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Development and Validation of a Prognostic Model for Risk Assessment of Unfavorable Outcomes in Patients with Diabetic Foot Syndrome and Concomitant Ischemic Heart Disease

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Abstract **Background:** Diabetic foot syndrome (DFS) combined with ischemic heart disease (IHD) represents a high-risk comorbid condition with frequent limb loss and mortality. No validated prognostic instrument integrating cardiac, metabolic, and angioarchitectural parameters exists for pre-interventional risk stratification in this population. **Methods:** A retrospective study included 58 patients with DFS and IHD who underwent X-ray endovascular interventions (XEI) at the Republican Specialized Center of Surgery named after V.V. Vakhidov (2015–2019). Binary logistic regression identified independent predictors of major amputation or 30-day mortality. Prognostic accuracy was evaluated by ROC analysis. **Results:** Unfavorable outcomes occurred in 13 patients (22.4%). Independent predictors were: LVEF <50% (OR=8.26; 95% CI: 2.03–33.55; p=0.003), angina CCS class III–IV (OR=7.24; p=0.017), Wagner stage IV–V (OR=6.47; p=0.013), heel or total foot involvement (OR=5.59; p=0.019), HbA1c ≥10% (OR=4.90; p=0.027), and crossover vascular access (OR=4.34; p=0.038). The composite model achieved AUC=0.915 (95% CI: 0.851–0.978), sensitivity 92.3%, specificity 84.4% - significantly superior to LVEF alone (AUC=0.772). **Conclusions:** The developed multifactorial prognostic model demonstrates high accuracy for pre-interventional risk stratification in patients with DFS and IHD and can guide individualized therapeutic decision-making.

Keywords Diabetic foot syndrome, Ischemic heart disease, Prognostic model, Logistic regression, ROC analysis, Amputation, Risk stratification, Endovascular intervention

1. Introduction

Diabetic foot syndrome (DFS) is one of the most severe complications of diabetes mellitus, determining a high incidence of amputations, disability, and mortality. According to the International Diabetes Federation, up to 25% of patients with diabetes mellitus develop ulcerative-necrotic lesions of the lower extremities during their lifetime, and five-year mortality following amputation exceeds 50%, comparable to oncological diseases [1]. DFS is not only a complication of micro- and macroangiopathy but also a marker of systemic vascular dysfunction, frequently coexisting with ischemic heart disease (IHD), which substantially worsens the clinical course and prognosis.

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More than 70% of patients with DFS have concomitant IHD, with verified systolic dysfunction (LVEF <50%) detected in one-third of patients, and prior myocardial infarction in every fifth patient [2,3]. Despite the introduction of high-technology X-ray endovascular interventions (XEI), a significant proportion of patients with DFS and IHD continue to experience unfavorable outcomes - major amputation, mortality, repeat interventions, and cardiac decompensation [4]. This is largely attributable to the traditional approach, in which revascularization of the lower extremity is planned without systematic assessment of myocardial reserve or cardiac functional status.

Current guidelines emphasize the necessity of integrating systemic vascular assessment and cardiac function into revascularization planning for patients with severe comorbid pathology [5,6]. However, formalized, validated prognostic tools that quantitatively integrate angioarchitectural, cardiological, and metabolic parameters for risk-adapted therapeutic

decision-making remain absent. This gap necessitates the development of an evidence-based predictive model capable of identifying patients at high risk of treatment failure prior to XEI in the setting of combined DFS and IHD.

2. Materials and Methods

Study design and patient population. This retrospective observational study was conducted at the Republican Specialized Center of Surgery named after Academician V.V. Vakhidov (Tashkent, Republic of Uzbekistan) between January 2015 and December 2019. The study cohort comprised 58 consecutive patients with confirmed DFS complicated by lower-limb ischemia and documented IHD who underwent XEI on lower extremity arteries under the standard institutional protocol operative at that time, without preliminary cardiac risk stratification.

