DOI: 10.15825/1995-1191-2026-1-128-137

RISK FACTORS FOR HUMORAL MYOCARDIAL REJECTION DURING THE FIRST YEAR AFTER HEART TRANSPLANTATION

Yu.V. Sazonova, P.A. Fedotov, M.A. Bortzova, M.A. Simonenko, L.O. Korneva, D.A. Kilina, A.S. Golovkin, O.V. Kalinina, M.Yu. Sitnikova, G.V Nikolaev, M.A. Karpenko

Almazov National Medical Research Centre, St. Petersburg, Russian Federation

Objective: to identify risk factors for antibody-mediated myocardial rejection (AMR) during the first year following heart transplantation (HT). **Materials and methods.** This retrospective study included 162 patients who underwent HT at Almazov National Medical Research Centre between 2010 and 2024. Clinical, laboratory, immunological, and morphological data were analyzed. Sensitization was assessed using Luminex multiplex assays and solid-phase ELISA. AMR was diagnosed based on endomyocardial biopsy with morphological and immunohistochemical evaluation in accordance with the 2013 ISHLT classification. Hemodynamically significant rejection was defined as AMR II–III in combination with graft dysfunction and/or the presence of donor-specific antibodies (DSA). Patients were stratified into three groups: (1) no sign of AMR (control); (2) isolated morphological signs of AMR (AMR II); and (3) hemodynamically significant AMR (AMR III, or AMR II with DSA and/or echocardiographic evidence of graft dysfunction). Discriminant analysis was used to evaluate the factors associated with the development of AMR. **Results.** Morphological signs of AMR were identified in 36.2% of patients, including 9.9% with hemodynamically significant rejection requiring specific therapy. Patients with AMR before HT showed significantly higher sensitization to HLA class I and II antigens (MFI >5000; $p < 0.05$), and following HT, a statistically significant excess of *de novo* antibodies persisted for 6–12 months compared with the control group ($p < 0.05$). In addition, AMR was associated with lower tacrolimus levels during the first two weeks after HT ($p = 0.002$) and reduced antimetabolite doses in the first month post-transplant ($p < 0.001$). Discriminant analysis of 15 variables yielded a model incorporating 9 significant predictors, enabling statistically reliable differentiation of patients with hemodynamically significant rejection from other groups ($F(18,222) = 12.463$; $p < 0.00001$). **Conclusion.** High levels of HLA sensitization before transplantation, suboptimal immunosuppression in the early postoperative period, and predictors identified in the discriminant analysis model are associated with an increased risk of developing hemodynamically significant AMR. The proposed model may be used for risk stratification and to individualize post-transplant follow-up.

Keywords: heart transplantation, antibody-mediated rejection risk factors, donor-specific antibodies.

INTRODUCTION

Cardiovascular diseases are the leading causes of death worldwide [1]. For patients with end-stage heart failure, HT continues to be the only effective treatment option [2]. Over recent decades, substantial progress in transplant outcomes has been achieved, driven by advances in surgical and anesthetic techniques, improvements in monitoring and therapeutic strategies, and the increasing individualization of immunosuppressive regimens [3].

In the context of these developments in modern transplantology, myocardial rejection – provided that optimal donor–recipient matching is achieved and immunosuppressive therapy is appropriately tailored to the recipient's immunological risk – is no longer the leading cause of mortality following HT, even in the early postoperative period [4].

Nevertheless, data from international registries indicate that the incidence of AMR has remained largely unchanged. Importantly, both clinically overt and subclinical forms of AMR have been shown to contribute to graft dysfunction and loss, as well as to the development of cardiac allograft vasculopathy [5].

The problem with AMR lies in the lack of uniform, standardized approaches for its timely diagnosis and, consequently, for the prevention and treatment of this complication. While the need to treat HC-AMR (AMR III) is well established, the optimal management of patients with mild to moderate AMR (AMR I–II), particularly in the absence of clinically significant graft dysfunction or circulating DSA, remains a subject of debate.

As a result, the reported incidence of AMR in the global literature ranges from 10% to 20% and is associated with a significant increase in adverse outcomes.

Corresponding author: Yulia Sazonova. Address: 2, Akkuratova str., St. Petersburg, 197341, Russian Federation. Phone: (911) 250-29-37. E-mail: yulia.via.sazonova@gmail.com

Histological and immunohistochemical criteria for AMR have been established by the International Society for Heart and Lung Transplantation (ISHLT). These include macrophage and neutrophil infiltration, endothelial swelling, and deposition of immunoglobulins and complement components – particularly C4d – within capillary endothelium. The diagnosis of HC-AMR (HC-AMR), however, relies on a comprehensive assessment that integrates pathological findings from endomyocardial biopsies (histological and immunohistochemical), evidence of graft myocardial dysfunction, and the presence of circulating DSA in the recipient's blood.

Risk factors for the development of AMR are currently the subject of extensive investigation. Proposed predictors include recipient- and donor-related variables such as sex, age, blood group incompatibility, cause of donor death, presence of pre-existing and donor-specific antibodies, patient adherence, the use of induction therapy, and immunosuppressant drug levels [6].

At the same time, advances in desensitization strategies and the increasing individualization of immunosuppressive regimens have significantly modified the prognostic relevance of several of these factors. For instance, recent ISHLT data suggest that the presence of pre-existing antibodies is not invariably associated with an increased risk of AMR, provided that appropriate prophylactic therapy is administered [8].

Particular attention should be directed toward identifying risk factors for HC-AMR, a severe form characterized by rapid progression, biventricular dysfunction, and a high risk of mortality. In this context, identification of predictors specific to this phenotype is essential for improving risk stratification, optimizing post-transplant monitoring, and enabling timely therapeutic intervention [9].

