Factors Affecting Outcome after Total Knee Arthroplasty in Patients with Diabetes Mellitus

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Purpose: To compare the clinical outcome and complications following total knee arthroplasty (TKA) in diabetic and non-diabetic patients, and to identify diabetes-related risk factors for negative outcomes. **Materials and Methods:** 222 primary TKAs in patients with diabetes were evaluated using Knee Society scores and Hospital for Special Surgery score. Postoperative complications were reviewed retrospectively. The mean follow-up was 53.2 months. The effect of diabetes-related factors and comparison with a matched control group were analyzed statistically. **Results:** Significant improvements were noted in all the scores after TKA ($p < 0.05$). There was no statistical difference in clinical sores between the diabetic and non-diabetic patients. In multivariate analysis associating age, gender and body mass index with pain and knee score at the latest follow-up, the average knee scores in normal and overweight group were found to be significantly higher than those in the obese group. The diabetic patients had an increased overall incidence of postoperative complications (17.6%) compared with the control group (8.1%) ($p < 0.05$). Particularly, the rate of wound complications such as skin necrosis, bulla formation or erythema with drainage was higher in the diabetic group ($p < 0.05$). Diabetes-related factors did not influence the incidence of complications. Associated diseases were the only significant risk factors correlated with wound complications and meniscal bearing dislodgement. **Conclusion:** Patients with diabetes can benefit from TKA, even though diabetic patients are at an increased risk for overall postoperative and wound complications. Preoperative factors such as obesity and associated diseases may adversely affect the clinical outcome of TKA in diabetic patients.

Key Words: Diabetes mellitus, total knee arthroplasty, clinical outcome, complication, risk factor

INTRODUCTION

The prevalence of diabetes is rising as the elderly population increases. In Koreans, the age-adjusted prevalence of diabetes is 7.6%, corresponding to 2.7 million with diabetes. The prevalence of diabetes increases with age and reaches its peak in the oldest age-group; in population of 60 - 69 years of age the prevalence of diabetes is about 20%.[1]

Diabetes has been known to adversely affect the musculoskeletal system, to delay collagen synthesis,[2,3] and to impair wound healing[4] and phagocytosis.[5] These factors may lead to higher risks of various infections and poorer wound healing after any surgical procedure. Some studies have shown an altered bone and mineral metabolism in diabetic animals and humans,[6-10] and the fracture healing process may be delayed by this condition.[11-14] Theoretically, these effects could contribute to prosthesis loosening in total joint replacement.

Total knee arthroplasty (TKA) is one of the most frequently performed orthopaedic operations in the elderly population. As TKA in diabetic patients has become more common, it has received increasing attention. Some authors have reported an increased rate of deep infection in diabetic patients,[15-18] while others have raised concerns over wound complications.[16-19]

The aim of our present study was to compare the clinical outcome and complications following TKA in a consecutive series of diabetic and non-diabetic patients, and to identify diabetes-related risk factors for negative outcomes.

MATERIALS AND METHODS

Patient characteristics

Between 1995 and 2004, 1581 primary TKA procedures were performed at our institution. Surgery was performed by one senior author. In this consecutive series, 222 primary TKAs (14%) in 171 patients with diabetes were available with a minimum follow-up period of 2 years. Only patients with osteoarthritis were included in the current study. The medical records of these patients were reviewed in detail to assess the demographic and medical features of each patient (Table 1). The study included 155 women (203 TKAs) and 16 men (19 TKAs) with a mean age of 67.6 years (range, 50 - 86 years) at the time of operation. Fifty-one patients had bilateral staged TKA. The mean duration of follow-up was 53.2 months (range, 24 - 132 months). Nine patients (5.3%) had previous knee procedures before definitive TKA; 5 received arthroscopic debridement, 1 high tibial osteotomy and 3 open reduction and internal fixation for distal femur or proximal tibial

fracture. To identify diabetes-related factors that affect the outcome after TKA, several diabetes associated variables were investigated, including duration of diabetes, the number of major systemic complications of diabetes, body mass index (BMI) and glycosylated hemoglobin values (HbA1c). Twenty-four patients (31 knees; 14%) were treated with insulin, and 147 patients (191 knees; 86%) were treated with oral hypoglycemics. The mean time from the onset of diabetes to the time of surgery was 7.6 years (range, 1 - 30 years). Twenty-nine patients (37 knees; 17%) had major systemic complications of diabetes at the time of surgery. Twenty-five patients (32 knees) had one complication, and four patients (5 knees) had two complications. The distribution of complications from diabetes is listed in Table 2. Table 3 shows associations with various diseases; the most common was hypertension associated with 148 knees (66.7%). Body mass index (BMI) is the ratio of weight to height, calculated by dividing the weight by the square of the height (kg/m^2). Patients were divided into three categories based on their BMI: individuals with a BMI of 20 - 25

