characteristics of included studies are presented in Table 1. These were published between 2003 and 2018. The total sample size was 13,393, of which 704 were in the SSI group and 12,689 the non-SSI group. Among these studies, nine^{28,31,32,35–37,40,41,43} were conducted in the US, two in

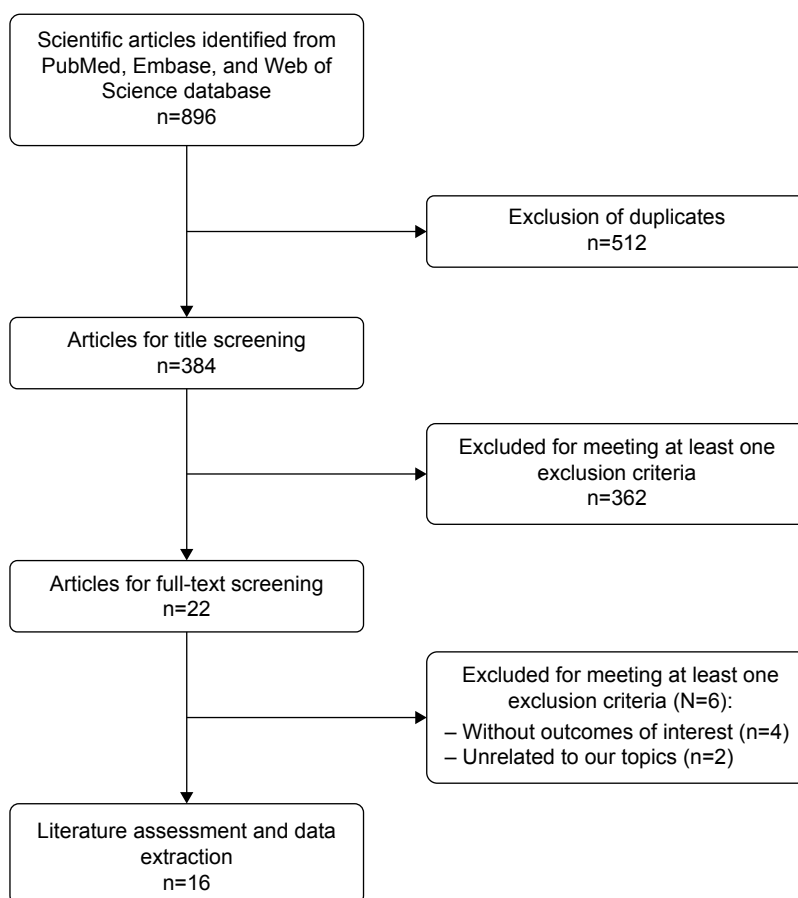


Figure 1 Eligibility of studies for inclusion in meta-analysis.

Table 1 Baseline characteristics of patients in trials included

Study	Country	Design	SSI group	Non-SSI group	Surgery	NOS score
Lim et al ²⁸	USA	Retrospective case-control	173	3,180	Single-level lumbar fusion surgery	7
Kim et al ²⁹	South Korea	Retrospective case-control	30	1,801	Posterior lumbar interbody fusion	7
Habiba et al ³⁰	Norway	Retrospective case-control	40	1,732	Lumbar disc herniation without laminectomy or fusion	7
Koutsoumbelis et al ³¹	USA	Retrospective case-control	84	168	Posterior lumbar instrumented arthrodesis	5
Lee et al ³²	USA	Retrospective case-control	15	134	Lumbar spine surgery	5
Liu et al ³³	China	Retrospective case-control	64	192	Posterior lumbar spinal surgery	6
Ogihara et al ³⁴	Japan	Prospective cohort study	24	2,712	Posterior lumbar spinal surgery	7
Chaichana et al ³⁵	USA	Retrospective case-control	37	780	Posterior instrumented lumbar fusion	5
Mehta et al ³⁶	USA	Retrospective case-control	24	274	Lumbar spinal fusion	7
Petilon et al ³⁷	USA	Propensity score-matched case-control study	30	30	Instrumented lumbar spinal fusion	6
Falavigna et al ³⁸	Brazil	Prospective cohort study	13	39	Lumbar arthrodesis	7
Schimmel et al ³⁹	the Netherlands	Retrospective case-control	36	135	Lumbar spinal fusion	5
Chen et al ⁴⁰	USA	Retrospective case-control	30	165	Lumbar spinal fusion	6
Blam et al ⁴¹	USA	Retrospective cohort	24	232	Lumbar spinal fusion	7
Lai et al ⁴²	China	Retrospective case-control	26	897	Lumbar spine surgery	6
Haleem et al ⁴³	USA	Retrospective case-control	54	218	Lumbar spine surgery	6

Abbreviations: NOS, Newcastle-Ottawa Scale; SSI, surgical site infection.

