

ANNUAL REPORT 2002

The Norwegian Renal Registry (Norsk Nefrologiregister)

This report will also be available on:
<http://www.nephro.no/registry.html>

Correspondence to:
Overlege dr.med Torbjørn Leivestad
Institute of Immunology, Rikshospitalet, N-0027 Oslo, Norway.
Fax: 47- 23 07 35 10. Tel: 47- 23 07 13 78.

Preface

The Norwegian Renal Registry (Norsk Nefrologiregister) was formally constituted in 1994 as collaboration between The Norwegian Renal Association (Norsk Nyremedisinsk Forening) and Rikshospitalet University Hospital, with the latter as the formal owner. National data on renal replacement therapy (RRT) had been collected within The Renal Association since 1980 in a less formalised manner, and the transplant centre had stored data on transplanted patients since the sixties. Further, Norwegian renal units had reported to the ERA-EDTA-registry since the late sixties.

According to its statutes, The Norwegian Renal Registry shall combine the handling of data for all these purposes. It shall present national statistical reports and form a basis for research. Reports for 1995 and 1996 in Norwegian, and since 1997 in English, have been distributed; the latter five have also been made available on Internet.

National organisation and policy

Norway has 4.53 mill. inhabitants (July 2002) and 19 counties with populations ranging from 73700 to 515000. Each county, except one, has a central renal unit and some have additional unit(s) run in close contact with the central unit. There is only one transplant centre (two during 1963-83). Pre-transplant work-up, as well as post-transplant follow-up beyond 3 months, is handled by the county-centres.

The county-centres are responsible for reporting data from day 1 on all patients receiving renal replacement therapy (RRT) for chronic renal failure within their area. Treatment of acute renal failure is not reported unless the failure is irreversible, in which case the whole treatment period is included. Minor changes of treatment modality, e.g. from HD to HDF or between CAPD and APD, are not reported. Similarly, temporary changes to HD for PD-patients are not reported. At intervals, cross-checking for unreported deaths is performed against official census data.

Transplantation has always been considered the treatment of choice, if possible with a living related donor. Since 1984, also spouse donors have been used. Acceptance criteria for transplantation have been wide, strict age limits have not been applied. Over time, an increasing number of non-transplantable patients have also been offered life-long dialysis.

Incidence and prevalence calculations in this report are based on the national population data from July 2002, although this in some instances may be slightly misleading since population changes have not been uniform in all counties during the period.

Incidence figures for 2002

During 2002 a total of 419 new patients (in 2001: 427) entered renal replacement therapy (RRT), i.e. 92.3 per mill. inhabitants.

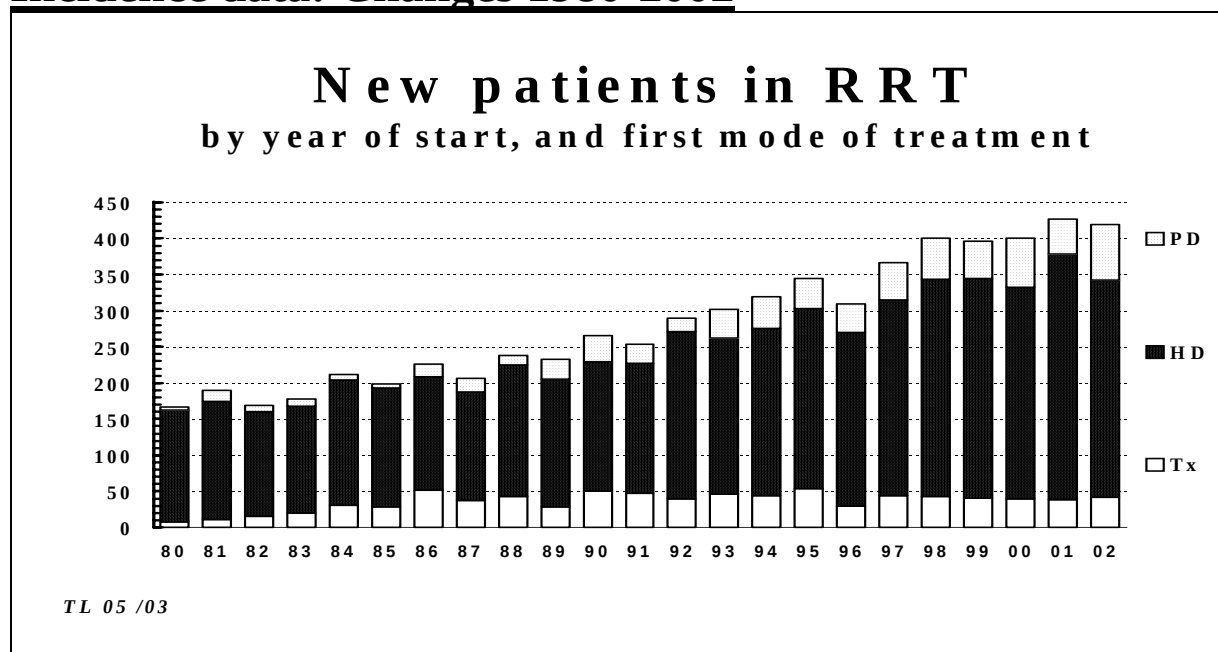
A majority of 68.0% were males and 32.0% females. Median age at start was 64.5 years, mean 60.3 years, ranging from 2 weeks to 87 years.

