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PREDICTING THE OUTCOME OF HEART TRANSPLANTATION FROM EXPANDED-CRITERIA DONORS USING REGRESSION ANALYSIS

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There is a growing need for tools that enable objective assessment of donor heart quality. One such approach is the use of regression models incorporating donor and recipient risk factors to predict surgical outcomes and potentially expand the donor pool by increasing the number of transplantations. **Objective:** to develop a model for estimating the total risk of one-year mortality in recipients using different categories of expanded-criteria donors (ECDs). **Materials and methods.** The study included 1,500 recipients who underwent orthotopic heart transplantation (OHT) at Shumakov National Medical Research Center of Transplantology and Artificial Organs over an 11-year period, from January 1, 2011, to December 31, 2021. The cohort comprised 1,281 men (85.4%) and 219 women (14.6%), aged 9 to 78 years (median age 49.0 [38.0–56.0] years). The heart transplants performed (n = 1,500) were divided into two clinical groups: group 1 (main group) comprised recipients who underwent OHT from ECDs (n = 1,060; 70.6%); group 2 (control group) included recipients who underwent OHT from standard-criteria donors (n = 440; 29.4%). Donor heart suitability for transplantation was assessed according to the 2023 criteria of the International Society for Heart and Lung Transplantation (ISHLT). **Results.** Donor- and recipient-related indicators were initially evaluated using univariate regression analysis. The final multivariate regression model included five donor-related factors – donor–recipient weight mismatch, donor age, high-dose cardiotonic therapy, coronary stenosis, and prolonged graft ischemia – and four recipient-related factors – total bilirubin >40 μmol/L, creatinine >110 μmol/L, international normalized ratio (INR) >1.4, and pre-transplant peripheral veno-arterial extracorporeal membrane oxygenation (pVA-ECMO). The highest odds ratios were observed for donor age, coronary stenosis, graft ischemia time exceeding 6 hours, and pre-transplant pVA-ECMO support. The predicted one-year mortality rate calculated using regression analysis showed a strong correlation ($R = 0.827$; $p < 0.001$) with the observed one-year mortality rate. Long-term survival was also analyzed across risk groups, with the worst outcomes observed in the high-risk group. **Conclusion.** The proposed statistical model provides a reliable prognostic accuracy for both early and long-term post-transplant survival. Its application at the stages of donor heart evaluation and donor–recipient matching may facilitate the use of a broader donor pool while enabling an objective assessment of recipient prognosis.

Keywords: heart transplantation, mechanical circulatory support, VA-ECMO, regression analysis.

INTRODUCTION

Given the current shortage of donor organs over recent decades, the use of hearts from expanded-criteria donors (ECDs) remains a practical strategy for increasing the availability of heart transplantation (HT), particularly for patients requiring urgent transplantation and/or those with a predicted poorer early or long-term post-transplant survival [1].

In Russian clinical practice, where implantable long-term mechanical circulatory support systems are not yet widely available, the use of suboptimal donor hearts represents a realistic approach to increasing the number of HT procedures performed. In this context, the experience of individual transplant centers is of considerable importance when determining the suitability of donor organs whose characteristics fall between those of an "ideal" and an "ineligible" donor.

Accordingly, there is a high need for the development of objective tools for assessing donor heart quality. One promising approach involves the creation of regression models incorporating donor- and recipient-related risk factors to predict postoperative outcomes and increase transplant activity [2, 3].

Research objective: To develop a cumulative risk model for estimating the one-year mortality associated with the use of ECDs (including cases of donor–recipient

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weight mismatch, donor age >55 years, high-dose cardiotonic therapy, coronary artery atherosclerosis, graft ischemia time exceeding 5 hours, ejection fraction (EF) <50%, left ventricular myocardial hypertrophy (LVH) >1.5 cm, systemic vascular resistance (SVR), and valvular pathology.

MATERIALS AND METHODS

The study included 1,500 recipients who underwent orthotopic heart transplant (OHT) at Shumakov National Medical Research Center of Transplantology and Artificial Organs over an 11-year period from January 1, 2011, to December 31, 2021. Among the recipients, 1,281 (85.4%) were men and 219 (14.6%) were women. Recipient age ranged from 9 to 78 years, with a median age of 49.0 years (interquartile range: 38.0–56.0 years).

