Predisposing factors for surgical site infection of spinal instrumentation surgery for diabetes patients

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Abstract

Purpose Diabetes mellitus (DM) is known as an important risk factor for surgical site infection (SSI) in spine surgery. It is still unclear however which DM-related parameters have stronger influence on SSI. The purpose of this study is to determine predisposing factors for SSI following spinal instrumentation surgery for patients with DM.

Methods 110 DM patients (66 males and 44 females) who underwent spinal instrumentation surgery in one institute were enrolled in this study. For each patient, various preoperative or intraoperative parameters were reviewed from medical records. Patients were divided into two groups (SSI or non-SSI) based on the postoperative course. Each parameter between these two groups was compared. Univariate and multivariate analyses were performed to determine predisposing factor for SSI.

Results The SSI group consisted of 11 patients (10 %), and the non-SSI group of 99 patients (90 %). Univariate analysis revealed that preoperative proteinuria ($p = 0.01$), operation time ($p = 0.04$) and estimated blood loss ($p = 0.02$) were significantly higher in the SSI group compared to the non-SSI group. Multivariate logistic regression identified preoperative proteinuria as a statistically significant predictor of SSI (OR 6.28, 95 % CI 1.58–25.0, $p = 0.009$).

Conclusions Proteinuria is a significant predisposing factor for SSI in spinal instrumentation surgery for DM patients. DM patients with proteinuria who are likely to suffer latent nephropathy have a potential risk for SSI. For them less invasive surgery is recommended for spinal instrumentation. In this retrospective study, there was no significant difference of preoperative condition in glycemic control between the two groups.

Keywords Spinal instrumentation surgery · Surgical site infection · Diabetes mellitus · Proteinuria · Microvascular disease · Diabetic nephropathy

Introduction

Surgical site infection (SSI) is one of the most disastrous complications of spinal surgery, especially of instrumentation procedure. Diabetes mellitus (DM) has been recognized as one significant risk factor for SSI in spinal surgery [1, 2]. When spinal instrumentation surgery is indicated for a DM patient, usually the surgeon pays attention to the history and the severity of DM to prevent various perioperative complications including SSI. However it is still unclear which DM-related parameters (i.e. treatment history, glycemic control condition, complications derived from hyperglycemia) have stronger influence on SSI. In patients with severe DM (i.e. HbA1c > 7.0 % or insulin dependence), perioperative glycemic control is recommended [3–5], however, few reports so far clarify the optimal target of perioperative glycemic control to prevent SSI [6]. The objective of this study is to review DM patients underwent spinal instrumentation surgery and to identify the predisposing factors for SSI.

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Materials and methods

From August 2003 to May 2011, a total of 676 spinal instrumentation surgeries were performed in a single hospital facility (K. K. H.). All patients had received HbA1c checks in preoperative screening, and those who had HbA1c > 6.5 % or had a history of DM diagnosis were all enrolled in this study. HbA1c measurement in this paper is described in Japan Diabetes Society (JDS) level, which is nearly equal to National Glycohemoglobin Standardization Program (NGSP) level-0.4 (%) [7]. A total 110 cases (16.4 %) with DM (66 males and 44 females) were extracted.

Postoperative SSI was determined according to the Centers for Disease Control and Prevention (CDC) definition [8]. DM patients were divided into SSI and non-SSI groups according to this definition. For comparison, SSI incidence was also investigated in non-DM patients ($n = 566$) who underwent spinal instrumentation surgery in the same period.

Surgical antimicrobial prophylaxis (AMP) was used as follows; Cephalosporin antibiotic (cefazolin or cefmetazole) was infused 30 min before skin incision and re-infused every 3 h during the procedure in all cases. Postoperative AMP course was not standardized and depended on each surgeon's decision. However, there was no significant difference in postoperative AMP period between DM and non-DM patients (4.67 vs. 4.71 days, $p = 0.88$, unpaired t test).

For each DM patient, the following preoperative or intraoperative parameters were reviewed from the clinical chart; patient's background, age at surgery, body mass index (BMI), American Society of Anesthesiologist (ASA) class, smoking history. Glycosuria and proteinuria, serum creatinine and blood urea nitrogen (BUN) were investigated. Glycosuria and proteinuria were graded qualitatively and <1+ were diagnosed as positive. As for glycemic control, consultation with diabetologist, preoperative hospitalization days for glycemic control, insulin dependence, late HbA1c, and serum glucose level the morning before the surgery were investigated. As for surgical parameters, operation time (OT) and estimated blood loss (EBL) were investigated.

