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ORIGINAL RESEARCH

The Efficacy of Diabetic Foot Treatment in a "TOSF" Pattern: A Five-Year Retrospective Study

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Aim: To evaluate the advantages and problems in the diagnosis and treatment of diabetic foot (DF) patients by analyzing the results of a 5-year follow-up of the organ system based (TOSF) treatment model.

Methods: A retrospective study was conducted in 229 patients with diabetic foot. Chi-square test and rank-sum test were used to analyze the effects of patients' general condition, behavioral and nutritional status, degree of infection (inflammatory markers), comorbidity, diabetic foot grade/classification, and revascularization on readmission rate, amputation rate, all-cause mortality, incidence of other complications, and wound healing time. Logistic regression was used to analyze the risk factors affecting the prognosis of diabetic foot. Kaplan-Meier survival curve was used to analyze the differences in amputation rate and mortality rate at each time point.

Results: This study showed that nutritional status, degree of infection, and revascularization influenced readmission rates. General condition, behavior and nutritional status, degree of infection, Wagner grade and revascularization affect the amputation rate. General conditions, behavioral and nutritional status, degree of infection, comorbidities, classification and revascularization affect the mortality of patients. Age and white blood cell(WBC) count affected the incidence of other complications. Influence of infection degree and Wagner grade and revascularization in patients with wound healing time. Revascularization was an independent protective factor for readmission, amputation, and mortality.Elevated serum inflammatory markers are an independent risk factor for amputation. Hypoproteinemia is an independent risk factor for mortality.

Conclusion: In the "TOSF" diagnosis and treatment pattern, diabetic foot patients have a good prognosis. Special attention should be paid to the screening and revascularization of lower extremity vascular disease in patients with diabetic foot.

Keywords: diabetic foot, organ system, revascularization

Diabetic foot(DF) is a refractory disease with a high global incidence and has become a serious public health problem. There are globally more than 463 million diabetes mellitus patients.[1] The International Diabetes Federation estimates that 9.1–26.1 million diabetic patients annually will develop DF,[2] and this is the most common cause of hospitalization for diabetes, with the characteristics of a long hospitalization time, treatment difficulties, and high medical costs.[3] In China, the incidence of new DF in diabetic patients within one year is 8.1%,[4] the annual amputation and mortality rates are 5.1% and 14.4%, respectively,[4] and the annual cost is 110 billion US dollars.[5] There are several current traditional treatment methods for diabetic foot ulcers (DFUs), such as conventional wound therapeutic (CWT), negative pressure wound therapy(NPWT), platelet-rich plasma gel (PRP), biological agents, skin grafts, and stem cell therapy, especially the latest method of autologous wound edge dotted full-thickness skin grafting for refractory ulcer wounds has achieved satisfactory clinical results.[6] However, the treatment of DF remains challenging because patients with DF have both medical and surgical conditions, it is obvious that a single department of treatment cannot meet such complex patient needs.There have been many reports globally on the treatment of DF by multi-disciplinary teams.[7,8] Most of the medical staff in these teams are scattered in their own diagnosis and treatment centers, therefore, the efficiency of works may be affected to a certain extent. Since our hospital began to implement the "Taking the organ

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system as the foundation (TOSF)" diagnosis and treatment pattern in 2015, the efficiency of patient diagnosis and treatment have been greatly improved.[9]

The "TOSF" pattern of DF diagnosis and treatment center of our hospital is as follows: the outpatient treatment island included endocrinology, vascular surgery, and diabetic foot clinics. Patients were admitted to the hospital at the discretion of the attending physician. On the day of admission, endocrine and vascular surgeons jointly made the preliminary diagnosis and treatment, consultation, and further examination plans. If the infection was serious, emergency debridement was performed after adequate assessment. The treatment plan was adjusted according to the patient's examination and condition changes, and the endocrinologist monitored blood glucose and be responsible for contacting the internal medicine specialists for treating related medical comorbidities (such as nephropathy, cardiac insufficiency, etc.). If combined with lower extremity arterial disease, revascularization was performed by vascular surgeons. And is responsible for contacting specialized surgeons to handle surgical comorbidities (such as debridement, toe amputation, wound repair, major amputation, etc.). The patient does not need to be transferred everywhere, and the medical staff surrounds the patient for treatment, so it's improved efficiency and prognosis. This article summarizes the 5-year follow-up results of the endocrine TOSF center for the diagnosis and treatment of DF.

Methods

A total of 257 patients with the first occurrence of diabetic foot admitted to our center from January 2016 to December 2017 were selected, and 229 patients who were followed up for 5 years were screened for this retrospective study. The data of patients were collected by reviewing inpatient and outpatient medical records and by telephone follow-up. Patient characteristics included: general conditions (sex, single foot/double feet, age, course of disease), behavior and nutritional status [smoking, hemoglobin A1c (HbA1c), albumin (Alb)], degree of infection/inflammatory markers [(white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)], comorbidities [coronary artery disease (CAD), cardiac dysfunction (CD), cerebral infarction (CI), renal insufficiency (RI), hypertension], and DF grading/classification and revascularization (Wagner grade, classification, revascularization or not). The outcome indicators included readmission rate, amputation rate, all-cause mortality, incidence of other complications, wound healing time (weeks), amputation time (weeks), and mortality time (weeks).

Criteria for diagnosis and classification of related diseases were: (1) Diabetic foot is defined as foot infection, ulcer and/or deep tissue destruction caused by nerve abnormalities and/or different degrees of vascular lesions in the distal lower limbs of diabetic patients.[10] (2) According to the albumin level, the patients were divided into two groups: ≥ 30 g/L and < 30 g/L.[11] (3) The degree of infection was divided into general infection and severe infection according to the results of inflammatory markers; general infection: WBC $\leq 12\times10^9$/L and $\geq 4\times10^9$/L, ESR ≤ 60 mm/h, CRP ≤ 32 mg/dL; and severe infection: WBC $> 12\times10^9$/L or $< 4\times10^9$/L, ESR > 60 mm/h, CRP > 32 mg/dL.[12,13] (4) Diabetic foot grading: Wagner grading was used;[14] ischemic diabetic foot was defined as an Ankle brachial index(ABI) < 0.90 and arterial stenosis $\geq 50\%$ or occlusion on ultrasound, computerized tomography angiography(CTA), or digital subtraction angiography(DSA). (5) All patients were treated by percutaneous transluminal angioplasty, and antegrade or retrograde puncture was selected according to the condition of the patient, as well as balloon dilatation or stent implantation.

