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Depth and combined infection is important predictor of lower extremity amputations in hospitalized diabetic foot ulcer patients

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Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, St. Paul's Hospital, The Catholic University of Korea, 180 Wangsan-ro, Dongdaemun-gu, Seoul 02559, Korea Tel: +82-2-958-2379 Fax: +82-2-968-7250 E-mail: leejm68@catholic.ac.kr **Background/Aims:** As the prevalence of diabetes mellitus and its complications increase rapidly, diabetic foot ulcers (DFUs), which are a major diabetic complication, are expected to increase. For prevention and effective treatment, it is important to understand the clinical course of DFUs. The aim of this study was to investigate the natural course and predictors of amputation in patients with DFUs who required hospitalization

Methods: A total of 209 patients with type 2 diabetes, aged 30 to 85 years, who visited emergency department or needed hospitalization due to DFUs were consecutively enrolled from May 2012 to January 2016, by retrospective medical record review. The main outcome was lower extremity amputation (LEA).

Results: Among 192 patients who completed follow-up, 113 patients (58.9%) required LEAs. Compared to patients without amputation, baseline levels of white blood cell counts and C-reactive protein were higher in patients with amputation. In addition, bone and joint involvement was more frequently observed in patients with amputation. Multivariable regression analysis revealed that combined infection (odds ratio [OR], 11.39; 95% confidence interval [CI], 2.55 to 50.93; *p* = 0.001) and bone or joint involvement (OR, 3.74; 95% CI, 1.10 to 12.70; *p* = 0.035) were significantly associated with an increased risk of LEA.

Conclusions: The depth of the wound and combined infection of DFU, rather than the extent of the wound, were significant prognostic factors of LEAs in patients with type 2 diabetes.

Keywords: Diabetes mellitus; Diabetic foot; Ulcer; Prognosis; Amputation

INTRODUCTION

The prevalence of type 2 diabetes is rapidly increasing. In 2012, diagnosed and undiagnosed diabetes among people aged 20 years or older was 12.3% in the United States [1]. The World Health Organization reported that the global prevalence of diabetes in adults over 18 years in 2014 was estimated to be 9% [2], and the estimated number of patients with diabetes worldwide was reported as 415 million in 2015 [3]. In Korea, according to the Korean National Health and Nutrition Examination Survey 2011, the prevalence of diabetes in Korea was 10.5% in adults over 30 years or older [4]. As the prevalence of diabetes mellitus (DM) and its complications increase rapidly, the incidence of diabetic foot ulcer (DFU) is also expected to increase [5]. According to the data from 'Di-



abetes in Korea 2007,' the 44.8% of the foot amputated patients in 2003 had diabetes [6]. Patients with diabetes were 10.1 times more likely to undergo foot amputation, and 7.8 times more likely to have foot ulcer [6]. In addition, about 73,000 non-traumatic lower-limb amputations were performed in adults aged 20 years or older with diagnosed diabetes in the United States in 2010 [1].

DFU is associated with a significant portion of admission, medical costs, disability, and mortality, and is the leading cause of non-traumatic lower extremity amputation (LEA) [7,8]. According to one study performed in Korea from December 1994 through December 2002, total medical costs (per capita) of foot amputation and foot ulcer in patients with diabetes were 2.0 and 1.7 times higher, respectively, than those of non-diabetic patients [9]. Mean hospital stay of foot amputation and DFU were 1.6 and 1.3 times longer, respectively, than those of non-diabetic patients [9]. Considering this increasing prevalence of diabetic vascular complications and its related health burden, early detection and prompt management of DFU are urgently required. In addition, for prevention and effective treatment of DFU, it is important to understand the risk factors and clinical course of DFU in patients with type 2 diabetes.

This retrospective cohort study aimed to investigate the predictors of LEA in patients with type 2 diabetes hospitalized for DFU.

METHODS

Patients

A total of 380 patients with type 2 diabetes, aged 30 to 85 years, who visited St. Vincent's Hospital in Korea for DFU management were recruited consecutively from May 2012 to January 2016 by retrospective medical record review. Among these patients, 229 subjects who visited the Emergency Department or needed hospitalization for DFU care were included. Twenty patients with type 1 DM, gestational DM, or any severe illness, such as liver cirrhosis, heart failure, and malignancy were excluded from the study. The patients with too little available clinical data from the medical record were also excluded (Fig. 1). The Catholic Medical Center Ethics Committee and the Institutional Review Board (IRB No: VC15OISI0207) approved this study. Written informed consents were obtained.

