

# Factors Affecting Length of Hospital Stay and Mortality in Infected Diabetic Foot Ulcers Undergoing Surgical Drainage without Major Amputation

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This study aimed to investigate factors affecting length of hospital stay and mortality of a specific group of patients with infected diabetic foot ulcer who underwent surgical drainage without major amputation, which is frequently encountered by orthopedic surgeons. Data on length of hospital stay, mortality, demographics, and other medical information were collected for 79 consecutive patients (60 men, 19 women; mean age, 66.1 [SD, 12.3] yr) with infected diabetic foot ulcer who underwent surgical drainage while retaining the heel between October 2003 and May 2013. Multiple linear regression analysis was performed to determine factors affecting length of hospital stay, while multiple Cox regression analysis was conducted to assess factors contributing to mortality. Erythrocyte sedimentation rate (ESR,  $P = 0.034$ ), glycated hemoglobin (HbA1c) level ( $P = 0.021$ ), body mass index (BMI,  $P = 0.001$ ), and major vascular disease (cerebrovascular accident or coronary artery disease,  $P = 0.004$ ) were significant factors affecting length of hospital stay, whereas age ( $P = 0.005$ ) and serum blood urea nitrogen (BUN) level ( $P = 0.024$ ) were significant factors contributing to mortality. In conclusion, as prognostic factors, the length of hospital stay was affected by the severity of inflammation, the recent control of blood glucose level, BMI, and major vascular disease, whereas patient mortality was affected by age and renal function in patients with infected diabetic foot ulcer undergoing surgical drainage and antibiotic treatment.

**Keywords:** Diabetic Foot; Foot Ulcer; Length of Stay; Mortality

## INTRODUCTION

Diabetic foot ulcer is a common and serious complication of diabetes mellitus (DM), which may require amputation or may lead to death (1-7). Concurrent infection with diabetic foot ulcer often aggravates disease progression and impedes wound healing and recovery, affecting patient prognosis (3). This condition frequently requires surgical drainage and subsequent antibiotic treatment, resulting in prolonged hospital stay; and despite these medical efforts and resources, treatment often results in death.

Orthopedic surgeons often encounter grave patients with diabetic foot ulcers and concomitant infections, requiring surgical treatment. Previous studies have reported that the length of hospital stay, as a surrogate of recovery time, and mortality are important outcomes of diabetic foot ulcers (2,3). However, factors affecting these outcomes have not been investigated in detail in patients with infected diabetic foot ulcers, requiring sur-

gical treatment. Knowledge of these factors would enable orthopedic surgeons to better predict patient prognosis and to provide such patients with clinical information on controllable prognostic factors. These measures would help reduce a considerable sociomedical burden since DM is increasing in incidence, and infected diabetic foot ulcer is a serious complication of DM frequently requiring hospital admission.

Therefore, the aim of our study was to investigate factors affecting the length of hospital stay and mortality of patients with infected diabetic foot ulcers requiring surgical drainage.

## MATERIALS AND METHODS

### Subjects and data collection

Consecutive patients with diabetic foot ulcers were enrolled in our hospital between October 2003 and May 2013; of these, patients with infected diabetic foot ulcers who underwent surgical drainage were selected. Patients without apparent infections

and those who had undergone immediate primary below-knee amputations were excluded from the study. Electronic patient medical records were reviewed, and data were collected on age, sex, body mass index (BMI), length of hospital stay, mortality, Wagner ulcer classification (Wagner stage), operative procedures (incision and debridement or primary major amputation), major vascular disease (cerebrovascular accident [CVA] or coronary artery disease [CAD]), ankle-brachial index [ABI] using Doppler, bacterial culture reports, and blood test results obtained on hospital admission (including hemoglobin, white blood cell count, total protein, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], blood urea nitrogen [BUN], serum creatinine [Cr], aspartate aminotransferase [AST], alanine aminotransferase [ALT], fasting blood glucose [Glu], and glycated hemoglobin [HbA1c]). When blood samples were obtained, they were immediately processed, refrigerated (if necessary), and transported to the central testing department in our hospital, where they were immediately analyzed.

The length of hospital stay was defined as the duration from the day of admission to the day of discharge, related only to the diagnosis and treatment of infected diabetic foot ulcers. We included Wagner stages III, IV, and V because stages I and II are not concurrent with infection according to the definition (6,8). We defined major amputation as amputation performed above the ankle level, such as Syme's amputation, below-knee amputation, and above-knee amputation.