Table 1. Demographic Data

Gender (No. of patients, %)	
Male	16 (9.4%)
Female	155 (90.6%)
Age (mean, range)	67.6 yrs (50 - 86)
Follow-up period (mean, range)	53 months (24 - 132)
Type of treatment (No. of patients, %)	
Insulin	24 (14%)
Oral hypoglycemics	147 (86%)
Duration of diabetes (mean, range)	7.6 yrs (1 - 30)
Number of complications of diabetes (No. of patients)	
0	142
1	25
2	4
Body mass index (BMI) (mean, range)	26.5 kg/m^2 (18.9 - 36.9)
Normal	74 knees (33.3%)
Overweight	119 knees (53.6%)
Obese	29 knees (13.1%)
Glycosylated hemoglobin value (HbA1c) (mean, range)	7.5% (4.4 - 12.2)
Previous knee surgery (No. of knees)	
Arthroscopic debridement	5
High tibial osteotomy	1
Open reduction and internal fixation	3

Table 2. Preoperative Systemic Complications Associated with Diabetes Mellitus

Complications	No. of patients (%)
Coronary arterial occlusive disease	10 (5.8)
Peripheral arterial occlusive disease	3 (1.8)
Cerebrovascular accident	5 (2.9)
DM neuropathy	6 (3.5)
DM retinopathy	4 (2.3)
DM nephropathy	5 (2.9)

Table 3. Associated Diseases

Diseases	No. of knees (%)
Hypertension	148 (66.7)
Hypothyroidism	1 (0.5)
Parkinsonism	2 (0.9)
Congestive heart failure	4 (1.8)
Cushing syndrome	10 (4.5)
Nephrotic syndrome	1 (0.5)
Liver cirrhosis	1 (0.5)

are considered normal weight; 25 - 30 overweight; and > 30 obese.[20-22] In the present study, the mean BMI was 26.5 kg/m^2 (range, 18.9 - 36.9). Seventy-four knees (33.3%) were associated with normal weight, 119 knees (53.6%) with overweight and 29 knees (13.1%) with obese. HbA$_{1c}$ is a useful index of blood glucose control over a period of 4 - 5 weeks.[23-25] HbA$_{1c}$ values, taken within 1 month before TKA to evaluate diabetes, were available for 185 knees with a mean HbA$_{1c}$ of 7.51% (range, 4.40 - 12.20). Antibiotic prophylaxis and a tourniquet were used in all patients. Prophylaxis for thromboembolism was not performed. All knees were approached through a standard medial parapatellar incision, and all patients received cefuroxime-impregnated cement (1 g of cefuroxime in 40 g of CMW) with mobile bearing low contact stress total knee system (Depuy, Warsaw, IN, USA). Full weight bearing ambulation and range of motion exercises were started on the first postoperative day.

Clinical evaluation

All the patients were identified only by the sequential number of TKA while administering rating scores and complications to stay blind to the patient's status as either a diabetes or control subjects. Patients were preoperatively evaluated according to the Knee Society clinical scoring system and then postoperatively at 6 weeks, 6 months, 1 year, and yearly thereafter.[26] Values for knee and function score were obtained to assess prosthetic knee and patient function separately. Pain score was also obtained from the knee scores comprising pain, range of motion and stability. Ratings of 90 - 100 were considered excellent, 80 - 89 good, 70 - 79 fair, and less than 70 poor. We also evaluated Hospital for Special Surgery (HSS) knee-rating scores.[27] Knees with a rating of 85 or more were designated as excellent, 70 - 84 good, 60 - 69 fair, and less than 60 poor. Perioperative and postoperative complications were noted retrospectively for all patients. Complications included wound complications, superficial or deep infection, meniscal bearing dislodgement, periprosthetic fracture, deep vein thrombosis (DVT), peroneal nerve palsy and other medical complications. Wound complications were defined as marginal skin necrosis, bulla formation or wound erythema with drainage that persisted longer than usual. To avoid observational bias, only the cases were determined to be adopted of which hospital stay was prolonged at least two days or more for wound management or additional use of intravenous antibiotics. Patients were clinically screened for DVT and it was confirmed with Doppler ultrasonography when diagnosis was suspicious.

