Statistical Report 2000

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Introduction

The Catalan Register of Renal Patients (RMRC) is a mandatory population-based register that compiles information on all patients undergoing Renal Replacement Therapy (RRT) in Catalonia.

At present, the RMRC forms part of the Public Health Department of the Catalan Health Service. It was created in 1984 to provide support for the Renal Failure Treatment Program of the Ministry of Health and Social Security of the Government of Catalonia. At the same time, the Commission for Control and Tracking for the Register was set up to ensure the confidentiality and quality of the data, and the adaptation of the Register to new needs for information related to nephrological care.

In 1988, an external validation was carried out. This reflected exhaustive reporting of variables and excellent agreement, thus helping to prove the validity of the data for carrying out clinical and epidemiological studies. These results may also be considered as a gauge of the correct functioning of the Register.

In 1990, the RMRC became a local register for the European Dialysis and Transplant Association (EDTA), to prevent duplication in the compiling of data by medical personnel. Since 1999 it has participated in the Collaborative Transplant Study (CTS) by sending information on renal transplants performed in Catalonia.

Since the creation of the RMRC, an annual **Statistical Report** has been published, the purpose of which is to present and disseminate the results of the data analysis. In accordance with the aims of the Register, this document contains information regarding the scope of the problems of treated end-stage renal failure (ESRF) in Catalonia, and the sociodemographic characteristics, morbidity and the mortality of patients in RRT. Part of the report is also given over to presenting the results of non-systematic research and information from databases outside the Register and from specific studies that contribute to an increased knowledge of treatment of ESRF in Catalonia, from both the clinical and epidemiological viewpoint.

This document is devoted in large part to presenting the data for the year 2000 and their evolution since 1984. This year the section on hemodialysis continues the study on vascular accesses, which got underway in 1996. The data compiled over this five-year period were analyzed in relation to the characteristics of patients, and a study was also carried out on mortality associated with the type of vascular access used during the first dialysis.

This year a specific study was carried out on renal dyslipemia and cardiovascular risk factors in patients on dialysis and transplant.

Material and method

Incidence and prevalence

Catalonia was used as the reference population for calculating incidence and prevalence, using the 1991 census for the 1992-1995 period and the 1996 census for the 1996-2000 period. Incidence refers to the number of patients residing in Catalonia who started RRT during the year in relation to the total population of Catalonia. Incidence rates are expressed per million population and year. Prevalence is defined as the total number of renal patients in RRT residing in Catalonia and living on December 31, also in relation to the global population of Catalonia. Prevalence rates are expressed per million population.

Certain tables refer to the total number of patients treated in Catalonia, resident and non-resident, which is specified in each case.

The rates corresponding to each health region have been standardized by age and gender for the purpose of comparison and thus prevent the effects caused by the composition of different population pyramids. The data have been standardized by the indirect method in the calculation of incidence rates, which allows the comparison of the rates of each health region (HR) with the global rate in Catalonia. Prevalence rates have been calculated by the direct method. The adult population (over 14 years of age) has been used for standardization. For this reason, since end-stage renal failure (ESRF) is less frequent in children, the standardized incidence and values of the incidence and the prevalence values are higher than the gross rates used for comparing data from Catalonia with those from other Spanish autonomous communities or other countries. The confidence interval (with a 95% confidence level) of the rates standardized by the indirect method has been calculated by the following formula (LONG, 1977):

$$\text{Specific rate} \pm 1{,}96 * \frac{\text{Global rate}}{\text{Theoretical cases}} * \sqrt{\text{Observed cases}}$$

To calculate the confidence interval (with a confidence level of 95%) of the standardized rates by the direct method, the following formula has been used (RUE, 1993):

$$\text{Specific rate} \pm 1{,}96 * \sqrt{\frac{\text{Specific rate of the HR stratum}}{\text{Population stratum- Catalonia}} * \left(\frac{\text{Population stratum- Catalonia}}{\text{Population of Catalonia}}\right)^2}$$

The SPSSx program was used for statistical analysis. The Chi-squared (χ^2) test was used to evaluate the independence of the qualitative variables; the Student-t test was used to compare two means; and the analysis of variance was used to compare more than two means.

Survival

The analyses of global survival for primary renal disease, by age group, by the number of concomitant diseases at the start of RRT and by level of functional autonomy were carried out with the new patients included in the Register from January 1, 1984 to December 31, 2000. These cases were recorded prospectively. This means that their reporting is exhaustive and an accurate follow-up of these patients is available.

To prevent any possible bias, patients who began treatment prior to the creation of the

Register were excluded from these analyses. The data from these patients were collected retrospectively and thus the information regarding certain cases is incomplete. Moreover, owing to the difficulty involved in recovering information on patients who have already died, cases that were still alive at the time of the data collection may be over-represented in this group of patients, especially those that never received transplants.

Survival related to treatment was calculated using each treatment cycle – as opposed to the patient – as the analysis unit. All treatment periods from January 1, 1984 to December 31, 2000 were studied. Changes in treatment were considered missing from the follow-up for the purpose of statistical calculation.

The survival of patients with transplants has been calculated for patients receiving transplants between January 1, 1984 and December 31, 2000. Multiple-transplant patients (kidney and pancreas, kidney and liver or double-kidney) were excluded from the study, since their characteristics differed from those of the other transplant recipients. The survival of the patient and of the transplant graft were calculated by type of transplant (from living donor or cadaver), and also by different immunocompatibility characteristics (by the number of HLA-DR, A or B matches and percentage of antibodies).

In the univariate analyses, the survival tables were computed using the actuarial method, and the level of statistical significance among the different curves of one same analysis was evaluated. Subgroups were compared globally, and in pairs, using the Gehan test (SPSS, 1983). The SPSSx program was employed.

The proportional risks model was used for the multivariate analysis, with the SPSS statistical package (SPSS, 10.0), which uses a modification of the Cox regression proposed by Breslow, in which the coefficients are estimated by means of the Newton-Raphson iterative algorithm. The statistical significance of the estimated relative risks was determined with the maximum probability method and the χ^2 test.

Evolution of treated end-stage renal failure in Catalonia

The global incidence and prevalence data on treated end-stage renal failure (ESRF) in Catalonia, and the number of transplants performed in 2000 are presented in Table 1 in absolute figures and in rates per million population (pmp), together with the number of deaths and the mortality rates, expressed per hundred patients.

Table 1. Global results of end-stage renal failure in Catalonia, 2000.

The prevalence rate has continued to grow in recent years (Table 2). The incidence rate, despite slight variations, continues to be one of the highest in Europe. This year the transplant rate rose slightly over last year. It is one of the highest in recent years, close to 60.1 transplants per million population. This rate is a measure of activity calculated from the total number of transplants performed, independently of the place of origin of the donor or recipient, in relation to the population of Catalonia. The mortality rate for this year was practically the same as that for the last three years.

Table 2. Evolution of treated end-stage renal failure in Catalonia, 1995-2000.

Description of the population in Renal Replacement Therapy

Sociodemographic data

Figure 1 shows the detailed evolution of the mean age of patients at the start of Renal Replacement Therapy (RRT) and survival cases by year's end. It also shows the evolution of the mean age of patients who died in 1986-2000. With regard to prevalence, the mean age continued to grow at the same rate as in previous years, thus maintaining quite a stable growth tendency. As for incidence, greater variation was seen than in the annual

means, since the number of new cases is lower than that of prevalent cases. Despite the fact that the tendency is in general on the rise, this year the increase was only two-tenths of one percent.

Figure 1. Evolution of the mean age of patients in RRT, 1984-2000.

In relation to the previous year, there has been a slight increase in the mean age of the prevalent population, for both men and women.

With respect to the evolution of the mean age of the patients that died during the period 1986-2000, the situation is similar to that of incidence: there are slight variations owing to the low number of cases, yet the global tendency is for patients in RRT to die at an increasingly advanced age. In the last year, the global mean dropped by almost one year. The men's group shows almost two years while among women the age increased by half a year.

Among RRT patients, there is a predominance of men (61.0%) and the age group with the most cases is 60 to 80 years for both sexes (44.5%).

Figure 2. Evolution of age at start of RRT in number of cases and percentages, 1984-2000.

Figure 3. Breakdown of treatment of ESRF incidence rates per age group and gender, 2000.

Figure 2 shows the breakdown of new cases, by age groups, for the period 1984-2000. In the under-60 age groups, it has been seen that, despite the fact that the number of new cases beginning RRT each year is still more or less stable, the percentage that these patients represent out of the total incidence for each year is progressively decreasing. In contrast, in the over-60 age groups, a gradual increase is seen, both in absolute figures and in their percentages. This growth in terms of the number of patients is much more significant in the over-70 groups. According to these data, the high incidence rates seen are steady on account of the inclusion of patients who are increasingly older. The breakdown of patients by age group in 2000 is practically equal to that of previous years.

Figure 4. Breakdown of treatment of ESRF prevalence rates by age group and gender, 2000.

Figures 3 and 4 show the incidence and prevalence rates by age group and gender. These rates increase with age, especially from the 35 to 44 year group to the 65-to-74-year group. In more elderly patients, the increase is less pronounced, and lowers in the over-84 year group. Rates for men have always been higher than rates for women although the breakdown is the same.

This year, a descriptive analysis of the sociodemographic variables modified in 2000 has been presented for the first time.

