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Outcomes of Foot and Ankle Surgery in Diabetic Patients Who Have Undergone Solid Organ Transplantation

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Abstract

Foot and ankle problems are highly prevalent in patients with diabetes mellitus (DM). Increased rates of surgical site infections and noninfectious complications, such as malunion, delayed union, nonunion, and hardware failure, have also been more commonly observed in diabetic patients who undergo foot and ankle surgery. DM is a substantial contributor of perioperative morbidity in patients with solid organ transplantation. To the best of our knowledge, postoperative foot and ankle complications have not been studied in a cohort of diabetic patients who previously underwent solid organ transplantation. The aim of the present study was to evaluate the outcomes of foot and ankle surgery in a cohort of diabetic transplant patients and to compare these outcomes with those of diabetic patients without a history of transplantation. We compared the rates of infectious and noninfectious complications after foot and ankle surgery in 28 diabetic transplant patients and 56 diabetic patients without previous transplantation and calculated the odds ratios (OR) for significant findings. The diabetic transplant patients who underwent foot and ankle surgery in the present cohort were not at an increased risk of overall complications (OR 0.83, 95% confidence interval [CI] 0.33 to 2.08, $p = .67$), infectious complications (OR 0.54, 95% CI 0.09 to 3.09, $p = .49$), or noninfectious complications (OR 1.14, 95% CI 0.41 to 3.15, $p = .81$). Four transplant patients (14.3%) died of non-orthopedic surgery-related events during the follow-up period; however, no deaths occurred in the control group. Diabetic patients with previous solid organ transplantation were not at an increased risk of developing postoperative complications after foot and ankle surgery, despite being immunocompromised. The transplant patients had a greater mortality rate, but their premature death was unrelated to their foot and ankle surgery. Surgeons treating transplant patients can recommend foot and ankle surgery when indicated. However, owing to the increased mortality rate and comorbidities associated with this high-risk group, we recommend preoperative clearance from the transplant team and medical consultations before performing surgery.

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Keywords

ankle; complication; diabetes mellitus; immunosuppression; risk; transplantation

Diabetes mellitus (DM) is a highly prevalent disease among orthopedic surgery patients, especially within the specialty of foot and ankle surgery. According to the Centers for Disease Control and Prevention's National Diabetes Fact Sheet 2014, an estimated 29.1 million Americans (9.1% of the population) have DM (1). DM is a global problem, with an estimated 285 million adults worldwide diagnosed with this disease in 2010, and this is projected to substantially increase to 439 million adults by 2030 (2). The complications of DM are associated with significant economic burdens. The International Diabetes Federation estimated that \$376 billion global health expenditures were spent in 2010 to prevent and treat DM and its complications. By 2030, the International Diabetes Federation projected expenditures will exceed \$490 billion (2). Patients with poorly controlled DM have been shown to be at a greater risk of the development of complications such as Charcot neuroarthropathy (CN), peripheral neuropathy, peripheral vascular disease, osteomyelitis, and renal-related metabolic bone disease, among others.

Postoperative orthopedic infectious complications of DM after foot and ankle surgery have been well documented in published studies. A retrospective study reported that diabetic patients who underwent foot and ankle surgery experienced an approximately fivefold increase in the rate of postoperative deep surgical site infections compared with patients without DM (13.2% versus 2.8%, respectively) (3). A recent prospective study demonstrated that patients with complications of DM, including neuropathy, peripheral arterial disease, and nephropathy, experienced a sevenfold increase in surgical site infection risk compared with patients without DM and without neuropathy and a nearly fourfold increase in risk compared with patients with uncomplicated DM (4). Diabetic patients have also been shown to experience greater rates of noninfectious orthopedic complications after foot and ankle surgery (5,6). Common complications have included impaired fracture healing, malunion, delayed union, nonunion, hardware failure, revision surgery, and amputation (7,8). In addition, diabetic patients with comorbidities such as heart disease, chronic obstructive pulmonary disease, hypertension, and previous hospitalizations have been shown to experience an increased risk of requiring long-term bracing, ranging from 15 months to 8 years after the initial foot and ankle fracture presentation, compared with their counterparts without DM (47% versus 14%, respectively) (9).

