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Kidney transplant patients at Ullevål Hospital 1963–83

ORIGINAL ARTICLE

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BACKGROUND

In the period November 1963 to July 1983, 118 patients received a kidney transplant at Ullevål Hospital. All future kidney transplants were subsequently performed at Oslo University Hospital, Rikshospitalet. The purpose of our study is to present demographic data and show patient and graft survival from the first patient cohort of kidney transplant recipients in Norway.

MATERIAL AND METHOD

The patients were identified in surgical protocols from Ullevål Hospital and the Norwegian Renal Registry using follow-up data up to December 2016. We recorded the patients' age and sex, cause of renal failure, donor characteristics, patient and graft survival, number of retransplants and cause of death.

RESULTS

118 patients: 38 women and 80 men, aged 14–67 years, received a transplant during the reference period. The most common indicators for transplantation were chronic glomerulonephritis (n = 61), chronic pyelonephritis (n = 20) and polycystic kidney disease (n = 14). Seventy-two patients (61 %) received a kidney from a deceased donor. After one year, 94 of the patients were still living (80 %), after five years, 66 of the patients (56 %) were still living, and after twenty years, the figure was 34 (29 %). Cardiovascular disease was the most common cause of death. The median graft survival was 3.8 years (quartile range 14.4 years). Thirty-two patients underwent retransplantation.

INTERPRETATION

Even in this pioneering era, patient survival rates and the functional life of donated kidneys were acceptable.

Main findings

Of 118 patients who received a kidney transplant at Ullevål Hospital in the period 1963–83, 61 % received a kidney from a deceased donor.

After 20 years, 29 % of the patients were still alive.

The median graft survival was 3.8 years.

Cardiovascular disease was the most common cause of death.

The first successful kidney transplant in Norway was performed at Ullevål Hospital on 5 November 1963 (1). The patient, a 35-year-old man, lived for 22 years after receiving a kidney donated by his mother. This operation was performed nine years after the world's first successful kidney transplant (2).

The first haemodialysis department at Ullevål Hospital was established in 1969. Prior to this, all haemodialysis was carried out at the Department of Experimental Medical Research at Ullevål Hospital, where Fredrik Kiil and Bjørn Amundsen developed the Kiil kidney dialysis machine, which performed its first successful haemodialysis in 1959. In 1969, a Nordic cooperation, known as Scandiatransplant, was established for the exchange of organs for transplantation (3). That same year, a national programme was initiated in Norway which offered kidney transplants to all renal failure patients who might benefit, with Ullevål Hospital and Rikshospitalet each covering their share of the country. The discovery of azathioprine as an immunosuppressive agent in 1963 was an important advancement in transplant medicine. Then in 1983, ciclosporin was adopted as an immunosuppressive drug, which led to a significant increase in organ transplants worldwide. At this point, an agreement was entered into between Ullevål Hospital and Rikshospitalet for all organ transplants in Norway to be performed at Rikshospitalet in Oslo (4).

In 1992, Gorlén et al. published a report on the first 69 patients to receive a kidney transplant at Ullevål Hospital in the period from 1963 to the start of 1978 (5). In our retrospective study, we included all patients who received a kidney transplant up to July 1983, with an observation period extending to December 2016.

We recorded the patients' age and sex, patient and graft survival after transplantation from living versus deceased donors, number of retransplants, cause of renal failure and patients' cause of death.

Material and method

This report is a retrospective descriptive study of the 118 patients who received a kidney transplant at Ullevål Hospital in the period from November 1963 to July 1983. The patients were identified based on handwritten surgical protocols at Surgical Department III, Ullevål Hospital, and from the Norwegian Renal Registry, which was formed in 2016 when the Norwegian Nephrology Registry and the Norwegian Renal Biopsy Registry were merged. The patients' records were retrieved from hospital archives.

Postoperatively, all patients received prednisolone therapy (7.5–10 mg daily) and azathioprine (1–1.5 mg per kg body weight daily) for immunosuppression. We do not have a full overview of the immunosuppressive therapy these patients received after all organ transplants, and a significant part of patient follow-up was transferred to Rikshospitalet in 1983. Data on retransplants, donor status and graft failure were retrieved from the Norwegian Renal Registry. The National Population Register was used to determine the date of death, and causes of death were taken from patient records.

We recorded patient survival one, five and twenty years after transplantation. Graft survival is defined as the time from transplantation to retransplantation or death due to renal failure, based on information from the patient record.

The endpoint of the observation was either the patient's death or 1 December 2016, when the study was concluded.

Statistics

Descriptive data are presented as median values and quartile ranges.

Ethics

The study was approved by the data protection officer at Oslo University Hospital and was deemed not subject to notification to the Regional Committees for Medical and Health Research Ethics (REC).

Results

A total of 118 patients: 38 women and 80 men, aged 14–67 years at the time of surgery, receive a transplant during the reference period (Figure 1). All had terminal renal failure and were receiving haemodialysis. The frequency of surgery increased from one to two patients per year in the 1960s to over ten per year in the late 1970s.

