A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery

Dan Xing · Jian-Xiong Ma · Xin-Long Ma ·
Dong-Hui Song · Jie Wang · Yang Chen · Yang Yang ·
Shao-Wen Zhu · Bao-Yi Ma · Rui Feng

Abstract

Objective To identify the independent risk factors, based on available evidence in the literature, for patients developing surgical site infections (SSI) after spinal surgery.

Methods Non-interventional studies evaluating the independent risk factors for patients developing SSI following spinal surgery were searched in Medline, Embase, Sciencedirect and OVID. The quality of the included studies was assessed by a modified quality assessment tool that had been previously designed for observational studies. The effects of studies were combined with the study quality score using a best-evidence synthesis model.

Results Thirty-six observational studies involving 2,439 patients with SSI after spinal surgery were identified. The included studies covered a wide range of indications and surgical procedures. These articles were published between 1998 and 2012. According to the quality assessment criteria for included studies, 15 studies were deemed to be high-quality studies, 5 were moderate-quality studies, and 16 were low-quality studies. A total of 46 independent factors were evaluated for risk of SSI. There was strong evidence for six factors, including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgical procedure. We also identified 8 moderate-evidence, 31 limited-evidence and 1 conflicting-evidence factors.

Conclusion Although there is no conclusive evidence for why postoperative SSI occurs, these data provide evidence to guide clinicians in admitting patients who will have spinal operations and to choose an optimal prophylactic strategy. Further research is still required to evaluate the effects of these above risk factors.

Keywords Surgical site infection · Spinal surgery · Postoperative infection · Risk factors · Systematic review

D. Xing and J.-X. Ma contributed equally to this work.

D. Xing · J.-X. Ma · X.-L. Ma (✉) · J. Wang · R. Feng
Department of Orthopaedics, Tianjin Medical University
General Hospital, 154 Anshan Street, Heping District, Tianjin
300052, China
e-mail: tjmuld@gmail.com

D. Xing · D.-H. Song (✉)
Department of Orthopaedics, Tianjin Gongan Hospital, 78
Nanjing Street, Heping District, Tianjin 300042, China
e-mail: yaoyanshi@sohu.com

X.-L. Ma · Y. Chen · Y. Yang · S.-W. Zhu · B.-Y. Ma
Department of Orthopaedics Institute, Tianjin Hospital, 406
Jiefang Nan Street, Hexi District, Tianjin 300211, China

Introduction

Surgical site infections (SSI) after adult spinal surgery are one of the most common causes of morbidity and mortality and have been reported to occur in 0.7–12.0 % of patients [39]. Spinal surgeries report a higher rate of infection compared with other orthopedic surgeries such as total hip arthroplasty [38]. According to the Center for Disease Control's National Nosocomial Infections Surveillance (NNIS) System, which reflects the rate of hospital-acquired infections in the United States, SSI is the third most commonly reported type of nosocomial infection, accounting for 14–16 % of all nosocomial infections [16]. Moreover, 77 % of acute mortalities in patients with SSI were found to be related to the infections [32]. It has also been reported that SSI can increase medical, social and economical costs for the patients by up to four times, as well as increase costs for hospitals

and the health insurance companies. Recognition of a patient's risk factors for SSI may allow for interventions that prevent severe infections. Thus, several studies were performed to identify the specific risk factors for SSI. Identifying risk factors may aid in preventing infections and the associated patient suffering.

The incidence of SSI after spinal surgery is influenced both by patient characteristics and pre- or intra-operative factors. A variety of risk factors for SSI following spinal surgery have been identified including diabetes, obesity, longer operation times, smoking, history of previous SSI, type of surgical approach, larger blood loss, and use of spinal instrumentation. Furthermore, some of the above factors are impossible to modify and their effects can also be compounded by interactions, so a zero rate of SSI risk cannot be expected. Therefore, orthopedic surgeons aims to minimize infection rates to an acceptably low level.

