Conventional and total orthotopic cardiac transplantation: a comparative clinical and echocardiographical study

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Abstract

Objective: Clinical interest has recently emerged in a new technique of heart transplantation with bicaval and pulmonary venous anastomosis. This technique is thought to improve left heart function and reduce thromboembolism. We have used this technique systematically since 1993. We compared the patients transplanted before September 1993 with the standard technique and the patients transplanted with the new technique. Methods: A total of 135 patients were transplanted at our institution from 1987 to 1995, 100 with the standard technique and 35 with the new technique. Of these, 95 survivors were studied by transthoracic and transesophageal echocardiography; 65 were transplanted with the standard technique (‘standard’ group) and 30 with the new technique (‘total heart’ group). All patients were free from rejection and in sinus rhythm when studied. Results: Both groups were similar in pretransplant characteristics. Operative data were similar with a limited increase in the ischemic time with the total heart technique (210 ± 73 min for ‘total heart’ vs. 196 ± 84 min for ‘standard’). Right heart catheterization showed comparable cardiac output and pulmonary pressures. Peripheral embolic events occurred in 9 patients in the ‘standard’ group and none in the ‘total heart’ group. The left atrium was larger in the ‘standard’ group (58 ± 6 vs. 42 ± 4 mm, \( P = 0.0006 \)). Left atrial spontaneous echo contrast was present in 32 patients in group ‘standard’ and none in ‘total heart’ group (\( P < 0.0001 \)), and left atrial thrombi were detected in 17 patients in group ‘standard’ vs. none in group ‘total heart’ (\( P = 0.01 \)). All patients with a history of embolism had left atrial thrombus and spontaneous echo contrast. Conclusion: This study showed a high incidence of left atrial spontaneous echo contrast and thrombi when using the standard technique, which was absent when using the total heart technique. Total heart transplantation with bicaval and pulmonary venous anastomosis should be preferred for heart transplantation. © 1997 Elsevier Science B.V.

Keywords: Heart transplantation; Echocardiography

1. Introduction

Heart transplantation is a worldwide accepted therapeutic option for the treatment of end-stage heart failure. Most of heart transplantations have been performed using the technique described by Lower and Shumway [7,9]. We have previously shown that patients transplanted using this technique not only have a high incidence of spontaneous echo contrast (SEC), but also left atrial thrombosis when examined by transesophageal echocardiography [5]. Left atrial enlargement, resulting from the addition of the donor to the recipient atrium, was thought to be responsible for blood stasis. The technique described by Dreyfus [6], using atrial anastomosis at the venous level on both sides, results in a
transplanted heart with a more normal anatomical configuration and normal size of both atria. This technique should therefore reduce blood stasis in the atria.

The purpose of this study was to compare two consecutive series of heart transplant recipients who underwent surgery at a single institution using both techniques. The incidence of spontaneous echo contrast (SEC) and thrombus in the left atrium was evaluated by transthoracic (TTE) and transesophageal echocardiography (TEE).

2. Material and methods

Surviving patients (95) out of a total of 135 patients who received a heart transplant at our institution between 1986 and 1995, were enrolled in this study. Of these, 100 patients underwent orthotopic heart transplantation using the standard technique originally described by Lower and Shumway [7,9] and 65 patients were studied and constituted the ‘standard’ group. Since September 1993, all patients were transplanted using the total atrioventricular transplantation described below [6], and 30 were included in the study. These form the ‘total heart’ group. All the survivors were included in the study except 2 patients in the ‘standard’ group who moved away from Rouen and were followed by another team.

2.1. Donor heart harvesting.

Some minor modifications are necessary to carry out harvesting for total heart transplantation. The superior vena cava (SVC) is transected as high as possible, usually above theazygos vein. The inferior vena cava (IVC) is transected at the diaphragmatic reflexion, leaving enough IVC for the liver harvest. The pulmonary veins are separately transected. A vertical incision in the left atrium is made between the superior and the inferior pulmonary veins to create a single orifice on each side.

2.2. Technique for the recipient.

Arterial canulation is done as usual. The superior vena cava is canulated high at the junction with the left innominate vein, and is dissected free circumferentially at the pericardial reflexion. The IVC is canulated at the level of the diaphragmatic reflexion. The recipient heart is explanted removing the posterior wall of both atria. The SVC is divided at the caval-atrial junction and the IVC is divided leaving a small cuff of right atrium. The left atrium is removed, leaving only two left atrial cuffs that include the ostiae of the pulmonary veins on either side. The implantation of the donor heart requires 6 anastomosis in the following order: left pulmonary veins, right pulmonary veins, SVC, IVC, pulmonary artery and aorta. Occasionally, when the lungs are harvested, a larger cuff is left around the pulmonary veins on the recipient left atrium to allow for safe anastomosis.