Information about the clinical and demographic characteristics was collected by careful medical record review. Hypertension was defined as systolic blood pressures \geq 140 mmHg, diastolic blood pressures \geq 90 mmHg, or the use of antihypertensive medications. Fasting and postprandial plasma glucose levels were measured using an automated enzymatic method (model 7600-110, Hitachi, Tokyo, Japan), and glycated hemoglobin (HbA1c) levels were measured using high-performance liquid chromatography with a reference range of 4.4% to 6.4% (Bio-Rad, Montreal, QC, Canada). Total cholesterol, triglycerides, low density lipoprotein, and high density lipoprotein cholesterol were measured enzymatically using an automatic analyzer (model 7600-110). Estimated glomerular filtration rate (eGFR) was assessed using the 4-component Modification of Diet in Renal Disease equation [10]. Baseline white blood cell (WBC) counts and C-reactive protein (CRP) were also measured. We defined smoking status as current or past smokers. Coronary artery disease was defined as a history of diag-



Figure 1. Study flow diagram. DFU, diabetic foot ulcer; ED, Emergency Department.

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nosed angina pectoris by coronary artery angiography, myocardial infarction, or coronary revascularization (coronary bypass surgery or coronary angioplasty) [11]. Stroke history included previous transient ischemic attack or cerebral infarction [11]. Diabetic retinopathy was defined as non-proliferating diabetic retinopathy of any severity and proliferating diabetic retinopathy, which was confirmed by ophthalmologist. Peripheral artery disease (PAD) was defined as ankle-brachial index (ABI) \leq 0.9 or compatible findings of PAD in peripheral arterial angiography or computed tomography (CT).

DFU outcome evaluation

We classified the DFU wounds according to extent, depth, and severity of infection of each wound at initial visit. When patient had multiple DFUs, the most significant ulcer was selected as the wound for assessment. The extent of the wound was estimated by multiplying the largest diameter by the second largest diameter measured perpendicular to the first diameter. We classified ulcers into one of the following groups: < 10, 10 to 25, and \geq 25 cm². We further classified ulcers by depth: superficial soft tissue, fascia/muscle/tendon level, and bone or joint level. An infected ulcer was defined as a wound with loss of epithelial continuity of overlying skin with both physical findings, such as pus or redness, heat sensation, fluctuation of surrounding tissue (which suggests fluid accumulation) [5], and one of the following signs or abnormal laboratory findings: fever, WBC $\ge 10 \times 10^9$ /L (normal reference range, 4.0 to 10.0 × 10⁹/L), or CRP \ge 0.50 (normal reference range, 0.01 to 0.47 mg/dL). All of the wounds were classified according to the University of Texas classification [5]. The main outcome in this study was LEA, including minor and major amputations. Minor amputation included toe, ray, transmetatarsal, and below-knee amputation. Major amputation was defined as above-knee amputation [12]. We also collected data on hospitalization days and deaths related to DFUs.

Management protocol for DFU and indications for amputations

When the DFU patients initially visited our hospital, the multidisciplinary team including an orthopedist or plastic surgeon, vascular surgeon, infectious disease specialists, and an endocrinologist decided the management of the DFU. After initial debridement, an assessment of the wound was performed. If the orthopedist or plastic surgeon decided that the wounds did not indicate a need for an emergency amputation, studies for the state of blood supply for the wound (CT angiography for peripheral arteries or arteriography) were done. And if the sign of infection was combined with the DFU, wound culture and administration of the empirical antibiotics (in most cases, 3rd line cephalosporins) were performed. Additionally, when extensive muscle necrosis or osteomyelitis was suspected, we considered the magnetic resonance imaging. After completion of all the above evaluation, the team determined whether to amputate the wound or not.

The followings are the indications for amputation at our hospital: (1) infection: life-threatening sepsis or septic shock; (2) blood supply to the tissues: severe peripheral arterial disease (impossible revascularization); and (3) other: extensive muscle necrosis. However, if the surgeon decides that the wound will heal, only debridement can be done to an ulcer which only involves a toe or part of a foot.

