

HEART TRANSPLANT: INDICATIONS AND PATIENTS' QUALITY OF LIFE

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Abstract: Heart failure has been increasing more and more in recent years due to the population's increased longevity, advances in the treatment of acute heart attacks with the use of thrombolytics and angioplasty, the expansion of cardiac interventions and improvements in the diagnosis of the syndrome. With the current modifications incorporated into pharmacological treatment, there has been an improvement in patient survival. Therefore, the evolution of cardiomyopathy to terminal forms is unquestionable due to the characteristics of the disease and, in these situations, transplantation may be the only alternative. Heart transplantation is the only effective way to restore the patient's hemodynamic functions, however it has different limitations and does not apply to all candidates. The limitation of viable organs is one of the biggest factors that impede the development of transplants. This problem becomes more evident when it comes to organs that are more sensitive to shock and ischemia injuries. Despite the great advances made in legislation on organ transplants, there is still a lack of an effective health policy aimed at promoting the recruitment and adequate maintenance of donors so that this situation can be reversed. The quality of donated organs and the serious clinical condition of candidates arriving at transplant centers are the main factors responsible for unsatisfactory results in the immediate phase of heart transplantation. The present study aims to present a review of the indications for heart transplantation and the quality of life of patients.

Keywords: Heart transplant; Indications; Quality of life.

INTRODUCTION

Heart failure (HF) affects at least 26 million people worldwide (KEPIŃSKA; ADAMCZAK; KAŁUŻNA-OLEKSY, 2019). In the United States alone, 6.2 million adults are affected, in addition to an incidence rate of approximately 21 per 1,000 inhabitants after the age of 65. According to projections, the situation is still likely to get worse, as estimates show that by 2030, more than 8 million people over the age of 18 will be affected in the country (TRUBY; ROGERS, 2020). Carrel and Guthrie, in 1905, unpretentiously performed the first heterotopic heart transplant by implanting a dog's heart into the cervical region of another animal (Carrel and Guthrie, 1905). However, the researchers' intention was focused on the development of vascular surgery. This line of research was so important at the time that it awarded the first author the Nobel Prize for physiology in 1915. In the following years, experimental research continued slowly, limited by the practicality of the method; however, with the development of extracorporeal circulation, studies were resumed with a view to orthotopic transplantation. Thus, in 1960, Lower and Shumway obtained the first series of successful experimental orthotopic transplants, whose technical principles were later applied in the first transplants in humans and remained practically unchanged until recently with the so-called classical technique (Lower and Shumway 1960). The first human heart transplant was performed by Hardy et al., in 1964, when they transplanted a monkey heart into a patient in severe cardiogenic shock, but without success; however, this achievement had the merit of demonstrating the feasibility of the method (Hardy et al., 1964). In 1966, Lower successfully transplanted hearts from cadavers that were resurrected for kidney donation into monkeys. Even though his studies were well known, they were

never published. Barnard, surprisingly, on December 3, 1967, at the University of Cape Town, South Africa, took the decisive step in heart transplantation in humans: his patient had a good initial clinical evolution, dying on the 18th postoperative day in consequence of pulmonary infection (Barnard, 1970). Kantrowitz et al., three days after this event, performed the world's second transplant on an 18-day-old patient with Ebstein's disease, whose survival was only six hours (Kantrowitz et al 1997). On January 2, 1968, Barnard performed his second transplant on a patient with ischemic cardiomyopathy, and Shumway, on January 6, 1968, the fourth in the world (Barnard, 1998).

METHOD

This is a literature review, of a narrative type, which aims to describe heart transplantation, its indications and the quality of life of patients, from a theoretical point of view, through materials that have already been published on the topic in question, through analysis and interpretation of the literature. The inclusion criteria were: articles in Portuguese and English; published between 2018 and 2023 and which addressed the themes proposed for this research, review-type studies made available in full. The exclusion criteria were: duplicate articles, available in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria.

The review was carried out from July to November 2023, through searches in the databases Virtual Health Library (VHL), Latin American and Caribbean Literature in Health Sciences (LILACS), National Institutes of Health's Library of Medicine (PubMed) and Scientific Electronic Library Online (SciELO). The following descriptors were used: "Heart transplant", "Quality of life", "Transplant indications", in order to find articles relevant

to the subject covered. After the selection criteria, 5 articles remained that were subjected to thorough reading for data collection. The results were presented in a descriptive way, divided into thematic categories addressing: describing the subtitles or points that were mentioned in the discussion.

