Excellent outcome of cardiac transplantation using domino donor hearts

Abstract  Objective. Domino cardiac transplantation affords flexible and optimal organ utilization, provides hearts unaffected by brain death, allows prospective tissue matching, and subsequent transplantation with short allograft ischemic times. A retrospective review of our experience with domino cardiac transplantation has been made. Methods. Seventy-two of 119 patients who underwent heart-lung transplantation from 1988 on served as domino cardiac donors (40 males, 32 females; mean age of 32 years; mean weight of 51 kg). The domino donor diagnoses were cystic fibrosis (n=47), bronchiectasis (n=9), primary pulmonary hypertension (n=6), emphysema (n=7), pulmonary fibrosis (n=2) and Eisenmenger’s syndrome (n=1). Forty-seven domino hearts were transplanted at our institution and 25 were exported to other centres in the United Kingdom. The 72 domino cardiac recipients were 62 males and 10 females, mean age of 47 years, mean weight of 60 kg, with ischemic heart disease (n=32), cardiomyopathy (n=36) and other conditions (n=4).

Results. There were four deaths (5.6%) at less than 30 days (2 from multiple organ failure, 1 from primary allograft failure and 1 from acute rejection). Actuarial survival estimates and 1 and 5 years were 77±5.2% and 69±6.3%, respectively. This compared favourably with survival data obtained in 234 non-domino cardiac recipients. In the patients transplanted at Papworth, there was no difference in the incidence of rejection (0.6±0.05 versus 0.7±0.03 events per 100 patient days for the first 12 months) or in the freedom from graft atherosclerosis (74±3% versus 70±3% at 5 years) between the domino and non-domino groups.

Conclusions. The use of domino hearts donated by recipients of heart-lung transplants is beneficial and is associated with an excellent early and longer-term outcome.

Keywords  Domino cardiac transplantation  
Heart-lung transplantation

Introduction

With the current critical shortage of donor organs worldwide, it is essential that all available organs are successfully transplanted. In domino cardiac transplantation, the normal heart of a heart-lung transplant recipient is transplanted into another recipient with end-stage cardiac failure. This procedure affords flexible and optimal organ utilization, provides hearts unaffected by brain death, allows the potential for prospective tissue matching, and subsequent transplantation with short ischemic times. At Papworth Hospital, combined heart-lung transplantation has been performed in patients with concomitant cardiopulmonary disease and remains the procedure of choice for patients with end-stage lung disease who require bilateral lung transplantation. The latter group
are the source of hearts for domino cardiac transplantation. We present a retrospective review of results of cardiac transplantation using these organs.

**Patients and methods**

Between November 1988 and September 1994, 119 patients underwent combined heart-lung transplantation at Papworth Hospital and 72 of these served as domino cardiac donors. Forty-seven domino hearts were transplanted at Papworth, and 25 were exported to other institutions in the United Kingdom. The indications for combined heart-lung transplantation in the domino cardiac donors were cystic fibrosis (47 patients), bronchiectasis (9), emphysema (7), primary pulmonary hypertension (6), pulmonary fibrosis (2) and Eisenmenger's syndrome (1). There were 40 males and 32 females with a mean age of 32 years and a mean weight of 51 kg.

Each potential domino cardiac donor was evaluated with a chest X-ray, electrocardiogram, and echocardiogram. All males over 35 years of age and females over 40 years of age, as well as patients with a family history of coronary artery disease or diabetes underwent coronary angiography and left ventriculography. Patients were excluded as domino donors in the presence of recurrent cor pulmonale, M-mode echocardiography showing a right ventricular cavity greater than 6 cm, severe tricuspid or pulmonary valve insufficiency, any other organic valve disease, two-dimensional echocardiography showing severe ventricular dysfunction and coronary artery disease demonstrated by coronary angiography. All patients donated their hearts according to guidelines issued by the Unrelated Live Transplant Regulatory Authority and the Human Organ Transplant (Unrelated Persons) Regulations 1989.