Statistical analysis

The statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the mean ± SD values or median (interquartile range), and categorical variables were presented as percentages. Continuous variables were compared with independent Student t tests, while categorical variables were compared using a chi-square tests and Fisher exact tests. Age, sex, smoking history, duration of DM, hypertension, prior amputation history, WBC, CRP, eGFR, oral anti-diabetic medication, antiplatelet agents, statin, presence of PAD, the depth and size of the wounds, and combined infection were included in the univariable analysis. Because there were not enough medical records about whether patients use insulin, the percentage of missing data regarding insulin use was 61.7%, which has potential for bias. Therefore, we excluded insulin use in statistical analyses. The predictive factors were analyzed using the multivariable logistic regression method, including those that were statistically significant in the univariable analysis. A p <0.05 was considered to be statistically significant. The results were reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Table 1. Baseline characteristics	s of study	participants
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Characteristic	Non-LEA (n = 79)	LEA (n = 113)	þ value
Male sex	25.0	37-4	0.395 ^a
Age, yr	61.8 ± 13.9	62.8 ± 12.5	0.616 ^b
BMI, kg/m ²	24.2 ± 3.7	23.5 ± 3.1	0.284 ^b
Hospital days, day	19.0 (10.0–31.0)	26.0 (18.0–38.0)	< 0.001 ^c
Duration of DM, yr	16.2 ± 10.3	16.0 ± 10.7	0.141 ^b
Smoking	31.6	27.4	0.355 ^a
Comorbidities			
Hypertension	21.9	22.4	0.294 ^a
ESRD	5.7	7.0	0.375 ^a
Stroke	4.7	7.8	0.423 ^a
CAD	3.1	6.8	0.271 ^a
Diabetic retinopathy	14.6	13.0	0.335 ^a
Laboratory findings			
WBC count, $\times 10^9/L$	9.7 ± 4.3	12.0 ± 5.9	0.004 ^b
CRP, mg/dL	4.7 ± 6.8	8.2 ± 8.0	0.002 ^b
Serum creatinine, mg/dL	1.1 (0.85–1.9)	1.00 (0.8–1.7)	0.539 ^a
eGFR, mL/min/1.73 m ²	54.6 (35.3–83.2)	64.0 (38.4–87.0)	0.536 ^a
Fasting plasma glucose, mg/dL	160.3 ± 78.2	184.2 ± 74.1	0.214 ^b
Baseline HbA1c, %	8.9 ± 2.3	9.0 ± 2.3	0.675 ^b
Total cholesterol, mg/dL	161.6 ± 54.6	159.2 ± 52.4	0.794 ^b
Triglyceride, mg/dL	141.4 ± 89.0	121.8 ± 72.0	0.165 ^b
HDL-C, mg/dL	35.8 ± 11.4	32.2 ± 10.3	0.058 ^b
LDL-C, mg/dL	95.3 ± 33.1	95.7 ± 40.4	0.981 ^b
ABI	0.97 ± 0.27	0.95 ± 0.27	0.650 ^b
Medications			
Oral anti-diabetic medications	23.5	34.9	0.240 ^a
Antiplatelet agents	14.6	20.3	0.514 ^a
Statin	13.5	15.6	0.297 ^a

Values are presented as percentage, mean \pm SD, or median (interquartile range). p < 0.05 was considered to be statistically significant. LEA, lower extremity amputation; BMI, body mass index; DM, diabetes mellitus; ESRD, end-stage renal disease; CAD, coronary artery disease; WBC, white blood cell; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ABI, ankle-brachial index.

^aChi-square tests and Fisher exact tests is used.

^bIndependent Student *t* tests is used.

^cMann-Whitney test is used.

RESULTS

Baseline characteristics of the study population

A total of 209 patients (131 males [62.7%], 78 females [37.3%]) were included in the study. After excluding 17 patients (8.1%) who were lost to follow-up, 192 patients

were analyzed.

Mean age was 62.7 ± 13.3 years, and mean duration of diabetes was 16.1 ± 10.5 years, respectively. Median hospitalization days was 23.0 days (interquartile range, 14.0 to 34.0) (Table 1).