Statistical Analysis

All data were analyzed using SPSS program version 17.0. Categorical variables such as general condition, behavioral and nutritional status, degree of infection (inflammatory markers), complications, classification of diabetic foot, and revascularization were expressed as percentages and analyzed by chi-square test (χ^2). Continuous non-normal distribution data such as wound healing time were expressed as median (25%, 75%) and analyzed by rank sum test. A p value of ≤ 0.05 was used as the level of significance. The odds ratio (OR) and 95% confidence interval (CI) of logistic regression analysis were used to evaluate the risk factors affecting the prognosis of diabetic foot. Kaplan-Meier survival curve was used to analyze the differences in amputation and mortality rates at each time point. A p value of ≤ 0.05 was considered to be the significance level.

Ethics

This study complies with the Declaration of Helsinki and the Ethics approval for this study was provided by the Medical Ethics Committee of Capital Medical University Affiliated Luhe Hospital(Luhe Hospital 2023-LHKY-064-02, on 2023/06/21). During their participation, participants gave written informed consent.

Results

A total of 257 patients were screened in this study, with 229 finally enrolled, thus a loss rate of 11.1%. There were 125 males (54.6%) and 104 females (45.4%). The median age was 64 (58, 74.5) years, ranging over 20–90 years. During the 5-year follow-up, 75 patients were readmitted (32.8%). The amputation rate was 12.2% (28 cases). The all-cause mortality rate was 21.4% (49 cases), and the top three causes of mortality were myocardial infarction (16 cases, 32.6%), cerebral infarction (13 cases, 26.5%), and CD (6 cases, 12.2%). Other complications occurred in 49 cases (21.40%), the top three diseases being myocardial infarction (11 cases, 22.4%), cerebral infarction (10 cases, 20.4%), and renal failure (8 cases, 16.3%). There were 171 cases of ischemic diabetic foot, accounting for 74.7%. Except for the amputation patients and those who died, the wounds of 163 patients were healed (71.2%), with a median healing time of 78 (47, 126) days.

The amputation rate was 16.8%, which was higher than the 6.8% of the female patients (Table 1). The mortality rate of patients aged < 65 years was lower than that of patients ≥ 65 years (8.5% vs 35.2%), whereas the incidence of other complications was higher than that of patients ≥ 65 years (27.2% vs 15.4%). The mortality rate of patients with disease duration < 10 years was lower than that of patients with disease duration ≥ 10 years (13.7% vs 26.3%).

In terms of behavior and nutritional status, the amputation and mortality rates in smoking patients were higher than those in non-smoking patients (16.9% vs 8.2%; 28.1% vs 15.6%, respectively) (Table 2). The readmission rate of patients with HbA1c ≤ 7% was lower than that of patients with HbA1c > 7% (20.7% vs 37.4%), and the mortality rate was lower than that of patients with HbA1c > 7% (9.6% vs 26.0%). The amputation rate was lower in patients with Alb ≥ 30 g/L than in patients with Alb < 30 g/L (8.8% vs 31.5%), as was the mortality rate (17.1% vs 45.8%).

The amputation rate of patients with WBC ≥ 4×10^9/L and ≤ 12×10^9/L was 6.2%, which was lower than that of patients with WBC < 4×10^9/L or > 12×10^9/L of 26.9% and the all-cause mortality was 18.0% and the incidence of other complications was 17.3% in the latter group, which were lower than the former group of 29.9% and 31.4%, respectively (Table 3). The readmission rate was 26.4% in patients with ESR ≤ 60 mm/h and 39.2% in patients with ESR > 60 mm/h. The amputation rate was 2.7% in patients with ESR ≤ 60 mm/h and 21.8% in patients with ESR > 60 mm/h. The all-cause mortality rate of patients with ESR ≤ 60 mm/h was 15.0%, which was significantly lower than of those with ESR > 60 mm/h of 27.9%, and the median wound healing time for the former was 66 (40.25, 91.0) days, which was significantly shorter than the 110 (69,167) days of the latter. The amputation rate was lower in patients with CRP ≤ 32 mg/dL than in those with CRP > 32mg/dL (7.2% vs 17.1%). The median wound healing time of 67 (40.25, 90.25) days in patients with CRP ≤ 32 mg/dL was shorter than in patients with CRP > 32 mg/dL [98 (62.0, 160.0) days].

In terms of comorbidities, the all-cause mortality in patients with coronary heart disease (CAD) was 31.1%, which was higher than the 18.2% in patients without CAD (Table 4). All-cause mortality was significantly higher in patients with CD than in patients without CD (58.9% vs 18.4%). All-cause mortality was higher in patients with cerebral infarction (CI) (34.5%) than in patients without CI (16.7%).

With regards to the diabetic foot grading/classification and revascularization, patients with Wagner grades 1–3 had a lower amputation rate (4.3%) than those with Wagner grades 4–5 (18.0%), and the median wound healing time was 54 (34.5, 79.25) days for the former, which was shorter than the 103 (75.5, 164.5) days of the latter(Table 5). The all-cause mortality of patients with non-ischemic DF was 8.7%, which was lower than that of patients with ischemic DF of 23.4%. There were 171 patients (74.7%) with ischemic DF. Among them, 72 patients with revascularization had lower readmission and amputation rates than those without revascularization (23.7% vs 38.4%; 5.6% vs 18.2%, respectively). The mortality rate was significantly lower (15.3% vs 33.4%), and the wound healing time was significantly shorter [78 (50, 100) days vs 98 (58, 174) days] in patients with revascularization compared with patients without revascularization.