China,^{33,42} and one each in South Korea,²⁹ Norway,³⁰ Japan,³⁴ Brazil,³⁸ and the Netherlands.³⁹ Most studies were performed with a retrospective case–control design, except three, which were prospective^{34,38} or retrospective⁴¹ cohort design. All patients had undergone lumbar fusion surgery or posterior lumbar spinal surgery. NOS scores ranged from 5 to 7, which indicated that these studies were of high quality.

Risk factors

Sex

The most important risk factors for SSI are presented in Table 2. Eleven studies investigated the relationship between sex and postoperative SSI.^{28–31,33,34,36–39,43} The pooled estimate showed that males had a significantly lower risk of developing postoperative SSI compared with females (RR 0.88, 95% CI 0.80–0.97; $P=0.008$; Figure 2). There was no significant heterogeneity among the studies ($I^2=49.2\%$, $P=0.032$).

Increased age

Eight studies assessed the relationship between increased age and postoperative SSI.^{32–35,38,41–43} The pooled result suggested that patients with SSI were older than those without (WMD 1.43 years, 95% CI 1.15–4.02; Figure 3); however, this difference was not significant ($P=0.2777$). This indicated that increased age was not a significant risk factor for SSI.

Table 2 Pooled estimates of RR (WMD)^a obtained from meta-analysis of risk factors of SSI following lumbar spine surgery

	RR	95% CI	P-value
Male sex	0.88	0.80–0.97	0.008
Diabetes	2.19	1.43–3.36	<0.001
Current smoking	0.89	0.75–1.06	0.178
ASA grade >II	2.63	0.84–8.27	0.098
Obesity	2.87	1.62–5.09	<0.001
Increased age ^a	1.43	–1.15 to 4.02	0.2777
BMI ^a	1.32	0.39–2.25	0.006
Duration of surgery ^a	24.96	14.77–35.15	<0.001
Duration of hospital stay ^a	2.07	0.28–3.87	0.024
Estimated blood loss ^a	106.90	–65.14 to 278.53	0.224
COPD	1.21	0.68–2.17	0.521
Hypertension	1.28	1.08–1.52	0.005
Cardiovascular disease	1.63	0.40–6.70	0.495
Rheumatoid arthritis	1.76	0.53–5.90	0.359
Osteoporosis	1.91	0.79–4.63	0.152
Allogeneic blood transfusion	1.39	0.59–3.27	0.457
Previous surgery	2.06	1.39–3.06	<0.001
Implanted instrument	1.41	1.19–1.66	0.533
Sleep apnea	1.00	0.18–5.35	1.00
Hypercholesterolemia	1.07	0.70–1.62	0.764

Note: ^aResults expressed as WMD with 95% CI.

Abbreviations: WMD, weighted mean difference; SSI, surgical site infection; ASA, American Society of Anesthesiologists; BMI, body-mass index.

Diabetes

Twelve studies investigated the relationship between diabetes and postoperative SSI.^{28,29,31–36,39,40,42,43} The pooled estimate suggested that diabetes patients had a 2.19-fold increased risk of developing SSI compared with those without diabetes (RR 2.19, 95% CI 1.43–3.36; $P<0.00$; Figure 4). Heterogeneity was significant ($I^2=90.1\%$, $P<0.001$), and thus we conducted sensitivity analysis. When we excluded a study with a relatively small sample ($n=149$),³² the pooled estimate of the remaining studies did not change substantially (RR 2.23, 95% CI 1.71–3.43; $P<0.001$), but heterogeneity was still present ($I^2=89.5\%$, $P<0.001$). Furthermore, we excluded studies one at a time, and overall estimates changed slightly, but heterogeneity was still observed.