In light of the above, a retrospective analysis of clinical, laboratory, and immunological risk factors associated with the development of hemodynamically significant antibody-mediated myocardial rejection during the first year after heart transplantation appears warranted.

Objective: to identify risk factors associated with AMR episodes within the first year following HT.

MATERIALS AND METHODS

This retrospective study included 162 HT recipients who were followed at Almazov National Medical Research Centre, St. Petersburg, Russia. The inclusion criteria were as follows: patients who underwent HT at the Center between 2010 and 2024, age ≥18 years, and provision of informed consent to participate in the study. The exclusion criteria were age <18 years and refusal to participate in the study.

Clinical and biochemical blood parameters were assessed using an Architect automated biochemical analyzer. Blood concentrations of calcineurin inhibitors were measured with a Luminex automated analyzer using an immunofluorescence assay. Drug levels were determined at the trough (C_0), 12 hours after the last administered dose.

Detection of antibodies to human leukocyte antigens (HLA) class I and II, both before and after heart transplantation, was performed using solid-phase enzyme-linked immunosorbent assay (ELISA) and multiplex analysis (Luminex). Recipient sensitization was evaluated based on the percentage of panel-reactive antibodies (PRA), calculated using the Match IT Antibody software (Immucor) for Luminex assays. Patients with anti-HLA antibody levels exceeding 10% PRA and mean fluorescence intensity (MFI) >5000 were classified as highly sensitized.

Instrumental diagnostic evaluation of AMR included standard transthoracic echocardiography (ECHO) and endomyocardial biopsy (EMB), followed by morphological and immunohistochemical assessment of biopsy specimens.

All patients received standard immunosuppressive therapy consisting of calcineurin inhibitors (tacrolimus), antimetabolites (mycophenolate mofetil or mycophenolic acid), and glucocorticosteroids, along with adjunctive treatments (e.g., antihypertensive and antithrombotic agents) as clinically indicated. Lipid-lowering therapy was routinely prescribed to all recipients, and prophylaxis against cytomegalovirus infection and Pneumocystis jirovecii pneumonia was administered during the first six months following transplantation. Patients with a high degree of pre-existing sensitization (PRA >10% and MFI >5000) underwent a desensitization protocol, which included extracorporeal hemocorrection techniques (plasma exchange or cascade plasmapheresis) in combination with intravenous human immunoglobulin administration.

Immediately prior to transplantation, donor–recipient compatibility was assessed using a complement-dependent lymphocytotoxic crossmatch assay.

The diagnosis of AMR was established based on histological and immunohistochemical evaluation of endomyocardial biopsy specimens and classified according to the 2013 ISHLT criteria. Hemodynamically compromising rejection (HC-R) requiring transfusion-based hemocorrection combined with desensitization therapy was defined as either morphologically confirmed severe AMR (AMR III) or moderate AMR (AMR II) accompanied by evidence of graft dysfunction on echocardiography and/or the presence of donor-specific antibodies in the recipient's circulation.

Statistical analysis was performed using IBM SPSS Statistics version 19.0 and STATISTICA version 10.0 (StatSoft Inc., USA). Both parametric and nonparametric

methods were applied to analyze the main patient characteristics. A p-value <0.05 was considered indicative of statistical significance. To identify variables distinguishing the study groups, stepwise discriminant function analysis was employed.

Study Design

Patients were stratified into three groups: Group 1 (recipients without evidence of AMR [control group]); Group 2 (recipients with isolated histological and immunohistochemical features of AMR [AMR II]; Group 3 (recipients with HC-AMR, defined as AMR III or AMR II in combination with DSA and/or echocardiographic evidence of graft dysfunction.

Baseline risk factors for AMR were assessed in patients with and without AMR. Subsequently, discriminant function analysis was performed to identify predictors of HC-R.

RESULTS

A total of 162 patients were included in the study, of whom 71% (n = 115) were male. The predominant underlying conditions leading to end-stage chronic heart failure were ischemic cardiomyopathy (50.8%) and dilated cardiomyopathy (40.1%). Other etiologies – including restrictive cardiomyopathy, congenital or acquired heart defects, and storage diseases – accounted for 9.1% of cases.

Prior to HT, 3% of patients with a high degree of pre-existing sensitization underwent a desensitization protocol consisting of transfusion-based hemocorrection (plasma exchange or cascade plasmapheresis) in combination with intravenous human immunoglobulin.

During the first postoperative year, morphological signs of AMR were identified in 36.2% (n = 59) of recipients. However, HC-R (Group 3), characterized by graft dysfunction and/or the presence of DSA and requiring intensive therapy, was observed in only 9.9% (n = 16) of cases. In 26.5% of recipients (n = 43; Group 2), isolated histological findings of AMR (AMR II) were not associated with DSA and did not result in impaired systolic function of the left or right ventricles or clinically significant diastolic dysfunction.

Among the 103 patients in the control group, no AMR episodes were recorded during the first year following transplantation.

No statistically significant differences were observed among Groups 1, 2, and 3 with respect to key clinical, laboratory, and diagnostic parameters, including the severity of chronic heart failure. A trend toward younger age was noted in Group 3 compared with the other groups (median 44 years *vs.* 52 and 53 years, respectively); however, this difference did not reach statistical significance (p > 0.05). The baseline characteristics of the recipients are summarized in Table 1.