Recently, Schuster et al. [51] published a systematic review on the risk factors for SSI after spinal surgery with the levels of evidence from the included studies. Pull et al. [45] also published a systematic review with appraised validity of identified risk factors for SSI. However, neither of these systematic reviews performed an evidence synthesis according to the study characteristics and the study quality score. We performed this systematic review of the literature to identify the independent risk factors for SSI in patients after spinal surgery and to grade the evidence according to the quality of included studies. This synthesis will provide an evidence base from which orthopedic surgeons can assess the probability of SSI for each patient. The ultimate goal is to decrease the risk for SSI and thereby decrease patient morbidity, mortality and healthcare costs based upon any identified independent risk factors.

Materials and methods

Search strategy

All methods used in this review followed the CRD, PRISMA [37], and MOOSE [53] guidelines. The primary sources of the reviewed studies were Medline, Embase, Sciencedirect, and OVID. The search included literature published exclusively in English up to June 2012 with no lower date limit on the search results. Searches included the terms "surgery", "spinal", "infection", "surgical", "spine", "prophylaxis", and "prevention". The electronic search was reinforced with manual searches for reference lists of all retrieved articles. In addition, all relevant conference databases that provided grey literature were also searched.

Eligibility of relevant studies

To begin, SSI was defined by the ICD-9-CM codes, National Nosocomial Infection Surveillance System (NNIS) definitions [40], Centers for Disease Control and Prevention (CDC) definitions [32], NHSN criteria [23] or other criteria such as definite pus discharge from the wound, local redness and heating, or identification of germs in exudates. We included studies in that (1) were observational in design, (2) consisted of a clearly defined group of adult patients, (3) investigated SSI (but were not limited to a specific pathogen) and (4) reported data on the independent risk factors for SSI but not on specific management strategies. However, studies were excluded if they were pediatric studies (age <18 years old), for the treatment of osteomyelitis, other than spinal surgery, or for evaluating antibiotics. Articles published in languages other than English were also excluded. Other excluding criteria included editorials, reviews and animal studies.

Study selection

Two reviewers (D. X. and XL. M.) independently analyzed each of the titles and abstracts based on the eligibility criteria. Articles that could not be excluded from our study based on the title and abstract were retrieved for independent full-text review by the same two reviewers. Any disagreements were resolved by consensus.

Data abstraction

The two independent reviewers (D. X. and JX. M.) extracted the following data from the qualifying articles. A form for extracting data, which had been previously piloted, was used to record information about population, study design, sample size, diagnosis, surgical procedure, and independent risk factors for SSI. The corresponding author of each study was contacted to obtain any missing information that was required. In the case of discrepancies, the third reviewer (Y. C.) was involved.

Quality assessment

The quality of the included studies was independently assessed by two authors (D. X. and Y. C.). The methodological quality of studies was evaluated using a previously designed criteria list (Table 1), which was adapted from Lievense et al. [31]. These systems were designed for methodological quality assessment of observational studies and had been used in previous observational systematic review articles [7, 22, 31]. Some of the original 15 criteria were not included in this review because they were not relevant to our topic or not specific to the study design of

Table 1 A list of criteria for the assessment of the methodological quality of included studies (adapted from Lievense et al. [31])

Item	Criterion	C/CC
Population		
1	Selection before infection was present or at uniform point	C/CC
2	Cases and controls were draw from the same population	CC
3	Participation rate ≥80 % for case	C/CC
4	Participation rate ≥80 % for control	CC
Study design		
5	Prospective design was used	C/CC
6	Follow-up time ≥30 days	C
7	Withdrawals ≤20 %	C
Data analysis		
8	Multivariate analysis performed	C/CC
9	Adjusted for at minimum age and sex	C/CC
Assessment of outcome		
10	Identification of infection assessed according to standard definitions	C/CC
11	Infection was assessed identical in studies population	C/CC
12	Presence of infection was assessed reproducibly	C/CC
Assessment of risk factors		
13	Exposure assessment was blinded	C/CC
14	Exposure was measured identical for cases and controls	CC
15	Exposure was assessed prior to the outcome	C/CC

Each item: scored as positive = 1, negative = 0, uncertain = ?