Figure 5 shows the differences in the family or cohabitation structure of patients who began RRT in 2000 by gender. Despite the fact that patients in RRT tend to have a spouse or partner, this percentage is higher among men. The family structure is also affected by the age of patients. The majority of patients (87.5%) living in a senior citizen's center or residence are over 64 years of age. In the 15-to-44-year age group the percentage of patients forming part of a couple is 50.5%; in the 45-to-64-year age group, it is 74.5%; in the 65-to-74-year age group it is 67.6%; and in the over-74 year age group it is 42.2%.

Figure 5. Breakdown by types of family or cohabitation structure by gender. New cases, 2000.

Figure 6. Breakdown by education level by age group. New cases, 2000.

The breakdown by education level is shown in Figure 6. The 15-to-44-year age group has the highest education percentage, with 16.5% having average-level education and 16.5% with higher education. These percentages lower as the age of the patients increases. Differences are also seen with regard to gender, since of the 6.1% patients with higher education, 79.2% are men. The same occurs with respect to average-level education (8.4% of patients) in which 81% are men.

Figure 7. Breakdown of the socioeconomic condition (category from the National Institute of Statistics- INE) by gender. New cases, 2000.

Figure 7 shows the socioeconomic status of patients who started RRT during 2000. 70.3% of patients or heads of family have steady employment; 11.5% are self-employed without employees; 7.7% are part-time or occasional workers; 5.2% work in a family business, 4% are businesspeople with personnel working under them; and the remaining 1.3% work in cooperatives. 21.3% of these patients are active workers (26.3% of men and 12.9% of women).

Type of presentation of end-stage renal failure

Since 1993, information has been compiled on patients beginning RRT to find out if starting treatment is due to the acute onset of the disease, the aggravation of a previously known disease or the normal evolution of the disease.

Figure 8 shows the breakdown of this variable for 1993-2000. Certain variations are seen although these are not reliable. What has lowered a great deal is the percentage of non-reported cases. In 1993 it was 12.6%, while in 2000 it was 0.5%.

When analyzing the type of presentation and age group, one notices that, as the age of the patient increases, the percentage of patients with a normal evolution of end-stage renal failure decreases (Figure 9).

Figure 8. Breakdown of type of presentation of end-stage renal failure. New cases, 1993-2000.

Figure 9. Breakdown of type of presentation of end-stage renal failure by age group. New cases, 1993-2000.

Figure 10. Breakdown of type of presentation of ESRF by primary renal disease. New cases 1993-2000.

Primary renal disease

With regard to incidence, a slight increase in glomerular nephropathies has been seen over last year and a decrease of those of polycystic etiology. Diabetic nephropathy continues to be the second most common cause of ESRF, followed by nephropathy of unknown etiology. Other diseases remain stable (Figure 11). Prevalence, on the other hand, has remained very stable in recent years, with a predominance of patients with glomerular pathology.

Each age group presents a different breakdown of primary renal diseases ($p<0.0001$). Thus in older groups, disease of unknown origin is very significant (30.7% in those over 74 years of age), owing to the difficulty involved in clearly establishing the etiology of renal failure in patients deteriorated by age and in those for whom the taking of a renal

biopsy might mean an added risk or low therapeutic benefit. On the other hand, glomerular diseases predominate in the 15-to-44-year group (33.5%) and polycystoses are on the rise after the age of 44. In children, close to 50% of patients suffer from a primary renal disease (PRD) included in the category of other diseases, including medullar cystic disease, cystinosis, prune belly syndrome and, above all, renal hypoplasias.

Since 2000 the Register has been compiling the way in which PRD diagnosis has been carried out: by biopsy, pathonomic tests or clinical suspicion. 72% of glomerular diseases, 51% of the nephropathies of the "other disease" group and 13% of interstitial diseases were diagnosed by biopsy. In the remaining categories this percentage is lower than 10%, since pathonomic tests were used to diagnose 94.5% of the polycystic nephropathies, and close to 30% of those of interstitial etiology, vascular and other diseases (Figure 12).

Figure 11. Incidence and prevalence by primary renal disease, 2000.

Figure 12. Diagnostic tests by primary renal disease. New cases, 2000.

2000 also marked the beginning of the systematic registering of the year the first visit to the nephrologist took place. Figure 13 shows the mean time passed between the first visit to the nephrologist and the start of RRT. Patients with a polycystic, glomerular or interstitial nephropathy were those treated for the longest time by the nephrologist, while diabetic patients and those belonging to the group of other nephropathies were those treated the shortest time.

Figure 13. Incidence and prevalence by primary renal disease, 2000.

Type of treatment

Figure 14 shows the breakdown of patients on December 31, 2000 by type of treatment. There is a lowering in the percentage of patients treated with assisted hemodialysis (AHD) in favor of patients with functioning renal transplants from cadavers (RTC) by 1.3%, while the percentage of other therapeutic techniques remains very low. Moreover, the percentage of patients with a functioning RTL remains stable (0.6%). The number of patients in continuous cycle peritoneal dialysis (CCPD) matches that of patients in continuous ambulatory peritoneal dialysis (CAPD).

64.3% of the youngest patients (under 45 years of age) have functioning transplants. This percentage drops to 30.1% in patients from 65-to-74-years of age. PD is used at the same rate for all age groups (close to 3%) but while CCPD is more significant in younger groups, CAPD is used on older patients.

When analyzing the breakdown by treatment type and age group in the period 1986-2000, we see that, in 1986 in the **0-to-44-year age group**, 38.1% of patients have a functioning transplant and 61.9% were on dialysis (D). From 1987 onward, this proportion was inverted since there were more patients with a functioning transplant. In 2000 this proportion was 64.3% with RT and 35.7% on dialysis.

In the **45-to-64-year age group**, the percentage of patients with functioning transplants in 1986 was 17.4%. In 1995 this proportion was similar to that of dialysis patients and in 2000 it rose to 57.5%. As for the **group of patients over 64**, in 1986 the percentage of patients with a functioning transplant was practically non-existent while in 2000 it represented 19.7% of patients in this age group (Figure 15).

Figure 14. Prevalence by treatment type, 2000.

Figure 15. Prevalence by treatment type, 1986-2000.

Table 3 shows the breakdown of treatment type by health region. The prevalence data are expressed in absolute figures and in percentages, while the incidence and mortality data are only presented in absolute figures. Figure 16 describes the flow between the different treatments during 2000, and the situation on December 31.

Table 3. Breakdown of treatment type by health region of residence, 2000.

Figure 16. Flow of patients residing in Catalonia and in Renal Replacement Therapy, 2000.

Dialysis

Hemodialysis

In 2000, the percentage of patients dialyzed in the health region of residence is the same as last year (87.8%). The remaining 12.2%, who had to travel to another health region for dialysis, were mainly patients from the health regions of Barcelonès Nord and Maresme, Costa de Ponent and Centre, who used the resources of nephrology services of the city of Barcelona for reasons of geographical proximity. The health region of Lleida was where the largest number of patients from outside Catalonia received dialysis. For the most part they came from the towns in the region of Franja de Ponent in Aragon (Table 4).

Table 4. Breakdown of dialysis patients by health region of residence and health region of treatment, 2000.

As in previous years, an analysis was carried out of the patients who start HD each year, including patients receiving HD as first RRT technique, those who had previously used other techniques (transplantation or peritoneal dialysis) and patients from other Spanish autonomous communities who receive dialysis in Catalonia. Figure 17 shows the entry points of patients to HD (columns on the left) and leaving points from this technique (column on the right).

It can be seen that the total number of patients who started HD (992) marks a slight drop over the previous year, during which time an increase of 100 patients was produced. Over the past four years, given the increase in new patients, there has been an increase in patients starting HD and using RRT as first technique, while the number of patients starting HD on account of graft failure or after having received PD remains quite stable. With regard to stopping HD, it can be seen that the number of deaths in this technique has risen considerably (500 deaths in the years 1996 and 1997, 573 in 1999 and 600 in 2000). This fact, together with the maintenance of a high transplantation rate, explains why the number of patients abandoning this technique has also continued to increase in recent years.

The annual differences between the two columns, entering and leaving the technique, show the demand for new openings in HD. There were 117 in Catalonia this year.

Figure 17. Flow of patients: Hemodialysis, 1991-2000.

Table 5 reveals the breakdown of entry of patients to AHD from each of the health regions of residence, during the period 1998-2000.

Table 5. Patients who start hemodialysis by health region of residence, 1998-2000.

Figure 18. Reason for switch from hemodialysis to peritoneal dialysis, 1993-2000.

Figure 19. Weekly hours of hemodialysis, 1990-2000.

Information concerning the reasons for switching from hemodialysis to peritoneal dialysis has been compiled since 1993 (Figure 18). Lack of vascular access was the main reason why patients left HD and switched over to PD (36.5%), followed by the patient's own choice (27.5%). The low number of cases (234) and the high percentage of cases for which this information is not reported (23.5%) still prevents the completion of more detailed studies to determine the influence of other factors such as primary renal disease, age or the length of time the patient has been on dialysis.

Concerning periodicity of treatment, the year 2000 saw a new reduction of the percentage of patients receiving dialysis less than 10 hours weekly. This phenomenon can be observed in Figure 19. Despite the fact that the vast majority of patients receive dialysis from 10 to 12 hours weekly, this percentage drops in favor of those who receive 9 hours per week, which went from 16% in 1990 to 31% in 1996, 28.0% in 1997 and 18.0% this year. This percentage of patients who receive dialysis 9 hours per week varies by gender (13.3% of men and 25.1% of women), age (7.7% of patients from 15-to-44-years of age, 12.1% of those from 45 to 64, 19.3% of those from 65 to 74 and 27.4% of those over 74) and the level of service of the center where they receive dialysis (7.3% of patients treated in nephrology departments, 23.0% treated in nephrological service units and 17.7% treated in dialysis centers). The percentage of patients receiving fewer than 9 hours or more than 12 hours of dialysis treatment remains close to 5%. 98% of patients receive 3 weekly sessions of hemodialysis.

