

Risk factors for surgical site infection following spinal surgery

A meta-analysis

Xinxin Zhang, MD^a, Peng Liu, MD^a, Jipeng You, MD^{b,*}

Abstract

Study design: A meta-analysis.

Background: We performed a meta-analysis to explore risk factors of surgical site infection (SSI) following spinal surgery.

Methods: An extensive search of literature was performed in English database of PubMed, Embase, and Cochrane Library and Chinese database of CNKI and WANFANG (up to October 2020). We collected factors including demographic data and surgical factor. Data analysis was conducted with RevMan 5.3 and STATA 12.0.

Results: Totally, 26 studies were included in the final analysis. In our study, the rate of SSI after spinal surgery was 2.9% (1222 of 41,624). Our data also showed that fusion approach (anterior vs posterior; anterior vs combined), osteotomy, transfusion, a history of diabetes and surgery, hypertension, surgical location (cervical vs thoracic; lumbar vs thoracic), osteoporosis and the number of fusion levels were associated with SSI after spinal surgery. However, age, sex, a history of smoking, body mass index, fusion approach (posterior vs combined), surgical location (cervical vs lumbar), duration of surgery, blood loss, using steroid, dural tear and albumin were not associated with development of SSI.

Conclusions: In our study, many factors were associated with increased risk of SSI after spinal surgery. We hope this article can provide a reference for spinal surgeons to prevent SSI after spinal surgery.

Abbreviations: BMI = body mass index, CI = confidence interval, OR = odds ratio, SSI = Surgical site infection.

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

1. Introduction

Surgical site infection (SSI), as the third most common complication, always brings in miserable and poor outcomes.^[1–3] Previous studies^[4–6] have been reported 0.2% to 16.1% occurrence of patients who underwent spinal surgery. Undoubtedly, SSI not only prolong hospital stay for the patients, but also increase medical, social, and economical costs. Thus, it is important to find the risk factors for SSI to lower rate of infection after spinal surgery.

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XZ and PL contributed equally to this work.

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Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

^a Emergency Department, Affiliated Hospital of Hebei University, No. 212 Road Yuhua Dong, Baoding, Hebei, China, ^b Medical Department, Affiliated Hospital of Hebei University, No. 212 Road Yuhua Dong, Baoding, Hebei, China.

* Correspondence: Jipeng You, Medical Department, Affiliated Hospital of Hebei University, No. 212 Road Yuhua Dong, Baoding, Hebei, China (e-mail: 405305757@gg.com).

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A variety of risk factors including diabetes, obesity, longer operation times, smoking, history of previous SSI, type of surgical approach, larger blood loss, and use of spinal instrumentation surgery have been mentioned by previous studies.^[7,8] As we know, many studies have reported the incidence and risk factors of SSI following spinal surgery, yet previous meta-analysis has just studied the epidemiological incidence of SSI after spinal surgery. To our knowledge, there is few meta analysis regarding risk factors of SSI after spinal surgery. Therefore, this study aims to explore incidence and risk factors of SSI following spinal surgery.

2. Methods

2.1. Statement of ethics

This study was approved by the institutional review board (IRB) of our hospital. An informed consent from the patients was not considered necessary by the Ethics Committee as our data originated from published papers. The present study has been conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

2.2. Search strategy

We searched for the English and Chinese language studies with the keywords: "surgical site infection" or "SSI", and "spinal surgery" in English database of PubMed, Embase, and Cochrane Library and Chinese database of CNKI and WANFANG. There was no limitation on the date of publication, which covered all previously published studies up to October 2020.

2.3. Eligibility criteria

Included articles must satisfy: study population must be adult patients (>18 years old); measured out comes of the incidence and risk factors of SSI after spine surgery; comparison: SSI group and non-SSI group; Studies were excluded if they were abstracts, letters, reviews or case reports; had repeated data; did not report outcomes of interest.

2.4. Data extraction and outcome measures

The data included the general characteristics of each study and the outcomes measured. General characteristics included first author, year of publication, country, the number of SSI patients and total patients, type of article, shown in Table 1. When the same population was reported in several publications, we retained only the most informative article or complete work to avoid duplication of information. Data were extracted independently by 2 authors. Any disagreements concerning paper eligibility were resolved by discussion and consensus. Test for risk of publication bias. We performed a visual inspection of the funnel plot for publication bias. The funnel plot should be asymmetric when there is publication bias and symmetric in the case of no publication bias. We performed Egger and Begg tests to measure the funnel plot asymmetry using a significance level of P < .10. The trim and fill computation was used to estimate the effect of publication bias. Sensitive analysis overall because of the low heterogeneity of every factor, so we do not calculate sensitive analysis.

2.5. Statistical analysis

Dichotomous outcomes were presented as odd ratios (OR) and 95% confidence intervals (CI) were calculated for outcomes,

Table 1

Characteristics of included studies.

while continuous variable were regarded as standardized mean difference (SMD) and 95% CI. A *P* value < .05 was judged as statistically significant. Random-effects or fixed-effects models were used depended on the heterogeneity of the studies included. Heterogeneity was analyzed with both the Chi squared test *I* square test, where *P* value of < .10 for the Chi squared and $I^2 > 50\%$ implied heterogeneity.^[9] All statistical analyses were performed using Review Manager version 5.3 (The Cochrane Collaboration, Oxford, UK) and STATA 12.0 (Stata Corporation, College Station, TX).

