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ORIGINAL RESEARCH

The effect of diabetes on perioperative complications following spinal surgery: a meta-analysis

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Background: Degenerative spinal diseases and diabetes mellitus (DM) have increasingly become a social and economic burden. The effect of DM on spinal surgery complications reported by previous studies remains controversial.

Methods: We searched MEDLINE, Cochrane CENTRAL, ScienceDirect, EMBASE, and Google Scholar to identify studies reporting the relationship between DM and spinal surgery complications. Two independent reviewers performed independent data abstraction. The I^2 statistic was used to assess heterogeneity. A fixed-effects or random-effects model was used for the meta-analysis.

Results: Twenty-four studies met the inclusion criteria. Surgical site infection and the incidence of deep venous thrombosis after spinal surgery were significantly higher in patients with than in patients without diabetes, and the length of hospital stay was significantly longer in patients with diabetes ($P<0.05$). No significant differences were observed in the risk of reoperation, blood loss, and operation time between patients with and those without diabetes ($P>0.05$).

Conclusion: Patients with diabetes have a higher risk when undergoing spinal surgery than patients without diabetes. Diabetes increases the risks of postoperative mortality, surgical site infection, deep venous thrombosis, and a prolonged hospitalization time after spinal surgery.

Keywords: diabetes mellitus, spine, surgery, complication

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases of blood glucose dysregulation that can cause complications and lead to target organ, peripheral vascular, and nerve dysfunction.[1] Previous studies showed that DM may affect the typical signs and symptoms of cervical spondylotic myelopathy[2] and could be a predisposing factor for the development of lumbar spinal stenosis.[3] Several studies have focused on the correlation between diabetes and complications of spinal surgery.[4,5] Previous studies have shown that glycemic control could reduce the risk of postoperative mortality, surgical site infection, venous thrombosis, and a prolonged length of hospital stay after spinal surgery in patients with diabetes.[6–9] Appaduray and Lo[10] demonstrated that hyperglycemia could increase the risk of poor outcomes such as infections and cardiovascular disease following lumbar spinal surgery. A recent study assessed the effect of glycemic control on perioperative complications in patients undergoing lumbar surgery and showed that poor glycemic control in patients with diabetes receiving degenerative lumbar spine surgery could increase the risk of acute complications and poor outcomes.[11] However, Arnold et al[12] reported that DM would not increase the risk of postoperative complications. Controversies regarding whether diabetes could increase the rate of complications associated with spinal surgery still exist.

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Moreover, the sample sizes of these studies were relatively small, which could restrict the conclusions. The purpose of the present study was to conduct a meta-analysis to assess the impact of DM on surgical outcomes in patients who receive spinal surgery.

Materials and methods

Search strategy

We conducted the present study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A computerized search was performed in the MEDLINE database, the Cochrane CENTRAL database, ScienceDirect, EMBASE, and Google scholar for relevant published studies through May 2018. The following search terms were used to maximize the search specificity and sensitivity: spine, surgery, and diabetes. The search strategy is presented in Figure 1, and included only studies conducted on humans for all published, unpublished, and ongoing trials. In addition, the WHO International Clinical Trials Registry Platform, the UK National Research Register Archive, and Current Controlled Trials were used for a further manual search for articles from Congresses that may have been missed in the database search from their inception to May 2018. The reference lists of all full-text papers were examined to identify any initially omitted studies.

Selection criteria

The studies that met the following criteria were included in the meta-analysis: 1) the study design was a cohort or case–control study; 2) the study included patients with and those without diabetes who were undergoing spinal surgery; 3) the study reported outcome measures, operation data, clinical function scores, recovery rates, and postoperative