Figure 20 shows the breakdown of patients by the number of weekly hours of hemodialysis and body surface. 52.3% of patients receiving dialysis 9 hours weekly or less are those with a body surface smaller than 1.7 m^2, while those receiving dialysis more than 12 hours weekly with the same body surface are 30.0%. Only 6 patients receiving dialysis less than 9 hours weekly have a body surface greater than 1.7 m^2. It has been seen that as the number of hours of hemodialysis increases, so does the mean body surface ($p<0.00001$). Patients receiving dialysis less than 9 hours weekly have a mean body surface of 1.63 m^2, those receiving 9 hours have 1.58 m^2, those receiving 10 to 12 hours have 1.69 m^2 and those receiving more than 12 hours have 1.82 m^2.

Figure 20. Percentage breakdown of patients in hemodialysis by number of hours of dialysis weekly and body surface, 2000.

Vascular access

This is the fifth consecutive year that data concerning vascular accesses has been collected. The 1996 statistical report devotes a chapter to this subject. The 1997 report not only provides a general description of the breakdown of the different types of vascular accesses, but also a study of the characteristics of patients who had 4 or more vascular accesses. A study was begun on the morbidity and mortality associated with the type of vascular access used in the first dialysis. The reports for 1998 and 1999 shows more in-depth research on the study of the risk factors involved in starting HD with a catheter and on associated mortality when starting HD with a catheter, respectively.

Of the 3,284 hemodialysis patients who were alive and residing in Catalonia on December 31, 2000, information was collected on 3,278 of them (99.9%). Of these, 2,770 (84.5%) received dialysis by means of an internal arteriovenous fistula (IAVF); 250 (7.6%) did so via different types of grafts; and 258 (7.9%) with temporary or permanent catheters.

The IAVF was the preferred type of vascular access, since it was used by 84.52% of patients. The predominant site was the carpus (63.6%) as opposed to the elbow (36.4%), and in both sites the upper left extremity was preferentially used.

This year the number of patients using a graft (250) was the same as those using a catheter (258). Heterologous grafts were used more frequently, since only 3.6% of these patients used saphenous vein grafts. Nearly half of the grafts were placed in the lower extremities.

Figure 21. Breakdown of vascular access type by PRD, 2000.

7.9% of the patients also use the catheter. There is a predominance of use in the shoulder girdle (93.4%) over the pelvic girdle (6.6%). The majority of non-permanent catheters are placed on the right side and they are distributed as follows: 24.6% in the subclavian vein, 68.3% in the jugular vein, 7.1% in the femoral vein. 50.0% of patients receive dialysis with a tunneled catheter (permcath).

Figure 22. Breakdown of vascular access type by age group, 2000.

Figure 23. Breakdown of the number of hospital admissions as a result of complications with vascular access, by type, 2000.

Figure 21 shows that diabetic and interstitial patients were those with a higher percentage of catheters, 11.9% and 9.5% respectively; while glomerular patients (4.5%) or those with renal polycystosis (5.4%) were those with the lowest percentage. There are also differences in the breakdown of vascular accesses depending on the age of the patient. As the age of the patient increases, so does the percentage of patients with a catheter and a graft (Figure 22).

The number of hospital admissions owing to complications of the vascular access of patients living on December 31, 2000 has been studied. Of catheterized patients, 61.2% did not require admittance at any time this year, 20% had to be admitted once, 11.6% twice and 7.2% more than twice. In the case of patients with an IAVF, the percentages were 90%, 7.3%, 2% and 0.7% respectively (Figure 23).

Peritoneal Dialysis

Figure 24 shows the study of flows of patients who started or abandoned peritoneal dialysis. The progressive increase of patients starting PD since 1992 was interrupted in 1995 and was briefly recovered in 1998 thanks to those who began PD as first technique. However this year it decreased once again. The number of patients who began PD as first technique this year was 58, compared to 79 in 1998. The number and breakdown of patients starting and abandoning this technique were very similar to those of previous years. This year the same number of patients initiating the technique abandoned it.

Figure 24. Flow of patients: peritoneal dialysis. 1991-2000.

Figure 25. Reason for switching from peritoneal dialysis to hemodialysis. 1993-2000.

Figure 26. Probability of developing peritonitis by PD technique. New cases of peritoneal dialysis, 2000.

Figure 25 shows the breakdown of reasons for switching from peritoneal dialysis to hemodialysis in 1993-2000. Infection of the peritoneum, together with associated disease or serious complication were the main reasons for the switchover, with 30.6% and 31.1% respectively, percentages which rise to over 40% if we take into account only the reported cases.

Of the patients who began PD this year, the probability has been studied of their developing a peritonitis as a result of the technique used (CCPD or CAPD). As Figure 26 shows, the probability accumulated over a year of a patient in CCPD having peritonitis is 24%, while if he follows CAPD treatment, it is 35%.

The 1996 report offers a more exhaustive analysis of peritoneal dialysis, with information on the different types of peritoneal dialysis, connections used, type of catheter, study of peritonitis episodes, etc.

Treatment with recombinant human erythropoietin

With regard to treatment with recombinant human erythropoietin (r-HuEPO), the 1996 report contains a study on the use of r-HuEPO in patients in RRT carried out jointly with the Register of the Advisory Committee for the therapeutic use of r-HuEPO. This section presents only an update based on certain variables from the Register such as age, gender, primary renal disease and health region of residence.

Figure 27. Breakdown of dialysis patients receiving treatment with r-HuEPO, by age and gender, 2000.

As every year, the percentage of patients treated with r-HuEPO continues to grow. In 2000 it was 90.3%, almost 10% more than the previous year. The percentage of women receiving treatment with r-HuEPO is always higher than that of men, in all age groups. In the under-15 age group, there were very few cases and thus the percentages may vary a great deal. In women, the percentages for the different age groups remain stable. In men, the percentage of treated patients decreases slightly with age until reaching the 45-to-64-year age group, at which point it rises slightly (Figure 27). The proportion of patients treated with this hormone is different for each of the primary renal diseases. The evolution of 1990-2000 shows the constant increase in these percentages. In the past year the percentages varied between 74.6% for patients with polycystosis and more than 93% for patients with interstitial, vascular nephropathy and those in the group of other nephropathies (Figure 28).

Figure 28. Evolution of percentage of dialysis patients receiving treatment with r-HuEPO by primary renal disease, 1990-2000.

Figure 29. Breakdown of percentage of dialysis patients receiving treatment with r-HuEPO by health region of residence, 2000.

Certain differences can be seen in the percentage of dialysis patients treated with r-HuEPO by health region of residence, although these are less significant as the years go by. The health region of Tortosa (75.3%) remains at the same level as last year while that of Barcelona Ciutat (90.5%), Costa de Ponent (93.6%) and Lleida (89.4%) show an increase and are on a par with the other regions, which vary between 88% and 92.2% (Figure 29).

Transplantation

This year, 366 renal transplants were performed in Catalonia, which means a slight increase over last year. This figure, expressed per million population, represents a transplant rate of 60.1 pmp, higher than the majority of European countries with major transplanting activity.

Figure 30 shows the global evolution since 1984 and by type of transplant. This year the number of live donor transplants (RTL) increased. There were in fact 8, five more than last year. The increase in kidney and pancreas transplants was maintained. In 1988, the first multiple kidney and liver transplant was performed, and since then there have been 45. Double kidney transplants (dual RT) were first carried out in 1997. This new modality

seeks to put available resources to better use, since it now admits certain kidneys as valid organs which, owing to their characteristics, would not be accepted individually for single-kidney transplants. This year 8 such transplants were performed, whereas last year no transplants of this type were done. Nonetheless, it should be pointed out that in 1999 the first simultaneous kidney and heart transplant was carried out.

Figure 30. Evolution of the number of transplants, 1984-2000.

Data concerning recipients

As has been seen in the breakdown by age and gender, an aging of the population in RRT is taking place. This fact is also reflected in the continuous increase in the mean age of patients when receiving a transplant. The evolution of this indicator is shown in Figure 31, together with the percentage breakdown by age group, of patients over 55 years of age who received transplants in the period 1990-2000. The mean age of patients at the time of receiving a transplant oscillates between 34.1 years in 1985 and 49.0 years in 2000.

As regards the breakdown by age groups, it has been seen that in 1990 the percentage of transplants to patients in the 55 to 59 year age group remains stable, but the percentage of patients over 60 years of age has increased since 1988, and that of patients over 64 since 1990, although they show more irregular behavior.

During this period (1984-2000), there has also been a marked increase in the number of transplants to diabetic patients, from 2.1% of the total transplants in 1985 to 9.8% in 2000. It should be noted here that this increase also implies a qualitative change, given that currently the majority of these transplants are simultaneous, involving kidney and pancreas. 21 such transplants were carried out in 2000.

Figure 31. Evolution of the percentage of renal transplants in those over 55 years of age and the mean age of patients who have received transplants, 1990-2000.

Table 6. Comparative data on renal transplants in Catalonia, 1984-1989, 1990-1994 and 1995-2000.

Table 6 presents a summary of the data from the different factors studied and groups the years into three periods. The first presents the transplants performed from 1984 to 1989, the second from 1990 to 1994 and the third from 1995 to 2000. The differences between the periods are always highly significant, with the exception of the data concerning retransplants, where the percentages are very similar for the three periods. In short, it can be said that transplants in Catalonia are now being carried out on older patients, with more HLA-DR matches and to a higher number of diabetic patients, mainly simultaneous kidney and pancreas transplants, while the proportion of retransplants has varied little.