3. Results

3.1. Study identification and selection

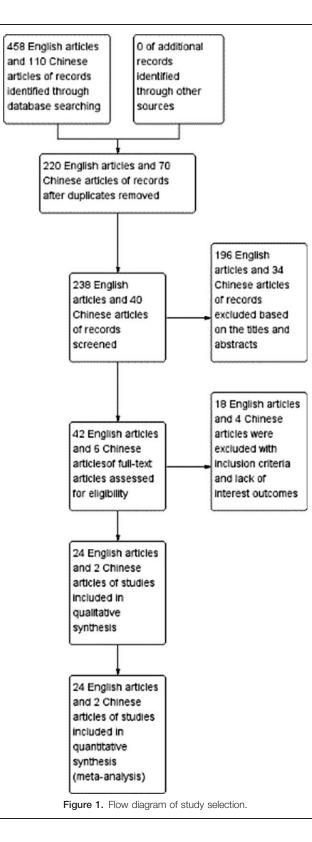
Initially, we collected totally 568 (458 English articles and 110 Chinese articles) records by the database search. Two hundred ninety records (220 English articles and 70 Chinese articles) were excluded due to repetition and 230 (196 English articles and 34 Chinese articles) records were removed for review based on the titles and abstracts. The remaining 48 records were retrieved for inclusion criteria and 15 (13 English articles and 2 Chinese articles) of them were excluded, 7 (5 English articles and 2 Chinese articles) did not report outcomes of interest. Finally, 26 (24 English articles and 2 Chinese articles) articles that met our inclusion criteria were included in the present meta-analysis. The selection process that included in this meta-analysis is shown in Figure 1.

3.2. Baseline characteristics and quality assessment

The main characteristics of the 26 articles (from 74 to 5803 patients) that published before October 2020 included in the

			No. of pa	articipants	
First author	Year	Country	ASD	Total	Study type
Amy M. Cizik ^[10]	2012	USA	63	1532	Retrospective
Andrew A. Fanous ^[11]	2019	USA	20	532	Retrospective
CJ. Lucasti ^[12]	2019	USA	13	74	Retrospective
Cindy R. Nahhas ^[13]	2017	USA	108	2548	Retrospective
John J. Lee ^[14]	2016	USA	15	149	Retrospective
Kotaro Satake ^[15]	2013	USA	11	110	Retrospective
Qi Lai ^[16]	2017	China	26	923	Retrospective
Satoshi Ogihara ^[17]	2015	Japan	24	2736	Retrospective
Satoshi Ogihara ^[18]	2018	Japan	26	4027	Retrospective
Satoshi Ogihara ^[19]	2019	Japan	20	623	Retrospective
Sjoerd P. F. T. Nota ^[20]	2015	USA	361	5761	Retrospective
Takashi Sono ^[21]	2018	Japan	10	637	Retrospective
Samer Habiba ^[22]	2017	Norway	40	1772	Retrospective
SHI Lei ^[23]	2017	China	36	3964	Retrospective
Oren G. Blam ^[24]	2003	USA	24	256	Retrospective
Nathan J. Lee ^[25]	2017	USA	140	5803	Retrospective
Muneharu Ando ^[26]	2014	Japan	8	294	Retrospective
Matt El-Kadi ^[27]	2019	USA	30	5065	Retrospective
Jin-Sol Han ^[28]	2016	Korea	10	280	Retrospective
Albert F ^[29]	2010	USA	46	830	Retrospective
Daniël M. C. Janssen ^[30]	2018	Netherlands	60	898	Retrospective
Eiichiro Iwata ^[31]	2016	Japan	5	85	Retrospective
Jin Hak Kim ^[32]	2015	Korea	30	1831	Retrospective
Yusuke Yamamoto ^[33]	2018	Japan	11	141	Retrospective
Can Yaldiz ^[34]	2015	Turkey	63	540	Retrospective
Ankit I. Mehta ^[35]	2013	USA	22	213	Retrospective





meta-analysis were presented in Table 1. Finally, 1222 patients were suffering from SSI after spinal surgery in total of 41,264 patients. According to the 26 included studies, the rate of SSI was 2.9% (ranged from 0.6%-17.6%).

Because all studies included were retrospective studies, we used the Newcastle Ottawa Quality Assessment Scale (NOQAS) to

18			
	1.5.1	-	

The	quality	assessment	according	to	the	Newcastle	Ottawa
Qual	lity Asse	ssment Scale	(NOQAS) c	of ea	ach s	study.	

Study	Selection	Comparability	Exposure	Total score
Amy M. Cizik ^[10]	3	3	2	8
Andrew A. Fanous ^[11]	3	2	3	8
CJ. Lucasti ^[12]	2	3	3	8
Cindy R. Nahhas ^[13]	2	3	2	7
John J. Lee ^[14]	3	3	2	8
Kotaro Satake ^[15]	3	2	2	7
Qi Lai ^[16]	3	3	2	8
Satoshi Ogihara ^[17]	2	3	3	8
Satoshi Ogihara ^[18]	3	3	2	8
Satoshi Ogihara ^[19]	3	2	3	8
Sjoerd P. F. T. Nota ^[20]	2	2	3	7
Takashi Sono ^[21]	3	2	3	8
Samer Habiba ^[22]	2	3	3	8
SHI Lei ^[23]	2	3	2	7
Oren G. Blam ^[24]	3	3	2	8
Nathan J. Lee ^[25]	3	2	2	7
Muneharu Ando ^[26]	3	3	2	8
Matt El-Kadi ^[27]	3	3	2	8
Jin-Sol Han ^[28]	2	3	3	8
Albert F ^[29]	3	2	2	7
Daniël M. C. Janssen ^[30]	3	2	3	8
Eiichiro Iwata ^[31]	2	3	3	8
Jin Hak Kim ^[32]	2	3	3	8
Yusuke Yamamoto ^[33]	3	2	2	7
Can Yaldiz ^[34]	3	3	2	8
Ankit I. Mehta ^[35]	3	2	3	8

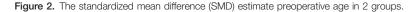
assess the quality of each study. This scale for non-randomized case controlled studies and cohort studies were used to allocate a maximum of 9 points for the quality of selection, comparability, exposure, and outcomes for study participants. Of these studies, 19 studies scored 8 points and 7 studies scored 7 points. Hence, the quality of each study was relatively high (Table 2).

