CHAPTER XI - Heart Transplant

Gunter LAUFER, PhD, Innsbruck, Austria,
Marian GASPAR, PhD, Timisoara, Romania

11. 1. Definition. The heart transplant is defined as total replacement of the heart of a patient in irreversible stage (end-stage heart failure) with the heart of a brain-dead donor. Heart transplant has become after four decades of cardiac surgical practice a standardized method of treatment, in case of end-stage heart failure, when no other conventional method is possible.

History. The first human heart transplant performed by Christian Barnard, in 1967, South Africa, was the result of long research of teams of doctors in America and Europe, and the visionary courage of a surgeon to move from experimental to clinical practice. Initial enthusiasm was followed by a period of deterrence due to the reactions of rejection and high mortality. A few years have passed before the discovery of more powerful immunosuppressive drugs (cyclosporine, tacrolimus, mycophenolate mofetil), which ensure a better resistance to organ rejection. The medical personality with the most important role in organ transplant was Alexis Carrel, his experimental work paving the way for clinical progress.

11. 2. Heart transplant stages

Basically, there are three stages in organizing a program of organ transplant:
- Pretransplant stage
- Transplant stage
- Posttransplant stage

Pretransplant Stage – The organizational phase of the program in the legal framework of the Organ Transplant Law. It establishes specialized centers that have the necessary competence to perform heart transplant.

The selection and composition of receptor transplant list involves investigating patients and defining the quality of Receiver based on clearer inclusion and exclusion criteria.
- Main indication - heart failure refractory to other treatment methods has recently changed. Adults represent 95% of patients on waiting lists, coronary disease and myopathies of different etiologies totalling over 45% of indications.

Heart Transplant Indications

I – Cardiomyopathies
- ischemic
- idiopathic (viral, toxic)
- valvular
- family
- restrictive

II – Congenital Heart Diseases
- complex anomalies that cannot be repaired
- acute or late myopathies after reparative surgery

III – Heart Rejection
- early
- chronic

IV – Rare Indications
- hypertrophic cardiomyopathy
- malignant arrhythmias
- cardiac tumors

**Selecting criteria of heart transplant patients**
- VOmax < 10 ml/kg/min
- NYHA functional class IV
- ejection fraction < 20 %
- mechanical assistance
- angina refractory to any other therapy

**Exclusion criteria of the receiver**
- Age – it is a controversial criterion. If a few years ago the age limit was 50 years, currently it is spreading over the age of 55 - 60 years.
- Pulmonary vascular resistances - if they are above 6 - 8 Wood units, heart transplant indication becomes risky, considering heart-lung transplant.
- Clinical criteria – they refer to the associated pathology that would limit long-term results - liver diseases as cirrhosis, liver tumors, chronic kidney failure, which would also require kidney transplant, diabetes mellitus, autoimmune diseases, severe mental affections.
- Social criteria - lack of social and family compliance

Once established the indication of transplant principle – the receiver is subject to additional tests - heart and other organs and systems- for creating a complete morpho-functional picture of the patient. The final accepting factor of the Receptor is the psychosocial factor, patient and family compliance.

The receiver is put on the centre waiting list and on the national and European list, to have maximum opportunities to benefit from a possible donor at some point in time.

**Management of Patients Put on the Waiting List**

Patients on the waiting list for heart transplant are approached by a multidisciplinary medical team in order to have better evaluation and balancing while waiting for the transplant. Those who are relatively stable can wait at home with established medication and regular
monitoring by cardiac surgery team. Patients in a critical condition wait in hospital connected to assist devices that support severely compromised heart function.

General measures refer to:
• Reducing salt intake below 2 g / day
• Reducing intake of fluids to 1-1.5 L / day
• Vaccination against pneumococcal infection, influenza
• Prohibition of alcohol
• Stop smoking
• Light walking exercise 20-30 minutes 4-5 times a week
• Reducing long-distance travel
• Control of patients with osteoporosis or hyperlipidaemia and their prior treatment
• Blood pressure control, diabetes mellitus control
• Cardiovascular specific medication - vasodilators - heart tonic - diuretics - beta-blockers, calcium channel inhibitors - antiarrhythmic medication - anticoagulant medication. Medication is customized to each patient and carefully examined by your cardiologist.
• Prompt and vigorous treatment of any infection (pulmonary, urinary, skin)
• Some patients require special measures of intensive care, admitted to hospital and examined by the heart transplant team.
• A separate issue is the patient under mechanical cardiac assistance until heart transplant.