Table 1

Recipient's characteristics

Indicator		Group 2 (AMR II according to morphological examination) N = 43	Group 3 (AMR II and III) N = 16	Group 1 (no rejection) N = 103	P
Age, years, Me [LQ; UQ]		52 [41; 59]	44 [30; 54]	53 [41; 57]	NS
Male sex, n (%)		29 (67%)	8 (50%)	78 (76%)	NS
BMI, kg/m^2, Me [LQ; UQ]		24 [22; 27]	22 [19; 24]	24 [21; 27]	NS
Diagnosis, n (%)	IHD	19 (44%)	3 (19%)	43 (42%)	NS
	DCM	11 (26%)	4 (25%)	25 (24%)	NS
	Other	13 (30%)	9 (6%)	35 (34%)	NS
UNOS status 1		8 (18.6%)	6 (37%)	10 (9.7%)	NS
LVEF, Simpson's method (%), Me [LQ; UQ]		23 [18; 25]	23 [14; 27]	22 [17; 27]	NS
LVEDV, mL, Me [LQ; UQ]		251 [193; 330]	200 [149; 325]	242 [207; 313]	NS
LVESV, mL, Me [LQ; UQ]		181 [143; 255]	174 [117; 258]	182 [148; 257]	NS
PVR, Wood units, Me [LQ; UQ]		2.8 [2; 3.7]	3.1 [2.5; 3.6]	2.6 [1.9; 3.4]	NS
NT-proBNP, pg/mL, Me [LQ; UQ]		3964 [2132; 6260]	3142 [1574; 7381]	3792 [2172; 5714]	NS

Abbreviations and group definitions: Group 1, recipients without antibody-mediated rejection (AMR; control group); Group 2, recipients with isolated histological and immunohistochemical evidence of AMR (AMR II); Group 3, recipients with hemodynamically compromising AMR (AMR III, or AMR II with donor-specific antibodies and/or echocardiographic evidence of graft dysfunction). BMI, body mass index; PVR, pulmonary vascular resistance; UNOS, United Network for Organ Sharing urgency status classification; NT-proBNP, N-terminal pro–brain natriuretic peptide; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; ME, median value; LQ/UQ, lower (25th) and upper (75th) percentiles; n, number of observations; NS, no statistically significant difference (p > 0.05).

Similarly, when comparing patients with and without histological evidence of rejection, no significant differences were identified in established risk factors, including history of pregnancy, prior blood transfusions, and use of mechanical circulatory support before HT (Table 2).

Analysis of the immunological profiles of patients across the comparison groups revealed a general trend toward higher anti-HLA antibody (AT) levels in recipients with AMR, both overall and across specific HLA classes. Notably, sensitization with AT levels up to 5000 MFI against HLA classes I and II was observed in patients with AMR even prior to transplantation ($p < 0.05$), whereas such sensitization was uncommon in the control group (Fig. 1).

Peak AT levels in the AMR group were detected within the first 6 months post-transplant, with levels exceeding 5000 MFI for HLA class I. In contrast, patients without rejection generally lacked significant sensitization ($p = 0.012$) (Fig. 2).

During the 6–12-month postoperative period, patients with AMR exhibited total AT levels, *de novo* AT, and sensitization to HLA class I that were more than twice those observed in the non-rejection group ($p < 0.05$) (Figs. 3 and 4).

Patients with AMR, like those without rejection, generally received induction therapy. However, rabbit anti-thymocyte immunoglobulin was used as the primary induction agent four times less frequently in patients

Table 2

Risk factors for antibody-mediated myocardial rejection

Indicator	AMR N = 59	No AMR N = 103	P
Pregnancy	18 (31%)	19 (18%)	NS
Blood transfusions prior to HT	20 (34%)	30 (29%)	NS
Mechanical circulatory support prior to HT	11 (19%)	10 (9.7%)	NS
Pre-transplant sensitization	15 (25%)	23 (22%)	NS
Induction immunosuppressive therapy present	46 (81%)	84 (82%)	NS
Rabbit antithymocyte globulin administered after HT	2 (3.4%)	14 (14%)	**0.036**

Abbreviation: AMR, antibody-mediated myocardial rejection; HT, heart transplantation; NS, no statistically significant difference.

