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Toe Wounds Treated with Percutaneous Transluminal Angioplasty and Toe Amputation in Hemodialysis Patients with Diabetic Nephropathy: Wound Sites and Outcomes 2 Years after Surgery

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Abstract

Introduction: When hemodialysis patients with diabetic nephropathy develop wounds on their feet, serious complications can occur. It is important to prevent wounds in those patients. In particular, a thorough follow-up is necessary for patients with a high risk of suffering a wound.

Patients and methods: Our study examined 26 patients with wounds confined to their toes for which percutaneous transluminal angioplasty and subsequent toe amputation were performed. The patients were able to ambulate after their wounds healed and therapeutic footwear was made. This study examined the outcomes 2 years after surgery, locations of amputated toes, and patients' history of coronary intervention.

Results and Discussion: The 26 patients consisted of 20 men (64.4 ± 10.2 years) and 6 women (74.8 ± 10.6 years), indicating a significantly higher age in women. There was a history of coronary intervention in 15 of 26 patients. Toe amputation consisted of the first toe in 13 toes, the second toe in 8 toes, the third toe in 3 toes, the fourth toe in 4 toes, and the fifth toe in 8 toes. There were significantly more first toes than other toes. There were 19 patients with only 1 affected toe. In these patients, the first toe was the most commonly affected toe, followed by the fifth toe. The outcomes 2 years after surgery were survival in 17 patients and death in 9 patients. The mean age was 64.2 years in patients who survived and 71.7 years in patients who died. Seven of nine patients who died had a history of coronary intervention. Of the 17 patients who survived, 6 patients had re-amputation within 2 years after initial surgery. Five of the six re-amputation cases involved toe amputation on the ipsilateral foot. Thus, a thorough follow-up is necessary if there is continued burden on the foot with surgery.

Keywords: Diabetes; Diabetic foot; Ulcer; Chronic renal failure; Hemodialysis; Toe amputation; Peripheral arterial disease; Critical limb ischemia; Prognosis

Introduction

There are 3 major underlying causes of diabetic foot ulcers: neuropathy (autonomic, motor, and sensory neuropathy), peripheral arterial disease, and infection. When autonomic neuropathy causes hypohidrosis, skin dryness and cracking occur and skin barrier function decreases. Therefore, a wound can develop even from a slight skin injury [1].

In the innermost layer of the skin, there are arteriole-venule shunts between arterioles and venules. These shunts are involved in the regulation of body temperature. When the skin is exposed to cold temperatures, shunts open to prevent a body temperature drop by allowing arteriole blood to bypass capillaries and to flow directly into venules. Arterioles and shunts are innervated by autonomic nerves. Thus, when diabetes causes denervation, shunts become dilated. As a result, the blood flow of capillaries decreases, leading to reduction in nutrients to the skin, oxygen partial pressure, and skin temperature. In addition, arterioles dilate due to denervation and the blood flow in venules increases. The resulting skin edema causes the exacerbation of diabetic foot lesions [1].

When there is motor neuropathy, the balance of the intrinsic muscles of the feet is affected and a foot deformity can occur. If joints protrude due to the foot deformity, calluses and ulcers can form due to mechanical stimulation from footwear. In some cases, joints become exposed and gangrene develops. When there is sensory neuropathy, patients cannot feel pain as a part of the physical defense system. In addition, when visual impairment develops due to diabetic retinopathy, patients might be unable to promptly discover ulcers and gangrene on their bodies [1].

Diabetes is a risk factor for peripheral arterial disease (PAD). A 1% increase in HbA1c increases the risk for PAD by 25-28%. When diabetic patients develop lower limb ischemia due to PAD, their foot wounds can become intractable [2,3]. The incidence of cellulitis is more than 9 times higher in patients with diabetes than in those without, and

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diabetic patients are prone to exacerbation of foot lesions because of their higher susceptibility to infection [4,5]. Renal insufficiency due to diabetic nephropathy is also a risk factor for PAD. Critical limb ischemia (CLI) is a severe condition of PAD, and CLI patients are known to have poor prognosis [6].

