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Prevalence and clinical features of metabolic syndrome in recipients after orthotopic heart transplantation

The aim – to determine the prevalence of metabolic syndrome (MS) in recipients after orthotopic heart transplantation (OHT) and to assess its clinical features.

Materials and methods. A retrospective analysis was conducted on 112 recipients who underwent orthotopic heart transplantation between 2019 and 2024 at the Heart Institute of the Ministry of Health of Ukraine. Patients were divided into two groups: Group A (n = 41) – with MS before transplantation, and Group B (n = 71) – without MS. Anthropometric, biochemical parameters, echocardiographic data, and survival rates were evaluated. The diagnosis of MS was established according to the NCEP-ATP III criteria.

Results. The proportion of males in Group A was higher (95.1 % vs. 78.9 %, p = 0.021). The mean age in Group A was 53 (46; 56) years, which was higher than in Group B (40 (32; 53), p = 0.003). MS was associated with a higher body mass index (p = 0.001), a greater prevalence of ischemic cardiomyopathy (41.5 % vs. 19.7 %, p = 0.043), and elevated creatinine levels (p = 0.016). One year after transplantation, the prevalence of MS increased to 50.5 % (p = 0.041), primarily due to elevated triglyceride levels (> 1.7 mmol/L, p = 0.014), increased blood pressure (≥ 130/85 mm Hg, p = 0.0001), and a rise in the proportion of recipients with diabetes mellitus or fasting glucose ≥ 5,6 mmol/L (p = 0.012). Kaplan – Meier survival analysis demonstrated that recipients with MS before OHT had significantly lower one-year survival compared to those without MS [(82.9 ± 5.9) % vs. (94.4 ± 2.7) %, p = 0.048].

Conclusions. MS is common among recipients after OHT and may worsen prognosis by increasing cardiovascular risk. The obtained results indicate the need for careful monitoring and correction of metabolic disorders in this patient population.

Key words: orthotopic heart transplantation, metabolic syndrome, survival, triglycerides, diabetes mellitus.

Metabolic syndrome (MS) is a complex pathological condition characterized by the simultaneous presence of several cardiovascular risk factors, including hyperglycemia, arterial hypertension, abdominal obesity and dyslipidemia. Its development is driven by intricate pathophysiological mechanisms, with insulin resistance and the accumulation of abdominal fat playing central roles in this process [1]. MS is closely associated with ischemic heart disease, acute cerebrovascular accidents and renal insufficiency. Moreover, it indicates biochemical changes in patients who have experienced a myocardial infarction [2, 3].

Overall, the prevalence of MS in the general population ranges from 18 % to 39 %, depending on diagnostic criteria and demographic differences [4]. MS holds particular significance in patients after orthotopic heart transplantation (OHT), as it may adversely affect long-term trans-

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plant outcomes. According to JM Sánchez-Gómez et al., metabolic syndrome occurs in approximately 40 % of patients after heart transplantation. The authors found that the presence of MS is associated with a twofold increased risk of developing cardiovascular diseases, cardiovascular mortality, non-fatal acute myocardial infarction and stroke. Additionally, MS is linked to a 1.5-fold increase in overall mortality among OHT recipients [5].

Despite significant progress in the treatment and management of patients after heart transplantation, MS remains a major concern, primarily due to the side effects of immunosuppressive therapy, which significantly impact long-term outcomes. Furthermore, the biochemical characteristics of MS are closely linked to the development and progression of cardiac allograft vasculopathy – a specific post-transplant complication characterized by diffuse intimal hyperplasia and fibrosis caused by chronic rejection, as well as associated cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia [6, 7].

Despite multiple studies, the impact of MS on the survival and function of the transplanted organ remains insufficiently explored.

The aim – to assess the prevalence and clinical characteristics of metabolic syndrome in recipients after orthotopic heart transplantation.

Materials and methods

Inclusion and Exclusion Criteria. This retrospective study included all cases (112) of orthotopic heart transplantation performed at the Heart Institute of the Ministry of Health of Ukraine in the period from 2019 to 2024. Exclusion criteria were the need for simultaneous transplantation of other organs and the age of the recipients less than 18 years.

