Body mass index and risk of surgical site infection following spine surgery: a meta-analysis

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Abstract

Purpose Inconsistent results have been reported in the literature on the association between obesity, expressed as increased body mass index (BMI), and risk for surgical site infection (SSI) following spine surgery. The objective of this study was to review and quantify the association between increased BMI and risk of spinal SSI in adults.

Methods We performed a comprehensive search for relevant studies using PubMed, Embase, and references of published manuscripts. Study-specific risk measures were transformed into slope estimates and combined using the random effects meta-analysis model to establish the risk of SSI associated with every 5-unit increase in BMI.

Results Thirty-four articles underwent full-text review. Variations were noted among these studies in relation to SSI diagnosis criteria and BMI cut-off levels used to define obesity. Data from 12 retrospective studies were included in the analyses. Results showed that BMI was significantly positively associated with the risk of spinal SSI. Unadjusted risk estimates demonstrated that a 5-unit increase in BMI was associated with 13 % increased risk of SSI [Crude odds ratio (OR): 1.13; 95 % CI: 1.07–1.19, $p < 0.0001$]. Pooling of risk estimates adjusted for diabetes and other confounders resulted in a 21 % increase in risk of spinal SSI for every 5-unit increase in BMI (adjusted OR: 1.21; 95 % CI 1.13–1.29, $p < 0.0001$).

Conclusion Higher BMI is associated with the increased risk of SSI following spine surgery. Prospective studies are needed to confirm this association and to determine whether other measures of fat distribution are better predictors of risk of SSI.

Keywords Surgical site infection · Spine surgery · Body mass index · Obesity · Meta-analysis

Introduction

Surgical site infections (SSIs) are defined by the Centers for Disease Control (CDC) National Nosocomial Infection Surveillance system (NNIS) as superficial, deep, or organ space infections occurring within 30 days after surgery (or within 1 year of hardware implantation) [1]. The European Centre for Disease Prevention and Control applies similar criteria for the surveillance of SSI in European hospitals [2]. Rates of SSI after spine surgery have varied in the literature depending on study population and operative factors such as the surgical approach and spinal instrumentation. For the years 2006–2008, the National Healthcare Safety Network (NHSN) reported mean SSI rates between 0.72 and 2.30 % for laminectomies and between 0.70 and 4.15 % for spinal fusions [3]. Estimates of the burden of SSI following orthopaedic procedures demonstrate a two- to fourfold increase in healthcare costs attributable to SSI [4, 5]. Orthopaedic SSIs have been found to prolong length of hospital stay by a median of 14 days, and to increase rehospitalisation rates by twofold due to additional treatments and procedures required such as operative debridement and revision surgery [4].

Preventive measures that have been implemented to decrease the risk of SSI include adherence to sterile

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techniques and administration of prophylactic antibiotics [6, 7]. Moreover, numerous studies have sought to identify risk factors for SSI following spine surgery to support surgical decision-making and introduce more tailored preventive measures. With the rising prevalence of obesity, its role as a risk factor for spinal SSI has been examined by several studies and systematic reviews. Findings from published systematic reviews indicate that studies that have established body mass index (BMI)-defined obesity as a statistically significant factor for spinal SSI were higher in number than those that have nullified the association [7–9]. The evidence for obesity as a risk factor for spinal SSI was rated as moderate to strong in strength [7, 9]. Several sources of heterogeneity between studies in the literature were identified including differences in study design, study population, surgical approach, definitions of obesity, and criteria applied to identify SSI cases [7–9]. Therefore, no pooled summary estimates were reported and conclusions were based on the number of times obesity was confirmed as a risk factor for SSI. Inferences based on this vote counting approach, however, provide no indication of the magnitude of the association and are often misleading due to inadequate power [10].