The heart transplants performed (n = 1,500) were divided into two clinical groups:

Group 1 (main group): recipients who underwent OHT from ECDs (n = 1,060; 70.6%); Group 2 (control group): recipients who underwent OHT from standard criteria donors (n = 440; 29.4%).

Assessment of donor heart suitability for transplantation was performed in accordance with the 2023 guidelines of the International Society for Heart and Lung Transplantation [4]. The pre-transplant clinical characteristics of recipients and donors are presented in Table 1.

Statistical analysis was performed using IBM SPSS Statistics 23 (IBM Corp., USA). In the main group, univariate regression analysis was initially conducted to identify factors associated with one-year mortality. Variables demonstrating statistical significance were sub-

Table 1

Pre-transplant clinical characteristics of recipients and donors in the main and control groups (n = 1500)

Indicator	Main group (n = 1060)	Control group (n = 440)	Significance of difference (p)
Heart recipients			
Age, years – Mean ± SD Median [Q1; Q3]	46.3 ± 11.0 48.0 [38; 56]	45.8 ± 13.0 48.0 [37.8; 56]	0.448
Sex (female) – (n/%)	173/16.4	46/10.5	0.002
Weight, kg – Mean ± SD Median [Q1; Q3]	79.5 ± 18.7 79 [66; 92]	79.9 ± 17.0 78 [70; 90]	0.699
BSA, m^2 – Mean ± SD Median [Q1; Q3]	1.9 ± 0.2 1.9 [1.7; 2.1]	1.9 ± 0.1 1.9 [1.8; 2.0]	1.000
BMI, kg/m^2 – Mean ± SD Median [Q1; Q3]	25.9 ± 5.2 25.5 [22.4; 29.4]	25.7 ± 3.9 25.3 [23.1; 28.4]	0.468
CHF stage IIB (n/%)	603/56.8	313/71.1	0.000
CHF stage III (n/%)	365/34.4	82/18.7	0.000
NYHA functional class Median [Q1; Q3]	3.3 ± 0.5 3 [3; 4]	3.2 ± 0.4 3 [2; 3]	0.000
VA-ECMO – (n/%)	343/32.4	96/21.8	0.000
TPG, mmHg – Mean ± SD Median [Q1; Q3]	10.0 ± 4.2 9 [7; 16]	8.8 ± 4.4 8 [6; 12]	0.000
TPVR, Wood units – Mean ± SD Median [Q1; Q3]	3.7 ± 1.2 2.8 [1.7; 4.0]	2.8 ± 1.5 2 [1.7; 3.6]	0.000
Heart donors			
Age, years – Mean ± SD Median [Q1; Q3]	46.3 ± 11.0 48 [38; 56]	38.5 ± 9.9 39 [31; 46.8]	0.000
Sex (female) – (n/%) Sex (male) – (n/%)	259/24.5 801/75.5	80/18.2 360/81.8	0.01
Female donor–male recipient pair – (n/%)	114/10.8	29/6.6	0.07
Weight, kg – Mean ± SD Median [Q1; Q3]	84.1 ± 17.6 80 [70; 90]	79.3 ± 11.7 80 [70; 87.3]	0.000
Donor-to-recipient weight ratio – Mean ± SD Median [Q1; Q3]	1.0 ± 0.3 1 [0.8; 1.3]	0.9 ± 0.2 1 [0.9; 1.1]	0.000
Stroke (donor) – (n/%)	804/75.8	233/53.0	0.000
MV duration, days – Mean ± SD Median [Q1; Q3]	2.5 ± 1.8 2.0 [1; 3]	2.8 ± 3.8 2.0 [1; 3]	0.038
Eurotransplant Heart Transplant Score, points	26.8 ± 12.4	24.4 ± 10.2	0.000

Abbreviations: SD, standard deviation; BSA, body surface area; CHF, chronic heart failure; NYHA, New York Heart Association; VA-ECMO, venoarterial extracorporeal membrane oxygenation; TPG, transpulmonary gradient; TPVR, total pulmonary vascular resistance; MV, mechanical ventilation.

sequently included in a multivariate logistic regression model.