Data Collection. An analysis was performed encompassing anthropometric parameters, baseline and dynamic blood pressure measurements, medical history data, etiology of heart failure, presence of comorbid conditions, initial echocardiographic findings (including left ventricular ejection fraction and pulmonary artery pressure), as well as biochemical markers such as NT-proBNP, creatinine, lipid profile, blood glucose, glycated hemoglobin and C-reactive protein levels. Additionally, the presence of metabolic syndrome and patient survival rates were assessed.

The diagnosis of metabolic syndrome was established if recipients met at least three out of five criteria according to the Third Report of the National Cholesterol Education Program (NCEP-ATP III) [1] *(Table 1)*.

Table 1
Criteria for metabolic syndrome according to National Cholesterol Education Program ATP III guidelines [1]

Criterion	Threshold Value
Abdominal obesity – Waist circumference, cm	
Men	> 102
Women	> 88
Triglycerides, mmol/L	≥ 1.7
HDL cholesterol, mmol/L	
Men	< 1.03
Women	< 1.29
Blood pressure, mm Hg	≥ 130/85
Fasting glucose, mmol/L	≥ 5.6

HDL – High-density lipoproteins.

The patients received the following immunosuppression regimen *(Table 2)*.

Ethical approval. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committees of the Heart Institute and Shupyk National Healthcare University of Ukraine.

Informed Consent. Given the retrospective nature of the study, informed consent for participation was not required.

Statistical Analysis. The study results were reported as mean (M) ± standard deviation (SD). In cases of non-normal data distribution, results were presented as median (Me) and the 1st (Q25) and 3rd (Q75) quartiles – Me (Q25; Q75).

For normally distributed data, the Student's t-test was used to determine statistical significance, whereas for non-normally distributed data, the Mann – Whitney U-test was applied. To analyze categorical variables, such as the frequency of postoperative complications in both groups, the Pearson's chi-square test or Fisher's exact test (where appropriate) was used.

Survival analysis was conducted using the Kaplan – Meier method, with group comparisons performed using the Log-rank test. A p-value of < 0.05 was considered statistically significant. All statistical calculations were performed using SPSS software version 26.0.

Results

From 2019 to 2024, a total of 112 orthotopic heart transplantations were performed at the

Table 2
Immunosuppression regimen used in the studied heart transplantation recipients

Drug	1st day	2nd day	3rd day and beyond
Methylprednisolone	125 mg – IV three times daily	0.8 mg/kg/day – per os divided into two doses	0.8 mg/kg/day – reduce the dose by 4 mg daily, first in the evening until complete withdrawal, then in the morning to 6–8 mg/day
Tacrolimus	0.03 mg/kg per os twice daily	under the control of tacrolimus levels	
Mycophenolate mofetil	1 g per os twice a day, provided that the leukocyte count is normal and there are no signs of infection		

Table 3
Baseline characteristics of recipients

Parameter	Total (n = 112)	Group A (n = 41)	Group B (n = 71)	p-value (A vs. B)
Male sex, n (%)	95 (84.8 %)	39 (95.1 %)	56 (78.9 %)	0.021
Age, years	48 (35; 56)	53 (46; 56)	40 (32; 53)	0.003
Etiology of HF, n (%)				
DCM	69 (61.6 %)	21 (51.2 %)	48 (67.6 %)	0.043
ICM	31 (27.7 %)	17 (41.5 %)	14 (19.7 %)	
Other causes	12 (10.7 %)	3 (7.3 %)	9 (12.7 %)	
BMI, kg/m^2	26.2 ± 4.84	29.6 ± 4.60	24.2 ± 3.84	0.001
Previous cardiac surgery, n (%)	9 (8.04 %)	7 (17.1 %)	2 (2.82 %)	0.008
Creatinine, μmol/L	115.6 ± 71.3	140.5 ± 69.5	101.2 ± 30.7	0.016
GFR, mL/min	86.8 ± 36.5	81.9 ± 41.2	89.9 ± 33.5	0.043
Smoking, n (%)	29 (25.9 %)	13 (31.7 %)	16 (22.5 %)	0.285
Atrial fibrillation, n (%)	28 (25.0 %)	12 (29.3 %)	16 (22.5 %)	0.427
Pacemaker, n (%)	23 (20.5 %)	9 (21.9 %)	14 (19.7 %)	0.778
MCS, n (%)	14 (12.5 %)	8 (19.5 %)	6 (8.45 %)	0.088
LVEF, %	20.4 ± 8.66	21.5 ± 8.14	19.8 ± 8.98	0.421
PAP, mm Hg	39.4 ± 19.5	41.1 ± 15.6	37.4 ± 17.3	0.103
NT-proBNP, pg/ml	8466 ± 5674	8263 ± 4218	8509 ± 3394	0.745