Statistical analyses

SSI incidence was compared between DM patients and non-DM patients using Fisher exact test. Each parameter of DM patients was compared between SSI and non-SSI groups using univariate analyses. Mann–Whitney U test was used for continuous variables between two groups and Chi square test was used for dichotomous and categorical variables. A $p < 0.05$ was accepted as significant.

Multivariate logistic regression was then performed to determine predictor for SSI. All univariate variables that were significantly different between the two groups were entered into a forward stepwise multiple logistic regression analysis. All analyses were performed using IBM SPSS Statistics version 19 (IBM; Armonk, New York, USA).

Results

Overall 11 patients (10 %) had a postoperative SSI in the DM patients; 7 (6.36 %) deep and 4 (3.64 %) superficial incisional. SSI cases in the non-DM patients who underwent spinal instrumentation were 6 (1.06 %). SSI incidence in DM patients was significantly higher compared to non-DM patients ($p = 0.000$). In DM patients, univariate analyses revealed that preoperative proteinuria ($p = 0.01$), OT ($p = 0.04$) and EBL ($p = 0.02$) were significantly higher in the SSI group compared to the non-SSI group (Table 1). There was no significant difference between the two groups in terms of other patient background factors (age, BMI, ASA, smoking, serum creatinine, and BUN) and glycemic control condition (late HbA1c, serum glucose, consultation rate to diabetologist, and preoperative hospitalization days). Proteinuria, OT, and EBL were thus entered into a logistic regression analysis. This analysis identified proteinuria as a significant predictor for SSI (OR 6.28, 95 % Confidence Intervals 1.58–25.0, $p = 0.009$) (Table 2).

Discussion

DM has been reported as an independent risk factor of postoperative infection in numerous spine surgeries [1, 2]. This is thought to be due to DM patient's immunocompromised state, reduced wound healing potential, and poor microvascularization [9].

Immunocompromised state is a sustained decrease in polymorphonuclear leukocyte function caused by continuous hyperglycemia [10]. These include abnormalities in granulocyte adherence [11], impaired phagocytosis [12], delayed chemotaxis [13], and depressed bactericidal capacity [12]. Furthermore, dysfunction of opsonization and immunoglobulin are reported to be induced by hyperglycemia [14].

As for wound healing, Hennessey reported that hyperglycemic state is associated with increased collagenase activity and decreased wound collagen content [14]. Goodson et al. [15] showed that hyperglycemia interferes with collagen synthesis and thus impairs wound healing.

DM is associated with the development of accelerated and premature atherosclerosis in blood vessels. Immune

Table 1 Univariate analyses between surgical site infection (SSI) and non-SSI groups

	SSI (<i>n</i> = 11)	Non-SSI (<i>n</i> = 99)	<i>p</i> value
Age at surgery (years)	66.2 ± 2.2	66.9 ± 1.0	0.51
BMI (kg/m ²)	24.3 ± 1.1	24.6 ± 0.4	0.58
ASA class 2	4 (36.4 %)	53 (53.5 %)	
ASA class 3	7 (63.6 %)	46 (46.5 %)	0.35
Smoking history (positive)	4 (36.4 %)	28 (28.6 %)	0.59
Glycosuria (<1+)	4 (36.4 %)	43 (43.4 %)	0.75
Proteinuria (<1+)	6 (54.5 %)	17 (17.2 %)	0.01
Diabetologist consultation history	10 (90.9 %)	83 (83.8 %)	0.68
Preop. hospitalization days	12.2 ± 3.8	7.2 ± 1.0	0.68
Insulin dependence	4 (36.4 %)	7 (7.1 %)	0.24
HbA1c (%)	6.88 ± 0.3	6.80 ± 0.1	0.72
Serum glucose (mg/dl)	128.4 ± 9.3	123.3 ± 3.6	0.63
Serum creatinine (mg/dl)	1.73 ± 0.75	0.99 ± 0.13	0.18
Serum BUN (mg/dl)	24.9 ± 4.6	19.2 ± 1.0	0.2
Operation time (min)	271.5 ± 23.3	225.9 ± 9.4	0.04
Estimated blood loss (ml)	909.0 ± 118.1	654.9 ± 60.6	0.02

BMI body mass index, *ASA class* American Society of Anesthesiologist class, *BUN* blood urea nitrogen

Table 2 Multivariate logistic regression analysis to determine predictor for SSI

	Odds Ratio	95 % confidence intervals	<i>p</i> value
Proteinuria (positive)	6.28	1.58–25.0	0.009
Operation time (min)	1.002	0.993–1.010	0.46
Estimated blood loss (ml)	1	0.999–1.002	0.66

mechanisms, altered macrophage function and the effects of advanced glycation end products (AGEs) lead to enhanced endothelial injury and microvascular disease [16]. These vascular changes cause thickness of vascular walls and reduced perfusion [16]. This poor microcirculation leads to tissue hypoxia as well as obstruction of antibiotics delivery, thus facilitating microorganism growth in surgical sites.