The technique of combined heart-lung transplantation with domino cardiac donation has been described in detail elsewhere [15]. Modifications to the technique of combined heart-lung transplantation were required, including inferior vena caval cannulation close to the diaphragm or via a femoral approach and cannulation of the innominate vein instead of the superior vena cava. The domino heart was excised following cardioplegic arrest (500 ml of St. Thomas' Hospital solution) with an adequate length of superior vena cava to preserve the sino-atrial node [3]. The heart was stored in 4°C lactated Ringer's solution prior to implantation. The current immunosuppression protocol is triple therapy with cyclosporine, azathioprine and corticosteroids.

The domino cardiac recipients consisted of 62 males and 10 females with a mean age of 47 years and a mean weight of 60 kg. The recipient diagnoses were cardiomyopathy (36 patients), ischemic heart disease (32), rheumatic heart disease (3) and congenital heart disease (1 patient). Donor and recipient age and weight, allograft ischemic time, length of stay in the intensive care unit and in hospital are expressed as a mean ± standard deviation (SD), or as a median and range. Differences between groups were assessed with the un-paired Student t-test or the Mann-Whitney test, as appropriate. Survival was calculated using the life-table method, and differences between groups were tested using the log-rank test. Statistical significance was defined at a probability value of less than or equal to 0.05.

**Results**

**Procedures**

Seventy-two domino cardiac transplant procedures were performed between November 1988 and September 1994. Forty-seven were transplanted at Papworth and 25 were exported to other centres in the United Kingdom. A domino heart was not used in 47 patients, 21 owing to Eisenmenger's syndrome and 26 because they failed to meet the inclusion criteria outlined above. Results obtained in a subgroup of these domino cardiac recipients have been the subject of previous reports [1, 13].

**Outcome of domino cardiac donors/heart-lung recipients** (Table 1)

There was no significant difference in the ischemic time, intensive care unit (ICU) or hospital stay, and 30-day, 1-year and 5-year survival (Fig. 1) between those heart-lung recipients who acted as domino donors and those who did not.

**Operative mortality**

Four patients (5.6%, one at Papworth and three elsewhere) died within 30 days of operation. Two died from multiple organ failure, one from primary allograft dysfunction and one from acute allograft rejection. The patient who died from primary allograft dysfunction received an apparently

<table>
<thead>
<tr>
<th>Table 1 Comparison of outcome between heart-lung transplant recipients who acted as domino cardiac donors and those who did not</th>
<th>Heart-lung recipient</th>
<th>Test significance level</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Domino donor</td>
<td>Non-domino donor</td>
</tr>
<tr>
<td>No. of patients</td>
<td>72</td>
<td>47</td>
</tr>
<tr>
<td>Ischemic time mean ± SD min (range)</td>
<td>184 ± 43.9 (93–297)</td>
<td>195 ± 43.1 (117–295)</td>
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<tr>
<td>Hospital stay median days (range)</td>
<td>27 (1–147)</td>
<td>31 (1–95)</td>
</tr>
<tr>
<td>Intensive care unit stay median days (range)</td>
<td>3 (1–56)</td>
<td>3 (1–44)</td>
</tr>
<tr>
<td>Actuarial survival 30-day</td>
<td>92 ± 3.3%</td>
<td>85 ± 5.2%</td>
</tr>
<tr>
<td>1-year</td>
<td>83 ± 4.7%</td>
<td>64 ± 7.2%</td>
</tr>
<tr>
<td>5-year</td>
<td>45 ± 9.0%</td>
<td>46 ± 10.6%</td>
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</table>
normal donor heart but the right ventricle was unable to overcome an elevated pulmonary vascular resistance of 7.5 Wood units.