Table 7 shows the breakdown of patients with functioning transplants in relation to the health region of residence and the health region of treatment, both for transplants performed this year and for all patients with functioning transplants followed in Catalonia.

Table 7. Breakdown of patients that have received transplants by health region of residence and treatment, 2000.

The percentage of patients from outside Catalonia who received a renal transplant this year was 9.3% (34 patients). In the early years, this percentage varied between 20% and a 25%; in 1995 it was 17.1%. This tendency could be explained by the increase in transplants carried out in other Spanish autonomous communities in recent years. This

year the patients not residing in Catalonia who received transplants in Catalan renal transplant units are above all from the Balearic Islands (13 patients), Valencia (4 patients), Aragon (4 patients) and Andalusia (4 patients).

Despite the continued increase of patients in RRT, the number of patients on the waiting list to receive a transplant has not increased in the same proportion. The number of patients on the waiting list is quite stabilized, in spite of a lowering of the percentage. An increase in the number of patients pending study (Figure 32) has also been seen. Another important development has been the spectacular increase in the number of patients excluded from the waiting list for clinical reasons since 1990. In 1989, 222 were excluded from the waiting list (6.3% of the total) for this reason, and in 2000, 942 (27.4%). This could have been prompted by a change in the reporting criterion, since it was at that time that the age limits for receiving a transplant were extended.

The percentage of patients on the waiting list (excluding patients pending clinical studies or histocompatibility and those who have functioning transplants) lowers with age, going from 85% of patients between 15 and 44 years to 0.8% in those over 74. Exclusion for clinical reasons accounts for close to 42.6% of patients from 45 to 74 years of age. There are significant differences in the waiting-list situation as a result of primary renal disease: more than 43.2% of glomerular dialysis patients are on the waiting list to receive a transplant, while only 12.8% of diabetic patients or 14.0% of vascular patients are. Moreover, diabetic patients make up the group with the greatest percentage of exclusions for clinical reasons (43.4%).

Figure 32. Situation of patients in RRT residing in Catalonia in relation to transplantation, 1990-2000.

Figure 33 shows the evolution of the waiting list for patients who initiated RRT in 1990-2000 and as first intention were not excluded from the waiting list for any reason (age, clinical reasons or voluntary exclusion). At the end of the first year 1.9% of patients had already received a transplant, 8% were on the waiting list with all studies completed and the remaining 90.1% were pending study. After 5 years, 35.2% had a functioning transplant, 20.8% were on the waiting list, 6.5% were pending studies, 16.8% were excluded and 20.7% had died. At the 10-year mark, 40.8% continued with a functioning transplant, 5% were on the waiting list to receive a transplant, 3.7% pending studies, 9.3% excluded and 41.2% had died.

Figure 33. Evolution of the situation on the waiting list and mortality. New cases not excluded from the list at start of RRT, 1990-2000.

Figure 34. Previous time on dialysis of patients who received a first renal cadaver transplant. Transplants 1986-2000.

Figure 34 shows the previous amount of time on dialysis of patients residing in Catalonia who received a first RTC in the period 1986-2000, expressed as the annual means and their respective 95% confidence interval. The global mean for the period was 39.6 months, while in 2000 this figure was 33.2 months. Despite these fluctuations, a clear downward tendency has been seen in the time spent on dialysis while awaiting a transplant.

Figure 35 shows the mean number of months on dialysis of patients living on December 31, 2000 who were on the waiting list for a first transplant (including patients pending clinical studies or histocompatibility), analyzed by the health region of residence. For Catalonia as a whole this time was 43.7 months. The health regions of Barcelonès Nord and Maresme and Tortosa were those with the lowest mean time on dialysis, this being less than 40 months.

Figure 35. Time on dialysis of patients on the waiting list (December 31, 2000) to receive the first renal transplant from a cadaver, by health region of residence.

Figures 36, 37 and 38 show the probability of receiving a transplant in relation to time in RRT and different factors. In the first figure, it is seen that, for patients as a whole, the cumulative probability at the second year is 35.6%, at the fourth year 59.4% and at the sixth year 70.3%. The following figure shows the same study in relation to age, and it can be seen that the probability of receiving a transplant is lower for older age groups. For patients under 14 years the cumulative probability of receiving a transplant is 55.5% in the first year, 77.8% in the second year; 87.0% in the third year, and 100% and in the sixth year. In the 15-to-44-year age group, this probability is 50.4% in the second year, 75.3% in the fourth year and 87.5% in the sixth year. In the 45-to-64-year age group it is 31.8% in the second year, 56.2% in the fourth year and 66.4% in the sixth year. Finally, in the 64-to-74-year age group it is 15.3% in the second year, 27.8% in the fourth year and 30.4% in the sixth year (Figure 37).

Figure 38 shows the same study by PRD. It can be seen that diabetic patients are those with the lowest probability of receiving a transplant, followed by vascular patients and those of unknown etiology.

Figure 36. Cumulative probability of receiving a first transplant. Patients on the waiting list at start of RRT, 1990-2000.

Figure 37. Cumulative probability of receiving a first transplant by age group. Patients on the waiting list at start of RRT, 1990-2000.

Figure 38. Cumulative probability of receiving a first transplant by PRD. Patients on the waiting list at start of RRT, 1990-2000.

Figure 39. Previous time on dialysis of patients who received a renal retransplant from a cadaver donor. Transplants 1986-2000.

With regard to time on dialysis prior to receiving a retransplant, no clear tendency is seen, unlike the situation with respect to time on dialysis prior to a first transplant. The patients who received a retransplant from a cadaver donor during the period 1986-2000 were on dialysis for a mean time of 42.2 months following the failure of the first graft. In the case of patients who received a retransplant in 2000, this time was 58.7 months. The annual number of retransplants was lower and therefore the 95% confidence intervals were wider (Figure 39).

The flow study of transplants (Figure 40) shows the previous treatment techniques of patients receiving a transplant and the number of patients receiving a transplant who started or resumed other techniques. Although the characteristics of patients with transplants have been discussed earlier, it is important to point out the existence of a small number of patients (8 patients this year) who received a transplant without undergoing any other previous replacement therapy; and too, the increase in patients who previously received peritoneal dialysis. In 1996 and 1997, the number of patients that received a renal transplant from outside Catalonia decreased; in 1998 it rose slightly and subsequently dropped once again to 9.3%.

Figure 40. Annual flow of patients: Transplants, 1991-2000.

The study of immunosuppressant treatments was carried out using data compiled from 1990 on. In the past three years, there has been an increase in the use of new drugs such as mycophenolate and tacrolimus, and a significant reduction in the use of cyclosporine A and azathioprine. The breakdown of the immunosuppressant drugs used

in the first six weeks following transplantation is shown in Figure 41, in which the drugs used in 1995 and in 2000 are compared. This year, given the changes in the immunosuppressant protocols, we have added a new anti-CD25 category (humanized and chimerized). There was a significant reduction in the use of cyclosporine A, azathioprine, GAL and OKT3 and an increase in mycophenolate, tacrolimus and anti-CD25.

Figure 42 shows the types of drugs used in the immunosuppressant maintenance treatment of patients with functioning transplants on December 31, 2000. A large difference is seen in the use of immunosuppressants in 1995 and in 2000. At present, corticoids, mycophenolate and tacrolimus are those that are used most. The use of the cyclosporine A and azathioprine has been greatly reduced.

Figure 41. Immunosuppressant drugs used during the first six weeks following transplantation. Transplants 1995 and 2000.

Figure 42. Immunosuppressant maintenance treatment for transplants functioning on December 31, 2000.

As in recent years, the Cockroft-Gault formula has been applied in order to estimate creatinine clearance. This employs serum creatinine and the age, weight and gender of the recipient. This test is very useful and accepted as an indirect measure of glomerular filtration.

Cockroft-Gault formula:

$$\text{Estimated creatinine clearance in men} = \frac{(140 - \text{age}) \times \text{body weight (kg)}}{\text{Serum creatinine mg/dL} \times 72}$$

$$\text{Estimated creatinine clearance in women} = \frac{(140 - \text{age}) \times \text{body weight (kg)}}{\text{Serum creatinine mg/dL} \times 85}$$

Figure 43 shows the estimated creatinine clearance, using this formula, for patients with functioning transplants on December 31, 2000 by gender. In general, the men had better glomerular filtration than the women, since only 11.5% had insufficient levels, under 30mL/min., whereas in the women this percentage was 17.7%.

Figure 43. Estimated serum creatinine clearance by gender. Patients with functioning transplants on December 31, 2000.

Glomerular filtration was also analyzed in relation to the ages of the recipient and the donor, as shown in Figures 44 and 45. The data presented correspond to the third update, on December 31. In both figures it can be seen that as the age increases, both of the recipient and of the donor, the levels of glomerular filtration are worse and the percentage of deaths of patients increases. Moreover, in both cases, the percentage of patients resuming dialysis is not very high.

Figure 44. Estimated serum creatinine clearance by age of recipient. Update in the third year following transplantation. Transplants 1990-1997.

Figure 45. Estimated serum creatinine clearance by age of donor. Update in the third year following transplantation. Transplants 1990-1997.