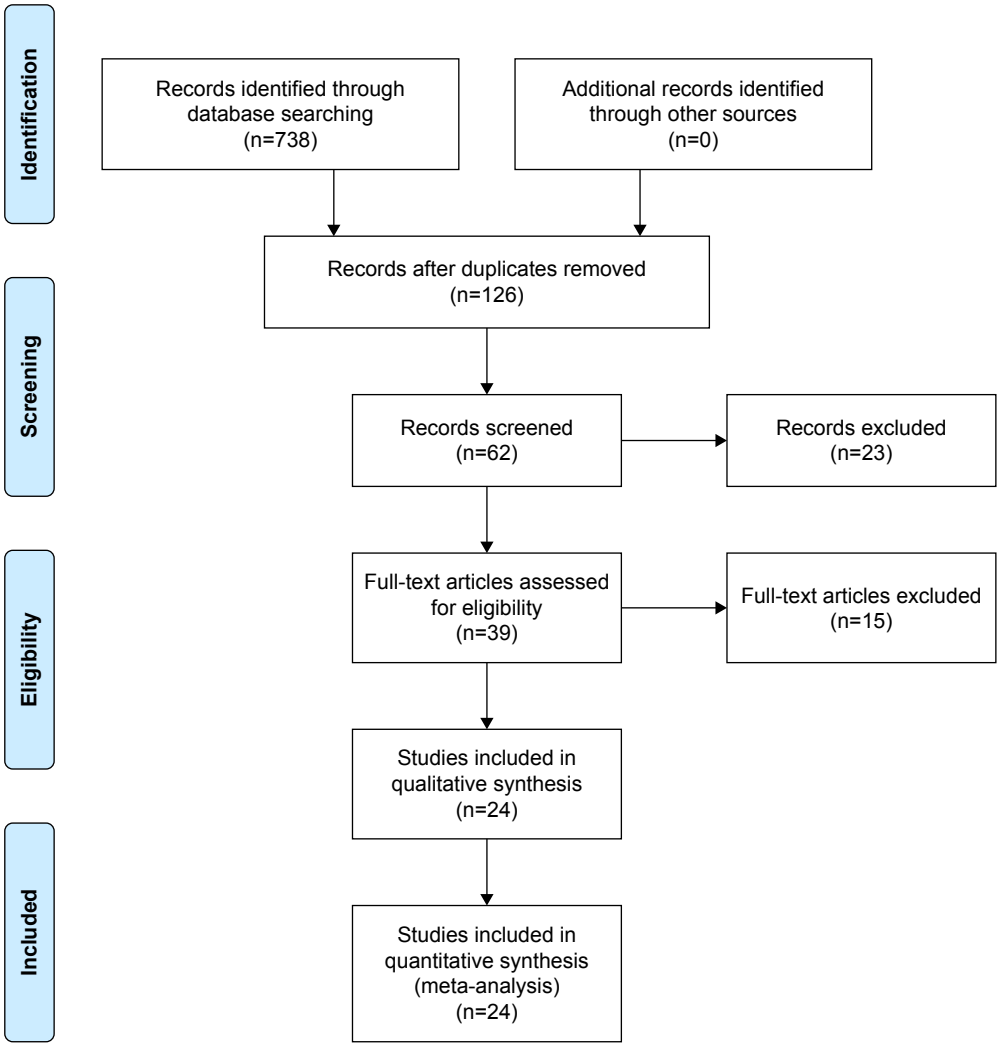

Figure 1 Flowchart of the study selection process.

complications; and 4) the study may have included any other outcomes.

The exclusion criteria included reviews, letters, case reports, systematic reviews, and studies that were unrelated to our topics.

Study selection

Two authors independently screened the article titles and abstracts based on the eligibility criteria, and intensive reading of the full texts was performed when the studies met the inclusion criteria. When a study could not be excluded immediately, disagreements were resolved by consensus with the senior investigator.

Data extraction

Data extraction was conducted according to the PRISMA statement, and data from eligible peer-reviewed articles were extracted by two independent authors. Any discrepancies between the two reviewers were resolved by discussion and consensus or, if necessary, by third-party adjudication. Authors of the studies were contacted for missing data or further information when necessary. The following outcomes were extracted from the included publications: 1) demographic data on the participants; 2) operation data, clinical function scores, recovery rates, and postoperative complications; and 3) any other outcomes mentioned in the individual studies.

Assessment of methodological quality

We assessed the methodological quality of included studies using the modified Newcastle–Ottawa Scale (NOS). This scale consists of three items for cohort study reports: patient selection, comparability of the intervention/control group, and outcome assessment. The quality scale ranges from 0 to 9 points. Articles were considered to be of high quality if the NOS score was >5 points.