In addition to foot-related complications, diabetic patients have a greater risk of the development of end-stage renal disease, coronary artery disease, and cardiomyopathy. Similarly, diabetic patients can have end-stage liver disease due to hepatitis, nonalcoholic fatty liver disease, and cirrhosis. Consequently, the rates of cardiac, pancreatic, renal, and liver transplantation have dramatically increased in this population within the previous 4 decades, largely owing to the continued success of immunosuppressive agents and biologic agents. Although diabetic patients have undergone solid organ transplantation with modest success rates, previous studies have demonstrated that the manifestations of DM significantly increase the risks and complications associated with transplantation. A

retrospective study reported a 40% decrease in the mean 5-year survival rates after orthotopic liver transplantation in diabetic patients compared with nondiabetic patients (10). Another retrospective study described lower mean 5-year survival rates and graft survival rates for diabetic patients after renal transplantation compared with nondiabetic patients (83% versus 93% and 74% versus 79%, respectively) (11). The success of simultaneous renal and pancreatic transplantation has also been reported (12). In addition to greater rates of mortality, solid organ transplantation has been associated with an increased risk of postoperative infections owing to the chronic use of immunosuppressive agents and antimicrobial prophylactic treatment-induced resistance. Additionally, 1 study reported that diabetic patients who underwent renal transplantation experienced an approximately twofold increase in overall bone fracture incidence compared with patients without DM (13).

Because of these comorbidities and the long-term immunosuppression, surgeons have traditionally been reluctant to operate on diabetic patients with previous solid organ transplantation owing to the presumed increased postoperative risks and complications. To the best of our knowledge, complications after foot and ankle surgery in diabetic patients who have previously undergone solid organ transplantation have not been studied. We hypothesized that the postoperative complication rates after foot and ankle surgery would be greater for diabetic transplant patients than for diabetic patients without a history of transplantation. The aim of the present study was to evaluate the outcomes of foot and ankle surgery in a cohort of diabetic patients with a history of solid organ transplantation and compare these outcomes with those of diabetic patients without a history of transplantation.

Patients and Methods

Approval was obtained from our local institution review board before beginning the present retrospective case-control study. We reviewed the foot and ankle surgical database of the senior author (D.K.W.), searching for diabetic patients who had previously undergone solid organ transplantation. A comprehensive foot and ankle registry was created in our division in January 2005, in which the data for every surgical patient were prospectively entered at the time of their surgery. Demographic data were entered into the spreadsheet, as were the “International Classification of Diseases, Ninth Revision” diagnosis codes for transplantation (V42.0), cardiac transplantation (V42.1), liver transplantation (V42.7), pancreatic transplantation (V42.83), and renal transplantation (V42.07) (14). Postoperative complications were recorded prospectively in the comprehensive foot and ankle registry by categorically denoting the absence (0) or presence (1) of specific complications. Once transplant patients had been identified from the comprehensive foot and ankle registry, the electronic inpatient and outpatient records and digital radiographs were reviewed from those patients who had undergone surgery by the senior surgeon (D.K.W.) from January 2005 until June 2013.

Our study group included patients with DM who were aged ≥ 18 years and had undergone previous solid organ transplantation and, subsequently, foot and ankle surgery. For the purposes of the present study, we defined solid organ transplantation as pancreatic, renal, hepatic, cardiac, and/or lung transplantation. The inpatient and outpatient records identified 28 consecutive patients who fit the study group inclusion criteria. Their data were abstracted

by the first author (R.H.Z.), who also determined the values to be used in the present research project.

The exclusion criteria included transplant patients who had previously been treated for active soft tissue infection (Current Procedural Terminology code 28002, “International Classification of Diseases, Ninth Revision” code 682) or osteomyelitis (Current Procedural Terminology code 28005, “International Classification of Diseases, Ninth Revision” code 730) (14,15). Patients with active infections were excluded, because one of the outcomes of interest was the occurrence of postoperative infection.