Logistic regression analysis showed that HbA1c > 7% and CAD were risk factors for readmission (Table 6). Revascularization was a protective factor for readmission. WBC > 12×10^9/L or <4×10^9/L and ESR > 60 mm/h were

Table 1 Effect of General Conditions on Prognosis

Grouping		Number N/%	Read mission N/%	Chi-Square value	P value	Amputation N/%	Chi-Square value	P value	Mortality N/%	Chi-Square value	P value	Other Complications N/%	Chi-Square value	P value	Number N/%	Healing Time (IQR, p25-p75)	T/Z value	P value
Gender	Man	125/54.6	44/35.2	0.749	0.387	21/16.8	5.363	0.021	30/24.0	1.109	0.292	21/16.8	3.459	0.063	82/65.6	79.5 (45.75, 128, 25)	−0.368	0.713
	Female	104/45.4	31/29.9			7/6.8			19/18.3			28/27.0			81/77.9	78 (53, 106.5)		
Age	<65	118/51.5	38/32.3	0.033	0.856	12/10.2	0.960	0.327	10/8.5	24.172	0.000	32/27.2	4.738	0.030	101/85.6	81 (50, 122)	−0.385	0.701
	≥65	111/48.5	37/33.4			16/14.5			39/35.2			17/15.4			62/55.9	76 (42, 126.25)		
Single/ Double	Single	212/92.6	75/32.8	0.230	0.631	28/12.3	3.350	0.067	49/21.4	0.346	0.556	49/21.4	1.821	0.177	155/73.1	77 (47, 117)	−1.268	0.205
	Double	17/7.4	7/41.2			5/29.5			5/29.5			1/5.9			8/47.1	115 (51.5, 195.25)		
Course of disease	<10	88/38.4	25/28.5	1.223	0.269	12/14.8	0.468	0.494	11/13.7	6.175	0.013	19/21.6	0.003	0.955	67/76.1	78 (48, 105)	−0.103	0.918
	≥10	141/61.6	50/35.5			15/10.7			37/26.3			30/21.3			96/68.1	77 (47, 141)		

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Table 2 Effect of Behavior and Nutritional Status on Prognosis

Grouping		Number N/%	Read mission N/%	Chi-Square value	P value	Amputation N/%	Chi-Square value	P value	Mortality N/%	Chi-Square value	P value	Other Complications N/%	Chi-Square value	P value	Number N/%	Healing Time (IQR, p25-p75)	T/Z value	P value
Smoke	Yes	107/46.7	33/30.9	0.333	0.564	18/16.9	3.952	0.047	30/28.1	5.265	0.022	19/17.8	1.583	0.208	64/59.8	80.5 (47.75, 150.5)	−0.763	0.445
	No	122/53.3	42/34.5			10/8.2			19/15.6			30/24.6			99/81.1	78 (47, 107)		
HbA1c	≤7	63/27.5	13/20.7	5.793	0.016	4/6.4	2.093	0.148	6/9.6	7.285	0.007	18/28.6	2.659	0.103	54/85.7	78 (54.5, 96)	−0.751	0.453
	>7	166/72.5	62/37.4			24/14.5			43/26.0			31/18.7			109/65.7	79 (45.5, 143)		
Alb	≥30	194/84.7	59/30.5	3.152	0.076	17/8.8	14.193	0.000	33/17.1	14.525	0.000	43/22.2	0.445	0.505	154/79.4	77.5 (46.75, 117)	−1.475	0.140
	<30	35/15.3	16/45.8			11/31.5			16/45.8			6/17.2			9/25.7	117 (60, 211.5)		

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Table 3 Effect of Degree of Infection on Prognosis

Grouping		Number N/%	Read mission N/%	Chi-Square value	P value	Amputation N/%	Chi-Square value	P value	Mortality N/%	Chi-Square value	P value	Other Complications N/%	Chi-Square value	P value	Number N/%	Healing Time (IQR, p25-p75)	T/Z value	P value
WBC (10^9/L)	≤12/≥4	162/70.7	49/30.3	1.577	0.209	10/6.2	18.911	0.000	29/18.0	4.024	0.045	28/17.3	5.570	0.018	130/80.2	77 (45.75, 107.25)	−1.578	0.115
	>12/<4	67/29.3	26/38.9			18/26.9			20/29.9			21/31.4			33/49.3	93 (53, 159)		
ESR (mm/H)	≤60	114/49.8	30/26.4	4.268	0.039	3/2.7	19.476	0.000	17/15.0	5.676	0.017	23/20.2	0.202	0.653	100/87.7	66 (40.25, 91.0)	−4.864	0.000
	>60	115/50.2	45/39.2			25/21.8			32/27.9			26/22.7			63/54.8	110 (69, 167)		
CRP (mg/dl)	≤ 32	112/48.9	34/30.4	0.570	0.450	8/7.2	5.280	0.022	23/20.6	0.097	0.756	23/20.6	0.097	0.756	88/78.6	67 (40.25, 90.25)	−4.167	0.000
	> 32	117/51.1	41/35.1			20/17.1			26/22.3			26/22.3			75/64.1	98 (62.0, 160.0)		

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Table 4 Effect of Comorbidities on Prognosis

Grouping		Number N/%	Read mission N/%	Chi-square value	P value	Amputation N/%	Chi-square value	P value	Mortality N/%	Chi-square value	P value	Other complications N/%	Chi-square value	P value	Number N/%	Healing time (IQR, p25-p75)	T/Z value	P value
CAD	Yes	58/25.3	23/39.7	1.681	0.195	9/15.6	0.783	0.376	18/31.1	4.289	0.038	17/29.4	2.892	0.089	32/55.2	78 (37.75, 127.0)	−0.033	0.973
	No	171/74.7	52/30.5			19/11.2			31/18.2			32/18.8			131/76.6	80/ (48.0, 117.0)		
CD	Yes	17/7.4	4/23.5	0.709	0.400	0/0.0	—	0.238	10/58.9	15.293	0.000	5/29.5	0.701	0.402	7/41.2	79 (21, 230)	−0.348	0.728
	No	212/92.6	71/33.5			28/13.3			39/18.4			44/20.8			156/73.6	78 (47.25, 121.5)		
Cerebral infarction	Yes	61/26.6	24/39.4	1.641	0.200	7/11.5	0.044	0.834	21/34.5	8.392	0.004	16/26.3	1.154	0.283	37/60.7	82 (49.5, 135.5)	−0.695	0.487
	No	168/73.4	51/30.4			21/12.5			28/16.7			33/19.7			126/75.0	76.5 (46.75, 117.0)		
RI	Yes	64/27.9	20/31.7	0.091	0.763	7/11.0	0.138	0.711	19/29.7	3.630	0.057	16/25.0	0.685	0.408	43/67.2	75 (45, 174)	−0.331	0.740
	No	165/72.1	55/33.4			21/12.8			30/18.2			33/20.0			120/72.7	78.5 (47.25, 119.75)		
Hypertension	Yes	121/52.8	37/30.6	0.550	0.458	14/11.6	0.103	0.748	31/25.7	2.720	0.099	28/23.2	0.464	0.496	78/64.5	76.5 (44.25, 108.5)	−0.877	0.380
	No	108/47.2	38/35.2			14/13.0			18/16.7			21/19.5			85/78.7	82 (49.5, 128.5)		