Statistical analysis

We used Review Manager 5.1 software for Windows (RevMan Version 5.1; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) for data analysis. Dichotomous outcomes are expressed as ORs with 95% CIs; continuous outcomes are expressed as the mean differences (MDs). Before the original data were synthesized, we used Cochran's Q chi-squared test and the I^2 statistic to assess the heterogeneity across studies. $P<0.1$ or $I^2>50\%$ was defined as significant heterogeneity. If substantial heterogeneity existed, a random-effects model (the DerSimonian–Laird method) was used; otherwise, a fixed-effects model (the Mantel–Haenszel method) was preferred to summarize the pooled data. When heterogeneity was present, a sensitivity analysis was conducted to identify the potential sources. Since the number of included studies was <10, an assessment of publication bias was not performed. $P<0.05$ was considered statistically significant.

Results

Search results

The search strategy identified 738 citations as potentially relevant literature reports. By scanning the titles and abstracts, 712 reports were excluded because of duplication or irrelevancy, because they were case reports or reviews, or because they were not comparative studies. Ultimately, 24 studies[6,8–30] were eligible for data extraction and meta-analysis (Table 1). No additional studies were obtained after the reference review. The search process is shown in Figure 1.

Study characteristics

The characteristics of the 24 included studies, which were published between 1993 and 2017, are shown in Table 1. The sample sizes of these studies ranged from 52 to 256,899 patients. Statistically similar baseline characteristics, such as the mean age and gender, were observed between both groups.

Quality assessment and level of evidence

Four of the included studies were prospective controlled studies, and 20 studies were retrospective controlled studies. The NOS scores were 5–8 for the included studies. The methodological quality assessment is presented in Table 1.

Meta-analysis outcomes

Blood loss

Usable data on blood loss were provided in 10 trials.[6,14,16,18,19,24,25,27,29,30] No significant heterogeneity was observed, and a fixed-effects model was used ($I^2=36\%$, $P=0.10$). Pooling of the results demonstrated that blood loss in the DM group was not significantly greater than that in the non-DM group (MD=0.55, 95% CI: –8.15 to 9.26, $P=0.90$; Figure 2).

Operation time

The operation time was provided in eight trials.[6,14,18,19,24,25,27,30] No significant heterogeneity was observed, and a fixed-effects model was used ($I^2=0\%$, $P=0.47$). Pooling of the results demonstrated that the operation time in the DM group

Table 1 Characteristics of included studies

Author	Study design	Diagnosis	Operative interventions	Sample size		Mean age (years)		NOS
				DM	Non-DM	DM	Non-DM	
Appaduray and Lo 2013[10]	Retrospective	Lumbar spondylolisthesis/ spinal stenosis/scoliosis	Decompression/fusion	115	444	66.5	54	7
Arinzon et al 2004[13]	Retrospective	Lumbar spinal stenosis	Decompression	62	62	70.5	72.4	7
Arnold et al 2014[12]	Prospective	Cervical spondylotic myelopathy	Decompression	42	236	60.12	55.66	8
Armaghani et al 2016[14]	Prospective	NS	Decompression/fusion	434	571	61	56	8
Browne et al 2007[8]	Retrospective	NS	Fusion	11,135	186,326	48.96		5
Chen et al 2009[15]	Retrospective	NS	Fusion	30	165	NS	NS	6
Cho et al 2012[16]	Retrospective	Thoracolumbar deformity	Spine corrective operation	23	23	61.1	59.2	8
Cook et al 2008[9]	Retrospective	Cervical spondylotic myelopathy	Fusion	3,432	34,300	60.48	54.23	7
Dokai et al 2012[17]	Retrospective	Cervical spondylotic myelopathy	Laminoplasty	13	65	72	71.1	7
Freedman et al 2011[18]	Retrospective	Lumbar spondylolisthesis/ spinal stenosis	Discectomy/ decompression	117	1,464	NS	NS	7
Glassman et al 2003[19]	Retrospective	NS	Fusion	94	43	63	59	6
Golinvaux et al 2014[20]	Retrospective	NS	Decompression/fusion	2,437	13,043	NS	NS	7
Guzman et al 2014[11]	Retrospective	Degenerative disease	Decompression/fusion	423,050	2,145,944	NS	NS	8
Hikata et al 2014[21]	Retrospective	Degenerative disease/ vertebral fracture/scoliosis	Fusion	36	309	64.3	63.8	7
Kawaguchi et al 2000[6]	Retrospective	Cervical spondylotic myelopathy	Laminoplasty	18	34	65.7	64.8	6
Kim et al 2015[22]	Prospective	NS	Decompression/fusion	6,268	28,650	NS	NS	8
Kim et al 2008[23]	Retrospective	Cervical spondylotic myelopathy	Laminoplasty	31	56	64.7	61.1	7
Liao et al 2006[24]	Retrospective	Degenerative spondylolisthesis	Fusion	39	298	60–70	60–70	7
Machino et al 2014[25]	Prospective	Cervical spondylotic myelopathy	Laminoplasty	115	444	66.5	54	7
Maloney et al 2017[26]	Retrospective	Lumbar disc herniation	Discectomy	126	126	59	59	6
Sharma et al 2013[27]	Retrospective	NS	Decompression/fusion	111	97	62	63	7
Silverstein et al, 2016[28]	Retrospective	Degenerative disease/ vertebral fracture/scoliosis	Lumbar decompression	30	182	NS	NS	7
Simpson et al 1993[29]	Retrospective	Lumbar disc herniation/ spinal stenosis	Decompression/fusion	62	62	63	63	6
Takahashi et al 2013[30]	Retrospective	Lumbar disc herniation/ spinal stenosis	Decompression/fusion	41	124	70.9	68	8

