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初发与复发性糖尿病足溃疡临床特征分析*

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【摘要】 目的 分析四川大学华西医院住院糖尿病足溃疡（diabetic foot ulcer, DFU）患者的临床特征，探究足溃疡复发的危险因素。**方法** 回顾性分析2012年1月1日–2020年12月31日在四川大学华西医院住院的817例DFU患者的临床资料，按照既往是否发生足溃疡，分为初发组（502例）和复发组（315例）。比较两组患者临床特征的差异，采用多因素logistic回归分析足溃疡复发的危险因素。**结果** 初发和复发性DFU患者以神经缺血性足溃疡为主，均好发于第一足趾和第五足趾。与初发DFU患者相比，Wagner 3级和创面位于胼胝的复发性DFU患者更多（P<0.05），但足坏疽（Wagner 4～5级）的患者更少（P<0.05）。复发性DFU患者的糖化血红蛋白、血小板计数和纤维蛋白原水平更低（P<0.05），血尿酸和血肌酐水平更高（P<0.05）；两组患者的血红蛋白、白细胞计数、估算肾小球滤过率、血沉和C-反应蛋白水平均无明显差异（P>0.05）。多因素logistic回归分析显示，男性（OR=1.555, 95%CI: 1.097～2.072, P=0.013）、糖尿病病程≥10年（OR=2.369, 95%CI: 1.473～3.810, P<0.001）、既往截肢史（OR=4.518, 95%CI: 2.386～8.553, P<0.001）、足部骨质疏松（OR=1.711, 95%CI: 1.065～2.751, P=0.027）、创面位于胼胝（OR=1.786, 95%CI: 1.058～3.012, P=0.030）和冠心病（OR=0.668, 95%CI: 0.453～0.987, P=0.043）与足溃疡复发相关。**结论** 男性、糖尿病病程超过10年、既往截肢史、足部骨质疏松和创面位于胼胝是DFU患者足溃疡复发的独立危险因素。因此，DFU患者即使足溃疡愈合，也应加强足部护理，降低足溃疡复发率。

【关键词】 糖尿病足溃疡 足溃疡复发 足胼胝 足溃疡诱因 危险因素

Clinical Characteristics of Diabetic Patients with Initial and Recurrent Foot Ulcers

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【Abstract】 Objective To explore the risk factors for the recurrence of foot ulcers by analyzing clinical characteristics of the patients with diabetic foot ulcers (DFU) in West China Hospital, Sichuan University. **Methods** A retrospective analysis was carried out with the clinical data of 817 DFU patients hospitalized at West China Hospital, Sichuan University between January 1, 2012 and December 31, 2020. The patients were divided into an initial ulceration group (502 cases) and a recurrent ulceration group (315 cases) according to their history of foot ulcers. The differences in clinical characteristics between the two groups were compared, and multivariate logistic regression analysis was conducted to identify the risk factors associated with the recurrence of foot ulcers. **Results** Initial and recurrent DFU patients both had predominantly neuro-ischemic foot ulcers, and the most common sites of ulceration were the first and fifth toes in both groups. Compared with the initial DFU group, more patients in the recurrent group had foot ulcers of Wagner grade 3 and ulcerous wounds located on calluses (P<0.05), and fewer patients in the recurrent group suffered from foot gangrene (P<0.05). Patients with recurrent DFU had lower glycated hemoglobin, platelet counts, and fibrinogen levels (P<0.05), and higher serum uric acid and creatinine levels (P<0.05). Hemoglobin, white blood cell count, estimated glomerular filtration rate, erythrocyte sedimentation rate and C-reactive protein levels were not significantly different between the two groups (P>0.05). Multivariable logistic regression analysis showed that male sex (OR=1.555, 95% CI: 1.097-2.204, P=0.013), duration of diabetes≥10 years (OR=2.369, 95% CI: 1.473-3.810, P<0.001), history of amputation (OR=4.518, 95% CI: 2.386-8.553, P<0.001), foot osteoporosis (OR=1.711, 95% CI: 1.065 to 2.751, P=0.027), ulcerous wound located on foot callus (OR=1.786, 95% CI: 1.058-3.012, P=0.030), and coronary heart disease (OR=0.668, 95% CI:0.453-0.987, P=0.043) were significantly associated with the recurrence of foot ulcers. **Conclusions** Male sex, duration of diabetes being over 10 years, history of previous amputation, foot osteoporosis, and ulcerous wounds located on foot callus are independent risk factors of recurrent foot ulcers in patients with DFU. Therefore, even after their foot ulcers have healed, special attention should be given to the care of foot for patients with DFU, which may reduce the

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recurrence of foot ulcers.