Surgical debridement and drainage were performed by eliminating all infected and nonviable tissues under spinal or general anesthesia. Intraoperative bacterial culture was performed using the tissue debris. If the toes were not viable, they were amputated at the time of debridement. Either a Penrose drain was placed to enhance postoperative drainage or the surgical wound remained open. Patients with suspicious ischemic foot were referred to the vascular surgery department preoperatively, and concurrent vascular intervention or bypass surgery was performed at the time of orthopedic surgery, based on the vascular surgeon's decision and ABI test.

Intravenous antibiotics were administered postoperatively according to the bacterial culture and antibiotic-sensitivity reports. Patients were discharged when the surgical wound was stable with minimal or no oozing, and blood test results (ESR and CRP) showed continuous improvement in inflammation.

### Statistical analysis

To summarize patient demographics, descriptive statistics such as mean, SD, and proportion were used. The Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables. Multiple regression analysis with stepwise selection was performed to examine the effects of the baseline variables, in which length of hospital stay was used as the dependent variable. To determine the survival rate and the hazard

ratio of mortality, we performed multiple Cox proportional hazards analysis with stepwise selection. The following factors were included in the analysis as possible predictors or confounders: age, sex, length of hospital stay, mortality, Wagner stage, ABI, ESR, CRP, BUN, Cr, AST, ALT, Glu, HbA1c, BMI, CVA, and CAD. All statistics were 2-tailed, and *P* values of  $< 0.05$  were considered significant. All analyses were performed using SPSS Statistics 20.0 for Windows (IBM Corporation, Armonk, NY, USA).

### Ethics statement

This retrospective study was approved by the institutional review board of Seoul National University Bundang Hospital (IRB No. B-1308/216-109). The board waived the patients' informed consent.

### RESULTS

A total of 330 patients with diabetic foot ulcers were enrolled based on electronic medical records; of these, 76 were excluded because they had no sign of infection and were assigned to Wagner stage I or II. Of the 254 patients with infected diabetic foot ulcers, 165 were treated conservatively without surgery were excluded, which were assigned to Wagner stage I and II with superficial infection. Ten patients who underwent primary below-knee amputation also were excluded, leaving 79 patients (60 men, 19 women; mean age, 66.1 [SD, 12.3] yr) with infected diabetic foot ulcers to be included in the data analyses (Fig. 1).

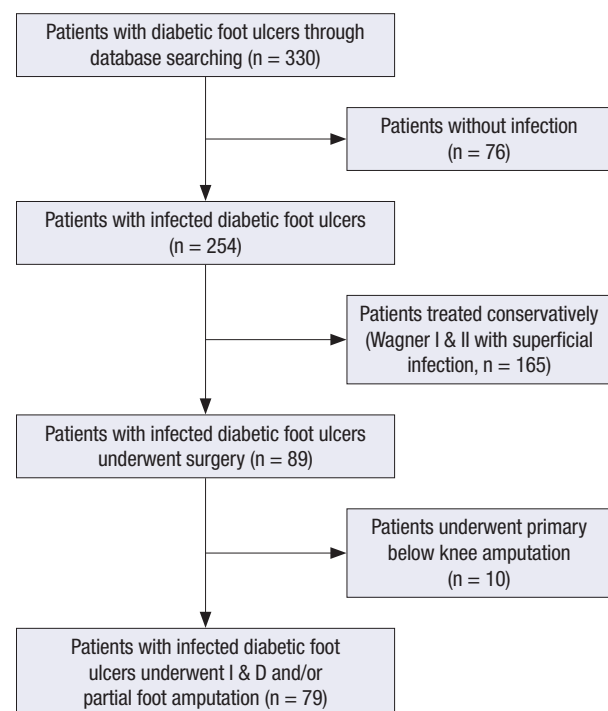


Fig. 1. This flowchart shows the strategy to identify patients with infected diabetic foot ulcers who require surgical drainage.

**Table 1.** Patient demographics and characteristics

Characteristics	Findings
Patients number	79
Mean age (yr)	66.1 (SD 12.3)
Body mass index (kg/m <sup>2</sup> )	22.2 (SD 3.5)
Sex	
Male	60 (75.9%)
Female	19 (24.1%)
Admission days	37.8 (SD 30.5)
Mortality (dead/alive)	10/69
Follow up duration (mon)	20.0 (SD 22.3)
Wagner classification	
Stage III	67 (84.8%)
Stage IV	12 (15.2%)
CVA and CAD	14/79 (17.7%)
ABI	0.98 (SD 0.31)
Hemoglobin (g/dL)	10.7 (SD 1.7)
WBC count (10 <sup>3</sup> /μL)	10.6 (SD 4.2)
Total protein (g/dL)	6.6 (SD 0.8)
ESR (mm/h)	68.6 (SD 29.3)
CRP (mg/L)	7.8 (SD 7.6)
BUN (mg/dL)	24.6 (SD 17.3)
Cr (mg/dL)	2.5 (SD 2.7)
AST (IU/L)	26.9 (SD 21.9)
ALT (IU/L)	25.5 (SD 38.1)
Glucose (fasting) (mg/dL)	185.5 (SD 112.6)
Hemoglobin A1c (%)	8.6 (SD 2.0)

