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(Accepted 9 December 1988)

Transplants from living donors in the United Kingdom and Ireland: a centre survey

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Abstract

A survey was carried out to determine for the first time the extent of transplantation from living donors in the United Kingdom and Republic of Ireland and the views of transplant surgeons regarding future developments. Questionnaires were sent to 32 transplant centres representing 18 health regions and covered their extent of experience of transplantation, sources of donors, ages of donors and recipients, outcome of transplantation, and views on expansion of living donor transplantation services. Replies received from 27 transplant centres representing 17 health regions gave data on more than 1200 transplants from living donors. Transplants from living donors accounted for 0-25% of the total experience of health regions. Two centres had abandoned living donor transplantation. Sixty per cent of transplant surgeons favoured expansion of the living donor programme to meet a shortage of kidneys from

cadavers, and the remainder thought that existing programmes were optimal.

Living donor transplantation promises to be an important factor in the future planning of health care resources.

Introduction

When reviewing kidney transplantation in Leicester during 1987 we found a reduction in the number of transplants (table) consequent on a diminishing supply of donor organs despite vigorous campaigns to encourage organ donation. No transplantations from living donors had been performed in the area since 1984 even though seven of the eight previous recipients had functioning grafts. Possible reasons for the decline in transplantations from living donors were the excellent survival of patients with grafts from cadavers after treatment with cyclosporin, uncertainty over the long

	From cadavers	From living donors
1975	5	
1976	6	
1977	13	
1978	17	1
1979	10	
1980	17	
1981	14	
1982	28	1
1983	41	1
1984	43	5
1985	38	
1986	51	
1987	38	

term effects of nephrectomy in donors, and the expectation that most patients would get a kidney from a cadaver soon after starting dialysis. In our review we found that patients received dialysis for an average of two years before transplantation.

Before considering an expansion of our living donor transplantation programme we decided to check how other centres were coping with this problem and first contacted the United Kingdom Transplant Service. Though it did not have a register of data on living donor transplants, it confirmed that the plateau in the supply of kidneys from cadavers and increasing demand for transplants in Leicester were reflected in national statistics.¹²

National comparisons can be made of living donor transplantation within Europe.³ Of the 14 000 kidneys transplanted in the United Kingdom, 10-12% have been from live donors. Countries in Europe vary enormously in their use of living donor transplantation to cope with their waiting lists for transplants. Often the percentage of kidneys from living donors is influenced by cultural and religious views or the acceptance of criteria for brain death. In Greece and Turkey living donors supply 60-90% of all transplants, whereas in Spain they supply 6%³; in the United States living donors supply 32% of all transplants.^{4,5} In view of these large differences we conducted a survey of living donor transplantation among centres in the British Isles.

Methods

In July 1987 questionnaires were sent to 32 transplant centres in 17 health regions in the United Kingdom and to the Republic of Ireland. The following topics were covered: date of first transplantation from a living donor; extent of transplantation experience; source of donors; ages of donors and recipients; outcome of transplantations; and views on expansion of the living donor transplantation programme. As there was no readily available information on the catchment area for donors for each renal transplant unit the centres were asked to define their boundaries.

Analysis of survival of grafts was complicated by the fact that the date of failure had not always been accurately recorded. The construction of survival curves based on such data has been discussed by Peto.⁶ Our method was similar to that advocated by Peto but reduced computation time by grouping the time scale. As most centres did not separate technical failures from those due to rejection all failures were grouped together. Grafts that were functioning when patients died were regarded as lost to follow up.

Results

Of the 32 transplant centres contacted, 27 replied, representing 17 health regions (including the Republic of Ireland). The data that were supplied varied enormously among centres but represented over 1200 transplants. Seven transplant centres gave information on transplants from living donors only as a percentage of their total transplants (including some transplants for temporary residents), and one centre gave a cumulative result for survival of 334 transplants from living donors. Altogether 654 transplantations were recorded in sufficient detail to permit analyses of source of donor and length of survival.

Though transplantation from living donors was first performed in Edinburgh and London in 1960, by far the greatest experience (334 transplants since 1968) has been in the south Thames area, based mainly on the transplant units of Guy's and Dulwich Hospitals. The next largest centre was Dublin with 134 transplants,

followed by Liverpool (119) and Newcastle upon Tyne (110). Two transplant units, Leicester and Sheffield, had abandoned living donor transplantation in favour of transplants from cadavers. The regional difference in experience of transplantation from living donors is best illustrated by the geographical distribution of the procedure (fig 1). It accounted for up to 25% of total transplantations among health regions, the lowest figures being found in the Midlands.