【Key words】 Diabetic foot ulcers Recurrent foot ulcers Foot callus Causes of foot ulcers Risk factors

糖尿病足溃疡(diabetic foot ulcer, DFU)是糖尿病最严重的并发症之一。全球DFU发生率约6.3%(95%*CI*: 5.4%~7.3%)[1]。文献报道,约40%DFU患者足溃疡愈合1年后复发,而3年和5年复发率分别为60%和65%[2]。在中国,50岁以上糖尿病患者新发足溃疡的年发病率为8.1%,足溃疡愈合1年后复发率约31.6%[3]。DFU不仅在原位复发,还可能在同侧足不同解剖部位甚至对侧肢体复发。ÖRNEHOLM等[4]报道,约38%的足溃疡复发位于对侧前足足底。DFU高复发率已成为临床亟待解决的难题。

既往足溃疡病史是DFU再次发生的最强预测因子[2]。针对复发性足溃疡患者,在专门的三级糖尿病足诊治中心进行正规随访和治疗至关重要。国际糖尿病足工作组(The International Working Group on the Diabetic Foot, IWGDF)指出,全面足部护理和足部手术是主要的预防性干预措施[5]。

因此,我们设计了一项横断面研究,以阐明本中心复发性DFU的临床特征,从DFU患者临床特征及足溃疡特点的角度,分析DFU复发的危险因素并优化临床诊断和治疗,对降低DFU患者的足溃疡复发率有着重要的意义。

1 对象与方法

1.1 研究对象

采用回顾性队列研究纳入2012年1月1日–2020年12月31日四川大学华西医院糖尿病足诊治中心收治的住院DFU患者。纳入标准:DFU的诊断符合IWGDF对糖尿病足的定义[6]——无论是初诊还是既往诊断糖尿病,有足部的皮肤感染、溃疡和(或)组织破坏,通常伴有下肢动脉病变或周围神经病变。排除标准:合并踝关节以上的下肢溃疡、手部溃疡等的糖尿病患者;痛风性溃疡、癌性溃疡等非DFU的糖尿病患者;长期使用糖皮质激素导致足溃疡的糖尿病患者。本研究经四川大学华西医院伦理委员会批准(2012年审119号)。

1.2 研究方法

通过电子病历系统收集所有患者的临床资料。①人口学资料,包括患者性别、年龄、糖尿病诊断时间、体质量指数(body mass index, BMI);②糖尿病治疗史(糖尿病是否规律治疗及监测血糖、是否皮下注射胰岛素治疗)、既往糖尿病足病史(既往足溃疡及截肢史)及个人史(吸烟史、饮酒史);③实验室检查,包括血常规、凝血常规、空腹血糖、糖化血红蛋白(glycated hemoglobin, HbA1c)、血尿酸、估算肾小球滤过率(estimated glomerular filtration rate, eGFR)、血沉、C-反应蛋白(C-reactive protein, CRP);④足溃疡评估,包括足部畸形、胼胝,溃疡位置、溃疡分类、诱因,足部骨髓炎、坏疽等。⑤辅助检查,包括踝肱指数(ankle brachial index, ABI)、足部X线摄片、足部MRI扫描、肌电图、下肢动静脉彩超等,评估患者是否合并糖尿病慢性并发症以及高血压、冠心病、高脂血症、高尿酸血症等合并症。按照既往是否发生足溃疡,将纳入患者分为复发性DFU和初发DFU患者组。复发性足溃疡定义为既往出现足溃疡的部位再次发生的溃疡,或者足部其他部位的新发溃疡。