Furthermore, recent data from several studies do not support an association between BMI-defined obesity and risk of spinal SSI. Results from the Spine Patient Outcomes Research Trial (SPORT) showed a non-significant difference in wound infection rates between the obese and non-obese cohorts undergoing surgical treatment for lumbar disc herniation [11]. Mehta et al. [27, 28] showed that BMI was not significantly associated with SSI in patients who underwent posterior lumbar fusion or cervical fusion surgeries. The authors demonstrated that the thickness of subcutaneous fat at the surgical site is more indicative of SSI risk than absolute BMI. Similarly, Waisbren et al. [12] showed that obesity measured by percent body fat (% BF) was associated with more than 5× higher risk of postoperative SSI, while obesity measured by BMI was not a risk factor for SSI. These results led to the proposition that measures of adiposity other than BMI, such as % BF and thickness of subcutaneous fat, are more sensitive measurements of the risk of SSI than BMI-defined obesity [12, 27, 28].

BMI is a measure of weight-for-height and is not a direct indicator of body fat. The World Health Organisation (WHO) uses BMI to classify adults into the following categories: normal range ($18.50 \leq \text{BMI} < 25 \text{ kg/m}^2$), overweight ($25 \leq \text{BMI} < 30 \text{ kg/m}^2$), and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) [13]. Direct indicators of adiposity in adults such as % BF are measured by other methods including bioelectrical impedance analysis (BIA) and dual energy X-ray absorptiometry. Several studies in the literature have used the cut-offs of 25 and 35 % BF for defining obesity in adult males and females, respectively. Nevertheless, the

WHO makes no recommendations about % BF thresholds that constitute obesity and there is currently no consensus regarding the criteria of % BF for the diagnosis of overweight and obesity [14, 15]. Furthermore, tools that accurately measure adiposity are expensive and not widely accessible. BMI remains the simplest and the most commonly used proxy for adiposity and has been widely used in practice and in the epidemiologic and medical literature. Therefore, establishing the strength of the association between BMI and risk of SSI remains relevant for clinical practice. Our aim in this study was to review and quantify the association between BMI and risk of SSI following spine surgery in the adult population. We performed a meta-analysis of observational studies to calculate a pooled estimate of the risk of spinal SSI in adults associated with every 5-unit increase in BMI.

Methods

Search strategy and inclusion criteria

We systematically searched PubMed and Embase databases for studies published up to February 2013. The search strategy consisted of combinations of the following terms: (“spine” OR “spinal”) AND (“surgery” OR “surgical”) AND (“surgical site infection” OR “wound infection” OR “dehiscence” OR “osteomyelitis” OR “abscess” OR “cellulitis”) AND (“obesity” OR “body weight” OR “body habitus” OR “body size” OR “adiposity” OR “body mass index” OR “BMI”). We also searched the reference lists of candidate studies, reviews, and other publications to identify further potentially relevant studies.

Studies were included if they met the following criteria: (1) the study provided original analysis on risk factors for spinal SSI which included an assessment of the association between SSI and obesity in adults, (2) the study provided quantitative risk estimates of the association between obesity and risk of spinal SSI with 95 % confidence intervals, or the study provided sufficient information to calculate risk estimates and their 95 % confidence intervals, (3) the CDC/NNIS criteria were applied for the selection of SSI cases, (4) a BMI scalar definition was used to define body weight. We excluded reviews, case reports, letters to editors, abstracts with no full reports, non-human and non-English language studies, and studies of paediatric populations.

Data extraction and level of evidence rating

The following data were extracted from eligible studies by one investigator (DYA) and reviewed by another (MMJ): first author and year of publication, country, study design,

type of surgery, spinal levels included, number of SSI cases, number of uninfected controls, BMI categories reported, results, and variables controlled for if multivariate analyses were performed. Ratings for the levels of evidence for each study were assigned using criteria established by Wright et al. [16] for prognostic studies.