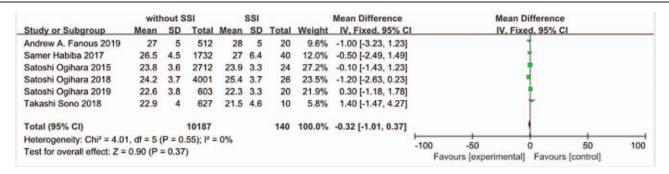
3.3. Assessment of risk factors of SSI 3.3.1. Age. Twelve studies^[10–21] reported age of patients at operational time between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity=.23; $I^2=21\%$, Fig. 2). The meta-analysis showed that age was not associated with a significant increase in the incidence of SSI (fixed-effects model; P=.57, SMD=-0.20, 95% CI [-0.88, 0.48], Fig. 2).

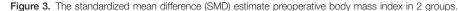
3.3.2. Body mass index (BMI). Six studies^[11,17–19,21,22] reported BMI of patients at operational time between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity = .55; $I^2 = 0\%$, Fig. 3). The meta-analysis showed that BMI was not associated with a significant increase in the incidence of SSI (fixed-effects model; P = .37, SMD = -0.32, 95% CI [-1.01, 0.37], Fig. 3).

3.3.3. Smoking. Twenty studies^[10–15,17–29] reported a history of smoking between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity = .54; $I^2 = 0\%$, Fig. 4). The meta-analysis showed that history of smoking was not associated with a significant increase in the incidence of SSI (fixed-effects model; *P*=.07, OR=1.15, 95% CI [0.99, 1.35], Fig. 4).

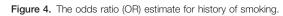
	wi	thout SS	1		SSI			Mean Difference		M	ean Differend	e	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	i	IV	Fixed, 95%	CI	
Amy M. Cizik 2012	49.4	16	1469	53.5	16.1	63	2.8%	-4.10 [-8.16, -0.04]			-		
Andrew A. Fanous 2019	61	18	512	65	14	20	1.2%	-4.00 [-10.33, 2.33]			-		
CHRISTOPHER J. LUCASTI 2019	50	15	61	47	17	13	0.5%	3.00 [-6.98, 12.98]					
Cindy R. Nahhas 2017	60.22	15.43	2440	61.71	13.97	108	6.3%	-1.49 [-4.19, 1.21]			1		
John J. Lee 2016	53.7	15.6	134	51.3	17.5	15	0.5%	2.40 [-6.84, 11.64]			+-		
Kotaro Satake 2013	66.9	1	99	66.2	2.2	11	26.7%	0.70 [-0.61, 2.01]					
Qi Lai 2017	54.93	0.5503	897	54.58	2.71	26	42.4%	0.35 [-0.69, 1.39]					
Satoshi Ogihara 2015	64	15	2712	67.5	13.2	24	1.6%	-3.50 [-8.81, 1.81]			-		
Satoshi Ogihara 2018	59.1	18.1	4001	61.3	12.9	26	1.9%	-2.20 [-7.19, 2.79]			-		
Satoshi Ogihara 2019	62.8	20	603	67.5	18	20	0.7%	-4.70 [-12.75, 3.35]			-+		
Sjoerd P. F. T. Nota 2015	55	16	5400	56	17	361	14.2%	-1.00 [-2.80, 0.80]			1		
Takashi Sono 2018	63.1	16.1	627	65.6	9.4	10	1.3%	-2.50 [-8.46, 3.46]			-		
Total (95% CI)			18955			697	100.0%	-0.20 [-0.88, 0.48]					
Heterogeneity: Chi ² = 14.00, df = 11	(P = 0.2)	3); I ² = 21	1%							1		1	100
Test for overall effect: Z = 0.57 (P =	0.57)	4							-100 F	-50 avours (experim	ental] Favou	50 rs [control]	100







	smoki	ng	witho	ut		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Takashi Sono 2018	3	84	7	553	0.6%	2.89 [0.73, 11.40]	
Sjoerd P. F. T. Nota 2015	43	473	318	5394	16.5%	1.60 [1.14, 2.23]	
SHI Lei 2017	8	973	28	2991	4.8%	0.88 [0.40, 1.93]	
Satoshi Ogihara 2019	2	60	18	563	1.2%	1.04 [0.24, 4.61]	
Satoshi Ogihara 2018	8	725	18	3302	2.3%	2.04 [0.88, 4.70]	
Satoshi Ogihara 2015	4	336	20	2400	1.7%	1.43 [0.49, 4.22]	
Samer Habiba 2017	12	608	28	1164	6.7%	0.82 [0.41, 1.62]	
Oren G. Blam 2003	8	104	16	151	4.3%	0.70 [0.29, 1.71]	
Nathan J. Lee 2017	26	1208	114	4595	16.5%	0.86 [0.56, 1.33]	
Muneharu Ando 2014	0	8	66	286	1.4%	0.20 [0.01, 3.42]	
Matt El-Kadi 2019	6	1225	24	3840	4.1%	0.78 [0.32, 1.92]	
Kotaro Satake 2013	4	32	7	78	1.3%	1.45 [0.39, 5.34]	
John J. Lee 2016	5	46	10	103	1.9%	1.13 [0.36, 3.53]	
Jin-Sol Han 2016	3	84	7	196	1.4%	1.00 [0.25, 3.96]	
Daniël M. C. Janssen 2018	20	285	40	613	8.4%	1.08 [0.62, 1.89]	
Cindy R. Nahhas 2017	21	420	87	2128	9.7%	1.23 [0.76, 2.01]	
CHRISTOPHER J. LUCASTI 2019	5	17	8	56	0.9%	2.50 [0.69, 9.03]	
Andrew A. Fanous 2019	22	418	9	323	3.4%	1.94 [0.88, 4.27]	
Amy M. Cizik 2012	18	456	45	1076	9.1%	0.94 [0.54, 1.64]	_
Albert F 2010	8	128	38	702	3.9%	1.16 [0.53, 2.56]	
Total (95% CI)		7690		30514	100.0%	1.15 [0.99, 1.35]	•
Total events	226		908			1.1	15 IN IN IN IN
Heterogeneity: Chi ² = 17.71, df = 19	(P = 0.54)	: I ² = 09	6				
Test for overall effect: Z = 1.79 (P =							0.01 0.1 1 10 100 Favours [experimental] Favours [control]



