Bicaval versus standard technique in orthotopic heart transplant: assessment of atrial performance at magnetic resonance and transthoracic echocardiography

Angelo Maria Dell’Aquila, Stefano Mastrobuoni, Gorka Bastarrika, Beltran Levy Praschner, Pedro Azcárate Agüero, Sara Castañó, Jesus Herreros and Gregorio Rabago

Department of Cardiovascular Surgery, Clinical University of Navarra, Pamplona, Spain
Department Radiology, Clinical University of Navarra, Pamplona, Spain
Department of Cardiology, Clinical University of Navarra, Pamplona, Spain

* Corresponding author. Höteweg 11, 48143 Münster, Germany. Tel: +49-1784509731; e-mail: am.dellaquila@gmail.com (A.M. Dell’Aquila).

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Abstract

Despite a more physiological morphology of atrial anastomosis in the bicaval technique with respect to standard biatrial anastomosis in orthotopic heart transplantation (OHT), the impact on the long-term outcome is still not clear. In this retrospective study, we sought to investigate the morphology and function of the atria through magnetic resonance imaging (MRI) and transthoracic echocardiography (TTE). Moreover, we aimed to analyse the accuracy of TTE with respect to MRI. Cox regression analysis of 216 consecutive patients receiving OHT between August 1987 and January 2010 identified only recipient age at the time of transplant to be an independent predictor of mortality ($P = 0.048$, odds ratio = 1.04). After a mean follow-up of 96.6 ± 77.7 months, 108 patients were alive, of which 35 were found to be eligible for MRI assessment. In this analysis, left and right atrial volumes were found to be significantly larger in the standard group in comparison with the bicaval group ($P = 0.001$), and no significant difference between the two techniques was observed in left and right atrio-ventricular output. Moreover, a significantly reduced accuracy was observed (CCC < 0.3) when TTE results were compared with MRI assessment in evaluating atrial dimensions. Although left and right atrial volumes are significantly larger in the standard group in comparison with the bicaval group, we concluded that no significant difference in the atrial output and survival between the two techniques could be demonstrated.

Keywords: Orthotopic heart transplantation • Bicaval technique • Standard biatrial • Magnetic resonance imaging • Transthoracic echocardiography

INTRODUCTION

Despite the improvement in pharmacological treatment of end-stage heart failure, cardiac transplantation and LVAD as destination therapy remain the only definitive treatment capable of improving the long-term survival [1, 2]. The standard biatrical technique introduced by Lower and Shumway [3] for orthotopic heart transplantation (OHT) has been adopted worldwide due to its simplicity and reproducibility. However, several studies have demonstrated that the drawback of this technique consists in enlarged atrial cavities without a physiological geometry between the donor and the recipient atrium [4]. Therefore, this ‘unphysiological’ geometry can lead to a higher incidence of atrioventricular valve incompetence and rhythm disturbances [4].

In 1991, Sievers et al. [5] introduced the bicaval technique. This technique, based on the preservation of the recipient’s right atrium, has the potential advantage to preserve the physiological right atrium conduction system and geometry [6]. Two recent meta-analyses [4–7] demonstrated a potential benefit of the bicaval technique over the standard technique although the long-term survival seems to be not different between the two techniques.

Thus, the question why long-term outcome seems to be only weakly influenced by the surgical technique remains to be addressed.

The aims of this study are (i) to evaluate the impact of the two surgical implantation techniques used in our institution for long-term survival, (ii) to assess the atrial and ventricular performances within the two techniques using cardiac magnetic resonance imaging (MRI) and transthoracic echocardiography (TTE) evaluation and (iii) to evaluate the accuracy of the TTE in estimating the atrial volumes and performances compared with that of the MRI technique.

MATERIALS AND METHODS

Study population

A total of 216 consecutive patients received OHT at our institution between August 1987 and January 2010. One hundred and
eight patients were alive at follow-up and were considered for inclusion in this study. Of those, all were examined with routinely TTE during hospital admission and if eligible with MRI.

The study protocol was approved by the institutional review board and all patients gave written informed consent. The clinical follow-up was completed at 99.5% on 1 February 2010.