During the follow-up, 38 patients (19.8%) needed re-



Table 2. Characteristics of diabetes mellitus foot ulcer and clinical course

Characteristic	Non-LEA (n = 79)	LEA (n = 113)	p value
Deformity	4.2	3.6	0.222 ^a
Trauma history	9.9	17.7	0.265 ^ª
Prior amputation history	3.7	6.2	0.808 ^a
Location of DFU			< 0.001 ^a
Planta	3.1	2.6	
Dorsum	4.7	3.6	
Toe	18.8	45.8	
Others	14.6	6.8	
Combined PAD	18.2	36.0	0.003 ^a
Extent of DFU, cm ²			0.059 ^a
< 10	16.1	14.1	
10 to < 25	8.4	7.3	
≥ 25	3.7	9.9	
Bone or joint involvement of DFU	6.8	26.6	< 0.001 ^a
Infection of DFU	19.3	55.7	< 0.001 ^a
Severity of stenosis of peripheral arteries of lower limbs ^b			0.405 ^a
Mild	2.1	2.1	
Moderate	2.1	6.3	
Severe	6.3	20.8	
Angioplasty during whole follow-up	10.9	13.0	0.493 ^a
Mean HbA1c during the follow-up	8.6 ± 2.1	8.4 ± 1.8	0.133 ^c
Re-hospitalization	6.8	11.0	0.470 ^a
Death	0.5	2.1	1.000 ^d

Values are presented as percentage or mean \pm SD. *p* < 0.05 was considered to be statistically significant.

LEA, lower extremity amputation; DFU, diabetic foot ulcer; PAD, peripheral artery disease; HbA1c, glycated hemoglobin. ^aChi-square tests and Fisher exact tests is used.

^bFindings from computed tomography angiography or percutaneous peripheral angiography. We classified the severity of stenosis of any arteries that perfused the DFU area as mild, moderate, and severe, which were confirmed by the expert radiologist or vascular surgeons.

^cIndependent Student *t* tests is used.

^dMann-Whitney test is used.

hospitalization because of worsening of initial DFU lesion or newly developed DFU (Table 2). Five enrolled patients (2.6%) died during hospitalization (four patients died from sepsis and one patient died from acute myocardial infarction).

Among this population, 113 patients (58.9%) required amputations (97 minor and 16 major amputations). Baseline levels of WBC counts and CRP were higher in the LEA group than those of the non-LEA group. However, there were no significant differences in duration of diabetes, presence of end-stage renal disease, cardiovascular disease, glycemic control status, lipid profile, and use of antiplatelet agents between LEA and non-LEA groups (Table 1).

Comparison between the group with LEA and non-LEA

Median hospital days were longer in the LEA group than in the non-LEA group (26 days vs. 19 days, p < 0.001) (Table 1). There was no statistical difference in prior amputation history or deformity between LEA and non-LEA group. Also, there was no statistical difference in the



Table 3. Logistic regression	n analysis for risk factors of	flower extremity amputation
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V	Univariable analysis		
variable	Odds ratio (95% CI)	p value	
Age	1.01 (0.98–1.03)	0.607	
Male sex	1.13 (0.63–2.05)	0.677	
Smoking	0.84 (0.45–1.59)	0.595	
Duration of DM	1.00 (0.97–1.03)	0.929	
Hypertension	0.71 (0.39–1.29)	0.257	
Prior amputation history	1.22 (0.46–3.25)	0.694	
WBC \geq 10, \times 10 ⁹ /L	1.92 (1.07–3.44)	0.030	
$CRP \ge 6, mg/dL$	3.46 (1.83–6.53)	< 0.001	
eGFR	1.00 (0.10–1.01)	0.409	
Oral anti-diabetic medications	1.34 (0.70–2.56)	0.384	
Antiplatelet agents	1.45 (0.51–1.81)	0.071	
Statin	0.79 (0.41–1.52)	0.485	
PAD	2.78 (1.41–5.49)	0.003	
Wound size, cm ²			
<10	1.00		
10 to < 25	1.01 (0.42–2.43)	0.992	
≥ 25	3.12 (1.14–8.54)	0.027	
Bone or joint involvement of DFU	4.11 (2.04–8.29)	< 0.001	
Combined infection of DFU	20.24 (7.96–51.49)	< 0.001	

CI, confidence interval; DM, diabetes mellitus; WBC, white blood cell; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; PAD, peripheral artery disease; DFU, diabetic foot ulcer.

mean HbA1c during whole follow-up period. The most common site for DFU was toe in both non-LEA and LEA group. While total prevalence of PAD was more prevalent in LEA patients, the total number of angioplasty procedures, including percutaneous ballooning and/or stenting and surgical bypass of peripheral artery during the whole follow-up period, was not significantly different in both groups. However, both infected ulcer and ulcer with bone or joint invasion were more frequently observed in LEA patients (Table 2).