Conventional triple drug immunosuppression therapy was used in all patients including cyclosporine A, azathioprine and steroids for maintenance immunosuppression with the addition of rabbit antilymphocyte globulins for induction. All patients received low molecular weight heparin until discharge, which was then substituted by oral antiplatelet therapy using aspirin at a daily dose of 250 mg.

2.3. Hemodynamic data.

An endomyocardial biopsy and a right heart catheterization were performed on the same day as the transesophageal echocardiography in all patients and no patient showed evidence of significant rejection on that biopsy. All patients were in regular sinus rhythm at the time of examination. Right heart catheterization was performed with a Swan–Ganz catheter allowing cardiac output evaluation. The following right heart pressures were also recorded: right atrial, right ventricular, pulmonary artery and pulmonary capillary wedge pressures.

2.4. Echocardiography.

Informed consent was obtained from all patients prior to the study. Transthoracic (TTE) and transesophageal echocardiography (TEE) were performed with an Acuson XP 128 echocardiograph (Acuson Inc) equipped with a high-frequency biplane phased-array transducer for transesophageal echocardiography. TTE enabled measurement of left atrial diameter, left ventricular diastolic and systolic diameter, ejection fraction calculation by the single-plane area-length method. Transmitral flow velocities were measured by Doppler flow echocardiography and early (E) and late (A) pic velocities were recorded which allowed the calculation of their ratio E/A.

Transesophageal echocardiography was possible in all patients using pharyngeal lidocaine anesthesia, midazolam intravenous administration, and antibiotic prophylaxis with amoxicillin. The morphology of the whole left atrium and the interatrial septum was carefully assessed, as well as all accessible anastomotic sites for both techniques. Spontaneous echo contrast (SEC) was defined as the presence of swirling smoke-like echoes within the atrial cavity [3].
Table 1
Baseline data of the patients transplanted using ‘standard’ and the total ‘heart techniques’

<table>
<thead>
<tr>
<th></th>
<th>Standard (65 patients)</th>
<th>Total heart (30 patients)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age HTx (y)</td>
<td>50 ± 11</td>
<td>47 ± 10</td>
<td>ns</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74 ± 12</td>
<td>73 ± 13</td>
<td>ns</td>
</tr>
<tr>
<td>Donor age (y)</td>
<td>30 ± 10</td>
<td>31 ± 9</td>
<td>ns</td>
</tr>
<tr>
<td>Preop diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated</td>
<td>36</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Schematic</td>
<td>21</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Valvular</td>
<td>8</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Ischemic time (mn)</td>
<td>196 ± 84</td>
<td>210 ± 73</td>
<td>ns</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (mn)</td>
<td>117 ± 38</td>
<td>123 ± 34</td>
<td>ns</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>510 ± 370</td>
<td>540 ± 380</td>
<td>ns</td>
</tr>
<tr>
<td>In-Hospital stay-time (d)</td>
<td>27 ± 11</td>
<td>26 ± 11</td>
<td>ns</td>
</tr>
<tr>
<td>Rejections</td>
<td>2 ± 3</td>
<td>1.5 ± 1</td>
<td>ns</td>
</tr>
<tr>
<td>Embolic episodes</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strokes</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower limb ischemia</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenteric ischemia</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to transplant (months)</td>
<td>26 ± 19</td>
<td>6 ± 4</td>
<td>.0002</td>
</tr>
</tbody>
</table>

2.5. Statistical analysis.

All values are expressed as mean ± S.D. Mann-Whitney U test and Fisher’s exact test were used to compare both groups when appropriate. A P value ≤ 0.05 was considered statistically significant. Multiple logistic regression analysis was used to determine independent predictors of SEC and left atrial thrombus testing recipient age (≥ 55), time elapsed since transplantation (≥ 6 months), left atrial size (≤ 55 mm), left ventricular ejection fraction (≤ 55%), and number of previous rejections (n ≥ 2).