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Table 5 Effect of *DF* Grading/Classification and Revascularization on Prognosis

Grouping		Number N/%	Read mission N/%	Chi-Square value	P value	Amputation N/%	Chi-Square value	P value	Mortality N/%	Chi-square value	P value	Other Complications N/%	Chi-Square value	P value	Number N/%	Healing time (IQR, p25-p75)	T/Z value	P value
Wagner grading	1–3	95/41.5	29/30.6	0bia.365	0.546	4/4.3	9.722	0.002	20/21.1	0.011	0.915	19/20.0	0.188	0.664	78/82.1	54 (34.5, 79.25)	−6.394	0.000
	4–5	134/58.5	46/34.4			24/18.0			29/21.7			30/22.4			85/63.4	103 (75.5, 164.5)		
classification	Non-ischemia	58/25.3	20/34.5	0.106	0.745	6/10.4	0.256	0.613	5/8.7	7.539	0.006	9/15.6	1.597	0.206	53/91.4	71 (42, 121)	−1.178	0.239
	ischemia	171/74.7	55/32.2			22/12.9			44/25.8			40/23.4			110/64.3	82 (55, 126)		
revascularization	Yes	72/42.2	17/23.7	4.169	0.041	4/5.6	5.221	0.022	11/15.3	7.111	0.008	18/25.0	0.179	0.627	59/81.9	78 (50, 100)	−2.050	0.040
	No	99/57.9	38/38.4			17/18.2			33/33.4			22/22.3			51/51.5	98 (58, 174)		

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Table 6 Logistic Regression Analysis of the Influence of Various Factors on Prognosis

Risk Factors	Readmission Rate		Amputation Rate		Mortality		Other Complications Rate	
	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value
Gender	1.583 (0.735–3.411)	0.241	2.062 (0.554–7.666)	0.280	0.638 (0.236–1.724)	0.376	0.561 (0.216–1.458)	0.235
Age	1.308 (0.657–2.602)	0.444	0.648 (0.202–2.079)	0.466	0.199 (0.087–0.453)	0.000	3.349 (1.560–7.189)	0.002
Single/Double	1.136 (0.347–3.714)	0.833	0.888 (0.159–4.956)	0.893	2.409 (0.540–10.745)	0.249	4.657 (0.567–38.213)	0.152
Course of disease	0.995 (0.511–1.938)	0.989	2.399 (0.961–5.984)	0.061	1.221 (0.489–3.053)	0.669	0.869 (0.395–1.913)	0.728
Smoke	0.510 (0.234–1.109)	0.089	1.372 (0.395–4.769)	0.619	1.727 (0.640–4.663)	0.281	1.233 (0.472–3.222)	0.669
HbA1c	2.565 (1.266–5.197)	0.009	2.226 (0.510–9.716)	0.287	2.345 (0.868–6.338)	0.093	0.657 (0.269–1.605)	0.356
Alb	1.556 (0.580–4.176)	0.380	2.649 (0.754–9.305)	0.128	3.380 (1.397–8.181)	0.007	0.324 (0.103–1.021)	0.054
WBC	0.753 (0.317–1.792)	0.522	2.576 (1.025–6.476)	0.044	1.668 (0.560–4.967)	0.358	4.306 (1.895–9.785)	0.000
ESR	0.477 (0.211–1.079)	0.076	6.309 (1.665–23.914)	0.007	1.696 (0.570–5.048)	0.206	1.075 (0.403–2.871)	0.885
CRP	1.433 (0.641–3.200)	0.381	1.894 (0.471–7.614)	0.368	2.015 (0.680–5.969)	0.206	1.080 (0.393–2.965)	0.882
CAD	2.167 (1.063–4.415)	0.033	3.400 (0.990–11.680)	0.052	0.659 (0.243–1.788)	0.413	2.184 (1.013–4.708)	0.046
CD	0.305 (0.083–1.119)	0.730	0.000	0.998	6.009 (1.755–20.580)	0.004	1.769 (0.406–7.714)	0.447
Cerebral infarction	1.604 (0.842–3.057)	0.151	0.510 (0.146–1.784)	0.292	2.045 (0.941–4.447)	0.071	1.703 (0.732–3.962)	0.216
RI	0.899 (0.453–1.784)	0.706	0.592 (0.179–1.959)	0.391	1.735 (0.720–4.180)	0.219	1.269 (0.561–2.870)	0.568
Hypertension	0.731 (0.388–1.380)	0.335	0.821 (0.250–2.694)	0.745	1.098 (0.443–2.722)	0.840	1.003 (0.443–2.273)	0.994
Wagner grading	1.048 (0.524–2.098)	0.894	0.295 (0.079–1.099)	0.069	1.136 (0.467–2.761)	0.778	1.041 (0.457–2.370)	0.924
Classification	0.938 (0.442–1.990)	0.867	0.838 (0.238–2.956)	0.784	0.443 (0.139–1.416)	0.170	0.360 (0.144–0.899)	0.029
Revascularization	0.496 (0.252–0.978)	0.043	0.265 (0.085–0.820)	0.021	0.361 (0.168–0.776)	0.009	1.167 (0.572–2.381)	0.672

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risk factors for amputation. Revascularization was a protective factor for amputation. Alb < 30 g/L and cardiac insufficiency were risk factors for mortality. Age < 65 years and revascularization were protective factors for mortality. Age < 65 years, WBC > 12×10^9/L or < 4×10^9/L and CAD were risk factors for other complications. Non-ischemic DF was a protective factor for other complications.

Revascularization was an independent protective factor for readmission, amputation, and mortality (Table 6). HbA1c > 7% was an independent risk factor for readmission. WBC > 12×10^9/L or < 4×10^9/L was an independent risk factor for amputation and other complications, while ESR > 60 mm/h was an independent risk factor for amputation. Alb < 30 g/L and cardiac insufficiency were independent risk factors for mortality. Age < 60 years was an independent protective factor for mortality and an independent risk factor for other complications.

Kaplan-Meier curve analysis showed the amputation rates at each time point of follow-up (Figure 1). Hereby, male, smoking, Alb < 30 g/L, WBC > 12×10^9/L or < 4×10^9/L, ESR > 60 mm/h, CRP > 32 mg/dL, and Wagner 4–5 patients were associated with a higher amputation rate, whereas for patients with revascularization it was lower. For mortality at each follow-up time point (Figure 2): age ≥ 65 years, disease duration ≥ 10 years, smoking, HbA1c > 7%, Alb < 30 g/L, WBC > 12×10^9/L or < 4×10^9/L, ESR > 60 mm/h, CAD, CD, cerebral infarction, and ischemic DF patients were associated with a higher mortality, whereas it was lower in patients with revascularization.