When CLI patients develop foot wounds, serious complications can occur. Wounds can worsen rapidly, and the patients might have to undergo a major amputation to save their lives. In fact, it is not rare for these patients to lose their lives due to sepsis caused by the infection of such wounds. Therefore, it is important to prevent wounds in CLI patients. In particular, a thorough follow-up is necessary for patients with a high risk of suffering a wound. Our study examined patients with wounds confined to their toes for which percutaneous transluminal angioplasty and subsequent toe amputation were performed. The patients were able to ambulate after the wound healed and therapeutic footwear was made. This study examined their outcomes thereafter. There is a Japanese custom of removing shoes inside homes, and Japanese people are often barefooted or in slippers indoors. Our study also investigated the differences in the incidence of amputation among toes in people who practice such a custom.

Patients and Methods

The subjects were patients undergoing hemodialysis due to diabetic nephropathy. In the period between January 2007 and October 2013, their toe wounds had been treated with percutaneous transluminal angioplasty to increase lower limb blood flow for limb salvage and subsequently treated with toe amputation. The subjects were patients who met the following 3 criteria: (1) there was no previous history of lower limb surgery, (2) foot wound healed after toe amputation, and (3) therapeutic footwear was made for ambulation after the wound healed. In a total of 26 subjects, this study examined their outcomes 2 years after surgery, locations of the amputated toes and their history of coronary intervention.

Statistical Analysis

Continuous variables such as age and index were expressed as mean ± standard deviation and were compared by Student's t test between two groups. Categorical variables such as dead or alive were expressed as count and percentage and were compared by Fisher's exact test. In all tests, $P<0.05$ (2 sided) was considered statistically significant and $0.05 \leq P<0.10$ (2 sided) was considered marginally significant. In case that the distribution of toe amputations is significantly unbalanced, the Haberman Residuals (Adjusted Standardized Residuals) was used to find the significantly larger number of toes with amputation using over 1.96 of this residual. Statistical analysis software was SAS Ver. 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The 26 patients consisted of 20 men (76.9%) and 6 women (23.1%). The age ranged from 44 to 85 years and the mean age was 66.8 years. The mean age was 64.4 ± 10.2 years in men and 74.8 ± 10.6 years in women, indicating a significantly higher age in women (p=0.039). All patients had type 2 diabetes. There was a history of coronary intervention in 15 of 26 patients (57.7%). Toe amputation was performed on the left foot in 13 patients, right foot in 12 patients, and both feet in 1 patient.

Toe amputation consisted of the first toe in 13 toes, the second toe in 8 toes, the third toe in 3 toes, the fourth toe in 4 toes, and the fifth toe in 8 toes (total of 36 toes). There was a significant difference in the distribution of these amputated toes (p=0.043). There were significantly more first toes than other toes (adjusted standardized residuals: 2.6) (Table 1).

There were 19 patients with only 1 affected toe. The affected toe was the first toe in 8 patients, the second toe in 2 patients, the third toe in 2 patients, the fourth toe in 2 patients, and the fifth toe in 5 patients. There was a marginally significant difference in the distribution of these amputated toes (p=0.052), and there were significantly more first toes than other toes (adjusted standardized residuals: 3.0) (Table 2). Seven patients had multiple affected toes on one foot.

The outcomes 2 years after surgery were survival in 17 patients and death in 9 patients, and the overall mortality rate was 34.6%. The mortality rate was 30.0% in men and 50.0% in women, indicating no significant difference (p=0.628). The mean age was 71.7 ± 9.9 years in patients who died and 64.2 ± 11.1 years in patients who survived, indicating no significant difference (p=0.102). Seven out of nine patients who died had a history of coronary intervention. Seven (46.7%) out of fifteen patients with coronary intervention died while only two (18.2%) out of eleven patients without coronary intervention died. However, there was no significant difference (p=0.217). Of the 17 patients who survived, 6 patients had re-amputation within 2 years after initial surgery due to wounds in their lower limbs, and 11 patients did not have re-amputation. Five out of six re-amputation cases involved toe amputation on the ipsilateral foot. The remaining case had ipsilateral knee disarticulation (Table 3).

Discussion

There are various levels of severity of diabetic ulcers as shown by several classification systems of diabetic ulcer severity [7]. One such ulcer is a toe wound that can develop as a complication of diabetes. Our study examined toe wounds in patients who were receiving hemodialysis due to diabetic nephropathy. Such wounds can worsen rapidly if revascularization and wound treatment are not performed [8]. Therefore, early discovery of wounds as well as prevention are important. It is essential to know the sites prone to wounds. When

Amputation	1st toe	2nd toe	3rd toe	4th toe	5th toe	Fisher
Yes	13 (25.0%)	8 (15.4%)	3 (5.8%)	4 (7.7%)	8 (15.4%)	p=0.043
No	39 (75.0%)	44 (84.6%)	49 (94.2%)	48 (92.3%)	44 (84.6%)	

The total number is the number of toes.

Table 1: Distribution of amputated toes in 26 patients.

Amputation	1st toe	2nd toe	3rd toe	4th toe	5th toe	Fisher
Yes	9 (23.7%)	2 (5.3%)	2 (5.3%)	2 (5.3%)	5 (13.2%)	p=0.052
No	29 (76.3%)	36 (94.7%)	36 (94.7%)	36 (94.7%)	33 (86.8%)	

The total number is the number of toes.

Table 2: Distribution of amputated toes in 19 patients with only 1 affected toe.

Patient	Age (years)	Gender	History of coronary intervention	Location of wounds	Two-year postoperative outcome
1	60	M	No	L) 1	Alive w/o re-amputation
2	86	F	Yes	L)4	Dead
3	76	M	Yes	L)3	Dead
4	66	M	Yes	R)1	Dead
5	60	M	Yes	L)1,2	Alive w/o re-amputation
6	52	M	No	L)5	Re-amputation of L) Residual Toe Amputation and Alive
7	60	F	Yes	R)1	Alive w/o re-amputation
8	54	M	Yes	R)5	Dead
9	78	M	No	R)2,5	Dead
10	71	M	Yes	L)5	Re-amputation of L) Residual Toe Amputation and Alive
11	69	F	Yes	L)1,2	Dead
12	79	M	No	R)1, L)1	Alive w/o re-amputation
13	68	F	No	R)1,2	Re-amputation of R) Residual Toe Amputation and Alive
14	63	M	Yes	R)1	Dead
15	59	M	No	R)5	Alive w/o re-amputation
16	85	F	No	L)1	L) Knee disarticulation and Alive
17	72	M	Yes	L)1,2	Dead
18	81	F	No	R)2	Dead
19	61	M	Yes	R)4,5	Alive w/o re-amputation
20	65	M	Yes	L)5	Alive w/o re-amputation
21	77	M	No	L)4	Re-amputation of L) Toe and Alive
22	75	M	Yes	L)1	Alive w/o re-amputation
23	67	M	Yes	L)2	Re-amputation of L) Toe and Alive
24	61	M	No	R)1	Alive w/o re-amputation
25	47	M	No	R)3	Alive w/o re-amputation
26	44	M	Yes	R2-5	Alive w/o re-amputation

M, Male; F, Female; R), Right; L), Left.

Table 3: Baseline characteristics and patient demographics.

patients have diabetic peripheral neuropathy, they might continue to wear ill-fitting footwear because they do not feel pain. If there is a mallet deformity or Charcot deformity, the protruded area can rub against the footwear, resulting in a wound. If a wound develops in the forefoot, the range of motion of the ankle can become limited, resulting in an equinus deformity in some cases. Such a deformity can worsen a wound because the forefoot is subjected to a strong impact force when landing or during the pushing-off phase of gait. Since this type of mechanical stimulation can be a factor that exacerbates wounds, the importance of footwear has been raised based on international evidence [9].

The history of shoes in Japan is less than 150 years and is short compared with that in the West. When buying shoes, people often place importance on style over function [10]. Japanese people customarily do not wear shoes in their homes. They generally remove their shoes at the entranceway, keeping the floors clean. People are often barefooted or wear slippers indoors. Slippers are light and comfortable and hotels and airlines provide slippers to be worn indoors. In Japan with such a custom, Japanese diabetic patients prefer sandals and slippers. In particular, patients with visual impairment tend to wear these types of footwear because they are easier to put on their feet. Sandals and slippers provide no support to the heels. When patients walk, their feet move back and forth and chafe against the slippers. Therefore, patients develop wounds on the lateral or medial side of their feet depending on their tendency (Figures 1A-1G).

Our study examined 26 patients. When patients with only one affected toe were examined, the first toe was the most commonly affected toe, followed by the fifth toe. When patients with multiple affected toes were included, the number of second toe amputations was equal to the number of fifth toe amputations. Half of the patients with second toe amputation also had a wound in the first toe. Thus, half of the patients with second toe amputation were thought to be severe first toe cases. For this reason, our institution had the first toe on the medial side of the foot as the most commonly amputated toe, followed by the fifth toe. As in our report, the first toe is the most commonly affected toe in numerous reports from many institutions. However, many reports have stated that the second toe was the second most commonly affected toe [11-13]. Thus, different studies had a different incidence of the affected toe, namely for the second toe and the fifth toe. It might be related to the forefoot alignment depending on race and custom of footwear. Another study examined diabetic foot ulcers and lower limb amputation. The difference was investigated between the left and right lower limbs as the affected limb, and the institution with more right-handed subjects reported more affected limb on the right side [11]. In our institution, there was no clear difference between the right and left sides.

The prevalence of PAD is greater in men than in women, and

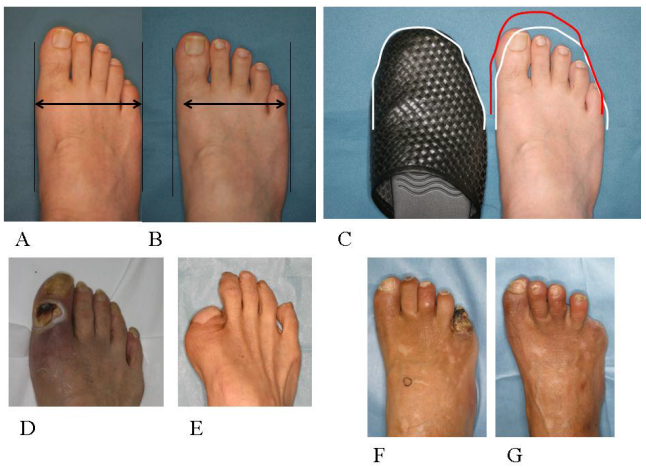

Figure 1: (A) In a non-weight-bearing condition. (B) In a weight-bearing condition. When the patient placed the weight on the foot in a standing position, the width of the foot increased (the lengths of double arrow lines in (A) and (B) were the same). (C) The red outline shows the outer edge of the slipper when the patient wore it in a seated position. The outer edge of the slipper moved to the position shown by the white outline when the patient walked. Thus, the slipper was poorly fitting and placed pressure on the foot. (D) When the patient walked wearing slippers, the load was on the medial foot. A wound developed on the first toe (Patient 4). (E) Patient 4: four months after surgery. (F) When the patient walked wearing slippers, the load was on the lateral foot and a wound developed on the fifth toe (Patient 8). (G) Patient 8: six months after surgery.

the ratio of men to women increases for CLI [6]. In our study, men accounted for 76.9% of the subjects. The mean age was 64.4 years in men and 74.8 years in women, suggesting that the age of onset was lower in men than women. When age increases, the risk for CLI increases due to arterial and non-arterial polymorbid conditions [14]. In our study, the mean age was 71.7 years in patients who died and 64.2 years in patients who survived, indicating a difference of 7.5 years albeit not significant. However, the mortality rate was higher in women than in men, and this result is thought to reflect that age is a stronger risk factor than gender.

Death occurs due to coronary artery disease (CAD) in 40-60% of PAD patients. The sensitivity of CAD diagnosis changes with the diagnostic method [6]. Thus, our study examined the history of coronary intervention to evaluate the presence of heart disease. Seven of out nine patients who died had a history of coronary intervention. Seven (46.7%) out of fifteen patients with coronary intervention died but only two (18.2%) out of eleven patients without coronary intervention died. In our study, the cause of death was not confirmed in 9 patients. The mortality rate was higher in patients with coronary intervention, although there was no significant difference. Of the 17 patients who survived, 6 patients had re-amputation within 2 years after initial surgery due to wounds in their lower limbs. Five of these six re-amputation cases involved toe amputation on the ipsilateral foot. Thus, a thorough follow-up is necessary when there is continued burden on the foot with surgery.

Conclusion

Our study examined hemodialysis patients with diabetic nephropathy who received PTA and toe amputation for toe wounds. The patients were able to ambulate after the wound healed and therapeutic footwear was made. In patients with only one affected toe, the first toe was the most commonly affected toe, followed by the fifth toe. Two years after surgery, the outcome was death in approximately 1 in 3 patients. There was a history of coronary intervention in approximately half of the patients who died. Two years after surgery, approximately 2 in 5 patients who survived did not develop a wound that required re-amputation. Five out of six re-amputation cases involved toe amputation on the ipsilateral foot. Thus, a thorough follow-up is necessary when there is continued burden on the foot with surgery.

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