Tabulated by first mode of treatment, and age at start of treatment:

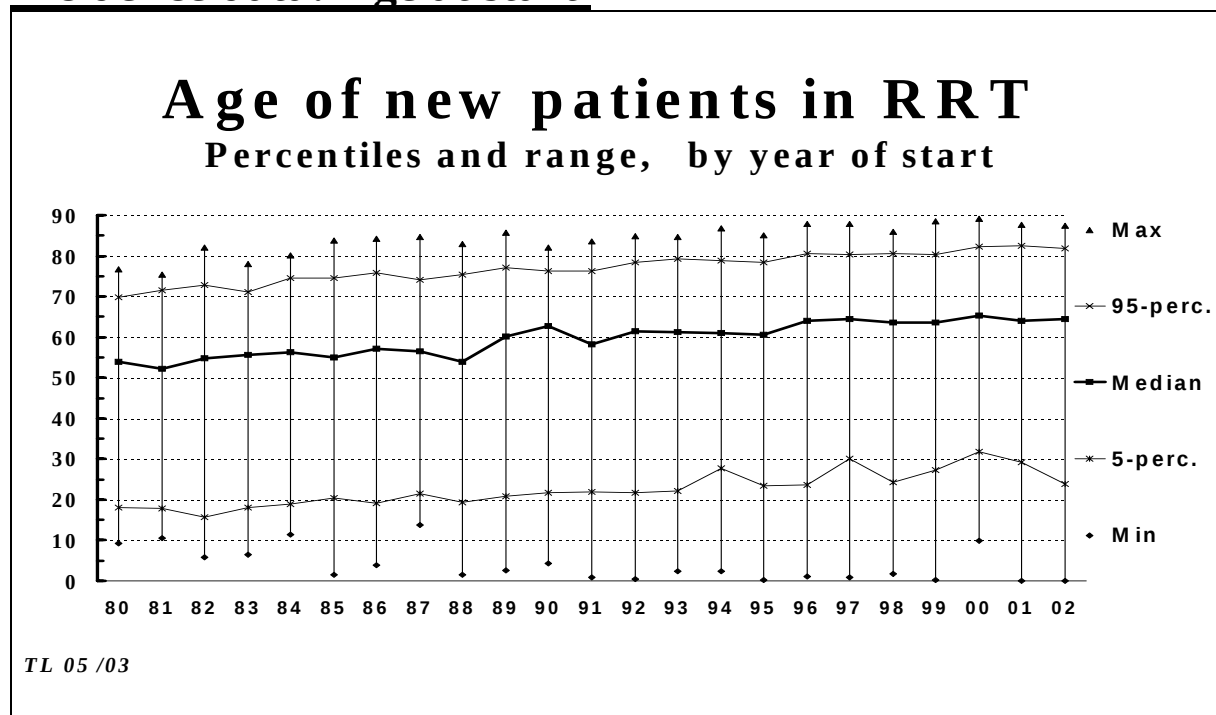
	< 15	15-24	25-34	35-44	45-54	55-64	65-74	75+	Total	in %
HD	4	11	11	20	40	61	79	74	300	71.7
PD	1	2	1	9	9	8	24	23	77	18.3
TX	4	3	3	9	9	11	3	0	42	10.0
Total	9	16	15	38	58	80	106	97	419	100
in %	2.1	3.8	3.6	9.1	13.8	19.1	25.3	23.2	100	

At start of treatment, 275 (65.6%) were considered by their nephrologist to be a potential candidate for transplantation, while 144 (34.2%) were accepted for life-long dialysis (constituting 40% of those starting with HD and 31% of those starting PD). Among patients starting dialysis in 2002, 25% were previously unknown to the renal unit when they presented with terminal renal failure, 54% were known and started RRT as planned, while 21% were known but had a hastened RRT-start.

Incidence data: Changes 1980-2002



Incidence data: Age at start



Since registration started in 1980 there has been a continuous shift in patient age. Both the maximum and the median age at start of RRT have increased. Also the 5-percentile and 95-

percentile values (i.e. including the majority of patients) have increased with a similar number of years. But also smaller children have been accepted, the youngest ever started PD in 2002 at age 13 days. The number of children below 15 years has not changed during the period - it has ranged from two to eight per year.

Incidence data: Primary renal disease

	1980-84	1985-89	1990-94	1995-99	2000-01	2002
Glomerulonephritis	34%	36%	31%	24%	19%	17%
Pyelo/interstitial nephr.	16%	14%	11%	12%	13%	11%
Polycystic diseases	10%	9%	9%	9%	8%	10%
Diabetic nephropathy	13%	12%	12%	11%	15%	12%
Amyloidosis	7%	6%	6%	4%	4%	3%
Vascular/hypertensive	5%	8%	18%	24%	28%	28%
Immune/systemic	4%	5%	4%	6%	3%	5%
Kidney tumour	1%	1%	1%	1%	1%	1%
Myelomatosis	3%	2%	1%	2%	3%	3%
Other defined	4%	4%	4%	3%	3%	5%
Unknown	3%	3%	3%	4%	4%	5%
N:	912	1106	1419	1817	830	419

The main change over time has been an increase of vascular/hypertensive nephropathy and a relative reduction of glomerulonephritis. Whether this only reflects changed coding practice or a true shift is not known.

Diabetic nephropathy has contributed 10-15% per year. Until 1995 sub-classification was not reliably registered. In 2002, 27 were registered as having Type I, 24 as Type II diabetes. In addition 44 patients with other types of primary renal disease were recorded having diabetes as a co-morbid factor (two were Type I and 42 Type II), thus 23% of new patients were diabetics.

