The current status of combined heart and kidney transplantation

JO CHIKWE, JOHN PEPPER

Abstract

Heart transplantation is an accepted therapeutic option in selected patients with end-stage heart failure. Up to 10% of patients develop renal failure while on the waiting list for heart transplantation. Renal dysfunction is a relative contraindication to heart transplantation. In order to establish current practice in UK heart transplant centres and overall surgical outcomes for combined heart and kidney transplantation, we surveyed the eight units currently responsible for heart transplantation, all but one of which had carried out at least one combined heart and kidney transplant. We obtained outcome data from the United Kingdom Transplant organisation. We found a wide variability in the level of renal function considered a contraindication to heart transplantation, and no consensus on the criteria for combined heart and kidney transplantation. The 30-day mortality was 14% (4/28) and survival at one, three, five and 10 years was 66.5 (95% confidence interval 57.3–75.7), 50.2 (40.3–60.1), 45.6 (35.6–55.7), and 30.8 (19.2–42.4) respectively, with significant variability between centres.

A prospective, controlled trial is needed to address these issues, but such a study remains extremely unlikely in the context of the increasing scarcity of organ donors.

Key words: heart transplantation, kidney transplantation, patient selection.

Br J Cardiol 2002;**9**:519–23

Introduction

Heart transplantation is an accepted therapeutic option in selected patients with end-stage heart failure. Whilst the indications for isolated heart transplantation are well established, experience suggests that there is little agreement regarding the management of patients with heart failure who have major impairment of other organ systems, such as the kidneys.

Department of Cardiac Surgery, Royal Brompton Hospital, Sydney Street, London, SW3 6NP.
Jo Chikwe, Specialist Registrar Cardiothoracic Surgery
John Pepper, Professor of Cardiothoracic Surgery
Correspondence to: Dr J Chikwe
(email: j.chikwe@medschl.cam.ac.uk)

Cardiac and renal disease frequently co-exist, not least because they share common aetiologies. Up to 70% of patients awaiting heart transplantation suffer from diabetes and atherosclerosis in addition to low cardiac output states, which in themselves predispose to renal impairment.[1] Progression of renal failure is common in the later stages of cardiac disease and up to 10% of patients develop end-stage renal failure while on the waiting list for heart transplantation.[1]

Native renal function may also be compromised following heart transplantation by factors including perioperative low cardiac output states, nephrotoxic antibiotics, and immunosuppressive regimes including calcineurin inhibitors. Although renal function can improve dramatically after restoration of blood flow, a minority of patients develop dialysis-dependent renal failure following heart transplantation. The survival of such patients post-heart transplantation is dramatically reduced:[2] a serum creatinine greater than 200 µmol/L or creatinine clearance of less than 40 ml/min are, therefore, relative contraindications to heart transplantation.[3]

Despite this, a small number of combined heart and kidney transplants have been reported.[4-19] There is a select group of patients for whom combined heart and kidney transplantation is an appropriate option and for whom the rigid application of guidelines would exclude potentially life-saving surgery. We therefore undertook a survey of heart transplant centres that had carried out at least one combined heart and kidney transplant to establish current practice in the UK.

Method

The eight units currently responsible for all combined heart and kidney transplants in the UK were contacted in a telephone survey. The structured telephone questionnaire asked how many such transplants had been done, whether there were any such patients currently on the waiting list or under consideration for transplantation, what level of renal dysfunction was considered a contraindication for heart transplantation alone, and whether there were any formal criteria for considering patients for combined heart and kidney transplantation.

Although survival data were requested from each unit, these were available for less than half of the patients transplanted. Survival data were obtained from registries maintained by United Kingdom Transplant (UKT) although these data are not unit-specific.

Actuarial patient survivals were calculated using the Kaplan-

Table 1. All combined cardiac and renal transplants by centre

Centre	Cases
A	12
B	6
C	4
D	2
E	1
F	1
G	1
H	1
I	0

Table 2. Renal cut-offs for heart only recipients by centre

Centre	Serum creatinine (μmol/L)	Creatinine clearance (ml/min)	Glomerular filtration rate	Proteinuria	Protocol
A	-	< 40	-	-	-
B	No fixed exclusion criteria for renal function				
C	-	-	< 40	-	Yes
D	-	< 50	< 50	-	-
E	> 200	< 30	-	-	-
F	-	< 50	-	-	Yes
G	Unable to contact				
H	No longer heart transplant unit				
I	> 100	< 50	-	-	Yes

Meier method. The 95% confidence intervals were computed as 1.96 times the standard error in each direction.

