Permanent and Temporary Pacemaker Implantation after Orthotopic Heart Transplantation

Fernando Bacal, Edimar A. Bocchi, Marcelo L. C. Vieira, Neusa Lopes, Luiz Felipe Moreira, Alfredo Fiorelli, Roberto Costa, Martino Martinelli, Noedir A. G. Stolf, Giovanni Bellotti, José Antonio F. Ramires

São Paulo, SP - Brazil

Purpose - *To determine the indication for and incidence and evolution of temporary and permanent pacemaker implantation in cardiac transplant recipients.*

Methods - *A retrospective review of 114 patients who underwent orthotopic heart transplantation InCor (Heart Institute USP BR) between March 1985 and May 1993. We studied the incidence of and indication for temporary pacing, the relationship between pacing and rejection, the need for pemanent pacing and the clinical follow-up.*

Results - *Fourteen of 114 (12%)heart transplant recipients required temporary pacing and 4 of 114 (3.5%) patients required permanent pacing. The indication for temporary pacing was sinus node dysfunction in 11 patients (78.5%) and atrioventricular (AV) block in 3 patients (21.4%). The indication for permanent pacemaker implantation was sinus node dysfunction in 3 patients (75%) and atrioventricular (AV) block in 1 patient (25%). We observed rejection in 3 patients (21.4%) who required temporary pacing and in 2 patients (50%) who required permanent pacing. The previous use of amiodarone was observed in 10 patients (71.4%) with temporary pacing. Seven of the 14 patients (50%) died during follow-up.*

Conclusion - *Sinus node dysfunction was the principal indication for temporary and permanent pacemaker implantation in cardiac transplant recipients. The need for pacing was related to worse prognosis after cardiac transplantation.*

Key-words: pacemaker, cardiac transplantation

Instituto do Coração do Hospital das Clínicas - FMUSP
Mailing address: Fernando Bacal - Rua João Castaldi, 217/42 - 04517-050 - São Paulo, SP - Brazil

Cardiac transplantation remains the treatment of choice for end-stage heart disease despite great advances in drug therapy [1].

Cardiac arrhythmias are not uncommon in those who experience denervation after heart transplantation, and temporary pacing might be necessary in the postoperative period [2-5]. Resting heart rate after transplantation has been shown to be about 100 beats per minute due to the absence of autonomic innervation; however soon after cardiac transplantation, some patients have a lower heart rate at rest [2-4,6-8]. Bradyarrhythmias occur in more than 50 % of recipients in the immediate postoperative period and are probably due to sinus node dysfunction, but atrioventricular conduction disturbances can also occur in some patients [4,9,10]. The mechanism of these disturbances remains poorly understood although rejection, prolonged ischemic time, specific anomalies of coronary artery anatomy and donor sinus node dysfunction have been suggested [3,9,11,12].

These arrhythmias are sometimes transient and asymptomatic and recovery of cardiac rhythm occurs overtime, although many authors suggest that sinus node dysfunction soon after transplantation is related to a poorer prognosis [13].

The purpose of this study was to determine the incidence of, indication for and evolution of temporary and permanent pacemaker implantation in cardiac transplant recipients.

Methods

A retrospective review of 114 patients who underwent orthotopic heart transplantation in InCor between March 1985 and May 1993 was performed.

The mean age was 46±11 years. The indications for transplantation included: dilated cardiomyopathy in 21%, *Chagas* disease in 21%, ischemic cardiomyopathy in 14% and rheumatic cardiomyopathy in 7%.

This study was undertaken to determine the incidence of and indication for temporary pacemakers, the relation-

ship between arrhythmias and rejection episodes, the evolution to permanent pacing and clinical follow-up.

Triple-drug therapy was used (steroids, azathioprine and cyclosporine). Those patients who did not tolerate cyclosporine in the early postoperative period received polyclonal serum (Atgam) for a 14 day period.

Right ventricular endomyocardial biopsies were performed in all patients in the first week after transplantation, and routinely if theGalio-67 test was positive or if allograft rejection was clinically suspected. The right internal jugular vein was punctioned with a 9F sheath and bioptome (clamp 9M-9F) under fluoroscopy, and three or four biopsy specimens were taken from the interventricular septum. Rejection criteria accepted were that reported by ISHLT [14].

Twenty-four-hour Holter monitoring was performed in patients with bradyarrhythmias, using a 2-channel recorder (*Maquette - Mac 15)* to determine the need for permanent pacing.