Independent predictors of one-year mortality ($p < 0.05$) were assigned weighted scores according to their odds ratios (ORs). Predicted one-year mortality scores were then calculated using the derived regression equation. Based on these scores, recipients were stratified into three risk categories: low-risk (≤10 points), medium-risk (11–15 points), and high-risk (≥16 points).

Predicted mortality rates were compared with observed mortality rates across the risk groups. To assess the accuracy of the model, the correlation between predicted and observed outcomes was evaluated using Pearson's correlation coefficient (r). Long-term survival by risk category was analyzed using the Kaplan–Meier method.

RESULTS

Using univariate regression analysis, 9 expanded-criteria donor variables were evaluated: donor–recipient weight mismatch, donor age >55 years, high-dose cardiotonic therapy, coronary artery stenotic disease, graft ischemia time >5 hours, EF <50%, LVH >1.5 cm, cardiopulmonary resuscitation (CPR), and valvular pathology. Among these variables, 5 factors demonstrated statistically significant associations with one-year mortality (Table 2).

Considering the potential impact of recipient-related factors on HT outcomes, they were also included in the analysis. Eight recipient parameters were assessed: total bilirubin >40 μmol/L, serum creatinine >110 μmol/L, international normalized ratio (INR) >1.4, pre-transplant veno-arterial extracorporeal membrane oxygenation (pVA-ECMO), recipient age >65 years, body mass index (BMI) >30 kg/m^2, transpulmonary gradient (TPG) >15 mmHg, pulmonary vascular resistance (PVR) >3 Wood units, and type 2 diabetes mellitus. Of these variables, 4 were identified as statistically significant predictors (Table 3).

The final multivariate regression model incorporated 5 donor-related factors and 4 recipient-related factors, demonstrating good predictive performance ($R^2 = 0.64$). The highest ORs were observed for donor age, stenotic

Table 2

Univariate regression analysis of donor-related risk factors for heart transplant from using expanded-criteria donors (n = 1,060)

Indicator	Single-factor (univariate) regression analysis	
	Odds ratio (OR) (95% CI)	p-value
Donor–recipient weight mismatch	1.785 (0.552–1.117)	0.002
Donor age >55 years	2.186 (1.669–2.884)	0.000
High cardiotonic (inotropic) therapy	1.999 (1.003–3.941)	0.005
Coronary stenosis	4.062 (2.070–7.973)	0.000
Graft ischemia time >6 hours	1.608 (1.446–1.867)	0.004
Left ventricular EF <50%	0.698 (0.386–1.262)	0.234
Left ventricular myocardial hypertrophy >1.5 cm	0.880 (0.585–1.326)	0.542
CPR	0.899 (0.305–2.649)	0.848
Valve disease	0.735 (0.153–3.541)	0.701

Abbreviations: EF, ejection fraction; CPR, cardiopulmonary resuscitation.

Table 3

Univariate regression analysis of recipient risk factors in heart transplant from expanded-criteria donors (n = 1060)

Indicator	Univariate analysis	
	OR (95% CI)	p-value
Total bilirubin >40 μmol/L	1.531 (0.381–0.740)	0.000
Serum creatinine >110 μmol/L	1.528 (0.317–0.879)	0.014
INR >1.4	1.540 (0.391–0.713)	0.000
Pre-transplant pVA-ECMO	2.277 (6.357–14.440)	0.000
Age >65 years	0.290 (0.646–4.317)	0.290
BMI >30 kg/m^2	0.468 (0.515–1.356)	0.468
TPG >15 mmHg, TPVR >3 Wood units	0.680 (0.785–1.450)	0.680
Type 2 diabetes	0.406 (0.646–1.193)	0.878

Abbreviations: OR, odds ratio; CI, confidence interval; INR, international normalized ratio; pVA-ECMO, peripheral veno-arterial extracorporeal membrane oxygenation; BMI, body mass index; TPG, transpulmonary gradient; TPVR, total pulmonary vascular resistance.

coronary artery disease, graft ischemia time >6 hours, and pre-transplant pVA-ECMO (Table 4).

