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Clinical Implication of Diabetes Mellitus in Primary Total Hip Arthroplasty

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Purpose: The purpose of this study was to investigate the effect of diabetes mellitus on primary total hip arthroplasty by comparing the clinical outcomes of patients diagnosed to have diabetes mellitus before the operation with those without diabetes.
Materials and Methods: A total 413 patients who underwent unilateral cementless total hip arthroplasty from June 2006 to May 2009 were recruited and divided into diabetic and non-diabetic groups. The comparative analysis between the two groups was made. We evaluated Harris hip score, postoperative complications such as wound problem, surgical site infection, other medical complication and length of stay in hospital as clinical parameters. Radiographic evaluations were also included to determine loosening, dislocation and osteolysis.
Results: Patients with diabetes had an increased incidence of orthopaedic complications including surgical site infection and mortality, but other medical complications were not increased in diabetic patients. All complications after primary total hip arthroplasty were associated with diabetes mellitus, but the degree of diabetes was not associated with complications.
Conclusion: Diabetes mellitus increases incidence of orthopaedic complications, particularly deep infection, after cementless primary total hip arthroplasty.

Key Words: Diabetes mellitus, Total hip arthroplasty, Infection, Complications

INTRODUCTION

World Health Organization reports that the number of patients who were diagnosed with diabetes mellitus had increased to 366 million in 2011 from 151 million in 2000. This number is expected to increase another 50.7% by 2030, which would be 552 million patients. In the Unites States, the prevalence of diabetes mellitus is estimated to be 10.9%[1]. Likewise, in South Korea, it has been continuously increasing with the prevalence of 6.4% in 2003 that is expected to be increased to 10.9% in 2030[2].

The importance of hyperglycemia measurement at admission cannot be stressed enough. Hyperglycemia is a known risk factor for mortality of surgical emergencies such as stroke, acute coronary syndrome, heart failure, pneumonia and trauma[3]. Furthermore, it negatively affects clinical outcomes of total hip arthroplasty, especially in terms of postoperative infection[3-9]. However, recent clinical developments in control and treatment of diabetes mellitus makes

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arthroplasty safe. This is why many surgeons and health care providers do not correctly weight the importance of diabetes mellitus before primary total hip arthroplasty. As an example, according to the guidelines for adequate reimbursement of Health Insurance Review and Assessment Service, there are no cautions or exceptions related to diabetes mellitus in determining the use of prophylactic antibiotics for the primary total hip arthroplasty[10](Table 1).

In the present study, we aimed to investigate the effects of diabetes mellitus on clinical outcomes of primary total hip arthroplasty by comparing these outcomes in patients with diabetes mellitus with those without diabetes.

MATERIALS AND METHODS

This was a retrospective case-control study. Among 616 cases of unilateral primary total hip arthroplasty which were performed at our institute from June 2006 to May 2009, 203 cases of resurfacing hip arthroplasty that were selectively performed on young and healthy patients were excluded. The remaining 413 cases of cementless primary total hip arthroplasty were included in this analysis. These patients were divided into the diabetic and non-diabetic groups. Patients were considered to have diabetes mellitus if they met at least one of these criteria: 1) Currently taking oral hypoglycemic agents and/or insulin after the diagnosis of diabetes mellitus. 2) Having blood glucose levels higher than 126 mg/dL after >8 hours fasting. 3) Showing blood glucose levels higher than 200 mg/dL after 2 hours of glucose ingestion (75 g) in oral glucose tolerance test. 4) Having glycated hemoglobin (HbA1c) levels of more than 6.5% and 5) carrying diabetic symptoms (e.g., excessive water drinking, hyperuresis, and weight loss) and a high glucose level (>200 mg/dL) in a random test. The degree of obesity was assessed by body mass index (BMI, kg/m^2) in which 25 or less was defined as normal and BMI>25 was classified as either overweight or obese.

Surgeries were performed by three surgeons using three types of cementless implants. In all cases, posterolateral approach was used in an operating room equipped with a combined laminar flow. Strict control of the traffic was maintained during the surgery, so that the number of un-scrubbed personnel would not exceed five. All participants in an operation were asked to wear body-exhaust suits. Unless otherwise specified, a first generation cephalosporin was administered to patients 30 minutes prior to make a skin incision. The drug was re-administered every two hours while the operation lasted. Patients were treated with prophylactic antibiotics for up to two days after the surgery. In patients with diabetes mellitus, maintenance solution was provided before and after the surgery in order to control the blood glucose level as suggested by an endocrinologist. Regardless of the status of diabetes mellitus, compression stockings were provided for all patients in order to prevent venous thromboembolism. Unless there was a known contraindication, all patients above the age of 45 years were treated with low molecular weight heparin, starting 12 hours after the surgery. Regardless of the groups, patients were allowed to walk with clutches after 2-3 days postoperatively.

