

New conduction defects and pacemaker implantation after heart transplantation

Kalp nakli sonrası yeni ileti defektleri ve kalp pili implantasyonu

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ABSTRACT

Background: This study aims to determine the incidence of new conduction defects and pacemaker implantation and to identify patient characteristics for a permanent pacemaker need after biatrial orthotopic heart transplantation.

Methods: Between February 1998 and August 2014, we retrospectively analyzed the data of 212 consecutive patients (147 males, 65 females; mean age 39.6±15 years; range 5 to 65 years) who underwent heart transplantation with biatrial cuff technique in our clinic. Baseline characteristics and postoperative data were compared among the patients who required a pacemaker or did not.

Results: The incidence of permanent pacing after heart transplantation was 6.4%. The most frequent reason for permanent pacing was symptomatic bradycardia. Previous cardiac surgery was associated with a non-significant trend toward a need for permanent pacing (p=0.056). The presence of a ventricular assist device was a found to be associated with both prolonged temporary and permanent pacemaker requirement after biatrial cardiac transplantation (p=0.021 and p=0.042, respectively).

Conclusion: Although bradyarrhythmia and need for temporary pacing were common in the early postoperative period, few of these patients needed permanent pacemaker implantation. The need for a permanent pacemaker seems to be more frequent after challenging operations, such as bridge to heart transplantation with a long-term ventricular assist device.

Keywords: Bradycardia; heart transplantation; pacemaker.

ÖZ

Amaç: Bu çalışmada biatriyal ortotopik kalp nakli sonrası yeni ileti defekti ve kalp pili implantasyon sıklığı belirlendi ve kalıcı kalp pili ihtiyacına yönelik hasta özellikleri tespit edildi.

Çalışma planı: Şubat 1998 - Ağustos 2014 tarihleri arasında kliniğimizde biatriyal teknik ile kalp nakli yapılan 212 ardışık hastanın (147 erkek, 65 kadın; ort. yaş 39.6±15 yıl; dağılım 5-65 yıl) verileri retrospektif olarak incelendi. Başlangıç özellikleri ve ameliyat sonrası verileri, kalp pili ihtiyacı olan ve olmayan hastalar arasında karşılaştırıldı.

Bulgular: Kalp nakli sonrası kalıcı kalp pili sıklığı %6.4 idi. Kalıcı kalp pili için en sık neden, semptomatik bradikardi idi. Geçirilmiş kalp cerrahisi, kalıcı kalp pili ihtiyacında anlamlı olmamakla birlikte bir artış ile ilişkilendirildi (p=0.056). Ventrikül destek cihazı varlığı, biatriyal kalp nakli sonrasında hem uzamış geçici hem de kalıcı kalp pili gereksinimi ile ilişkili bulundu (sırasıyla p=0.021 ve p=0.042).

Sonuç: Bradikardi ve geçici kalp pili ihtiyacı erken ameliyat sonrası dönemde sık görülmesine rağmen, bu hastaların çok az bir kısmında kalıcı kalp pili implantasyonu gerekli oldu. Kalıcı kalp pili ihtiyacı, özellikle uzun süreli ventrikül destek cihazlı kalp nakli köprülemesi gibi zorlu ameliyatlarda daha sık görülmektedir.

Anahtar sözcükler: Bradikardi; kalp nakli; kalp pili.



The incidence of sinus bradycardia and rhythm disturbances including junctional rhythms which occur after orthotopic cardiac transplantation has been reported to be 64%.^[1] With pacing for sinus node dysfunction early after heart transplantation, the sinus node may recover and permanent pacing may not be necessary in the long-term follow-up.^[2] In addition, some studies have focused on an explanation for post-transplantation sinus node dysfunction; ischemia, rejection, surgical trauma, drug therapy, and increased donor age are some of the accused factors.^[2-7] Also, surgical trauma-induced dysfunction has brought biatrial and bicaval techniques into question.^[2,4,8-11]

In this study, we aimed to determine the incidence of cardiac pacing in our cardiac transplant population and to identify patient characteristics or events which may predict which patients will require pacing after biatrial cardiac transplantation.