Discussion

Diabetic foot has become a global medical problem due to its characteristics of high disability and mortality rates and considerable cost. In particular, the disease involves complex anatomical sites and pathophysiology, and there are various problems that need to be resolved concurrently, including blood glucose control, internal medical complications, local wound management, vascular diseases, and infection,[15] thus the diagnosis and treatment through a single discipline is frequently ineffective. In recent years, ever more centers have adopted the model of "Multidisciplinary collaboration" for DF diagnosis

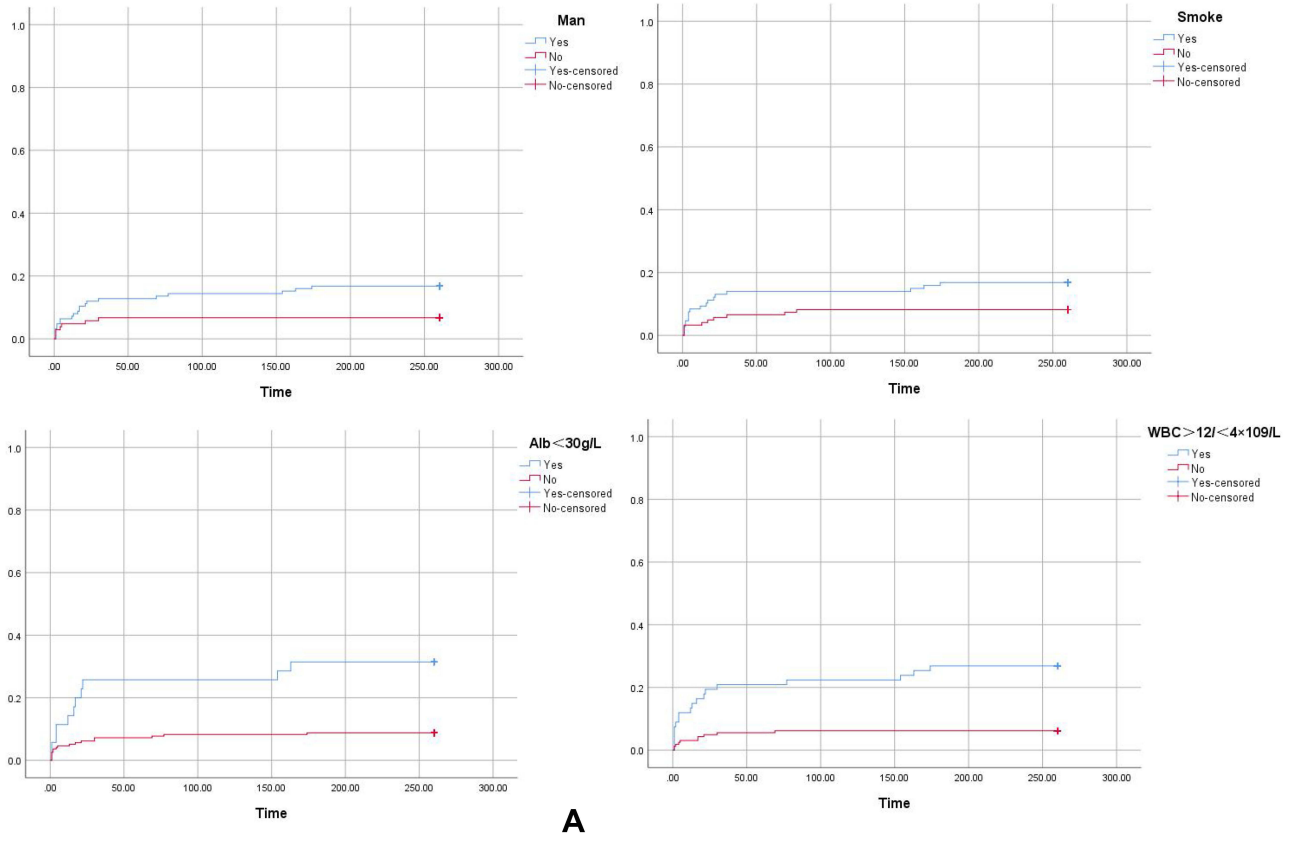

Figure 1 Continued.