C, applicable to case-series studies; CC, applicable to case control studies

the included studies. Therefore, our methodological assessment tool was based on 12 criteria that were specific to case-series studies, which were scored as positive (1), negative (0), or unsure (?). Included studied were classified into three different quality levels (high, moderate, low quality) according to their methodological quality score, which is presented in Table 2. A consensus method was used to resolve differences in quality rating, with a third reviewer (XL. M.) available for consultation if needed.

Evidence synthesis

Given the heterogeneity of the included studies and independent risk factors, we were unable to perform a meta-analysis directly. In addition to assessing the quality of the studies, we graded the body of evidence. Therefore, we summarized the results using the model of "best-evidence synthesis" (Table 2) by which the potential risk factors were classified. The risk factors of included studies with

Table 2 Criteria for quality of the included studies and best-evidence synthesis

| Item	Level	Criteria for inclusion
Level of studies	High-quality studies	Multivariate analysis performed and had a quality score ≥8
	Moderate-quality studies	Multivariate analysis performed but had a quality score <8 or
		No multivariate analysis performed and had a quality score ≥5
	Low-quality studies	No multivariate analysis performed and had a quality score <5
Level of evidence	Strong evidence	Minimum of three high-quality studies with generally consistent findings
	Moderate evidence	Minimum of two moderate-quality studies with generally consistent findings
	Limited evidence	Minimum of one low-quality study with generally consistent findings
	Conflicting evidence	Converse findings in >50 % of the studies
	No evidence	No study could report a positive correlation between certain factors and outcomes

different methodological qualities were summarized according to the quantity and quality of relevant studies. This is a less-common approach, but is increasingly recognized as pertinent because it provides a conclusion that incorporates both the quality of studies and their outcomes [6, 19, 31, 55]. Using the key elements for grading systems suggested by the US Agency for Healthcare Research and Quality [59], we rated the evidence by synthesis according to five levels: no, conflicting, limited, moderate or strong evidence. "Strong evidence" means that further study is very unlikely to change our confidence in the estimate of effect. "Moderate evidence" means that further research is likely to have an impact on our confidence in the estimate of the effect and may change the results. "Low evidence" means that further research is very likely to change the results. "Conflicting evidence" means that any estimate of effect is very uncertain. "No evidence" means that no statistically analyzed or discussed factors are presented.

Results

Study identification

From our research, we identified 412 potential citations after duplications were excluded. After screening the titles and abstracts of these citations, we identified 177 publications for full-text reading. Based on the full-text

Fig. 1 Flow diagram of the selection process for relevant studies
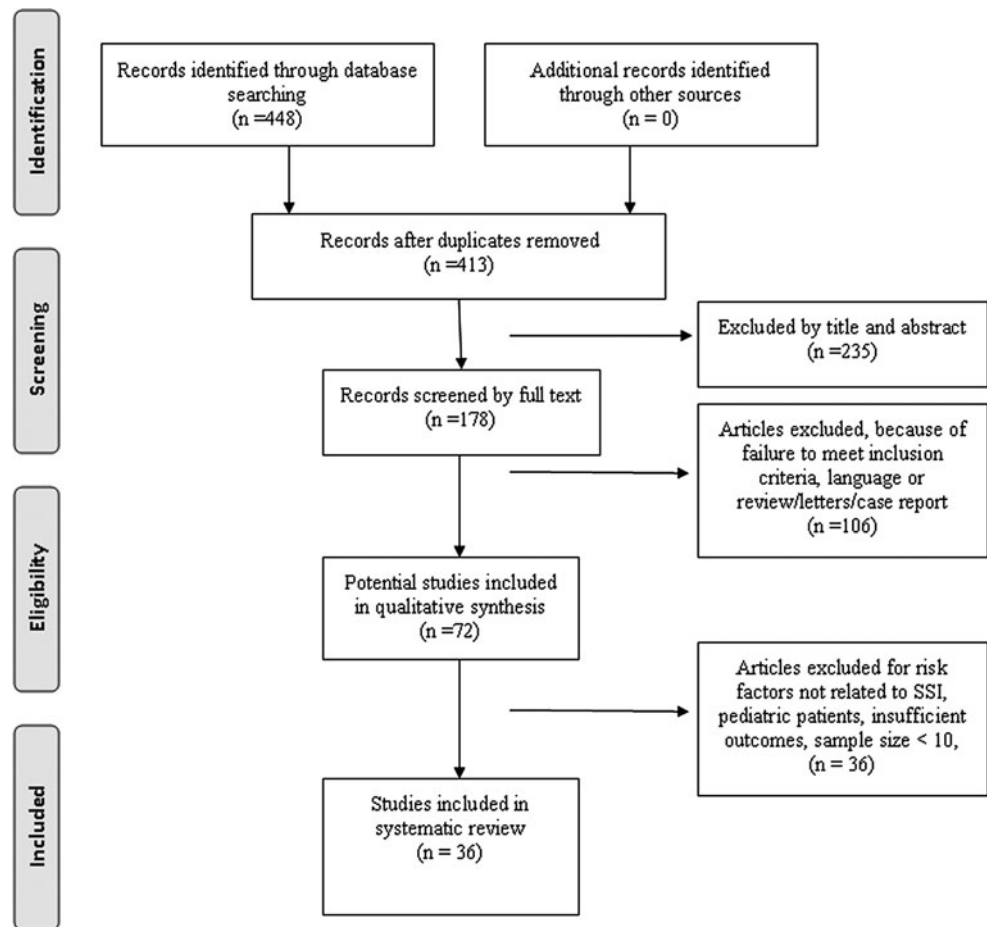
screening, 36 studies were included ultimately in the current review. The most frequent reason for exclusion was the inclusion of pediatric patients (Fig. 1).