3. Results

Our experience with heart transplantation began in 1987. Since then, 100 patients have been transplanted using the standard technique. Since September 1993, 35 patients have received a heart transplant using the total heart technique. Operative mortality was 13.6 ± 2.8% in the whole series and actuarial survival was 79.3 ± 3.4% at 1 year and 65.4 ± 4.3% at 5 years. There has been no statistically significant difference between both groups in terms of operative mortality and survival. Among the 95 patients enrolled in this study, 65 were transplanted using the standard technique (group ‘standard’) and 30 using the total atrioventricular technique (group ‘total heart’). Both groups were comparable for age and weight at transplantation, pretransplant diagnosis, donor age, in-hospital stay-time and number of rejections as shown in Table 1. The time required for completion of all the anastomosis was longer using the total heart technique (20–30 min), but cardiopulmonary bypass time did not significantly increase. Ischemic time was longer in the ‘total heart’ group, but this increase did not reach statistical significance. If we compare the total population, 100 patients operated with the standard technique and 35 patients operated with the total heart technique, ischemic time was significantly different, 212 ± 73 min, for total heart vs. 194 ± 85 min. For the standard technique, P = 0.03. Blood loss during the first postoperative day was not increased by the use of the total heart technique.

Despite antiplatelet therapy, peripheral arterial embolism occurred in 9 patients 6–36 months after transplantation (Table 1). Embolic events only occurred in the ‘standard’ group. All patients who had experienced an embolism subsequently received oral anticoagulant therapy. Spontaneous echo contrast in the left atrium was observed by TEE in all patients with a history of peripheral emboli, as well as the presence of intra atrial thrombus. None of the patients transplanted with the total heart technique showed signs of peripheral embolism. Linear regression analysis did not uncover a discriminant factor in the ‘standard’ group between patients with or without a history of peripheral emboli. No arrhythmias were found when patients presented embolic events either in emergency room or at Holter studies made during the following days.

Hemodynamic data and major echocardiographic findings are summarized in Table 2. There was no significant difference between both groups regarding hemodynamic data. Pulmonary capillary wedge pressure was not significantly different between both groups, and was not increased with the enlargement of the left atrium in the ‘standard’ group. By conservation of the recipient atria, using the standard technique, the resulting left atrium is significantly enlarged when compared to the total heart technique, and the left atrial...
size is also largely greater than the upper limits for the normal left atrium. Doppler echocardiography showed a normal left ventricular filling pattern in the ‘total heart’ group with normal and regular E and A waves, whereas in the ‘standard’ group, left ventricular filling pattern was highly variable from cycle to cycle as shown by a greater variability of the E/A ratio from cycle to cycle. This variability reflects the asynchronous activity of the recipient’s left atrium and the transplanted atrium.

Spontaneous echo contrast or left atrial thrombosis could not be shown in any patient by transthoracic echocardiography. The presence of SEC could be demonstrated in 32 out of 65 patients (49%) in the ‘standard’ group and in none of the ‘total heart’ group (P < 0.0001). Using logistic regression analysis, the operative technique was the only predictive factor for the presence of SEC. The presence of left atrial thrombosis was demonstrated by TEE in 17 out of the 65 patients enrolled in the ‘standard’ group and in none of the patients enrolled in the ‘total heart’ group (P = 0.01).

The thrombus was localized in the left atrial appendage in 9 patients, on the posterior wall in 5 patients and on the suture line in 3 patients. Using logistic regression analysis, the operative technique was the only predictive factor associated with the presence of left atrial thrombosis. When left atrial thrombosis was present, SEC was also present in all patients. Within the ‘standard’ group, no evidence of a predictive factor for SEC or left atrial thrombosis was observed.

In the ‘total heart’ group, morphologic analysis and Doppler study did not show any stenosis at the anastomotic sites of the pulmonary veins and the SVC.

4. Discussion

The standard surgical technique for heart transplantation described by Shumway and coworkers [7,9] has been used worldwide for most heart transplantsations for the last 30 years. It is a simple, highly reproducible and efficient technique allowing a rapid surgical procedure and eliminating the risk of technical failures. The manner in which the atrial anastomosis are made results in an enlargement of both atria and to some degree a distortion of the donor atria. The anatomic and physiologic abnormalities have been extensively analysed by transesophageal echocardiography [1,8]. The left atrium is enlarged with a snowman aspect due to the suture line between the recipient and the donor left atrium protruding in the atrial cavity. Persisting electrical and mechanical activity in the remainder of the recipient atria results in asynchronous contractions of both components of the left atrium modifying the filling pattern of the left ventricle. Both the enlargement of the atria and the asynchronous contraction can promote blood stasis and the occurrence of spontaneous intra-atrial echo contrast and left atrial thrombosis. Only transesophageal echocardiography has been able to detect spontaneous echo contrast and left atrial thrombosis in transplanted patients [1]. Furthermore, we suggest that TEE should be proposed to all patients transplanted using the standard technique. Presence of spontaneous echo contrast has been shown to increase the thromboembolic risk for valvular patients [3]. In our experience, SEC was associated with left atrial thrombus in 50% of the patients, and in the absence of SEC none of the patients presented an embolism or atrial thrombosis. Oral anticoagulation therapy was administered in all patients presenting atrial thrombosis but not in patients presenting only SEC.