The aim of these measures in the waiting period is to bring the patient in the best shape possible, haemodynamically and functionally, to increase the success rate when transplantation is performed.

Evaluation and Management of Organ Donors

The donor is a patient who, as a result of a severe aggression (an accident with head injury, extensive cerebral hemorrhage, brain tumor), is in the state of - Brain Death - with vital functions (heart, lung) sustained mechanically, by respiratory ventilation and cardioactive medications. Making the diagnosis of - Brain Death – an irreversible state of the human being - is one of the hardest and most responsible diagnoses. Complex medical teams have set universal criteria for declaring brain death. The diagnosis of brain death (under the Romanian legislation) is established on the following criteria:

1. Clinical examination
   • The state of deep coma, flaccid, areactive
   • The absence of brain stem reflexes (corneal and photomotor reflex)
   • The absence of spontaneous ventilation confirmed by apnea test (at a PaCO2 of 60 mmHg)
   • Two routes EEG, performed every 6 hours, to test the absence of brain electrical activity
2. The cause of brain death must be clearly established.
3. Exclusion of other reversible causes which would produce a clinical picture and EEG, similar to that of brain death (hypothermia, CNS depressant drugs.)
4. The diagnosis of brain death will be made by two different anesthesiologists or by an anesthesiologist and a neurologist or neurosurgeon, by two repeated examinations at six-hour intervals (Law No. 65, 2006).

Organ harvesting can also be done by living donors, relatives, or those who are compatible only for paired organs, kidneys and parts of organs, liver, lung, without jeopardizing the donor's life, with their legal agreement and without being the subject of organ trafficking, under human, not material considerations.

Organ donation law may be different from country to country. For example, in Romania it is compulsory to obtain family consent while in Austria the implied consent law is enforced.

Within the legal framework of the organ transplantation law, after establishing the possible existence of an organ donor, the stage of - Organ Donor Management – i.e. a complex, high performance and professional responsibility process, begins.

Brain death induces a series of disorders in organs and systems:
- haemodynamic instability
- loss of heat control
- hydroelectrolytic instability
- metabolic disorders

Inadequate donor management can lead to irreversible damage of harvested organs which causes transplant failure.

The donor is clinically examined and biochemically investigated. Transplant teams are previously told that there is a potential organ donor, in order to begin the local organizing program. Donor’s general data, sex, weight, height, blood group and Rh, absence of active infection or presence of HIV infection, markers of hepatitis B and C are transmitted.

Several aspects of the donor are examined next:
- Diagnosis of brain death
- Complex intensive care
- Investigation of possible contraindication factors: HIV, hepatitis B, C
- Investigation of each organ function: heart, lung, liver, kidney, using specific methods. ECG, echocardiac or even angiocoronarography is performed in heart transplant, in order to exclude any cardiac pathology.
- Obtaining family consent
- Organizing the Moment of Organ Harvesting, coordination and synchronization of teams that can come from different remote medical centers.

The organ harvesting stage is coordinated by the medical team of the hospital where the donor is. The organ harvesting protocol is well established and respected by all teams,
specialized and trained specifically in the Organ Transplant Program. We do not accept any amateurism or interests other than the medically-moral ones in the community interest.

The heart is harvested after being properly protected with special cardioplegic solution. It is kept in sterile bags (three different bags), filled with cold saline solution and placed in a plastic container, filled with ice, for protection during transport. The heart harvesting team notes the donor’s data and announces the team that prepares the Receiver and performs the heart transplant. It is a race against the clock that must unfold perfectly. The harvested heart must be implanted as soon as possible, in the 4-6 hours that are considered time limits of accepted ischemia. Transportation from the place of harvest is done by medical ambulance if the distance is small or by plane if it is at long distances. Synchronization of the harvesting team with the one that prepares the receiver is ensured by phone all the time.