Inclusion criteria: confirmed type 2 diabetes mellitus; clinically and instrumentally verified chronic lower-limb ischemia (Fontaine stage IIb–IV); ulcerative or necrotic foot lesions (Wagner stage I–V); documented IHD based on clinical history, ECG findings, echocardiographic wall motion abnormalities, or prior coronary angiography; complete clinical, laboratory, and angiographic records. Patients with decompensated NYHA class IV heart failure, acute coronary syndrome within 30 days prior to XEI, advanced renal failure requiring dialysis, or incomplete follow-up data were excluded.

For the purposes of prognostic model construction, patients were dichotomized by outcome: unfavorable outcome - major amputation (above ankle level) or all-cause mortality within 30 days of XEI (n=13); favorable outcome - all remaining patients with limb preservation, including those requiring minor amputation with retained weight-bearing function (n=45).

Clinical and instrumental assessment. Severity of peripheral ischemia was graded using the Fontaine classification. Tissue destruction extent was assessed by the Wagner classification. Cardiac functional status was evaluated by the NYHA functional classification for heart failure and the Canadian Cardiovascular Society (CCS) angina grading. LVEF was measured by transthoracic echocardiography (Simpson biplane method, Philips Affiniti 50, Netherlands). HbA1c was determined by high-performance liquid chromatography (HPLC) on a Bio-Rad D-10 analyzer (USA), calibrated per IFCC/NGSP standards. Digital subtraction angiography (DSA) was performed on an Azurion fluoroscopic system (Philips, Germany). Angiographic parameters analyzed included number of affected arterial segments, anatomical level of involvement, and distal runoff status. Vascular access was categorized as ipsilateral antegrade femoral or contralateral crossover. Procedural strategy was classified as balloon angioplasty alone (PTBA) or combined with stenting (PTBA+stenting).

Statistical analysis. Data were analyzed using IBM SPSS Statistics v.26.0 (USA) and Microsoft Excel 2019. Continuous variables are presented as M±SD. Between-group comparisons used the Student's t-test or Mann-Whitney U test; categorical variables were compared by χ^2 or Fisher's exact test. Statistical significance was set at $p<0.05$.

Binary logistic regression was performed to identify independent predictors of the unfavorable primary outcome. Variables with $p<0.10$ in univariable analysis were entered into the multivariable model using stepwise forward selection. For each retained predictor, regression coefficient (B), odds ratio (OR) with 95% CI, and p-value are reported. Prognostic model accuracy was assessed by ROC curve analysis with calculation of AUC, sensitivity, specificity, and Youden index (J = sensitivity + specificity − 1). The optimal probability threshold was determined at the maximum Youden index value.

3. Results and Discussion

Baseline characteristics by outcome. Among 58 patients, unfavorable outcomes (major amputation or 30-day mortality) occurred in 13 (22.4%), while 45 (77.6%) had favorable outcomes. Significant between-group differences were identified across clinical, metabolic, cardiac, and angioarchitectural parameters (**Table 1**).

Table 1. Distribution of clinical-laboratory and instrumental parameters in patients with DFS and IHD according to treatment outcome (n=58)

Parameter	Unfavorable outcome (n=13)	Favorable outcome (n=45)	p-value
Age ≥70 years, n (%)	9 (69.2%)	12 (26.7%)	<0.01
HbA1c ≥10%, n (%)	8 (61.5%)	9 (20.0%)	<0.01
Fontaine stage III–IV, n (%)	11 (84.6%)	14 (31.1%)	<0.001
Wagner stage IV–V, n (%)	10 (76.9%)	9 (20.0%)	<0.001
Heel or total foot involvement, n (%)	9 (69.2%)	6 (13.3%)	<0.001
LVEF <50%, n (%)	11 (84.6%)	5 (11.1%)	<0.001
CHF NYHA class II–III, n (%)	9 (69.2%)	5 (11.1%)	<0.001
Angina CCS class III–IV, n (%)	8 (61.5%)	2 (4.4%)	<0.001
Prior myocardial infarction, n (%)	7 (53.8%)	2 (4.4%)	<0.001
PTBA+stenting vs. PTBA alone, n (%)	10 (76.9%)	10 (22.2%)	<0.001
Contralateral crossover access, n (%)	9 (69.2%)	9 (20.0%)	<0.001