Clinical data was reviewed for all patients in medical records. Excluding four patients who had died in follow-ups, all patients were followed for at least two years. Age, gender, height, weight, body mass index, operative diagnosis, diagnostic status for diabetes mellitus, HbA1c,

Table 1. Exceptional Rules for Prophylactic Antibiotics Use

Total days of prophylactic antibiotics (inpatient + discharge medication)
Exceptional criteria
- Emergency operation, infection before surgery, simultaneous operation, postoperative fever (3 days after surgery), massive transfusion, mechanical ventilation, postoperative infection, missed prophylactic antibiotics
- First operation of two-stage bilateral athroplasty, second operation of two-stage bilateral total hip arthroplasty
- No records on end time of surgery/end day of antibiotics
Prescription rate of antibiotics in discharge medication
Exceptional criteria
- Emergency operation, infection before surgery, simultaneous operation, postoperative fever (3 days after surgery), massive transfusion, mechanical ventilation, postoperative infection
- First operation of two-stage bilateral athroplasty, second operation of two-stage bilateral total hip arthroplasty

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waiting days for operation after hospitalization, days in hospital, postoperative drainage and amount of blood transfusion were recorded and used as variables in statistical analysis. As for the results of operation, Harris hip score before and after the operation, all orthopedic complications including wound problem, surgical site infection, loosening, osteolysis, dislocation, reoperation and medical complications were assessed. Patients were examined at six weeks, three months, six months, and a year after the surgery. Afterwards, they were examined annually. In order to investigate the association between diagnosis of diabetes mellitus and clinical outcomes, all available clinical records were analyzed. For statistical analyses, Fisher's exact probability test and Studen's t-test were used. If multiple variables had shown statistically significant association in univariate analyses, multivariate analysis was performed using binary logistic regression analysis. All statistical analyses were done with IBM SPSS Statistics software (version 22.0; IBM Co., Armonk, NY, USA) and *P*-values less than 0.05 were considered as statistically significant.

RESULTS

1. Clinical Outcomes

Of 413 patients, 41 patients (10%) were in the diabetes mellitus group and 372 patients (90%) were in the non-diabetes mellitus group. Twenty five (61%) and 16 (39%) patients were male and female, respectively, in the diabetes mellitus group. The average age of patients was 56 years (35-84 years) and the average follow-up period was 26 months. The average BMI was 24.5. There was no statistically significant difference in age, gender, follow-up period and the degree of obesity between the two groups (Table 2). The average level of HbA1c was found to be 7.26% (6.5-10.5%) in the diabetes mellitus group. The Harris hip scores for diabetes mellitus group and non-diabetes mellitus group before the operations were 63 and 65 (P=0.295), respectively, and by the final follow-up, it was found to be 92 and 94 (P=0.3), respectively, which was not significantly different.

2. Complications

Over the follow-up period, one patient (4.1%) in diabetes mellitus group and three patients (0.8%) in non-diabetes mellitus group had died. The mortality was significantly higher in diabetes mellitus group (Table 3, P=0.04). The patient who died after 47 months of surgery from the diabetes mellitus group was deceased because of multiple operations for the periprosthetic fractures. One patient from the non-diabetes mellitus group died a week after the surgery because of pulmonary thromboembolism. The other two patients died due to unrelated reasons after 18 and 19 months postoperatively.

Eight (1.9%) orthopedic complications were found. Five cases with complications were in the diabetes mellitus group and three cases (0.80%) were in non-diabetes mellitus group, creating a significantly higher number of complications in the diabetes mellitus group (Table 3, P=0.00). Complications of our study were surgical site infection (4 cases; all in diabetes mellitus group), dislocation (3 cases; 1 case in the diabetes mellitus group and 2 cases in the non-diabetes mellitus group) and periprosthetic femoral fracture (1 case; in

Table 2. Demographic Data

Chracteristics	Group		*P*-values
	DM	Non-DM	
Number of patients	41	372	
Gender			0.74
Male	25 (61)	216 (58)	
Female	16 (39)	156 (42)	
Age (year)	56 (35-84)	51 (16-95)	0.06
Follow up (month)	26	34	0.10
BMI (kg/m^2)	24.5	23.61	0.37
HbA1c (%)	7.26 (6.5-10.5)		