In the period 1990-2000, 3,616 transplants were performed. Of these, 689 cases of graft failure and 337 patient deaths were reported. The breakdown of the main causes of graft

loss varies in relation to the time passed following the transplant. These causes were analyzed in two periods, by the time in which graft failure took place: at the first year of transplant or in subsequent years. 29.4% of the cases of graft loss during the first year following transplantation were due to chronic transplant nephropathy (acute or chronic rejection), 27.8% to complications, 3.6% to hyperacute rejection and 1.4% to abandonment of immunosuppressant treatment. The cause was not reported in only 4.1% of the cases.

The main cause of graft loss following the first year of transplantation was also chronic transplant nephropathy (46%). 4.1% of cases were produced by a recurrence of the PRD and 1.9% for abandonment of immunosuppressant treatment. Cause of graft loss was unknown in 8.7% of the cases (Figure 46).

Figure 46. Breakdown of causes of graft loss by time passed since transplantation. Transplants 1990-2000.

The causes of kidney loss in the first year following transplantation fall into two categories: those that are due to graft failure and those caused by the death of the patient (with or without a functioning kidney). In 1984 and 1985 the percentage of transplanted kidney loss was approximately 11% owing to the death of the patient and 14% owing to graft failure, while in recent years these figures have been 5% and 10%, respectively. Figure 47 shows the evolution in the time of both categories. It can be seen that since 1998 there has been a very significant reduction in kidney loss in the first year following transplantation, a development that may be the result of using new drugs. In the last year, losses due to graft failure were 4.2% and those caused by death of the patient, 3.4%.

In the breakdown of transplanted kidney loss by age, it can be seen that as age increases, the percentage of losses owing to rejection is clearly reduced (from 24.3% of transplants to patients under 15 years of age to 8.3% in patients over 59 years of age). In contrast, those caused by death of the patient increase with age (4.3% in patients under 15 to 17.8% in patients over 59). It should also be pointed out that patients from 15 to 54 years of age show a global percentage of transplanted kidney loss that is lower than the remaining categories (27.0% of all transplants carried out in the period 1990-2000).

In spite of the foregoing, it is essential to put all these data into perspective, since this analysis has not taken into account the time that the transplant has been functioning (in other words, “exposure time”). Also and as commented earlier, transplants to older people and diabetic patients have increased significantly in recent years, meaning that the exposure time of these patients is shorter than for groups of patients with standard PRD or those under 55 years of age. For this reason, these data have to be analyzed together with those obtained in the survival analysis of patients who have received a transplant and grafts by age and PRD, since this study does indeed take into account the time that patients have had a functioning transplant.

Figure 47. Evolution of percentages of graft failure and of death of the patient in the first year following transplantation. Transplants 1990-1999.

Donor data

During 1995, donor data on age, gender and cause of death were collected retrospectively as far back as 1990. The inclusion of these new factors has improved the quality of the analysis presented with respect to cadaver transplants.

Figure 48 shows the aging of donors. In 1990, the kidneys of donors over 50 years of age represented 20% of the total, while in 2000 they accounted for 45.3%. Furthermore, in this last year the number of kidneys provided by donors 70 years of age or older was 10.9%, while in the period 1990-1994 it varied between 1% and 2%. As a result, the

mean donor age has gone from 31.4 years in 1990 to 45.8 years in 2000, moving up one year over 1999.

Figure 48. Evolution of the breakdown of renal transplants from cadaver donors over 50 years of age, and of the mean donor age, 1990-2000.

Figure 49. Evolution of the breakdown of renal transplants from cadaver donors by cause of donor death. Transplants 1990-2000.

In recent years, certain variations were produced in the typology of donors, who, as mentioned, are increasingly older. Analyses of the causes of death have pointed to a reduction in donors who died from cranioencephalic traumas (CET) and an increase in donors from cerebrovascular accidents (CVA) (Figure 49).

In order to relate the donor's age with that of the recipient, this year the age groups were recalculated. **Young recipients** are now those under 60 years of age and **old recipients** are those 60 years of age or older. Similarly **young donors** are under 60 years and **old donors,** 60 or older.

The following figure presents an analysis of the estimated creatinine clearance, using the Cockroft-Gault formula, of patients who received a renal transplant from a cadaver donor, bearing in mind the ages of both donor and recipient. All serum creatinine levels used in the analysis correspond to the measurements taken on December 31 of the third year following transplantation. The categories of non-functioning kidney (dialysis) and death of patient are included among the different levels of estimated creatinine clearance.

In the third follow-up, young recipients with renal transplants from young donors had better glomerular filtration, which was normal in 33.9% of cases. In contrast, young recipients who received kidneys from an old donors not only had worse estimated creatinine clearance (>59mL/min, 12.1%), but also suffered greater mortality than those who have received kidneys from young donors (7.6% compared to 3.6%). Even though 13.9% of the old recipients who received transplants from young donors had good glomerular filtration, they also showed a higher percentage of mortality (15.9%, while old other old recipients that received organs from older donors only had 12.4%) (Figure 50).

Figure 50. Estimated creatinine clearance of patients who received transplants from cadaver donors by ages of donor and recipient, in the third follow-up, 1990-1997.

To ensure correct analysis of these data, they should be studied together with the survival curves of the patient and the graft, by donor characteristics.

The following figures analyze certain aspects of renal transplantation. Figure 51 shows the evolution of the time of cold ischemia of the organs used in the transplants from the period 1990-2000. Here a tendency towards reduction is seen. In 1991, the mean hours of ischemia were 23.2 and this year 17.2. The number of days of hemodialysis following transplantation has also decreased: the mean for 1991 was 4.2 days and that of 2000, 1.3 days (Figure 52). Figure 53 shows the percentage of acute tubular necrosis, although in this case the reduction of this type of episodes does not seem to be as clear. It must be taken into account that the number of non-reported cases in these last analyses was much greater (more than 30%).

Figure 51. Time of cold ischemia of transplanted kidneys. Transplants 1990-2000.

Figure 52. Days of post-transplantation HD. Transplants 1990-2000.

Figure 53. Percentage of patients with episodes of acute tubular necrosis. Transplants 1990-2000.

Morbidity

Concomitant diseases

Morbidity was analyzed for patients living at the end of the year in relation to different parameters, such as PRD, age and last treatment type. In the first case, a classification was used that is often employed by the EDTA: **standard disease** (codes 00 to 66), **diabetes** (codes 80 and 81) and **other** (codes 82 to 99). As of last year, fifteen concomitant diseases have been analyzed instead of thirteen, since arterial hypertension and (AHT) and irreversible visual deficit have been included. In Figure 54 it can be seen that diabetic patients suffered from a greater number of cardiovascular diseases (ischemic heart disease, cardiomyopathy, circulatory disorders, cerebrovascular disease and vascular diseases), while the rest of the concomitant diseases studied are broken down in a more homogeneous manner. The mean number of diseases, not counting AHT, is similar to last year (1.90 for the standard renal disease group, 3.13 for the diabetic group and 2.78 for the rest) in all groups. The means presented in the figure include AHT.

Figure 54. Concomitant diseases by primary renal disease. Cases on December 31, 2000.

With respect to the different age groups, the elderly show the highest percentage of concomitant diseases. 28% to 40% of patients over 64 years of age and 30% to 50% patients over 74 of age presented cardiovascular disease or chronic respiratory disease. 46% of patients from 64 to 74, and 65% of those over 74 suffered from arthropathies. As regards the group from 45-to-64-years of age, the percentage with which these diseases were presented oscillates between 7% and 25%. Finally, in the group of patients from 15-to-44-years of age, these percentages are around 5%, except in the case of cardiomyopathy, diseases of the esophagus, stomach and duodenum, and arthropathy, which are present in between 10% and 20% of the cases, and in vascular diseases, present in 25% of the cases. The percentage of tuberculosis and diabetes is lower than 9% in the three age groups. Chronic liver disease affects between 5% and 20% in the different age groups (Figure 55).

Figure 55. Concomitant diseases by age group. Cases on December 31, 2000.

Figure 56. Concomitant diseases by last treatment. Patients from 45-to-64-years of age with standard PRD and on the waiting list for RT. Cases on December 31, 2000.

Since the populations in each of the treatments differ in such parameters as age or primary renal disease, which, as has been seen, influence in the morbidity of patients, the study has been repeated, adjusting the populations with respect to these factors to make them more homogeneous. Thus, in each of the three treatment groups, patients were selected who were over 44 years of age and under 65 with standard PRD and, in the case of dialysis patients, those included on the transplant (RT) waiting list. The results are shown in Figure 56. The mean ages for these new groups were 54.62 years for dialysis patients (361 cases) and 55.10 for patients with a functioning transplant (1,095 cases). Generally speaking, the means of concomitant diseases were equal, even though dialysis patients still maintained a higher mean, and had higher percentages than patients with functioning transplants for the majority of pathologies. The most frequent diseases present in dialysis patients, apart from hypertension, were arthopathy (33.8%), cardiomyopathy (18.8%), diseases of the esophagus, stomach or duodenum (22.7%)

and chronic liver disease (16.1%). The most frequent diseases in the patients with a functioning transplant were, above all, vascular disease (15.3%) and chronic liver diseases (16.0%).

Table 8. Main concomitant diseases, 2000.

To summarize this section, Table 8 presents the main concomitant diseases at the beginning of RRT in new cases in 2000 and of all patients living by the end of the year. Comparing these results with those obtained last year, it has been seen that, on the one hand, the patients who started RRT this year had a slightly higher number of concomitant pathologies, especially in relation to arthopathy, diabetes and circulatory disorders, although these variations were of little significance due to the low number of cases. A slight increase in some pathologies and a reduction in others were also been seen for the total group of patients on December 31.

