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Review Article — *Special issue: Heart Failure*

Metabolic profile of patients after heart transplantation

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ABSTRACT

Orthotopic heart transplantation improves life expectancy and quality of life in patients with severe heart failure. After transplantation, metabolic complications are frequent. They are caused particularly by immunosuppressive therapy. In our cohort of 315 patients, 52% of patients had diabetes mellitus together with hyperlipoproteinemia, 41% of patients had hyperlipoproteinemia without diabetes, 3% of patients had diabetes mellitus without hyperlipoproteinemia and only 4% of patients had none of these disorders. Therapeutic options with respect to interactions with immunosuppressive therapy are discussed in this article.

Contents

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1. Introduction

In the last two decades, orthotopic heart transplantation (HTX) has become an established method for the treatment of severe heart failure. Heart transplantation is a treatment option that significantly improves quality of life and prognosis of patients with terminal heart failure. Owing to long-term survival of transplanted patients, this treatment is associated with various late complications. The most important complications are rejection, infection, or cancer, but also metabolic complications, accentuated by lifelong immunosuppressive treatment.

1.1. *Metabolic syndrome*

Metabolic syndrome is a cluster of typical risk factors, which often occur together and arise from insulin resistance. It is ranked among diseases of affluence. Presence of metabolic syndrome increases the chance of developing premature atherosclerosis and cardiovascular diseases and also increases the risk of developing type 2 diabetes mellitus and some frequent types of cancer. Metabolic syndrome according to the Czech Institute of Metabolic Syndrome is defined as the presence of at least 3 risk factors listed below:

(1) Central obesity—waist circumference ≥102 cm in men, ≥88 cm in women
(2) Triglycerides ≥1.7 mmol/L (or hypolipidemic therapy)
(3) HDL cholesterol <1.0 mmol/L in men, <1.3 mmol/L in women
(4) Blood pressure ≥130/≥85 mmHg or antihypertensive therapy
(5) Fasting plasma glucose ≥5.6 mmol/L, or impaired glucose tolerance, or type 2 diabetes mellitus

1.2. *Hyperlipoproteinemia*

Hyperlipoproteinemia occurs in 60–80% of patient after heart transplantation. It is associated with several risk factors as history of coronary artery disease, history of lipid abnormalities, body mass index ≥25 kg/m^2, high dose of corticosteroids, and cyclosporine or sirolimus administration.

Cyclosporine increases cholesterol level, particularly its LDL fraction [1]. One of the possible mechanisms is injury of cell membrane, which is involved in LDL cholesterol clearance. This can probably lead to LDL cholesterol rise [2]. Higher plasmatic concentrations of cyclosporine decrease activity of lipoprotein lipase, which can cause increase in triglyceride level. Changes in lipid metabolism occur already in the first 3–6 months after transplantation [3]. Cyclosporine decreases clearance of prednisone, which can cause insulin resistance, increased synthesis of free fatty acids, and increased production of VLDL particles [4].

Newer immunosuppressive agent, calcineurin inhibitor tacrolimus has a less adverse effect on lipid profiles than cyclosporine. In the retrospective study of 194 patients after heart transplantation who were switched from cyclosporine to tacrolimus, levels of total and LDL cholesterol significantly decreased, and levels of HDL cholesterol significantly increased [5].

A negative effect of sirolimus (rapamycin) on lipid profiles has also been reported. The data were mostly gathered from patients after kidney transplantation. In a group of patients after kidney transplantation where sirolimus had been added to cyclosporine with corticosteroids, cholesterol and triglyceride levels increased significantly. The rise was dependent on the dose of sirolimus [6].

There is not enough data evaluating the effect of mycophenolate mofetil on lipid levels after organ transplantation.

Corticosteroid administration is associated with increased hepatic production of VLDL and rise in triglycerides and total cholesterol levels. It is caused by increased activity of acetyl-CoA carboxylase, increased synthesis of free fatty acids, and inhibition of lipoprotein lipase. Moreover, these effects are emphasized by cyclosporine, which decreases prednisone clearance.

1.3. *Diabetes mellitus*

According to ISHLT registry, the prevalence of diabetes mellitus before heart transplantation was 22%, and cumulative incidence of new-onset diabetes was up to 32% in the fifth year after heart transplantation [7]. Risk factors for developing diabetes mellitus that were reported in patients after liver or kidney transplantation were diabetes in family history, age over 40 years, metabolic syndrome, impaired glucose tolerance before transplantation, hepatitis C, immunosuppressive drugs, or obesity. In one study, family history and higher glycemia before transplantation (5.6 vs. 5.2 mmol/L in patients who did not develop diabetes) were found to be predisposing factors for developing diabetes mellitus after heart transplantation [8].

The major predisposing condition in the development of diabetes mellitus is the treatment with corticosteroids, though other immunosuppressants, particularly tacrolimus, contribute to its development as well [9].

2. Results

A total of 315 patients after heart transplantation treated at our department were included in this study. This representative sample comprises 263 men and 52 women. The aim of our study was to explore how many patients after heart transplantation suffer from diabetes mellitus and/or hyperlipidemia, and also how are these disorders treated in this setting.

After data collection, all patients were divided in four groups as shown in Fig. 1 (numbers of patients are listed below):

- Patients with diabetes mellitus and hyperlipidemia—165.
- Patients with diabetes mellitus and without hyperlipidemia —9.
- Patients without diabetes mellitus and with hyperlipidemia —128.
- Patients without diabetes mellitus and without hyperlipidemia—13.