Combined heart and kidney transplantation

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The first reported combined heart and kidney transplant occurred in 1978.[1] The patient died of gram negative sepsis 15 days after transplantation. It was not until 1986 that a case was reported with long-term (> 18-month) survival.[2] Since that time, there have been more than 40 publications examining the pros and cons of simultaneous heart and kidney transplantation. Initial reports consisted mainly of small case series demonstrating proof of concept and adequate 1–3 year survival, mostly in line with that of heart transplantation alone.[3-5] Later it was noted that simultaneous transplantation seemed to protect against rejection of the heart transplant (although different immunosuppressive protocols were frequently employed) and that rejection of one organ often occurred independently of immunological damage to the other.[4,6] More recently, a number of papers have examined the ethics of organ allocation and the use of cyclosporin-sparing immunosuppressive regimes to minimise renal toxicity following transplantation.[7]

Outcomes of combined transplantation

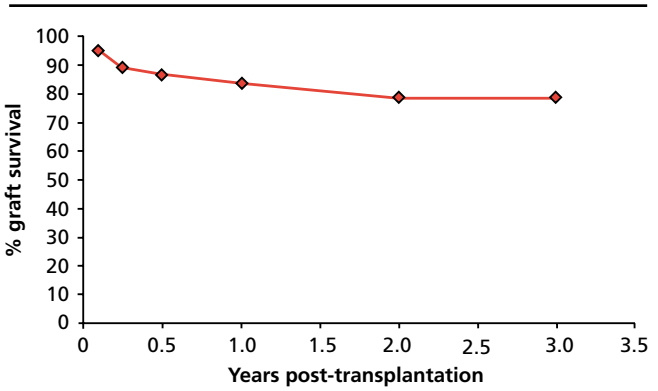
In recent reviews of more than 100 historical cases, actuarial survival of the combined transplants averaged 67% at two years, which is similar to results for isolated heart transplantation but shorter than for isolated kidney transplantation (mean survival approximately 85%)[6,8] (figure 1). Long-term follow-up data from the modern era are, however, scarce. This, together with the scarcity of donor organs and uncertainty about the precise indications for combined organ transplantation, have led some to argue that combined transplantation should not be undertaken.[9] This is a complex issue beyond the scope of this editorial. However, it should be noted that there are many circumstances in which organs are transplanted to patients with known risk factors for premature graft failure, so survival cannot be the sole discriminator in this debate.

Indications for combined transplantation

Two main patient groups have been considered for combined transplantation:

1. Patients with end-stage heart disease and fixed (irreversible) renal disease; and,
2. Patients with end-stage renal disease and severe cardiac disease not amenable to other treatment.

Figure 1. Actuarial graft survival of combined heart and kidney transplantation



Adapted from Castillo-Lugo JA, Brinker KR[8]

In practice, the vast majority of combined transplants have come from group 1 and the underlying cardiac disease has usually been cardiomyopathy or coronary ischaemia. The published literature has rarely distinguished between these two groups, however, and it is not possible to determine whether survival outcome differs between them.

The selection of candidates for combined transplantation is fraught with difficulty. For example, in group 1, renal

impairment is often due to pre-renal failure or pump failure, both of which may reverse after isolated heart transplantation. While combined heart and kidney transplantation has obvious advantages, technical difficulties and the shortage of donor kidneys mandate that dual transplantation be avoided unless it is certain that native kidney function has truly failed. The problem is to define the selection criteria for a combined transplant and the cut-off for renal function, above which simultaneous transplantation is precluded. While guidelines are available from UK Transplant, these are couched in very vague terms and are only advisory.[10]

Conversely, in group 2, most nephrologists recognise the role of intravascular volume overload as a major cause of the cardiac dysfunction seen in patients on dialysis. For many patients with apparent two organ failure, isolated kidney transplantation significantly improves cardiac dysfunction through an improvement in salt and water balance, and possibly from improvement of direct uraemic cardiotoxicity (still debated). Single transplantation may also reduce arteriovenous shunting, improve blood pressure control, and assist the correction of anaemia. Many patients considered for dual transplantation may, therefore, not require a combined approach. A policy of sequential kidney followed (if necessary) by heart transplantation may be more logical in these circumstances.

The UK experience

In this edition of *The British Journal of Cardiology*, Chickwe and Pepper (see pages 519–23) present the UK experience of simultaneous heart-kidney transplantation. The paper raises a number of important issues. First, it (somewhat controversially) suggests that the outcome of combined transplantation in the UK does not compare well with published single centre series in the USA and Europe. This may reflect publication bias, with transplant centres tending to only report better outcomes. Indeed, only 40–50% of all combined transplants reported to national registries ever make their way into the published literature.[4] However, there are alternative explanations. Patients may have been selected differently – if so, are the criteria currently applied in the UK sufficiently robust? The differences may reflect different immunosuppressive protocols or immunological factors – can anything be learnt from this? More worryingly, the differences may reflect the small numbers of combined transplants performed at each transplant centre in the UK, with learning curves that are never fully scaled. Such a scenario would argue strongly that combined transplantation should be centralised into a smaller number of transplant centres. As suggested by Chikwe and Pepper, a case control study might be an appropriate way to investigate this further.

A second issue relates to the way in which patients are currently selected for combined transplantation. It is clear that transplant units adopt their own, arbitrary criteria for acceptable pre-transplant renal function, rather than following a national guideline. This needs to be reconsidered, especially since several units do not appear to use accurate isotopic or inulin-based measurements of glomerular filtration rate in their pre-transplant assessment.

Third, there has been very little debate within the UK with regard to organ allocation for simultaneous transplantation. Given the increasing transplant waiting lists, is it appropriate that kidneys (for example) be allocated for combined transplantation, especially when they will be of a superior quality to much of the remaining (kidney) transplant pool? The present paper does not directly address this issue and it would be instructive for further work to include details of patient diagnosis at the time of entry onto the transplant waiting list, and any ethical review undertaken as part of pre-transplant work-up.

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