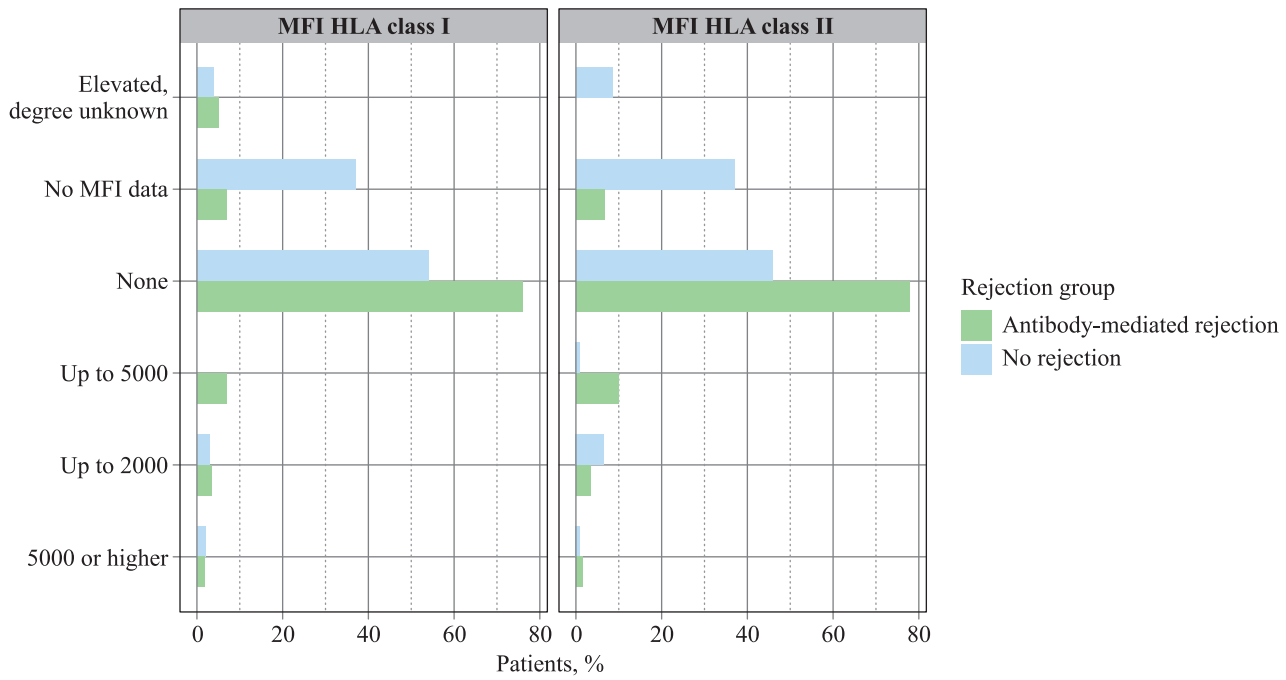

Fig. 1. Mean fluorescence intensity of antibodies to HLA class I and II before heart transplantation in patients with antibody-mediated rejection

with AMR compared to those without rejection. Specifically, only 3.4% of patients in the AMR group received this therapy, versus 14% in the non-rejection group. This difference was statistically significant ($p = 0.036$; $\chi^2 = 4.387$), reflecting a variation in treatment approaches between the groups (Table 2).

Tacrolimus trough levels during the first two weeks after transplantation were lower in patients who developed AMR compared with those who did not (median 11.4 [8.2–13.6] *vs.* 12.4 [10.1–15.0] ng/mL, $p = 0.002$). Similarly, immunosuppressant dosing during the first month post-transplant differed significantly between groups ($p < 0.001$), with patients experiencing AMR receiving lower median doses (1000 mg) compared to patients without rejection (1500 mg) (Fig. 5).

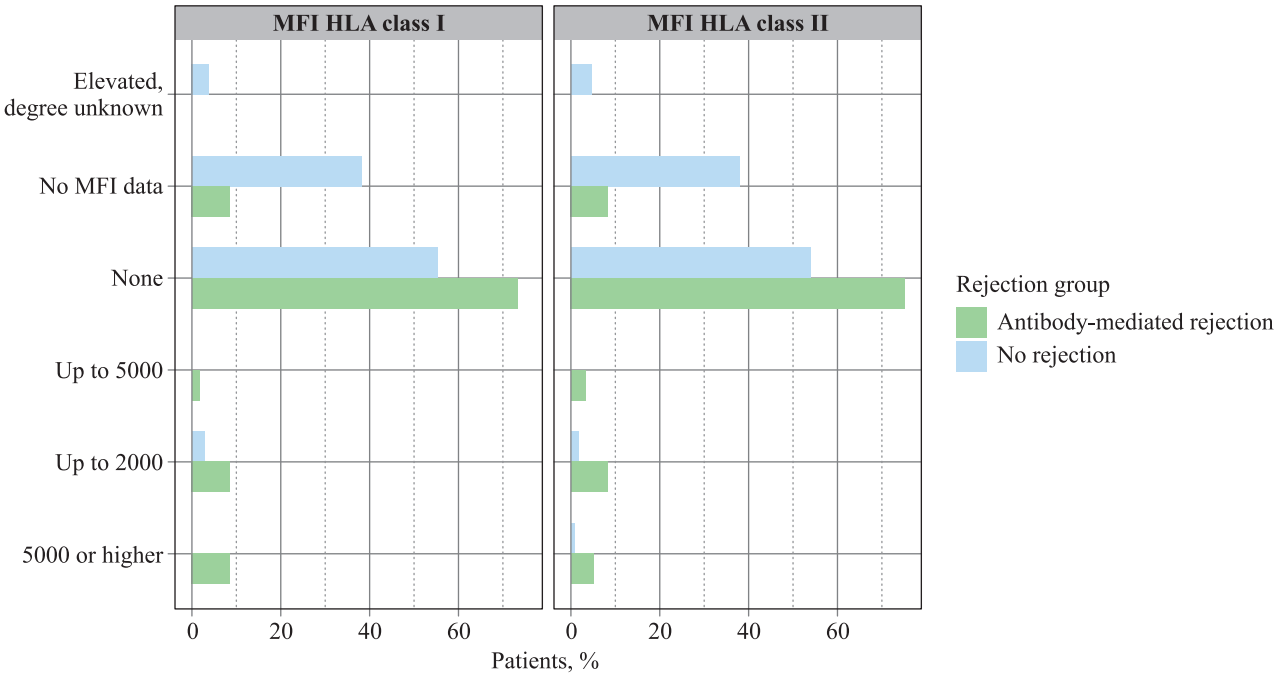

Fig. 2. Mean fluorescence intensity of antibodies to HLA class I and II during the first 6 months after heart transplantation in patients with antibody-mediated rejection