	male	1	fema	le		Odds Ratio		0	ds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	M-H,	Fixed, 95% C		
Albert F 2010	11	220	35	610	3.8%	0.86 [0.43, 1.73]			-		
Amy M. Cizik 2012	34	876	29	656	6.9%	0.87 [0.53, 1.45]			-		
Andrew A. Fanous 2019	12	253	8	279	1.6%	1.69 [0.68, 4.20]			+		
CHRISTOPHER J. LUCASTI 2019	2	27	11	47	1.6%	0.26 [0.05, 1.28]	-		-		
Cindy R. Nahhas 2017	52	1055	56	1493	9.6%	1.33 [0.90, 1.96]			-		
Daniël M. C. Janssen 2018	32	440	28	458	5.5%	1.20 [0.71, 2.04]					
Eiichiro Iwata 2016	1	51	4	34	1.0%	0.15 [0.02, 1.41]	-		-		
Jin Hak Kim 2015	16	1248	14	583	4.1%	0.53 [0.26, 1.09]			-		
Jin-Sol Han 2016	6	175	4	105	1.0%	0.90 [0.25, 3.25]			-		
Muneharu Ando 2014	4	151	4	143	0.9%	0.95 [0.23, 3.85]					
Nathan J. Lee 2017	55	2380	85	3423	14.8%	0.93 [0.66, 1.31]			-		
Oren G. Blam 2003	17	189	7	67	2.0%	0.85 [0.33, 2.14]		_			
Qi Lai 2017	20	570	6	353	1.6%	2.10 [0.84, 5.29]				S	
Samer Habiba 2017	22	1024	18	748	4.4%	0.89 [0.47, 1.67]			-		
Satoshi Ogihara 2015	18	1572	6	1164	1.5%	2.24 [0.88, 5.65]				-	
Satoshi Ogihara 2018	23	2792	3	1234	0.9%	3.41 [1.02, 11.37]					
Satoshi Ogihara 2019	9	331	11	292	2.5%	0.71 [0.29, 1.75]					
Sjoerd P. F. T. Nota 2015	197	3041	164	2720	35.1%	1.08 [0.87, 1.34]			+		
Yusuke Yamamoto 2018	3	54	8	87	1.3%	0.58 [0.15, 2.29]			-		
Total (95% CI)		16449		14496	100.0%	1.05 [0.93, 1.20]			+		
Total events	534		501			500 Section 2010 (2010)			1		
Heterogeneity: Chi ² = 23.79, df = 18	(P = 0.16);	12 = 24	%				-	1	-	1	
Test for overall effect: Z = 0.79 (P =							0.01	0.1 [experiment	al] Favours	10	10

Figure 5. The odds ratio (OR) estimate for gender.

3.3.4. Sex. Nineteen studies^[10–13,16–20,24–26,28–33] reported sex between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity=0.16; I^2 =24%, Fig. 5). The meta-analysis showed that gender was not associated with a significant increase in the incidence of SSI (fixed-effects model; *P*=.43, OR=1.05, 95% CI [0.93, 1.20], Fig. 5).

3.3.5. *Diabetes.* Seventeen studies^[10–14,16–19,21,23,25–30] reported a history of diabetes between SSI group and non-SSI group. There was not significant in the test for heterogeneity and

the studies had low heterogeneity (*P* for heterogeneity = .29; I^2 = 14%, Fig. 6). The meta-analysis showed that a history of diabetes was associated with a significant increase in the incidence of SSI (fixed-effects model; *P*<.00001, OR=1.78, 95% CI [1.49, 2.14], Fig. 6).

3.3.6. Hypertension. Seven studies^[10,11,13,16,25,26,29] reported a history of hypertension between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity=.26; I^2 = 22%, Fig. 7). The meta-analysis showed that a history of