HF – heart failure; DCM – dilated cardiomyopathy; ICM – ischemic cardiomyopathy; BMI – body mass index; GFR – glomerular filtration rate; MCS – mechanical circulatory support; LVEF – left ventricular ejection fraction; PAP – pulmonary artery pressure; NT-proBNP – N-terminal pro-B-type natriuretic peptide.

Heart Institute of the Ministry of Health of Ukraine. The median age of recipients at the time of transplantation was 48 (35; 56) years, with males comprising 84.8 % (95 individuals) of all heart transplant recipients. The most common cause of end-stage heart failure in these patients was dilated cardiomyopathy (DCM), identified in 69 cases (61.6 %).

Based on the presence of metabolic syndrome according to the NCEP ATP III criteria, all recipients were divided into two groups:

- Group A (n = 41) – Recipients with metabolic syndrome before transplantation.
- Group B (n = 71) – Recipients without metabolic syndrome before transplantation.

Detailed characteristics of the study groups are presented in *Table 3*.

Thus, as shown in Table 3, recipients with metabolic syndrome were significantly older (53 [46; 56] years vs. 40 [32; 53] years, p = 0.003) and had 16.2 % (p = 0.021) higher proportion of males compared to those without the syndrome.

Table 4
Prevalence of metabolic syndrome before and one year after heart transplantation

Criteria for metabolic syndrome	Before OHT (n = 112)	One Year After OHT (n = 101)	p-value
Triglycerides ≥ 1.7 mmol/L or medication use	51 (45.5 %)	64 (63.4 %)	0.014
HDL-C < 1.03 mmol/L in men, < 1.29 mmol/L in women	37 (33.0 %)	29 (28.7 %)	0.495
Diabetes or fasting glucose ≥ 5,6 mmol/L	44 (39.2 %)	57 (56.4 %)	0,012
Blood pressure ≥ 130/85 mmHg	28 (25.0 %)	59 (58.4 %)	0.0001
Waist circumference > 102 cm in men, > 88 cm in women	23 (20.5 %)	31 (30.7 %)	0.088
Metabolic syndrome, n (%)	41 (36.7 %)	51 (50.5 %)	0.041

HDL-C – high-density lipoproteins.

Moreover, ischemic cardiomyopathy was significantly more common as the etiology of heart failure among recipients with metabolic syndrome by 13.8 % (p = 0.043) compared to those without the syndrome *(Table 3)*.

Additionally, recipients with metabolic syndrome had a 13.0 % (p = 0.001) higher body mass index and a 14.3 % (p = 0.008) higher frequency of previous cardiac surgical interventions *(Table 3)*. They also had 28.0 % (p = 0.016) higher mean creatinine levels alongside with 9.77 % lower glomerular filtration rate (p = 0.043) compared to recipients without metabolic syndrome *(Table 3)*.

Further, an analysis of metabolic syndrome prevalence dynamics before and one year after transplantation showed an increase in the syndrome's frequency by 13.8 % (p = 0.041) one year post-OHT compared to the preoperative prevalence *(Table 4)*. Notably, among the 51 patients diagnosed with metabolic syndrome one year after OHT, 33 (64.7 %) had already met the criteria for metabolic syndrome before transplantation.

As seen in *Table 4*, the increase in the prevalence of metabolic syndrome was primarily driven by a significant rise of 17.9 % (p = 0.014) in the number of recipients with triglyceride levels ≥ 1.7 mmol/L, a substantial increase of 33.4 % (p = 0.0001) in recipients with blood pressure values ≥ 130/85 mm Hg, and a 17.2 % increase in the number of recipients with diabetes mellitus or fasting glucose levels ≥ 5,6 mmol/L (p = 0.012). At the same time, one year after OHT, there was a trend toward a reduction in the number of recipients with HDL cholesterol levels < 1.03 mmol/L in men or < 1.29 mmol/L in women (p = 0.495) *(Table 4)*.