Characteristics of studies included in the analysis

Characteristics of the studies are presented in Table 3. A total of 36 studies were included involving 2,439 patients with SSI after spinal surgery. The number of subjects in each study ranged from 45 to 24,774. The number of patients with SSI ranged from 6 [30] to 752 [56]. All of the investigations evaluated the risk factors for SSI after spinal surgery. These articles were published between 1998 and 2012. Included studies consisted of 14 (38.9 %) case–control studies (602 patients) and 22 (61.1 %) case-series studies (1,837 patients). There were 23 studies conducted in the USA, 3 in Japan, 2 in Taiwan, 2 in Netherlands, 2 in Korea, and 1 each in Lebanon, Italy, China and Austria. Twenty-six studies (72.2 %) reported the level of the spine in question: the cervical spine was operated on in 15 studies, the thoracic spine in 19 studies, the lumbar spine in 25 studies, and the sacral spine in 12 studies. Although 13

of the 36 studies did not provide data on the average age of patients, the lowest and highest mean ages reported by the remaining studies were 44 and 72.1 years. The most frequently performed surgical procedures were spinal fusion and spinal laminectomy/decompression. A variety of definitions were used to define SSI after spinal surgery. Although most of the studies used the criteria established by the Center for Disease Control and Prevention (CDC), other studies reporting SSI included findings from physical examinations, anamnesis, radiographic investigations, blood tests, MRI findings, and applied treatments. Although statistical methods were used in all 30 studies, multivariate regression analysis was performed in only 20 of 30 studies.

Quality of included studies

According to the methodological quality criteria for observational studies, 15 studies (41.7 %) were deemed to be high-quality studies, 5 (13.9 %) as moderate-quality studies and 16 (44.4 %) as low-quality studies, as presented in Table 3.