1.3 统计学方法

分类变量以例数(%)表示,组间比较采用χ^2检验或Fisher确切概率法;连续变量用$\bar{x}\pm s$或中位数(四分位间距)表示,组间比较采用t检验或Mann-Whitney U检验。采用二元logistic回归分析影响足溃疡复发的相关因素。$P<0.05$为差异有统计学意义。

2 结果

2.1 初发与复发性DFU患者的一般情况比较

最终纳入DFU患者共817例,其中初发和复发性DFU患者分别为502例(61.4%)和315例(38.6%)。如表1所示,复发性DFU患者的糖尿病诊断时间比初发DFU患者更长($P<0.001$)。与初发DFU患者相比,复发性DFU患者中入院前不正规治疗糖尿病、接受胰岛素和既往有截肢史的患者更多($P<0.05$)。两组患者住院时间、年龄、性别、BMI、吸烟史、饮酒史和糖尿病家族史无明显差异($P>0.05$)。

如表2所示,与初发DFU患者相比,复发性DFU患者合并糖尿病视网膜病变、糖尿病心脏自主神经病变和糖尿病胃肠自主神经病变的患者更多($P<0.05$),两组患者中糖尿病周围神经病变和糖尿病膀胱自主神经病变均无明显差异($P>0.05$)。复发性DFU患者合并冠心病的患者更少($P=0.037$),而高血压、高尿酸血症、高脂血症和慢性肾脏疾病差异均无统计学意义($P>0.05$)。

2.2 复发性DFU患者的足溃疡的特点

如表3所示,初发和复发组中,均以神经缺血性足溃疡为主;好发于第一足趾,其次为第五足趾和足跟。足溃

表 1　初发与复发性DFU患者的基本特征比较

Table 1　Comparison of basic data between the initial and recurrent DFU groups

Item	Initial DFU group (n=502)	Recurrent DFU group (n=315)	P
Hospital stay/d, median (P_{25}-P_{75})	31 (18-56)	31 (17-55)	0.488
Age/yr., $\bar{x} \pm s$	65.5±12.0	65.8±11.7	0.722
Male/case (%)	309 (61.6)	212 (67.3)	0.096
BMI/(kg/m^2), $\bar{x} \pm s$	23.3±3.5	23.4±3.4	0.665
Duration of diabetes/years, $\bar{x} \pm s$	10.9±7.6	13.1±7.7	<0.001
State of treatment and control of blood glucose/case (%)			0.006
Regular	6 (1.2)	4 (1.3)	>0.05
Relatively regular	122 (24.3)	64 (20.3)	>0.05
Irregular	327 (65.1)	236 (74.9)	<0.05
Untreated	17 (3.4)	2 (0.6)	<0.05
Newly diagnosed diabetes	30 (6.0)	9 (2.9)	<0.05
Insulin therapy before admission/case (%)	340 (67.7)	247 (78.4)	0.001
Tobacco smoking past and present/case (%)	271 (54.0)	163 (51.7)	0.533
Alcohol abuse past and present/case (%)	205 (40.8)	125 (39.7)	0.743
History of previous amputation before admission/case (%)	20 (4.0)	54 (17.1)	<0.001
Family history of diabetes/case (%)	153 (30.5)	105 (33.3)	0.393

BMI: Body mass index.

表 2　初发与复发性DFU患者的糖尿病慢性并发症和合并症比较

Table 2　Comparison of chronic complications and comorbidities of diabetes between the initial and recurrent DFU groups

Complication and comorbidity	Initial DFU group (n=502)	Recurrent DFU group (n=315)	P
Diabetic retinopathy/case (%)	200 (39.8)	150 (47.6)	0.029
Diabetic peripheral neuropathy/case (%)	479 (95.4)	306 (97.1)	0.216
Cardiac autonomic neuropathy/case (%)	360 (71.7)	250 (79.4)	0.014
Diabetic gastrointestinal autonomic neuropathy/case (%)	120 (23.9)	97 (30.8)	0.030
Diabetic bladder autonomic neuropathy/case (%)	255 (50.8)	159 (50.5)	0.929
Hypertension/case (%)	354 (70.5)	226 (71.7)	0.697
Coronary heart disease/case (%)	136 (27.1)	65 (20.6)	0.037
Hyperuricemia/case (%)	62 (12.4)	47 (14.9)	0.293
Hyperlipidemia/case (%)	118 (23.5)	78 (24.8)	0.682
Chronic kidney disease/case (%)	344 (68.5)	221 (70.2)	0.623