11.3. Heart Transplant Stage - Surgical Technique

Heart transplant stage starts when the donor’s existence is announced and the receiver on the waiting list is chosen. Medical responsibility is maximum in each stage of the transplant program. Once the receiver is chosen, based on the Rh blood group compatibility, size, absence of absolute contraindications, he is brought from home or if hospitalized, the process of preoperative preparation begins - complex, well standardized.

After all, the surgery stage seems to be the simplest, when all teams meet in the operating room and the donated heart implantation begins.

The surgical technique used in most heart transplant centers is the bicaval orthotopic transplantation technique. After excision of the recipient heart, suture of donated heart begins - left atrium - inferior vena cava-superior vena cava-pulmonary artery-aorta (Fig.)
After finishing cardiac sutures, declamping of the heart which beats for another human being for the first time is performed next.

In case of heterotopic transplant, the two hearts - the receiver’s heart which remains in place and the donor’s heart are connected to function in parallel (Fig.).

Perioperative management of cardiac transplanted patient has many common points with that of a routine cardiac surgery. However, there are many specific problems to be solved.

Heart reperfusion after declamping (ischemia time being longer than in usual heart surgery), is longer (one or more hours).
haemodynamic instability - can be caused by a long ischemia time, more than 4 hours, poor protection of the donor during intensive care

denervated transplanted heart responds differently to hypovolemia and hypotension

intraoperative monitoring by transesophagian cardiac Echo allows good assessment of hemodynamic function and scientific guidance of cardioactive medication

rhythm disorders are also common and should be corrected

preoperative pulmonary hypertension may cause problems of right ventricular function

postoperative bleeding is more common post-transplant due to preoperative anticoagulation program in which many receivers are involved

likewise, transplanted patients are more susceptible to infection during the entire period of post-transplant life.

Post-Transplant Patient Management

The most delicate postoperative aspect is that of the immunosuppressant medication - to prevent both acute and chronic heart rejection.

Immunosuppressant medication is the combination of:

• Ciclosporin - inhibitor of calcineurin
• Azathioprine or mycophenolate mofetil- antimitotic medication
• Prednisone
• medications recently introduced - rapamycin, binductin Q, antilymphocite polyclonal or monoclonal preparations anti-CD3 or anti-iterleukine 2- make progress in preventing acute and chronic rejection.

Monitoring for signs of possible acute rejection is done by performing myocardial biopsies and a highly specialized medical supervision.

Complications after Cardiac Transplantation

The immediate complications may be common to open heart surgery or specific:

• postoperative bleeding, which requires reintervention for hemostasis. In heart transplant, suture lines are broader and are possible bleeding sites
• acute rejection may occur immediately or in the first week, despite the immunosuppressive drugs
• infection is a serious problem due to immunitary depression
• neuropsychiatric disorders - may occur in the immediate post-transplant period due to steroid medication.

Other complications may also occur later in post-transplant evolution:
• late cardiac rejection
• coronary disease of transplanted heart - miointimal hyperplasia may develop even three months after transplant. It has a severe evolution and may result in patient death. The cause of the accelerated coronary disease is not precisely known, it seems to be associated with viral infection with cytomegalovirus. Stentation or coronary grafting may be attempted but it usually results in re-transplantation.
• malignant tumors

11. 4. Cardiac Transplant Results
Operative mortality decreased to 3-5%, one-year survival may reach 85%, five-year survival can be 70%, 10-year 40% and 15-year 25%. Early child mortality in the first post-transplant year is higher - 20%. Further improvement of immunosuppressive drugs and more intensive postoperative care (intramyocardial ECG by pace-maker technology) can improve the results of this outstanding therapy.

Perspectives
The problem of the transplant program still stands. There is a large discrepancy between the growing number of patients on the waiting list and the reduction of donor allografts. Thus, in the U.S.A., they reached a total of 4070 heart transplants in 1995, and then in 2002 it declined to 3000 due to fewer donors. Xenografts, that is the heart harvested from other species than the human one, is still under research. Extremely high costs of heart transplantation, dependence on expensive post-transplant medication and repeated medical checks are more problems that reduce the number of procedures.