Statistical analysis

BMI category-specific risk measures for spinal SSI were transformed into incremental estimates associated with every 5 kg/m² increase in BMI by the method of trend estimation described by Berlin et al. [17]. These estimates were derived via the synthesis of regression slopes for each study based on the assumption of a positive linear trend between the natural logarithm of odds ratio (OR) and BMI for different exposure categories. The value assigned to each BMI category was the mid-point for closed intervals and the value 20 % higher than the low end of an interval for open-ended upper intervals [17]. Open-ended lower intervals (e.g. BMI <25) were transformed into closed categories by assigning the lower limit of the normal BMI range (18.50 kg/m²) as the lowest end of the interval. Separate analyses were performed for non-adjusted and adjusted risk estimates.

Data were pooled using the random effects meta-analysis model and statistical significance for heterogeneity between studies was assessed using Cochran's *Q* statistic. The inconsistency (*I*²) statistic was used to determine the proportion of true heterogeneity across studies. Values of 25, 50, and 75 % were considered indicators for low, moderate, and high true heterogeneity, respectively [18]. We performed sensitivity analyses by omitting a single study at a time to assess the influence of each study on the summary estimates. "Small-study effects", of which publication bias is a possible source, were investigated using funnel plots and Egger's regression asymmetry test [19]. Trim and fill analyses were used to examine the potential impact of studies missing due to publication bias on summary results [20].

A two-sided *p* value <0.05 was considered significant. Statistical analyses were performed using Excel (Version 12.3.5, Microsoft Corporation) and the 'meta' package [21] for R (Version 2.15.2, R Foundation for Statistical Computing, Vienna, Austria).

Results

Literature search and systematic review results

A flowchart of the search and study selection process is shown in Fig. 1. The electronic search identified a total of

128 citations (57 from PubMed and 71 from Embase). After screening titles and abstracts and removal of duplicates, 29 studies were retrieved for further full-text assessment. Five additional potentially relevant studies were identified from reference lists. Of the 34 articles that underwent full-text review, 12 [22–33] met eligibility criteria for inclusion in the meta-analysis and 22 were excluded. The most common reasons for exclusion of the 22 studies were: criteria for the diagnosis of SSI not reported and/or CDC/NNIS criteria not applied [34–47], non-scalar definitions of obesity used [47–49], risk estimates of the association between obesity/BMI and SSI not reported or raw data not provided to calculate risks [44, 47, 50–53], and analyses restricted to deep wound infections [54, 55].

Study characteristics

Characteristics of the studies are summarised in Table 1. A total of 12 studies were included involving 446 patients with spinal SSI. Eleven of the twelve studies were conducted in the USA and one conducted in Japan. All studies were based on retrospective data collection from patients' medical records. Five studies were rated as level of evidence grade II and seven were rated as grade III. The lumbar spine was the most commonly operated on spinal level (in 8 out of 10 studies that reported the spinal level under study), while the cervical, thoracic, and sacral spines were operated on in five studies. The most frequently performed surgical procedures were fusions and laminectomies.

Although all of the 12 studies applied the CDC/NNIS criteria for the diagnosis of SSI, different BMI cut-off levels were used. Moreover, ten studies reported unadjusted risk estimates, while six reported estimates adjusted for other confounders using multivariate analyses. Diabetes was the most common variable controlled for in four out of the six studies. Eleven studies reported risk measures in the form of OR, whereas one [24] used the Cox proportional hazards regression model to estimate risk. We pooled the two types of metrics together because they approximate one another in outcomes with rates <10 % and for risks smaller than 2.0 [56].

Meta-analysis of increased BMI and the risk of spinal SSI

Data from ten studies were combined to calculate the unadjusted crude summary estimate of the association between BMI and risk of spinal SSI. The forest plot in Fig. 2 shows the transformed study-specific estimates and the results of the random effects meta-analysis. The summary OR was 1.13 (95 % CI 1.07–1.19, *p* < 0.0001), indicating that a 5-unit increase in BMI was associated

Fig. 1 Flow chart of search strategy and study selection

with 13 % increase in the risk of SSI. Moderate heterogeneity was noted between the ten studies ($I^2 = 56.1\%$, p for Q test = 0.015).