We used 2-to-1 control-to-study match criteria to select 56 control patients with DM and without a history of solid organ transplantation who had undergone foot and ankle operative procedures similar to those of the study group counterparts. The 2-to-1 match was used to increase the power of the present study and, at the same time, minimize the loss with the small number of case-control sets available from our database (16). A sample size estimation was not performed, because a pilot study had not been performed and no previous studies have addressed this topic. The control group was matched for sex, age, and length of orthopedic surgery time. The patients in the present study were matched according to the operative time rather than the specific foot and ankle procedure to increase the inclusion criteria pool and control for variability. For the purposes of the present study, we assumed that, in general, patients with similar operative times had undergone similar categories and complexities of foot and ankle reconstruction. We extracted the following baseline characteristics from each patient in the study: sex, age, operative time, solid organ transplantation history, follow-up period after orthopedic surgery, diabetic status, duration of DM, blood glucose level, hemoglobin A1c (HbA1c), creatinine, Michigan Neuropathic Screening Instrument (MNSI) score, history of insulin use, American Society of Anesthesiologists classification, body mass index (BMI), and neuropathic status.

Peripheral neuropathy was clinically diagnosed using the MNSI score (score ≥ 2.5) (17). This validated instrument relies on Semmes-Weinstein monofilament testing, vibration testing using the 128-Hz tuning fork, an Achilles reflex assessment, the presence or absence of ulceration, and the presence or absence of deformity such as claw toes or CN. Diabetic neuropathy was confirmed in patients using a quantitative neurologic examination, coupled with nerve conduction studies (18). Four plantar sites (first and fifth metatarsal heads, plantar hallux, and heel) were tested using the 5.07 Semmes-Weinstein monofilament. These 4 sites represented a slight modification from the original description of the MNSI. Patients who could sense all 4 sites with their eyes closed received a score of 0 for each foot. Patients who were unable to sense the monofilament in 1 of the 4 sites received a score of 0.5 for each foot. Patients who were unable to sense 2 of the 4 sites received a score of 1.0 for each foot. Vibratory sensation was evaluated using the 128-Hz tuning fork at the dorsal hallux. Patients who felt the vibration consistent with the duration that the examiner felt while holding the 128-Hz tuning fork received a score of 0 for each foot. Patients who initially felt the vibration but were unable to sense it after 5 seconds of dampening by the examiner received a score of 0.5 for each foot. Patients who were unable to sense the vibration at all or with noted absence within 5 seconds received a score of 1.0 for each foot. The Achilles reflexes were evaluated in a standard musculoskeletal manner. An intact reflex

without reinforcement received a score of 0 for each foot. An intact reflex with reinforcement (clasping the hands and fingers together with the Jendrassik maneuver) received a score of 0.5 for each foot. An absent reflex received a score of 1.0 for each foot. Patients with a foot ulcer received a score of 1.0 for each foot. Patients without foot ulcers received a score of 0 for each foot. For the purposes of the present study, we defined neuropathic deformity as multiple claw toes involving both feet or the presence of CN. Claw toes and CN were evaluated both clinically and radiographically. The presence of a deformity received a score of 1.0, and the absence of a deformity received a score of 0. The maximum score per foot was 5, and the combined maximum total score for both feet was 10. The MNSI was used as a measure of peripheral neuropathy in our diabetic patient population (17).

Malunion was defined as healed bone fractures or arthrodeses in less than optimal positions. Delayed union was defined as bone fractures or arthrodeses that had not healed within 6 months of the foot and ankle operation. Nonunion was defined as the absence of bone healing after 1 year. Owing to the high prevalence of patients with neuropathy, the presence of pain was an unreliable marker of nonunion. Thus, we relied on the radiographic findings to include hardware failure. All complications were determined by the single academic foot and ankle surgeon (D.W.K.) who performed the operations. The data obtained regarding diabetic status, insulin use, and neuropathic status were recorded using a binary yes (1) or no (0) system, in which patients either had or did not have the complication documented in their electronic medical records.

The 28 transplant patients underwent a combined total of 67 foot and ankle surgical procedures, and the control group underwent 118 procedures. Some patients underwent multiple procedures during their surgery, including midfoot arthrodesis, bone graft harvesting, and Achilles tendon lengthening. The various surgical procedures in the study and control group are listed in Table 1. The mean interval from solid organ transplantation until foot and ankle surgery was 67.9 (range 10 to 170) months. Two patients in the study group required amputation surgery. A toe amputation was performed for a nonhealing ulcer, and another patient underwent transtibial amputation for a nonreconstructable, nonbraceable Charcot deformity of the foot. Of the 28 transplant patients, 16 (57.1%) had a diagnosis of CN compared with 19 (32.7%) of the 56 control patients ($p = .06$). All the cases of CN, in both the transplant and control groups, had been present before the foot and ankle surgery. Noninfected foot ulcers were present in 4 (14.2%) of 28 transplant patients and 6 (10.7%) of 56 control patients ($p = .07$). Our standard perioperative prophylactic antibiotic coverage for both study and control group inpatients consisted of 1 g (body weight <180 lb) or 2 g (body weight ≥ 180 lb) of intravenous cefazolin administered within 1 hour before the start of surgery. Inpatients received additional doses every 8 hours for the first 24 hours. For patients with documented penicillin allergies, either 1 g of intravenous vancomycin or 600 mg of clindamycin was administered. At our institution, transplant patients also received lifelong chemoprophylaxis with 800 mg of oral trimethoprim-sulfamethoxazole 3 times weekly. This was not altered during the perioperative period.