Each statistically significant variable was assigned a weighted point value, and predicted mortality was calculated using a regression-based scoring system derived from the cumulative score (Table 5).

Predicted one-year mortality rates obtained through regression analysis demonstrated a strong positive correlation with observed one-year mortality ($R = 0.827$; $p < 0.001$).

Based on the estimated risk of death within one year after HT, recipients were stratified into three risk categories: low-risk (≤10 points), medium-risk (11–15 points), and high-risk (≥16 points).

The predicted one-year mortality closely corresponded to the observed mortality across the risk groups,

Table 4

Multivariate regression analysis of donor and recipient risk factors in heart transplantation (n = 1060)

Indicator	Multivariate regression analysis	
	OR (95% CI)	p-value
Donor–recipient weight mismatch	1.961 (0.690–1.324)	0.001
Donor age >55 years	5.852 (0.889–11.184)	0.001
High-dose cardiotonic therapy	1.560 (0.908–1.974)	0.001
Donor coronary stenosis	8.142 (0.769–15.695)	0.001
Graft ischemia time >6 hours	3.844 (1.497–7.434)	0.001
Total bilirubin >40 μmol/L	1.970 (0.662–1.420)	0.001
Serum creatinine >110 μmol/L	1.260 (0.339–0.992)	0.047
INR >1.4	1.320 (0.566–1.108)	0.043
Pre-transplant pVA-ECMO	3.910 (0.219–6.538)	0.001

Abbreviations: OR, odds ratio; CI, confidence interval; INR, international normalized ratio; pVA-ECMO, peripheral veno-arterial extracorporeal membrane oxygenation.

Table 5

Risk stratification scale for early postoperative mortality after heart transplantation from suboptimal donors (n = 1060)

Indicator	OR (95% CI)	Points
Donor–recipient weight mismatch (ratio <1.2)	1.961	2
Donor age >55 years	5.852	6
High-dose cardiotonic therapy	1.560	2
Coronary stenosis	8.142	8
Graft ischemia time >6 hours	3.844	4
Total bilirubin >40 μmol/L	1.970	2
Serum creatinine >110 μmol/L	1.260	1
INR >1.4	1.302	1
Pre-transplant pVA-ECMO	3.910	4
Maximum total score	**30**	

Donor–recipient risk scale	Prediction of 1-year mortality
10	**11.4%**
12	**12.4%**
14	**13.6%**
16	**15.2%**
18	**18.5%**
20	**20.3%**
22	**22.0%**
24	**24.4%**
26	**26.0%**
28	**28.2%**
>29	**>30%**

Table 6

Distribution of recipients by 1-year mortality risk groups

	Low-risk group	Medium-risk group	High-risk group
Risk scale scores	<10 points	11–15 points	≥16 points
Predicted 1-year mortality (%)	≤11.2	11.2–14.8	>14.8
Observed 1-year mortality (%)	10.0	12.2	14.6
Number of risk factors (%)			
0–1	100	88.2	29
2–3	–	11.8	68.4
4–5	–	–	2.6

with rates of 10.0%, 12.2%, and 14.6%, respectively (Table 6).

An analysis of long-term survival according to risk category was also performed, with the poorest outcomes observed in the high-risk group (Fig.).

DISCUSSION

Given the persistent shortage of donor hearts, the use of ECD organs remains an important and clinically relevant strategy. It has been suggested that broader utilization of all available donor hearts could substantially alleviate the current organ shortage [5].