Values are presented as number (%), mean (range), or number only.
DM: diabetes mellitus, BMI: body mass index.

diabetes mellitus group). To find the association with surgical site infection, we performed univariate analyses using all formerly described variables and found that the diagnosis of diabetes mellitus was the only variable that significantly associated with surgical site infection (*P*=0.00). In the diabetes mellitus group, no significant correlations was found between the level of HbA1c and surgical site infection (*P*=0.43), and all orthopedic complications (*P*=0.59). Although other medical complications seemed to be more prevalent in diabetes mellitus group, it did not reach a statistically significant level (Table 3, all *P*>0.05). In the univariate analysis of orthopedic complications, four variables (i.e., age, diabetes mellitus, waiting days for operation after hospitalization and total days in hospital) were found to be have a statistically significant association (Table 4). In the multivariate analysis, diagnosis of diabetes mellitus (*P*=0.001; odds ratio [OR], 15.13; 95% confidence interval [CI], 3.11-73.67) and total days in hospital (*P*=0.005; OR, 1.04; 95% CI, 1.01-1.07) were found to be significantly associated with the development of orthopedic complications (Table 5).

DISCUSSION

Numerous factors are reported to be responsible for complications after the total hip arthroplasty. Of known complications, surgical site infection is associated with the underlying diseases such as diabetes mellitus, inflammatory diseases, decreased immunity, hemophilia[3] and high BMI[5,8,11,12]. On the other hand, other earlier studies have shown that young age[5], retaining a suction drain for more than 48 hours[13], previous history of infection and previous history of surgeries increase the risk of postoperative infection[5]. In a number of publications, it is demonstrated that complications of total hip arthroplasty are increased in patients with diabetes mellitus[3-9]. Similarly, we found a significant

Table 3. Complications and Mortality

Complication	Group		*P*-value
	DM	Non-DM	
Death	1 (4.1)	3 (0.8)	0.04
Orthopedic complications			
Surgical site infection	4 (9.8)	-	0.00
Dislocation	1 (4.1)	2 (0.5)	0.17
Osteolysis	-	1 (0.3)	
Periprosthetic fracture	1 (4.1)	-	
Other medical complications	1 (4.1)	1 (0.3)	0.06

Values are presented as number (%),
DM: diabetes mellitus

Table 4. Relationship between the Occurrence of Orthopedic Complications and Variables*

Variable	*P*-value
Age	0.02
Gender	0.15
Body weight	0.14
Height	0.07
BMI	0.14
Delay prior to surgery	0.03
Days of admission	0.01
Amount of transfusion	0.16
Hemovac-drainage	0.08
Presence of DM	0.00
Diagnosis	0.88

* Results of univariate analysis.
BMI: body mass index, DM: diabetes mellitus.

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increase of orthopedic complications in the diabetes mellitus group. Marchant et al.[14] investigated the association between the degree of diabetes mellitus and complications. They showed that uncontrolled diabetes mellitus is associated with more than three folds increase in risk of stroke, two folds increase in risk of surgical site infections and three folds increase in risk of mortality. In addition, incidence of urinary tract infection, intestinal obstruction, postoperative bleeding, and transfusion were also increased.

With HbA1c level, which is the most commonly accepted parameter for the severity of diabetes, different studies have shown conflicting results in the association between complications and the degree of diabetes mellitus. Iorio et al.[4] reported comparable results with no association between blood HbA1c level and complications while Harris et al.[15] observed an increased risk of complication in total hip arthroplasty (n=6,088) with HbA1c level above 7%. Similarly, Stryker et al.[16] demonstrated that patients with HbA1c levels above 6.7% experience an increase in postoperative wound complications. The association between elevated levels of HbA1c and complications remains unclear. However, the relationship between the clinical result and serum glucose level, which is the more traditional parameter to determine the degree of diabetics, is relatively clear. Mraovic et al.[6] emphasized the significance of blood glucose level by demonstrating the increased risk of infection even in none diabetic patients who show the fasting blood glucose levels of above 140 mg/dL one day after operation.

The glycemic goal that is recommended by the American Diabetes Association is HbA1c below 7.0%, the average pre-meal blood glucose of 90-130 mg/dL and the average post-meal blood glucose of <180 mg/dL. Rizvi et al.[17] recommended postponing surgeries for several weeks to months in patients who had not reached this glycemic goal. They also recommended to maintain the glucose level between 140-180 mg/dL for severe patients who are about to have major surgeries. Another piece of recommendation for patients without severe diabetes is to keep the fasting glucose levels and random blood glucose levels under 140 mg/dL and 180 mg/dL, respectively.