Abbreviations: DM, diabetes mellitus; NOS, Newcastle–Ottawa Scale; NS, not state.

was not significantly longer than that in the non-DM group (MD=1.36, 95% CI: –2.22 to 4.94, P=0.46; Figure 3).

Length of hospital stay

Data from five studies were available to examine the length of hospital stay.[8,18,24,27,29] Significant heterogeneity was observed, and a random-effects model was used (I^2=91%, P<0.001). Pooling of the results demonstrated that the length of hospital stay in the DM group was significantly longer than that in the non-DM group (MD=1.00, 95% CI: 0.29–1.71, P=0.02; Figure 4).

Mortality

Six studies reported postoperative mortality.[8,9,11,18,20,29] No significant heterogeneity was observed (I^2=0%, P=0.48); therefore, a fixed-effects model was used. Pooling of the results demonstrated that the incidence of postoperative mortality in the DM group was significantly higher than

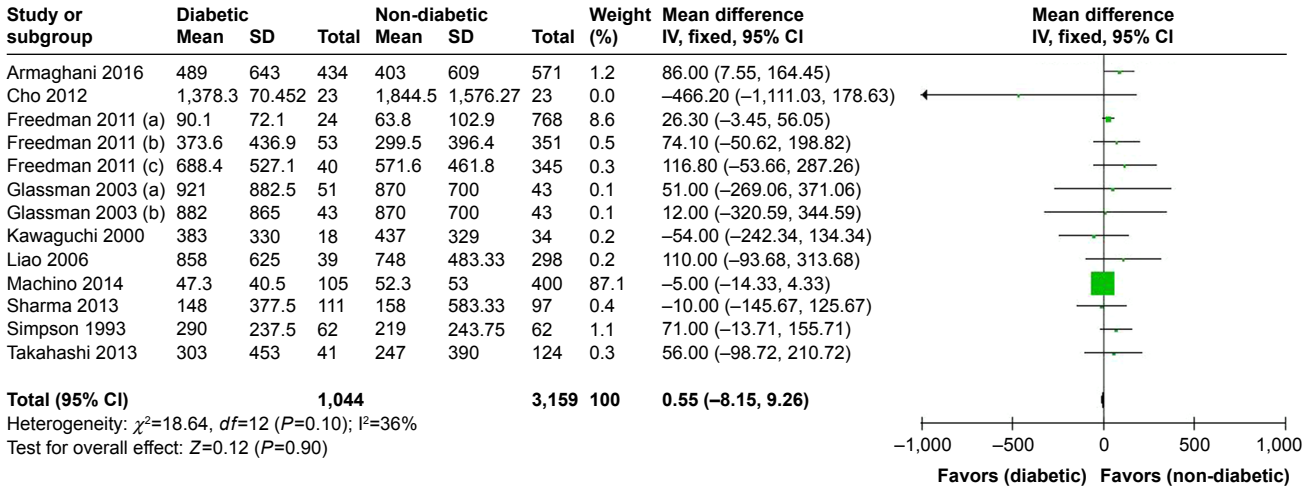

Figure 2 Forest plot showing blood loss.

that in the non-DM group (OR=1.44, 95% CI: 1.33–1.56, $P<0.001$; Figure 5).