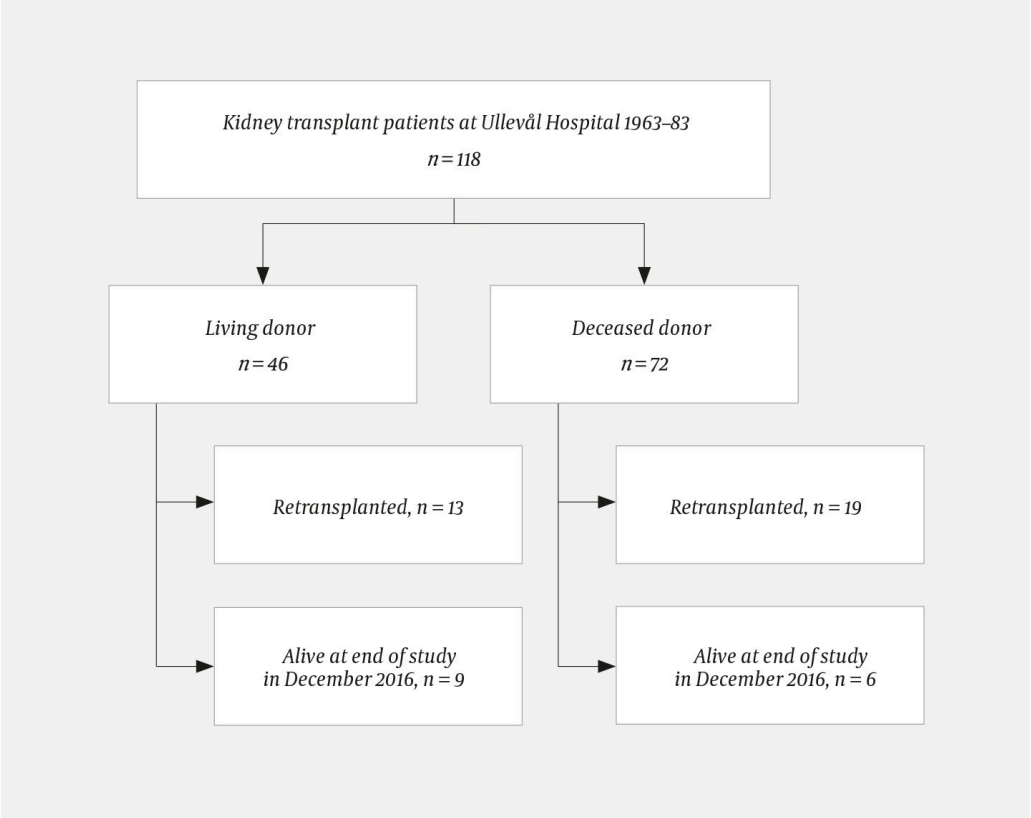

Figure 1 Patients in the study.

The cause of renal failure was chronic glomerulonephritis in 61 patients, chronic pyelonephritis in 20, polycystic kidney disease in 14, nephrosclerosis in 5 and congenital nephritis in 2. Sixteen patients had renal failure due to other factors.

Forty-six patients (39 %) received a living donor kidney transplant (Table 1). Thirteen of these subsequently underwent retransplantation: 3 with a kidney from a living donor and the remainder from a deceased donor.

Table 1

Kidney transplant patients at Ullevål Hospital 1963–83. Patient characteristics and graft survival after living and deceased donor transplants. Figures are given as a percentage (%) unless otherwise specified.

	Living donor	Deceased donor	Total
No. of patients (women)	46 (15)	72 (23)	118 (38)
Median patient age, years (quartile range)	32 (20)	50 (19)	42 (23)
Median donor age, years (quartile range)	52 (16)	39 (30)	44 (26)
No. of retransplants	13 (28)	19 (26)	32 (27)
1-year survival, patients	43 (93)	51 (71)	94 (80)
5-year survival, patients	36 (78)	30 (41)	66 (56)
20-year survival, patients	20 (43)	14 (19)	34 (29)
Median patient survival, years (quartile range)	14 (30)	4 (13)	7 (23)
Median graft survival, years (quartile range)	12 (27)	2 (7)	4 (14)

Seventy-two patients (61 %) received a transplant from a deceased donor (Table 1). Retransplantation was subsequently performed on 19 of these using a kidney from a deceased donor.

Among the total of 32 patients who underwent retransplantation during the period, 22 received a second transplant and 10 received two further transplants, i.e. a total of 160 transplants were performed on the 118 patients.

The median survival for a transplant was 12.4 years (quartile range 26.9 years) in patients with a living donor transplant and 1.8 years (quartile range 6.7 years) for the deceased donor group.