FIG 1—Transplantation centres and their catchment areas. Circles indicate locations of centres; numbers within circles are percentage of living donor transplantations performed each year. Figures for the Thames areas include 11 transplant centres. Replies from South Thames areas were pooled. —=Boundaries of health region; ----=boundaries of catchment area of centre

Of the 654 transplants from living donors, most were from the siblings (369; 56%), parents (249; 38%), and children (16; 2%) of recipients. The relationship of seven (1%) donors was unknown, and five twins, three uncles or aunts, one niece, and four unrelated donors represented <1% each of transplants.

Though the ages of most recipients were known, the ages of less than half of the donors had been recorded. Most recipients were aged 25-34, as were the donors, although the overall trend was for donors to be older than recipients.

Survival was based on known survival time in 102 of

FIG 2—Estimated survival of kidney grafts from all, sibling, and parent living donors. Estimates based on known survival time in 102 of 142 failures among 609 transplants

142 failures among 609 cases for which we had information. Figure 2 shows that an estimated 89% of grafts survived after one year, 76% after five years, and 66% after 10 years. Long term graft survival was better for kidneys donated by siblings than by parents. Data were insufficient for us to construct survival curves for grafts from other groups of donors. The worst results were among the recipients aged under 24, and results were surprisingly good in recipients aged over 49 (fig 3).

FIG 3—Estimated survival of kidney grafts from living donors according to age of recipient. Estimates based on known survival time in 102 of 142 failures among 609 transplants

Centres were invited to comment on the expansion of living donor transplantation. Most (60%) centres commented that it should be expanded to cope with the shortfall of kidneys from cadavers. Some centres stated limitations: one would consider living donor transplantation only for children and another only for identical twins, though two centres were considering transplantation from unrelated donors, usually spouses.

Discussion

Although the information requested in this survey was not detailed, the response is comparable with that in recent American studies.⁵ Our findings reinforce recent recommendations for better data on availability of donors within different district health authorities.⁷ The Department of Health does not have an accurate map of the catchment areas of each transplant unit. Though many transplant centres cover an area that coincides with the boundaries of the health district, some do not. We believe that our map (fig 2) is the first compilation of areas for retrieval of cadavers as recognised by transplant coordinators. With the emergence of smaller transplant centres the renal unit may treat patients from a large district and the regional neurosurgical unit may lie in a separate district, as is the case for Leicester. Organs are shared equitably as a result of a local rather than a national agreement. Transplant centres that have a large population receiving dialysis but lack a major donor centre because of geographical boundaries may need to make greater use of living donor transplantation if waiting lists are to be kept to reasonable levels.

A great deal can be learnt from a collaborative experience in transplantation. Even from our limited analysis it was clear that grafts from siblings fare much better in the long term than those from parents, which confirms the findings in large series in the United States and Europe.^{8,9} Poor long term survival of grafts was found among younger recipients (aged under 24).

The relative age difference between donor and recipient may be important in future planning. Few centres were prepared to transplant a child's kidney to an adult, and most sibling donors had an age difference of no more than 10 years from their recipient. Centres may favour different matching and treatment regimens, such as donor specific transfusion.¹⁰ An awareness of these differences among centres has been of benefit in transplantation from cadavers, and information should clearly be shared if transplantation from living donors is to expand more widely.^{11,12}

If living donor transplantation is to be more widely accepted then both doctors and patients need to be familiar with its potential benefits and hazards. The advantages may be seen as excellent survival of grafts, short waiting time, and a cost saving to the NHS. Despite the advances in immunosuppressive treatment over the past 20 years the survival of transplants from cadavers with cyclosporin treatment is only now approaching the one year survival of 80-90% obtained with transplants from living donors.¹³

The excellent long term results of living donor transplantation shown in this study (60% survival at 20 years) is in contrast to the poor long term results predicted for transplants from cadavers in patients treated with azathioprine and cyclosporin.¹⁴ National statistics show that many patients wait more than two years for a reasonably matched kidney from a cadaver.¹⁴ Prolonged dialysis is expensive both financially and in terms of hardship to the family.^{15,16} A successful transplant saves the NHS £30 000,¹⁷ and on average it costs less than £500 for routine investigations (for example, intravenous urography, renal arteriography) of a potential donor.¹⁸

The disadvantages of living donor transplantation have been well established in American series and relate mainly to the risk of mortality or morbidity in the donor.^{19,21} Though one in 1600 donors die after nephrectomy,⁵ this risk has been estimated to be less than that of dying from a road traffic accident. Postoperative morbidity has been estimated to be 1-2%, the main problems being deep venous thrombosis, pulmonary embolism, and wound infection.^{11,18,20} The longer term consequences of donating a kidney have been investigated intensively over the past few years.²²⁻²⁵ Recent reviews of 25 years of follow up found no significant risk to the donor in surviving with a single kidney provided that recognised criteria for selection had been used.^{5,24,25} Though proteinuria has been found in one third of donors, it is non-progressive and believed to be related to hereditary factors.⁵ Only two of almost 10 000 living donors have been reported to have developed end stage renal failure.²⁴