Table 3 Study characteristics

N	Study	Setting	Years	Design	Date collection	No. of patients with SSI	Mean age	Spinal levels included	Study quality (score)
1	Ahn [2]	Korea	2000–2009	CS	Retrospective	32	59.1	NR	Low (4)
2	Cizik [13]	USA	2003–2004	CS	Retrospective	63	NR	C, T, L, S	Moderate (7)
3	Abdul-Jabbar [1]	USA	2005–2010	CS	Retrospective	193	56.5	C, T, L, S	High (13)
4	Mehta [35]	USA	2006–2008	CS	Retrospective	24	56	L	Low (4)
5	Gruskay [21]	USA	2005–2009	CS	Retrospective	216	>18	C, T, L	Low (4)
6	Rao [47]	USA	2008–2008	CCS	Retrospective	57	55	NR	Moderate (7)
7	Chikawa [12]	Japan	2001–2008	CS	Retrospective	9	57.4	NR	Low (4)
8	Chen [10]	China	1992–2007	CCS	Retrospective	16	NR	S	High (8)
9	Lee [28]	Korea	2004–2008	CS	Retrospective	15	72.1	L	Low (3)
10	Schimmel [50]	The Netherlands	1999–2008	CCS	Retrospective	36	NR	T, L	High (9)
11	Watanabe [57]	Japan	2006–2006	CS	Retrospective	14	53	C, T, L	High (9)
12	Pull [43]	USA	1998–2005	CS	Retrospective	20	55.8	T, L, S	Moderate (5)
13	Schwarzkopf [52]	USA	2002–2007	CCS	Retrospective	61	56	T, L	Moderate (6)
14	Pull [44]	USA	1996–2005	CS	Retrospective	46	55.4	C, T, L, S	High (11)
15	Veeravagu [56]	USA	1997–2006	CS	Retrospective	752	NR	C, T, L, S	High (12)
16	Boston [8]	USA	2003–2005	CCS	Retrospective	55	44	NR	High (9)
17	Pull [42]	USA	1996–2005	CS	Retrospective	132	55.6	C, T, L, S	High (11)
18	Demura [14]	Japan	1993–2003	CS	Retrospective	8	56	C, T, L	Moderate (7)
19	Chen [11]	USA	2003–2008	CS	Retrospective	27	NR	L	Low (3)
20	Maragakis [33]	USA	2001–2004	CCS	Retrospective	104	59.4	NR	High (10)
21	Olsen [40]	USA	1998–2002	CCS	Retrospective	56	52.4	C, T, L, S	High (10)
22	Friedman [18]	USA	NR	CCS	Retrospective	41	53	C, T, L, S	High (9)
23	Liao [30]	Taiwan	1995–1997	CS	Retrospective	6	NR	L	Low (4)
24	Kanafani [24]	Lebanon	2001–2003	CCS	Retrospective	27	59	NR	Low (4)
25	Fang [17]	USA	1991–1997	CCS	Retrospective	48	47.8	NR	High (8)
26	Kuo [27]	Taiwan	1997–2002	CS	Retrospective	30	64.1	NR	Low (3)
27	Olsen [39]	USA	1996–1999	CCS	Retrospective	41	54.3	L, S	High (9)
28	Apisarnthanarak [3]	USA	1998–2000	CCS	Retrospective	13	64	NR	Low (4)
29	Banco [5]	USA	1994–1997	CS	Prospective	72	NR	NR	High (11)
30	Rechtine [48]	USA	1986–1997	CCS	Retrospective	12	NR	T, L	Low (4)
31	Weinstein [58]	USA	NR	CS	Retrospective	46	57.2	C, T, L, S	Low (3)
32	Klekamp [25]	USA	1989–1995	CCS	Retrospective	35	NR	C, T, L	Low (2)
33	Wimmer [61]	Austria	1989–1993	CS	Retrospective	22	NR	C, T, L	Low (3)
34	Mastronardi [34]	Italy	1999–2001	CS	Retrospective	9	NR	C, T, L	Low (4)
35	Willems [60]	The Netherlands	1989–2001	CS	Retrospective	17	NR	C, T, L	Low (3)
36	Koutsoumbelis [26]	USA	2000–2006	CS	Retrospective	84	61.0	L, S	High (10)

N number, *CS* case-series study, *CCS* case–control study, *NR* not reported, *C* cervical spine, *T* thoracic spine, *L* lumbar spine, *S* sacral spine

Evidence level of independent risk factors

There were 46 potential independent risk factors that were identified by more than one study and were included in the final analysis. As shown in Table 4, six were identified as strong-evidence factors, including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgical procedure. There were eight moderate-evidence independent risk factors identified including level of spinal surgery, number of spinal levels operated on, surgery involving the sacrum or pelvis, larger intraoperative blood loss, surgery with spinal instrumentation, earlier surgery, blood transfusions and ASA (American Anesthetists Society score) classification. Thirty-one limited-evidence independent risk factors were identified, presented in Table 4. Only the number of resident surgeons

participating in the operative procedure was identified as a conflicting-evidence factor.