Table 2. Logistic regression results: independent predictors of unfavorable outcome (major amputation or 30-day mortality) in patients with DFS and IHD

Risk Factor	B	OR (Exp B)	95% CI	p-value
LVEF <50%	2.11	8.26	2.03–33.55	0.003
Angina CCS class III–IV	1.98	7.24	1.42–36.90	0.017
Wagner stage IV–V	1.87	6.47	1.48–28.26	0.013
Heel or total foot involvement	1.72	5.59	1.34–23.23	0.019
HbA1c ≥10%	1.59	4.90	1.18–20.41	0.027
Contralateral crossover access	1.47	4.34	1.06–17.81	0.038
PTBA+stenting (vs. PTBA alone)	1.31	3.70	0.98–13.95	0.051*

B - regression coefficient; OR - odds ratio; 95% CI - 95% confidence interval.
** Included in model as clinically significant marker of angioarchitectural severity despite p=0.051.*

Table 3. Comparative ROC analysis: composite prognostic model versus single-parameter LVEF criterion in patients with DFS and IHD

Prognostic Instrument	AUC	95% CI	Sensitivity (%)	Specificity (%)
Composite prognostic model	0.915	0.851–0.978	92.3	84.4
LVEF <50% (single criterion)	0.772	0.645–0.899	84.6	88.9

Table 4. Sensitivity, specificity, and Youden index of the prognostic model at different probability thresholds

Probability Threshold	Sensitivity (%)	Specificity (%)	Youden Index (J)
0.30	100.0	64.4	0.644
0.40	100.0	75.6	0.756
0.50	92.3	84.4	**0.768**
0.60	84.6	88.9	0.735
0.70	76.9	93.3	0.702

Bold indicates optimal threshold.

Patients with unfavorable outcomes demonstrated substantially more severe cardiac dysfunction, advanced metabolic decompensation, and more complex angioarchitectural disease. LVEF <50% was present in 84.6% of the unfavorable group versus 11.1% in the favorable group ($p<0.001$). Angina CCS class III–IV was observed in 61.5% versus 4.4% ($p<0.001$), and prior myocardial infarction in 53.8% versus 4.4% ($p<0.001$). These findings are consistent with data from Okamoto et al. [7], who demonstrated that myocardial dysfunction was the strongest independent predictor of non-healing in diabetic foot ulcers after revascularization, and from Yammine et al. [8], confirming IHD severity as the leading determinant of amputation risk in patients with critical limb ischemia. Among technical parameters, contralateral crossover access - a surrogate marker of proximal occlusive disease severity - was required in 69.2% of unfavorable versus 20.0% of favorable cases ($p<0.001$).

Logistic regression results. Multivariable logistic regression retained six statistically significant independent predictors of major amputation or 30-day mortality (**Table 2**). The strongest predictor was LVEF <50% (OR=8.26; 95% CI: 2.03–33.55; p=0.003), indicating an 8-fold increase in risk of amputation or death in the presence of this parameter. This finding aligns with Wang et al. [9], who demonstrated in a meta-analysis that LVEF <45% increases the risk of vascular reconstruction failure by more than 2.5-fold.

Angina CCS class III–IV emerged as the second strongest predictor (OR=7.24), followed by Wagner stage IV–V (OR=6.47), heel or total foot involvement (OR=5.59), HbA1c ≥10% (OR=4.90), and contralateral crossover access (OR=4.34). The requirement for combined PTBA+stenting showed a clinically relevant trend at the boundary of statistical significance (OR=3.70; p=0.051), reflecting the role of procedural complexity as an indicator of advanced angioarchitectural disease. Parameters including age ≥70 years, prior myocardial infarction, CHF NYHA class II–III, and Fontaine stage III–IV did not reach independent statistical significance in the multivariable model, although their cumulative effect on outcome is clinically acknowledged [10,11].