Reoperation

The number of patients who underwent reoperation was provided in six studies.[12,16,19,22,27,30] No significant heterogeneity was observed ($I^2=0\%$, $P=0.56$); therefore, a fixed-effects model was used. Pooling of the results demonstrated that the incidence of reoperation in the DM group was not significantly higher than that in the non-DM group (OR=1.18, 95% CI: 0.99–1.40, $P=0.07$; Figure 6).

Infection

Seventeen studies reported the postoperative incidence of infection.[8–13,15,18–21,24–27,29,30] Significant heterogeneity was observed, and a random-effects model was used ($I^2=61\%$, $P=0.0005$). The meta-analysis revealed that the postoperative incidence of infection was significantly higher than that in the non-DM group (OR=1.88, 95% CI: 1.46–2.42, $P<0.001$; Figure 7).

Deep venous thrombosis (DVT)

Five studies reported the postoperative incidence of DVT.[8,11,12,19,20] No significant heterogeneity was observed, and a fixed-effects model was used ($I^2=6\%$, $P=0.37$). The meta-analysis revealed that the postoperative incidence of DVT was significantly higher than that in the non-DM group (OR=1.49, 95% CI: 1.40–1.58, $P<0.001$; Figure 8).

Discussion

The present study indicates that diabetes increases the risks of postoperative mortality, surgical site infection, DVT, and prolonged hospitalization time after spinal surgery.

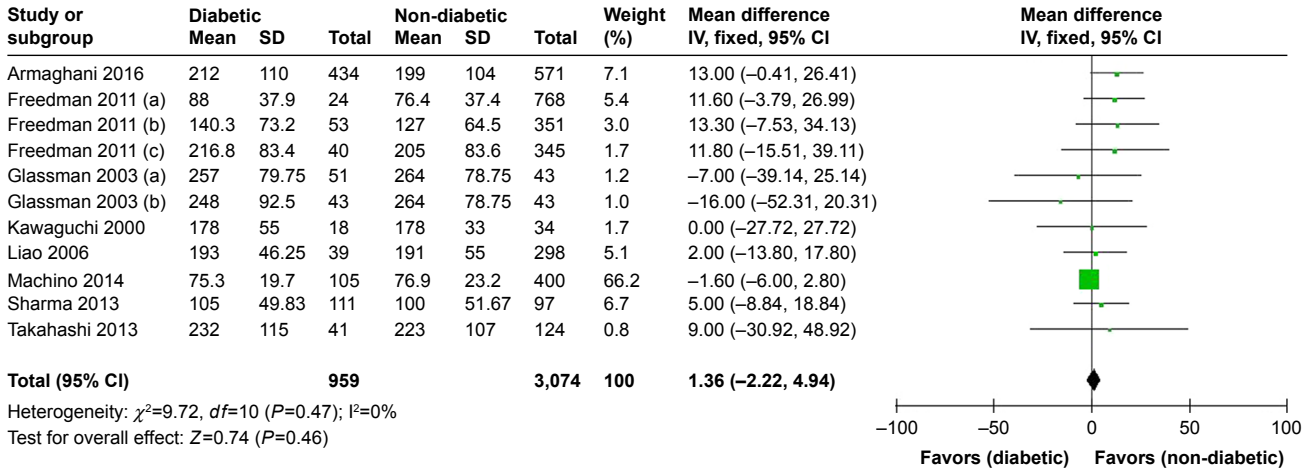

Figure 3 Forest plot showing operation time.