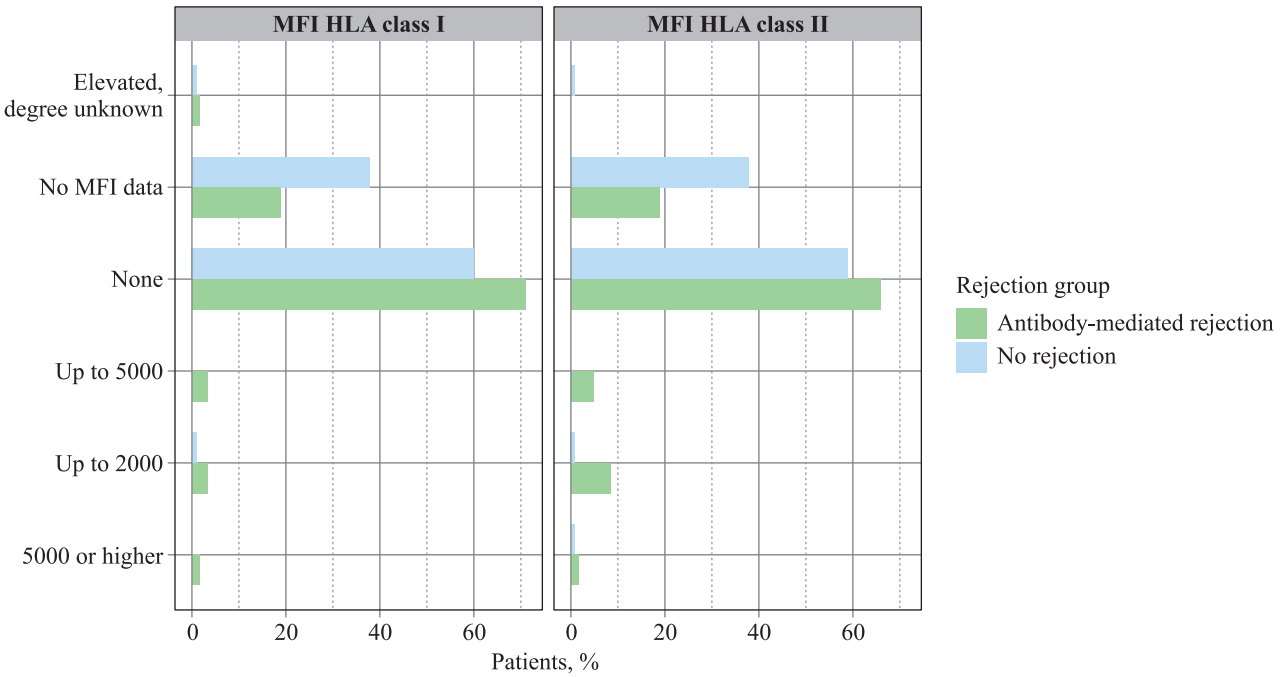

Fig. 3. Mean fluorescence intensity of antibodies to HLA class I and II at 6–12 months after heart transplantation in patients with antibody-mediated rejection

A stepwise discriminant analysis was conducted using a general model incorporating 15 variables. The final model retained 9 features, enabling statistically significant discrimination between patients with HC-R requiring treatment and those without rejection or with subclinical rejection, $F(18, 222) = 12{,}463$, $p < 0.00001$ (Table 3, Fig. 6).

During the construction of the discriminant function (DF), no misclassifications requiring treatment were observed in the HC-R patient group. Among patients without rejection, 9 misclassifications were identified out of 89 individuals, and in the group with subclinical rejection not requiring treatment, 18 misclassifications occurred among 30 patients. Analysis of these misclassifications revealed no abnormal variables necessitating