Discussion

Surgical site infections following spinal surgery are frequently seen and have been previously linked to the length of surgical procedure, morbidity, and mortality. Therefore, it is important to identify variables that increase the risk of SSI so that strategies can be developed to minimize patient risk. The purpose of this systematic review was to identify independent risk factors for adult patients who develop SSI after spinal surgery and to synthesize these risk factors according to the level of available evidence, based on the methodological quality of the included studies.

Although multiple risk factors for SSI have previously been identified, there had been no synthesis of the evidence according to different level of study quality. In agreement with other review articles, Pull et al. [45]. reviewed 24 studies and reported 73 different types of factors related to SSI. Schuster et al. [51] reviewed 32 studies to evaluate the influence of perioperative risk factors and therapeutic interventions on SSI and rated level of evidence according to a certain methodological criteria. However, the authors evaluated the risk factors without an evidence-based synthesis. While the above reviews partly agreed with our results, the present systematic analysis introduced a quality assessment of the included studies and performed an evidence synthesis to evaluate the independent risk factors for SSI after spinal surgery, according to the differing quality levels of the studies.

Because of study heterogeneity, it was impossible to pool data between studies and conduct a meta-analysis to determine the estimates the effects of each risk factor. However, the evidence synthesis method is also a useful method for arriving at clinical recommendations. In the present systematic review, we only included observational studies, which might result in an incomplete detection of preoperative exposures and a higher bias of risk. In addition, heterogeneity of the included studies was induced, to a certain degree, by surgical approach, study population, preoperative state, primary disease, surgical techniques of surgeons, and different indications for surgery. Accordingly, while the results of this systematic review should be considered valid, these methodological quality considerations should be taken into account when interpreting the findings.

By conducting this systematic review of the current evidence base of 36 included studies, we have identified 6 strong-evidence independent risk factors, including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgery procedure. Diabetes

was associated with increased risk for SSI, with some studies reporting an odds ratio as high as 4.2 [18]. Diabetic patients are known to be susceptible to postoperative SSI due to their immunocompromised state, reduced wound healing potential and poor microvascularization. In addition, diabetes impairs wound healing because microangiopathic changes lead to local tissue ischemia [20] and lower tissue concentrations of antibiotics. Thus, tight regulation of serum glucose levels may decrease the incidence of SSI following spinal surgery [15]. Moreover, several studies reported that elevated preoperative or postoperative serum glucose level, which was regarded as a limited-evidence risk factor in the present study, was independently associated with an increased risk of SSI [30, 40]. Koutsoumbelis et al. [26] reported that postoperative serum glucose levels were significantly higher in the infected group, but they were not a risk factor according to a multivariate logistic regression analysis. Therefore, while preoperative and postoperative regulation of serum glucose levels had weaker evidence for being a risk factor than diabetes, it may influence us to pay more attention to the regulation of serum glucose levels pre- and post-operatively. Obesity was found to be an independent risk factor for SSI. The obese patients have thick subcutaneous adipose layers that form dead space after closure of the surgical wound. Thus, the necrosis of local fat can result in a localized wound infection. The use of subcutaneous drains to prevent dead space or recommending weight loss preoperatively may be effective strategies for preventing SSI. Although the different cutoffs (BMI >30 or BMI >35) or different definitions for obesity were utilized in different studies, the influence of obesity on SSI showed a similar trend. Therefore, weight loss may lower risk of SSI after spinal surgery. Our results confirmed the finding that patients who smoked had an increased risk for SSI. Smoking impairs wound healing because microvascular traction leads to tissue ischemia. Thomsen et al. [54] reported that patients may benefit from intensive preoperative smoking cessation interventions, which must have been initiated at least 4 weeks before surgery and have included nicotine replacement therapy. Therefore, patients have to stop smoking before surgery. Longer operative times were found to have a higher risk for SSI. The reason may be that longer surgical procedures result in increased duration of tissue traction and resulting ischemia and necrosis. Longer surgical procedures can also increase the risk of wound contamination. Although longer operative times were dictated mostly by the surgical complexity of the procedure, they can be mitigated by factors such as the proficiency of the surgeon and the operation methods [32]. The proper methods, which can minimize tissue necrosis and decrease infection rates, include releasing the tension on self-retractors often [49] and frequent irrigation of the