	diabet	es	witho	ut		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Albert F 2010	5	55	41	575	5.1%	1.27 [0.53, 3.09]	
Amy M. Cizik 2012	14	167	49	1365	7.6%	2.34 [1.32, 4.14]	
Andrew A. Fanous 2019	6	81	14	451	3.0%	2.39 [0.94, 6.03]	
CHRISTOPHER J. LUCASTI 2019	4	14	9	60	2.4%	1.90 [0.68, 5.30]	
Cindy R. Nahhas 2017	18	340	90	2208	17.1%	1.30 [0.79, 2.13]	- - -
Daniël M. C. Janssen 2018	7	73	53	825	6.1%	1.49 [0.70, 3.16]	
Jin-Sol Han 2016	6	406	24	1425	7.6%	0.88 [0.36, 2.13]	
John J. Lee 2016	2	51	8	229	2.1%	1.12 [0.25, 5.13]	
Matt El-Kadi 2019	4	24	9	125	2.1%	2.31 [0.78, 6.91]	
Muneharu Ando 2014	10	827	20	4238	4.6%	2.56 [1.20, 5.45]	
Nathan J. Lee 2017	4	56	4	238	1.1%	4.25 [1.10, 16.48]	
Qi Lai 2017	29	848	111	4955	23.1%	1.53 [1.02, 2.28]	
Satoshi Ogihara 2015	17	399	9	524	5.5%	2.48 [1.12, 5.51]	
Satoshi Ogihara 2018	5	313	19	2423	3.1%	2.04 [0.77, 5.42]	
Satoshi Ogihara 2019	5	457	21	3570	3.4%	1.86 [0.70, 4.91]	
SHI Lei 2017	3	76	17	547	2.9%	1.27 [0.38, 4.23]	
Takashi Sono 2018	12	377	24	3587	3.2%	4.76 [2.40, 9.44]	
Total (95% CI)		4564		27345	100.0%	1.78 [1.49, 2.14]	•
Total events	151		522				
Heterogeneity: Chi ² = 18.60, df = 16	(P = 0.29)	; ² = 14	%				
Test for overall effect: Z = 6.26 (P <	0.00001)						0.01 0.1 1 10 10 Favours [experimental] Favours [control]

Figure 6. The odds ratio (OR) estimate for history of diabetes.

	hyperter	nsion	witho	ut		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-I	H. Fixed, 95% Cl
Albert F 2010	17	259	29	571	10.7%	1.31 [0.71, 2.43]		
Amy M. Cizik 2012	30	464	33	1068	11.8%	2.17 [1.31, 3.60]		
Andrew A. Fanous 2019	10	228	10	304	5.2%	1.35 [0.55, 3.30]		
Cindy R. Nahhas 2017	63	1380	45	1168	29.3%	1.19 [0.81, 1.76]		
Muneharu Ando 2014	3	109	5	184	2.3%	1.01 [0.24, 4.33]	-	
Nathan J. Lee 2017	90	3162	50	2641	33.4%	1.52 [1.07, 2.15]		
Qi Lai 2017	4	249	22	674	7.4%	0.48 [0.17, 1.42]		
Total (95% CI)		5851		6610	100.0%	1.38 [1.13, 1.69]		•
Total events	217		194			2012		
Heterogeneity: Chi ² = 7.71	, df = 6 (P	= 0.26);	$ ^2 = 22\%$					
Test for overall effect: Z =	3.12 (P = 0	0.002)					0.01 0.1 Favours [experime	1 10 100 ental] Favours [control]

hypertension was associated with a significant increase in the incidence of SSI (fixed-effects model; P=.002, OR = 1.38, 95% CI [1.13, 1.69], Fig. 7).

3.3.7. Steroid use. Nine studies^[13,16,18,19,23–27] reported steroid use between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity = .21; I^2 = 27%, Fig. 8). The meta-analysis showed that steroid use not was associated with a significant increase in the incidence of SSI (fixed-effects model; P=.92, OR = 1.02, 95% CI [0.71, 1.46], Fig. 8).

3.3.8. Osteoporosis. Two studies^[16,25] reported osteoporosis between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity =.51; $I^2 = 0\%$, Fig. 9). The meta-analysis showed that osteoporosis was associated with a significant increase in the incidence of SSI (fixed-effects model; P < .0001, OR = 2.04, 95% CI [1.43, 2.93], Fig. 9).

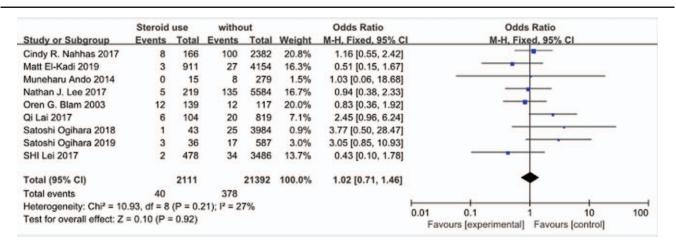
3.3.9. *Previous surgery.* Eight studies^[14,17,21–23,27,29,30] reported previous surgery between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity = .50; $I^2 = 0\%$, Fig. 10). The meta-analysis showed that previous surgery was associated with a significant increase in the incidence of SSI

(fixed-effects model; *P*=.03, OR=1.40, 95% CI [1.04, 1.89], Fig. 10).

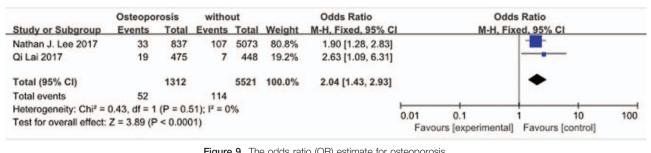
3.3.10. Albumin. Two studies^[14,24] reported albumin of patients at operational time between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity = .66; $I^2 = 0\%$, Fig. 11). The meta-analysis showed that albumin was not associated with a significant increase in the incidence of SSI (fixed-effects model; P = .18, SMD = 0.13, 95% CI [-0.06, 0.331], Fig. 11).

3.3.11. Osteotomy. Two studies^[20,25] reported osteotomy between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity=.46; I^2 =0%, Fig. 12). The meta-analysis showed that osteotomy was associated with a significant increase in the incidence of SSI (fixed-effects model; *P*<.00001, OR = 2.03, 95% CI [1.49, 2.77], Fig. 12).

3.3.12. Transfusion. Four studies^[13,23,30,34] reported transfusion between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (*P* for heterogeneity=.64; I^2 =0%, Fig. 13). The meta-analysis showed that transfusion was associated with a significant increase in the incidence of SSI (fixed-effects model; P<.002, OR=2.03, 95% CI [1.49, 2.77], Fig. 13).