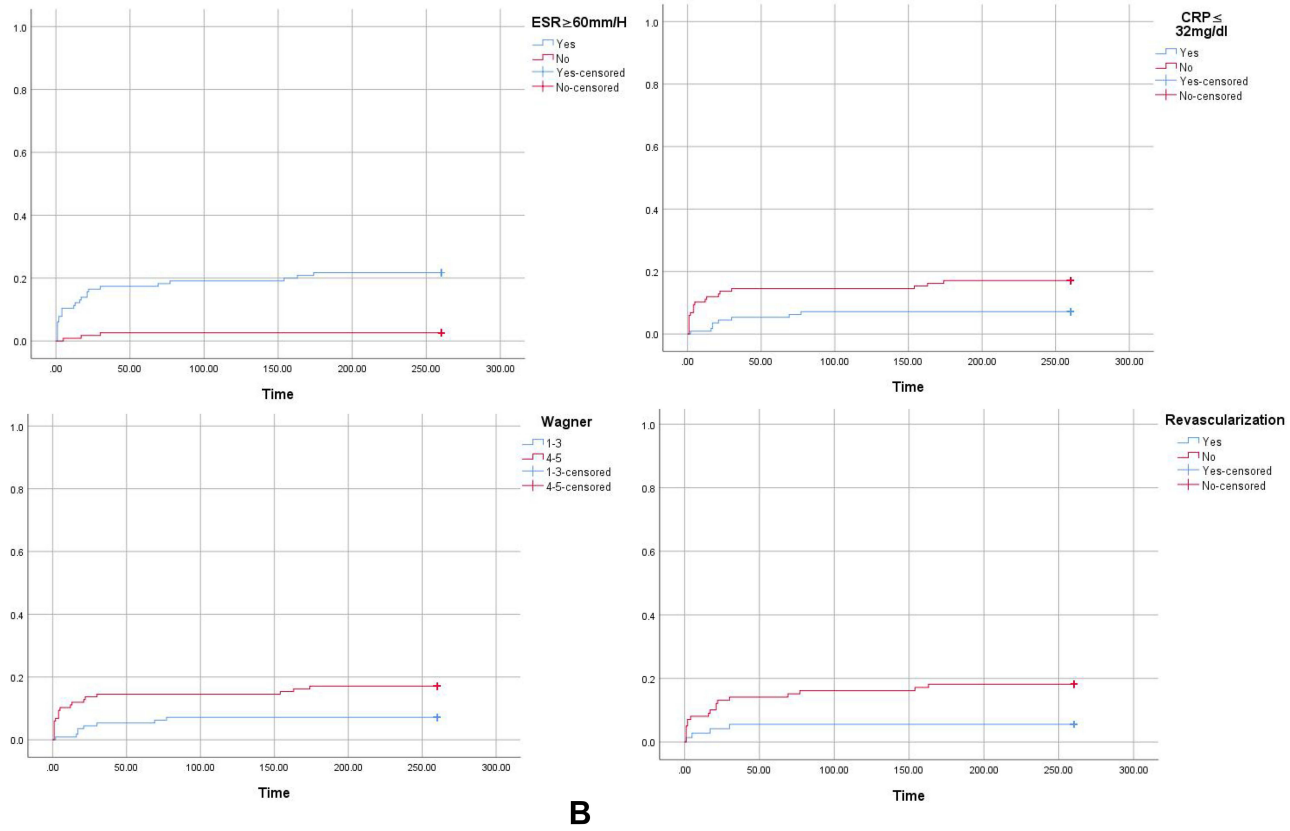

Figure 1 (**a**) Kaplan-Meier curve analysis of the influence of each factor on amputation time. Amputation rates by each follow-up time point: They were higher in male patients than in female patients (p=0.023), higher in smokers than in non-smokers (p= 0.042), lower in patients with albumin ≥30g/L than in patients with albumin < 30g/L (p= 0.000). The patients with WBC ≤12×10^9/L and ≥4×10^9/L were lower than those with WBC > 12×10^9/L and < 4×10^9/L (p=0.000). (**b**) Kaplan-Meier curve analysis of the influence of each factor on amputation time. Amputation rates by each follow-up time point: The patients with ESR ≤60mm/H were lower than those with ESR > 60mm/H (p=0.000). The levels of CRP in patients with CRP≤32mg/dl were lower than those in patients with CRP > 32mg/dl (p=0.019), and those in patients with Wagner regrade 1–3 were lower than those in patients with Wagner grade 4–5 (p=0.002), and those in patients with revascularization were lower than those in patients without revascularization (p=0.016).

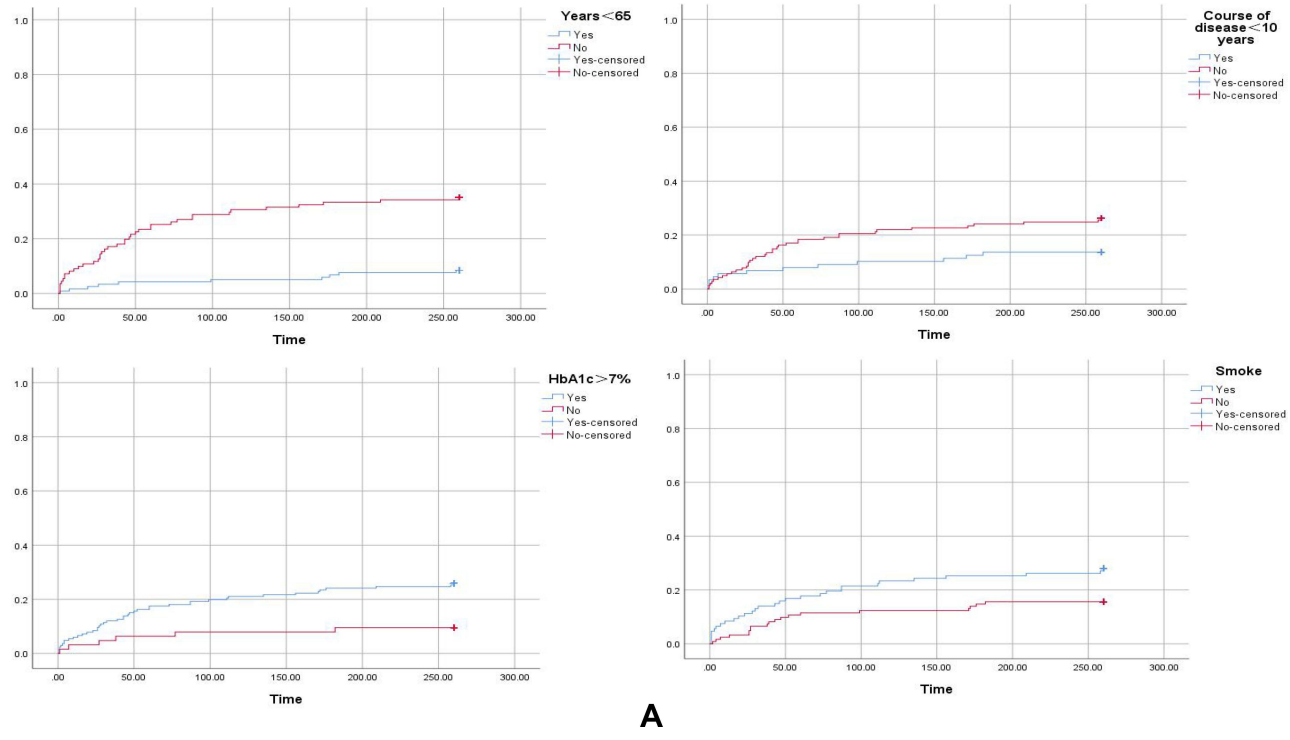

Figure 2 Continued.