An adjusted summary estimate was calculated from six studies. The forest plot in Fig. 3 shows the transformed study-specific estimates and the results from random effects meta-analysis. A 5-unit increase in BMI was found to be associated with 21 % increase in the risk of SSI (adjusted OR: 1.21; 95 % CI 1.13–1.29, $p < 0.0001$). Heterogeneity between the six studies was not significant ($I^2 = 28.7\%$, p for Q test = 0.220).

Sensitivity analyses and publication bias

Influence analysis for the unadjusted estimate showed that the study by Koutsoumbelis et al. [26] was responsible for almost all heterogeneity detected between the ten studies. Elimination of this study resulted in zero heterogeneity across the remaining studies ($I^2 = 0.0\%$, p for Q test < 0.0001) but did not significantly influence the magnitude of the summary estimate. For the adjusted summary effect, influence analysis showed that no single study had a major effect on heterogeneity or on the summary estimate.

Table 1 Characteristics of individual studies

Study	Country	Study design	LOE ^a	Type of surgery	Spinal levels	No. of SSI cases	Mean age (years)	% Females	BMI (kg/m ²) category	Variables controlled for
Apisarnthanarak et al. [22]	USA	Retrospective CCS	III	Laminectomies and/or spinal fusions	NR	13	64 ^b	54	>27.8 for males and >27.3 for females	NA
Boston et al. [23]	USA	Retrospective CCS	III	Fusions, laminectomies, and other non-infection procedures	NR	55	44 ^b	62	≥30	NA
Chen et al. [24]	USA	Retrospective review	II	Elective posterior instrumented lumbar arthrodeses	L	27	NR	NR	>35	NA
Friedman et al. [25]	USA	Retrospective CCS	III	Laminectomies	C, T, L, S	41	53	41	>35 ^d	Nonwhite race, diabetes, and noncervical laminectomy
Koutsoumbelis et al. [26]	USA	Retrospective CCS	III	Posterior lumbar or lumbosacral instrumented arthrodesis	L, S	84	61	65.6	≥30	Female sex, diabetes, COPD, osteoporosis, CHD, blood loss (>500 ml), dural tear, and total of ≥10 people in operating room
Mehta et al. [27]	USA	Retrospective review	II	Instrumented posterolateral lumbar fusions	L	24	56	42	≥30 ^d	NA
Mehta et al. [28]	USA	Retrospective review	II	Posterior cervical spinal fusions with the use of instrumentations	C	22	61	36	≥30 ^d	NA
Olsen et al. [29]	USA	Retrospective CCS	III	Laminectomies and/or fusions by neurosurgeons	C, T, L, S	41	54.3	51.2	>35 ^d	Postoperative incontinence, posterior approach, tumour resection
Olsen et al. [30]	USA	Retrospective CCS	III	Laminectomies, and/or arthrodeses by orthopaedic surgeons	C, T, L, S	46	52.4 ^c	52.4 ^c	>30 ^d	Diabetes, elevated serum glucose level, suboptimal timing of prophylactic antibiotics, cervical level surgery, and ≥2 resident surgeons in operating room
Sciubba et al. [31]	USA	Retrospective review	II	Sacral tumour resections with or without instrumentations	S	18	45.6 ^c	56.5 ^c	≥30	NA
Schwarzkopf et al. [32]	USA	Retrospective CCS	III	Laminectomies, spinal fusions, decompressions, and discectomies	T, L	61	56	46	BMI used as a continuous variable	Blood transfusions
Watanabe et al. [33]	Japan	Retrospective review	II	Arthrodeses, fusions, decompressions, and tumour resections	C, T, L	14	49	35.7	>25	Male sex, age >60 years, smoking history, diabetes, trauma, instrumentation, duration of operation >3 h, blood loss >300 g, and saline irrigation

BMI/ body mass index, CCS case–control study, NR not reported, OR odds ratio, C cervical, T thoracic, L lumbar, S sacral, LOE levels of evidence, NA not applicable, SD standard deviation

^a Levels of evidence based on Wright et al. [16]

^b Median age

^c Values are for all patients (cases and controls)