The dominant role of systemic cardiac parameters - particularly LVEF and angina class - confirms that hemodynamic reserve directly conditions the functional efficacy of peripheral revascularization, even when macroscopic flow restoration is technically achieved [12]. Advanced tissue destruction (Wagner IV–V) and proximal foot involvement (heel, total foot) reflect the biological state of affected tissues at the time of intervention, which substantially limits regenerative capacity and increases susceptibility to secondary infection [13].

ROC analysis and probability thresholds. The composite prognostic model demonstrated high discriminatory accuracy with AUC=0.915 (95% CI: 0.851–0.978). At the optimal

probability threshold of P=0.50, the model achieved sensitivity 92.3%, specificity 84.4%, and Youden index J=0.768. This significantly exceeded the discriminatory performance of LVEF <50% alone as a single predictor (AUC=0.772; 95% CI: 0.645–0.899; sensitivity 84.6%, specificity 88.9%), confirming the superiority of the multifactorial approach over single-parameter assessment (**Table 3**).

Analysis of model performance across different probability thresholds demonstrated that at P=0.30, sensitivity reached 100.0% with specificity of 64.4% (Youden index 0.644), suitable for initial risk screening. At P=0.50, the optimal balance was achieved (J=0.768). At P=0.70, specificity rose to 93.3% with sensitivity 76.9% (J=0.702), appropriate for decision-making regarding high-technology invasive interventions where avoiding unnecessary procedures is prioritized (**Table 4**).

The model enabled stratification of patients into three risk zones: low risk (P<0.40) - primary XEI on lower extremity arteries is indicated without mandatory preliminary cardiac intervention; intermediate risk (P=0.40–0.60) - multidisciplinary council decision required with expanded cardiological assessment; high risk (P>0.60) - priority cardiac evaluation and correction of coronary blood flow before peripheral revascularization is warranted. This risk-stratified approach forms the basis for the individualized therapeutic algorithm further developed in the main study [14].

The superiority of the composite model over isolated LVEF assessment is illustrated by the following clinical observation: a patient with LVEF=52% (formally preserved function) but with heel localization (Wagner stage V), HbA1c=11.2%, and CCS class III angina had a calculated risk of 0.84, and treatment resulted in amputation despite technically successful PTBA. In contrast, a patient with LVEF=55%, isolated finger ulcer (Wagner stage II), and HbA1c=8.3% had a calculated risk of 0.32 and achieved complete wound healing within 38 days of XEI [14]. These observations confirm that isolated cardiac parameters do not sufficiently reflect the overall biological and vascular risk in this comorbid population, which necessitates integration of metabolic and angioarchitectural variables into the decision-making framework [15].

4. Conclusions

A multifactorial prognostic model was developed and validated for quantitative assessment of unfavorable outcome risk (major amputation or 30-day mortality) in patients with diabetic foot syndrome and concomitant ischemic heart disease undergoing X-ray endovascular interventions. Six independent predictors were identified: LVEF <50% (OR=8.26), angina CCS class III–IV (OR=7.24), Wagner stage IV–V (OR=6.47), heel or total foot localization (OR=5.59), HbA1c ≥10% (OR=4.90), and contralateral crossover vascular access (OR=4.34).

The composite model demonstrated high discriminatory accuracy (AUC=0.915), substantially superior to isolated LVEF assessment (AUC=0.772). At the optimal probability threshold of 0.50, sensitivity reached 92.3% and specificity 84.4%. Defined risk strata (low: P<0.40; intermediate: P=0.40–0.60; high: P>0.60) provide a practical framework for prioritizing either lower-extremity or coronary revascularization in individualized treatment planning.

Routine application of this model in pre-procedural assessment may reduce the frequency of unnecessary interventions in high-risk patients, guide sequencing of revascularization strategies, and ultimately contribute to a reduction in amputation rates and perioperative mortality in patients with severe vascular comorbidity.

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