3.3.13. Dural tear. Six studies^[17-19,23,30,34] reported dural tear between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity = .25; $I^2 = 25\%$, Fig. 14). The meta-analysis showed that dural tear was not associated with a significant increase in the incidence of SSI (fixed-effects model; P = .91, OR = 1.02, 95% CI [0.71, 1.47], Fig. 14).

3.3.14. Duration of surgery. Six studies^[11,14,19,22,24,30] reported duration of surgery between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity = .34; $I^2 = 11\%$, Fig. 15). The meta-analysis showed that duration of surgery was not associated with a significant increase in the incidence of SSI (fixed-effects model; P=.13, SMD=-6.21, 95% CI [-14.32, 1.90], Fig. 15).

3.3.15. Blood loss. Four studies^[11,19,21,30] reported blood loss between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity

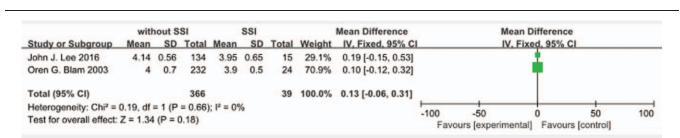
(P for heterogeneity = .18; I^2 = 39%, Fig. 16). The meta-analysis showed that blood loss was not associated with a significant increase in the incidence of SSI (fixed-effects model; P=.08, SMD=76.02, 95% CI [-8.23, 160.26], Fig. 16).

3.3.16. Number of fusion level. Six studies^[10,11,14,21,30,31] reported the number of fusion level between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (P for heterogeneity = .77; $I^2 = 0\%$, Fig. 17). The meta-analysis showed that the number of fusion level was associated with a significant increase in the incidence of SSI (fixed-effects model; P < .00001, SMD=-0.37, 95% CI [-0.54, -0.21], Fig. 17).

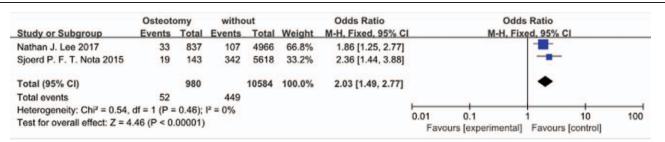
3.3.17. Surgical location (cervical, thoracic, lumbar). Six studies^[11,14,21,30,31,35] reported surgical location (cervical, thoracic, lumbar) between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the studies had low heterogeneity (3 P for heterogeneity = .52, .31, .35,respectively; $I^2 = 0\%$, 16%, 10%, respectively, Fig. 18). The

	previous su	irgery	witho	out		Odds Ratio	(Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	М-Н.	Fixed, 95% Cl	
Albert F 2010	29	471	12	263	20.8%	1.37 [0.69, 2.74]			
Daniël M. C. Janssen 2018	19	253	41	645	30.8%	1.20 [0.68, 2.10]			
John J. Lee 2016	4	17	11	132	2.8%	3.38 [0.94, 12.17]			
Matt El-Kadi 2019	8	775	22	4290	9.6%	2.02 [0.90, 4.56]			
Samer Habiba 2017	5	255	35	1517	14.2%	0.85 [0.33, 2.18]	-		
Satoshi Ogihara 2015	7	427	17	2309	7.5%	2.25 [0.93, 5.45]			
SHI Lei 2017	4	483	32	3481	11.1%	0.90 [0.32, 2.56]	· · · · · · · · · · · · · · · · · · ·		
Takashi Sono 2018	3	100	7	537	3.1%	2.34 [0.60, 9.21]			
Total (95% CI)		2781		13174	100.0%	1.40 [1.04, 1.89]		•	
Total events	79		177						
Heterogeneity: Chi2 = 6.32, d	f = 7 (P = 0.50)); l ² = 0%	6						100
Test for overall effect: Z = 2.2	24 (P = 0.03)	60 - E					0.01 0.1 Favours [experimer	1 10 ntal] Favours [control]	100

Figure 10. The odds ratio (OR) estimate for previous surgery.









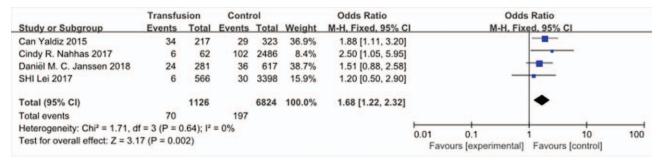


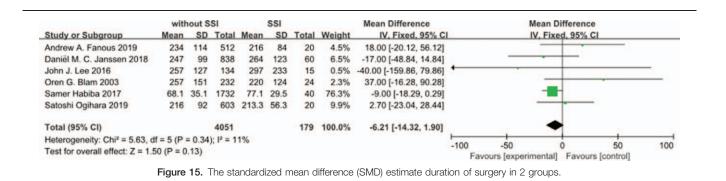
Figure 13. The odds ratio (OR) estimate for transfusion.

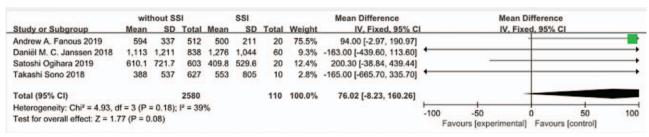
meta-analysis showed that surgical location (cervical vs thoracic; thoracic vs lumbar) was associated with a significant increase in the incidence of SSI (fixed-effects model; P < .0001, < .0001; OR = 0.44,95% CI[0.34,0.58]; OR = 1.70,95% CI[1.33,2.16],

respectively, Fig. 18). However, the meta-analysis showed that surgical location (cervical vs lumbar) was not associated with a significant increase in the incidence of SSI (fixed-effects model; P=.09; OR=0.82, 95% CI[0.65,1.03], Fig. 18).