^d Results also reported for other categories

Fig. 2 Forest plot of study-specific and combined summary unadjusted OR for every 5-unit increase in BMI from ten studies using the random effects model **Fig. 3** Forest plot of study-specific and combined summary adjusted OR for every 5-unit increase in BMI from six studies using the random effects model

The funnel plots are shown in Fig. 4. Egger's regression test for funnel plot asymmetry was not statistically significant for either the unadjusted ($p = 0.82$) or adjusted ($p = 0.57$) estimates. The test, however, has low power when the number of studies included in the meta-analysis is <10 [57]. Trim and Fill analyses showed that two studies might be missing in the case of the unadjusted risk estimate, while one study might be missing in the case of the adjusted estimate. Adjustment for missing studies did not meaningfully affect the magnitude or strength of evidence for both the re-estimated unadjusted (OR: 1.15; 95 % CI 1.09–1.20) and adjusted (OR: 1.20; 95 % CI 1.12–1.28) risks.

Discussion

Results on the association between BMI-defined obesity and risk of spinal SSI have been inconsistent. Variations were noted among studies in relation to SSI diagnosis criteria and obesity definitions. It has been suggested that

differences in BMI groupings could partly explain the mixed findings reported in the literature [58]. Moreover, some evidence suggests that categorising BMI could lead to biased results and influence the internal validity of epidemiologic studies [58]. Therefore, in this meta-analysis we transformed category-specific effects into estimates on a continuous BMI scale to establish the risk of SSI associated with every 5-unit increase in BMI. We pooled results from individual studies by restricting analyses to data based on the CDC/NNIS criteria for diagnosing SSI in the adult population. Our results demonstrate a positive relationship between BMI and risk of SSI after spine surgery, with an increase in risk found for both the unadjusted and adjusted pooled estimates. The unadjusted results showed a 13 % increase in SSI risk, while adjustment for confounders showed a 21 % increase in risk for every 5-unit increase in BMI. Diabetes was controlled for in four out of the six studies that have performed multivariate analyses. Although patients with high BMI are at increased risk for diabetes, the persistence of the association between BMI and SSI after adjusting for diabetes indicates that high

Fig. 4 Funnel plots of studies included in the meta-analysis **a** unadjusted odds ratio (OR) and **b** adjusted OR

BMI is a risk factor for SSI independent of the influence of diabetes. The adjusted results mean that, for example, individuals with BMI of 30 kg/m² would have 21 % higher risk of spinal SSI than those with BMI of 25 kg/m². We point out that due to the log-linear model assumed between SSI risk and BMI, a 10-unit increase in BMI would increase the risk of spinal of SSI by 46 % and not by 42 % as would be expected in a linear relationship.

The exact biological mechanisms that link increased BMI with SSI remain to be fully elucidated. Obese patients have thicker layers of subcutaneous fat, which require higher retraction forces and raise the risk of dead space formation upon closure of the wound [41]. These factors could lead to increased tissue necrosis and poor vascular perfusion that impede bacterial oxidative killing by neutrophils and result in wound infection [25]. In addition, adipose tissue is a source of pro-inflammatory cytokines known to cause insulin resistance and increase the risk of infection [59]. However, evidence suggests that increased body mass does not always equate to increased body fat, and varying degrees of correlation between BMI and body fat

have been reported in the literature. In a large multi-ethnic US study, Romero-Corral et al. [60] found that BMI had a higher correlation with lean mass than with % BF in males and a higher correlation with % BF than with lean mass in females. A BMI cut-off of ≥ 30 kg/m² for obesity has good specificity but low sensitivity to detect adiposity [60, 61]. Other cut-off values for obesity result in a trade-off between sensitivity and specificity [60]. Waisbren et al. [12], found a quadratic non-linear relationship between BMI and % BF, while Mehta et al. [27] found no significant correlation between BMI and the thickness of subcutaneous fat measured at the level of L4 in adult patients undergoing lumbar surgery. Thickness of subcutaneous fat and % BF were shown to be significant risk factors for SSI while BMI was not [12, 27, 28]. Therefore, measures of fatness other than BMI may serve as better predictors of SSI. However, assessment of risk of SSI based on these measures of fatness is limited by practical considerations, and BMI remains the simplest and most commonly used indicator for obesity.