Immunosuppressive regimen

Between June 1984 and February 1997, the immunosuppressive regimen was based on cyclosporine (CsA), azathioprine and prednisone. The monoclonal antibody OKT3 (Ortho Pharmaceutical Corp, Raritan, NJ, USA) was used for induction therapy only in patients with chronic renal failure or arterial hypertension in order to use lower doses of CsA in the immediate postoperative period or delay in the beginning of CsA itself. Since February 1997, the immunosuppression regimen consisted of Daclizumab (Zenapax®; Hoffmann-LaRoche, Mississauga, ON, Canada) 1 mg/kg intravenously (i.v.) within 12 h of transplantation and a second dose 1 mg/kg i.v. 2 weeks thereafter; corticosteroids (methylprednisolone 500 mg intra-operatively, then 125 mg twice a day i.v. for 36 h, followed by oral prednisone 1 mg/kg/day tapered to 0.1 mg/kg/day for the first 6 months when steroids were definitively suspended); Mycophenolate Mofetil (CellCept®, Hoffmann-LaRoche) at a dosage of 0.5–1.0 g twice a day to target a through level of 3–5 ng/ml; Tacrolimus (Prograf®, Fujisawa, Munich, Germany) 1–4 mg twice a day to target a through levels of 10–15 ng/ml for the first 3 months and 5–10 ng/ml thereafter.

Eligibility for MRI and image acquisition protocol

Exclusion criteria to MRI investigation were the usual contraindications to MRI: allergy to iodated contrast media, renal failure (creatinine >1.4 mg/dl), atrial fibrillation or frequent extrasystolia (more than four premature beats per minute), claustrophobia and patients with magnetic resonance unsafe ferromagnetic objects such as pacemaker or ICD.

MRI studies were performed in a 1.5-T MRI system (Magnetom Symphony with quantum gradients; maximum gradient amplitude 30 mT/m; slew rate, 125 mT/m/s; Siemens Healthcare, Erlangen, Germany) using a four-element-phased array coil. Retrospectively, ECG-gated 7–9 contiguous axial 5 mm slice-thickness cine loops encompassing the entire left atrium were acquired using a steady-state free precession sequence. Reconstructed images were transferred to the same external workstation. No medication was given to lower or stabilize the heart rate prior to scanning.

Transthoracic echocardiography

Transthoracic two-dimensional echocardiograms, M-mode recordings and Doppler ultrasound measurements were performed using a Sonos 7500 ultrasound system (Phillips). All echocardiographic studies were performed by two cardiologists who were blinded to the previous operation techniques. LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD) were measured from M-mode recordings using leading edge methodology according to the American Society of Echocardiography criteria [8]. LV volumes, LVEF as well as atria volumes were determined using the Simpson rule. Diastolic function was assessed by measuring E and A waves of the mitral filling pattern by pulsed echo-Doppler technique in four-chamber apical views. Moreover, early (E) and late (A) pic velocities were recorded in order to calculate their ratio E/A.

Statistical analysis

Normal distribution of data was assessed with the Shapiro–Wilk test. Data are summarized as mean ± SD. Paired sample Student’s t-test was used to estimate atrial and ventricular parameter differences for respective TTE and MRI values. Univariate regression analysis was used first to define the relationship between categorical or continuous variables and the occurrence of death. Clinical characteristics such as donor/recipient age, height, weight, pathology determining heart failure, ischaemic time, bypass time and transplantation technique were entered into the model. Variables with a P value of ≤0.2 were entered into a multivariate model for Cox regression analysis with stepwise selection to determine the independent predictors of mortality. A P value <0.05 was considered to be statistically significant. The cumulative survival curve was computed according to the Kaplan–Meier method, and comparison between the groups was performed using the log-rank test. Moreover, in order to identify the independent predictors of atrial enlargement, univariate analysis followed by multivariate linear regression analysis was made.

Bland and Altman plots including mean differences and limits of agreement were generated to ascertain the degree of agreement between TTE and MRI results for each pair of atrial parameters [9]. Calculation of concordance correlation coefficient (CCC) allowed assessing the degree of concordance for each measured variable and estimating the interobserver variability [10]. The CCC can range from 0 to 1, with CCC of 0 representing no agreement and CCC of 1 meaning perfect reliability. For linear correlation analysis, the Pearson correlation coefficient R was calculated defining correlation as poor (r = 0.0–0.09), minimal (r = 0.1–0.40), moderate (r = 0.41–0.60), good (r = 0.61–0.80) and excellent (r = 0.81–1.0). Data analysis was performed using commercially available statistical software packages (MedCalc, Version 9.3.0.0. Med-Calc Software; Mariakerke, Belgium and SPSS for Windows, Version 15.0/SPSS Inc., Chicago, IL, USA).