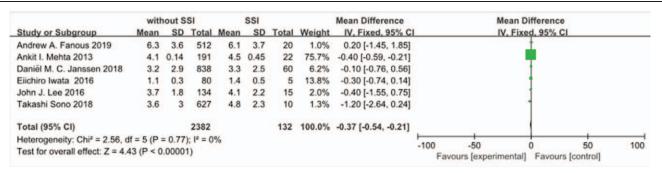
	Dural t	ear	witho	ut		Odds Ratio	Odd	s Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fix	ed, 95% Cl
Can Yaldiz 2015	12	141	51	399	43.2%	0.63 [0.33, 1.23]		-
Daniël M. C. Janssen 2018	9	91	51	807	16.5%	1.63 [0.77, 3.42]		-
Satoshi Ogihara 2015	3	277	21	2459	7.5%	1.27 [0.38, 4.29]		
Satoshi Ogihara 2018	3	256	23	3771	5.1%	1.93 [0.58, 6.48]		
Satoshi Ogihara 2019	3	45	17	578	4.1%	2.36 [0.66, 8.37]	-	· · · ·
SHI Lei 2017	7	916	29	3048	23.6%	0.80 [0.35, 1.84]	_	-
Total (95% CI)		1726		11062	100.0%	1.02 [0.71, 1.47]		•
Total events	37		192					
Heterogeneity: Chi ² = 6.69, d	f = 5 (P =	0.25); 1	= 25%				0.01 0.1	1 10 100
Test for overall effect: Z = 0.1	2 (P = 0.9	1)					0.01 0.1 Favours [experimental]	1 10 100 Favours [control]













3.3.18. Fusion approach (anterior, posterior, combined). Six studies^[14,19,20,24,26,35] reported fusion approach (anterior, posterior, combined) between SSI group and non-SSI group. There was not significant in the test for heterogeneity and the

studies had low heterogeneity (3 *P* for heterogeneity = .30, .70, .32, respectively; $I^2 = 17\%$, 0%, 14%, respectively, Fig. 19). The meta-analysis showed that fusion approach (anterior vs posterior, anterior vs combined) was associated with a significant

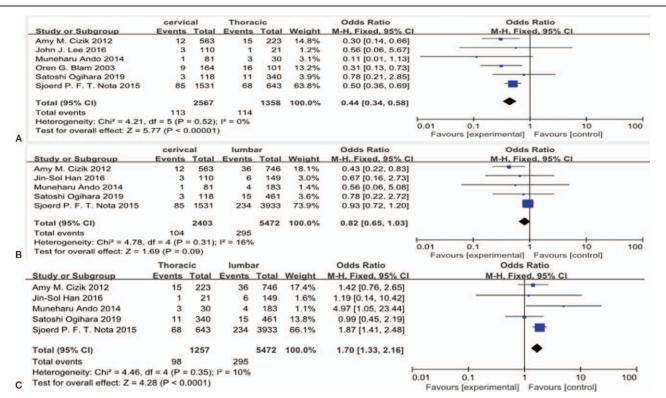


Figure 18. A. The odds ratio (OR) estimate for surgical location (cervical vs thoracic, lumbar). B. The OR estimate for surgical location (cervical vs lumbar). C. The OR estimate for surgical location (thoracic vs lumbar).

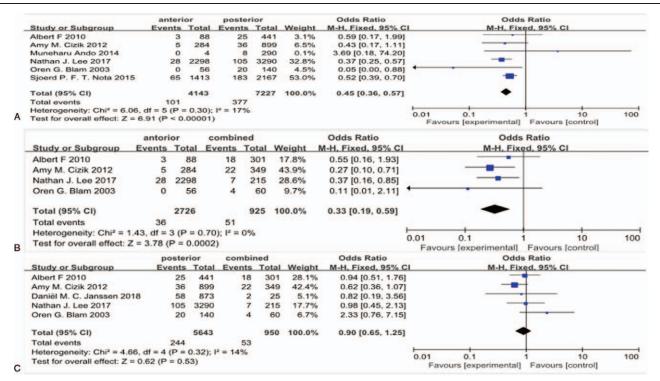


Figure 19. A. The odds ratio (OR) estimate for fusion approach (anterior vs posterior). B. The OR estimate for fusion approach (anterior vs combined). C. The OR estimate for fusion approach (posterior vs combined).

increase in the incidence of SSI (fixed-effects model; P < .0001, =.0002, respectively; OR = 0.45, 95% CI[0.36,0.57]; OR = 0.33, 95% CI[0.19,0.59], respectively, Fig. 19). However, the metaanalysis showed that fusion approach (posterior vs combined) was not associated with a significant increase in the incidence of SSI (fixed-effects model; P = .53; OR = 0.90, 95% CI[0.65,1.25], Fig. 19).

3.3.19. *Publication bias.* After a detection of publication bias by STATA 12.0, there was no publication bias found for all included studies (all P > .05).

4. Discussion

SSI is a common disease after spinal surgery in clinic, which may bring great burden on individuals and society. Thus, it is important to find risk factors for SSI after spinal surgery in order to minimize risk as far as possible. Patient characteristics including age, obesity, diabetes, presence of more than 3 comorbid diseases, urinary incontinence, tobacco use, poor nutritional status, nonsteroidal anti-inflammatory drugs use and surgical factors containing revision surgery, posterior surgical approach, tumor resection, increased estimated blood loss, prolonged surgical time and multilevel surgery fusions extending to the sacrum have been identified as risk factors for SSI in previous studies.^[7,36,37] However, the risk factors remain debated due to relatively small numbers of patients.