Current smoking

Nine studies investigated the relationship between current smoking and postoperative SSI.^{28,30–32,34,35,37,39,43} Pooled estimates showed that current smokers had a comparable rate of postoperative SSI than nonsmokers (RR 0.89, 95% CI 0.75–1.06; $P=0.178$; Figure 5). This indicated that current smoking did not increase the risk of postoperative SSI in patients with lumbar spine surgery. Heterogeneity was not significant ($I^2=46.2\%$, $P=0.062$).

Obesity

Six studies investigated the relationship between obesity and postoperative SSI.^{30–32,35,36,43} The pooled result showed that obesity patients had a 2.87-fold increased risk of SSI than those of normal weight (RR 2.87, 95% CI 1.62–5.09; $P<0.001$). This indicated that obesity was a significant risk for SSI. There was no significant heterogeneity among the studies ($I^2=43.4\%$, $P=0.078$).

ASA grade >2

Four studies investigated the relationship between American Society of Anesthesiologists (ASA) grade and postoperative SSI.^{28,30,34,43} Pooled estimates suggested that patients with ASA grade >2 had a similar rate of postoperative SSI compared with those with ASA grade 1–2 (RR 2.63, 95% CI 0.84–8.27; $P=0.098$). This demonstrated that ASA grade >2 did not increase the risk of postoperative SSI. Heterogeneity was not significant ($I^2=45.6\%$, $P=0.073$).

BMI

Nine studies investigated the relationship between body-mass index (BMI) and postoperative SSI.^{30,32,34,36,37,39,41–43}

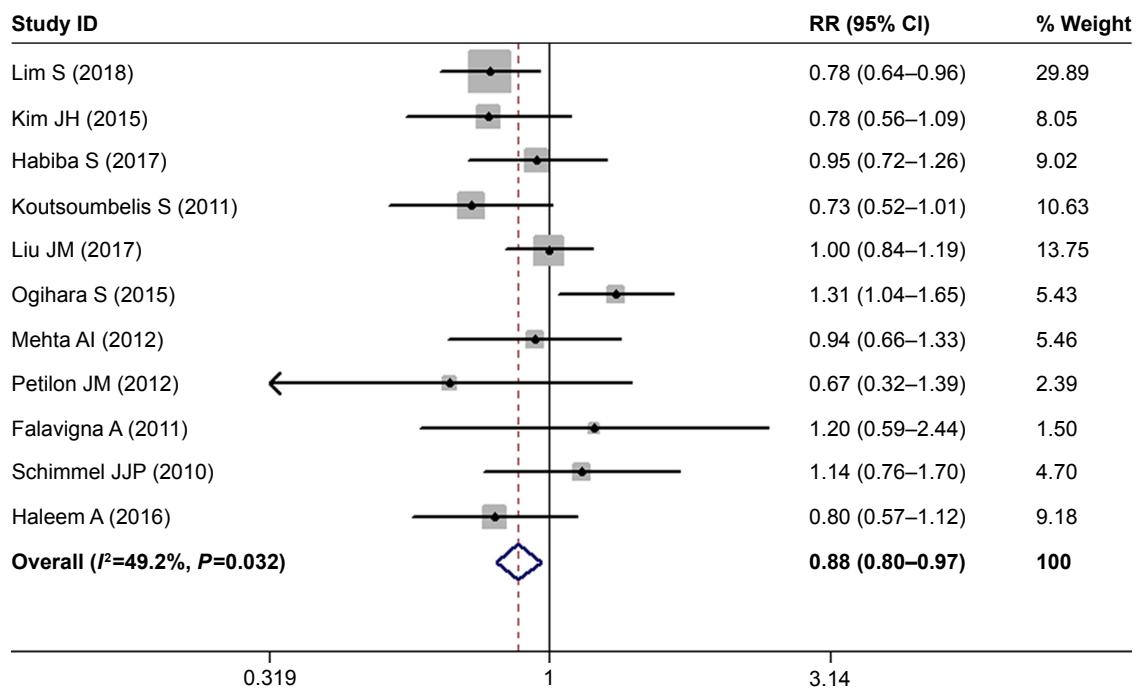


Figure 2 Forest plot showing the relationship between male sex and postoperative surgical site infection.