Table 9 shows that, of the patients living on December 31, 404 had diabetes mellitus (DM) as a concomitant disease. Of these patients, 258 (63.9%) had type 2 DM, 76 patients (18.8%) had DM secondary to other diseases, 25 patients (6.2%) presented type 1 DM, and the 45 remaining patients (11.1%) had an unspecified DM.

Malignant neoplasms

Figure 57 shows the breakdown of malignant neoplasms by gender. The most frequent neoplasias in the men were skin processes, in 3.0%, processes of the urinary system in 2.9% and gastrointestinal processes in 1.8%. 2.3% of the women suffered from breast cancer, 1.8% had skin cancer and 1.1% had cancer of the urinary system. The older groups were affected by the most frequent malignant neoplasms (urinary system, genital and gastrointestinal), except for skin cancers, which most often affected patients between 45 and 64 years of age.

A more in-depth treatment of this subject is found in the 1995 Statistical Report, which, using the actuarial method, examines the appearance of malignant neoplasms throughout the time in RRT, on the basis of various factors such as treatment type, site of origin of the neoplasia, gender and age group.

This year, the probability study of the appearance of malignant neoplasms was carried out using the new cases for the period 1990-2000. Overall, it was seen that the probability of appearance of malignant neoplasms was 9.8% at 5 years after starting RRT, and 15.7% at 10 years, and that the probability of malignant neoplasms appearing was higher in men than in women ($p=0.002$). This probability was 11.8% for men and 7.8% for women at 5 years after starting treatment and 18.6% and 12.2% respectively, at 10 years.

Figure 57. Breakdown of malignant neoplasms by gender. Cases on December 31, 2000.

Another factor showing significant statistical differences was age; the probability of appearance of malignant neoplasms increased considerably in the older age groups of patients. Whereas in the groups of patients between 45 and 64 years of age, it was 16.6% at 10 years after starting RRT, in the 64-to-74-years this reached 23.3%, and in patients over 74 years, 38.4% in the same period ($p<0.0001$).

Table 9 shows the probability of the appearance of different types of neoplasias at 5 and 10 years after starting treatment (dialysis or transplant). The most frequent are those of urogenital, gastrointestinal, and dermatological origin.

Table 9. Probability of appearance of different malignant neoplasms in RRT patients, 1990-2000.

Hepatitis C virus

For the eighth consecutive year, the Catalan Register of Renal Patients has compiled information on this subject in the annual patient follow-up, with the purpose of contributing information on the appearance of new cases and the risk factors associated with this problem. This year, as in 1999, we have devoted special attention to the follow-up of patients who started Renal Replacement Therapy from 1995 on. For this reason, some of the following data refer only to these patients, while other data refers to the situation of patients living on December 31.

Figure 58. Percentage of patients with antibodies to HCV by last treatment. Cases on December 31, 2000.

Figure 59. Probability of developing HCV seroconversion. New cases 1995-2000.

The percentage of non-reported cases has continued to decrease. In 1998, it was 8.9% (504 patients); in 1999, 7.8% (462 patients); and this year it was 3.4% (210 patients). The majority of the non-reported cases were patients who received a transplant for whom their serology was unknown or not reported. The percentage of patients with antibodies to HCV by last treatment appears in Figure 58. If patients whose cases were not reported are excluded, the percentage of patients with antibodies to HCV receiving HD on December 31, 2000 is 19.1%, lower than last year, and that of those with a functioning transplant is 26.1%, also lower than last year. The percentage of infected patients receiving peritoneal dialysis continues to be lower than for other treatments (8.9%).

The global rate of seroconversion of patients in the period studied is 1.84 per 100 people/ year of follow-up. This year the probability of seroconversion by time in RRT has also been calculated. This analysis is an approximation since only the year of seroconversion is known, not the exact date. With this information, and bearing in mind that conversion took place at the end of the year in which it was reported, cumulative probability has been calculated. It is shown in Figure 59.

A multivariate analysis has also been carried out, for analyzing possible risk factors, such as age, gender, primary renal disease, time in RRT, treatment with blood products, installation of shunts and catheters, surgical treatment and transplants. None of these factors were found to have a significant statistical relationship.

Level of functional autonomy

This variable is measured with a scale based on the Karnofsky activity scale adapted by Gutman for patients on dialysis (GUTMAN, 1981). This scale allows the level of functional autonomy to be measured in five categories:

1. Carries out practically normal physical activity (**Normal**).
2. Carries out almost normal physical activity most of the time. (**Almost normal**).
3. Carries out limited physical activity. Can care for oneself. (**Limited**).
4. Requires special services most of the time. Cannot care for oneself. (**Special services**).
5. Requires hospitalization or continuous services (**Continuous services**).

The patients who began Renal Replacement Therapy this year showed a distribution of their level of functional autonomy that was quite similar to that of previous years. In Figure 60 it can be seen that, of the patients who started RRT this year, the percentage of those with a good level of functional autonomy is similar to last year. 58.8% of the total group carried out normal or almost normal physical activity the greater part of the time, while few patients (2.8%) required hospitalization or continued services. Nonetheless, this figure shows that the breakdown throughout the period is very stable, and the

reduction in the percentage of non-reported cases stands out.

Figure 61 shows the breakdown of the level of functional autonomy of patients by age group on December 31, 2000. The percentage of patients who could carry out normal or almost normal physical activity lowers with age. 89% of the children showed normal physical activity while in the group of those over 74 years of age, this percentage was 13.9%.

Functional autonomy is also affected by certain pathologies such as diabetes and vascular diseases, and by the type of treatment. More than 90% of patients who received a transplant had a normal or almost normal level of autonomy.

Figure 60. Level of functional autonomy of new cases by year RRT was begun, 1993-2000.

Figure 61. Level of functional autonomy by age group. Cases on December 31, 2000.

Smoking and patients in RRT

Like last year, this year's follow-up includes information on the use of tobacco by 5,116 patients (83.5% response rate). These patients were asked if they were regular smokers, occasional smokers, ex-smokers or non-smokers. They were also inquired about their daily tobacco consumption and, in the case of ex-smokers, how many years ago they had stopped.

Figure 62. Breakdown of smoking among patients in RRT by last treatment, 2000.

Figure 63. Smoking among dialysis patients by age group and gender, 2000.

Figure 64. Proportion of smokers by age group and gender in the population of Catalonia (1994) and dialysis patients (2000).

Figure 65. Proportion of ex-smokers by age group and gender of the population of Catalonia (1994) and dialysis patients (2000).

Figure 62 shows the smoking behavior of patients in RRT by last treatment. Among patients with a functioning transplant the percentage that chose not to reply was very high (36.9%) and therefore the data for this group are not very representative. With respect to patients on hemodialysis or peritoneal dialysis, the percentage of non-smokers was 54% and 59% respectively. For this reason, the following analyses refer only to dialysis patients.

Figure 63 shows the breakdown of tobacco use by dialysis patients. The results are very similar to those of last year, where it was seen that patients who were regular or occasional smokers were for the most part young. The percentage of ex-smokers rises with age in men but lowers in women. As for patients who had never smoked, the percentage was quite stable among men, but with women it rose with age, reaching almost 100% in women over 74.

Figures 64 and 65 present the breakdown by age and gender of smokers and ex-smokers, both dialysis patients and the general population of Catalonia. Both populations, dialysis patients and the general population of Catalonia, showed similar patterns of behavior in relation to smoking, in spite of the fact that the percentage of smokers per age group was lower among patients in RRT than in the general population, for both men and women. In relation to the data presented last year, a reduction was seen in the

percentage of male smokers, in all age groups. The highest percentage of ex-smokers is among men over 45.

Survival

Survival of the patient in Renal Replacement Therapy

The global survival of patients residing in Catalonia who started Renal Replacement Therapy in the period 1984-2000 is given in Figure 66. Survival until the first year was 86.7%; to 5 years, 56.2%; and to 10 years, 35.9%. The mean time of survival was of approximately 6 and a half years.

Figure 66. Survival of patients in Renal Replacement Therapy. New cases 1984-2000.

Figure 67. Survival of patients in Renal Replacement Therapy by age at the start of treatment. New cases 1990-2000.

Table 10. Univariate and multivariate survival analyses of patients over 14 years of age in RRT (Cox Regression). New cases 1990-2000.

When analyzing survival by age groups (Figure 67 and Table 10) it can be seen that this worsens at 5 years. For the group of patients over 74 years of age it was only 22% for the same period.

Children have a slightly lower survival probability than young patients, especially in the earliest years and this is practically equaled in the fifth year (95% in the first year and 90% in the fifth year). Figure 67 shows that the differences in survival probability of patients between 20 and 50 years of age are relatively small and increase with age. Table 10 presents the results obtained in the univariate analysis (at one year and at five years) and multivariate analysis of the survival of new cases over 14 years of age (1990-2000), using the Cox regression method (COX, 1972), where the significance of each of the factors analyzed was studied: gender, age, PRD, level of functional autonomy, situation on the waiting list for a transplant, and morbidity at the start of treatment (the table only shows diseases with statistical significance).

The first column shows the factor studied; the second, the number of patients included in each of the categories of each variable; the third, the univariate probability of surviving the first year; the fourth, the univariate probability of surviving the fifth year; and the fifth, the multivariate risk, which is to say the risk adjusted to the other factors. For example: the patients belonging to the 45-to-64-year age group, at the start of the treatment, had a risk of dying 2.55 times that of the patients belonging to the 15-to-44-year age group, provided that they were in the same condition with regard to the other factors studied (PRD, level of functional autonomy, situation on the waiting list and concomitant diseases). In the case of the qualitative variables, the first category of each variable was taken as a reference and assigned a risk of 1. Thus, the patients with a diabetic nephropathy were shown to have a risk of dying 1.65 times that of glomerular patients, adjusted for the rest of variables studied. These results were very similar to those obtained in previous years (VIDAL, 1991). The last column shows the 95% confidence interval of the multivariate risk.