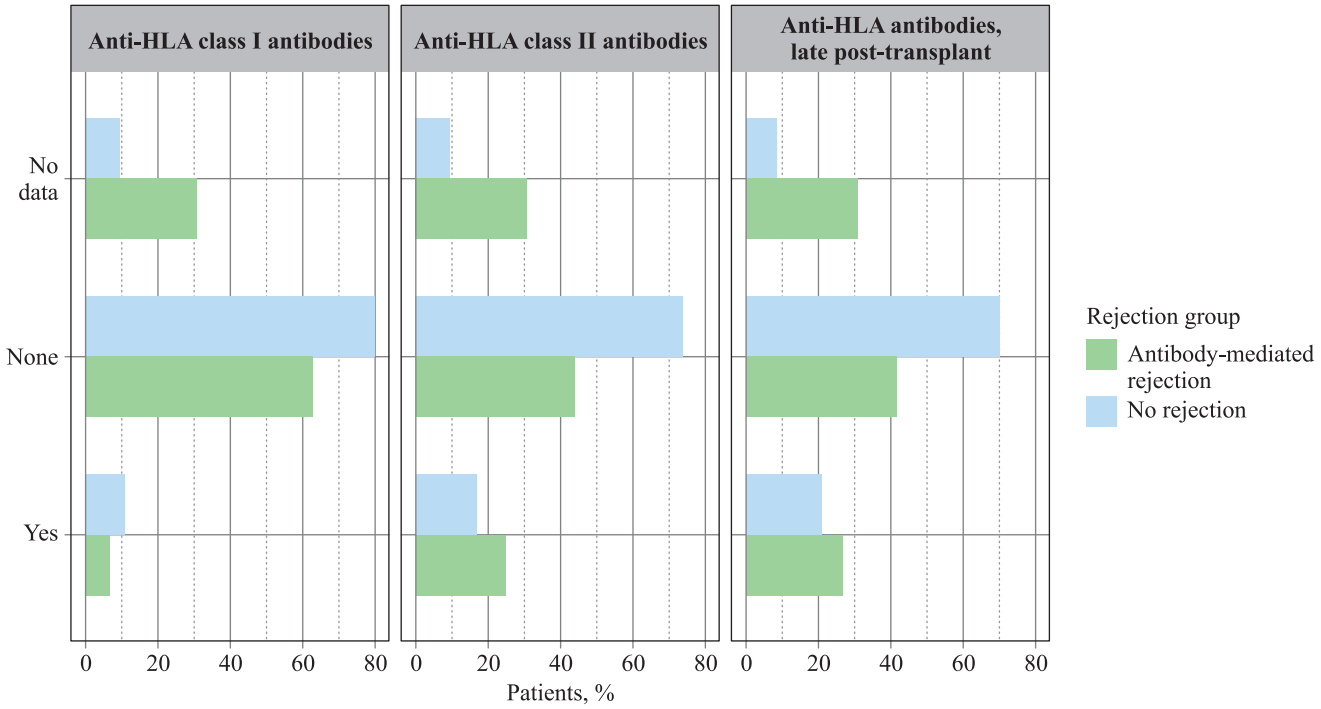

Fig. 4. Levels of pre-existing anti-HLA antibodies and *de novo* anti-HLA antibodies at 6–12 months after heart transplantation in patients with antibody-mediated rejection

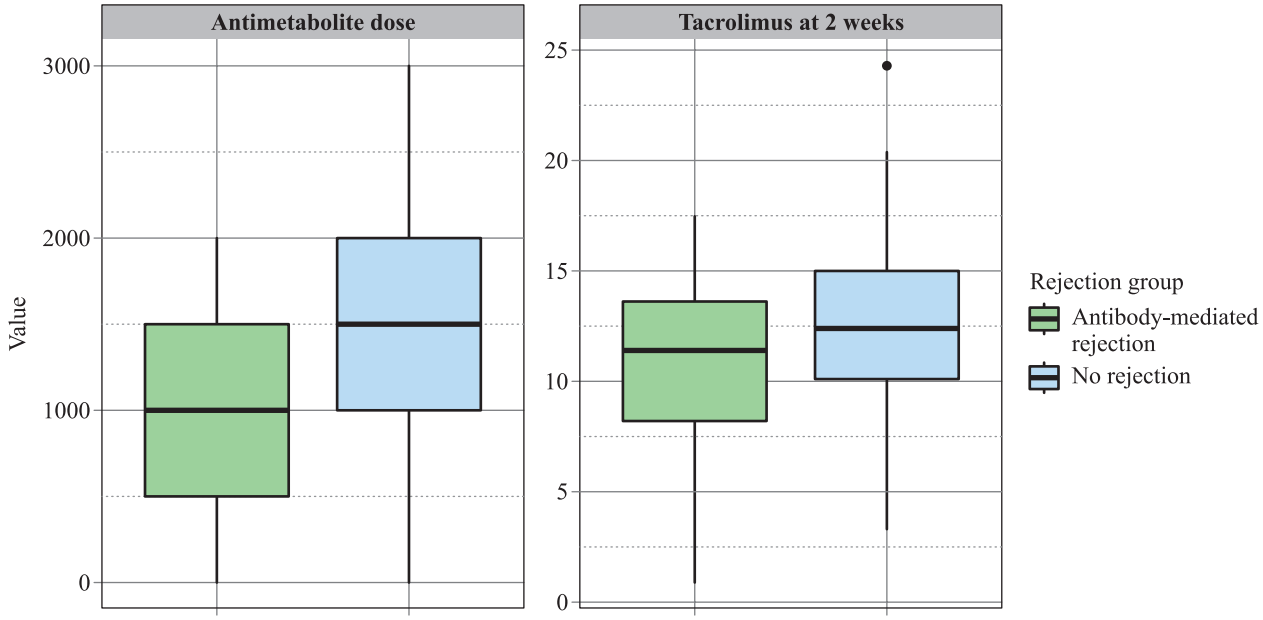

Fig. 5. Antimetabolite dosing and tacrolimus trough level 2 weeks after heart transplantation in rejection and non-rejection groups

Table 3

Discriminant analysis parameters for nine significant indicators (Wilks' lambda = 0.24739; approx. F(18, 222) = 12.463; p < 0.00001)

Indicator	Wilks' Lambda	Partial Lambda	F-remove (2,111)	p-value	Toler.	1-Toler. (R-Sqr.)
Post-transplant desensitization therapy	0.630422	0.392419	85.93045	0.000000	0.803934	0.196066
Antimetabolite dose	0.273039	0.906059	5.75427	0.004190	0.760040	0.239960
Tacrolimus trough level at 2 weeks after HT	0.263866	0.937557	3.69638	0.027918	0.936610	0.063390
Patient compliance	0.259201	0.954430	2.64989	0.075127	0.766998	0.233002
Early antibodies after HT	0.256655	0.963899	2.07866	0.129941	0.797085	0.202915
Body mass index	0.262669	0.941829	3.42792	0.035929	0.152929	0.847071
Body weight	0.259829	0.952126	2.79062	0.065695	0.130678	0.869322
Sex	0.257379	0.961188	2.24107	0.111135	0.561731	0.438269
ABO blood group mismatch	0.252805	0.978581	1.21480	0.300684	0.945481	0.054519