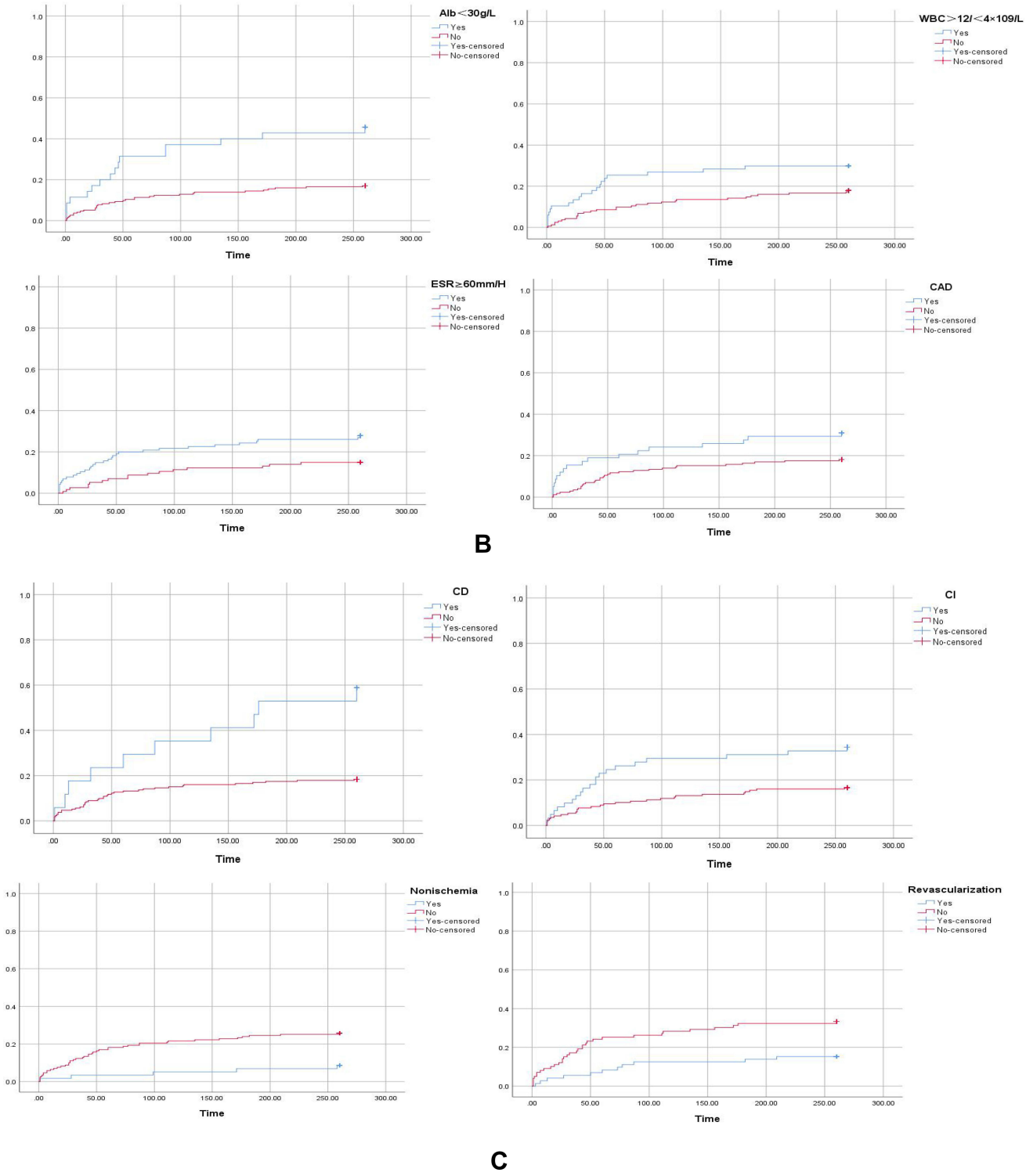

Figure 2 (**a**) Kaplan-Meier curve analysis of the effect of each factor on time to death. Mortality at each event point: There was lower in Patients younger than 60 years than in those older than 60 years(p=0.000).Patients with disease duration less than 10 years were less than those with disease duration more than 10 years (P=0.027); patients with Hba1c ≤7% were less than those with Hba1c > 7% (p=0.009), patients with smoking were more than those with non-smoking (P= 0.021). (**b**) Kaplan-Meier curve analysis of the effect of each factor on time to death. Mortality at each event point: Patients with albumin≥30g/L was lower than that of patients with albumin < 30g/L (p=0.000); Patients with white blood cell ≤12×10^9/L and ≥4×10^9/L was lower than that of patients with white blood cell > 12×10^9/L and < 4×10^9/L (p=0.027). Patients with ESR≤60mm/H were lower than those with ESR > 60mm/H (p= 0.014), patients with CAD, were higher than those without CAD (p=0.027). (**c**) Kaplan-Meier curve analysis of the effect of each factor on time to death. Mortality at each event point: patients withCD (p= 0.000) and cerebral infarction(CI) (p= 0.003) were higher than those without those diseases(p= 0.003); Patients with non-ischemic *DF* was lower than ischemic *DF* (P =0.007). Patients with revascularization were less than those without revascularization (p=0.007).

and treatment, and achieved significant results.[16,17] According to the "TOSF" pattern, our center has established an endocrine center.[8] Patients can complete the entire course of disease diagnosis and treatment in the same medical center. It is convenient for patients and improves the efficiency of medical staff. The Department of Endocrinology and the Department of Vascular Surgery were set up in the same ward. The Department of Endocrinology solves the management of blood glucose control and medical complications. Vascular surgery addresses wound management, revascularization, and infection control, and the doctors in two specialties work together on daily rounds to solve patient problems and develop treatment plans. Clearly, this mode can be more active in the diagnosis and treatment of patients and can better apply the advantages of multidisciplinary collaboration. On the, this study retrospectively analyzed the 5-year follow-up results of 229 patients basis on the "TOSF" pattern of DF. The prognosis of the "TOSF" pattern and the factors affecting DF prognosis were analyzed.

From the overall situation of the 5-year follow-up, the readmission rate was 32.75%, which was better than the 1-year readmission rate of 31.6% shown in a previous study.[10] The amputation rate was 12.23%, while previous studies showed that this of hospitalized patients was 11.4%–21.5%, which was approximately the same.[18–20] The all-cause mortality rate was 21.4%, which was lower than the 32.7% reported by Chu et al.[21] The incidence of other complications and mortality was 21.4%, and the two most frequent diseases were cardiovascular and cerebrovascular diseases. Few studies have been conducted on the healing time of DF, with a median overall healing time of 78 days in the present study. However, the rate of severe DF was higher in the present study (54.5%) than in the national survey (28.8%).[22] Moreover, the proportion of ischemic DF (74.7%) was much higher than that in the China DIA-LEAD study (21.2%).[23] As previously mentioned, the patients in our study were sicker, but the prognosis was better than that in other previous studies.[18–23]

From the general situation of patients, male patients accounted for 54.6%, and their amputation rate of 16.8% was higher than the 6.8% of female patients, which was consistent with the results of previous studies.[24,25] This is associated with men's poor physical and mental self-care ability as well as poor joint flexibility and higher foot pressure.[26–28] Patients aged < 65 years accounted for 51.5%, which was also in agreement with the trend of diabetic foot in youth.[26] The mortality rate of patients aged < 65 years was 8.5%, which was lower than that of patients aged ≥ 65 years, which was consistent with the results of other studies that an increase of age led to greater mortality.[29] However, the higher incidence of other complications in younger patients was inconsistent with other studies,[26] and we propose that the higher mortality rate in elderly patients may have led to that result. The longer the course of the disease, the higher is the prevalence and mortality of diabetic foot,[3,26] which is consistent with the results of the present study. The results suggested that male, older age, and longer disease duration are associated with a worse prognosis.