Previous meta-analysis just have been studied epidemiological incidence of SSI after spinal surgery. As for as we known, there was few meta-analysis regarding few risk factors of SSI after spinal surgery. Thus, we perform a meta-analysis to evaluate the risk factors associated with SSI.^[10–35] The incidence of SSI was

2.9% (1222 of 41,624) in our study. Our data also showed that fusion approach (anterior vs posterior; anterior vs combined), osteotomy, transfusion, a history of diabetes, previous surgery, and hypertension, surgical location (cervical vs thoracic; lumbar vs thoracic), osteoporosis and the number of levels fused were associated with development of SSI. However, age, sex, a history of smoking, BMI, fusion approach (posterior vs combined) were, surgical location (cervical vs lumbar), duration of surgery, blood loss, using steroid, dural tear and albumin not associated with development of SSI.

Qi^[16] discovered that there was a close relation between diabetes and SSI. Actually, our result was consistent with that of Qi. Patients with diabetes may have lesions in the small vessels and the microvasculature.^[38] Therefore, when the vessels are cut, large vessels and microvessels may be occluded, leading to ischemia and hypoxia in the incision tissue and, finally, to infection or a lack of healing at the surgical site. Although many articles found negative correlation between hypertension and SSI, both Amy M. Cizik^[35] and Nathan J. Lee^[25] reported that hypertension was related with SSI. In the present study, our results implied that hypertension was considered as a risk for SSI after spinal surgery. But we do not understand the reason. Qi Lai^[16] was the first to discover the close relation between osteoporosis and SSI following lumbar surgery, which the same with our results. However, the mechanism of osteoporosis and SSI is needed to explore in further study.

Albert $F^{[29]}$ did not find significant relation between the previous surgery and SSI and he believed old scar tissue was not responsible for the increased risk for SSI. However, Cindy R. Nahhas^[13] found that reoperation was significantly associated with wound complication. In our study, previous surgery was found to be a risk of SSI after spinal surgery. As for the reason, we

inferred that it may be relation to reduction of white blood cell in tissue of scar. Both Nathan^[13] and Sjoerd P^[20] showed that operative procedure with osteotomy was association with SSI after spinal surgery, which was the same with our finding. As we known, it need more surgical time to perform osteotomy, which markedly increase the incidence of infection due to more time exposure in the air and even transfusion to perform osteotomy. In term of transfusion, no significantly relation was found by Daniël M.^[30] While Cindy R. Nahhas^[13] and Can Yaldiz^[34] demonstrated that transfusion could markedly increase the risk of SSI after spinal surgery. Studies have reported that the immunosuppressive effects of perioperative transfusion may increase the risk of infection at least 2-fold. Regarding the number of fusion level, we proved that it was a risk of SSI. It was easily understood that we spent more operative time and even patients had more blood loss and need more transfusion when we performed more fusion level, which would significantly increase the risk of SSI.

Recently studies tried to compare the rate of SSI for anterior vs posterior spinal surgery and many of these studies offer conflicting views. Pradhan^[39] indicated that there was no statistical significance between surgical approaches to fusion. However, Memtsoudis obtained an opposite result by reviewing 261,356 patients and demonstrated that anterior and anterior-posterior fusions were significantly associated with higher rates of complications than posterior fusions. In this meta-analysis, fusion approach (anterior vs posterior, anterior vs combined) was proved to be associated with a significant increase in the incidence of SSI, whereas fusion approach (posterior vs combined) was not associated with it. Anterior approach have a great merit in term of increasing surface area available for fusion and avoiding damage to the posterior supporting muscles. Additionally, a dead space caused by muscle dissection following posterior spinal fusion may predisposes patients to infection more than anterior fusion.^[39-41]

Jin-Sol Han^[28] did not find significant relation between surgical location (cervical, thoracic, and lumbar) and SSI after spinal surgery. While Amy M. Cizik^[35] demonstrated that surgical location (cervical, thoracic, and lumbar) was closely association with infection after spinal surgery. Our finding presented that surgical location (cervical vs thoracic and thoracic vs lumbar) was associated with a significant increase in the incidence of SSI, but surgical location (cervical vs lumbar) was not risk for SSI. There is a possible reason may explain these results. We need more surgical time to perform thoracic surgery because it is more risky and difficult than cervical and lumbar surgery, which is easier to cause infection due to exposure from the air for more time.

Many factors including age, history of smoking, BMI, operative time, and blood loss, were not statistically associated with SSI in the present analysis. Especially, in our study, a history of smoking (P=.07) and blood loss (P=.08) had a negative correlation with SSI. However, we still clinically regard these as potential risk factors of SSI.

There were several limitations in this study. First, we just evaluated SSI totally, which includes superficial and deep SSI. We would discuss superficial and deep SSI respectively in the further study. Second, some factors had 2 included studies. Mentioned above might impact the accuracy of results. Third, some factors, like C-reactive protein (CRP) or other laboratory index, might be risk factors for SSI. Because related studies were few and could not get pooled result, we excluded them.

In conclusion, fusion approach (anterior vs posterior and anterior vs combined), osteotomy, transfusion, diabetes, previous surgery, hypertension, surgical location (cervical vs thoracic and lumbar vs thoracic), osteoporosis and the number of levels fused were associated with a significant increase in the incidence of SSI. In this meta-analysis, we can clearly see which kind of people more likely had SSI after surgery. This article not only provides a reference for spinal surgeons, but also shares decision-making and communication with patients undergoing spinal surgery because some of these factors, such as diabetes, can be adapted during workup. Meanwhile it is helpful for the future study on SSI. Further large-scale, well-designed studies are urgently needed.

Author contributions

Software: Xinxin Zhang. Writing – original draft: Peng Liu. Writing – review & editing: Jipeng You.

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