In this study, DM patients with proteinuria had a significantly higher incidence of SSI. Usually proteinuria or albuminuria of DM patients suggests the presence of nephropathy and it precedes the deterioration of creatinine clearance. Diabetic nephropathy or retinopathy is derived from general microvascular disease following continuous hyperglycemic state. Thus proteinuria is closely related to vascular disease in DM patients.

This relationship has been reported in various papers. Epidemiological studies have shown that microalbuminuria is an independent risk factor for arteriosclerosis [17]. A cross-sectional association possibly exists between increased urinary albumin excretion and the presence of sub-clinical atherosclerosis [18]. Microalbuminuria is

related to endothelial dysfunction and increased oxidative stress [19].

HbA1c and serum glucose are good indicators of glycemic control condition in daily or monthly terms. However they cannot reveal directly the existence of micro- or macrovascular disease caused by hyperglycemia state over the long term. On the other hand, proteinuria of DM patients could be a good indicator of vascular compromise according to the mechanisms described above.

Proteinuria is easily detectable by simple urinary examination. Diabetic nephropathy in mild or moderate stage demonstrated only microalbuminuria or proteinuria without renal dysfunction. Thus urinary examination could be a useful tool to expose the diabetic vascular compromise in preoperative screening. We could pay special attention to the DM patients with proteinuria in terms of potential SSI risk.

If we could detect DM patients with high SSI risk by some background factor preoperatively, it might be possible to decrease incidence of SSI by changing treatment strategy.

As for surgical parameters, OT and EBL are both significantly higher in the SSI group. This result is similar to other reports [2, 9] and shows that invasive procedure is related closely to SSI. Less invasive surgery is appropriate especially for DM patients with proteinuria. If spinal instrumentation is indicated in such a case, care should be taken to reduce OT as well as EBL.

Generally perioperative glycemic control for DM patients is thought to be an important procedure to prevent various complications including SSI. Tight glycemic

control has been reported to reduce infection rates following various surgeries [3–5]. On the other hand, recent meta-analyses [20] and multicenter studies [21] concluded that intensive insulin therapy significantly increased the risk of hypoglycemia and conferred no overall mortality benefit among critically ill patients. The association between perioperative blood glucose range and the incidence of postoperative infection remains unclear in the majority of surgical patients due to lack of evidence [6].

Leukocyte deficiencies and wound healing impairment appear to be reversible and to improve with tight glycemic control [12, 13, 22]. On the other hand, severe vascular compromise developed from endothelial dysfunction caused by long term hyperglycemia is not reversible even following glycemic control [18, 23]. Exogenous hyperinsulinemia was reported to activate NAD(P)H in rat aortic endothelium [24].

Some studies suggested that hyperinsulinemia causes endothelial dysfunction and the development of atherosclerosis in DM patients [18, 25].

In this study, the glycemic control situation (diabetologist consultation history and preoperative hospitalization for glycemic control) is similar in both groups and no significant difference was observed in terms of HbA1c and serum glucose level preoperatively. In other words, the SSI group had achieved glycemic control as good as the non-SSI group. Although glycemic control might work on SSI reduction, we cannot yet conclude that the present glycemic control was the “silver bullet” for SSI prevention.

This study has some limitations. The sample size was relatively small and SSI cases were especially scarce. Blood and urinary examinations were performed only once preoperatively, and timing of sampling was not standardized. Thus the reproducibility of each parameter was unclear. The protocols of perioperative glycemic control were not established in this series. The target of glycemic control and monitoring frequency of serum glucose were completely dependent on each diabetologist’s own experiences. Furthermore there had been no systemic protocol for SSI prevention throughout study term and other factors which are not related to DM could influence SSI incidence.

SSI incidence in this DM series was however significantly high (10 %) compared to non-DM patients (1.06 %). Although the causes of SSI are thought to be multifactorial [1, 2], some DM-related parameters probably contribute strongly to SSI.

This is the first study which indicates the relationship between DM background and SSI risk in spinal instrumentation surgery. Proteinuria suggesting diabetic nephropathy is a significant predisposing factor for SSI. Less invasive surgery is recommended for spinal instrumentation for DM patients with proteinuria.

Conflict of interest None.

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