CVA, cerebrovascular accident; CAD, coronary artery disease; ABI, ankle brachial index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BUN, blood urea nitrogen; Cr, serum creatinine; AST, aspartate aminotransferase; ALT, alanine aminotransferase. Normally distributed data recorded as mean (standard deviation).

The average length of hospital stay and the follow-up period were 37.8 (SD, 30.5) days and 20.0 (SD, 22.3) months, respectively. During the follow-up period, 10 patients (12.7%) died. The cause of deaths were pneumonia in three patients, CVA in two, heart failure in two, CAD in one, sepsis in one, and lung cancer in one. The survival rates at 12- and 28-months postoperatively were found to be 88.8% and 80.9%, respectively. There were 67 patients assigned to Wagner stage III and 12 to Wagner stage IV (Table 1). Bacterial culture reports revealed 58 patients had monomicrobial infection, 4 had polymicrobial infection, and 17 had sterile culture. Overall, 79 bacteria were isolated from 62 patients. *Staphylococcus aureus* was the most common pathogen isolated, followed by *Pseudomonas aeruginosa*, *Morganella morganii*, and *Escherichia coli*. Antibiotics that showed high sensitivity rate for Gram negative bacteria were; amikacin (92.9%), imipenem (92.9%), piperacillin/tazobactam (88.1%), ceftazidime (81.0%), cefotaxime (80.6%), and aztreonam (78.6%). Antibiotics that showed high sensitivity rate for Gram positive bacteria were; vancomycin (100%), teicoplanin (100%), rifampin (100%), trimethoprim/sulfamethoxazole (90.9%), and chloramphenicol (87.5%).

In multiple linear regression analysis, BMI ( $P = 0.001$ ), presence of major vascular disease (CVA or CAD) ( $P = 0.004$ ), HbA1c ( $P = 0.021$ ), and ESR ( $P = 0.034$ ) were found to be significant in-

**Table 2.** Effects of BMI, CVA&CAD, HbA1c and ESR on hospital stay in multiple linear regression model with stepwise selection method

Dependent variable (hospital stay)	Beta	Standard error	t	P value
Constant	-115.525	26.293	-4.394	0.001
BMI	4.016	0.848	4.736	0.001
CVA and CAD	24.368	6.635	3.673	0.004
HbA1c	2.839	1.041	2.728	0.021
ESR	0.223	0.091	2.457	0.034
Age	0.243	-	1.558	0.154
Sex	0.177	-	1.123	0.291
AST	-0.192	-	-1.122	0.291

R<sup>2</sup> = 0.742. BMI, body mass index; CVA and CAD, cerebrovascular accident and coronary artery disease; ESR, erythrocyte sedimentation rate.

**Table 3.** Effects of age and BUN on mortality in multiple Cox regression model with stepwise selection method

Dependent variable (mortality)	HR	95% CI	SE	P value
Age	1.557	1.141 to 2.216	0.159	0.005
BUN	1.112	1.014 to 1.220	0.047	0.024
BMI	0.867	0.671 to 1.120	0.130	0.274

HR, hazard ratio; SE, standard error; CI, confidence interval; BUN, blood urea nitrogen.

dependent factors affecting the length of hospital stay (Table 2).

Multiple Cox regression analysis showed that age ( $P = 0.005$ ) and serum BUN ( $P = 0.024$ ) were significant independent factors affecting mortality (Table 3).

## DISCUSSION

This study investigated factors affecting the length of hospital stay and mortality in the management of infected diabetic foot ulcers requiring orthopedic surgery without major amputation. Our study involved a different cohort than that used in previous studies investigating the prognosis of diabetic foot ulcers in that, our patients underwent orthopedic surgery (drainage and/or partial foot amputation) for infected diabetic foot ulcers. Our results showed that the length of hospital stay was affected by the severity of inflammatory reaction (ESR), the recent control of blood glucose level (HbA1c), BMI, and major vascular disease (CVA or CAD). Patient mortality was affected by age and renal function (BUN).