Cardiovascular disease is often present at start of RRT. Symptomatic heart disease was reported in 161 (38%); five out of these had a previous heart transplant. Cerebrovascular disease was reported in 47 and peripheral arteriosclerotic disease in 60 patients.

Prevalence data: Status by 31.dec. 2002.

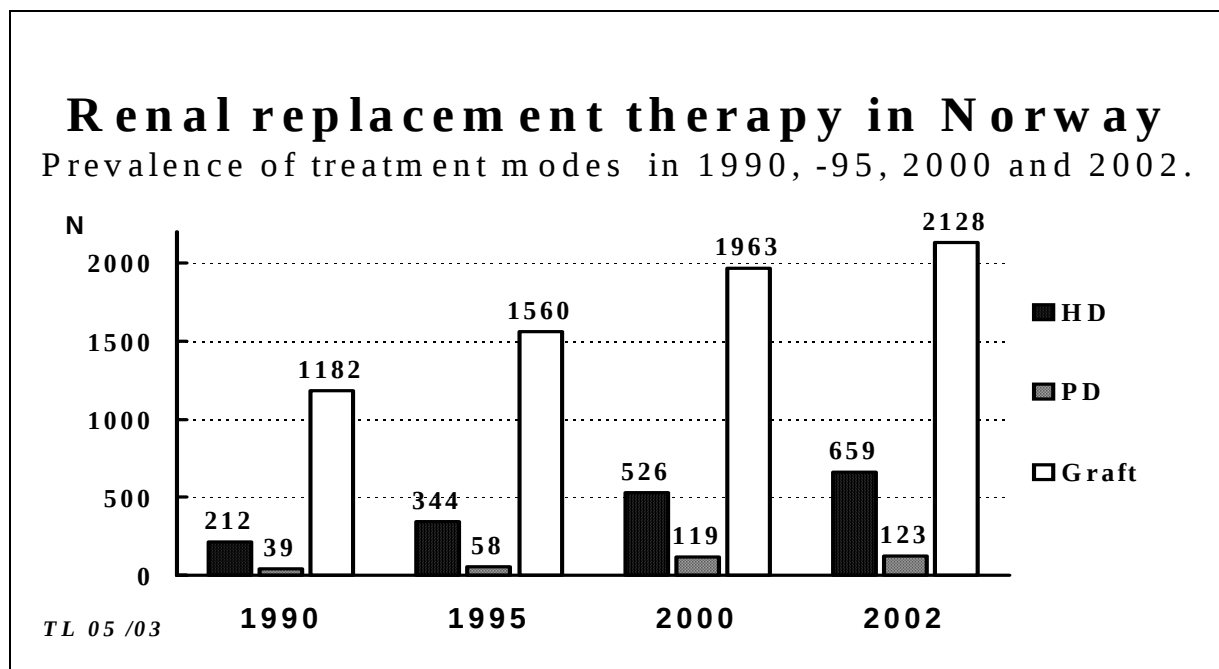
By the end of 2002, 2910 patients in Norway received renal replacement therapy, i.e. 641.4 per million inhabitants. This represents an increase of 151 patients or 5.5 % since 2001.

Gender: 64.0% males and 36.0% females.

Median age by the end of the year was 55.8 years, mean 55.0 years and range 0.5-90.2 years.

Tabulated by last mode of treatment, and age by end of 2002:

	< 15	15-24	25-34	35-44	45-54	55-64	65-74	75+	Total	in %
HD	0	10	28	55	77	130	166	193	659	22.6
PD	1	5	4	14	18	18	21	42	123	4.2
TX	31	67	220	351	517	489	334	119	2128	73.1
Total	32	82	252	420	612	637	521	354	2910	100
In %	1.1	2.8	8.7	14.4	21.0	21.9	17.9	12.2	100	



Death in RRT in 2002:

A total of 270 patients in renal replacement therapy died during 2002, i.e. 8.5% out of the 3178 persons at risk. Among these, 68% were males and 32% females. Median age at death was 73 years, mean 70.0 years, and the range 2-89 years. Median time from start of RRT until death was 25 months, with a range spanning from day one to more than 33 years.

The final mode of treatment was HD for 177 patients and PD for 27, while 66 died with a more or less well-functioning graft. Seven died within two months after graft loss; thus 73 deaths were termed 'TX-related'. 41 patients died following termination of treatment, 11 of those because the patient refused further treatment.

As in previous years, cardiac (30%) complications were the most frequent causes of death, followed by infections (22%), vascular complications (14%), and malignant tumours (12%).

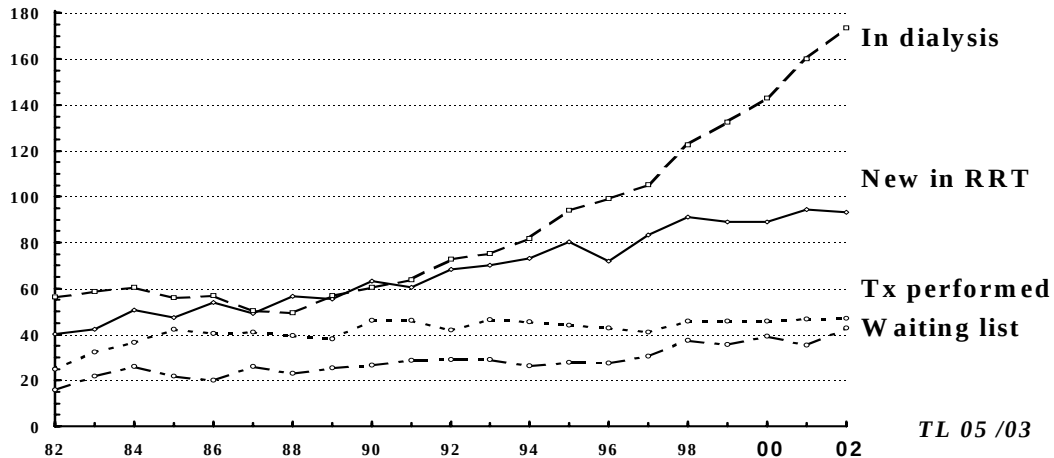
Transplantation and waiting lists:

A total of 213 renal transplants were performed at Rikshospitalet University Hospital in 2002, i.e. 47.0 per million inhabitants. In 98 (46.0%) the graft came from a living donor (LD), 25 of those were biologically unrelated to the recipient (mainly spouses). Among the LD-graft recipients 32 were grafted pre-emptively and 3 received a second graft after rejection of the first without new dialysis. 118 patients received a cadaveric graft (CD), 11 were pre-emptively transplanted, while one had a second graft without entering dialysis. There were 191 first grafts (93 LD and 98 CD), 16 were second grafts (5 LD, 11 CD) and 6 third grafts (all CD). Simultaneous kidney + pancreas transplantation was performed in 15, one patient with a functioning kidney graft received isolated Langerhans Islet cells.

In principle, transplantation is offered to all patients considered to profit from it, with no strict upper or lower age limit. The age of the 98 first cadaveric graft recipients in 2002 ranged from 8 to 80 years, with a mean age of 54.1 y. Out of these, 24 % were above the age of 65 and 4% were 75 or older. The 93 recipients of a first living donor graft were from 1.2 to 74 years, mean 45.3 y. Re-graft recipients (n=22) were younger, from 17 to 65 years, mean 43.1 y.

Renal replacement therapy in Norway

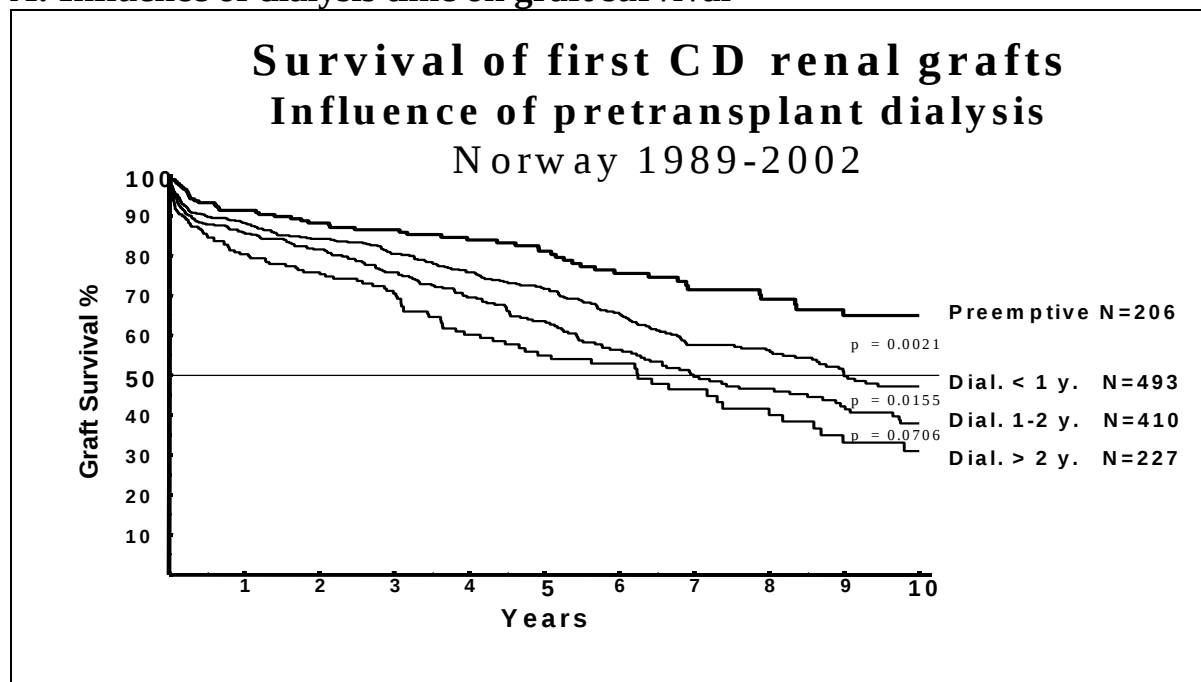
Status by end of year - pats. pr mill. inhabitants



By end 2002, 195 patients (43.0 per mill.) were on the active waiting list for a CD renal graft. This represented an increase of 35 patients (22%) since 2001. Among those waiting by Dec.31, median time on the list was 9 months. 40% had waited less than 6 months, 71% less than one year and 12% more than two years. The 115 recipients given a CD-graft in 2002 had a median waiting time of 12 months and a maximum of 55 months at the time of grafting. Among the 782 patients in dialysis treatment by Dec.31, 331 (42%) were for various reasons not considered candidates for a new renal graft.

Renal graft survival.

