MEDICAL PRACTICE

*Contemporary Themes***Selection and procurement of hearts for transplantation**

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Abstract

The success of orthotopic heart transplantation depends wholly on satisfactory function of the new heart on completion of the operation. This in turn depends on the quality of the donor heart before its removal, the effectiveness of the methods used to preserve it during transport from the donor to the recipient hospital, and the accuracy of the operative procedure. From January 1979 to December 1983, 62 donor hearts were transplanted into 61 recipients at Papworth Hospital. These hearts were selected from 250 offered for consideration. The most common reasons for not proceeding with an initial inquiry were failure of the donor to meet the medical criteria for selection (77 cases) and lack of intensive care facilities or staff shortages such that a transplant could not be accommodated at the time of inquiry (80). Eight early deaths occurred, of which three were due to primary failure of the donor heart. Actual one and three year survivals for the whole programme were 58% and 50% respectively, the current actual one year survival being 70%.

Forty per cent of patients selected for transplantation died while waiting for a heart to become available. Their average survival time was 46 days.

The number of donor hearts referred for transplantation depends on public attitudes towards organ transplantation, the willingness of doctors looking after brain dead patients to seek permission from relatives for the heart to be donated, and the cooperation of local

kidney transplant surgeons. A larger number of suitable donor hearts to choose from would enable more patients to be treated, as transplant operations could be arranged so that existing facilities were used to their maximum capacity.

Introduction

A successful, active cardiac transplant programme requires an adequate supply of suitable donor hearts. The ability to diagnose brain stem death accurately and with confidence is essential.¹ Doctors must be willing to ask for the organ to be donated once brain death has occurred, and relatives need to agree. Likewise the good will of kidney transplant surgeons, without whose cooperation the acquisition of donor hearts would be impossible, is most important. Finally, now that the concept of obtaining donor hearts from hospitals far distant from the transplant centre is firmly established^{2,3} there is a continuing need for improved methods of myocardial preservation.

This paper describes our experience during the past five years.

Patients and methods**SELECTION CRITERIA**

Just as potential recipients of heart transplants need careful selection, so do cardiac donors need to satisfy specific criteria. The prevalence of undetected coronary disease in the general population has made us unwilling to accept hearts from patients older than 35. Another reason for using hearts from young donors has been the demonstration by the Stanford group that accelerated graft arteriosclerosis tends to develop more rapidly in recipients of hearts from donors aged over 35.⁴ Compatibility of the size of the heart between recipient and donor is also occasionally a consideration: generally it is impracticable to consider hearts from donors aged less than 15 for a normal sized adult recipient. ABO blood group compatibility is essential. A negative cross match between donor lymphocytes and recipient serum is necessary before transplantation unless the recipient has previously been shown to have no preformed cytotoxic antibodies

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to a wide panel of different serum samples. Tissue typing is performed on all recipients and donors, but we do not at present regard HLA and DR mismatching as a contraindication, and usually there are more important factors that determine which particular recipient a donor heart should be used for.

Relevant medical information about the donor is obtained by telephone at the time of initial referral. There should be no history of cardiac disease, systemic infection, or malignancy other than primary cerebral tumour. Severe chest trauma may preclude donation of the heart, although a decision on this will usually be deferred until after the heart has been inspected. A brief period of cardiac arrest at the time of injury or during resuscitation is not necessarily a contraindication, providing a stable circulation is subsequently restored. This should be achieved, however, without dependence on high dose inotropic support, which undoubtedly impairs the performance of a heart after transplantation.

DIAGNOSIS OF BRAIN DEATH

Brain death is diagnosed by doctors entirely independent of the transplant team and according to the criteria defined by the conference of medical royal colleges and their faculties in the United Kingdom in 1976.¹ This report and its 1979 addendum⁵ and the general acceptance of their conclusions by the medical profession set the scene for the greater availability of suitable donor hearts. The final decision, however, rests with the relatives of the potential donor, who must give free consent before any organs are removed for transplantation. Many of the hearts offered to us have come as a direct result of relatives agreeing to the donation of kidneys and then asking specifically whether use might also be made of the heart or other organs.

THE DONOR OPERATION

When an offer of a suitable donor heart is received arrangements are made to admit a recipient of appropriate blood group. Normally the patient chosen is the one who has been waiting longest, but occasionally we disregard priority on the waiting list if we know that the condition of a particular recipient is deteriorating rapidly.