RESULT AND DISCUSSION

In 2019 alone, for example, more than 3,000 people were treated with a left ventricular assist device (LVAD) in the United States, and more than 3,000 patients received heart transplants in the same country, with an additional 3,500 patients awaiting transplant (TRUBY; ROGERS, 2020). Within this heterogeneous group, advanced HF plays a relevant role, as its complete definition is mandatory for the appropriate application of therapy, such as heart transplantation or long-term mechanical circulatory support devices (MCS) (CRESPO-LEIRO et al., 2018). Epidemiological data on prevalence and incidence regarding advanced disease are still inconsistent, but it is estimated that this disease represents approximately 1% to 10% of the general HF population. This information is explained by the increase in the global burden of HF, better treatment and increased survival of these patients (CRESPO-LEIRO et al., 2018; TRUBY; ROGERS, 2020).

Zerbini and Decourt, on May 26, 1968, performed the first heart transplant in Latin America and the seventeenth in the world, in a patient with dilated cardiomyopathy (Zerbini and Decourt, 1968). Two other patients underwent surgery, one of them surviving for more than a year, before this program was interrupted due to difficulties in controlling rejection and infection. This same attitude was already spreading in different centers that had started their programs for the same reason. However, the poor results obtained with the new method did not discourage the Stanford University team, led by Shumway,

who kept their program active. This attitude was also followed by a few other groups, but it was fundamental in establishing the classic criteria regarding the selection of donors, recipients and the conduct of the transplant itself. The experience accumulated during this period provided important support for the resumption of transplants in the 1980s, with the introduction of cyclosporine into the immunosuppressive regimen. Grattan et al., in 1990, described the accumulated experience of eight years of heart transplantation, now with the use of cyclosporine in which a significant improvement in patient survival can be noted to 80.7% in the first year and 59.7% in the fifth year after the operation (Grattan et al.,1990).

The most recent registry from the International Society for Heart and Lung Transplantation, from 2008, presents the accumulated experience of more than 74,000 heart transplants performed in different centers spread across different countries, of which more than half were performed in the United States of America (International Society for Heart and Lung Transplantation, 2008 2008). In 1999, the I Guideline on Heart Transplantation was established in Brazil and until then, 792 heart transplants had been registered, carried out in 16 active centers, and currently these numbers have practically doubled (I Guideline on Heart Transplantation 1999). Heart transplantation in our country has grown very slowly for a series of reasons that include different aspects, such as the need for better quality donors and the lack of interest on the part of hospitals themselves in maintaining active programs for remuneration that does not meet the real costs.

ASSESSMENT OF THE HEART TRANSPLANT CANDIDATE

MANDATORY ASSESSMENT

- History, physical examination and nutritional status.
- Kidney, liver and thyroid function. Abdominal ultrasound.
- Complete blood count, coagulogram, urinalysis, Na⁺/K⁺, blood glucose, EPF, PSA, cholesterol, triglycerides. Mammogram and Pap smear.
- Electrocardiogram, Chest X-ray and Doppler Echocardiogram.
- Complete hemodynamic study with determination of PVR.
- Blood type and antibody panel. Serology: HIV, CMV, EBV, VDRL, Toxoplasmosis, Chagas, Hepatitis B and C.

VO₂MAX IN CF III OR DOUBTFUL.

- Psychological, social, dental and gynecological assessment.

EXPENDABLE ASSESSMENT

- Radioisotope ventriculography and Coronarioventriculography.
- Endomyocardial biopsy, 24h Holter, VO₂max and catecholamine measurement.
- Creatinine clearance, serology for herpes simplex, chickenpox and rubella
- Assessment of psychiatry, pulmonology or neurology.
- Assessment of myocardial viability in ischemic cardiomyopathy.
- Fecal parasitology, PSA, CMV, EBV and HLA.

During clinical evaluation, the aim is to confirm the severity of the heart disease; rule out the possibility of optional therapies, such as myocardial revascularization or valve replacement; verify the absence of contraindications and estimate the short-term prognosis so that the patient can be included

on the waiting list. The biggest discussion occurs when establishing the real moment of indication for transplantation, in critically ill patients who have contraindications related to the procedure. Once transplantation is indicated, those conditions that increase morbidity and mortality in the post-transplant period must be excluded.