It is worth noting that survival analysis using the Kaplan – Meier method demonstrated that recipients with metabolic syndrome

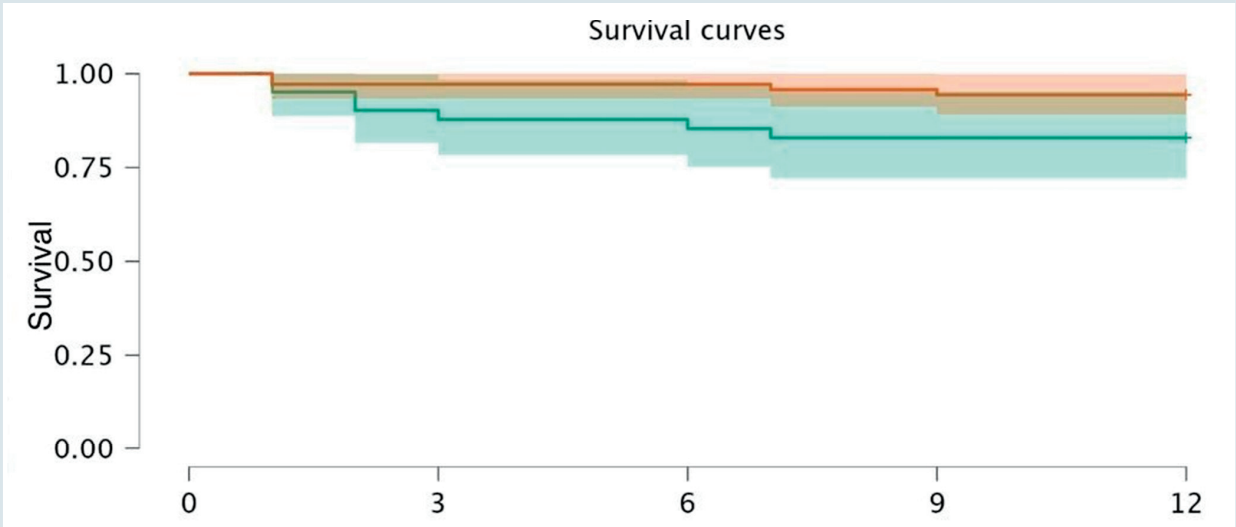

Figure. **Kaplan – Meier analysis of one-year survival among patients in the study groups**

before heart transplantation had significantly lower one-year survival rates compared to those without metabolic syndrome [(82.9 ± 5.9) % vs. (94.4 ± 2.7) %, p = 0.048] *(Figure)*.

Discussion

The results of our study confirm that metabolic syndrome is a common phenomenon among patients after orthotopic heart transplantation. Moreover, its prevalence increases after transplantation, which may indicate a significant impact of concomitant immunosuppressive therapy on the metabolic state of patients.

An analysis of the baseline characteristics of the recipients showed that patients with MS were significantly older, had a higher proportion of males and diagnosis of ischemic cardiomyopathy compared to patients without MS. These findings are consistent with literature data indicating a higher prevalence of metabolic disorders among older individuals and patients with ischemic heart disease [8, 9].

Among the factors that may have contributed to the increased prevalence of MS after transplantation, immunosuppressive therapy should be highlighted, as it is known to affect glucose metabolism, lipid profile, and blood pressure regulation [10]. In our study, we observed a significant increase in the proportion of patients with hypertriglyceridemia, impaired glycemia and arterial hypertension after transplantation. At the same time, the prevalence of low levels of HDL cholesterol remained largely unchanged.

From a long-term perspective, the presence of MS before transplantation was associated with lower survival rates after OHT. Kaplan – Meier survival curve analysis demonstrated significantly worse outcomes among recipients with MS, which is consistent with the findings of S. Sponga et al. [4]. Specifically, the authors reported that five-year survival was significantly lower in patients with pre-transplant MS (65 % vs. 78 %, p < 0.01) as well as in those with MS one year post-transplant (78 % vs. 89 %, p < 0.01) compared to recipients without the syndrome.