Management of the haemodynamic state of the donor after the diagnosis of brain death generally remains with the local clinician in charge. Ventilation is continued, and any tendency to hypotension is treated initially by infusion of large volumes of crystalloid or colloid solutions.⁶ Only in the rare instances of failure to respond to increased fluid replacement is inotropic support in the form of a dopamine infusion resorted to, and this preferably only as a temporary measure. Antibiotics are continued and vasopressin given if diabetes insipidus develops.

All operations to remove the heart from the donor have been undertaken in the referring hospital. The team, comprising surgeon, theatre nurse, and technician, goes to the hospital, where the final evaluation of the cardiovascular state of the donor is made. This includes a review of the medical notes, a careful physical examination, and inspection of a recent electrocardiogram and chest radiograph.

The time when the operation on the donor is started depends on the preparation of the recipient after his admission to Papworth and the expected transportation time between the donor hospital and Papworth. Unless previous cardiac surgery has been performed the recipient is not usually anaesthetised until the donor heart has been inspected and safely removed.

If, as is usually the case, the kidneys are also to be used for transplantation the local kidney transplant surgeon first mobilises these individually, but he does not cross clamp the abdominal aorta until the heart has been excised. This is accomplished after systemic heparinisation and during venous inflow occlusion; the aortic root is then perfused with one litre of cold cardioplegic solution. The heart is removed and cooled rapidly by serial passage through bowls of cold saline and stored in a sterile plastic bag containing cardioplegic solution at 2-4°C, which in turn is placed in a Coolbox in which the temperature is regulated. This method of preserving the heart has been shown to be safe experimentally for ischaemic periods of up to 16 hours,⁷ but in clinical practice we would not wish to exceed four hours. It should be emphasised that the quality of the heart at the time of removal, which has to be considered with regard to the particular characteristics, such as size and pulmonary vascular resistance, of the recipient for whom it is intended, is just as important as the duration of subsequent ischaemia, if not more so.

Results

During the period January 1979 to December 1983, 250 inquiries concerning cardiac donation were received by Papworth Hospital. Sixty two of these hearts were used for 61 recipients, one patient undergoing retransplantation three years after his original operation because of the development of coronary arterial disease in the transplanted heart. All but one of the 62 donor hearts came from within the United Kingdom (figure). Donor hearts were brought to Papworth by road in 15 instances and by a combination of road and air transport in the remainder. Transport arrangements were usually coordinated with the aid of the United Kingdom Transplant Services in Bristol. The total time for which the donor heart is ischaemic, which includes the time for excision, transportation, and implantation, depends chiefly on travel time and has varied from 96 to 252 minutes (mean 164 minutes).

We were unable to proceed with 188 inquiries about possible heart donation. Although 77 potential donors were rejected on the basis of not fulfilling the necessary medical criteria (chiefly being the wrong age or showing haemodynamic instability), a further 80 hearts could have been used had it not been for insufficient local facilities, chiefly lack of a transplant cubicle or pressure on beds in the intensive care unit (55 occasions), or insufficient trained nursing or medical staff to look after the patient (25 occasions). Permission to remove the heart for the purpose of transplantation was not forthcoming on 19 occasions, and in nine instances there was insufficient time between the offer of the heart and the time proposed for removal of the other organs to enable a potential recipient to be admitted and the surgical team to arrive at the donor hospital in time. Three hearts were rejected for miscellaneous reasons.

The table shows the age, sex, blood group, and cause of death of the donors from whom hearts were obtained. Details from inquiries about the 188 hearts that were not used are also included when known. Cerebral trauma, usually as a result of road traffic accidents, a high proportion of which were motorcycle accidents, was by far the commonest cause of brain death. Many patients with cerebral trauma had severe associated skeletal and soft tissue injuries. Other less common causes of brain death included spontaneous intracranial haemorrhage, respiratory arrest, and primary brain tumour.

Other donor organs removed concurrently with the hearts included

Origin of donor hearts.