Table 4 Strong-, moderate-, limited- and conflicting-evidence independent risk factors associated with patients developing SSI after spinal surgery

Evidence level	Independent risk factors related to SSI	Infected patients number of high-quality studies	Infected patients number of moderate-quality studies	Infected patients number of low-quality studies
Strong evidence	Obesity/BMI	1,256 [18, 26, 33, 39, 40, 42, 44, 56]	201 [13, 43, 47, 52]	63 [35, 60, 61]
	Longer operation time	1,107 [8, 10, 17, 33, 42, 56]		31 [12, 61]
	Diabetes	1,163 [17, 18, 26, 40, 42, 50, 56, 57]	8 [14]	127 [11, 24, 27, 28, 30, 61]
	Smoking	836 [17, 50, 56]		22 [61]
	History of previous SSI	226 [17, 42, 44]		
	Type of surgery procedure	470 [1, 33, 39, 42]	20 [43]	62 [2, 27]
Moderate evidence	Spinal level of surgery	41 [18]	63 [13]	
	Number of spinal levels operated	229 [1, 50]		39 [28, 35]
	Surgery involving the sacrum or pelvis	297 [1, 33]		
	Larger intraoperative blood loss	216 [26, 42]		31 [12, 61]
	Surgery with spinal instrumentation	856 [33, 56]		127 [12, 24, 27, 28, 58]
	Previous surgery	52 [10, 50]		
	Blood transfusions	752 [56]	61 [52]	
	ASA classification	856 [33, 56]		
Limited evidence	Hypertension		63 [13]	
	Invasiveness index		63 [13]	
	Renal disease		63 [13]	216 [21]
	Bony or connective tissue neoplasm	193 [1]		
	Skin to lamina distance			24 [35]
	Thickness of subcutaneous fat			24 [35]
	Surgical case order			
	Drain duration		57 [47]	
	Male gender		57 [47]	
	Hemodialysis			9 [12]
	Albumin count	16 [10]		
	Trauma	14 [57]		
	Insufficient intraoperative irrigation	14 [57]		
	Dependent functional status	752 [56]		
	Disseminated cancer	752 [56]		46 [58]
	Presence of comorbidities	139 [8, 26]		
	Preoperative irradiation		8 [14]	
	Exposure to razor shaving	104 [33]		
	Intraoperative administration of a F_iO_2 less than 50 %	104 [33]		
	Suboptimal timing of prophylactic antibiotic therapy	56 [40]		
	Pre-/post-operative elevated serum glucose level	56 [40]		6 [30]

Table 4 continued

Evidence level	Independent risk factors related to SSI	Infected patients number of high-quality studies	Infected patients number of moderate-quality studies	Infected patients number of low-quality studies
	Age	48 [17]	57 [24, 27]	
	Alcohol abuse	48 [17]	57 [25, 61]	
	Dural tear	84 [26]	13 [3]	
	The use of glue to cement the dural patch		13 [3]	
	Postoperative incontinence	41 [39]		
	Surgery for tumor resection	41 [39]		
	Complete neurologic deficit		12 [48]	
	Steroid therapy		22 [61]	
	Extended preoperative hospitalization		22 [61]	
	Indication for surgery		9 [34]	
Conflicting evidence	The number of resident surgeons participating in the operative procedure	212 [5, 26, 40]		