Control group

To compare the outcome after TKA in diabetic patients with that of non-diabetic patients, a randomized matching with controls was done from the same series using computer generated matching process. Non-diabetic patients were matched one to one with diabetic patients, based on the following criteria:[17,19] (1) age at surgery (within 5 years), (2) gender, (3) diagnosis of arthritis, (4) length of follow-up period (within 1 year), (5) implant design, and (6) BMI (same BMI category). Characteristics of the control and diabetic groups are compared in Table 4. There were no statistical differences in any of the

matching criteria between the two groups.

Table 4. Comparison of Diabetic and Control Groups

	Diabetic	Control
Age (yrs)	67.6	67.4
Gender (No. of patients)		
Male	16	16
Female	155	155
Diagnosis	OA (100%)	OA (100%)
Follow-up period (months)	53.2	54.4
Body mass index (kg/m^2)	26.5	25.9

OA, osteoarthritis.

Statistical assessment

Univariate analyses were performed to idenfity significant preoperative factors of the measured outcome. *P* values less than 0.05 were considered significant. The paired t-test was performed to determine whether there was a significant improvement in the clinical scores after TKA. Clinical scores were compared with those of the control group using the Student's t-test. Overall and individual complication rates were compared with the chi-square test. The relationship between clinical scores and continuous variables, such as duration of diabetes, BMI and the value of HbA$_{1c}$, were analyzed using the Pearson correlation coefficients test. In addition, analysis of variance (ANOVA) was used when the comparison was performed with respect to BMI subgroups. However, in a number of major systemic complications of diabetes, the samples of group "2" did not fulfill the normality test, therefore, they were correlated with the clinical scores using the Kruskal-Wallis test as a nonparametric test. The chi-square test was used to analyze the effect of diabetes-related factors on complication rates.

Once possibly significant predictors of outcome had been identified by this method, multivariate analysis was carried out to identify any predictors that would independently alter outcome. Computation was performed with the Statistical Analysis System (SAS Institute, Cary, North Carolina, USA).

RESULTS

Clinical results

In the diabetic group, the average preoperative Knee Society knee score was 50 ± 16, and the average pain and function scores were 22 ± 10 and 47 ± 14, respectively. There was a significant improvement in all the scores ($p < 0.0001$) after TKA. At the latest follow-up, knee, pain, and function scores had increased to 92 ± 12, 45 ± 9 and 74 ± 20, respectively (Table 5). There was also improvement in the HSS score from 66 ± 10 to 89 ± 10 ($p < 0.0001$) (Table 6). The control group also showed a significant improvement in the Knee Society scores and HSS score (Tables 5 and 6). At the latest follow-up examination, there was no pain in 112 knees (50.5%), mild pain in 102 (45.9%), moderate pain in 6 (2.7%) and severe pain in 2 (0.9%). One hundred and seventy seven (79.7%) knees were rated excellent, 21 (9.5%) good, 16 (7.2%) fair, and 8 (3.6%) poor according to the Knee Society rating scale.

Table 5. Average Knee Society Scores

Score	Diabetic status	Preoperative	Last follow-up
Knee	Yes	50 ± 16	92 ± 12
	No	52 ± 17	92 ± 10
Pain	Yes	22 ± 10	45 ± 9
	No	23 ± 10	45 ± 8
Function	Yes	47 ± 14	74 ± 20
	No	50 ± 13	74 ± 20

Table 6. Average Hospital for Special Surgery Scores

Diabetic status	Preoperative	Last follow-up
Yes	66 ± 10	89 ± 10
No	66 ± 11	89 ± 9

There were no statistically significant differences in the average preoperative Knee Society knee, pain and function scores between the diabetic and control groups ($p > 0.05$). Likewise, there were no statistical differences in the average postoperative knee, pain, and function scores between the two groups (Table 5). There were no significant differences in the average preoperative

and postoperative HSS score between the two groups (Table 6).