The rate of surgical site infection after primary total hip arthroplasty is 1-2%. Multi-institutional and multi-national research studies found slightly higher rates (higher than 2%)[18,19]. In the present study, we found an infection rate of 0.95% in all patients, yet this number reaches 10% if the analysis is limited to the diabetes mellitus group that is a statistically significant difference. Bolognesi et al.[20] found no significant association between diabetes and surgical site infection in joint replacement surgery. These authors had only investigated the infection before discharge, which automatically excludes infections that develop over time. In another study with a larger number of patients (350 diabetic patients from 4,241 patients), Iorio et al.[4] showed that diabetes mellitus creates a four-fold increase in risk of infection after the joint replacement surgery. In particular, they found 11.4 folds higher risk of infection in patients who underwent primary total hip arthroplasty, which is very similar to our results. Malinzak et al.[5] investigated 6,108 patients and found a three-fold increase in risk of infection after joint replacement in the diabetic patients. In addition, Jämsen et al.[3] and Lai et al.[21] also reported 4.5-fold and 4-fold increase in risks of infection, respectively. Pedersen et al.[22] found that diabetic patients are more likely to have a reoperation.

In our study, diabetes mellitus was the only factor significantly associated with surgical sites infection; hence, multivariate analysis was not performed. However, when we analyzed the relationship between the clinical variables and complications (including infection), multiple variables were shown to be significantly associated. Diagnosis of diabetes mellitus and the days in hospital were significantly associated

Table 5. Relationship between the Occurrence of Orthopedic Complications and Variables*

Variables	*P*-value	OR (95% CI)
Age	0.92	1.00 (0.95-1.07)
Presence of DM	0.00	15.13 (3.11-73.67)
Delay prior to surgery	0.54	1.02 (0.96-1.09)
Days of admission	0.01	1.04 (1.01-1.07)

* Results of multivariate analysis using significant factors in univariate analysis.
OR: odds ratio, CI: confidence interval, DM: diabetes mellitus.

with complications in multivariate analysis.

Postoperative infection affects the patients, their families and the society. Therefore, continuous efforts are made to lower this risk; starting with the study of Sir John Charnley[23] followed by the use of ultra clean air[24], and recommendations on prophylactic antibiotics[25,26]. Likewise, we made every effort to reduce infection by following domestic and international recommendations; yet, our effort seemed not sufficient to the patients in diabetes mellitus group. Therefore, we believe that diabetes mellitus itself should be considered as high-risk for orthopedic complication, particularly infection, after total hip arthroplasty. Once found, clear and specifics measures should be taken to reduce complications regardless of the degree of diabetes mellitus.

Interestingly, we did not find any significant difference in other orthopedic complications such as dislocation and aseptic loosening between the two groups. This is in agreement with prior reports such as the study of Bolognesi et al.[20] and Pedersen et al.[22]. Although there was another medical complication found in both the diabetes mellitus and non-diabetes mellitus groups, no statistical significance was noted.

This study was done retrospectively and other medical and functional impairments were not investigated. Furthermore, statistical significance could be limited due to a small number of complications. Effects of surgeries on both sides, duration of diagnosis of diabetes mellitus and other accompanying diseases were not considered in our study. Lastly, other drugs (e.g., antithrombotics) which are used in these patients were not included in the analysis. However, the authors were able to confirm the effects of diabetes mellitus on complications after total hip arthroplasty, in particular, infection. Therefore, it is strongly recommended to provide enough explanations for patients and their caregivers about the risks of orthopaedic complications, especially surgical site infection in diabetic patients before total hip arthroplasty. In addition, all possible active measures (e.g., modulating types and duration of prophylactic antibiotics) as well as blood glucose control should be made prior to surgery.

CONCLUSION

We were able to confirm that preoperative diagnosis of diabetes mellitus significantly increased the risk of orthopedic complications after cementless primary total hip arthroplasty, in particular, surgical site infection. Therefore, it is recommended to examine the preoperative status of diabetes mellitus and to educate patients about complications, which includes surgical sites infection. In addition, we recommend considering the patients with diabetes mellitus as a high-risk group. All possible prophylactic treatments should be initiated in order to lower the rates of postoperative complications in this specific patient-group.

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