Pooled estimates suggested that patients with high BMI values had a higher risk of developing SSI than those with normal BMI (WMD 1.32 kg/m², 95% CI 0.39–2.25; $P=0.006$). This indicated that BMI was a significant risk factor for postoperative SSI. Heterogeneity was not significant ($I^2=48.3\%$, $P=0.067$).

Duration of surgery

Ten studies investigated the relationship between duration of surgery and postoperative SSI.^{29–33,37,39,41–43} Pooled estimates suggested that patients with longer surgeries were more likely to develop SSI (WMD 24.96 minutes, 95% CI 14.77–35.15; $P<0.001$). This indicated that prolonged surgery was an

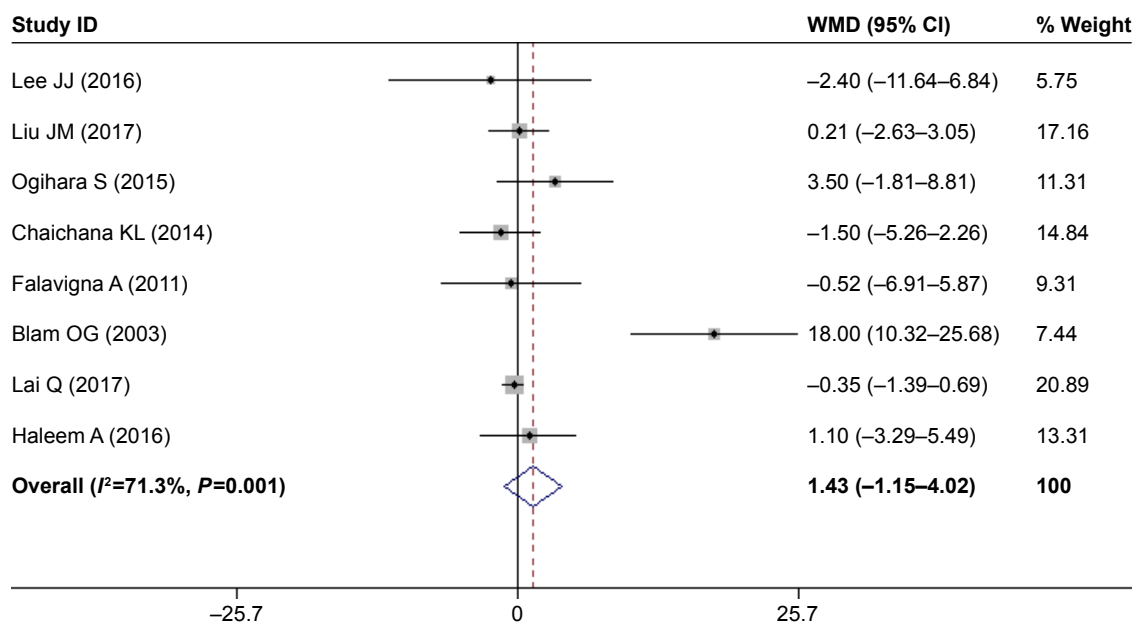


Figure 3 Forest plot showing relationship between increased age and postoperative surgical site infection. Note: Weights are from random-effects analysis.