Univariate analysis suggested that age, gender and BMI might affect the clinical outcomes. A significant relationship between other predictors and clinical outcomes could not be detected ($p >$ 0.05). However, associated diseases and the number of diabetic complications were related with preoperative pain scores. For the number of diabetic complications, the median value was 10 for group 2, 20 for group 1, and 30 for group 0 ($p = 0.0035$), and 30 in patients without associated diseases, 20 with hypertension, 20 with congestive heart failure, and 15 with Cushing syndrome ($p = 0.0096$).

Dividing the BMI into 3 subgroups, the mean postoperative pain score was 44 ± 6 in the normal weight group, 46 ± 7 in the overweight group, and 41 ± 14 in the obese group ($p = 0.0182$). The mean postoperative knee score was 92 ± 10 in the normal weight group, 94 ± 8 in overweight group, and 86 ± 24 in obese group ($p = 0.0109$). Multivariate analysis associating age, gender and BMI with the pain and knee score at the latest follow-up was performed. Once the analysis was carried out, the differences in the knee scores were all significant, whereas only the difference in the pain score was significant between the overweight and obese groups.

Postoperative complications

The diabetic group had an increased overall incidence of postoperative complications compared with the matched control group (17.6% vs.

8.1%; $p = 0.0029$). The rate of wound complications was significantly higher in patients with diabetes than in patients without diabetes (9.5% vs. 5.0%; $p = 0.0461$). The rate of dislodgement was 2.7% in diabetic versus 0.5% in non-diabetics and was found to be not significantly different ($p = 0.0585$). The rates of other complications were not statistically different (Table 7). Peroneal nerve palsy, serious medical complications and medial instability were not observed in the control group.

Six meniscal bearing dislodgements occurred postoperatively at an average of 18.8 months (range, 2 - 48) and were treated with meniscal bearing exchange. One each superficial wound infection occurred in the both groups, and they were treated with debridement of the wound and intravenous antibiotics. Two deep infections (0.9%) occurred in the diabetic group, whereas one deep infection (0.5%) in the control group. The deep infections in the diabetic group occurred 11 weeks and 33 months postoperatively, and the causative microorganisms were methicillin-resistant coagulase negative streptococcus and *Escherichia coli*, respectively. The deep infection in the control group occurred 36 months postoperatively, and the causative organism was *Acinetobacter baumannii*. These infections were treated with debridement of the joint and intravenous antibiotics, and the infected implants were retrieved and replaced with an antibiotic impregnated cement spacer. Definitive revisional total knee arthroplasty was performed 6 months later. Clinical features of the diabetic patients with deep infection are listed in Table 8. The patients were diagnosed as diabetes

Table 7. Postoperative Complications

Complication	Diabetic knees (%)	Control knees (%)	*p* value
Wound complication	21 (9.5)	11 (5.0)	< 0.05
Meniscal bearing dislodgement	6 (2.7)	1 (0.5)	ns
Superficial wound infection	1 (0.5)	1 (0.5)	ns
Deep joint infection	2 (0.9)	1 (0.5)	ns
Periprosthetic fracture	1 (0.5)	1 (0.5)	ns
Deep vein thrombosis	2 (0.9)	3 (1.4)	ns
Peroneal nerve palsy	1 (0.5)	0 (0)	ns
Medical complication	3 (1.4)	0 (0)	ns
Medial instability	2 (0.9)	0 (0)	ns
Overall	39 (17.6)	18 (8.1)	< 0.05

ns, not significant.

Table 8. Clinical Features of Diabetic Patients with Deep Infection

	Patient 1	Patient 2
Type of treatment	Oral hypoglycemics	Oral hypoglycemics
Duration of diabetes	1 yr	1 yr
Complication of diabetes	None	None
BMI (kg/m^2)	28.6	23.4
HbA1c (%)	7.4	-
Associated disease	Hypothyroidism	Hypertension
Previous surgery	None	O/R and I/F

O/R, open reduction; I/F, internal fixation.

one year before surgery and had no complication of diabetes preoperatively. One diabetic patient with peroneal nerve palsy underwent electrical stimulation therapy and showed recovery of ankle dorsiflexion 3 weeks postoperatively and big toe extension one year postoperatively. There were no perioperative mortalities in our series.