We searched the risk factors for LEA (Table 3). After adjustment for age, smoking, presence of hypertension or PAD, prior amputation history, eGFR, wound extent, combined infection, and bone or joint involvement of ulcer, multivariable logistic regression analysis results showed that combined PAD (OR, 4.39; 95% CI, 1.33 to 14.55; p = 0.016), combined infection of DFU (OR, 11.39; 95% CI, 2.55 to 50.93; p = 0.001), and the depth (bone or joint involvement of ulcer) (OR, 3.74; 95% CI, 1.10 to 12.70; p = 0.035) were significant prognostic factors in patients with type 2 diabetes who needed hospitalization due to DFUs (Table 4).

DISCUSSION

In this retrospective cohort study, we investigated the clinical outcome of DFUs in patients with type 2 diabetes who visited the Emergency Department or required hospitalization via outpatient clinic due to DFUs, and analyzed the data of those patients to illustrate several predictors of LEA.

DFU is a disastrous complication of diabetes, often leading to LEA. According to data from the National Hospital Discharge Survey, 28.4 LEA events occur per 10,000 patients with diabetes, and LEA among adults with diabetes was 10 times higher than for those without diabetes in 2010 [13].



Table 4. Logistic regression analysis for risk factors of lowe	r
extremity amputation	

Variable	Multivariable analysis		
variable –	Odds ratio (95% CI)	p value	
Age	1.01 (0.96–1.06)	0.798	
Smoking	0.76 (0.19–3.03)	0.694	
Hypertension	0.57 (0.18–1.87)	0.355	
Prior amputation history	2.03 (0.33–12.53)	0.445	
eGFR	1.00 (0.99–1.01)	0.915	
PAD	4.39 (1.33–14.55)	0.016	
Wound size, cm ²			
< 10	1.00		
10 to < 25	0.52 (0.14–1.89)	0.320	
≥ 25	1.91 (0.43–8.45)	0.392	
Bone or joint involvement of DFU	3.74 (1.10–12.70)	0.035	
Combined infection of DFU	11.39 (2.55–50.93)	0.001	

CI, confidence interval; eGFR, estimated glomerular filtration rate; PAD, peripheral artery disease; DFU, diabetic foot ulcer.

There have been many studies about the risk factors for DFU development; several risk factors for DFU have been reported, such as male sex, older age, history of previous ulcer, smoking, longer duration of diabetes, hypertension, neuropathy, PAD, deformity of foot, poor glycemic control, nephropathy, retinopathy, and nephropathy, etc. [14-17]. In contrast, there are not many longitudinal studies for prognosis of DFU have been reported. Several studies suggested the predictors of LEA such as older age, nephropathy, peripheral arterial disease, sensory neuropathy, uncontrolled DM, and infection [18]. However, there are still not many prospective cohort studies with a multicenter and relatively large sample size to evaluate the predictors of LEA at the present time.

After initial assessment of DFU, a treatment strategy should be established according to the proven risk factors and severity of each wound, as many clinical practice guidelines recommend [2]. Therefore, prognosis of DFU and predictors of LEA should be well understood [19].

The LEA rate (58.9%) in this study was higher than

those of other epidemiological studies of LEA for DFU (13.7%) [17]. This can be explained by higher baseline severity of the DFU wound (according to University of Texas classification, 64 patients [33.3%] were over class IIB), as many of our patients were admitted via emergency room for untreated chronic wound or referred from primary care for unhealed wound despite treatment. Lower limb amputation due to DFUs contributes to increased medical costs. Depending on hospitalization/non-hospitalization, diabetic foot amputation was associated with 1.6 or 2.1 times more annual days of healthcare use, and 2.0 or 2.3 times higher total medical cost than non-diabetic foot amputation. DFU was associated with 1.7 or 3.2 times higher total medical cost [6].

One of the important predictors for LEA in this study was depth of wound. On the basis of anatomy of foot and several classification system, we classified ulcers by depth: superficial soft tissue, fascia/muscle/tendon level, and bone or joint level [20]. Whether or not DFU invades the bone or joint level may be an especially important factor for prediction of prognosis. While several studies regarded the extent of the wound as an important factor related to LEA, it was not a significant predictor of LEA in our analysis [20]. This may suggest that decisions in the management of DFU could be dependent on the depth of wound, rather than extent of the wound.