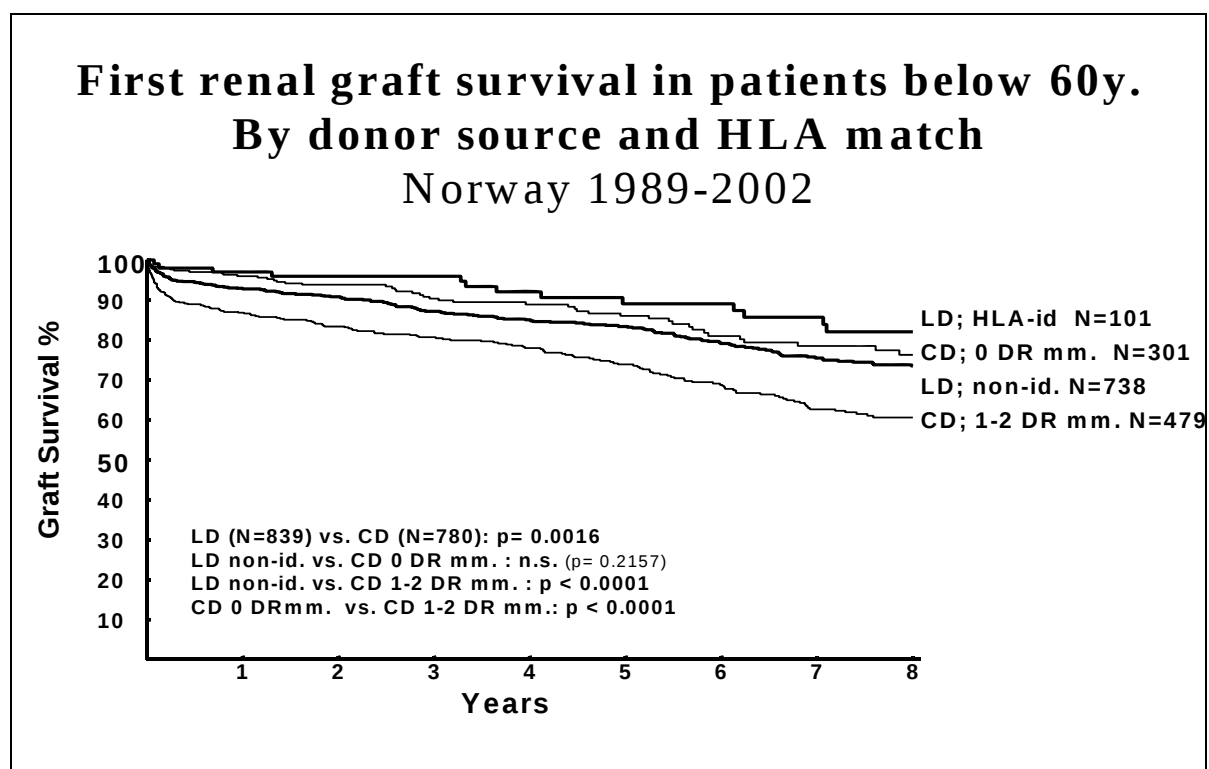
A: Influence of dialysis time on graft survival



Since the start of the Norwegian transplant program, pre-emptive transplantation has been advocated. Avoiding dialysis would both reduce patient inconvenience and save health costs. During 1989-2002 this was achieved in 37% of the recipients of a first LD-graft and in 15% of recipients of a first CD-graft. The survival analysis above would indicate that pre-emptive transplantation is advantageous in terms of graft survival. However, the mean age differs significantly between the groups (pre-emptive: 50y; <1y: 53.4y; 1-2y: 57.6y; >2y: 58.1y). Further, the donor age was higher and the proportion of HLA-DR mismatched grafts were higher among those who had spent more than one year on dialysis (with no difference between the pre-emptive and the less than one year group). Thus, the worsening prognosis with longer dialysis time could well be due to other factors than the prolonged dialysis.

B: Influence of age and of donor & compatibility on graft survival

A high proportion of Norwegian transplant candidates are aged, these often have more arteriosclerotic (and other) extrarenal complications. We therefore analysed separately the graft survival among the younger (age < 60 years, presumably few with advanced complications) and the older (age > 60 years, presumably many with advanced complications). Similar data were presented during the “XIX International Congress of The Transplantation Society” in Miami in August 2002 (but further updated here).