疡诱因中, 以物理性因素为主, 其中压力性占比最高, 其次为术后伤口和烫伤。与初发DFU患者相比, 复发性DFU患者中创面位于胼胝及Wagner 3级DFU患者更多(P< 0.05), 但足坏疽(Wagner 4级和Wagner 5级)的患者更少(P< 0.05)。

如表4所示, 初发和复发DFU两组患者下肢动脉病变、ABI、足部畸形、足部骨质疏松和骨髓炎无明显差异(P> 0.05)。复发性DFU患者的基线HbA1c、血小板计数和纤维蛋白原水平更低(P< 0.05), 血尿酸和血肌酐水平更高(P< 0.05); 两组患者基线血红蛋白、白细胞计数、eGFR、血沉和CRP水平无明显差异(P> 0.05)。

2.3　影响糖尿病患者足溃疡复发的因素

如表5所示, 对影响足溃疡复发的因素〔性别(男 = 1, 女 = 0), 糖尿病持续时间(< 5年 = 0, 5 ~ 9年 = 1, ≥ 10年 = 2)、有无冠心病(有 = 1, 无 = 0)、有无糖尿病视网膜病变(有 = 1, 无 = 0)、有无糖尿病心脏自主神经病变

表 3 初发与复发性DFU患者的足溃疡特点比较

Table 3 Comparison of foot ulcer characteristics between the initial and recurrent DFU groups

Characteristic	Initial DFU group (*n*=502)	Recurrent DFU group (*n*=315)	*P*
Wagner grade/case (%)			0.074
1	25 (5.0)	14 (4.4)	>0.05
2	83 (16.5)	55 (17.5)	>0.05
3	201 (40.0)	150 (47.6)	<0.05
4	181 (36.1)	85 (27.0)	<0.05
5	12 (2.4)	11 (3.5)	>0.05
Foot deformities/case (%)	91 (18.1)	60 (19.0)	0.742
Callus/case (%)	213 (42.4)	136 (43.2)	0.834
Wound located on callus/case (%)	42 (8.4)	44 (14.0)	0.011
Foot osteoporosis*/case (%)	414 (82.5)	275 (87.3)	0.064
Classification of foot ulcers/case (%)			0.433
Neuropathic foot ulcers	133 (26.5)	90 (28.6)	—
Neuro-ischemic foot ulcers	241 (48.0)	157 (49.8)	—
Ischemic foot ulcer	128 (25.5)	68 (21.6)	—
Single ulcer/case (%)	298 (59.4)	206 (65.4)	0.084
Foot ulcer site#/case (%)			0.170
First toe	78 (26.2)	40 (19.4)	—
Second toe	19 (6.4)	15 (7.3)	—
Third toe	13 (4.4)	18 (8.7)	—
Fourth toe	27 (9.1)	15 (7.3)	—
Fifth toe	37 (12.4)	33 (16.0)	—
Dorsum	34 (11.4)	18 (8.7)	—
Palms	27 (9.1)	14 (6.8)	—
Heel	35 (11.7)	23 (11.2)	—
Inner planta	8 (2.6)	11 (5.4)	—
Lateral planta	20 (6.7)	19 (9.2)	—
Foot ulcer causes/case (%)			0.301
Physical causes	303 (60.4)	196 (61.0)	—
Pressure	91 (18.1)	45 (14.3)	—
Surgical wound	47 (9.4)	45 (14.3)	—
Scalding	45 (9.0)	31 (9.8)	—
Injury	13 (2.6)	10 (3.2)	—
Others	107 (21.3)	61 (19.4)	—
Chemical causes	10 (2.0)	4 (1.2)	—
Unknown	189 (37.6)	119 (37.8)	—
Osteomyelitis/case (%)	264 (52.6)	175 (55.6)	0.408
Foot gangrene/case (%)	192 (38.2)	96 (30.5)	0.024

*: The numbers of valid cases of foot osteoporosis in initial and recurrent DFU groups were 443 and 284, respectively; #: The data only show cases with a single foot ulcer.