RESULTS

Among the 216 patients receiving OHT in our institution, 117 were transplanted with the standard technique and 99 with the bicaval technique. One hundred and eight patients were alive after a mean follow-up of 96.61 ± 77.74 months. Preoperative demographic data are showed in Table 1.

Donor and recipient age, and the graft ischaemic time, were significantly higher in the bicaval group in comparison with the standard group (Table 1). Thirty-day mortality was comparable in both groups (6.9% in biatral versus 8.08%, P = 0.8).

Kaplan–Meier analysis revealed a survival of 79.3, 71.2, 56.9%, at 1, 5, 10 years for the standard group and 84.7, 74.5, 60.5% for the bicaval group (Fig. 1). Comparison between the two
groups using the log-rank test revealed no significant difference ($P = 0.29$) (Fig. 2).

Cox regression analysis identified recipient age at the time of transplant to be an independent predictor of mortality ($P = 0.048$, odds ratio = 1.04, CI = 1.01–1.03).

### Morphology and heart performance at MRI

Following the above-mentioned criteria for MRI assessment eligibility, we were able to recruit 35 patients (preoperative demographic data are showed in Table 2). Allograft morphologic analysis with MRI did not show any significant anastomotic stenosis or the presence of clot at the level of right and left atrium in both groups.

Left and right ventricular dimensions as well as the ejection fraction (EF) and the left ventricular mass were within the normal range in both groups and no significant difference was detected between the two techniques (Table 3).

The left and the right atrium were significantly enlarged in the standard technique compared with the bicaval group. Mean end-diastolic and end-systolic volumes of the right atrium were 152 and 115 ml versus 83 and 43 ml in standard and bicaval groups, respectively ($P < 0.001$). For the left atrium, mean end-diastolic and end-systolic volumes were 119 and 87 ml in the bicaval group versus 195 and 160 ml in the standard group ($P = 0.003$). The right atrial EF (RAEF) was significantly higher in the bicaval group than that in the standard group (0.47 versus 0.25, $P < 0.001$). Similarly, the left atrium EF was higher in the bicaval group than that in the standard group (LAEF) (0.27 versus 0.19, $P = 0.002$). The left and right atrial output did not show any significant difference between the two groups (Table 3).

Linear multivariate regression analysis identified the standard technique as the only predictive factor of right ($P = 0.001$) and left atrial enlargement ($P < 0.001$).

### Morphology at TTE and comparison with MRI

Using TTE, no statically significant difference was observed in left ventricular dimensions and volumes between the standard group and the bicaval group (Table 4).

The left and the right atrium were significantly enlarged ($P < 0.02$) in the standard technique compared with the bicaval group. Moreover, a normal left ventricular filling pattern with normal and regular E and A waves was proved in all ventricles. Mean volumes of the right and left atria of both groups are shown in Table 4.
In none of the cases (35 patients), severe as well as moderate tricuspid regurgitation (TR ≥ 2) was observed. The incidence of mild TR was 42.2% in the entire cohort and it was more pronounced in the standard group (22.8 versus 20%, P = 0.7).

A systematic underestimation of left atrial volumes by TTE when compared with MRI was observed. Left atrial volumetric quantification determined by TTE revealed a mean EDV of 88.59 ± 37.85 and a mean ESV of 71.18 ± 29.73, whereas MRI showed a mean EDV of 153.17 ± 69.35 and a mean ESV of 119.64 ± 65.2 (Fig. 2).

A systematic underestimation was also observed in measurement of right atrial volumes by TTE when compared with MR. TTE revealed a mean EDV of 71.18 ± 29.76 and a mean ESV of 51.15 ± 21.0; whereas MR shows a mean EDV of 114.22 ± 49.09 and a mean ESV of 75.53 ± 46.69 (Fig. 3). This underestimation was less remarkable in right atrial volumes in the bicaval group (Table 5).