The median survival for patients was 14 years (quartile range 30 years) in the case of a living donor and 4 years (quartile range 13 years) with a deceased donor. Median survival by age at the time of surgery in five-year age groups was comparable between living donor transplant patients and deceased donor transplant patients (data not shown). At the end of the study, 15 patients were still alive, with a median observation period of 41.4 years. Nine of these patients originally had living donor transplants; five of this sub-group subsequently underwent retransplantation while four still had a functioning original transplant. Six of the surviving patients had originally received a deceased donor transplant. Three of these underwent retransplantation, while three had a functioning original transplant.

The main causes of death in the cohort were cardiovascular disease and stroke, sepsis, pneumonia and cancer (Table 2).

Table 2

Causes of death among kidney transplant recipients at Ullevål Hospital 1963–83 who died before the end of the study in 2016 (n = 103). Based on information in patient records.

Cause of death	No. of patients
Cardiovascular disease	28
Cancer	14
Sepsis	14
Stroke	10
Pneumonia	8
Other causes	20
Not known	9
Total	103

Discussion

The years 1963–1983, when 118 patients received transplants at Ullevål Hospital, represent a pioneering period in the history of organ transplantation, before approval of ciclosporin in 1983 made organ transplantation an accepted treatment option throughout the world. In November 1963, when the first transplantation was performed on a patient with subsequent long-term survival, there were very few reports in Europe of allografts with more than a few months' survival.

According to the Norwegian Renal Registry, the median graft survival in recent years is 12 years for a deceased donor kidney transplant and 15 years for a living donor kidney transplant. The increase in graft survival is largely due to the use of calcineurin inhibitors, namely ciclosporin and tacrolimus. It is interesting to note that both donor types are represented among the patients who still had a functioning original transplant at the end of the study after a median observation period of 41.4 years.

Some studies have found that kidneys donated from a living donor are associated with longer patient survival than kidneys from a deceased donor (5), (6–9), while other studies have found no association between patient survival and donor status (5, 6). A study by Gorlén et al. of the 69 first kidney transplant patients at Ullevål Hospital showed that patients with a deceased donor kidney transplant had a higher mortality rate than patients with a kidney from a living donor (5). Our study also found longer median survival among patients who received a kidney from a living donor, but these patients were generally younger than those who received a transplant from a deceased donor, which may explain the longer survival in this group. For patients within the same five-

year age group at the time of surgery, the median survival appears to be roughly the same for living and deceased donor transplants (data not shown). However, unlike Gorlén et al., we have not corrected for other variables that may affect survival, such as donor age, dialysis duration, or HLA incompatibility.

The study by Gorlén et al. of some of the same patient cohort showed 55 % and 44 % average survival rates after 10 and 20 years respectively (5). We found an overall median survival rate after 10 and 20 years of 45 % and 29 % respectively (data not shown in the results for 10 years). However, the patients in our study were generally older than the patients in the first published report.

Patient survival in our study is comparable to the findings in the 1977 study by Henari et al. (10), where long-term haemodialysis was compared with kidney transplantation in 200 patients, and the study by Bradley et al. which reported long-term survival in 177 patients who received kidney replacement therapy in the form of haemodialysis as opposed to transplantation (12). Both studies were conducted before the introduction of ciclosporin, and the former did not differentiate between living donor and deceased donor transplant patients.

The causes of renal failure were reported in the medical records as clinical diagnoses without biopsy, with chronic glomerulonephritis, chronic pyelonephritis and polycystic kidney disease being the three most common. Patients with diabetes, which is one of the most common underlying conditions among today's renal failure patients, were not previously offered transplantation.

Arteriosclerosis leading to cardiovascular disease and stroke was registered as the most common cause of death among study participants. The second most common cause was infections leading to sepsis and pneumonia. It is likely that infections are related to immunosuppression. These findings are consistent with other reports (2, 13). Malignancy as a cause of death was somewhat more frequent than in comparable studies. This is assumed to be due to the long observation period and the fact that the patients were followed up into old age.

One of the weaknesses of the study is that not all relevant data were collected. We have not registered how much or what type of immunosuppressive therapy the patients received after 1983. It would have been interesting to include this data in the study. We also did not contact the surviving patients at the end of the study for their subjective assessment of their quality of life following transplantation. We used the data provided in patient records and are aware that this is not always quality assured.

The strength of the study is the complete records for the first 118 transplant patients at Ullevål Hospital after November 1963, in terms of patient and graft survival with a follow-up period of more than 40 years.

Our conclusion is that the results from Ullevål Hospital are comparable with reports from other transplant centres within the same timeframe. Patient survival and graft function must be regarded as satisfactory in relation to contemporaneous treatment options. Some of the patients still had a functioning transplant at the end of the study. We believe that the observed difference in patient survival between living versus deceased donor transplants is largely due to the age range of the patients. Although we did not examine the

patients' quality of life, we must assume that this often improved following transplantation, not least because haemodialysis was clearly much more of a burden in times gone by than it is today.

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