In this study, length of hospital stay was used as a surrogate of recovery time from infected diabetic foot ulcer. Our study showed a greater length of hospital stay than that reported in other studies (2,7). This is because our cohort included severer diabetic foot ulcers with concomitant infection than that taken in a previous study (2), and we endeavored to salvage the limb without major amputation, which required subsequent intravenous antibiotic treatment causing prolonged hospital admission compared with that in another study (7). On the other hand, it should be considered that the length of hospital stay can be

affected by differences in medical care and socioeconomic systems used in different hospitals (1,9). This study was performed in South Korea, where more than 95% of the population are insured by National Health Insurance System and are considered to easily access medical system.

In our study, length of hospital stay was affected by severity of inflammatory reaction (ESR), the recent control of blood glucose level (HbA1c), BMI, and major vascular disease (CVA or CAD) at the time of hospital admission. These results are concurrent with those of a previous study, which reported that HbA1c level is an independent predictor for length of hospital stay in diabetic patients with sepsis (10). Another previous study showed that BMI was associated with immunologic dysfunction (11), which could explain our result that the patients with higher BMI showed longer length of hospital stay in our infected diabetic foot cohort. There is little supportive evidence on whether the presence of major vascular disease (CVA or CAD) increases the length of hospital stay in patients with infected diabetic foot ulcers. One possible explanation for this result is that patients with major vascular diseases are likely to take anticoagulant medication, which can increase the incidence of excessive oozing and hematoma at the surgical site, providing a media for bacterial growth and impeding infection control, as observed in other orthopedic surgeries (4,12). Another explanation could be the higher incidence of concurrent peripheral arterial disease in patients with CVA and CAD, which impedes wound healing progression (13). However, this issue requires further investigation in patients with diabetes.

The mortality rate of patients with infected diabetic foot ulcers was associated with age and renal function (BUN) in our study, which is supported by the results of a previous study (14). Regarding renal function, Lewis et al. (15) showed that the presence of end-stage renal disease and chronic kidney disease were independent risk factors for the development of diabetic foot ulcers, and patients with renal diseases also had higher mortality rates than patients without renal diseases. Previous studies have reported that patients with diabetic foot ulcers may experience higher mortality rates than expected (16,17). Boyko et al. (18) noted that diabetic foot ulceration serves as a marker for other associated diseases that increase mortality risks.

Our bacterial culture specimens were obtained intraoperatively to reduce the contamination of normal skin flora. A considerable portion of our specimens showed sterile culture, but this is comparable to the results of a previous study reporting sterile culture in 21% of the patients (19). This high rate of sterile culture might have been caused by preoperative exposure to antibiotic treatment before the culture specimens were obtained. The most common pathogens identified were *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which suggests that they should be the targets of empirical antibiotic treatment for diabetic foot infection. However, the culture results did not affect

the length of hospital stay or mortality of patients with infected diabetic foot ulcers in this study. Antibiotics sensitivity test showed amikacin (92.9%) and imipenem (92.9%) were drug of choice for Gram negative bacteria, and vancomycin (100%), teicoplanin (100%), and rifampin (100%) were that for Gram positive bacteria. Amikacin and vancomycin need to be used cautiously for patients with diabetic nephropathy.

There are some limitations to be addressed in this study. First, this study was retrospective; therefore, the data were not strictly controlled, and the accuracy of the clinical data depended on medical record review. Second, our hospital is a tertiary referral center for complex foot and ankle diseases; therefore, our results may not be applied to the general diabetic population. Third, the follow-up period was somewhat short, which could have affected accurate analysis of mortality data. Fourth, data on diabetic neuropathy was not included in the data analysis, which is considered to be one of important factor in the development and progression of diabetic foot ulcer.

The length of hospital stay was affected by the severity of inflammation (ESR), the recent control of blood glucose level (HbA1c), BMI, and major vascular disease (CVA or CAD). Patient mortality was affected by age and kidney function (BUN). These results provide useful clinical information regarding the prognosis of patients with infected diabetic foot ulcers who undergo surgical drainage and antibiotic treatment.

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## DISCLOSURE

The authors have no potential conflicts of interest to disclose.

## AUTHOR CONTRIBUTION

Conception and coordination: Kim TG, Park MS, Lee KM, Lee TS, Kim BK. Acquisition of data: Kwon SS, Yoon C, Jung KJ, Lee TS, Kim BK. Analysis of data: Moon SY, Park MS, Kwon SS, Yoon C, Jung KJ. Manuscript preparation: Kim TG, Moon SY, and Lee KM. Manuscript approval: all authors.

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