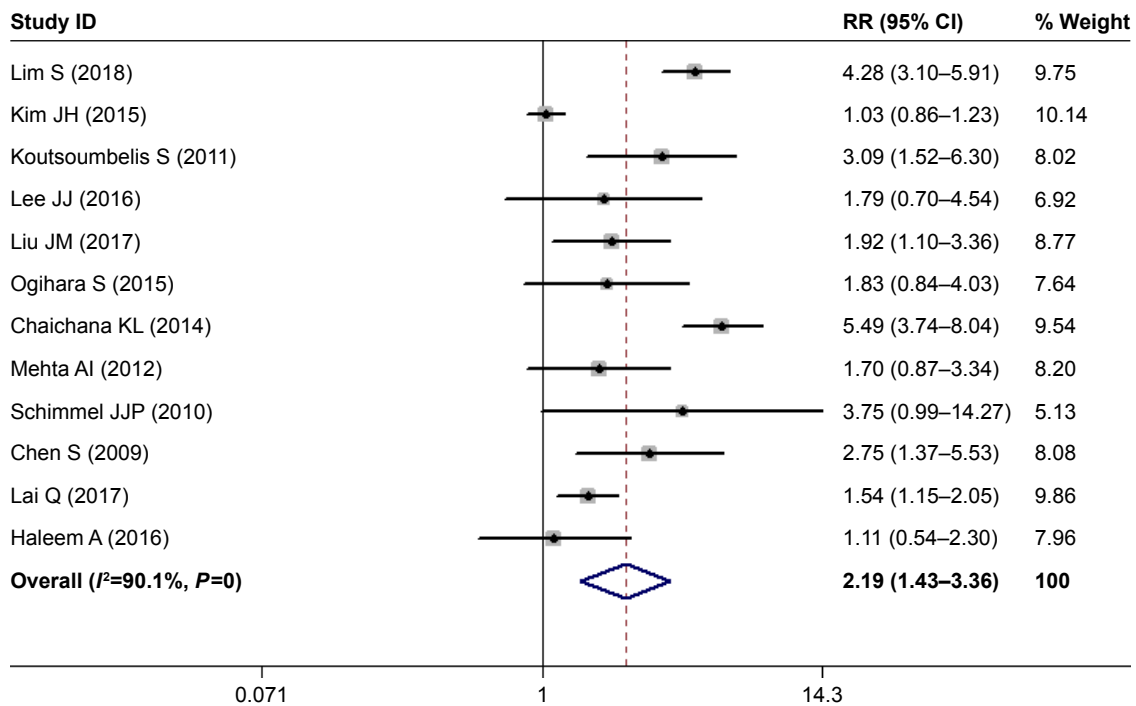


Figure 4 Forest plot showing the relationship between diabetes and postoperative surgical site infection. **Note:** Weights are from random-effects analysis.

increased risk for SSI. Heterogeneity was not significant ($I^2=33.9\%$, $P=0.267$).

risk of SSI (WMD 2.07 days, 95% CI 0.28–3.87; $P=0.024$). This indicated that prolonged hospital stays increased the risk of SSI. Heterogeneity was not significant ($I^2=29.6\%$, $P=0.384$).

Duration of hospital stay

Five studies investigated the relationship between duration of hospital stay and postoperative SSI.^{30,31,35,37,41} Pooled estimates suggested that patients with longer hospital stay had a higher

Estimated blood loss

Four studies investigated the relationship between estimated blood loss and postoperative SSI.^{33,37,41,42} The pooled result

