Cardiac retransplantation as a promising treatment option for late graft failure — Zabrze experience

Grzegorz M. Kubiak1, 2, Radosław Kwieciński1, 2, Michał Zakliczyński1, 2, Michał Hawranek3, Jerzy Nożyński4, Bogumila Król5, Piotr Przybyłowski1, 2, Alexander Suchodolski1, Michał O. Zembala1, 2

1Department of Cardiac Surgery and Transplantation, Medical University of Silesia in Katowice, School of Medicine with the Division of Dentistry in Zabrze, Silesian Centre for Heart Diseases, Zabrze, Poland
2Department of Heavy Cardiopulmonary Respiratory Failure and Mechanical Circulatory Support, Silesian Centre for Heart Diseases, Zabrze, Poland
33rd Department of Cardiology, SMDZ in Zabrze, Medical University of Silesia in Katowice, Silesian Centre for Heart Diseases, Zabrze, Poland
4Department of Histopathology, Silesian Centre for Heart Diseases, Zabrze, Poland
5Department of Cardiosurgery, Transplantation, and Vascular and Endovascular Surgery, Office of Transplant Coordination, Silesian Centre for Heart Diseases, Zabrze, Poland

INTRODUCTION

Heart failure (HF) emerges as a heterogenic entity with widespread distribution in the population of developed countries [1]. HF, with its typical clinical scenario, is characterised by frequent decompensations, hospital readmissions, and poor quality of life. Renal dysfunction, being common in groups of patients with HF, is associated with raised morbidity and mortality. Late graft failure (LGF), after orthotopic heart transplantation (OHT), may occur in the cardiac transplant recipient milieu, especially given that the time elapsed from the procedure is related to the raised risk of coronary artery vasculopathy (CAV). Despite the fact that many patients suffering from end-stage HF (ESHF) are eligible for mechanical circulatory support as a destination therapy, OHT is a better alternative, particularly in long-term observation [2].

METHODS

The rationale of the study was to compare the renal function before and after orthotopic cardiac retransplantation (ReOHT). We present two cases of patients referred for ReOHT due to LGF on the background of CAV. Despite the fact that many patients suffering from end-stage HF (ESHF) are eligible for mechanical circulatory support as a destination therapy, OHT is a better alternative, particularly in long-term observation [2].

After ReOHT, a three-drug immunosuppressive regimen consisting of tacrolimus, mycophenolic acid, and prednisone was introduced in both patients. Remarkably, the initiation of tacrolimus administration was postponed three days after the surgery, and the drug was carefully dosed until therapeutic plasma concentrations were obtained. Therefore, induction of immunosuppression using basiliximab was carried out in both patients.
Patient R.B. underwent surgery in July 2017 and C.J. in January 2018. To the best of our knowledge, during the last year (until May 2018), three ReOHT operations were carried out in Poland, all in our centre. The third patient underwent surgery in April 2018, and currently the follow-up is too short to draw meaningful conclusions. The two patients we describe are still under surveillance. Noticeably, we persistently observe significantly higher GFR values than before the operation. Kidney function of the patient C.J. was not significantly deteriorated, even though he had received high doses of glucocorticosteroids due to a single episode of acute cellular rejection.

The data was statistically analysed as follows: distributions of the parameters were assessed using the Shapiro-Wilk test. Variables were expressed as the mean ± standard deviation. Variables with normal distribution were compared using Student t test. Variables with abnormal distribution were compared using the Mann-Whitney U test. Differences were considered statistically significant if p < 0.05. Analyses were performed using Statistica 10 with the medical package (Statsoft Inc., Tulsa, OK, USA).

RESULTS AND DISCUSSION

In patient J.C., GFR and creatinine values before vs. after cardiac retransplantation were 28.0 ± 4.4 mL/min/1.73 m² vs. 43.0 ± 9.4 mL/min/1.73 m² (p = 0.002) and 246 ± 42 µmol/L vs. 171 ± 59 µmol/L (p = 0.001), respectively. In patient R.B., GFR and creatinine values before vs. after cardiac retransplantation were 27.0 ± 4.7 mL/min/1.73 m² vs. 56.3 ± 14.1 mL/min/1.73 m² (p = 0.007) and 310 ± 59 µmol/L vs. 156 ± 53 µmol/L (p = 0.007), respectively. The data are depicted in Figure 1.

Nearly 100 (n = 98) patients were referred for OHT in the year 2017 in Poland, which, considering the permanently growing population of HF patients from the epidemiological point of view, is highly insufficient. Notably, organ availability...
Cardiac retransplantation plays a key role in limiting the number of surgical procedures, therefore the idea of ReOHT grew in the controversial environment of previously reported unequivocal results [3]. The frequency of ReOHT as a method of choice in the management of acute rejection and chronic graft failure varies in the literature between 2% and 5% and is engaged more often in American institutions as compared to others. Because ReOHT was reported to be associated with increased mortality compared to primary OHT at one (19% vs. 16%), five (37% vs. 28%), and 10 years (54% vs. 40%), it is crucial to discriminate the potential risk factors for poor outcomes [4]. Interestingly, both OHT and ReOHT groups of patients were characterised by similar short- and mid-term, and different long-term survival results. The significance of differences in survival rates emerges with the time elapsed from the initial surgical procedure [5]. Patients suffering from late graft failure due to CAV have better outcomes, so the role of careful patient selection deserves emphasizing. Lietz and Miller [6] assessed survival rates of patients with ESHF on the basis of the United States United Network of Organ Sharing (UNOS) database and reported that they significantly improved over time from 49.5% in 1990 to 69.0% in 2005. Multivariable analysis revealed that serum creatinine level > 1.5 mg/dL was associated with an increased risk ratio (RR) of death (RR 1.77; 95% confidence interval 1.47–2.12; p < 0.001). Strikingly, progressive deterioration of renal function expressed as a gradual decrease of GFR in post-transplant patients was simultaneously observed by many researchers. Al Aly et al. [7] found a significant difference between GFR prior to transplantation (63.8 ± 18.4 mL/min/1.73 m²) and at five years (54.4 ± 15.5 mL/min/1.73 m²) and 10 years (52.7 ± 23.6 mL/min/1.73 m²) post-transplantation (p ≤ 0.006 for both). A significant linear correlation between GFR and time after OHT was reported by Przybyłowski et al. [8] (r = –0.59, p < 0.001). Ostermann et al. [9] compared the GFR values at registration and transplantation in nearly 900 patients submitted to OHT. In 214 (24.9%) patients renal function deteriorated to the extent that they entered a lower GFR group. A total of 67 (8.8%) patients moved from a standard risk group with GFR > 50 mL/min/1.73 m² and 30-day mortality of 9.5% to a group with increased 30-day mortality rate of 16.7% (p = 0.06). ESHF and graft failure are two different clinical scenarios with a similar physiological background. The impairment of the LV systolic function results in organ hypoperfusion; therefore, a significant GFR decrease is reported to be an eligible marker associated with poor outcomes.

In conclusion, whether the positive fluctuation of GFR and creatinine values observed in the laboratory findings will have a positive impact on prognosis in our group of patients requires further observation. It is important to keep in mind that ReOHT is a feasible option of treatment for patients with LGF, especially on the background of CAV, offering good short- and mid-term results basically undifferentiated from the initial OHT procedure.

Acknowledgements

We would like to thank the anonymous reviewer who significantly contributed to the final version of the manuscript.

Conflict of interest: none declared

References


www.kardiologiapolska.pl