RISK FACTORS IN HEART TRANSPLANTATION

- Age.
- Coexisting illnesses with a poor prognosis.
 - Infiltrative or inflammatory cardiomyopathy.
 - Irreversible pulmonary arterial hypertension.
 - Irreversible parenchymal lung diseases.
 - Acute pulmonary thromboembolism.
 - Severe cerebral or peripheral vascular disease.
 - Irreversible renal or hepatic dysfunction.
 - Peptic ulcer, diverticulosis or active diverticulitis.
 - Insulin-dependent diabetes with visceral changes.
 - Obesity or severe osteoporosis.
 - Active infection or coexisting neoplasia.
 - Psychosocial instability, drug addiction or both.

INDICATIONS FOR HEART TRANSPLANT

ABSOLUTE INDICATIONS FOR TRANSPLANT

AFTER OPTIMIZATION OF THERAPY

1. $VO_2\max < 10$ ml/kg/min, having reached the anaerobic limit. CF IV.
2. Recurrent hospitalizations for heart failure.
3. Limiting myocardial ischemia and not susceptible to revascularization or

angioplasty, with $EF < 20\%$.

4. Recurrent and refractory symptomatic ventricular arrhythmias.
5. Patients in priority situations.

RELATIVE INDICATIONS FOR TRANSPLANT

AFTER OPTIMIZATION OF THERAPY

1. $VO_2\max < 14$ ml/kg/min and limitation of daily activity. CF III-IV.
2. Recurrent hospitalizations for CHF. Water accumulation due to renal hypoperfusion.
3. Limiting myocardial ischemia and not susceptible to revascularization or angioplasty.
4. Frequent ventricular arrhythmia with a history of sudden death.

Inappropriate indications for transplant

1. Ejection fraction $< 20\%$, isolated. CF I-II.
2. Stable angina with ejection fraction $> 20\%$.
3. Previous ventricular arrhythmias. $VO_2\max > 14$ ml/kg/min, without other factors.

PRIORITY CRITERIA

1. Cardiogenic shock when using catecholamines.
2. Cardiogenic shock when using circulatory assistance or mechanical ventilation
3. Acute retransplantation due to primary graft failure.
4. Malignant and uncontrollable cardiac arrhythmias.

DONOR SELECTION

The success of the transplant depends, among other factors, on the quality of the graft, and it must be ensured that it is capable of maintaining adequate hemodynamic conditions for the recipient after implantation and is free from transmitting infectious or tumoral diseases. To obtain organs in adequate conditions, it is necessary that the donor continues to be treated as a critical patient even after confirmation of brain death.

In Brazil, through Resolution Number: 1346 of 08/08/91, the Federal Council of Medicine published the criteria adopted in the diagnosis of brain death, which in essence do not differ from those universally accepted. Even though investment has been increased to increase the number of organ donors for transplantation, the quality of the organs still leaves something to be desired, which is the biggest factor in the refusal of donated organs.

Chest radiography, electrocardiogram and echocardiogram are fundamental exams in the evaluation of heart donors, and, in special situations, cardiac catheterization. Laboratory investigation includes serology for syphilis, hepatitis, Chagas disease and AIDS. Serology determinations for cytomegalovirus and toxoplasmosis are valuable in the patient's clinical follow-up.

In the clinical diagnosis of brain death, it is mandatory to know the cause of the coma, to exclude the possibility of metabolic or exogenous poisoning. The following neurological parameters must be observed: deep apperceptive and reactive coma; apnea; paralytic mydriasis; absence of oculomotor and corneal-palpebral reflexes. To confirm the clinical diagnosis of brain death, the parameters described above must remain unchanged for a period of more than six hours. Its laboratory documentation is mandatory and must be carried out using one of the methods that confirms the absence of cerebral flow, such

as arteriography, scintigraphy or transcranial ultrasound, or that proves cerebral inactivity, such as electroencephalogram or evoked potential.

The criteria adopted in the selection of heart donors are stricter than those applied to other organs, and may differ between teams or the clinical conditions of the recipient. The lack of donors has motivated the extension of the age range limits up to 50-55 years: above 40 years for

For men and over 45 years of age for women, the use of coronary angiography is recommended, taking into consideration, the risk of coronary artery disease. This guidance becomes more important for donors with a history of smoking, diabetes mellitus, high blood pressure or stroke victims.

