PART III

TRANSPLANTATION  CLINICAL REPORTS

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Renal Transplantation as the Method of Choice for Treatment of Chronic Renal Failure

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Introduction

With the progressive development of dialysis facilities and increasing transplantation activity, different programmes for the treatment of terminal renal failure have been elaborated in different countries and in different kidney centres, either with a more or less integrated programme of treatment as in Boston (Lowrie et al, 1973) and Australia (Mathew et al, 1975) or a more or less competitive programme between dialysis and transplantation as in Germany. This has influenced both the selection of patients and the choice of treatment, which makes a direct comparison of results achieved by the two methods of treatment hard to make.

In Göteborg the clinical renal transplantation programme was started in January 1965 with the support of two sets of dialysis equipment. With this shortage of dialysis facilities the only alternative to death of the patient was renal transplantation. Renal transplantation was therefore, from the very start, taken as the method of choice for the treatment of patients with terminal renal failure and this principle was quite stable for the ten year period 1965–1975. Progressive development of dialysis capacity and increasing confidence in transplantation led to a rapid increase in the total number of patients demanding kidney transplantation, which is illustrated in Figure 1. A balance between the demands for and the possibility of performing renal transplantation was reached during the spring of 1974 and was valid also for 1975. This balance was true for the country as a whole and has in consequence both shortened the waiting time for a kidney graft and increased the possibility of a choice of treatment. Therefore the period from January 1965 until July 1975 represents a unique period in our programme for the evaluation of renal transplantation as the only definite method of treatment.
MATERIAL AND METHODS

Selection of recipients. Patient evaluation and selection was made at a weekly board meeting attended by nephrologists, transplant surgeons and physicians in charge of the histocompatibility unit. In the absence of any other form of definite treatment for chronic renal failure we felt a compulsion to offer a kidney transplant to all patients irrespective of age and cause of renal failure provided a graft was available and the patient at that time was in a condition to stand the operative procedure. Many patients with several high risk factors were accepted including those in a terminal phase of uraemia with pulmonary oedema, pericarditis and hyperpotassaemia. Only patients with advanced coronary artery disease, active severe infection, extrarenal malignant disease and advanced mental disease were excluded from transplantation.

The goal with this transplantation programme was to offer all patients in terminal renal failure a kidney graft, including use of retransplantation in cases of graft failure. The development of the programme is illustrated in Figure 2, which gives the number of transplantations performed year by year as primary grafts and as regrafts. As seen from Figure 3 the proportion of kidneys from living and from cadaveric donors varied during the years. There was a decline in the use of living donor kidneys during the years 1969, 1970 and 1971. This decline was a consequence of the hope that a cadaveric organ selected by means of HLA matching would give as good a chance for success as a related donor organ with comparable histocompatibility. As this expectation was not fulfilled, the living donor
Figure 2. Annual frequency of renal transplantation distributed as first, second, third and fourth transplantations

Figure 3. Annual distribution of living and cadaveric organs used for transplantation

was again preferred whenever available and suitable. Only 15% of the grafts came from living donors in our series of transplantations.

Access to Donor Organs

A major limiting factor for the progress of this programme was the availability of donor organs in sufficient numbers and of acceptable quality. The majority of grafts had to be sought from cadaveric donors. To obtain a sufficient number of kidneys from cadaveric donors, all neighbouring hospitals were stimulated to
become involved in a donor organisation working so that either a surgeon at that hospital removed the kidneys, or that a member of our transplant team went to the hospital to remove the organ. Most of our cadaveric grafts were obtained from hospitals other than our own. Despite these efforts to obtain donor kidneys there was a shortage of kidneys for transplantation throughout the period. This led to the use of many organs of poor quality.

The quality of the graft will determine the risks for the recipient and the functional outcome of the graft. This quality may be defined in two ways, viability and tissue compatibility. A major threat to a patient was to receive a graft with more than 40 minutes of warm ischaemia. Such grafts were followed by a 20% higher initial mortality compared with grafts with shorter warm ischaemic time. The main threat to the patient from such delayed organ removal from a cadaveric donor was septic complications which accelerated in frequency and severity with increasing time of warm ischaemia.

The ambition to transplant only grafts with none or only one or two incompatibilities in the HLA system involved several untoward consequences. Many patients with uncommon combinations of antigens could receive a graft of sufficient compatibility only after a long waiting period or never. During the prolonged waiting period many patients became sensitised against transplantation antigens which further restricted their chances for a suitable graft. A number of patients with blood group O had to be deferred for patients of other blood groups having closer HLA compatibility. A residual group of patients with blood group O thereby accumulated. The preservation period became prolonged and the costs increased. Even if there were no doubt that the outcome of transplantation between HLA compatible donor—recipient pairs was quite superior to transplantation between less compatible pairs, our overall graft survival was not so definitely improved as to counterbalance the negative consequences for a total care programme based on cadaveric organs. This compatibility ambition was therefore relaxed after 1972. This is one explanation for the improved balance between patients awaiting transplantation and the ability of the programme to treat more patients sooner.