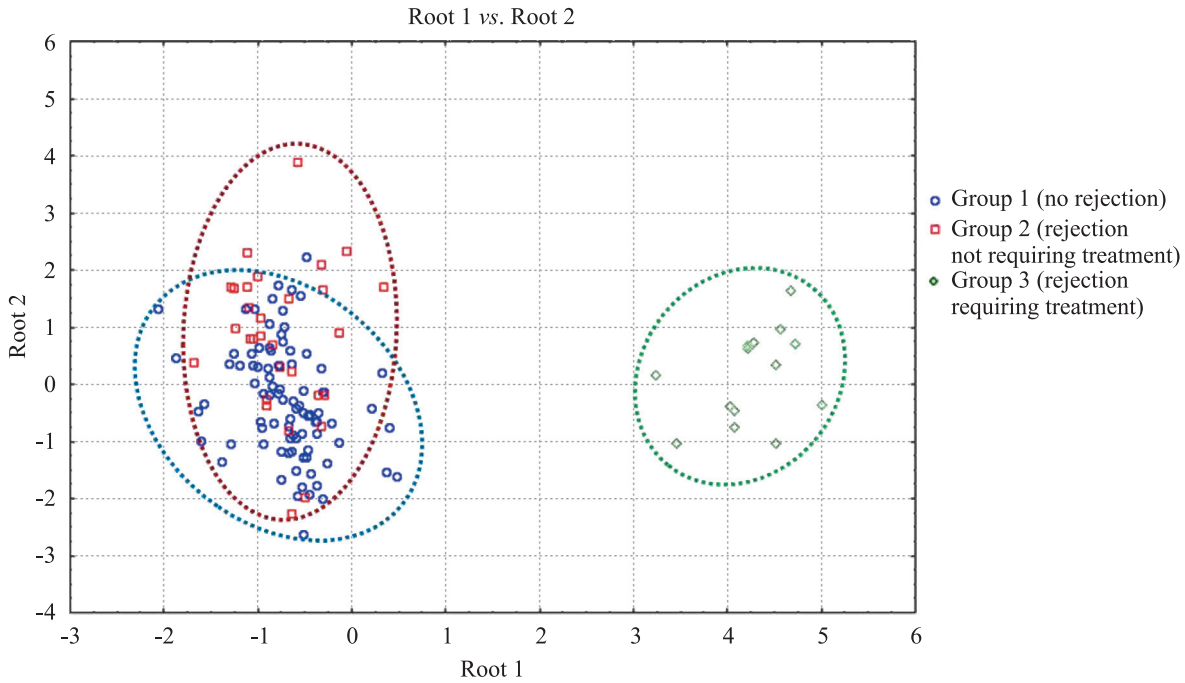

Fig. 6. Graphical representation of the discriminant model

exclusion. Importantly, the DF correctly identified 100% of recipients with rejection requiring treatment.

DISCUSSION

AMR is among the most severe complications following HT, with a substantial impact on both survival and long-term prognosis [10]. It remains a leading cause not only of graft dysfunction but also of cardiac allograft vasculopathy and sudden death [6, 11]. The incidence of AMR) within the first 12 months post-transplant may exceed 30%, a finding corroborated by our data: 36.4% of recipients exhibited AMR according to the 2013 ISHLT criteria, with 9.9% demonstrating HC-R requiring intervention.

Despite advances in noninvasive diagnostic approaches for myocardial transplant rejection, endomyocardial biopsy continues to be the established "gold standard" for definitive diagnosis [12, 13].

Our results further underscore the clinical heterogeneity of AMR: among the 59 patients with morphological evidence of AMR (AMR II), only 16 required therapeutic intervention. This observation aligns with current understanding that asymptomatic or subclinical AMR is common and necessitates comprehensive evaluation integrating histology, echocardiographic assessment, and serological data [13].

An interesting finding of our study was the difference in the use of induction therapy: only 3.4% of patients who developed AMR received rabbit anti-thymocyte immunoglobulin, compared with 14% in the non-rejection group ($\chi^2 = 4.387$; $p = 0.036$). This observation may suggest a potential protective effect of more intensive in-

duction therapy in sensitized recipients. Previous studies have similarly demonstrated the efficacy of rabbit antithymocyte immunoglobulin in preventing AMR among patients at high immunological risk.

In our analysis of risk factors, particular attention was given to the role of DSA. The presence of class I DSA, or both class I and class II DSA, was associated with the highest risk of hemodynamically compromising AMR. These findings are consistent with international guidelines, which highlight the importance of monitoring DSA not only pre-transplant but also throughout the first year following solid organ transplantation.

Our study also revealed that patients who developed AMR were more likely to test positive for anti-mitochondrial antibodies (AMA) prior to HT, with titers ≤5000 MFI, whereas sensitization was almost absent in the control group. AMA levels peaked within the first 6 months post-transplant in patients with AMR and remained approximately twice as high as in the control group during the latter half of the year. These findings highlight the importance of prospective immunological screening both before and after HT.

A key outcome of this study was the application of discriminant analysis using 15 clinical and immunological variables to predict HC-R. The final model, which incorporated 9 significant predictors, demonstrated high accuracy in distinguishing patients requiring treatment from those without rejection or with subclinical AMR ($F(18, 222) = 12.463$, $p < 0.00001$). These results underscore the potential utility of discriminant analysis for clinical risk stratification of hemodynamically compromising AMR and for guiding individualized monitoring and therapeutic strategies.

This study identified several key factors associated with AMR, including high levels of pre-existing sensitization, suboptimal induction therapy, inadequate immunosuppressive control, and the presence of *de novo* anti-HLA antibodies. These parameters may serve as the foundation for creating an immunological risk score and developing personalized monitoring strategies.

The future of transplant medicine lies in the integration of molecular diagnostics, predictive analytics, and individualized treatment approaches. Identification of risk factors for HC-AMR and the development of stratification models represent important steps toward improving post-transplant survival and reducing the incidence of complications such as graft dysfunction and cardiac allograft vasculopathy.

CONCLUSION

High levels of HLA sensitization prior to transplantation, suboptimal immunosuppressive control during the early postoperative period, and the development of *de novo* anti-HLA antibodies within the first year after transplantation are associated with an increased risk of AMR. The discriminant model developed using key clinical and immunological parameters demonstrates potential for risk stratification and personalized patient monitoring. These findings highlight the importance of close immunological surveillance and optimization of immunosuppressive therapy in high-risk recipients. Future studies should aim to validate this model, assess its impact on therapeutic decision-making, and investigate the long-term effects of individualized immunomonitoring on transplant outcomes.