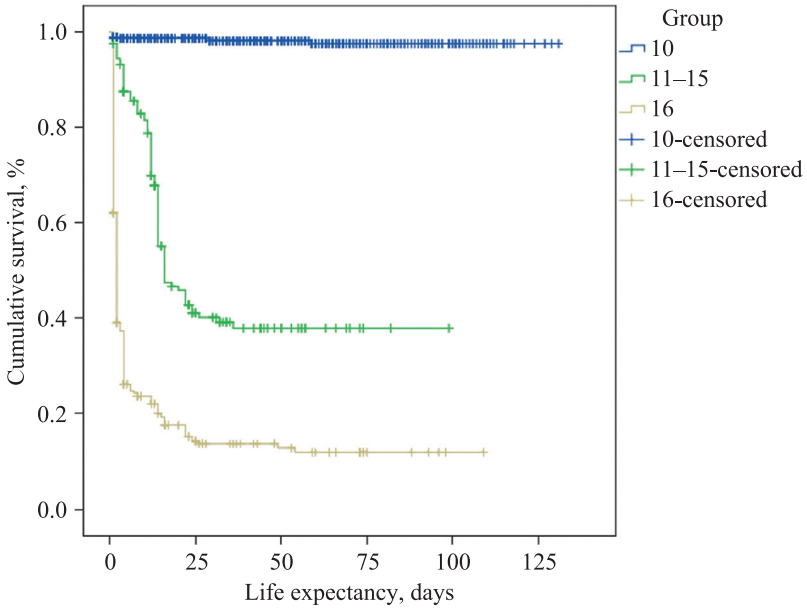

Fig. Long-term survival of heart transplant recipients from expanded-criteria donors stratified by risk group

In the present study, the number of annual HTs performed using ECDs increased from 46% in 2011 to a peak of 72.1% in 2019 during the study period from January 1, 2011, to December 31, 2021. Overall, the majority of the donor pool (70.6%) consisted of ECDs. These criteria included prolonged graft ischemia time, donor age 45–55 years, concomitant but potentially correctable valvular heart disease, coronary artery disease, donor–recipient weight mismatch exceeding 20%, reduced left ventricular systolic function, LVH, high-dose sympathomimetic therapy, prior CPR, methanol poisoning, and combinations of these factors.

HTs from donor organs with one or more risk factors may be justified in recipients requiring urgent transplantation; however, such procedures are associated with an increased likelihood of adverse postoperative outcomes [6]. At present, there are no universally accepted guidelines regarding the use of suboptimal donor hearts, resulting in substantial variability in donor selection strategies among individual transplant centers and regional or interstate organ allocation systems [3, 7].

The increase in the number of HTs performed at many transplant centers has paralleled the expansion of donor eligibility criteria. Outcomes following transplantation using ECDs remain mixed, with studies reporting either comparable or less favorable early- and long-term survival rates relative to standard-criteria donor transplantation. It is evident that the outcomes of HTs from ECDs depend not only on donor-related characteristics but also on recipient pre-transplant factors, including recipient age, presence of chronic pulmonary disease, repeat transplantation, severity of pre-transplant pulmonary hypertension, and multiple organ dysfunction [2, 8].

Given this, it appears justified to develop a statistical prediction model based on extensive institutional experience and a large series of transplantations performed using ECD hearts. Such a model would enable estimation of the risk associated with HT depending on the presence, number, and combination of expanded donor criteria, as well as their interaction with recipient pre-transplant factors.

Based on univariate analysis, several donor-related risk factors were examined, five of which demonstrated statistical significance: donor–recipient weight mismatch ($p < 0.002$), donor age >55 years ($p < 0.001$), high-dose cardiotonic therapy ($p < 0.005$), stenotic coronary artery disease ($p < 0.001$), and graft ischemia time >6 hours ($p < 0.004$).

Analysis of recipient-related risk factors identified the following significant predictors: total bilirubin >40 μmol/L ($p < 0.001$), serum creatinine >110 μmol/L ($p < 0.014$), INR >1.4 ($p < 0.001$), and pre-transplant pVA-ECMO ($p < 0.001$).

These variables were subsequently incorporated into a multivariate regression model for predicting the risk associated with HT. The highest ORs were observed for donor age, pre-existing donor stenotic coronary artery disease, graft ischemia time exceeding 6 hours, and recipient pre-transplant pVA-ECMO.

In the present study, predicted 1-year mortality demonstrated a strong positive correlation with observed 1-year mortality ($R = 0.827$; $p < 0.001$). Furthermore, analysis of long-term survival revealed the poorest outcomes in recipients classified within the high-risk group.

CONCLUSION

The developed statistical model provides a reliable prognostic tool for predicting survival in both the early and long-term post-transplant periods. It can be effectively applied during donor heart assessment and

donor–recipient matching, enabling broader utilization of available donor organs while ensuring an accurate assessment of the recipient's prognosis.

The authors declare no conflict of interest.

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