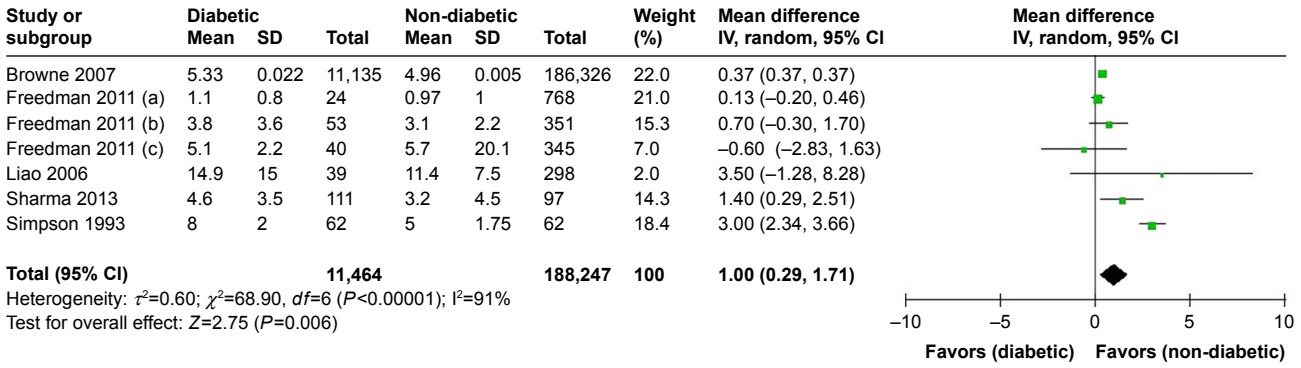

Figure 4 Forest plot showing length of hospital stay.

Four prospective controlled studies and 20 retrospective controlled studies were included. Although the NOS scores of the included studies are high (ranging from 5 to 8), the limitations inherent in this methodology weakened the level of evidence and should be considered when interpreting the findings of the present meta-analysis.

In 2010, the number of deaths caused by DM reached approximately 1.3 million worldwide, and the disease burden is several times greater in the elderly.[11,31] A large proportion of patients undergoing degenerative spine surgery are elderly, and therefore the impact of DM on surgical outcomes is of great interest. Currently, only a few studies have described the outcomes of spinal surgery in patients with DM. However, previous reports have relatively small sample sizes, which limit the conclusions that can be widely applied to clinical practice.[6,7,30]

Our meta-analysis demonstrates that patients with diabetes undergoing spinal surgery had increased odds of mortality. However, there is no clear and direct evidence to confirm that DM is an independent risk factor for postoperative mortality. Comorbidities including cardiovascular and cerebrovascular diseases, respiratory diseases, urinary system diseases, and nervous system diseases may have had additional influences on the outcomes for patients following spinal surgery, according to some studies.[11,12,18,25] Guzman et al[11] and Farrell and Moran[32] indicated that people with DM are more likely to have these comorbidities. Furthermore, Hamdan et al[33] and Carson et al[34] reported that comorbidities could increase inpatient mortality following spinal surgery. Therefore, a significant difference exists between the mortality rate of patients with diabetes undergoing spinal surgery and that of patients without diabetes.

No significant difference was found in the reoperation rate between patients with and without DM following spinal surgery. The reasons for reoperation included dysphagia (following cervical operation), malpositioning of the implant, or a postoperative deformity. Some studies[12,19] have shown that reoperation is not closely related to the presence of diabetes.

We also found that the risk of surgical site infection and DVT was higher in patients with DM following spinal surgery than in patients without DM. Many risk factors affect

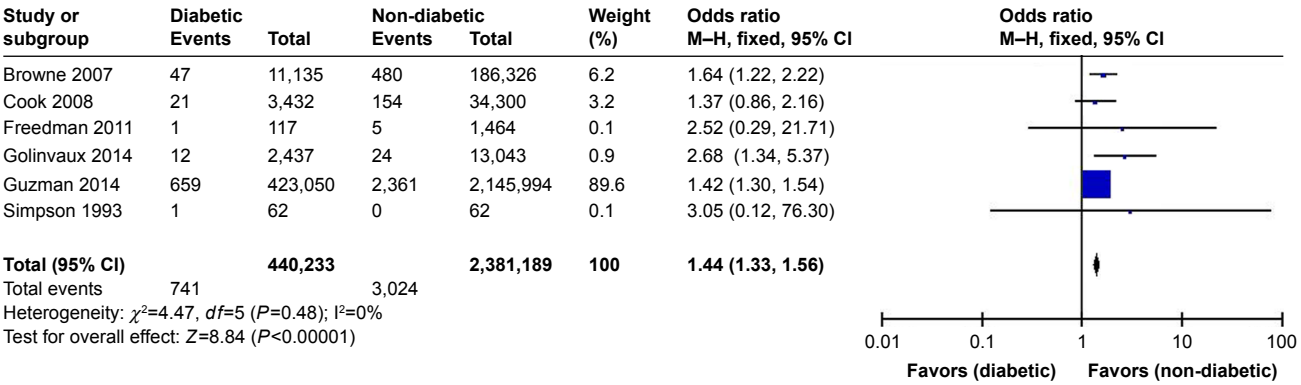

Figure 5 Forest plot showing mortality.
Abbreviation: M–H, Mantel–Haenszel.