In calculating the left atrial dimensions, TTE has showed a mean poor agreement (EDV: CCC = 0.3) (ESV: CCC = 0.22), as well for the right atrial dimensions (EDV: CCC = 0.18) (ESV: CCC = 0.27) (Table 5).

**DISCUSSION**

Our data demonstrate that there is no significant difference in the long-term survival between patients receiving the standard biatrial technique versus the bicaval technique in OHT. Although the standard biatrial technique results in significantly larger atrial volumes, the haemodynamic performance of the left and right atrium is similar between the two groups.

It is well known that the standard technique remains a simple, highly reproducible and efficient technique, reducing the risk of technical failures and allowing a shorter ischaemic time due to a lower number of anastomosis than the bicaval technique [11]. However, it has been demonstrated that this technique may lead to morphological atrial alterations and hence interfere with haemodynamic, electrophysiology and valvular function of the donor heart [7].

Schnoor et al. confirmed in a recent meta-analysis [7], the superiority and the evidence of clinically relevant benefits of the bicaval technique over the standard technique in terms of lower incidence of TR, preservation of the sinus rhythm, reduced early atrial pressure and ultimately reduced perioperative mortality. In another recent study, Davies et al. [12], analysing the United Network for Organ Sharing database, concluded that OHT performed with bicaval anastomoses have a small but significant survival advantage compared with biatrial anastomoses. However, using the same database but not considering the

### Table 3: Haemodynamic data at MRI of patients transplanted using the ‘standard’ and the bicaval techniques

<table>
<thead>
<tr>
<th></th>
<th>Standard group, n = 16</th>
<th>Bicaval group, n = 19</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Bpm</td>
<td>85.94 ± 8.35</td>
<td>87.21 ± 11.96</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>106.58 ± 22.58</td>
<td>94.08 ± 21.76</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>37.11 ± 15.58</td>
<td>28.82 ± 11.78</td>
<td>NS</td>
</tr>
<tr>
<td>LV output (l/min)</td>
<td>66.26 ± 7.04</td>
<td>70.14 ± 6.37</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>107.08 ± 23.87</td>
<td>108.89 ± 23.31</td>
<td>NS</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>45.73 ± 15.33</td>
<td>45.78 ± 13.09</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>58.16 ± 6.57</td>
<td>58.33 ± 7.03</td>
<td>NS</td>
</tr>
<tr>
<td>RV output (l/min)</td>
<td>5.25 ± 0.92</td>
<td>5.42 ± 0.94</td>
<td>NS</td>
</tr>
<tr>
<td>LAEDV (ml)</td>
<td>152.82 ± 48.50</td>
<td>159.57 ± 28.05</td>
<td>0.01</td>
</tr>
<tr>
<td>LAESV (ml)</td>
<td>62.49 ± 17.12</td>
<td>41.23 ± 19.27</td>
<td>0.004</td>
</tr>
<tr>
<td>LA output (l/min)</td>
<td>3.00 ± 0.68</td>
<td>2.77 ± 0.73</td>
<td>NS</td>
</tr>
<tr>
<td>RA output (l/min)</td>
<td>5.25 ± 0.92</td>
<td>5.42 ± 0.94</td>
<td>NS</td>
</tr>
<tr>
<td>RAEDV (ml)</td>
<td>115.95 ± 42.96</td>
<td>43.63 ± 11.15</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RAESV (ml)</td>
<td>71.23 ± 31.44</td>
<td>44.10 ± 19.73</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>RA output (l/min)</td>
<td>3.28 ± 0.74</td>
<td>3.49 ± 0.85</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Table 4: Haemodynamic data at TTE

<table>
<thead>
<tr>
<th></th>
<th>Standard group, n = 16</th>
<th>Bicaval group, n = 19</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV (ml)</td>
<td>123.64 ± 30.77</td>
<td>108.31 ± 31.6</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>39.14 ± 19.43</td>
<td>36.63 ± 15.41</td>
<td>NS</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>67.27 ± 7.99</td>
<td>65.83 ± 8.15</td>
<td>NS</td>
</tr>
<tr>
<td>LAEDV (ml)</td>
<td>110.15 ± 39.04</td>
<td>70.63 ± 26.26</td>
<td>0.02</td>
</tr>
<tr>
<td>LAESV (ml)</td>
<td>71.23 ± 31.44</td>
<td>44.10 ± 19.73</td>
<td>0.005</td>
</tr>
<tr>
<td>RA output (l/min)</td>
<td>84.06 ± 23.90</td>
<td>59.91 ± 30.46</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RAEDV (ml)</td>
<td>62.49 ± 17.12</td>
<td>41.23 ± 19.27</td>
<td>0.004</td>
</tr>
</tbody>
</table>

LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; RAEDV, right ventricular end-diastolic volume; RAESV, right ventricular end-systolic volume; E/A, (E) and late (A) pic trans-mitral velocities; LAEDV, left atrium end-diastolic volume; LAESV, left atrium end-systolic volume; RA, right atrium; RAESV, right atrium end-diastolic volume; RAEDV, right atrium end-systolic volume; NS, not significant.
missing data, Weiss et al. [13] showed no difference in the long-term survival between the bicaval and standard techniques.

In the present study, we did not observe a trend towards a better survival in the bicaval group compared with the standard technique (P = 0.29).

A possible explanation can be due to the fact that despite the significantly larger dimensions and a lower EF in the standard technique, the right and left atria are able to maintain a normal function by means of atrial output. This discrepancy between different atrial EF with similar output in the two techniques can be due to the asynchronous movement of the residual recipient atrial walls during the systole in the standard group. These phenomena can underestimate the atrial EF in the standard group. Moreover, the TTE data have confirmed a normal left ventricular filling pattern with normal and regular E and A waves in all ventricles. Therefore, it can be speculated that the haemodynamic parameter at rest in the presence of sinus rhythm and normal compliant ventricle is the same. Conversely, in ‘stress situations’ such as weaning from cardiopulmonary bypass or in the early post-operative period, a synchronous atrial contraction may ‘help’ a stiffer ventricle due to ischaemic arrest also exposed to eventual elevated pulmonary pressures of recipient.

Another aim of the current study was to evaluate the clinical use of TTE in the follow-up of transplanted patients compared with MRI. We demonstrated that TTE has remarkable limits in estimating atrial cavities in OHT patients with a high tendency towards underestimation. That can be due to the frequent presence of wall irregularity of atrial anastomoses.

Bouchart et al. [11] suggest that transoesophageal echocardiography (TEE) should be applied in all patients transplanted by the standard technique due to the possible risk of spontaneous echo contrast and atrial thrombosis. Also CT has been shown to be an optimal follow-up diagnostic tool [14]. Moreover, it has been confirmed to be an optimal method in detecting cardiac allograft vasculopathy [15].

We think that TTE must remain the method of choice in transplant follow-up, but we suggest that a more aggressive imaging method such as the above-mentioned CT, TEE or MR should be also used especially in patients transplanted with the standard technique.

In conclusion, our findings confirm that the bicaval technique should remain the preferable technique with the main goal to minimize the dimensions of the atria. Furthermore, taking into account the limits of TTE, a more invasive imaging in transplanted patients must be taken into consideration during the follow-up period.

**Limitations**

Two important limitations of this study are the retrospective study design and the low number of patients recruited for the MRI examination due to the strict MRI recruitment protocol. Thus, analysis of arrhythmia was not available because the MRI protocol included only patients with sinus rhythm. Moreover, TTE analysis showed no severe and moderate TR. The incidence of mild TR was 42.2% in the entire cohort and it was more pronounced in the standard group (22.8 versus 20%, P = 0.7). We think that this difference did not reach the statistical significance due to the low number of patients.

Other limitations are the follow-up time difference as well as donor and recipient age difference between the two techniques. Those problems have been faced by entering those variables (the date of transplant to the date of MRI follow-up and age of donor recipient) into the linear regression multivariate model. The donor and recipient age difference between the two techniques are a consequence of different time of applications of the two techniques. The bicaval technique was introduced in our centre in March 1997. Since then all patients underwent the bicaval technique. Over the years, the development of newer immunosuppressive agents and the improvement of transplantation intensive care have allowed the extension of transplant indications to older patients. Those improvements have also allowed the inclusion of older donors in our transplant programme.

**Conflict of interest:** none declared.

**REFERENCES**