Patients' behavior and nutritional status have a major impact on DF prognosis. In the present study, the proportion of smoking patients was 46.7%, which was significantly higher than 10.14% reported by Al-Rubeaan et al.[15] Moreover, the higher amputation rate and mortality rate in this study were consistent with Aidin's study,[30] which may be due to smoking being an important risk factor for vascular diseases.[3,31] HbA1c is recognized as an index to evaluate the level of blood glucose control in diabetic patients,[32] and the American Diabetes Association recommends that the HbA1c level be reduced to 7.0%.[33] Similar to the study of Gerstein et al,[34] elevated HbA1c resulted in increased mortality. This also explains why the lower readmission rate in this study in patients with high HbA1c. Alb is an important nutrient for the human body[35] and is essential for the maintenance of the body's hemodynamics.[36] A decrease of Alb can increase the mortality of patients.[37] By contrast, Alb supplementation can reduce the risk of mortality by 25%,[38] and hospitals in China generally stipulate that patients with serum Alb < 30 g/L can be supplemented[11.] The present study similarly showed that hypoproteinemia was associated with increased mortality and amputation rates. Therefore, smoking cessation, good glycemic control, and high-quality protein supplementation can significantly improve DF prognosis.

The severity of infection is an important factor in determining DF prognosis.[39,40] At present, the commonly used serological inflammatory markers to reflect DF infection severity include WBCs, CRP, and the ESR.[41] When WBC < 4×10^9/L or > 12×10^9/L, CRP > 32 mg/dL, and ESR > 60 mm/h, this frequently indicates the presence of deep tissue infection or severe infection.[12,13] Previous studies have shown that elevated WBC and CRP are associated with an increased amputation rate,[42,43] while an elevated ESR frequently indicates the presence of osteomyelitis,[44] which can significantly increase the risk of major amputation.[45] This study not only showed that abnormal inflammatory markers were associated with an increased amputation rate, but also suggested that an abnormal WBC count in severe infection was associated with increased all-cause mortality and other complications, an increased ESR was associated with a greater readmission rate and all-cause mortality, and an increased ESR and CRP were

associated with a prolonged wound healing time. Therefore, the inflammatory markers of patients on admission are important indicators for the disease prognosis.

Hypertension, renal insufficiency, and cerebral infarction were the top three complications in the present study. The study of Zheng and Yao[46] showed that the main causes of mortality of diabetic foot were cardiovascular and cerebrovascular diseases, and our study also showed that the mortality of patients with CAD, CD, or CI was significantly higher than that of patients without such complications. The study by Morbach et al[47] showed that 50% of mortalities in DF were caused by heart disease, with which the present study was consistent. From the present study, it is suggested that attention should be paid to the cardiovascular and cerebrovascular complications in patients with DF and to avoid the occurrence of adverse events.

The grade, classification, and revascularization of DF also directly affect its prognosis. Several studies have shown that the higher the Wagner grade, the greater the amputation risk,[48,49] with which our study was consistent. In addition, our study showed that patients with a lower Wagner grade exhibited a shorter wound healing time. The proportion of ischemic DF in this study was 74.7%, which was much higher than the 21.2% in the China DIA-LEAD study,[23] and the combined ischemia was associated with amputation and mortality through DF.[19,50] By contrast, in our study, the amputation rate of patients with ischemic DF was not significantly increased, and the wound healing time was similar to that of patients with non-ischemic diabetic foot, indicating that revascularization can significantly reduce the amputation rate[51] and shorten the wound healing time,[39] with which our study was consistent. Our study also showed that revascularization was associated with reduced readmission and mortality. It is suggested that revascularization is of great significance in DF treatment.

The risk factors for DF amputation include increased WBC,[52] elevated HbA1c,[18] ischemia,[48] and a higher Wagner grade.[50] Relative risk factors include poor general condition,[52] lack of multidisciplinary collaboration,[53] and poor preventive measures.[54] Our study was consistent with this. In addition, the present study showed that elevated CRP is a risk factor for amputation, and a severe abnormal WBC count and elevated ESR are independent risk factors for amputation. Revascularization was an independent protective factor for amputation. Risk factors for mortality in patients with DF include its severity,[55] combined ischemia,[56] age,[57] and combined heart disease,[58] with which our study was also similar. Our study also demonstrated that hypoproteinemia and CD were independent risk factors for mortality, while revascularization and age < 60 years were independent protective factors for mortality.

In addition, elevated HbA1c and CAD were risk factors for readmission, and revascularization was an independent protective factor for readmission. Age < 65 years, severe abnormal WBC count, and CAD were risk factors for other complications. Non-ischemic DF was a protective factor for other complications. In conclusion, the severity of infection and nutritional status have a major impact on DF prognosis, and greater attention should be paid to the screening of lower extremity vascular disease and the significance of revascularization in DF treatment.

Limitations of This Study

Our study was a single-center retrospective study, such that the results have some limitations. Because we have only recently implemented the "TOSF" pattern, the sample size is small and we are still inexperienced, but some studies have reported that there is a "learning curve" for multidisciplinary collaboration, and over time, the team cooperation improves and the major amputation rate decreases.[6] Despite these limitations, our study provides a new approach for DF management with a multidisciplinary team and preliminarily results indicated a favorable outcome for patients.

Conclusion

This study of a novel "TOSF" multidisciplinary collaboration model for DF diagnosis and treatment has preliminarily showed a good prognosis for patients with DF. It confirmed the importance of the prognostic factors of DF in previous studies. In particular, our study confirmed the significance of inflammatory markers in the prognosis of patients, and the positive effect of albumin supplementation on the prognosis. Special attention should be paid to the screening and revascularization of lower extremity vascular disease in patients with DF. In the future, we will increase the number of patients to improve the study, and may also establish a special DF ward and team to deal with the difficult problems of DF patients.

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Disclosure

The authors declare no conflicts of interest in this work.

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