There are important differences in the survival of patients as a function of their primary renal disease. The glomerular and polycystic patients had similar results, especially in the first three years; these patients had the highest percentage of survival, around 95% at the first year. These differences increased at the fifth year: the glomerular patients had a survival rate of 69% while that of polycystic patients was 79%.

Patients with an interstitial pathology had survival rates of 88% at the first year and 63% at the fifth year. Vascular patients, patients with other pathologies and those of unknown etiology had similar survival rates: 81%, 80% and 86%, respectively in the first year and 45%, 47% and 52% in the fifth year. Diabetics had the worst survival rate (80% in the first year and 32% in the fifth). When adjusting for other factors that affect survival it can be seen that the patients with the lowest risk of dying are the polycystic patients, while those with the greatest risk belong to the categories of other primary renal diseases and diabetic patients (Table 10, multivariate risk).

Survival has also been analyzed by various morbidity factors such as level of functional autonomy, situation on the waiting list and certain concomitant diseases at the time of starting Renal Replacement Therapy. As the level of functional autonomy at the start of the treatment worsened, the survival rate decreased significantly, at one year and at five years, and the risk of dying adjusted by the other factors increased. It was 2.51 times higher in patients needing special services than in those who had a normal level of functional autonomy.

Survival of the patient on dialysis

Hemodialysis

Table 11. Univariate and multivariate survival analyses of patients over 14 years of age in HD (Cox Regression). Treatment cycles 1990-2000.

This section examines the survival of patients receiving treatment with hemodialysis. The analysis unit is the treatment cycle. Table 11 shows the results obtained in the univariate and multivariate survival analyses of patients on hemodialysis. Variables with statistical significance were used in the model. The results are very similar to those seen in the global analysis of patients in RRT and only some of the concomitant diseases that significantly affect the survival of the patient have changed. The rest of the variables behave in similar fashion.

Peritoneal dialysis

The survival of patients treated for peritoneal dialysis has also been separately analyzed. No differences were found in relation to gender or primary renal disease, but differences were found concerning the patient's age when starting treatment. As can be seen in Table 12, the age when starting treatment is a most significant factor for survival. Patients over 74 years of age have a risk approximately 4 times higher than those of 15 to 44, adjusting for all the other factors. Patients needing special care have 3.44 times the risk of dying than those with a normal level of functional autonomy. The concomitant diseases at the start of the treatment cycle that have statistical significance are cardiomyopathy, diabetes and chronic liver disease.

Table 12. Univariate and multivariate survival analyses of patients over 14 years of age on PD (Cox Regression). Treatment cycles 1990-2000.

Survival of patients that have received a transplant and graft survival

Seeking a more updated view of these results, this year the majority of the data presented in this section are from the period 1990-2000. Figure 68 shows the survival of the 4,689 grafts from cadaver donors carried out in Catalonia in the period 1984-2000. This is 68% at 5 years and 49% at 10 years. Once the first year hurdle has been surpassed, the chances of losing the graft are lower than 5% per year. The survival of the patient is 90% at 5 years and 82% at 10 years. Mortality takes place mainly during the first year and is lower 2% per year. These results are quite satisfactory, especially if it is taken into account that the Register contains all patients, a considerable number of which received a transplant more than 10 years ago, and that more than 20% of the recipients are over 54 years of age. This fact must be borne in mind when comparing the results with those of

other similar studies. The results concerning patients who received transplants from living donors are better yet (the survival rate of such patients is 96% at 5 years and 91% at 10 years; that of the graft is 76% and 58% respectively).

Figure 68. Survival of patients and grafts in transplants from cadaver donors. Transplants 1984-2000.

Table 13 shows survival of patients and grafts at one year, three years and five years, for the different types of transplants and periods. The results obtained are very similar to those of previous years.

The survival of patients and grafts following simultaneous kidney and liver transplants is only presented at one year and three years, given the low number of cases available.

This year, the study of kidney transplants by periods has also been divided into three intervals: 1984-1989, 1990-1994 and 1995-2000. Some differences have been seen with respect to survival of the patient between the last period and the two previous periods. Graft survival shows progressive improvement from one period to the next, although this is more significant between the first and second periods than between the second and the third. It should be taken into account that there has been an increase in the mean age of the recipients and of the number of their risk factors, as has been discussed in the section dealing with the recipient's characteristics. This same reflection is also applicable to both patient and graft survival, since in recent years the characteristics of donors have changed (they are older and there have been fewer deaths from of cranioencephalic injuries) but despite these factors, graft survival has also improved. In addition, this year a new period of analysis has been created, from 1998 to 2000, since an important change in graft survival has taken place.

Table 13. Survival of the patient and of the graft by type of transplant and time period (actuarial analysis).

Figure 69. Survival of grafts in transplants from cadaver donors by period. 1990-1997 and 1998-2000.

Table 14. Survival of patients with renal transplants from cadaver donors by age of the recipient and primary renal disease (actuarial analysis). Transplants 1990-2000.

Figure 70. Survival of grafts in transplants from cadaver donors by age of donor. Transplants 1990-2000.

Figure 71. Survival of grafts in transplants from cadaver donors by age of donor and recipient. Transplants 1990-2000.

The increasingly high number of patients who have received more than one transplant (413 in the period 1990-2000) makes it necessary to treat the retransplant group separately. The differences between the survival of the recipient of the first and of the second transplant are not significant. With regard to graft survival, the differences are higher in the first transplants. At three years the survival of the second graft is 73%, more than 10% lower than that of the first ($p<0.0001$). These figures show a very acceptable survival probability rate for the patients that are given a second opportunity.

Figure 72. Survival of grafts in transplants from cadaver donors by gender of donor and recipient. Transplants 1990-2000.

When analyzing survival by the age of the patient when he received the transplant (Table

14), it can be seen that patients under 55 years of age present a percentage of 94% at five years and that this lowers gradually (87% for patients from 55 to 59 years of age, 80% for the patients from 60 to 64 and 71% for patients over 64). Survival analysis by PRD (Table 14) shows results that are very similar to those obtained in other years: the survival probability of the patient at five years is 91% for those who have a standard PRD, 83% for diabetics and 87% patients with another PRD (p=0.001).

Figure 70 shows how graft survival worsens as the donor's age increases. This effect is especially significant when donors are over 60 years of age and even more so when they are over 70.

Figure 71 shows graft survival in relation to the age of the **recipient** (**young**: under 60 years of age; **old**: 60 years of age or older) and that of the **cadaver donor** (**young**: under 60 years of age; **old**: 60 years of age or older), which are the same age groups used in the section of data concerning the donor.

Graft survival in patients of 60 years of age or older is similar, regardless of whether the kidney is from a young or old donor, while in the recipients under 60 years of age, graft survival varies a great deal according to the age of the donor. At five years, the group of young patients who had received transplants from young cadaver donors showed a graft survival rate of 76%. On the other hand, if donors were old the survival rate was 66% (p<0.00001).

Table 15. Univariate and multivariate analyses of graft survival (Cox Regression). Transplants from cadaver donor, 1990-2000.

Figure 72 shows that, globally speaking, there are no significant statistical differences in graft survival in relation to gender of the donor and recipient. The longest graft survival is found in those cases where the gender of the donor coincides with that of the recipient, although there are only statistically significant differences in male recipients who have had better results if the donors were also men.

Table 15 presents the results obtained in the univariate and multivariate analyses of graft survival using the method actuarial and a Cox Regression, respectively. As commented earlier, the multivariate analysis takes into account all factors that might influence survival (which were included in the regression model) and calculates the risk for each of them, while adjusting for all the others. In this case the factors studied are age of the donor and recipient at the time of the transplant, the maximum and final percentage of antibodies, HLR-DR matches and whether or not the patient has diabetes mellitus, circulatory cardiac disorders or a chronic obstructive lung disease.

Summing up then, graft survival in relation to HLA-DR antigen matches between donor and recipient of the grafts from cadaver carried out in Catalonia in the period 1990-2000 is best in the group of patients with transplants performed with two HLA-DR matches. At 5 years this is 74%, 6% higher than that for patients that have received a transplant without any matching (p=0.0007). These data confirm the tendency seen in previous series of transplants, published in older reports. There were no statistically significant differences in the graft survival analysis in relation to the matching of locus A and locus B.

The fact that recipients have antibodies against HLA antigens prior to transplanatation creates the need to find donors that present antigens against which the antibodies of the recipient will not react. This is one of the most important obstacles to finding suitable donors. The analysis of graft survival depending on whether or not the recipient has antibodies that react to the panel of HLA antigens (Panel Reacting Antibodies -PRA) is carried out by separately taking into account the existence of antibodies immediately

prior to the transplant (final-PRA) and the maximum level of antibodies that the patient may have presented at any time during treatment (maximum-PRA). For patients without antibodies (maximum-PRA between 0% and 10%), graft survival is 73% at the fifth year; for patients with few antibodies (maximum-PRA between 11% and 50%) it is 68%; while for patients with many antibodies (hypersensitive, maximum-PRA >50%) it is 63%. This difference is also seen when only the percentage of antibodies at the time of the transplant is taken into account. Graft survival at five years is 72% for recipients without antibodies (final PRA between 0% and 10%), 64% for sensitive recipients (final-PRA between 11% and 50%) and 54% for hypersensitive patients (final-PRA >50%). These data show that the presence of antibodies (PRA) in the recipient is one of the most important factors in renal graft survival. Thus, the presence of antibodies at the time of transplantation, even at low levels, is a factor that must be considered for long-term immunosuppressant treatment.