Total heart transplantation has been introduced in clinical practice by Dreyfus in 1991 [6] after having been described as early as 1959 by Web and Neely [10]. Its major advantage is in performing a complete anatomical transplantation of the whole heart with normal morphology of both atria and normal atrioventricular interactions. No clear cut evidence supporting the advantages of this technique have been reported to date in the literature in terms of clinical outcome, hemodynamics and exercise tolerance [2,4,6]. The potential drawbacks of this technique are essentially an increase in the time needed to complete the six anastomoses and the potential hazard of bleeding from the inaccessible medial aspects of the pulmonary vein anastomosis. In our experience, the increase in the ischemic
time has been acceptable remaining below 4 h, and bleeding has not been a concern in any of the patients transplanted with the total heart technique. The total heart technique may have some potential hazards in the pediatric population. Great care should be taken at the SVC anastomosis. Our experience was limited to one 10-year-old boy who had no anastomotic stenosis at the 18-months follow-up angiogram. The extended graft procurement allows for facing many donor anatomical abnormalities. The major advantage of the new technique in our experience is the complete disappearance of thromboembolic complications, left atrial thrombus and spontaneous echo contrast in the left atrium. It is unlikely that these findings can be explained by the longer follow-up time in the ‘standard’ group.

5. Conclusion

The standard orthotopic heart transplantation technique described by Lower [7,9] is still the gold standard for heart transplantation in the world. The enlarged resulting left atrium with prominent suture lines and asynchronous contractions of the recipient and donor atria may be responsible for the high incidence of left atrial thrombus in these patients. The total heart technique prevents these complications without increasing the operative risk and is for us the technique of choice for orthotopic heart transplantation.

References


Appendix A. Conference discussion

Dr Moidl (Vienna, Austria): I have a question. Do you use low dose aspirin routinely after cardiac transplantation?

Dr Bouchart: As I said, we gave these patients low molecular weight heparin until discharge and then they receive 300 mg of aspirin per day for the rest of their lives.

Dr Hagl (Heidelberg, Germany): Congratulations on this nice study. I wonder whether you have any data on AV valve function in the series of patients where you use the ‘total orthotopic technique’? Due to our limited experience with six cases, the post-operative function of both the tricuspid and mitral valve is much better preserved using the bicaval and bipulmonary various connection. From preliminary echo-studies, we may suggest that atrial and atrioventricular geometry is normal in the hearts transplanted this way. Thrombus formation may depend on atrial geometry and therefore size of both atria. Using the Shumway-Lower technique, the atria do not necessarily have to be as huge as you showed us. In our experience with more than 150 cases, we have seen only one thromboembolic complication.

Dr Bouchart: In our experience, there was a little bit more mitral insufficiency and tricuspid insufficiency with the standard technique. I agree that the presence of thrombus is mainly related to the large size of the atrium and the best way to reduce the size of the atrium is to remove all of the atrium.

Dr Nagele (Hamburg, Germany): Have you data on how many patients are in fibrillation of the recipient atrium and are the embolic events you reported a possible problem of patients who are in fibrillation of the recipient atrium.

Dr Bouchart: There was no significant data about that in our series.

Dr Rahman (Manchester, England): We totally agree with your concepts and congratulate you on your results. For the last 5 years, we have been convinced about the disadvantages of the standard technique and we have been using the standard technique with a view to reduce the problems arising from the right side of the heart, including tricuspid incompetence, etc. However, we did do two or three total replacements. Have you had any technical problems as regards the suture line and did you have to go back for bleeding?

Dr Bouchart: No. I think one of the points is to really coagulate all of this pericardial reflection before you make the suture when you remove the atria, so you dont have bleeding. We didn’t have trouble with the suture line; it never happened in our experience. The only thing we had was one patient, who had low arterial pressure when he went on the right side. This goes on for a couple of days only. Afterward, the heart is quite immobolized in the pericardium and there is no such trouble.

Dr Rahman: But if you remove the lungs to be transplanted somewhere else, you are left with a small left atrium and you will have to leave some of the recipients left atrium to compensate for this, or do you use pericardial patches as we did, in one or two cases.

Dr Bouchart: It has never been a problem in our experience. You leave a small cuff of atrium at the time, and if you want, you can leave just the posterior wall, so you can have a very small cuff of left atrium, but it has never been so in our experience.