PATIENTS AND METHODS

The study group consisted of 212 consecutive patients, (147 males, 65 females; mean age 39.6±15 years; range 5 to 65 years) who underwent heart transplantation with biatrial cuff technique at our institution between February 1998 and August 2014. The patient records were analyzed to identify individuals who required prolonged temporary pacemaker, as defined within the first 24 hours after transplantation and permanent pacemaker (PPM) implantation. Baseline characteristics at the time of transplantation including patient age, donor age, ischemic time, cardiopulmonary bypass (CPB) duration, and cardiac surgery history (i.e. coronary artery bypass grafting, valve replacement, congenital correction), preoperative ventricular assist device (VAD) implantation were compared among patients who required pacing and did not. Nine patients died

in the early postoperative period and PPM need was analyzed in 203 patients. Simple statistical analyses and T-table testing were used to make comparisons. Correlations were tested by the Pearson correlation coefficient. A *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics are shown in Table 1. The most frequent etiology of end-stage heart failure was dilated cardiomyopathy (65.5%) in 212 patients. Total of 102 patients had a history of cardiac surgery; 18 of them had coronary artery bypass grafting, 21 had valve replacement, three had congenital correction operation, and 60 had VAD support prior to transplantation. The mean donor age was 29.3±11.4 (range 7 to 59) years. Biatrial orthotopic heart transplantation procedure was performed in all patients.^[12] DDD mode (Dual chamber pacing, Dual sensing, Dual inhibitions) for pacing was used in all patients during operation by implanting two atrial and two ventricular epicardial pace wires.

A total of 100 patients (47.2%) experienced relative bradycardia requiring prolonged temporary pacing after transplantation during the first 24 hours of intensive care unit follow-up. Permanent pacemaker was placed in 13 patients (6.4%) after biatrial orthotopic heart transplantation. While 10 patients required early implantation before discharge (mean time 16.6±12.2 days), three patients required late implantation (mean time 2169±167.1 days) during long-term follow-up. There was no difference in the development of coronary allograft vasculopathy or rejection episodes at the time of PPM implantation.

Among the patients who needed PPM, five (38.4%) had PPM implantation during early postoperative

Table 1. Baseline clinical characteristics of heart transplant recipients

Baseline characteristics	n	%	Mean±SD
Recipient age (years)			39.6±15
Gender			
Male	147	69.3	
Ischemic heart disease	5	23.5	
Dilated cardiomyopathy	139	65.5	
Others*	23	10.8	
Preoperative cardiac surgery**	102	48.1	
Ventricular assist device	60	28.3	
Preoperative intra-aortic balloon pump	2.4	5	

SD: Standard deviation; * Hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, restrictive cardiomyopathy, congenital heart disease; ** Coronary artery bypass grafting, valve replacement, congenital correction, ventricular assist device implantation.

Table 2. Baseline characteristics of heart transplant recipients according to need for permanent cardiac pacing

	No pacing (n=190)			Permanent pacing (n=13)			p
	n	%	Mean±SD	n	%	Mean±SD	
Recipient age (years)			39.9±15			37.2±18.4	0.53
Donor age (years)			28.9±11.4			32±10.8	0.37
Ischemic time (min)			175.4±59.4			188.1±65	0.46
Cardiopulmonary bypass duration (min)			129.5±56			139±63.3	0.56
PCWP (mmHg)			23.6±8.2			24.3±8.8	0.81
MPAP (mmHg)			32.4±10.5			30.5±12	0.57
Ventricular assist device	52	27.3		7	53.8		0.042
Preoperative cardiac surgery*	90	47.4		9	69.2		0.056

SD: Standard deviation; PCWP: Pulmonary capillary wedge pressure, MPAP: Mean pulmonary arterial pressure; * Coronary artery bypass grafting, valve replacement, congenital correction, ventricular assist device implantation.

period due to bradycardia and hemodynamic instability requiring continuous temporary pacing support. Two patients (15.4%) had third-degree atrioventricular block, two (15.4%) had junctional rhythm requiring PPM, and one patient (7.7%) needed an implantable cardioverter defibrillator due to recurrent ventricular arrhythmia. Indications for PPM implantation in the late postoperative period included sinus node dysfunction, complete atrioventricular block, and symptomatic bradycardia.

The comparisons of the recipient age, donor age, cardiac ischemic time, CPB time duration, baseline pulmonary vascular wedge pressure, and mean pulmonary arterial pressure between two groups are shown in Table 2.