Temporary pacing was indicated in patients with type II second degree AV block, complete AV block and symptomatic sinus node dysfunction. Temporary stimulation was undertaken with epicardial electrode pacing during the surgical procedure or, if necessary, an endocardial electrode was positioned by right internal jugular vein puncture.

In the postoperative period, patients were given cardioactive drugs (dobutamine, dopamine, isoprenaline) in order to achieve a positive chronotropic and inotropic effect.

Survival analysis during the first 180 postoperative days was done through the actuarial method. The curves obtained were compared through theWilcoxon test.

The study period was divided into early (first 15 postoperative days) and late (after second week) periods.

Results

Of the 114 patients who had heart transplants, 14 (12.2%) underwent artificial cardiac stimulation with a temporary pacemaker and 4 received permanent pacing (tables I and II).

The indications for temporary pacemaker implantation were: sinus node dysfunction in 11 patients, type II second degree AV block in one patient and complete AV block in 2 patients.

Ten patients required a temporary pacemaker in the early postoperative period and 4 patients required one in the late period.

Acute rejection was confirmed in three patients who needed an early temporary pacemaker, and when treated with pulsetherapy with methylprednisolone 1.0 g daily for three days, normal rhythm was achieved. All late patients experienced rejection, and in two patients, in inspite of specific treatment no rhythm recovery occurred. Seven patients who needed a temporary pacemaker died during the study period, five in the early period and two after hospital discharge (one due to infection and the other due to rejection). Main causes of death in the early stages were: low cardiac output, acute rejection and failure of temporary pacemaker stimulation (occurred in one patient).

In 4 patients (3.5%) the indication for permanent pacing was sinus node dysfunction in 3 patients (one for rejection) and atrioventricular block in one patient (rejection). Only one of these patients had received previously temporary pacing.

Of the 11 patients who underwent temporary pacing due to sinus node dysfunction, 6 patients recovered normal cardiac rhythm. Two patients with atrioventricular block did not return to a normal heart rate. However, the patient with type II second degree AV block recovered normal cardiac rhythm in the early period.

Patients who did not require temporary pacing, survived longer than those who required pacing; in the first 180 postoperative days (76% versus 50%, $p<0.001$). Actuarial survival curves are given in table I.

Discussion

During the surgical procedure used for orthotopic

Table I - Temporary pacemaker implant

Patient	Age/ Sex	Postoperative day implant	Indication	Rhythm recovery	Rejection	Follow-up
1	58/M	IPOP	SND	Yes	No	Alive
2	35/M	7th PO	SND	No	No	Alive
3	65/M	IPOP	TAVB	No	No	Dead
4	54/M	8th PO	SND	No	Yes	Dead
5	45/M	IPOP	SND	Yes	No	Alive
6	48/M	30thPO	SND	No	Yes	Dead
7	48/M	18th"PO	SND	Yes	Yes	Dead
8	48/M	IPOP	SND	Yes	No	Dead
9	46/M	6th PO	SND	Yes	Yes	Alive
10	16/M	30th PO	TII 2ndDAVB	Yes	Yes	Alive
11	46/M	IPOP	SND	No	No	Dead
12	57/M	4th PO	SND	No	No	Dead
13	37/M	2 years	TAVB	No	Yes	Alive
14	42/M	15th PO	SND	Yes	Yes	Alive

IPOP- immediate postoperative period (within first 24h); PO- postoperative period; SND- sinus node dysfunction; TII 2nd DAVB- Type II 2nd degree atrioventricular block; TAVB total atrioventricular block.

Table II - Permanent pacemaker implant

Patient	Previous temporary pacing	Postoperative day implant	Indication	Rejection	Follow-up
1	7th PO	57th PO	SND	No	Alive
2	-----	0th PO	SND	No	Alive
3	2 years	2 years	TAVB	Yes	Alive
4	17th PO	44th PO	SND	Yes	Alive

PO- postoperative period; SND sinus node dysfunction; TAVB total atrioventricular block.

cardiac transplantation, the posterior portions of donor preserved right and left donor atria are left *in situ* with the sinus node and its neural connections undisturbed [15]. The transplant recipient thus has two sinus nodes with electrical activity and eletrocardiography expression totally independent of the surface eletrocardiogram. The donor sinus node is responsible for electrical stimulation despite its anatomical and functional denervation [3,13,16]. Normal sinus node function is dependent on a complex balance between intrinsic sinus node electrophysiologic properties, sinoatrial conduction properties and a number of extrinsic factors, the most important of which is the autonomic nervous system [17]. Although reinnervation after cardiac transplant has been observed in animal models, complete restoration of normal myocardial innervation in human transplantation has not been observed, although evidence of partial recovery does exist [17,18]. Cardiac frequency in a denervated heart is regulated according to venous return, atrial receptor stimulation, atrial stretching and circulating catecholamine levels [17-19].