Results

The questionnaire was completed by telephone or by fax by seven of the eight units contacted, accounting for 27 of the 28 combined heart and kidney transplants carried out in the UK. Information was provided by six transplant co-ordinators, one specialist registrar and one transplant research fellow.

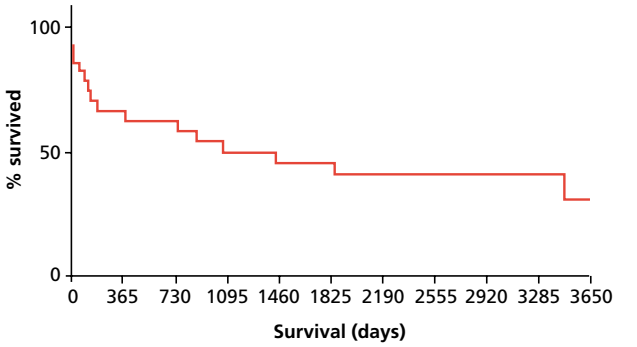
Twenty-eight combined heart and kidney transplants were carried out in the UK between 1986 and January 2002.[20] Three centres account for over two thirds of these cases (table 1), which include two heart/lung and kidney transplants.

Two patients at two units were on the waiting list for combined heart and kidney transplantation at the time of the questionnaire, and one patient was being considered for inclusion to the waiting list.

All respondents were aware of the UKT guidelines on renal dysfunction in heart transplantation which recommend listing only patients with a serum creatinine of < 200 μmol/L, or creatinine clearance of > 40 ml/min, for heart transplantation alone. In practice, however, the renal criteria used by individual units varied widely (table 2). The majority of units (5/7) used creatinine clearance in preference to serum creatinine (2/7) or a formal measure of glomerular filtration rate (2/7). For those units measuring creatinine clearance, the lower limit for acceptance onto the waiting list ranged from 30 ml/min (1/7), 40 ml/min (1/7) to 50 ml/min (3/7). For the two units using serum creatinine, the acceptable upper limit was 100 μmol/L in one unit, and 200 μmol/L in the other. The cut-offs for glomerular filtration rates were < 50 ml/min (1/7) and < 40 ml/min (1/7). One unit did not use absolute values of renal function as a contraindication to heart only transplantation.

Three units had written protocols for exclusion from the heart only waiting list. No unit had formal criteria for placing patients on a waiting list for combined heart and kidney transplantation. The very small number of such candidates was cited by four co-ordinators as the main reason for not establishing formal criteria; the division of the decision-making process between separate heart and kidney transplant teams was cited by two respondents. All respondents described the scarcity of donor organs as forcing a move away from exploring combined organ transplantation as an option in more patients.

Figure 1. Kaplan-Meier survival curve showing outcome of combined heart and kidney transplants



The outcome of each of the 28 combined heart and kidney transplants is summarised in table 3, and as a survival curve in figure 1. Of the 28 combined transplants, 82% (23/28) of the patients were male and the mean age was 44.4 (range 11–63). The 30-day mortality was 14% (4/28) and survival at one, three, five and 10 years was 66.5 (95% confidence interval 57.3–75.7), 50.2 (40.3–60.1), 45.6 (35.6–55.7), and 30.8 (19.2–42.4) respectively. There were no data available on organ rejection-free periods and the mortality data from UKT was not unit-specific. The 28 combined heart and kidney transplants represent less than 0.1% of the total number of the heart transplants performed in the United Kingdom in the same period.