DISCUSSION

A few studies evaluated the effect of diabetes on outcome following TKA. Serna et al. investigated the effect of various diagnosis, the use of cement versus cementless fixation, preoperative deformity, the number of prior surgeries, patient weight greater than 80 kg, and Chanley functional class, and suggested the necessity to examine the degree of glucose control in terms of its effect on the final outcome. To our best knowledge, the current study is the first attempt to examine the effect of diabetes-related factors (duration of diabetes, number of complications of diabetes, body mass index, HbA_{1c} value, type of treatment of diabetes, dose of insulin) on the clinical ratings and the incidence of postoperative complications rates.

In the present study, there was a significant improvement in HSS and Knee Society scores between preoperative and postoperative values for both control and diabetic groups, and these improvements of the scores were associated with pain relief and reflected changes in walking distance and gait aids. In diabetic patients, sensory and autonomic neuropathy can exist at subclinical levels,[28] and the resulting loss of pain perception may contribute to higher Knee Society

knee and pain scores in patients with diabetes. In addition, combined chronic complications of diabetes and medical comorbidities may have an adverse effect on the function and mobility of patients. These ideas are supported by Meding et al.,[29] who reported higher knee and pain scores and lower function scores in patients with diabetes. Papagelopoulos et al.[19] also reported lower function scores in diabetic patients; whereas the Knee Society knee score and HSS scores were lower in patients with diabetes in their series. Likewise, Serna et al.[17] reported lower HSS scores in patients with diabetes. Those authors recognized that diabetes might influence clinical outcome. However, the influence of diabetes-related factors on clinical outcome was not addressed in their study. We demonstrated that there was no difference in clinical scores between the diabetic and non-diabetic patients, and univariate analysis revealed that BMI was the single significant diabetes-related predictor on clinical outcome. It appears, therefore, that the lower knee score in the obese group is largely due to the lower pain score. Low postoperative pain scores have been attributed to the increased rates of postoperative patellofemoral symptoms among obese patients.[30-32] There have been a number of reports on the outcomes of TKA among obese patients, and there is a general consensus that obese patients have satisfactory clinical and radiological results in the long-term.[32-34] Adverse outcomes have been reported in highly or morbidly obese patients,[34,35] however the current study did not include morbidly obese patients and involved only one patient with a BMI greater than 35 kg/m^2. This may explain the lack of difference in postopera-

Table 9. Statistical Analysis of the Relationships between Preoperative Factors and Postoperative Complications

	Cx 1*	Cx 2[†]
Duration of diabetes	0.8307	0.4052
No. of complications of diabetes	0.4737	1.0000
Body mass index	0.1023	0.3069
HbA1c value	0.4078	0.1921
Type of treatment of diabetes	0.1778	0.5625
Dose of insulin[‡]	0.4180	-
Previous surgery	0.4106	1.0000
Associated diseases	0.0014*	0.0195*

*wound complications.
[†]meniscal bearing dislodgement.
[‡]the statistical analysis was done with Student's t-test for dose of insulin, chi-square test for others.

tive complication rates between the subgroups of BMI in the current study.

There was higher overall postoperative complication rate in diabetic patients, but all the individual complication rates were not statistically different. The most common complications were wound complications (9.5%) and meniscal bearing dislodgement (2.7%). Wound complications after TKA in diabetic patients has been described by several authors;[15-19] however, the definitions of wound complications are somewhat different in each study. Meding et al. defined it as skin necrosis, superficial infection, and wound dehiscence, while Papagelopoulos et al. defined it as wound dehiscence, hematoma, and wound discharge. Other groups defined wound complications as superficial infection.[16-18] Furthermore, the published rate of wound complications varies from 1.2% to 12%. The rate observed in the current study (9.5%) is not directly comparable with other studies, because it represents marginal skin necrosis, bulla formation, or wound erythema with drainage that persisted longer than usual. There were 14 cases of erythema, 5 cases of necrosis, and 2 cases of bulla formation. No wound dehiscence was observed. These are minor complications compared with those reported by other authors, and none of them caused significant morbidity.