Postoperative prolonged temporary pacemaker was associated with higher PPM rates ($p=0.027$). Prolonged temporary pacemaker requirement was significant ($p=0.017$), whereas PPM requirement was slightly, but non-significantly ($p=0.056$) more frequent in patients with a history of cardiac surgery (i.e. coronary artery bypass grafting, valve replacement, congenital correction and VAD implantation). The subgroup analysis showed that the presence of VAD was correlated with both prolonged temporary pacemaker and PPM implantation ($p=0.021$ and $p=0.042$, respectively).

DISCUSSION

Following transplantation, most of donor hearts are functionally depressed, thereby, requiring support with positive chronotropic agents or temporary pacing for the first 24 hours. Temporary pacing early after the operation, a common procedure, may enhance the cardiac performance. The incidence and indications for pacemaker implantation following cardiac

transplantation differ among studies, ranging from 6 to 23%.^[13] Most of these studies have reported sinus bradycardia, slow junction rhythm, sinus arrest, or sinus node dysfunction as the primary reasons, while about 10% of pacemaker implantation is due to second- and third-degree heart block. Extended ischemic duration, allograft rejection, and damaged sinoatrial node of the donors' heart during the transplantation are the main reasons for sinus node dysfunction.^[2-4] Most of these studies performed pacemaker implantation prior to hospital discharge, usually between seven and 21 days following transplantation. Similarly, our results showed a consistent incidence rate of PPM implantation.

Furthermore, in our study, symptomatic bradycardia was the most common reason for PPM implantation. In case of symptomatic bradycardia requiring prolonged temporary pacing, theophylline was administered before PPM implantation. There were no significant differences in cardiac ischemic time, CPB time duration, baseline pulmonary vascular wedge pressure, and the mean pulmonary arterial pressure among the patients who required pacemaker implantation and did not. Several studies reported ischemic time as the main cause of postoperative sinus node dysfunction,^[1,5] while some authors^[14,15] demonstrated no correlation between ischemic time and a subsequent need for pacing.

In addition, most studies reported an increased incidence of PPM with the biatrial technique.^[2,4,8] Randomized trials also showed that permanent pacing requirement reduced with bicaval technique.^[9-11] The bicaval technique of orthotopic heart transplantation, in contrast to the biatrial technique, is considered to better preserve the right atrial anatomy and, thus, is associated with less sinus node dysfunction. Meta-analyses of prospective trials revealed significant

superiority of the bicaval technique in comparison to the biatrial procedure for sinus rhythm.^[16] Meyer et al.^[10] showed significant reduction in the need for PPM insertion at 30 days (biatrial vs. bicaval 13% vs. 0%, $p=0.008$) and 90 days (17% vs. 1.8% $p=0.01$) post-transplantation with the bicaval technique. However, variable results were attained from studies comparing bicaval and biatrial anastomosis for regarding a pacemaker need. For instance, in a study of bicaval anastomosis, pacing was not required in any of 100 consecutive patients.^[17] In two randomized trials, permanent pacing was not required in any patients undergoing bicaval anastomosis, but in five (6.7%) of 75 patients undergoing biatrial anastomosis.^[18,19] Our cohort was comprised of those undergoing biatrial orthotopic heart transplantation, and our results are in consistent with the literature data.

The patients with a history of cardiac surgery tended to require PPM ($p=0.056$) in our study. When analyzed on its own, the presence of VAD was associated with PPM requirement ($p=0.042$). These results may indicate that besides the prior history of cardiac surgery, bridge to transplantation, in particular, may be a risk factor PPM. We believe that the surgical challenge caused by dense adhesions secondary to prior cardiac surgery might have yielded such a result.

Our study had some limitations due to its retrospective nature and small sample size. Pacing criteria were clinically derived and some data were limited by loss to follow-up.

In conclusion, although bradyarrhythmia was common in the early postoperative period after biatrial technique and prolonged temporary pacing is commonly required, few patients needed PPM implantation. As surgical technique seems to be a major predictor of who will be more likely to require permanent pacing, the presence of VAD results in more challenging surgery and may lead to pacing postoperatively.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

- Jacquet L, Ziady G, Stein K, Griffith B, Armitage J, Hardesty R, et al. Cardiac rhythm disturbances early after

orthotopic heart transplantation: prevalence and clinical importance of the observed abnormalities. *J Am Coll Cardiol* 1990;16:832-7.