An expansion of living donor transplantation could take place in two stages. Firstly, relatives could, depending on their cultural and religious views, be routinely screened as possible donors. Secondly, family members other than blood relatives could be considered as a source of kidneys. The prospect of using an unrelated living donor has been widely discussed in recent years, but the debate that rightly outlawed payment for transplantation cast a shadow over the ethics of expanding living donor transplant programmes.^{26,27}

The spouse most commonly carries the burden of the ailing patient and has most to gain from the wellbeing that a successful transplant restores. Recent studies suggest that spouse to spouse kidney transplantation with combined immunosuppressive treatment can result in excellent graft function.²⁸ In the United States 16% of transplant centres surveyed used living donors who were not blood relatives; 40% were prepared to consider spouse to spouse donation.¹⁹ Provided that families can be given adequate information and support and donors are carefully selected⁵

the option of renal transplantation from living donors should be more widely discussed.

We thank the many clinicians and transplant coordinators who contributed to this survey and Mrs Carole Austin, who typed the manuscript.

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(Accepted 23 November 1988)

Human gastric mucosal bleeding induced by low dose aspirin, but not warfarin

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Abstract

Objective—To investigate the suitability of treatment with low dose aspirin or warfarin, or both, as possible prophylaxis against cardiovascular disease by determining the effect on gastric mucosal bleeding.

Design—Randomised crossover trial.

Setting—Academic department of therapeutics.

Subjects—Twenty healthy male volunteers aged 19-22.

Interventions—On separate occasions and in randomised order all subjects received aspirin 75 mg, warfarin, or aspirin 75 mg combined with warfarin. Each treatment was given for 12 days or (when warfarin was used) for longer if necessary until the international normalised ratio of the prothrombin time was stable at 1.4-1.6.

End point—Loss of blood over 10 minutes into gastric washings.

Measurements and main results—Bleeding over 10 minutes into gastric washings under baseline conditions and after five days, and at end of each regimen of treatment. Aspirin 75 mg increased bleeding from 0.60 (95% confidence interval 0.36 to 0.99) $\mu\text{l}/10$ minutes to 1.26 (0.71 to 2.25) $\mu\text{l}/10$ minutes at five days, with no evidence of either progressive change or adaptation thereafter. Warfarin had no effect on bleeding either alone or when combined with aspirin.

Conclusions—Aspirin 75 mg causes gastric mucosal bleeding. Low dose warfarin neither induces gastric mucosal bleeding nor enhances that caused by aspirin.

Introduction

Thrombosis is a common feature of both unstable angina and death from ischaemic heart disease and unstable angina. This may be related to enhanced

platelet activity^{1,2} or increased amounts of fibrinogen and factor VII, which have been associated with fatal and non-fatal ischaemic heart disease.³⁻⁶ The effect that aspirin has on the function of platelets has been shown to reduce morbidity and mortality in patients with unstable angina and myocardial infarction and to be probably beneficial in the primary and secondary prevention of myocardial infarction.⁷⁻²⁰ Trials have tended to use progressively lower doses of aspirin as these cause maximum inhibition of synthesis of thromboxane by platelets, have a minimal effect on synthesis of prostacyclin by vessel walls, and substantially prolong the bleeding time.²¹⁻²³ For these reasons doses of aspirin of less than 100 mg a day might theoretically be more effective than higher doses, but for the same reasons they might render patients prone to bleeding that is also seen with higher doses.⁷⁻²⁰

Anticoagulant treatment with warfarin has also been used to prevent myocardial infarction. Although it is probably beneficial,²⁴ its continued use causes a progressive increase in bleeding.²⁵ An alternative approach is to use lower doses to normalise the increased activity of factor VII found in patients prone to vascular disease,⁶ but whether this would cause less bleeding is as yet unproved.

Possibly optimum benefit would accrue from combining low doses of aspirin and warfarin, and this approach is to be investigated by the Medical Research Council in a large community based study.²⁶ Because a combination of treatments has the potential to enhance harm (particularly gastrointestinal bleeding) as much as benefit we investigated the effect of low doses of aspirin and warfarin, alone and in combination, on gastric mucosal bleeding.

Subjects and methods

Twenty healthy non-smoking male volunteers aged 19 to 22 participated in the study. They did not have a

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Br Med J 1989;298:493-6