The presence of arterial hypotension or the use of vasoactive drugs in high doses, for a period longer than 12-24 hours, constitute risk factors for transplantation and are often responsible for the appearance of graft dysfunction in the postoperative period. Cardiac arrest alone is not a criterion for excluding the organ, as long as after the event, it remains stable hemodynamic conditions. The donor's body weight must not be less than 20% of the recipient's weight, especially when the recipient has high pulmonary resistance, preferring larger donors.

The search for organs remotely is a reality and aims to increase the number of transplants. The method was pioneered in hearts by the Stanford group and corresponds to around 80% of transplants in international experience. The heart ischemia time must not exceed the limit of 4 to 6 hours for the transplant to be performed safely.

Histocompatibility between the donor and recipient is assessed by mandatory compatibility between the ABO blood groups and by obtaining a negative result from the donor's lymphocyte crossmatch with the

recipient's serum (crossmatch).

In recipients whose lymphocyte reactivity is less than 10%, compared to a panel of lymphocytes, there is no obligation to wait for the results of the cross-match before starting the operation. The Rh factor is not valued in the case of organ transplants and HLA compatibility has only retrospective value.

Operation on the donor

Median thoracotomy is the access route for exposing intracavitary organs. In the macroscopic evaluation of the heart, attention must be paid to the presence of hematomas or abnormalities in ventricular contraction. The performance of the right ventricle can be assessed by delicate compression of the pulmonary trunk or by increasing venous return by placing the donor in the Trendelenburg position. Palpation of the coronary arteries and aorta helps identify atheromatous plaques or thrills, indicative of coronary or valvular disease. Heparin is administered at a dose of 400 IU/kg of body weight, intravenously, before organ removal begins. The aorta is occluded near the emergence of the brachycephalic trunk, followed by the infusion of crystalloid cardioplegic solution at 4°C and the infusion of cold saline into the pericardial sac. The cardiac chambers are kept decompressed, avoiding distension. After removal, the heart is immediately transported in sterile plastic bags and immersed in ice-cold saline at 4°C. In the final preparation of the heart, the pulmonary vein orifices may or may not be joined, depending on the technique adopted for the implant.

CONCLUSION

Heart transplantation is the gold standard definitive surgical approach in the treatment of refractory heart failure. However, the shortage of donors limits the carrying out of a greater number of heart transplants, a situation in which the use of mechanical circulatory assistance devices has been increasing.

With well-established indications and contraindications, in addition to diagnosis and treatment of rejection, through defined immunosuppression protocols, the results of heart transplantation are very favorable. Among the early complications that can impact survival, we highlight primary graft dysfunction, right ventricular dysfunction and infections; Late complications include graft vascular disease and neoplasms. Despite the difficulties in performing heart transplantation, especially due to the scarcity of donors and the high mortality on the waiting list in Brazil, there is great potential both in increasing effective donors and in the use of circulatory assistance devices, which could come to positively impact the number and results of heart transplantation.

QUALITY OF LIFE OF PATIENTS

Considering the results obtained by the study on the quality of life of heart transplant patients, the largest population analyzed was male, with a predominance of ages between 50 and 60 years. The most recurrent transplant time was two to eight years, and the most common etiology was dilated cardiomyopathy. The predominance of these variables also influences the quality of life of heart transplant recipients, taking into consideration, that age predisposes to greater dependence and more associated comorbidities, which directly impact the transplant and encourage polypharmacy, which also makes medication adherence difficult. The transplant time of two years is still considered a recent time, with

adaptations, longer follow-ups, which reflects on the quality of life of heart transplant patients (ALMEIDA ET AL. 2017).

Regarding the variables of the instrument used, a quality standard was found to be fair to good, involving the physical, psychological, social relationships and environment domains, according to the answers described by the participants.

In the study, the social relationships domain of transplant recipients was the one that remained most in the regular average,

due to the decrease in relationships between friends and family. Other relevant issues were the possibility and availability of practicing leisure activities, with transplant recipients in the study referring to a reduction and even the non-practice of any leisure activity, due to restrictions and a reduction in financial resources. These problems have a significant impact on psychological and behavioral issues, altering the quality of sleep, work capacity and how these individuals enjoy life (World Health Organization, 1997).

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