Discussion

The first successful combined heart-kidney transplant was reported in 1986,[9] and was followed in the literature by a number of case series.[1,10-18, 21] While it has become apparent that renal failure

Table 3. Combined thoracic and kidney transplants, UK and Republic of Ireland

Date of transplant	Organ	Patient survival (days)	Graft survival (days)	Graft status
11.11.1995	heart/lung		1,881	functioning
	kidney		1,776	functioning
30.3.1986	heart		5,181	functioning
	kidney+			
7.7.1994	heart		2,454	functioning
	kidney		2,566	functioning
30.6.1988	heart	879	879	failed?/died
	kidney	879	704	failed/died
31.7.1990	heart		4,003	functioning
	kidney		1,959	functioning
4.3.1991	heart		3,496	functioning
	kidney		1,611	functioning
6.3.1991	heart	381	381	failed/died
	kidney	381	381	died wfg*
10.1.1991	heart	3,685	3,462	died
	kidney	3,685	1,832	died
2.8.1991	heart		2,180	functioning
	kidney		1,644	functioning
13.11.1992	heart	131	131	failed/died
	kidney	131	131	died wfg*
22.10.1993	heart/lung	1	1	failed/died
	kidney	1	1	died wfg*
9.7.1994	heart	180	180	failed/died
	kidney	180	180	failed/died
14.10.1992	heart		3,291	functioning
	kidney		3,246	functioning
29.5.1997	heart	13	13	failed?/died
	kidney	13	13	failed/died
1.1.1998	heart		1,055	functioning
	kidney+			
30.7.1994	heart	1,067	1,067	died wfg*
	kidney	1,067	1,067	died wfg*
10.11.1994	heart		1,847	failed
	kidney		1,847	failed
24.4.1996	heart	46	46	failed?/died
	kidney	46	46	failed?/died
2.6.1996	heart		1,847	functioning
	kidney		1	failed
7.9.1998	heart	115	115	died wfg*
	kidney	115	115	died wfg*
28.6.1997	heart		1,434	functioning
	kidney+			
23.7.1998	heart		1,065	functioning
	kidney		1,065	functioning
7.3.1999	heart		746	functioning
	kidney		746	functioning
26.7.1999	heart	2	2	failed/died
	kidney	2	2	died wfg*
12.2.2001	heart		86	functioning
	kidney		73	functioning
21.4.2001	heart		93	functioning
	kidney		83	functioning
15.5.2001	heart	5	5	failed?/died
	kidney	5	5	failed?/died
3.10.2001	heart+			
	kidney+			

Key: * wfg = with functioning graft; + = no follow-up

Key messages

- Combined heart and kidney transplantation is an appropriate option for a select group of patients
- Few units have established formal criteria for the indications for combined heart and kidney transplantation; the renal criteria used by individual units vary widely
- Survival rates in the UK for combined heart and kidney transplantation are substantially lower than those for unmatched heart transplantation
- The scarcity of donor organs mean very few combined heart and kidney transplants take place in the UK

is no longer an absolute contraindication to heart transplantation, there is still no clear consensus as to the indications for combined heart and kidney transplantation. As the number of patients eligible for transplantation expands in response to advances in therapeutics, and the shortage of suitable organs worsens, the clinical questions of if and when this is an appropriate procedure are complicated by ethical issues of organ availability.

The largest study describing the outcomes of combined heart and kidney transplantation showed no statistically significant difference between survival at 24 months in 82 patients undergoing combined heart and kidney transplantation and unmatched patients undergoing isolated heart transplantation.[15] This is not the case in the UK where survival figures for combined heart and kidney transplantation are substantially lower than those for unmatched isolated heart transplantation. One, three and five-year survivals for isolated heart transplantation from UK Transplant are 83 (95% confidence intervals 79–86), 73 (69–76) and 66 (62–69) respectively.[20] Published single centre data on combined heart and kidney transplantation is significantly better than the collated UK survival data. This suggests that with optimal patient selection and management, survival figures closer to those for heart transplantation alone could be achieved.[16] It remains unclear what the procedure of choice is in patients with renal failure due to cardiac insufficiency. A prospective, controlled trial is needed to address these issues. Such a study remains extremely unlikely in the context of the increasing scarcity of organ donors and the small numbers of potential patients. At a minimum, a detailed case-controlled, retrospective comparison should be made between the 28 combined heart and kidney transplant recipients and isolated heart transplant recipients, matched for both levels and underlying cause of renal dysfunction, to determine the best management of patients with renal failure due to cardiac insufficiency.

Acknowledgements

We are grateful to Philip Pocock at United Kingdom Transplant for providing access to the UKT database, and the transplant

units who provided data for this study. We thank Drs Henry Purcell and Peter Andrews for suggesting this study and for helpful comments.

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