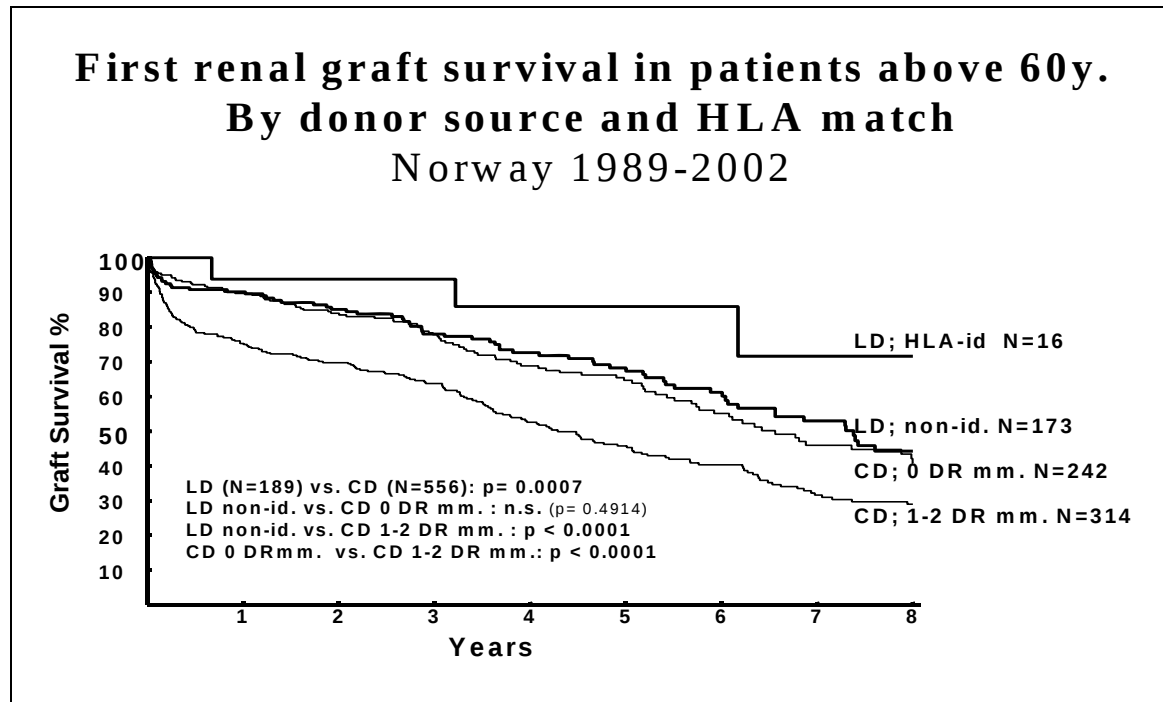
As appears, in general the survival of LD grafts is superior to that of CD grafts. HLA-identical sibling grafts tend to do best, although the differences compared to the HLA-DR compatible CD grafts and the non-identical LD grafts did not reach significance. HLA-DR mismatched CD grafts have the poorest survival.

When a similar analysis is performed censoring for death with functioning graft, DR compatible

CD grafts have a significantly lower risk of being lost than non-identical LD grafts.

It is generally held that the immune response tends to be reduced by age. This seems to contrast with our finding that among the recipients above 60 years (below), the influence of

mismatches on graft survival seems even greater than among the younger. However, a death-censored analysis fails to demonstrate any significant graft loss difference between the groups.



The likelihood of early rejection episodes was lower in the older groups compared to the younger, although this difference was significant only among the recipients of DR mismatched CD grafts. Thus it would seem that the increased risk of acute rejection episodes from HLA incompatibility more often results in patient death with a still functioning graft among the older recipients.

Patient status and treatment.

By the end of each year the registry distributes a patient questionnaire asking for patient status and actual treatment as well as complications during the treatment year. Data are requested for all dialysis patients starting RRT before Dec.1 and for all transplanted patients with more than 4 months observation since their latest transplant.

By now (July 2003), the 2002-response rate for dialysis patients is 95.2% and for transplanted patients 95.5%. The following calculations are based on received reports only.

Rehabilitation status: Five main groups have been defined:

	Working	Able to work	Self-caring	Need of assist	Need for care
Dialysis	8%	39%	34%	14%	6%
Transplant	48%	20%	28%	4%	1%

Blood pressure: Hypertension is a problem, both in dialysis and after transplantation. The table shows blood pressure (BP) groups and the most widely used drugs:

	Dialysis	Transplanted
BP > 140/90	48%	26%
BP >130/80 and $\leq$ 140/90	27%	36%
BP $\leq$ 130/80	25%	38%
Beta-blocker	52%	35%
Calcium-channel-blocker	42%	46%

ACE-inhib./AT-blocker	29%	40%
-----------------------	-----	-----

75% of dialysis patients and 78% of the transplanted use one or more antihypertensive drugs (diuretics not included). Among those not using antihypertensive drugs, 13% of the transplanted and 30% of the dialysis patients had BP > 140/90.

Erythropoietin (EPO): 92% of dialysis patients and 5% of transplanted patients use EPO.

D-vitamin: 69% of dialysis patients and 14% of transplanted use active vitamin D₃.

Statins:

42% of dialysis patients and 50% of transplanted patients either use a statin or participate in a double blind study ("Alert").

Immunosuppressive drugs:

Until 1983 azathioprine with prednisolone was standard therapy after transplantation. Since then, ciclosporine and prednisolone, most often combined with azathioprine, has been standard. During the later years mycophenolate and tacrolimus and also rapamycin have been used. Based on the received 2002-reports, 81% use ciclosporine, 11% use tacrolimus, 50% use azathioprine, 27% mycophenolate and 2% rapamycin. 98% of transplanted patient use prednisolone. Among those using a calcineurin-inhibitor only 66% have reached the daily prednisolone-dose of 5mg (or less) recommended for patients with stable function. In some few it has been deliberately withdrawn.

Graft function:

Grouped by serum creatinine concentration, 22% have a value $\leq 100\mu\text{mol/L}$, 48% in the range 101-150, 20% 151-200, 5% 201-250 and 4% above 250. Serum creatinine below 125 (upper normal male value) was found in 48% of calcineurin-inhibitor users and in 67% of those without. The latter group mainly consists of patients transplanted before ciclosporine, and with a high proportion of HLA-identical sibling graft recipients.

For 7% of patients a diagnosis of chronic rejection has been made, in 68% of these this diagnosis has been verified by biopsy.