As noted by J. Stehlik et al., metabolic disorders in post-transplant patients may be associated with the development of transplant coronary vasculopathy or chronic rejection, which are among the leading causes of graft dysfunction and mortality during long-term follow-up after heart transplantation [11].

Transplant coronary vasculopathy is a rapidly progressing form of atherosclerosis that occurs exclusively in the graft and develops due to endothelial dysfunction of multifactorial origin. Since metabolic syndrome is accompanied by chronic systemic inflammation, which contributes to endothelial dysfunction, its impact on the development of this complication appears to be entirely plausible [8].

Metabolic syndrome after orthotopic heart transplantation is a dynamic clinical entity driven not only by preexisting cardiometabolic risk factors but also by the metabolic footprint of lifelong immunosuppression and postsurgical physiology. Contemporary International Society for Heart and Lung Transplantation (ISHLT) guidance stresses that therapeutic efforts must begin before discharge and continue lifelong, with the dual aims of curbing cardiovascular morbidity – including cardiac allograft vasculopathy (CAV) – and safeguarding renal function [12]. Our approaches to MS correction are described below.

Early, individualised lifestyle optimisation remains the foundation of care. Cohort data demonstrate that strict adherence to high-quality dietary patterns – most consistently a Mediterraneanstyle diet – limits posttransplant weight gain and visceral adiposity, thereby tempering dyslipidaemia and insulin resistance [13]. Supervised aerobic or combined aerobicresistance cardiac rehabilitation instituted within the first postoperative months improves peak VO_2 and endothelial function; programmes incorporating short blocks of highintensity interval work appear particularly effective in stable recipients [14].

Pharmacological tailoring complements behavioural measures. Highintensity statin therapy is mandatory unless contraindicated, yet nearly one recipient in five fails to attain contemporary lowdensity lipoprotein cholesterol (LDLC) targets. Adjunctive proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition with evolocumab or alirocumab yields additional LDLC reductions of 50–60 percent without compromising safety and is now advised when LDLC persists above 1.4 mmol/L despite maximally tolerated statins, or when statin intolerance precludes dose escalation [15]. Attention is increasing towards sodium–glucose cotransporter-2 (SGLT2) inhibition; emerging registry and proofofconcept data suggest that empagliflozin produces glucoselowering, natriuretic and renoprotective effects in transplant recipients, with neutral effects on tacrolimus troughs and infection rates [16]. Metformin remains firstline for newonset diabetes after transplantation provided the estimated glomerular filtration rate exceeds 30 mL/min,

and glucagonlike peptide1 receptor agonists may be considered when obesity is a dominant driver of poor metabolic control.

Metabolic hypertension demands vigilant evaluation because even modest elevations in systolic pressure accelerate graft vasculopathy. The 2024 European Society of Cardiology (ESC) guideline advocates an ambulatory or home bloodpressure target of < 130/80 mm Hg for transplant survivors, achievable in most cases with a renin – angiotensin system blocker plus a dihydropyridine calciumchannel blocker once drug – drug interactions are excluded. Singlepill combinations strengthen adherence and should be prioritised [17].

Weight management frequently requires structured, multidisciplinary programmes. Where class II–III obesity persists after six to twelve months of optimised medical therapy, glucagonlike peptide1 receptor agonists or SGLT2 inhibitors can be considered. Bariatric surgery may be contemplated in carefully selected recipients with refractory morbid obesity, preferably 24 months or more after transplantation when immunosuppression is stable.

Longterm success hinges on seamless coordination among transplant cardiology, endocrinology, nephrology, dietetics and physiotherapy. Routine audit of metabolic targets, coupled with patient education and digital health engagement, underpins adherence and timely therapeutic intensification. A holistic, evidencebased strategy offers the best prospect of blunting the cardiovascular and renal sequelae of MS in heart transplant recipients.

Overall, the findings highlight the necessity of close monitoring and management of metabolic disorders in patients after heart transplantation. Optimizing immunosuppressive therapy strategies, individualized management of patients with metabolic syndrome risk factors and the active implementation of non-pharmacological approaches (lifestyle modification, dietary behavior correction) may contribute to improved prognosis and increased survival rates in transplant recipients.