122 kidneys (of which two were not suitable for transplantation), three livers, six pancreases, and 52 corneas. The early function of kidneys transplanted from multiorgan donors has been no different from that of those from kidney only donors.⁸ Likewise, the function of the transplanted hearts has been satisfactory in all cases except three. In retrospect these three cases were avoidable errors of judgment. One heart was taken from a donor with a primary brain tumour and associated severe cachexia requiring considerable inotropic support at the time of removal; it subsequently failed to function satisfactorily. Another heart had a congenital anomaly comprising atresia of the ostium of the coronary sinus with anomalous drainage to the innominate vein. This was not detected at the time of removal or insertion of the heart, and the patient died six days later from low cardiac output due to progressive myocardial oedema. The third case was an emergency in which the prospective recipient was being maintained with an intra-aortic balloon pump with supportive partial cardiopulmonary bypass. In full knowledge of the potential risks we accepted a heart from a 45 year old donor who had died as a result of accidental ergot poisoning. This heart never worked well, and the patient died 13 days later. Another patient, with moderately increased pulmonary vascular resistance, received a rather small heart, which, though its early function was good, remained dependent on isoprenaline support and failed after three weeks when affected by a rejection episode that in other circumstances should have been reversible. These deaths, when added to a further four early deaths unrelated to function of the donor heart, result in an early postoperative mortality, defined as death at or within 30 days of transplantation, of 13%. There have been 15 further deaths between five weeks and three years after transplantation, so that 38 of the 61 patients are currently alive. Figures for survival at one and three years are 58% and 50%, respectively for the whole programme; our current actual survival at one year is 70%.

Characteristics of population offering cardiac donation

	Hearts used	Hearts not used
Mean age (and range) (years)	23 (15-45)	24 (8-53)
Sex:		
Male	47	104
Female	15	66
Unknown		18
Blood group:		
O	24	45
A	32	84
B	6	14
AB		5
Unknown		40
Cause of death:		
Cerebral trauma	44	102
Intracranial haemorrhage	9	41
Respiratory arrest	6	9
Primary brain tumour	3	3
Overdose		5
Miscellaneous		7
Unknown		21
Total	62	188

Discussion

Unlike other forms of transplantation, when, for example, if a kidney fails to function the patient can be given dialysis until recovery occurs, the heart must work satisfactorily as soon as the operation has been completed. By careful selection and preservation of donor organs, followed by scrupulous attention to operative detail, the early function of the transplanted heart should be excellent and perioperative mortality low. Some of the patients have been moribund at the time of transplantation, and it has been gratifying to observe how rapidly organ systems previously compromised by severe chronic congestive cardiac failure can recover after a normal cardiac output has been established. The importance of an adequate supply of suitable donor hearts and the events surrounding the donor operation are therefore readily apparent.

Initially, we had extreme difficulty in obtaining donor hearts. Some kidney transplant surgeons were understandably apprehensive about the reintroduction of heart transplantation in Britain and the adverse effect this might have on the supply of kidneys. Others, however, were more cooperative, and as

general confidence in the procedure grew so too did the offers of donor hearts.

Public opinion has inevitably also been an important factor. During 1979 we were able to perform only three transplant operations, but when two of these were seen to be successful, with the patients obviously enjoying a return to normal activities, we began to receive offers of donor hearts that arose specifically as a result of relatives requesting that this be considered after they had agreed to kidney donation. Conversely, the *Panorama* programme on television in September 1980, which in a most irresponsible yet effective way cast doubt on the British criteria for the diagnosis of brain death, resulted in a considerable reduction in referral of all organs for transplantation, which took more than a year to recover from.

The size of the potential donor pool for cardiac transplantation is difficult to assess. Most donors die as a result of road traffic accidents, and in England and Wales in 1980 there were nearly 6000 deaths from this cause. Of these, perhaps one quarter were in the age group 15-35 years, and half of these were a direct result of cerebral trauma. Although many of these potential donors might not be suitable for cardiac transplantation, there must be many more than are currently being referred to this hospital—that is, 250 in five years.

We acknowledge that seeking permission from distressed relatives for organs to be donated can be a difficult task and that, if permission is granted, the subsequent referral to a transplant centre entails extra work for the local medical and nursing staff. The justification can only be that other patients stand to benefit from the generosity of spirit that is associated with organ donation. For our part, although we are obviously never in a position to ask directly for hearts to be donated, we have tried to facilitate procedures for doctors referring organs by distributing widely to appropriate centres a booklet (available on request from Papworth Hospital) outlining our criteria for selection and other requirements and also by ensuring that telephone inquiries are dealt with quickly.

If the present number of referrals of donor hearts could be increased this would be of great benefit. Having more hearts to choose from would allow our limited resources to be used more effectively as transplant operations could be spaced more efficiently. At present many weeks may go by without an offer of a donor heart, only to be followed by perhaps three offers within 10 days, all of which we feel obliged to use in the knowledge of the continuing unpredictable supply. With such increased efficiency, more patients could be treated and we could go some way towards rectifying the present situation in which 40% of the patients selected for heart transplantation die on our waiting list.

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