Other predictors of LEA included the presence of PAD and the combined infection of ulcer. PAD is most easily detected by the ABI that is generally used. An angiography may reveal significant macrovascular disease requiring intervention. In this study, PAD was defined as ABI \leq 0.9 or compatible findings of PAD in peripheral arterial angiography or CT. In terms of degree of ischemia, arterial oxygen supply can also be measured by transcutaneous oximetry. A transcutaneous oxygen tension higher than 30 mmHg correlates with a high likelihood of wound healing. However, transcutaneous oxygen tension requires expensive equipment and a trained technician, and it cannot be routinely used [18]. Although there was more moderate to severe stenosis of arteries in LEA patients, there was not a statistically significant difference between patients with LEA and non-LEA.

A total of 76 patients among 192 DFU (39.6%) had a percutaneous lower extremity angiography or lower extremity CT angiography at baseline examination. We classified the severity of stenosis of any arteries that perfused the DFU area as mild, moderate, and severe, which were confirmed by the expert radiologist or vascular surgeons. Although there was more moderate to severe stenosis of arteries in LEA patients, there was not a statistically significant difference between patients with LEA and non-LEA (Table 2). However, we believe that the statistical analysis for the characteristics of vascular stenosis would not be enough due to the small number of PAD evaluation.

There are many studies that suggest combined infection of DFU as a poor prognostic factor [21]. Therefore, pathogen-specific antibiotics therapy is one of the important factors for optimal treatment of DM foot infection, and should be included in the protocol for managing DFU in each hospital. There are several points to consider in the development of the protocol. First, the frequency and range of resistance to antibiotics are different in many regions [21]. Therefore, epidemiologic studies to investigate the pathogen that is the most common or the most virulent in each hospital are essential. Each pathogen's resistance to antibiotics also should be investigated. Second, proper identification techniques need to be introduced because the pathogens which are elucidated under the current culture-based techniques are not necessarily the most clinically important organisms [20].

The method used to elucidate the causative organisms in DFU was a wound discharge swab in this study. Therefore, cultured organisms include not only the true pathogen but also normal flora of the patient's skin. Some patients visited our hospital after several days of treatment with antibiotics. For that reason, organisms were not included in the analyses in this study.

Considering that important predictors for LEA in this study were the depth of wound and combined infection, for comprehensive management and improved wound care, a multidisciplinary team approach, including orthopedist, plastic surgeon, vascular surgeon, and infectionologist seems to be essential in the initial management of DFU [8,19].

In general, adequate glycemic control is essential for prevention of DFUs and LEAs [20,22]. However, the mean HbA1c level during the follow-up period was not different between the LEA and non-LEA groups in this study. Glycemic control cannot be shown as important for DFU

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treatment due to the small sample size and retrospective design of our study. Metabolic correction, including high glucose, blood pressure, and lipid profile within target range, with prompt infection control, should be emphasized in DFU patients with type 2 diabetes.

There are several limitations in this study. First, due to the retrospective study design, we could not assess presence of diabetic neuropathy. Because most patients were referred from other primary care, available baseline data for diabetic complications was not sufficient, and additional examinations for neuropathy were not possible on severely damaged wounds. As the included patients were those who required admission, and the patients with too little available clinical data from the medical record were also excluded, selection bias has to be taken into account. Other limitations of this study include relatively small sample size, retrospective design, and single center studies. A larger, prospective study will be needed to validate the findings of the present investigation. Additionally, as many studies suggest that infection of DFU is an important predictor for LEA [21,23], the difference in organisms and antibiogram of each DFU should be identified in the future for proper treatment of DFU.

In conclusion, in cases of severe DFU requiring hospitalization, the LEA risk was high in patients with type 2 diabetes. Therefore, DFU prevention is essential. Routine examination of the feet is necessary during routine clinical practice. Whenever DFU is identified, prompt management of DFUs by a multidisciplinary team would play an important role in lowering the LEA rate.

KEY MESSAGE

- In case of severe diabetic foot ulcer (DFU) enough to hospitalization, the lower extremity amputation (LEA) risk was high in patients with type 2 diabetes.
- 2. The depth of the wound, combined infection and peripheral artery disease were significant prognostic factor of LEA while the extent of the wound was not. Multidisciplinary team approach is important in management of DFU.



Conflict of interest

No potential conflict of interest relevant to this article was reported.

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