Our outcome assessment consisted of the overall postoperative complications, postoperative infectious complications, postoperative noninfectious complications (malunion, delayed

union, or nonunion), and mortality. Because of the small number of patients in our study, we combined malunion, delayed union, and nonunion into the outcome of noninfectious complications. The Clinical and Translational Science Institute (CTSI) at the University of Pittsburgh provided statistical assistance with our report. Their statistical consultation was supported by the National Institutes of Health (grant UL1-TR-000005). Statistical analyses of the differences in the overall incidence of postoperative complications, postoperative infectious complications, postoperative noninfectious complications (malunion, delayed union, and nonunion), and mortality were investigated using a logistic regression model with robust standard errors. The former allowed for prediction of yes/no postoperative complication outcomes, and the latter accounted for clusters of patients in the 2-to-1 matched data set, with each variable pair of 3 patients representing 1 study patient and 2 control patients. The paired *t* test was used for categorical analyses of the baseline patient characteristics, including sex, age, and length of orthopedic surgery. A clustered logistic regression model with robust standards was also used for analyses of the follow-up period, diabetic status, DM duration, blood glucose, HbA1c, creatinine, MNSI score, insulin use, American Society of Anesthesiologists classification, BMI, and neuropathic status. Statistical significance was set at an α value of 0.05 ($p < .05$) with associated 95% confidence intervals (CIs).

Results

The patient baseline characteristics are listed in Table 2. No significant differences were seen in sex, age, or operative time between our study and matched control groups. The study group consisted of 18 males (64.3%) and 10 females (35.7%), and the control group included 36 males (64.3%) and 20 females (35.7%), affirming the 2-to-1 control-to-study match ratio. The mean age of the transplant cohort was 53.9 (range 35 to 68) years and that of the diabetic control cohort was 53.4 (range 18 to 69) years (95% CI -1.05 to 2.20 , $p = .48$). The mean foot and ankle operative time in the transplantation cohort was 91.9 ± 69.7 (range 15 to 257) minutes and that of the diabetic control cohort was 90.8 ± 63.4 (range 23 to 215) minutes (95% CI -9.47 to 11.49 , $p = .84$).

The patient demographic information is listed in Table 2. The mean follow-up period for the entire study cohort was 58.6 (range 3.1 to 350) weeks. The transplant patients were followed up for a mean of 84.6 (range 5.6 to 350) weeks and the control patients for a mean of 45.6 (range 3.1 to 125.4) weeks (95% CI 1.001 to 1.02 , $p = .004$). The transplant patients were 5 times more likely than the control patients to have type 1 DM (odds ratio [OR] 5.1, 95% CI 2.33 to 11.2, $p < .001$). The transplant patients had had DM for a mean of 24.2 (range 1 to 48) years before their foot and ankle surgery procedure. The control patients had had DM for a mean of 12.4 (range 1 to 46) years (95% CI 1.04 to 1.13 , $p < .001$) before their foot and ankle procedure. The transplant patients had a mean HbA1c level of 6.81% (range 4.9% to 9.1%), and the control patients had a mean HbA1c level of 7.69% (range 5.0% to 12.4%, 95% CI 0.49 to 0.89 , $p = .006$), although the fasting serum glucose level on the day of surgery was not significantly different between the 2 groups ($p = .29$). The study group had a mean BMI of 29.0 (range 18.3 to 46.8) kg/m^2 , and the control group had a mean BMI of 33.6 (range 19.2 to 59.4) kg/m^2 (95% CI 0.85 to 0.99 , $p = .03$).