In the immediate postoperative period and also in the first few weeks after transplantation, sinus or junctional bradycardia occur in more than 50% of recipients [2,3,5,8,11]. Donor sinus node dysfunction is the most common cause of bradyarrhythmia reported after transplantation [4,9,10,20]. Some authors believe that the presence of sinus node dysfunction may be seen as evidence of a worse prognosis after transplantation. These data are similar to ours. In the group that required artificial cardiac stimulation, the mortality was 50% at 180 days follow-up. Hemodynamic dysfunction, myocardial damage and rejection may contribute to this prognosis. In an attempt to control bradyarrhythmias, we may use drugs such as isoprenaline, dopamine, dobutamine, terbutaline, theophylline. Artificial cardiac stimulation is indicated if no response to drugs occurs [3,17].

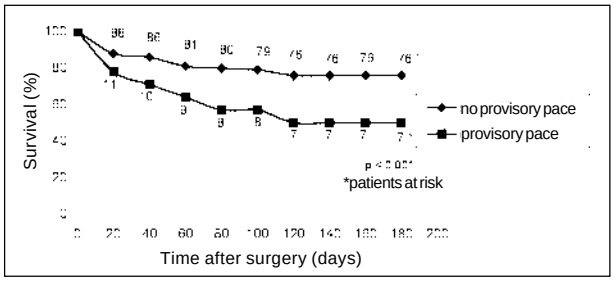

Fig. 1 - Actuarial Survival curve transplantation patients.

The incidence of temporary and permanent pacing after transplantation has varied from 4% to 24% in several studies. Indications for permanent pacing are: sinus node dysfunction (mainly), type II second degree atrioventricular block, and total atrioventricular block. Our data confirmed these findings [4,5,8,12,21,22].

The etiology of permanent sinus node dysfunction is multifactorial, and rejection, sinus node ischemia during transplant organ transport, surgical maneuvers, anomalies in the sinus node artery, prolonged ischemia time in the perioperative period, sinus node dysfunction prior to thesurgical act, and myocardial fibrosis after cyclosporine. Local trauma to the superior vena cava, donor age, inadequate denervated heart response to vasoactive amines and previous use of antiarrhythmic drugs, especially amiodarone, may be involved [4,5,8,9,11,12,13,17,23].

The optimum timing of permanent pacing is still controversial and must reflect the compromise between the advantages of early pacemaker implantation and the risks of delaying this procedure. According to some authors epicardial pacing wires are usually removed on day 21 afterthe operation, and a decision regarding permanent pacing is made at this point [3]. As part of the routine, an epicardial pacemaker is implanted in the postoperative period of cardiac surgery. At the end of the operation, an epicardial electrode is implanted in order to guarantee temporary stimulation in case of bradyarrhythmias soon after surgery. However, epicardial pacing in recipients may present difficulties due to rejection, fibrosis after rejection and myocyte fibrosis after cyclosporine [8].

In our series, rejection occured in 30% of patients with temporary and permanent pacing. Studies in retransplantation or necropsy have shown that cardiac conduction tissue is a specific target related to allograft rejection [13]. The arteries to sinoatrial and atrioventricular tissue are frequently involved in both an acute cellular reaction and in the chronic intimal fibro-cellular rejection reaction, causing sinus node dysfunction [24].

The beneficial hemodynamic effects of atrial contribution must be considered when deciding the optimal mode of pacing of patients undergoing cardiac transplantation, although some authors advocate only ventricular stimulation [3]. Implantation of rate responsive pacemakers is based on the observation of chronotropic incompetence noticed after cardiac transplantation [9,12]. Chronotropic response to exercise is abnormal in transplanted patients due to autonomic denervation [8,11]. Stimulation must be individualized using an atrioventricular pacemaker whenever it is possible,

and a rate responsive pacemaker in patients who have chronotropic incompetence [25,26].

In our series we used a dual chamber pacemaker in 4 patients with permanent pacing, a rate responsive pacemaker being necessary in only one of them.

Sinus node dysfunction was the main indication for temporary and permanent pacing in our patients. In patients who required temporary pacing, the mortality was 50%, and the need for pacing was related to a poor prognosis in cardiac transplantation evolution.

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