Dialysis treatment:

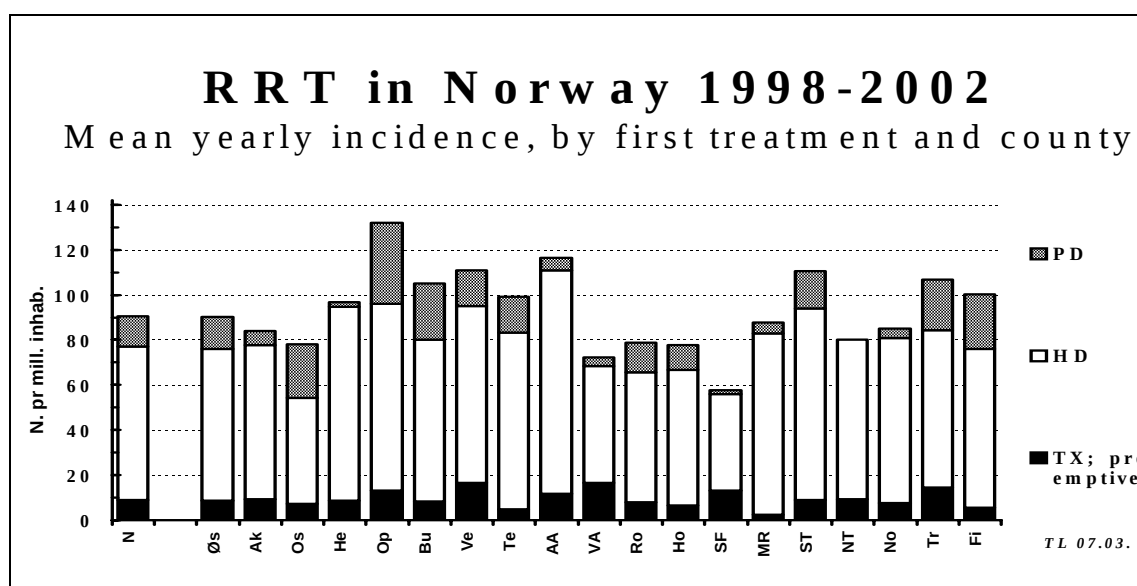
Among HD/HDF patients, only two were on home dialysis. HDF was reported in 65 (11%). Most patients (68%) receive 3 treatment sessions per week, 26% receive 1-2 sessions and 5% receive 4 or more. 21% are treated for 15 or more hours/week, and 25% for less than 10 hours. KT/V would be a better indicator of dialysis adequacy; collection of this still awaits a better standardisation.

Among PD patients, 34% use APD, none use IPD. A few get additional HD, but are categorised as PD-patients. 26% of PD-patients are noted to have had one or more peritonitis episodes during 2002, a further 8 of the HD patients had PD-peritonitis during 2002.

Regional differences within Norway

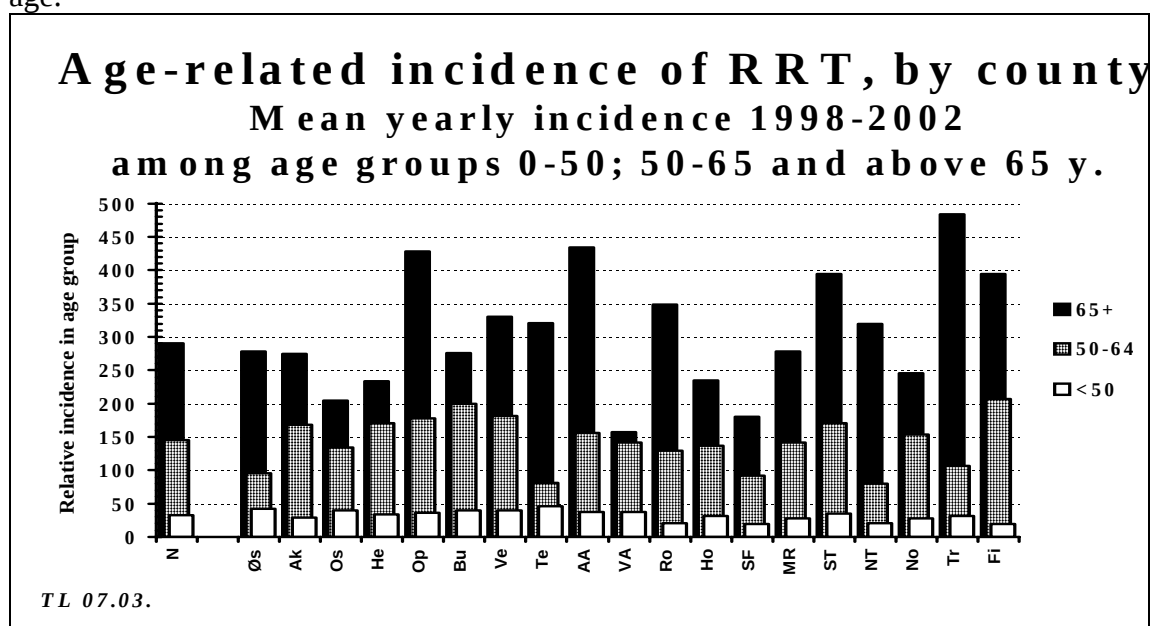
Incidence:

During all the years since data collection was started, the number of patients reported has differed substantially between centres, also after correction for population size. Further the first mode of treatment (HD, PD or pre-emptive transplant) for new patients differs considerably. In the following figure, patients were grouped by county of domicile at RRT-start and the incidences were calculated as a yearly mean for the five-year period 1998-2002:



As appears, the mean yearly incidence of RRT-start varied from 58 to 132 pr. million. Noticeably, the county having the lowest incidence (Sogn og Fjordane) is also known to be where people live the longest and have the lowest general morbidity. Although there is national consensus that pre-emptive transplantation is preferable, this was only achieved in 10%; in the individual counties this figure ranged from 3% to 23%. In some counties PD is rarely used, in others up to 31% of new patients have this as first treatment mode. 75% received HD as first treatment mode, in the counties this ranged from 60% to 92%.