Clustered logistic regression model analyses of the serum creatinine, neuropathic status, MNSI score, insulin use, and American Society of Anesthesiologists classification did not demonstrate any significant differences ($p > .05$) between the transplant and nontransplant patients (Table 2). The prevalence of neuropathy in the patients with DM who had undergone solid organ transplantation before foot and ankle surgery (93%) was similar to the rate in the patients with DM but without a history of transplantation (88%; $p = .39$).

Of the patients in the study cohort, 23 (82.1%) had undergone renal transplantation, 11 (39.3%) pancreatic transplantation, 4 (14.3%) hepatic transplantation, and 2 (7.14%) cardiac transplantation. No patients in the present study had undergone lung transplantation. The total number of transplantations do not sum to 28 because 9 patients (32.1%) had undergone simultaneous pancreatic-renal transplantation, and 4 patients (14.3%) had undergone staged renal and pancreatic transplantation. Another 4 patients (14.3%) had undergone repeat transplantation procedures for previously failed organ transplantation attempts. Males constituted most of the solid organ transplantation recipients (64.1%).

The postoperative complications of the transplant patients who underwent foot and ankle surgery are also listed in Table 2. Seven transplant patients (25.0%) experienced postoperative complications compared with 16 control patients (28.5%; OR 0.83, 95% CI 0.33 to 2.08, $p = .70$). Two transplant patients (7.14%) experienced postoperative infectious complications compared with 7 control patients (12.5%; OR 0.54, 95% CI 0.09 to 3.09, $p = .49$). Of the transplant patients, 5 (17.9%) experienced postoperative noninfectious complications compared with 9 control patients (16.1%; OR 1.14, 95% CI 0.41 to 3.15, $p = .81$). One of the noninfectious complications in the transplant group included the reactivation of CN after attempted ankle arthrodesis. This resulted in nonunion with hardware failure, which was successfully salvaged with tibiototalcaneal arthrodesis. The inpatient and outpatient electronic medical records identified 4 patients (14.3%) in the transplant study cohort who died during the follow-up period. No patients in the control cohort died during the same interval. The deaths of the transplant patients resulted from non-orthopedic surgery-related events: 2 (7.14%) had died of cardiac arrest (both 3 years after foot and ankle surgery), 1 (3.57%) of septicemia (1 year after foot and ankle surgery of an opportunistic fungal infection), and 1 (3.57%) of respiratory failure after repeat aortic valve surgery (4 years after foot and ankle surgery). No statistical evaluation of mortality was performed because none of the control patients had died during our study period, making the OR impossible to calculate.

Discussion

Increased rates of postoperative healthcare-associated infections in diabetic patients with previous foot and ankle surgery are well established in the published data. The effects of DM on postoperative noninfectious complications, such as malunion, delayed union, nonunion, and hardware failure, have also been described (7,8). The effect of solid organ transplantation on overall patient survival, infection, and disease progression has been an area of intense research. However, to the best of our knowledge, little research has been reported quantifying the potential for adverse effects during the postoperative transplantation period in the high-risk diabetic population. Traditionally, surgeons have been hesitant to

perform foot and ankle surgery on diabetic patients with previous solid organ transplantation under the assumption that the additional risks posed by both DM and solid organ transplantation would potentiate postoperative complications, including increased morbidity and mortality. Anecdotally, we observed that transplant patients generally exhibited successful foot and ankle surgery with complication rates similar to those of diabetic patients without a history of transplantation, prompting us to conduct the present retrospective, case-control study.

The results of the present study have demonstrated that diabetic patients with previous solid organ transplantation are not at an increased risk of developing postoperative infectious and noninfectious complications after orthopedic surgery compared with diabetic patients without a history of transplantation. Although the rate of noninfectious complications (OR 1.14) was greater in the diabetic transplant patients, this cohort had a lower likelihood of developing overall postoperative complications (OR 0.83) and postoperative infectious complications (OR 0.54). It is possible that the reduction in infections in the study group resulted from 2 factors. First, the transplant patients had a lower mean HbA1c compared with the control patients, and optimum glycemic control has previously been shown to reduce the rate of surgical site infection (4). Second, at our academic institution, all transplant patients receive 800 mg of oral trimethoprim-sulfamethoxazole 3 times weekly for life. This implementation of prophylactic antibiotic usage might have played a role in preventing the development of postoperative infectious complications.

An important finding of the present study was the difference in mortality between the transplant patients (14.3%) and control patients (0%). This difference highlights the potential for those with a history of solid organ transplantation to be at an increased risk of premature mortality. Because no control patients died in the present retrospective study, we were unable to perform a statistical analysis to compare these 2 cohorts. However, the hospital electronic medical records indicated that the causes of mortality were unrelated to the foot and ankle reconstruction (cardiac arrest, septicemia, cessation of respiration) and occurred 1 to 4 years after orthopedic surgery.

The transplant patients had a significantly longer follow-up period after foot and ankle surgery (84.6 weeks) than the control patients (45.6 weeks; $p = .004$). This increased follow-up interval most likely resulted from 2 reasons. First, the senior surgeon (D.K.W.) demonstrated additional concerns about the risks and complications posed by both solid organ transplantation and foot and ankle surgery. Second, at our institution, patients who undergo solid organ transplantation are followed up for life by the transplantation team. Other significant differences between the study and control groups were observed. In addition to the transplant patients having a fivefold increased likelihood of having type 1 DM, these patients exhibited a longer DM duration, lower BMI, and lower HbA1c levels compared with the control patients. The improved long-term glycemic control in patients who had previously undergone solid organ transplantation might have resulted from the contribution of pancreatic transplantation and vigilant, lifelong follow-up care by our academic institution's transplantation team.

The present study had several limitations that should be acknowledged. First, the nature of the retrospective analysis relied on the accuracy of the electronic medical records for data collection and review, which could only be as valid as the documentation. Second, a measurement bias was a possibility between the study and control groups, although this likelihood was minimized because a single foot and ankle surgeon performed all the operations for both patient groups. We attempted to minimize the measurement bias between the study and control groups by providing all patients with equivalent intraoperative antibiotic prophylaxis and similar perioperative care. The only difference in postoperative care was the use of 800 mg of oral trimethoprim-sulfamethoxazole 3 times weekly for life for the transplant patients. Third, a nonresponder bias was potentially present, because some patients were followed up for a longer period than others (i.e., transplant cohort). We acknowledge that more complications might have been identified if longer follow-up data were available for both patient groups. Fourth, an interviewer bias was potentially present, because the primary surgeon (D.K.W.) determined all outcomes and complications. Fifth, the inclusion of different risk factors might have influenced the incidence of postoperative complications. We attempted to address these issues and confounders through proper matching of study and control groups according to sex, age, and foot and ankle operative time. Sixth, the small sample size of our transplant cohort ($n = 28$) was a weakness that limited our ability to assess the effect of the type of DM, duration of DM, BMI, and HbA1c levels on the postoperative outcomes. Owing to the small sample size, the present study was underpowered to definitively state that no real differences exist between the transplant and control groups. Therefore, a type II error could have been a possibility and would have led us to wrongfully conclude that no significant differences exist between our 2 patient groups. Normally, an a priori power analysis is performed before beginning a study with 80% power and an α of 0.05. The prestudy calculations of an adequate sample size are determined from pilot studies or previous studies, neither of which was available for reference for our diabetic transplant cohort. A post hoc sample size analysis indicated that approximately 1900 transplant patients and 3800 control patients would be necessary to achieve 80% power in detecting a significant difference in overall complications, numbers virtually impossible to achieve with our research objectives and inclusion criteria. Seventh, we acknowledge that our method of identifying eligible patients was another potential weakness of the present study. A coding bias was potentially present, because we searched for eligible patients to include using the diagnosis and procedural codes. We recognize that different clinicians might use alternative methods of coding for similar diagnoses and/or surgical procedures. We recognize that these variables are important in foot and ankle surgery, and our goal is to periodically re-evaluate our transplant patients. Another limitation of the present study was that our 2 groups were not matched for specific surgical procedures, although the operative time was similar. As presented in Table 1, the procedures between the 2 groups were similar but not identical. The transplant group appeared to be representative of a high-risk academic diabetic foot and ankle practice, because 57% of the patients had CN and 50% underwent some type of arthrodesis, in addition to adjunctive procedures such as partial osteotomy, tendon lengthening, and tendon transfer. Our transplant cohort tended to have a greater prevalence of CN ($p = .06$) and foot ulcers ($p = .07$) than our control group.

CN has been closely associated with solid organ transplantation, in particular, simultaneous pancreatic-renal transplantation (19,20). One study reported that nearly 5% of simultaneous pancreatic-renal transplantation patients developed CN during their first post-transplant year, a frequency dramatically greater than that of the general diabetic population (19). Foot and ankle surgeons who treat transplant patients should be aware of the potential for their patients to develop CN owing to the adverse metabolic bone effects of chronic immunosuppressive agents. Bone loss and fractures are frequent complications after solid organ transplantation, and patients who require long-term glucocorticoids for immunosuppression are at increased risk of CN (19).

Owing to the comparable postoperative complication rates between the transplant and nontransplant cohorts, surgeons treating diabetic transplant patients can recommend foot and ankle surgery when needed. Despite the high risk of perioperative complications and comorbidities in the transplant cohort (57% with CN, 93% with peripheral neuropathy), this group did not demonstrate greater rates of adverse outcomes compared with our control group, with the numbers available (3,4). Although our results did not demonstrate differences in outcomes, surgeons should interpret our data within the context of the small sample size of patients studied, because the possibility of a type II error exists. Owing to the increased mortality rates and comorbidities associated with this high-risk group, we recommend preoperative clearance from the transplantation team and medical consultants before performing foot and ankle surgery.

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Table 1

Surgical procedures

Procedure	Transplant Cohort (n = 28)	Control Group (n = 56)
Application of external fixation	4	4
Arthrodesis of the foot or ankle	14	28
Arthroplasty forefoot	1	3
Exostectomy/ostectomy	14	16
Hammertoe correction	10	13
Harvesting of tibial bone graft	2	4
Ligament repair	0	1
Open reduction and internal fixation of foot fracture	1	3
Osteotomy of foot or ankle	5	15
Hardware removal	3	8
Tendon lengthening	8	14
Tendon transfer	3	5
Toe amputation	1	2
Transtibial amputation	1	2
Total number of procedures	67	118

Table 2

Comparison of transplant patients and control patients

Variable	Transplant Patients (n = 28)	Diabetic Control Patients (n = 56)	OR (95% CI)	p Value
Mean age (y)	53.9 ± 7.60	53.4 ± 9.48	—	.48
Sex			—	
Male	18 (64)	36 (64)		1.00
Female	10 (36)	20 (36)		
Operative time (min)	91.9 ± 69.7	90.8 ± 63.4	—	.84
Follow-up period (wk)	84.6 ± 89.9	45.6 ± 34.1	1.01 (1.001 to 1.02)	.004
DM type 1	14 (50.0)	9 (16.7)	5.11 (2.33 to 11.2)	<.001
DM type 2	14 (50.0)	46 (83.7)	0.20 (0.089 to 0.43)	<.001
DM duration (y)	24.2 ± 11.9	12.4 ± 11.4	1.08 (1.04 to 1.13)	<.001
BMI (kg/m ²)	29.0 ± 7.50	33.6 ± 7.61	0.92 (0.85 to 0.99)	.031
Glucose level (mg/dL)	130.3 ± 61.1	149.1 ± 52.6	0.99 (0.98 to 1.01)	.29
Hemoglobin A1c (%)	6.81 ± 1.23	7.69 ± 1.68	0.66 (0.49 to 0.89)	.006
Creatinine level (mg/dL)	2.24 ± 1.87	1.25 ± 1.17	1.64 (0.87 to 3.10)	.13
Neuropathy	26 (92.9)	49 (87.5)	2.17 (0.37 to 12.8)	.39
MNSI score (0 to 10)	7.13 ± 2.71	6.23 ± 2.84	1.13 (0.91 to 1.42)	.27
Insulin use	18 (64.3)	38 (67.9)	0.85 (0.34 to 2.13)	.73
ASA classification	3.00 ± 0.471	2.98 ± 0.301	0.43 (0.07 to 2.51)	.30
Overall complications	7 (25)	16 (28.5)	0.83 (0.33 to 2.08)	.67
Infectious complications	2 (7.1)	7 (12.5)	0.54 (0.09 to 3.09)	.49
Noninfectious complications	5 (17.9)	9 (16.0)	1.14 (0.41 to 3.14)	.81
Mortality	4 (14.3)	0 (0)	NA	—

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; MNSI, Michigan Neuropathic Screening Instrument; OR, odds ratio.

Data presented as mean ± standard deviation or n (%).