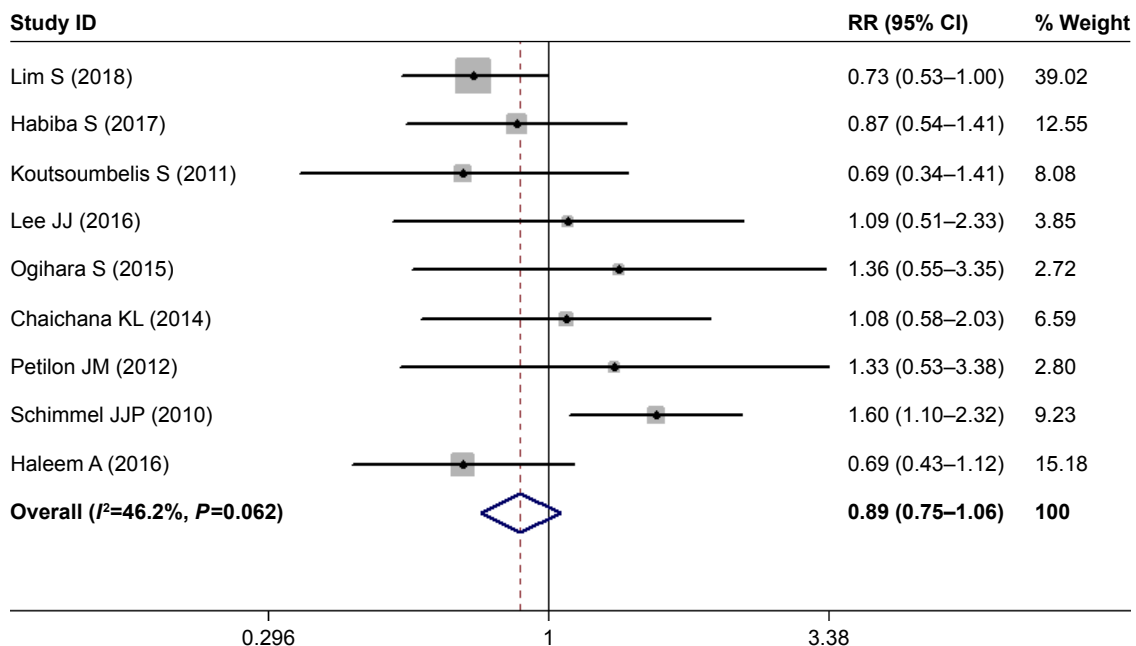


Figure 5 Forest plot showing the relationship between current smoking and postoperative surgical site infection.

showed that patients with greater blood loss had a higher risk of SSI (WMD 106.9 mL, 95% CI 65.14–278.53); however, this was not significant ($P=0.224$). This indicated that increased blood loss was not a significant risk factor for SSI in patients who had undergone lumbar spine surgery. Heterogeneity was not significant ($I^2=44.2\%$, $P=0.0698$).

Chronic obstructive pulmonary disease

Five studies investigated the relationship between COPD and postoperative SSI.^{28,31,39,42,43} Pooled estimates suggested that patients with COPD had a similar rate of SSI as those without (RR 1.21, 95% CI 0.68–2.17; $P=0.521$). This indicated that COPD was not a significant risk factor for SSI in patients who had undergone lumbar spine surgery. Heterogeneity was not significant ($I^2=13.8\%$, $P=0.292$).

Publication bias

Assessment of publication bias using Begg's and Egger's tests showed that there was no potential publication bias across the included studies (Egger's test, $P=0.473$; Begg's test, $P=0.527$).

Discussion

The present study was a meta-analysis of eligible studies with the objective of identifying risk factors for SSI following lumbar spinal surgery. Our study suggested that female sex, diabetes, obesity, BMI, prolonged operation time, prolonged hospital stay, hypertension, and previous surgery were risk factors for SSI in patients who had undergone lumbar spinal surgery, whereas, current smoking, ASA grade >2, increased age, COPD, cardiovascular disease, rheumatoid arthritis, and osteoporosis were not.

To the best of our knowledge, this is the first comprehensive meta-analysis to investigate risk factors for SSI in patients who have undergone lumbar spinal surgery. Our study indicated that patients with diabetes had a 2.19-fold increased risk of developing postoperative SSI compared with those without. Findings from the present study were consistent with most of the studies included, except three,^{29,32,34} which found that diabetes was not a risk factor for SSI. Lee et al³² retrospectively analyzed 149 adult patients who had undergone lumbar spine surgery with a midline posterior approach. Among these patients, 15 experienced postoperative SSI and 134 had no infection.³² The prevalence of patients with diabetes in the SSI and non-SSI groups was 26.7% (four of 15) and 14.9% (20 of 134), respectively, which were not significant ($P=0.249$).³² Similarly, Kim et al²⁹ undertook a review of a case series to identify risk factors for SSI in posterior lumbar interbody fusion, and they also reported a

negative relationship between diabetes and SSI. In that study, 80% (24 of 30) of patients in the SSI group had diabetes compared with 77.8% (1,401 of 1,801) in non-SSI group.²⁹ However, in another retrospective study of 2,715 patients investigating risk factors for SSI following posterior lumbar spinal surgery, the authors suggested that diabetes was an independent risk factor for SSI.³³ The rate of diabetes in SSI and control groups was 25% (16 of 64) and 13% (25 of 192), respectively, which demonstrated that diabetes patients were at higher risk of developing SSI.³³ The inconsistent results of these three studies are difficult for us to explain, since they all had large samples and used multivariate logistic regression analyses to reduce the influences of selection bias in retrospective studies.