surgical wound with saline during surgical procedures [9]. Moreover, full and long-term training for surgeons must be required to improve surgical proficiency. The history of previous SSI also significantly increased the risk of SSI. Although patients may not have any symptoms or signs of active infection, bacteria can remain encapsulated in the scar tissue. Bacteria may lie dormant until being released by a new surgery, which will lead to wound contamination [42]. If surgeons can determine the organism that caused the prior SSI before a revision surgery, an appropriate prophylactic antibiotic regimen may help to minimize the risk of SSI. A posterior surgical approach was independently associated with an increased risk of SSI. Levi et al. [29] found that all deep wound infections in patients for whom surgery involved spinal instrumentation occurred after a posterior approach. Wimmer et al. [61] reported that most of their patients with SSI had previously undergone surgery that involved posterior fusion and placement of instrumentation. Therefore, interventions to reduce the risk of SSI must focus on methods to reduce contamination of the posterior wound with urinary, fecal or skin flora. More attention must be paid to antisepsis of the posterior wounds, both in the hospital and by caregivers after discharge.

Beyond the six discussed risk factors for which there is strong evidence, we identified eight moderate-evidence factors. Friedman et al. [18] reported that laminectomy at a level other than cervical was one of independent risk factors. This may be attributed to the fact that laminectomy at a level other than cervical was always performed via a posterior approach, which has been identified as a strong-evidence risk factor. Mirza et al. [36] demonstrated that the number of levels operated on and blood transfusion were associated with longer surgical procedures, which was regarded as one of the strong-evidence risk factors. Therefore, an increased number of operated levels and blood transfusion may increase the risk of SSI. Although spinal instrumentation was regarded as foreign body that may increase the risk of infection, instrumentation could stabilize the motion segment, which could theoretically decrease inflammation due to instability and promote bone healing [41]. Using instrumentation had an effect on risk of SSI due to increased dead space by foreign bodies and longer operative times [27]. Surgery involving the sacrum or pelvis was a moderate risk factor because it may be associated with larger blood loss and longer operative times. As one of the moderate-evidence factors, larger blood loss may be directly associated with blood transfusion, which results in immune suppression in the recipient [46] and an increased risk of infection for all types of surgery [4]. Previous surgery may result in bowel and bladder dysfunction or complex tissue reconstruction, which to some extent may increase the risk of SSI after

spinal surgery. We also identified 31 limited-evidence factors, and only the number of resident surgeons participating in the operative procedure was identified as a conflicting-evidence factor. A better understanding of these independent risk factors could help to identify patients at different degrees of risk for SSI and help to develop interventions. Future studies are required to evaluate the effects of these risk factors.

The limitations of this systematic review primarily include the following: (1) systematic reviews of observational studies remain contentious in research [6, 18, 19, 55]. Although the criteria of methodological quality assessment and evidence synthesis have been adopted by several systematic reviews recently [6, 19, 55], the choice of this method is still under dispute. (2) Observational studies were sensitive to selection, detection, performance and publication bias and confounds. Publication bias occurs for the following reason: significant conclusions are easier to publish. Moreover, most authors prefer significant results by multivariate analysis. (3) Heterogeneity of included studies was induced by surgical approach, patient selection, preoperative state, surgical techniques of surgeons, analysis of putative risk factors, different indication for surgery, and definitions of SSI outcomes. (4) The classification of the evidence is weakened by heterogeneity and the varying methodological quality of the included studies. The evidence synthesis might overestimate the predicted effects and should be interpreted with the above limitations in mind.

Conclusion

This systematic review provided an overview of the current knowledge concerning independent risk factors for patients with SSI after spinal surgery. It included 36 studies involving 2,439 patients with SSI after spinal surgery. Although the available observations form a heterogeneous group, and there is no conclusive evidence, we have identified six strong-evidence risk factors including obesity/BMI, longer operation times, diabetes, smoking, history of previous SSI and type of surgical procedure. We also identified 8 moderate-evidence, 31 limited-evidence and one conflicting-evidence risk factor. We believe disclosure of these data will provide evidence to guide clinicians who treat patients with spinal surgery. However, high-quality studies are still required to clarify or to evaluate the effects of these risk factors. They should be based on a prospective design and with a large sample size. Multivariate analysis should be performed to adjust for, at a minimum, age, gender, primary diagnosis and comorbidities. In addition, details of interventions before surgery and preoperative exposures should be specified and randomized. Meanwhile,

the results of the analysis should be fully presented, including negative factors.

Conflict of interest The authors declare that they have no conflict of interest.

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