This study has several limitations. First, it is based on a retrospective analysis of medical records, which may introduce information bias due to potential inaccuracies or incomplete data. Second, the study's limited sample size may restrict the generalizability of the findings to a broader patient population. Additionally, the analysis was conducted within one year post-transplantation, which does not allow for an assessment of the long-term impact of metabolic syndrome on survival, graft function, and the risk of allograft vasculopathy development.

Conclusions

Recipients with metabolic syndrome were significantly older (53 [46; 56] years vs. 40 [32; 53] years, p = 0.003), had a 16.2 % higher proportion of males (p = 0.021), a 13.8 % higher prevalence of ischemic cardiomyopathy (p = 0.043), a 13.0 % higher body mass index (p = 0.001), and a 14.3 % higher frequency of previous cardiac surgical interventions (p = 0.008) compared to recipients without metabolic syndrome.

An analysis of metabolic syndrome prevalence dynamics before and one year after orthotopic heart transplantation revealed a 13.8 % increase in the syndrome's frequency (p = 0.041) one year post-transplant compared to the preoperative rate. This increase was associated with a higher incidence of hypertriglyceridemia (p = 0.014), impaired glycemia (p = 0.012) and arterial hypertension (p = 0.0001), which are key components of metabolic syndrome.

Recipients with metabolic syndrome before heart transplantation had significantly lower one-year survival rates compared to those without metabolic syndrome [(82.9 ± 5.9) % vs. (94.4 ± 2.7) %, p = 0.048].

Доступність даних:	Data availability:
Дані можуть бути надані за обґрунтованим запитом.	*Data can be provided upon reasonable request.*
Джерела фінансування:	Sources of funding:
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Не передбачене темою і концепцією роботи.	*Not provided for by the topic and concept of the work.*
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Поширеність і клінічні особливості метаболічного синдрому в реципієнтів після ортотопічної трансплантації серця

Мета роботи – визначити поширеність метаболічного синдрому (МС) у реципієнтів після ортотопічної трансплантації серця (ОТС) та оцінити його клінічні особливості.

Матеріали і методи. Проведено ретроспективний аналіз 112 реципієнтів, які перенесли ОТС у 2019–2024 рр. у ДНП «Інститут серця МОЗ України». Пацієнти були розподілені на дві групи: група А (n = 41) – з МС до ТС, група Б (n = 71) – без МС. Оцінювали антропометричні, біохімічні показники, дані ехокардіографії та рівень виживання. Діагноз МС визначали за критеріями NCEP-ATP III.

Результати. Частка чоловіків у групі А була вищою (95,1 % проти 78,9 %, p = 0,021). Середній вік у групі А – 53 (46; 56) років, що перевищує відповідний показник у групі Б (40 (32; 53), p = 0,003). МС був асоційований із вищим індексом маси тіла (p = 0,001), наявністю ішемічної кардіоміопатії у більшості випадків (41,5 % проти 19,7 %, p = 0,043) та вищим рівнем креатиніну (p = 0,016). Через рік після ТС поширеність МС зросла до 50,5 % (p = 0,041), що було зумовлено підвищенням рівня тригліцеридів (≥ 1,7 ммоль/л, p = 0,014), артеріального тиску (≥ 130/85 мм рт. ст., p = 0,0001) та зростанням частки пацієнтів із цукровим діабетом чи глюкозою натще ≥ 5,6 ммоль/л (p = 0,012). Аналіз виживання за методом Каплана – Мейєра показав, що реципієнти з МС до ТС характеризувалися статистично значущо нижчим показником однорічного виживання порівняно з реципієнтами без МС [(82,9 ± 5,9) % проти (94,4 ± 2,7) %, p = 0,048)].

Висновки. МС є поширеним серед реципієнтів після ОТС і може погіршувати прогноз унаслідок підвищення серцево-судинних ризиків. Отримані результати свідчать про необхідність ретельного моніторингу та корекції метаболічних порушень у цієї категорії пацієнтів.

Ключові слова: ортотопічна трансплантація серця, метаболічний синдром, виживання, тригліцериди, цукровий діабет.