RESULTS

During this 10-year period 552 consecutive patients were transplanted with the aid of 110 living donor grafts and 646 cadaveric donor grafts, of which 208 were regrafts to 161 patients with failed primary grafts. The overall outcome is summarised in Figure 4. At the close of this investigation 314 patients were alive. Eighty-three per cent of the recipients survived one year and 70% five years and more when a living donor graft was used. With the use of cadaveric grafts 70% of the recipients survived one year and 50% five years or more. These survival figures express the total mortality which includes all deaths occurring after prolonged dialysis treatment following graft failure.

Patient survival gradually improved during this 10-year period. The mortality
Figure 4. Overall results during the 10-year period 1965–1975

Figure 5. Annual survival rate of patients (PS) at 3 months and 12 months after transplantation and graft survival rate (GS) at 12 months
in the first 3 months post-transplantation decreased from 18% to 1.6% for recipients of living donor grafts, and from 35% to about 10% for recipients of cadaveric organs as seen from Figure 5. The one year patient survival slowly improved from about 60% to 70% for recipients of cadaveric organs and from 75% to 85% for recipients of living donor grafts. The one year survival of cadaveric grafts did not however improve despite the histocompatibility matching ambitions and modifications to the immunosuppressive regimen. A decreased mortality was achieved despite a growing number of high risk patients accepted for transplantation during the period and despite no improvement in graft survival.

DISCUSSION

Improved patient survival reflects improved patient care, with increasing dialysis facilities to balance increasing transplantation activity rather than true scientific advance. Improved survival of the recipients of living donor grafts reflects, on the other hand, the importance of selection of related donor–recipient pairs according to histocompatibility matching and the gain from growing clinical experience, since no real advance in immunosuppression has occurred during this 10-year period.

At a critical evaluation of the present outcome of kidney transplantation and of dialysis treatment, transplantation is still debited with a higher initial mortality. However, after three years of treatment the two methods have an equal percentage of patients alive as seen from Figure 6. With a prolonged follow up period beyond three years transplantation may be credited with a lower mortality than chronic dialysis. This is probably a consequence of the superior rehabilitation

![Graph showing patient survival over time](image)

Figure 6. Patient survival following chronic dialysis according to Brunner et al (1975) and following renal transplantation in Göteborg

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which is possible with a well functioning graft and implies a retardation of the otherwise progressive vascular disease which follows uraemia and which is poorly controlled by dialysis treatment.

When comparing the risks involved with the two methods it is important to emphasise that the initial risk of transplantation is counterbalanced by a lower mortality in the long run, and that patient mortality following transplantation is decreasing.

CONCLUSIONS

A balance between the actual need to provide treatment for all patients in terminal renal failure who wanted active treatment and the possibility of satisfying this need was achieved during a 10-year period. In a total care programme for terminal renal failure transplantation must remain the main method of definitive treatment for the following reasons:

- Full rehabilitation is possible
- Mortality after 3 years of treatment is lower with transplantation than with chronic dialysis
- Early mortality can be reduced when dialysis capacity is sufficient to balance the transplantation activity
- Transplantation requires less manpower and is much cheaper
- More transplantation centres must therefore be established

References


Docherty, P (1971) Uremivårdens kostnadsproblem. Läkartidningen, 68, 4757


Open Discussion

ANDREUCCI (Naples) I think that transplantation is the best way to treat patients, but I am just wondering whether this comparison between dialysis and transplantation is acceptable because usually for transplantation we select patients. We have many patients who cannot be transplanted because of their clinical condition; they will remain on dialysis, but this will decrease the calculated survival rate of patients on dialysis.

GELIN I fully agree with you that there are groups of patients who are very
unsuitable for transplantation. Those accumulating specific antibodies are one
group, and there are diseases which are unsuitable for treatment with dialysis,
but they are quite few. An integrated programme with both dialysis and trans-
plantation I think has worked out in Australia, and the dialysis capacity which
is built up should be used for those who are unsuitable for transplantation. That
would be, on a national scale, the most efficient programme.

HABERAL (Ankara) What is the main cause of mortality in the early period?

GELIN In the period until 1972, sepsis was the main peril — in the early phase.
In the late phase it is still the cardiovascular deaths. They kill about 50% of the
successfully grafted patients.

HABERAL Can I continue? Do you have any problems with thromboembolism?

GELIN We have had four deaths from thromboembolism in this series, but we
have had 18 cases with thrombosis. We have a very active programme, trying to
prevent thrombosis by haemodilution with low molecular weight dextran for the
first three days after transplantation. This might be one reason for the low figure
in our series.

HABERAL Do you have any explanation for this thromboembolic phenomenon?

GELIN Thromboembolism following transplantation has quite a complicated
aetiology. There is the operative trauma, but there is also an initiation of the
coaulation system. The action of the antigen-antibody complex activates the
Hagemann factor and then you have the coagulation system activated. So you see
there are at least two important factors activating the coagulation system.