The incidence of meniscal bearing dislodgement has been reported to vary from 0.83% to 9.3%.[36,37] The current study revealed a dislodgement rate of 2.7%. Joint sepsis has been a matter of concern after TKA in diabetic patients. England et al.[16] reported a deep infection rate of 7% and a wound

complication rate of 12% in diabetic patients after TKA. In that series, the rate of deep joint infection in diabetic patients was 10 times higher than the reported incidence of sepsis in non-diabetic patients, therefore they suggested the use of antibiotic-impregnated cement. Chiu et al.[15] performed a prospective randomized study to evaluate the role of cefuroxime-impregnated cement in the prevention of deep infection at primary TKA in patients with diabetes. They found no cases of deep infection in the group with cefuroxime-impregnated cement compared with a deep infection rate of 13.5% in the control group, and concluded that cefuroxime-impregnated cement was effective in the prevention of deep infection in patients with diabetes and suggested routine addition of cefuroxime. Its thermal stability and biological effectiveness in cement as well as good clinical result have been well documented, therefore we have routinely been using cefuroxime-impregnated cement for primary TKA, vindicating the idea that prophylactic use of antibiotic bone cement should be the standard of practice for primary TKA.[38] Meding et al. also added cefuroxime to cement and reported a deep infection rate of 1.2% in diabetic patients and 0.7% in nondiabetic patients, which are comparable with ours. In their study, all deep infections occurred in patients with insulin-dependent diabetes, whereas all deep infections in the current study occurred in patients who were treated with oral hypoglycemics (Table 8). Therefore, diabetes-related factors appear to have little influence on the rate of deep infection.

A higher than expected aseptic loosening rate in

patients with diabetes has been reported by several authors.[19,29] With a mean follow-up period of 4.3 years, Meding et al. demonstrated that the rate of aseptic loosening was significantly higher in patient with diabetes (3.6%) than with non-diabetic patients (0.4%). After a mean follow-up of 8 years, Papagelopoulos et al. reported the aseptic loosening rate of 7.4%, which was higher than the control group. However, there are also various studies showing contradictory outcomes. With the mean follow-up of 4.2 years. Chiu et al.[15] reported no aseptic loosening, whereas others[16-18] have reported the rate of aseptic loosening, ranging from 2 to 3% with the mean follow-up from 3.6 to 4.5 years, however only 1 or 2 aseptic loosenings were included in the series. Similarly, there was no aseptic loosening after a mean follow-up of 4.4 years in our series. After all, diabetes theoretically could contribute to implant loosening, nevertheless, reported incidences are not consistent: There seem to be other factors such as demographic differences besides diabetes in developing aseptic loosening.

The current study represents a retrospective review of clinical outcomes and postoperative complications in diabetes following TKA. While BMI standards reported by WHO expert committee were used in this study, several authors have raised a concern for its inability to detect differences and account for changes by age, gender,[39] and ethnic group.[40-43] However, the purpose of those studies were to precisely estimate the true association between adiposity and disease risk. Judging from the fact that the outcomes after TKA are affected by mechanical aspect rather than the possibility of cardiovascular disease, we think that it is a logical way to make BMI standard as an international classification to compare with existing studies.

Univariate analysis to identify a significant predictor of postoperative complications was possible only for wound complications and meniscal bearing dislodgement, because the number of patients with other complications was too small. As listed in Table 9, preoperative factors associated with diabetes did not affect the rate of wound complication and meniscal bearing dislodgement. The only significant preoperative factor affecting the complication rates was

associated disease. Patients who had iatrogenic Cushing syndrome before TKA had an odds ratio of 19 for wound complications and 38 for meniscal bearing dislodgement compared with patients without associated disease, and power analysis showed a power of 0.95 and 0.80, respectively, validating the ratios.

In conclusion, our present results indicate that patients with diabetes have preoperative clinical conditions similar to non-diabetic patients and benefit equally well from TKA. However, the diabetic patients were at an increased risk for overall postoperative complications and wound complications. Preoperative factors such as BMI and associated diseases may adversely affect the clinical outcome of TKA in diabetic patients. Therefore, it is necessary to balance the benefits of TKA against the risks and exercise extra caution in patient selection.

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