Study or subgroup	Diabetic Events	Total	Non-diabetic Events	Total	Weight (%)	Odds ratio M–H, fixed, 95% CI
Arnold 2014	0	42	4	236	0.6	0.61 (0.03, 11.50)
Cho 2012	14	23	17	23	3.0	0.55 (0.16, 1.92)
Glassman 2003	21	81	7	37	3.2	1.50 (0.57, 3.92)
Kim 2015	170	1,173	461	3,619	86.9	1.16 (0.96, 1.40)
Sharma 2013	24	111	16	97	6.0	1.40 (0.69, 2.82)
Takahashi 2013	2	41	1	124	0.2	6.31 (0.56, 71.46)
Total (95% CI)		**1,471**		**4,136**	**100**	**1.18 (0.99, 1.40)**
Total events	231		506			

Heterogeneity: χ^2=3.95, *df*=5 (*P*=0.56); I^2=0%
Test for overall effect: *Z*=1.79 (*P*=0.07)

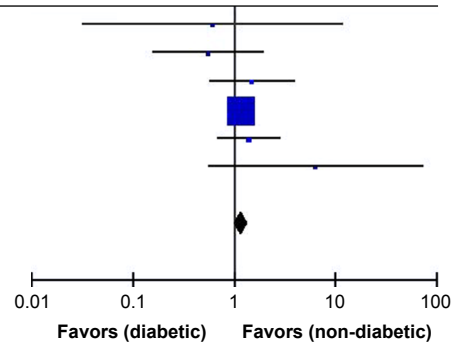

Figure 6 Forest plot showing reoperation.
Abbreviation: M–H, Mantel–Haenszel.

Study or subgroup	Diabetic Events	Total	Non-diabetic Events	Total	Weight (%)	Odds ratio M–H, random, 95% CI
Appaduray 2013	16	115	35	444	8.9	1.89 (1.00, 3.55)
Arinzon 2004	3	62	1	62	1.1	3.10 (0.31, 30.67)
Arnold 2014	3	42	6	236	2.7	2.95 (0.71, 12.28)
Browne 2007	76	11,135	604	186,326	16.9	2.11 (1.66, 2.68)
Chen 2009	9	30	18	165	5.4	3.50 (1.39, 8.80)
Cook 2008	9	3,432	98	34,300	8.1	0.92 (0.46, 1.82)
Freedman 2011	4	177	34	1,464	4.5	0.97 (0.34, 2.77)
Glassman 2003	11	97	2	43	2.3	2.62 (0.56, 12.38)
Golinvaux 2014	74	2,437	261	13,043	16.4	1.53 (1.18, 1.99)
Guzman 2014	2,028	423,050	7,296	2,145,994	19.8	1.41 (1.34, 1.48)
Hikata 2014	6	36	10	309	4.3	5.98 (2.03, 17.60)
Liao 2006	4	39	2	298	1.9	16.91 (2.99, 95.71)
Machino 2014	2	105	1	400	1.0	7.75 (0.70, 86.28)
Maloney 2017	11	126	6	126	4.6	1.91 (0.68, 5.34)
Sharma 2013	0	110	4	97	0.7	0.09 (0.00, 1.77)
Simpson 1993	6	62	0	62	0.7	14.38 (0.79, 261.05)
Takahashi 2013	0	41	1	124	0.6	0.99 (0.04, 24.82)
Total (95% CI)		**441,096**		**2,383,493**	**100**	**1.88 (1.46, 2.42)**
Total events	2,262		8,379			

Heterogeneity: τ^2=0.08; χ^2=41.50, *df*=16 (*P*=0.0005); I^2=61%
Test for overall effect: *Z*=4.90 (*P*<0.00001)

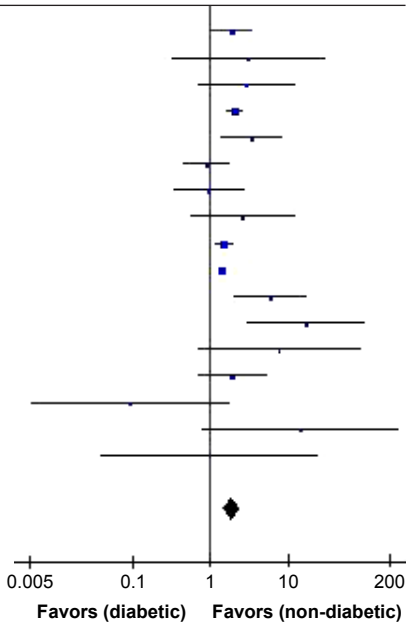

Figure 7 Forest plot showing infection.
Abbreviation: M–H, Mantel–Haenszel.