- Herre JM, Barnhart GR, Llano A. Cardiac pacemakers in the transplanted heart: short term with the biatrial anastomosis and unnecessary with the bicaval anastomosis. *Curr Opin Cardiol* 2000;15:115-20.
- Jones DG, Mortsell DH, Rajaruthnam D, Hamour I, Hussain W, Markides V, et al. Permanent pacemaker implantation early and late after heart transplantation: clinical indication, risk factors and prognostic implications. *J Heart Lung Transplant* 2011;30:1257-65.
- Cantillon DJ, Gorodeski EZ, Caccamo M, Smedira NG, Wilkoff BL, Starling RC, et al. Long-term outcomes and clinical predictors for pacing after cardiac transplantation. *J Heart Lung Transplant* 2009;28:791-8.
- Miyamoto Y, Curtiss EI, Kormos RL, Armitage JM, Hardesty RL, Griffith BP. Bradyarrhythmia after heart transplantation. Incidence, time course, and outcome. *Circulation* 1990;82:313-7.
- Heinz G, Kratochwill C, Koller-Strametz J, Kreiner G, Grimm M, Grabenwöger M, et al. Benign prognosis of early sinus node dysfunction after orthotopic cardiac transplantation. *Pacing Clin Electrophysiol* 1998;21:422-9.
- Holt ND, Tynan MM, Scott CD, Parry G, Dark JH, McComb JM. Permanent pacemaker use after cardiac transplantation: completing the audit cycle. *Heart* 1996;76:435-8.
- Woo GW, Schofield RS, Pauly DF, Hill JA, Conti JB, Kron J, et al. Incidence, predictors, and outcomes of cardiac pacing after cardiac transplantation: an 11-year retrospective analysis. *Transplantation* 2008;85:1216-8.
- Deleuze PH, Benvenuti C, Mazzucotelli JP, Perdrix C, Le Besnerais P, Mourtada A, et al. Orthotopic cardiac transplantation with direct caval anastomosis: is it the optimal procedure? *J Thorac Cardiovasc Surg* 1995;109:731-7.
- Meyer SR, Modry DL, Baaney K, Koshal A, Mullen JC, Rebeyka IM, et al. Declining need for permanent pacemaker insertion with the bicaval technique of orthotopic heart transplantation. *Can J Cardiol* 2005;21:159-63.
- Davies RR, Russo MJ, Morgan JA, Sorabella RA, Naka Y, Chen JM. Standard versus bicaval techniques for orthotopic heart transplantation: an analysis of the United Network for Organ Sharing database. *J Thorac Cardiovasc Surg* 2010;140:700-8.
- Lower RR, Shumway NE. Studies on orthotopic homotransplantation of the canine heart. *Surg Forum* 1960;11:18-9.
- Melton IC, Gilligan DM, Wood MA, Ellenbogen KA. Optimal cardiac pacing after heart transplantation. *Pacing Clin Electrophysiol* 1999;22:1510-27.
- DiBiase A, Tse TM, Schnittger I, Wexler L, Stinson EB, Valentine HA. Frequency and mechanism of bradycardia in cardiac transplant recipients and need for pacemakers. *Am J Cardiol* 1991;67:1385-9.
- Chau EM, McGregor CG, Rodeheffer RJ, Frantz RP, Olson LJ, Daly RC, et al. Increased incidence of chronotropic incompetence in older donor hearts. *J Heart Lung Transplant* 1995;14:743-8.
- Schnoor M, Schäfer T, Lühmann D, Sievers HH. Bicaval

- versus standard technique in orthotopic heart transplantation: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg* 2007;134:1322-31.
17. Trento A, Takkenberg JM, Czer LS, Blanche C, Nessim S, Cohen MH, et al. Clinical experience with one hundred consecutive patients undergoing orthotopic heart transplantation with bicaval and pulmonary venous anastomoses. *J Thorac Cardiovasc Surg* 1996;112:1496-502.
 18. el Gamel A, Yonan NA, Grant S, Deiraniya AK, Rahman AN, Sarsam MA, et al. Orthotopic cardiac transplantation: a comparison of standard and bicaval Wythenshawe techniques. *J Thorac Cardiovasc Surg* 1995;109:721-9.
 19. Deleuze PH, Benvenuti C, Mazzucotelli JP, Perdrix C, Le Besnerais P, Mourtada A, et al. Orthotopic cardiac transplantation with direct caval anastomosis: is it the optimal procedure? *J Thorac Cardiovasc Surg* 1995;109:731-7.