This study was supported by a grant from the Russian Science Foundation (No. 24-15-20016 – https://rscf.ru/project/24-15-20016/) and a grant from the St. Petersburg Science Foundation (Agreement No. 24-15-20016, dated May 24, 2024).

The authors declare no conflict of interest.

REFERENCES

1. *Sadeghpour Tabaei A, Hashemi P*. Intra-operative Risk Factors Affecting Mortality after Heart Transplantation: A Referral Center Experience in Iran. *Iran J Med Sci*. 2024; 49 (6): 359–368. doi: 10.30476/ijms.2023.99165.3122, PMID: 38952641.
2. *DeFilippis EM, Kransdorf EP, Jaiswal A, Zhang X, Patel J, Kobashigawa JA et al*. Detection and management of HLA sensitization in candidates for adult heart transplantation. *J Heart Lung Transplant*. 2023; 42 (4): 409–422. doi: 10.1016/j.healun.2022.12.019.
3. *Chambers DC, Perch M, Zuckermann A, Cherikh WS, Harhay MO, Hayes D et al*. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-eighth adult lung transplantation report – 2021; Focus on recipient characteristics. *J Heart Lung Transplant*. 2021; 40 (10): 1060–1072. doi: 10.1016/j.healun.2021.07.021, PMID: 34446355.
4. *Shah KB, Flattery MP, Smallfield MC, Merinar G, Tang DG, Sheldon EH et al*. Surveillance Endomyocardial Biopsy in the Modern Era Produces Low Diagnostic Yield for Cardiac Allograft Rejection. *Transplantation*. 2015; 99 (8): e75–e80. doi: 10.1097/TP.0000000000000615.
5. *Coutance G, Kransdorf E, Aubert O, Bonnet G, Yoo D, Rouvier P et al*. Clinical Prediction Model for Antibody-Mediated Rejection: A Strategy to Minimize Surveillance Endomyocardial Biopsies After Heart Transplantation. *Circ Heart Fail*. 2022; 15 (10): e009923. doi: 10.1161/CIRCHEARTFAILURE.122.009923, PMID: 36200456.
6. *Kilic A, Weiss ES, Allen JG, Conte J V, Shah AS, Baumgartner WA et al*. Simple score to assess the risk of rejection after orthotopic heart transplantation. *Circulation*.

2012; 125 (24): 3013–3021. doi: 10.1161/CIRCULATIONAHA.111.066431, PMID: 22634267.

7. *Chih S, Chruscinski A, Ross HJ, Tinckam K, Butany J, Rao V*. Antibody-mediated rejection: an evolving entity in heart transplantation. *J Transplant*. 2012; 2012: 210210. doi: 10.1155/2012/210210, PMID: 22545200.
8. *Kobashigawa J, Colvin M, Potena L, Dragun D, Crespo-Leiro MG, Delgado JF et al*. The management of antibodies in heart transplantation: An ISHLT consensus document. *J Heart Lung Transplant*. 2018; 37 (5): 537–547. doi: 10.1016/j.healun.2018.01.1291, PMID: 29452978.
9. *Farcas AO, Stoica MC, Maier IM, Maier AC, Sin AI*. Heart Transplant Rejection: From the Endomyocardial Biopsy to Gene Expression Profiling. *Biomedicines*. 2024; 12 (8): 1926. doi: 10.3390/biomedicines12081926, PMID: 39200392.
10. *Saldan A, Mengoli C, Sgarabotto D, Fedrigo M, Angelini A, Feltrin G et al*. Human cytomegalovirus and Epstein–Barr virus infections occurring early after transplantation are risk factors for antibody-mediated rejection in heart transplant recipients. *Front Immunol*. 2023; 14: 1171197. doi: 10.3389/fimmu.2023.1171197, PMID: 37256129.
11. *Cross AR, Glotz D, Mooney N*. The Role of the Endothelium during Antibody-Mediated Rejection: From Victim to Accomplice. *Front Immunol*. 2018; 9: 106. doi: 10.3389/fimmu.2018.00106.
12. *Goldberg JF, Mehta A, Bahniwal RK, Agbor-Enoh S, Shah P*. A gentler approach to monitor for heart transplant rejection. *Front Cardiovasc Med*. 2024; 11: 1349376. doi: 10.3389/fcvm.2024.1349376, PMID: 38380175.
13. *Nguyen VP, Kobashigawa JA*. Antibody-medicated rejection after heart transplantation: diagnosis and clinical implications. *Curr Opin Organ Transplant*. 2020; 25 (3): 248–254. doi: 10.1097/MOT.0000000000000754, PMID: 32304428.
14. *Zuckermann A, Schulz U, Deuse T, Ruhpawar A, Schmitto JD, Beiras-Fernandez A et al*. Thymoglobulin induction in heart transplantation: patient selection and implications for maintenance immunosuppression. *Transpl Int*. 2015; 28 (3): 259–269. doi: 10.1111/tri.12480, PMID: 25363471.
15. *Van den Broek DAJ, Meziyerh S, Budde K, Lefaucheur C, Cozzi E, Bertrand D et al*. The Clinical Utility of Post-Transplant Monitoring of Donor-Specific Antibodies in Stable Renal Transplant Recipients: A Consensus Report With Guideline Statements for Clinical Practice. *Transpl Int*. 2023; 36: 11321. doi: 10.3389/ti.2023.11321, PMID: 37560072.

The article was submitted to the journal on 18.07.2025