表 4　初发与复发性DFU患者的相关检查结果比较

Table 4　Comparison of findings from relevant examinations between the initial and recurrent DFU groups

Item	Initial DFU group (*n*=502)	Recurrent DFU group (*n*=315)	*P*
Arterial ultrasound of lower extremity/case (%)			0.684
Normal	23 (4.8)	10 (3.3)	—
Arteriosclerosis	182 (37.7)	111 (36.2)	—
Arterial stenosis	61 (12.6)	39 (12.7)	—
Arterial occlusion	217 (44.9)	147 (47.9)	—
ABI/case (%)			0.164
≤0.4	8 (2.8)	11 (5.3)	>0.05
>0.4-≤0.7	57 (19.8)	34 (16.5)	>0.05
>0.7-≤0.9	39 (13.5)	22 (10.7)	>0.05
>0.9-≤1.3	179 (62.2)	130 (63.1)	>0.05
>1.3	5 (1.7)	9 (4.4)	>0.05
HbA1c/%, $\bar{x} \pm s$	8.8±2.4	8.3±2.0	0.001
Hb/(g/L), $\bar{x} \pm s$	112.5±22.7	114.4±20.5	0.249
PLT/($\times 10^9 L^{-1}$), median (P_{25}-P_{75})	226.0 (164.5-293.0)	203.5 (154.0-265.8)	0.003
WBC/($\times 10^9 L^{-1}$), $\bar{x} \pm s$	7.99±3.93	7.93±3.68	0.851
FIB/(g/L), $\bar{x} \pm s$	4.61±1.47	4.27±1.44	0.001
UA/(μmol/L), $\bar{x} \pm s$	310±108	335±106	0.001
Crea/(μmol/L), median (P_{25}-P_{75})	108.0 (79.3-171.0)	114.3 (85.5-174.5)	0.024
eGFR/(mL/[min·1.73 m^2]), $\bar{x} \pm s$	76.4±32.4	72.6±30.7	0.102
ESR/(mm/1 h), $\bar{x} \pm s$	61.9±34.5	56.8±31.4	0.182
CRP/(mg/L), median (P_{25}-P_{75})	10.1 (3.5-34.3)	10.2 (3.4-28.5)	0.624

The numbers of valid cases of arterial ultrasound of lower extremity, ABI, HbA1c, Hb, PLT, WBC, FIB, UA, Crea, eGFR, ESR and CRP in the initial DFU group were 483, 288, 440, 474, 473, 474, 301, 303, 498, 496, 171, and 480, respectively, while those for the recurrent DFU group were 307, 206, 291, 304, 304, 459, 301, 312, 314, 310, 134, and 307, respectively; ABI: Ankle-brachial index; HbA1c: Glycosylated hemoglobin; Hb: Hemoglobin; PLT: Platelet count; WBC: White blood count; FIB: Fibrinogen; UA: Serumuric acid; Crea: Serum creatinine; eGFR: Estimated glomerular filtration rate; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

表 5　住院DFU患者足溃疡复发相关的多因素logistic回归分析

Table 5　Multivariable logistic regression analysis of recurrent foot ulcers in the hospitalized patients with DFU

Factor	*OR* (95% *CI*)	*P*
Gender (male)	1.555 (1.097-2.204)	0.013
Duration of diabetes<5 years	1.000	0.001
<10 years	1.552 (0.888-2.715)	0.123
≥10 years	2.369 (1.473-3.810)	<0.001
History of amputation	4.518 (2.386-8.553)	<0.001
Foot osteoporosis	1.711 (1.065-2.751)	0.027
Wound located on callus	1.786 (1.058-3.012)	0.030
Coronary heart disease	0.668 (0.453-0.987)	0.043

Corrective factors: Diabetic retinopathy, cardiac autonomic neuropathy, diabetic gastrointestinal autonomic neuropathy, foot gangrene, HbA1c, serum uric acid, and serum creatinine. *OR*: Odd ratio; *CI*: Confidence interval.

（有= 1, 无= 0）、有无糖尿病胃肠自主神经病变（有= 1, 无= 0）、创面是否位于胼胝（是= 1, 否= 0）、是否足部骨质疏松（是= 1, 否= 0）、是否足部坏疽（是= 1, 否= 0）、既往有无截肢史（有= 1, 无= 0）、HbA1c（≤7%= 0, > 7% ~ 9%= 1, > 9%= 2）、血尿酸（≥420 μmol/L= 1, < 420 μmol/L= 0）、血肌酐（连续性变量）〕纳入多因素logistic分析, 结果显示, 性别、糖尿病诊断时间、既往有无截肢史、有无足部骨质疏松、创面是否位于胼胝和是否合并冠心病与足溃疡复发显著相关。男性DFU患者的足溃疡复发风险是女性的1.555倍（95%*CI*: 1.097 ~ 2.204, *P*= 0.013）。与糖尿病病程不足5年的DFU患者相比, 糖尿病病程≥10年的DFU患者足溃疡复发风险是其的2.369倍（95%*CI*: 1.473 ~ 3.810, *P*< 0.001）。既往有截肢史的DFU患者足溃疡复发风险是既往无截肢史DFU患者的4.518倍（95%*CI*: 2.386 ~ 8.553, *P*< 0.001）。有足部骨质疏松的DFU患者足溃疡复

发风险是无足部骨质疏松的DFU患者的1.711倍(95%*CI*: 1.065 ~ 2.751, *P*= 0.027)。与无胼胝的DFU患者相比,创面位于胼胝的DFU患者复发风险是其的1.786倍(95%*CI*: 1.058 ~ 3.012, *P*= 0.030)。与没有冠心病的DFU患者相比,合并冠心病的DFU患者足溃疡复发风险降低(*OR*= 0.668, 95%*CI*: 0.453 ~ 0.987, *P*= 0.043)。

3 讨论

DFU的高复发率与下肢缺血、感染、糖尿病周围神经病变和足部生物力学负荷异常有关[7-9]。本研究发现与DFU复发相关的因素包括性别、糖尿病病程、既往截肢史、有无足部骨质疏松和创面是否位于胼胝。男性的足溃疡复发率较女性更高,可能与男性更多地从事体力劳动以及不同于女性的生活方式有关[8]。针对DFU复发的危险因素,不同的临床研究结果并非完全一致。一项Meta分析[8]研究结果显示,DFU复发的危险因素包括男性、吸烟、糖尿病病程长、既往溃疡累积时间、足底溃疡、糖尿病周围血管病变和周围神经病变。其中糖尿病病程长是发生血管病变的基础[10]。

截肢是DFU复发的最强预测因子,这与既往研究结果一致[2, 11-12]。截肢可以去除局部感染病灶,避免严重的菌血症和多器官损伤,从而降低严重DFU患者的住院死亡率[13]。但无论是截趾还是截肢都会导致足畸形和足部功能改变,增加新发溃疡的风险[14]。本研究中,复发性DFU患者中足溃疡诱因以截肢(趾)为主的手术创伤导致的足溃疡比例较初发足溃疡患者增加了4.9%,正是提示截肢本身是足溃疡复发的一个重要诱因。MOLINES-BARROSO等[15]进一步提出,应将小截肢后的节段水平与足溃疡复发风险纳入以确定更精确的小截肢模式。因此,对于有截肢指征的患者,不仅要谨慎选择截肢方式,还需在出院后进行定期随访和专业足部护理,预防足溃疡的复发。

本研究中超过80%的DFU患者合并足部骨质疏松,足部骨质疏松与足溃疡复发显著相关。目前国内外几乎没有针对DFU患者发生足部骨质疏松相关的临床研究。由于足溃疡和(或)局部肌肉受损,患足运动能力受限、负重减少甚至制动、足部骨骼机械受力减少,导致成骨和破骨细胞功能失衡,局部骨量丢失[16]。此外,创面感染、骨髓炎、骨折等因素进一步降低足部骨量,导致局部骨质疏松。因此,对于足溃疡愈合的糖尿病患者,有必要进行患足关节、肌肉功能锻炼和康复治疗,预防局部骨质疏松及DFU的复发。

本研究还发现,足部胼胝处发生溃疡是复发性足溃疡的危险因素。目前,足胼胝被认为是足溃疡前期,与周围皮肤相比,胼胝处的压力增加20倍[17]。胼胝的形成与活动时局部机械应力增加导致异常的足部力学改变、甚至出现足部畸形、穿戴不合适的鞋具有关[18]。2019年IWGDF指南[19]强调,去除胼胝可以有效降低足压,增加局部血液供应,促进伤口愈合。皮肤早期损害包括胼胝、水泡及出血是DFU复发的强预测因子,如果能及时规范化发现并处理,可预防足溃疡的发生[2]。此外,减压鞋的穿戴或者使用减压鞋垫等减压治疗,可进一步降低足溃疡的复发[20]。

值得注意的是,更多的复发性足溃疡患者入院前接受胰岛素治疗,其HbA1c明显低于初发DFU患者,这可能是由于曾经发生DFU的患者对糖尿病足有更深入的认识。这提示了糖尿病高危足的筛查和糖尿病教育的重要性。在本研究中,复发DFU患者中合并冠心病的患者较初发DFU患者更少,这可能与合并冠心病的DFU患者长期接受抗凝和(或)抗血小板治疗及他汀类降脂药的使用有关。因此推测,冠心病并非是糖尿病患者足溃疡复发的保护因素,而是其正规治疗后的额外获益。但是本研究尚未将药物及血管介入等治疗的相关指标纳入研究分析,因此这种推测还需研究进一步证实。

无论是初发还是复发性DFU患者,第一足趾和第五足趾是足溃疡发生风险最高的部位。PETERSEN等[21]研究发现最常见的DFU复发部位依次是第一跖骨头(41%)、第一足趾(32%)和第五跖骨头(16%),约48%的足溃疡在对侧肢体复发。糖尿病下肢动脉狭窄或者闭塞以及保护性感觉缺失既是DFU发生的主要原因,亦是足溃疡复发的危险因素,而病变通常累及双下肢,这也是足溃疡在对侧肢体复发的原因之一[9, 21]。另外,DFU患者即使足溃疡愈合,可能存在步态改变导致健侧足底压力分布异常,这或许是对侧足溃疡发生率高的另一原因[22]。因此,对于预防DFU复发,除了规律治疗糖尿病下肢动脉病变及周围神经病变,还应重视双足而非仅仅患足保护。

本研究是一项单中心回顾性研究,可能对结果造成一定的偏倚。此外,本研究未能进行长期预后分析,还需要对患者进行出院后的随访,进一步探究足溃疡复发相关因素。

综上,男性、糖尿病持续时间、既往截肢史、足部骨质疏松和创面位于胼胝是复发性DFU的独立危险因素。因此,DFU患者应加强血糖的控制,早期筛查并治疗危险因素,及早干预心血管危险因素,加强足部关节、肌肉功能锻炼,特别是足部减压和专科足部护理,以降低DFU的复发。

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参 考 文 献

[1] ZHANG P, LU J, JING Y, *et al*. Global epidemiology of diabetic foot ulceration: A systematic review and meta-analysis. Ann Med, 2017, 49(2): 106–116.

[2] ARMSTRONG D G, BOULTON A J M, BUS S A. Diabetic foot ulcers and their recurrence. N Engl J Med, 2017, 376(24): 2367–2375.

[3] JIANG Y, WANG X, XIA L, *et al*. A cohort study of diabetic patients and diabetic foot ulceration patients in China. Wound Repair Regen, 2015, 23(2): 222–230.

[4] ÖRNEHOLM H, APELQVIST J, LARSSON J, et al. Recurrent and other new foot ulcers after healed plantar forefoot diabetic ulcer. Wound Repair Regen, 2017, 25(2): 309–315.

[5] BUS S A, LAVERY L A, MONTEIRO-SOARES M, *et al*. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev, 2020, 36 (Suppl 1): e3269[2022-07-22]. https://doi.org/10.1002/dmrr.3269.

[6] VAN NETTEN J J, BUS S A, APELQVIST J, *et al*. Definitions and criteria for diabetic foot disease. Diabetes Metab Res Rev, 2020, 36(Suppl 1): e3268[2022-07-22]. https://doi.org/10.1002/dmrr.3268.

[7] HINCHLIFFE R J, FORSYTHE R O, APELQVIST J, *et al*. Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). Diabetes Metab Res Rev, 2020, 36(Suppl 1): e3276[2022-07-22]. https://doi.org/10.1002/dmrr.3276.

[8] HUANG Z H, LI S Q, KOU Y, *et al*. Risk factors for the recurrence of diabetic foot ulcers among diabetic patients: A meta-analysis. Int Wound J, 2019, 16(6): 1373–1382.

[9] PETERS E J, ARMSTRONG D G, LAVERY L A. Risk factors for recurrent diabetic foot ulcers: Site matters. Diabetes Care, 2007, 30(8): 2077–2079.

[10] GIRACH A, MANNER D, PORTA M. Diabetic microvascular complications: Can patients at risk be identified? A review. Int J Clin Pract, 2006, 60(11): 1471–1483.

[11] CHENG Y, ZU P, ZHAO J, *et al*. Differences in initial versus recurrent diabetic foot ulcers at a specialized tertiary diabetic foot care center in China. J Int Med Res, 2021, 49(1): 300060520987398.

[12] APELQVIST J, LARSSON J, AGARDH C D. Long-term prognosis for diabetic patients with foot ulcers. J Intern Med, 1993, 233(6): 485–491.

[13] CHALYA P L, MABULA J B, DASS R M, *et al*. Surgical management of diabetic foot ulcers: A Tanzanian university teaching hospital experience. BMC Res Notes, 2011, 4: 365[2022-07-22]. https://doi.org/10.1186/1756-0500-4-365.

[14] QUEBEDEAUX T L, LAVERY L A, LAVERY D C. The development of foot deformities and ulcers after great toe amputation in diabetes. Diabetes Care, 1996, 19(2): 165–167.

[15] MOLINES-BARROSO R J, LÁZARO-MARTÍNEZ J L, ÁLVARO-AFONSO F J, *et al*. Validation of an algorithm to predict reulceration in amputation patients with diabetes. Int Wound J, 2017, 14(3): 523–528.

[16] BITENC-JASIEJKO A, KONIOR K, GONTA K, *et al*. Prophylaxis of pain and fractures within feet in the course of osteoporosis: The issue of diagnosing. Pain Res Manag, 2020, 2020: 1391026[2022-10-04]. https://doi.org/10.1155/2020/1391026.

[17] DAVIS F M, KIMBALL A, BONIAKOWSKI A, *et al*. Dysfunctional wound healing in diabetic foot ulcers: New crossroads. Curr Diab Rep, 2018, 18(1): 2.

[18] FREEMAN D B. Corns and calluses resulting from mechanical hyperkeratosis. Am Fam Physician, 2002, 65(11): 2277–2280.

[19] BUS S A, VAN NETTEN J J, HINCHLIFFE R J, *et al*. Standards for the development and methodology of the 2019 International Working Group on the Diabetic Foot guidelines. Diabetes Metab Res Rev, 2020, 36 Suppl 1(Suppl1): e3267[2022-07-22]. https://doi.org/10.1002/dmrr.3267.

[20] ULBRECHT J S, HURLEY T, MAUGER D T, *et al*. Prevention of recurrent foot ulcers with plantar pressure-based in-shoe orthoses: the CareFUL prevention multicenter randomized controlled trial. Diabetes Care, 2014, 37(7): 1982–1989.

[21] PETERSEN B J, ROTHENBERG G M, LAKHANI P J, *et al*. Ulcer metastasis? Anatomical locations of recurrence for patients in diabetic foot remission. J Foot Ankle Res, 2020, 13: 1[2022-07-22]. https://doi.org/10.1186/s13047-020-0369-3.

[22] GALEA A M, SPRINGETT K, BUNGAY H, *et al*. Incidence and location of diabetic foot ulcer recurrence. Diabetic Foot J, 2009, 12(4): 181–186.

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