Study or subgroup	Diabetic Events	Total	Non-diabetic Events	Total	Weight (%)	Odds ratio M–H fixed, 95% CI
Arnold 2014	0	42	1	236	0.0	1.85 (0.07, 46.10)
Browne 2007	20	11,135	318	186,326	2.3	1.05 (0.67, 1.65)
Glassman 2003	0	94	1	43	0.1	0.15 (0.01, 3.76)
Golinvaux 2014	46	2,437	163	13,043	3.2	1.52 (1.09, 2.11)
Guzman 2014	1,328	423,050	4,507	2,145,994	94.3	1.50 (1.41, 1.59)
Total (95% CI)		**436,758**		**2,345,642**	**100**	**1.49 (1.40, 1.58)**
Total events	1,394		4,990			

Heterogeneity: χ^2=4.27, *df*=4 (*P*=0.37); I^2=6%
Test for overall effect: *Z*=12.99 (*P*<0.00001)

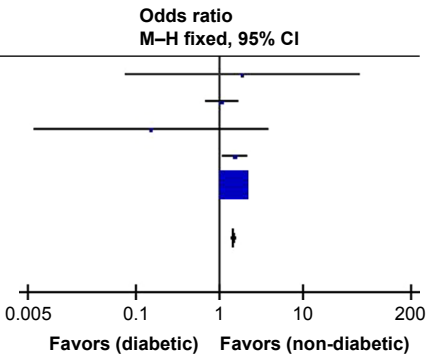

Figure 8 Forest plot showing deep venous thrombosis.
Abbreviation: M–H, Mantel–Haenszel.

wound healing, including a lack of platelet-derived growth factor, neutropenia, tissue hypoxia, and microvascular disease.[35,36] In addition, fibroblasts and collagen deficiency can lead to delayed wound healing.[37] Immune dysfunction is caused by the effects of DM increasing the probability of infection of the surgical site. DM is a chronic systemic disease characterized by high concentrations of glucose in the blood. Jones and Mitchell[38] also reported that a high concentration of glucose in blood vessels leads to increased vascular endothelial damage, which results in a higher risk of venous thrombosis. Therefore, patients with DM are more likely to develop venous thrombosis than those without DM following spinal surgery.

The results showed no significant difference in the operation time or blood loss between patients with and those without diabetes following spinal surgery, which is consistent with the results of several studies.[6,16,18,19,24,27,29,30] However, the length of hospital stay for patients with DM was longer than that for patients without diabetes, which may be related to the treatment of surgical site infections and other complications. Some papers have reported that the prolonged hospitalization time is related to the further regulation of blood glucose.[27]

There are some limitations in our meta-analysis: 1) no specific type of DM has a greater impact on spinal surgery, and it is not known whether spinal surgery will affect HbA1c; 2) the small sample sizes in the literature may have affected the final results; 3) differences in diabetes duration, treatment, complications, or comorbidities could have affected the findings and, similarly, the definition of diabetes was not standardized across the included studies and therefore it is likely that each study cohort may have affected the findings of the study; 4) this article did not compare the various types of spinal surgeries in detail, and different surgical methods may prolong the operation time and increase blood loss and the probability of surgical site infections, which may have impacted the evaluated results; and 5) most of the studies were performed on patients of the same nationality, and the lack of a regional comparison may affect the generalization of the results.

Conclusion

The effect of spinal surgery in patients with DM is more prominent and serious than that in patients without diabetes, and the mortality rate, surgical site infection rate, risk of venous thrombosis, and length of hospital stay are increased in patients with diabetes. Given this finding, physicians should pay attention to this risk to avoid complications.

Author contributions

WL and RS conducted the literature search and determined studies for exclusion and inclusion. WL and HJ extracted data from the included studies, performed the meta-analysis, and drafted the manuscript. WL, RS, and XM conceived the idea for the study, designed the study, and critically revised the manuscript for important intellectual content. All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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