Long-term survival

There were 12 (17.6%) late deaths from infection (4 patients), cerebrovascular disease (3), malignancy (1), renal failure (1) and for unknown reasons (2). Actuarial survival at 1 and 5 years were 77±5.2% and 69±6.3%, respectively (Fig. 2).

Permanent pacemaker

Three patients (4.2%) required implantation of a permanent pacemaker during the early post-transplant period for persistent bradycardia. There have been no late pacemaker insertions. The requirement for permanent pacing was no different from that of the non-domino group.

Outcome of domino cardiac transplants at Papworth compared with non-domino cardiac transplants at Papworth (Table 2)

During the same time period, 234 non-domino cardiac transplants were performed at Papworth. The non-domino allograft ischemic time was longer than that of the domino hearts (P<0.05) by 50 min. There was no difference in the ICU or hospital stay, 30-day, 1-year and 5-year survival (Fig. 2), the incidence of rejection or the actuarial freedom from graft atherosclerosis at 1 and 5 years between the two groups.

Outcome of domino cardiac transplants at Papworth compared with those exported to other centres (Table 3)

The mean age of the recipients of exported domino hearts was less than that of the Papworth recipients. The donor heart ischemic times at Papworth were predictably shorter than those of the exported organs. There was, however, no difference between the ICU or hospital stay or the 30-day, 1-year and 5-year survival (Fig. 3) between the two groups.

Discussion

The first description of domino cardiac transplantation in Europe was by Yacoub et al. in 1988 [18] and that in the United States was by Baumgartner et al. in 1989 [2]. The procedure has been more popular in Europe [19] and other countries such as Australia [4] than in North America. This has been due to logistic difficulties in transporting the domino allograft to a distant institution for transplantation [14] and also due to a prevailing thought that double lung trans-
Table 2 Comparison of outcome between domino and non-domino cardiac transplants performed at Papworth hospital

<table>
<thead>
<tr>
<th>Test significance level</th>
<th>Domino cardiac transplants</th>
<th>Non-domino cardiac transplants</th>
<th>No. of patients</th>
<th>Ischemic time mean ± SD min (range)</th>
<th>Hospital stay median days (range)</th>
<th>Intensive care unit stay median days (range)</th>
<th>Actuarial survival 30-day</th>
<th>1-year</th>
<th>5-year</th>
<th>Linearised incidence of rejection (events/100 patient-days) during first 12 months</th>
<th>Freedom from graft atherosclerosis 1 year</th>
<th>5 years</th>
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<tr>
<td></td>
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<td></td>
<td>72</td>
<td>147 ± 57.6 (39 - 320)</td>
<td>23 (7 - 61)</td>
<td>2 (1 - 22)</td>
<td>92 ± 3.3%</td>
<td>77 ± 5.2%</td>
<td>69 ± 6.3%</td>
<td>0.6 ± 0.05</td>
<td>98 ± 1%</td>
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<td>234</td>
<td>194 ± 58.3 (52 - 340)</td>
<td>22 (1 - 105)</td>
<td>2 (1 - 49)</td>
<td>90 ± 2.0%</td>
<td>79 ± 2.8%</td>
<td>62 ± 4.4%</td>
<td>0.7 ± 0.03</td>
<td>98 ± 1%</td>
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Table 3 Comparison of outcome between domino cardiac transplants performed at Papworth hospital and those performed at other centres in the United Kingdom