As the criteria used to define overweight and obesity in children are different from those used for adults, we

emphasise that results from this meta-analysis do not apply to the paediatric population. In addition, the study has some limitations. Results were based on an assumption of a log-linear model between risk of SSI and increased BMI. Several studies have demonstrated a U-shaped relationship between BMI and risk of mortality, with increased mortality rates at low and high BMI ranges [62]. This has been ascribed to the limited ability of BMI to distinguish between lean mass and body fat at the intermediate BMI ranges [60]. We could not assess the possibility of threshold, U- or J-shaped effects across BMI ranges due to lack of sufficient data from individual studies [63]. Moreover, we could not perform separate analyses by gender. If BMI has a stronger correlation with lean mass in males and a stronger correlation with % BF in females as some research suggests [60], then the risk estimates for the association between BMI and SSI would be expected to be higher in females than in males.

Our meta-analysis of retrospective observational studies included five level II and seven level III studies. Thus, the meta-analysis is prone to the influence of confounding and biases that are inherent to the individual studies [64, 65]. To address the possible effects of confounding, we performed analyses for both unadjusted and adjusted effects. However, we could not rule out that other confounding factors that were not measured might have biased the results. Residual confounding in individual studies remains an important source of bias in meta-analyses of observational studies [64]. Furthermore, moderate significant heterogeneity was observed between studies of the unadjusted risk estimate. Influence analysis showed that this heterogeneity was mostly due to the high OR reported by Koutsoumbelis et al. [26]. However, after adjusting for confounders, the study's results approximated those from other studies. Thus, when the adjusted risks were pooled, heterogeneity across studies was reduced and was not significant.

Publication bias, the selective publication of studies with positive outcomes, could undermine the validity of meta-analysis [65]. Our meta-analysis was restricted to studies that have been published in English. There is evidence that positive results are more likely to be published in English [66]. Thus, our summary risk estimates might have been over-estimated. Although Egger's test analyses showed no evidence for funnel plot asymmetry, we were unable to reliably assess the presence of publication bias due to the small number of studies included. Based on the trim and fill method, the impact of potentially missing studies on the estimated risks was negligible.

Although with some limitations, our findings have both clinical and epidemiological significance. Obesity is a growing public health problem with evidence of a shift in population trends towards higher BMI. The number of patients with elevated BMI undergoing spine procedures,

therefore, is rising [67]. Patients with higher BMI have been found to have lower serum and tissue concentrations of prophylactic antibiotics and, thus, inadequate protection against SSI [68]. Evidence-based guidelines evaluating the prophylactic use of antibiotics in spine surgery published by the North American Spine Society [6] concluded that obese patients have a higher risk for SSI than non-obese patients when the standard doses of prophylactic antibiotic are given. Nevertheless, no sufficient evidence was found in the literature to recommend modifications in antibiotic prophylaxis for patients with high BMI. These findings emphasise the importance of incorporating BMI into risk stratification models that would allow for recommendations to be made in relation to proper pre-operative weight management and modifications in antibiotic protocols. The current NNIS risk index, a risk scoring system developed to predict risk of postoperative SSI, is based on three indicators: the American Society of Anaesthesiologists (ASA) score, wound type, and duration of surgery [69]. The index does not contain many underlying patient factors such as increased BMI, and alternative scoring models have been found to achieve better predictive performance [70]. Our study identifies increased BMI on a continuous scale as an independent risk factor for spinal SSI and demonstrates that categorisation of BMI can greatly influence study results. Future studies based on prospective data collection are needed to confirm the association between increased BMI and spinal SSI and to determine if other measures of fat distribution are more sensitive indicators of risk of SSI.

Conflict of interest None.

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