In the present study, we found that obesity was a significant risk factor for SSI in patients who had undergone lumbar spinal surgery. These results were in line with previous studies.^{31,32,36} Koutsoumbelis et al collected 3,218 patients who had undergone posterior lumbar instrumented arthrodesis,³¹ and found that 42.9% (36 of 84) of them who developed SSI had obesity compared with 7.1% (12 of 168) of patients who had no SSI.³¹ The OR for obesity was 9.75 (95% CI 4.70–20.21, $P<0.001$), indicating that patients with obesity had 9.75-fold increased risk of developing SSI than those without. Consistent with these results, Lee et al³² reported that obesity was associated with a 4.09-fold increased risk of SSI (OR 4.09, 95% CI 1.32–12.7; $P=0.015$). In that study, the obesity rate in the SSI and non-SSI groups was 66.7% (ten of 15) and 32.8% (44 of 134), respectively, which indicated that obese patients were more likely to develop SSI than normal patients.³² When obese patients are undergoing surgery, it is necessary to cut through a large amount of oily liquid. The surgical incision is filled with sterile gauze, and bacteria can become embedded in the incision.⁴² This increases the risk of infection. Moreover, previous studies^{2,44} have demonstrated that BMI is a risk factor for postoperative complications: when BMI is increased by 5 kg/m², the risk of postoperative SSI is accordingly increased by 10%.

Consistently with prior studies, prolonged operations were significantly associated with postoperative SSI.^{29,31,33} Kim et al²⁹ analyzed 1,831 patients who had undergone posterior lumbar interbody fusion, and found that SSI patients had had longer surgery than those in the non-SSI group. In that study, operation times in SSI and non-SSI groups were 195.3 minutes and 177.1 minutes ($P=0.008$), respectively,²⁹ suggesting that prolonged surgery increased the risk of SSI. Similar results were found in another study, which assessed risk factors for SSI among patients with posterior lumbar instrumented arthrodesis.³¹ In that study, the duration of

surgery in SSI and non-SSI groups was 373.1 ± 167.1 minutes and 291.6 ± 130.7 minutes, respectively.³¹ The difference between them was significant ($P < 0.001$), which confirmed the role of prolonged surgery in postoperative SSI. However, in another case–control study,³⁷ a negative relationship was found between duration of surgery and SSI. In that study, the authors performed a propensity-score-matched case–control study of 60 patients who had undergone instrumented lumbar fusion.³⁷ The operating time for SSI patients was less (259.27 minutes) than non-SSI patients (288.17), and the difference between them was not significant ($P = 0.298$).³⁷ The negative result might be explained by the small sample.

Previous surgery was another risk factor for SSI, and this result was comparable to previous studies.^{35,39} Ogihara et al performed prospective multicenter surveillance to determine the risk factors for SSI in adult patients who had undergone lumbar spinal surgery.³⁴ They enrolled 2,736 patients, and 24 (0.9%) developed SSI.³⁴ The prevalence of patients who had had previous surgery in deep SSI and nondeep SSI groups was 29.2% and 15.5%, respectively, suggesting that previous surgery was an increased risk for postoperative SSI.³⁴ Chaichana et al performed a study with 817 consecutive cases, and found previous surgery was associated with 2.994-fold increased risk of SSI (RR 2.994, 95% CI 1.26–9.35; $P = 0.009$).³⁵ It was assumed that patients who had had previous lumbar spine surgery typically had longer surgeries, which increased procedural complexity and propensity for durotomies, thereby increasing the risk of SSI.⁴⁵

Limitations

This study has several potential limitations. First, in some outcomes, substantial heterogeneity was identified among the included studies. Despite sensitivity analysis being performed to detect potential sources of heterogeneity, no valuable information was found. Second, most of the studies were conducted with a retrospective design, and their results might be biased by the inherent disadvantages. This may have had a potential impact on our pooled estimates.

Conclusion

Our study indicates that female sex, diabetes, obesity, BMI, prolonged operation, prolonged hospital stay, hypertension, and previous surgery are independent risk factors for SSI following lumbar spine surgery, whereas, current smoking, ASA grade >2 , increased age, COPD, cardiovascular disease, rheumatoid arthritis, and osteoporosis are not. Knowing these risk factors, surgeons could adequately analyze and

evaluate risk factors in patients, and then develop prevention measurements to reduce the rate of SSI.

Disclosure

The authors report no conflicts of interest in this work.

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