<table>
<thead>
<tr>
<th>Test significance level</th>
<th>Papworth</th>
<th>Other centres</th>
<th>No. of patients</th>
<th>Ischemic time mean ± SD min (range)</th>
<th>Intensive care unit stay median days (range)</th>
<th>Hospital stay median days (range)</th>
<th>Actuarial survival 30-day</th>
<th>1-year</th>
<th>5-year</th>
<th>Linearised incidence of rejection (events/100 patient-days) during first 12 months</th>
<th>Freedom from graft atherosclerosis 1 year</th>
<th>5 years</th>
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<tr>
<td></td>
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<td></td>
<td>47</td>
<td>125 ± 42.4 (39 - 213)</td>
<td>3 (1 - 25)</td>
<td>23 (7 - 61)</td>
<td>96 ± 2.9%</td>
<td>82 ± 6.0%</td>
<td>72 ± 8.2%</td>
<td>P = 0.047</td>
<td>98 ± 1%</td>
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<td></td>
<td></td>
<td>25</td>
<td>186 ± 61.6 (82 - 336)</td>
<td>3 (1 - 21)</td>
<td>26 (12 - 60)</td>
<td>84 ± 7.3%</td>
<td>68 ± 9.6%</td>
<td>62 ± 10.2%</td>
<td>P = 0.200</td>
<td>98 ± 1%</td>
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</table>

plantation, rather than combined heart-lung transplantation, is the procedure of choice for patients with end-stage septic lung disease [6].

A contentious issue is whether heart-lung transplantation with domino cardiac donation represents satisfactory use of the offered heart-lung block. Another option is to allocate the organs to three different recipients (two single lung transplants and one heart transplant) rather than two, as in our report. This dilemma is greatest in patients with cystic fibrosis and emphysema where some centres prefer to manage these patients with lung transplantation alone. A potential advantage of double lung replacement is the retention of an innervated heart which may be of benefit in terms of exercise tolerance. Advocates of this approach believe that heart-lung transplantation in these situations places the transplanted heart at risk of rejection, coronary artery disease or both [6]. We have shown that cardiac rejection in the absence of lung rejection is rare, and we have abandoned surveillance endomyocardial biopsies in heart-lung recipients [8]. Our experience suggests it is the presence of obliterative bronchiolitis, and not graft coronary artery disease, that has determined long-term survival [16]. Graft coronary artery disease is present to some extent in a number of patients, but is seldom clinically significant [16].

The domino procedure affords maximal organ usage when heart-lung transplantation is used in patients having bilateral lung transplantation. There are several theoreti-
A final potential, but not thoroughly evaluated, advantage is that of prospective human leukocyte (HLA) matching. Knowledge of the donor's HLA status well in advance of the transplant procedure may allow close HLA matching with the potential, for an improved recipient survival [7] and may also facilitate the transplantation into a recipient with high levels of panel reactive antibodies, thus obviating the need for a time-consuming cross-match on the day of transplantation. We have successfully used prospectively matched donor hearts on several occasions.

Domino cardiac donation means that the heart-lung recipient operation is performed with separate vena caval anastomoses rather than a single right atrial anastomosis. This modification has not compromised the outcome in these patients [1], nor has the fact that heart-lung recipients donate their hearts influenced their survival. Techniques of preservation of the sino-atrial node have been described [3, 17]. In our experience there has been no increased requirement for permanent cardiac pacing in the recipients of domino hearts. The bicaval anastomoses result in the maintenance of right atrial shape with the potential for a lower incidence of post-transplant tricuspid regurgitation.

Close co-operation exists between the various thoracic organ transplant units in the United Kingdom. This has allowed a free exchange of domino hearts between groups. Groups in the United Kingdom that perform only cardiac transplantation frequently offer an intact heart-lung block to another group that performs heart-lung transplantation in exchange for the domino heart.

Heart-lung transplantation remains our procedure of choice for patients requiring bilateral lung transplantation. In experienced hands, the procedure is technically easier to perform and therefore the lung ischemic time is shorter. Whether the longer ischemic times with bilateral lung transplantation result in a greater incidence of obliterative bronchiolitis is unknown. The incidence of airway anastomotic problems appear to be lower in recipients of heart-lung transplants [11].

In conclusion, domino cardiac transplantation can increase the number of cardiac transplant procedures performed whilst maintaining excellent early and long-term results. The controversy related to the allocation of heart-lung blocks remains unresolved until the long-term results of single and bilateral lung transplants are known.

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References