We have previously reported marked differences in the age distribution of incident patients. In 2002 mean age of new patients ranged from 52.3 to 67.6 years. For the five-year period 1998-2002 we have calculated the mean yearly relative take-on rate of patients of patients in three different age populations: less than 50 years; 50-64 years; and those above 65 years of age.

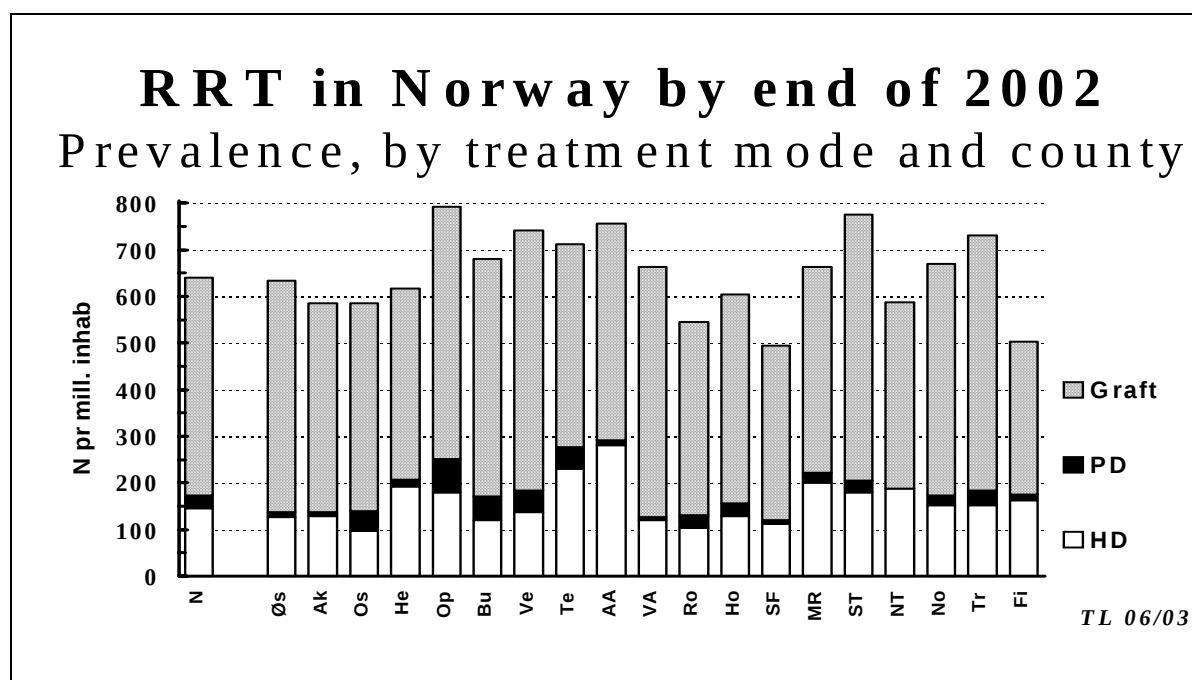


As appears from the figure, the mean RRT-incidence among persons below 50 years does not seem to differ much, though ranging from 19 to 46 pr. mill. inhabitants. In the age group 50-64 years, the RRT-incidence ranges from 81 to 207 pr. mill. (mean 145); while among the population of 65 years and above the incidence ranged from 157 to 484 pr. mill. inhabitants (mean 291). The reasons for such marked geographical differences are not clear.

The proportion of the new patients in 2002 who first presented in the renal unit with a terminal renal failure also varied considerably between counties – from 10% and up to 60%. In the majority of these cases the diagnosis would imply that renal failure has developed gradually over years. Thus, in most counties there must be a need for improved co-operation within the primary health service in order to achieve early referrals.

Prevalence:

Again, the data demonstrate great differences between the counties. In all counties the majority of patients have a functioning graft, constituting from 61% to 81% of the total RRT-population. The dialysis prevalence ranges from 121 to 291 per mill. inhabitants in the counties, indicating great differences in workloads and costs. In some counties, two out of three dialysis patients are not considered candidates for a new graft, in others this applies only to 10-15%. But counties with high dialysis prevalence do not necessarily have a high prevalence of 'non-transplantable' patients.



Concluding remarks:

Even if it may seem that the incidence increase during the latest years has levelled off, the prevalence of RRT-patients will continue to increase in the coming years. The marked county differences may indicate that we still can expect further increased national incidence. Unless a corresponding rise in kidney donation (both living and cadaveric donors!) is achieved, the number of patients in dialysis will rise and they will constitute an increasing proportion of the RRT-population.

Compared to the Swedish RRT-incidence (125 per million in 2002) and prevalence (756 per million), Norwegian numbers still are low. There are no obvious reasons for such a difference between our two nations that are so similar in most respects. Therefore, the Norwegian health service needs to prepare for accommodating a significantly increased number of RRT-patients in the coming years.

*Report completed 21.07.2003
Torbjørn Leivestad M.D.*

Appendix:

