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Long-term outcome following heart transplantation: current perspective

Markus J. Wilhelm

Clinic for Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland

Correspondence to: Markus J. Wilhelm, MD. Clinic for Cardiovascular Surgery, University Hospital Zurich, Rämistrasse 100, 8091 Zurich, Switzerland. Email: markus.wilhelm@usz.ch.

Abstract: Heart transplantation keeps its leading position in the treatment of end-stage heart failure (HF). Survival rates and functional status following heart transplantation are excellent, particularly if compared to medical therapy. The process of acute and chronic transplant rejection, however, and the sequelae of immunosuppression, such as infection, malignancy and renal insufficiency, prevents even better results. Therapy with current mechanical circulatory support devices is associated with improving outcome and may become competitive to heart transplantation, at least in selected patients. But long-term results are not yet available.

Keywords: Heart transplantation; immunosuppression; transplant rejection; ventricular assist device

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Introduction

Heart transplantation has been established as gold standard in the treatment of patients with end-stage heart failure (HF). It is considered after medical and resynchronisation therapy have failed. State-of-the-art medical therapy comprises treatment with betablockers, angiotensin-converting inhibitors or angiotensin-II antagonists, and diuretics including aldosterone receptor antagonists (1). In addition to pharmacological therapy, cardiac resynchronisation therapy is installed, if the preconditions are given (2). In patients with a moderate or higher degree of mitral insufficiency, the relatively new technique of mitral clipping is applied (3). Only after all these measure have not been successful in improving the degree of HF, heart transplantation remains the final option. Due to the growing number of patients with severely advanced HF and, at the same time, the stagnating number of available donor hearts, heart transplantation remains an option only for a limited number of those patients. Mechanical circulatory support with the most recent devices could become an alternative, since it currently achieves survival rates in selected patients which approach those after heart transplantation (4). However, reliable survival data are only available over the short term of a few years, in contrast to heart transplantation where we are able to oversee outcome over a period of three decades and more (5). The same is true for the spectrum of specific adverse events which are inherent to each of those therapies. It is a rather demanding challenge to recommend the appropriate therapy to an individual patient on the basis of the currently available outcome data. With this background in mind, the present article intents to review the actual outcome after heart transplantation with respect to survival and adverse events.

Survival of heart transplant recipients

Survival after heart transplantation is excellent, particularly if it is compared with the natural course of end-stage HF. The most recent data of the registry of the International Society of Heart and Lung Transplantation indicates a current 1-year survival of 84.5% and a 5-year survival of 72.5% (5). This has significantly improved as compared to the 76.9% 1-year survival and 62.7% 5-year survival in the 1980s. The development of new immunosuppressive drugs which allow a variety of immunosuppressive regimens, tailored to

the individual patient, has contributed to this success, since rejection and the adverse effects of immunosuppression could be better controlled. After 20 years, ca. 21% of patients are still alive, according to the international registry (5). In some experienced centers, long-term survival is reported to be even higher (6-9). The University Hospital Zurich has achieved a 20-year survival rate of 55.6% (10).

The improvement in outcome over the decades is related mainly to an increase in survival over the first year. After this period, the attrition rate of ca. 3-4% per year has remained similar over the different eras. This might be attributable to the fact that it was not possible to reduce the incidence of long-term complications after heart transplantation, such as chronic allograft vasculopathy (CAV) and malignancies, which account for ca. 35% of all deaths after 10 to 15 years (5).

Complications following heart transplantation

Conditions such as CAV, malignancy, infection, acute rejection and renal insufficiency have a major impact on outcome following heart transplantation.

Chronic allograft vasculopathy (CAV)

Five years after heart transplantation, ca. one third of patients are diagnosed with CAV. After ten years, CAV occurs in more than 50% of patients. This has an important impact on survival. More than three years after transplantation, CAV accounts for ca. 10% of deaths annually (5).

The incidence of CAV has not been changed much over the years, despite the availability of modern immunosuppressive drugs. The freedom form CAV at 5 years following heart transplantation only increased by 3% from 67% to 70% in the first decade of this century as compared the decade before (5).

In our own experience, CAV has been less frequently the cause of death as compared to other studies. Possible explanations for this phenomenon could be the annual performance of angiographies which lead to early detection of potentially lethal stenoses, and the routine administration of statins which have been shown to limit progression of CAV (10).

Malignancies

Currently, 15% of patients suffer from a malignancy 5 years after transplantation. This is only 3% less as compared to the previous decade in the 1990s. After 10 years, 35% of patients are affected by malignancies (5). The predominant malignancy is skin cancer. More than 5 years after transplantation, malignancy accounts for ca. 22% of deaths annually (5). As for CAV, there has been not much change over the decades. With specific measures, however, incidence and death rate might be reduced. Thus, we have reported that, after 10 years, the incidence of malignancies stays at ca. 25%, which is 10% lower as reported by the ISHLT (5,10). This relative success may have been achieved by the frequent check-ups in specialised outpatient clinics, as well as by the routine application of statins which we have shown to improve malignancy-free survival (11).

Infection

Infection constitutes a serious condition, predominantly within the first year after transplantation when it causes 30% of deaths. In the following years, the death rate decreases to 10% annually (5). The high incidence of infection-related deaths within the first year might be explained by the higher dosage of immunosuppression which is required to control the more intense immune reponse early after transplantation. After reduction of immunosuppression in the following years, the risk of infection-related death is reduced.

Acute rejection

Acute rejection episodes account for ca. 10% of deaths within the first three years after transplantation. Later, the incidence and impact on death decreases markedly (5). However, it has been shown that acute rejection triggers progression of CAV with all its consequences on transplant performance and death.

Renal insufficiency

Renal insufficiency develops as side effect of immunosuppressive drugs, particularly calcineurin-inhibitors such as cyclosporin and tacrolimus. They are given on an already impaired kidney function which is the result of a long-standing cardiac low-output syndrome. Five years after transplantation, 16% of patients have severe renal dysfunction which is defined as creatinine >2.5 mg/dL, dialysis or renal transplant. After 10 years, 30% of patients are effected Renal failure accounts for 8% of deaths 10 years following transplantation (5).

Functional status

Heart transplantation enables most of the patients with previous terminal HF to get back to a normal life. Three years after transplantation, ca. 75% of patients are not limited in their daily activities and live with no or only minimal symptoms, as indicated by a Karnofsky-Index of >90% (5). Five years after transplantation, 45% of patients, who are in working age, work at least part time (5). Exercise capacity after transplantation, as objectively measured by peak oxygen uptake, can reach values comparable to those of healthy individuals, particularly after a specified training program (12).

Summary

Heart transplantation currently remains the treatment of choice for patient with severely advanced HF. No other treatment option, such as medical therapy or electrical and mechanical devices, can compete with the excellent results, particularly over the long-term. However, rejection and the consequences of immunosuppressive therapy still constitute an unsolved problem which limit the success of heart transplantation. Mechanical circulatory support with modern devices appears to become an important contender with the potential to replace heart transplantation, at least in selected patients. For this to occur, however, mid- and long-term survival rates as well as data on functional outcome and quality of life have to become available which show that the results with mechanical devices are comparable or better than those after heart transplantation. A prerequisite for such outcome will be the further advancement of device technology with respect to biocompatibility and transcutaneous energy transfer.

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References

1. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012;14:803-69.
2. Steffel J, Rempel H, Breitenstein A, et al. Comprehensive cardiac resynchronization therapy optimization in the real world. Cardiol J 2014;21:316-24.
3. Maisano F, Franzen O, Baldus S, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. J Am Coll Cardiol 2013;62:1052-61.
4. Kirklin JK, Naftel DC, Pagani FD, et al. Sixth INTERMACS annual report: a 10,000-patient database. J Heart Lung Transplant 2014;33:555-64.
5. Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report--2014; focus theme: retransplantation. J Heart Lung Transplant 2014;33:996-1008.
6. Deuse T, Haddad F, Pham M, et al. Twenty-year survivors of heart transplantation at Stanford University. Am J Transplant 2008;8:1769-74.
7. Ongcharit P, Wongkietkachorn K, Sritangsirikul S, et al. Heart transplantation 1987--2007: 20 years' experience at Chulalongkorn hospital. Transplant Proc 2008;40:2591-3.
8. Roussel JC, Baron O, Périgaud C, et al. Outcome of heart transplants 15 to 20 years ago: graft survival, post-transplant morbidity, and risk factors for mortality. J Heart Lung Transplant 2008;27:486-93.
9. Ozduran V, Yamani MH, Chuang HH, et al. Survival beyond 10 years following heart transplantation: The Cleveland Clinic Foundation experience. Transplant Proc 2005;37:4509-12.
10. Rodriguez Cetina Biefer H, Sündermann SH, Emmert MY, et al. Surviving 20 years after heart transplantation: a success story. Ann Thorac Surg 2014;97:499-504.
11. Fröhlich GM, Rufibach K, Enseleit F, et al. Statins and the risk of cancer after heart transplantation. Circulation 2012;126:440-7.
12. Dall CH, Snoer M, Christensen S, et al. Effect of high-intensity training versus moderate training on peak oxygen uptake and chronotropic response in heart transplant recipients: a randomized crossover trial. Am J Transplant 2014;14:2391-9.

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