Mortality

In 2000 the mortality of patients in Renal Replacement Therapy was 9.9% (675 patients): **15.4%** in the group of patients on **hemodialysis**, **13.6%** in those on **peritoneal dialysis** and **1.8%** in patients with **functioning transplants**. The number of patients in RRT who died during 2000 was higher than that of last year, but the percentage of patients treated went from 10.1% to 9.9%. The breakdown of the causes of death is practically the same. The most common cause was cardiac disease, which accounted for 34.5% of all deaths this year (Table 16). The group of deaths from unknown causes continues to be quite significant, despite the fact that this year shows a decrease over last year.

Table 16. Breakdown of the causes of death, 2000.

When examining the main causes main of mortality of this population, in the period 1990-2000 more closely, it can be seen that the deaths caused by cardiac diseases affect, above all, patients over 44 years of age, with 1,826 cases (Table 17). In the 45-to-64-year age group, the breakdown of cardiac causes was 34.7% for infarctions and 39.3% for cardiac arrest. The percentage of infarctions lowered with age to 28.6% in the 65-to-74-year age group, and 19.8% in those over 74. The percentage of cardiac arrest rose to 46.7% and 54.3% respectively in these two age groups.

Table 17. Breakdown of causes of death by age group, 1990-2000.

Table 18. Breakdown of causes of death by PRD, 1990-2000.

Table 19. Breakdown of causes of death by last treatment, 1990-2000.

With regard to the causes of death of vascular origin, it should be stressed that 49.7% of the total of this category (449/903 cases) are due to cerebrovascular accidents.

Neoplasias are the primary cause of death in the miscellaneous group, and for this reason they constitute a new group this year. Of these, 40 were induced by immunosuppressants, and the remaining 390 were registered as other neoplasias. The most common cause of death in this miscellaneous group was the cachexia (34.0%), which affected patients over 64 above all.

Among infections, attention should be drawn to septicemia, which was the cause of death for 431 patients (48.8% of infections), representing 7.7% of the global mortality for the period 1990-2000.

Figure 73 shows the breakdown of the causes of death over the first five years of RRT. The analysis has been carried out with the new cases from the period 1990-2000. No new temporal pattern is seen in the breakdown of causes of death since the percentages

remain very similar, regardless of time in RRT. Thus, mortality for cardiac reasons is the main cause of death, close to 35% in all intervals. This miscellaneous category shows growing mortality since they rise from 8.9% in the first year to almost 12% in the fourth year of treatment, while causes of unknown origin remain at between 7% and 10%. The other causes show no specific behavioral pattern.

Figure 73. Breakdown of causes of death over time in RRT, 1990-2000.

Figure 74. Number of deaths of patients during the first year of RRT. New cases 1984-1999.

Figure 74 shows the evolution of mortality during the first year of treatment, both in absolute figures (the value represented by the columns is found in the vertical axis on the left: number of patients who died) and in the percentage of the annual incidence (the value represented by each of the points on the line is read in the vertical axis on the right: percentage). An increasing tendency is seen in the number of patients who died before completing a full year of RRT. On the other hand, the percentage that this number of patients represents in the annual incidence varies over the years, although in the last four years there has been a strong increase. Thus, of the new patients in 1986, 9.4% died during the first year of treatment. This percentage rose to 14.6% in 1992, dropped to 9.6% in 1993 and rose to 13.1% in 1994 and 18.2% in 1995. In 1997, it decreased again, only to increase once more to 15.7% in 1999. Mortality for patients who began RRT in 2000 cannot yet be analyzed, since there are patients who have not finished the first year of treatment.

Figure 75. Mortality rates during the first year of RRT by age groups. New cases 1990-2000.

Figure 76. Standard mortality ratio (SMR) during the first year of RRT (95% confidence interval). New cases 1990-2000.

Mortality in the first year was also analyzed as a function of the different age groups and compared with global mortality in Catalonia. Figure 75 shows the global mortality rates in Catalonia by age groups in 1996, and the mortality rates in RRT, by age groups, during the first year of treatment. The specific rates for renal patients were calculated from the mortality of the first year of treatment of the group of patients who started RRT between 1990 and 2000. This figure shows how the mortality rates of the population of Catalonia and the population of the Register increase with age. For all age groups, the mortality rates of the population in RRT are much higher. Figure 76 shows the relation that exists between the two rates. Despite the fact that the over-84 year age group presents a higher mortality rate (over 413.8 per 1,000 patients), this mortality rate is only 2.5 times that of the population of Catalonia, while the rate for the 45-to-54-year age group (45.8 per 1,000) is 14.5 times higher than that of the Catalan population of this same age. Globally then, the population in RRT has a mortality rate 7.1 times that of the Catalan population.

Geographical breakdown

Geographical breakdown of resources

In the Order of June 16, 1987, for the implementation of the Service Program for Persons with Renal Failure, the functional structure of nephrological service was established at the following levels (Figure 77):

Nephrology Departments (ND). Nephrology departments constitute the basic framework in which services are developed for patients with renal failure in Catalonia, and will guarantee all treatment alternatives for renal failure. Their sphere of influence

corresponds to a specific geographical area. Their functions are:

- To collaborate in the planning of the coverage that the services
- To carry out the prevention, diagnosis and prescription of Renal Replacement Therapy
- To control the quality of all nephrology service units and dialysis centers, which are the reference services
- To participate in the Register of Renal Patients
- In the case of the Departments that have a Rental Transplant Unit (RTU), to assume responsibility for the management of the waiting list for transplants
- To participate in training programs
- To carry out research projects

Nephrology Service Units (NSU). Nephrology service units are those that form part of an accredited general hospital and provide simple nephrological services, in addition to functioning as dialysis centers. Functionally, they depend on a nephrology department and also foster active home dialysis programs.

Figure 77. Functional levels of nephrological services in Catalonia.

Dialysis centers (DC). Dialysis centers are those health centers that, under the supervision of a reference nephrology department, provide dialysis as replacement treatment for patients with chronic end-stage renal failure and ensure clinical supervision.

Figure 78 presents the geographical breakdown of resources for treatment of renal failure in Catalonia by the different treatment levels.

Figure 78. Nephrology resources for the treatment of chronic renal failure in Catalonia, 2000.

Geographical breakdown of patients

Table 20 shows the evolution of the incidence rates of patients in RRT from 1998 to 2000, standardized, by age and gender, by the indirect method and calculated with the population over 14 years of age. Table 21 presents the evolution of the prevalence rates of patients in RRT, also from 1998 to 2000. The rates were standardized by age and gender, by the direct method with the population over 14 years of age. In these tables, the first column corresponds to the number of cases, the second to the standard deviation and the third to the standardized rate. In the case of incidence, it should be borne in mind that, due to the low number of patients, small variations produce significant changes in the rates. This does not occur with prevalence.

Table 20. Incidence of patients in RRT by health region for persons over 14 years of age. Rates per million population, 1998-2000.

Table 21. Prevalence of patients in RRT by health region for persons over 14 years of age. Rates per million population, 1998-2000.

Figure 79. Incidence of treated end-stage renal failure by health region for persons over 14 years of age. Rates per million population, 2000.

Figure 80. Prevalence of treated end-stage renal failure by health region for persons over 14 years of age. Rates per million population, 2000.

This effect can also be seen in Figures 79 and 80, which only present the incidence and prevalence rates for treated renal failure for 2000, with their 95% confidence intervals. The 1996 census for Catalonia was used as a reference population for estimating the rates, and these were standardized by age and gender.

Figure 81 shows the evolution of the prevalence rates of patients in RRT in rural areas (under 10,000 inhabitants) and urban areas (over 10,000 inhabitants). The changes seen in these rates show improvement in accessibility to RRT for the rural population and, therefore, greater equity in the breakdown of nephrology resources for the treatment of chronic renal failure in Catalonia. Furthermore, it can be seen that the tendency in the last three years is not entirely clear, which might explain why the rates corresponding to 1996-2000 were calculated using the population of Catalonia from 1996.

Figure 81. Evolution of prevalence rates of treated end-stage renal failure in rural and urban areas, 1984-2000.

Study of Dyslipemia

Introduction

Taking advantage of annual data-gathering for updating of the Register, the specific study for this year was that of dyslipemia and cardiovascular risk, for which reason the following questions were included for all patients (undergoing dialysis and with transplant):

The cholesterol figure
The HDL figure
The LDL figure
The triglycerides figure
Type of treatment: statins, fibered and/or resins

Despite the fact that this information was requested of all patients alive as of 31 December, there was a better response amongst patients undergoing dialysis than amongst those with a functioning transplant. The analyses presented were broken down according to the last type of treatment.

Results

Of the 3,282 living patients undergoing hemodialysis at December 31, 2000 information on cholesterol was obtained in 96.8% of the cases, on HDL in 67.8% of the cases, on LDL in 62.3%, on triglycerides in 92.5% and on treatment in 99.0% of the patients. Of the 159 living patients undergoing peritoneal dialysis at December 31, 2000, information on cholesterol was obtained in 98.1% of the cases, on HDL in 60.4% of the cases, on LDL in 58.5%, on triglycerides in 96.9% and on treatment in 100% of the patients. Of the 2,173 patients from 6 kidney transplant units, with a functioning transplant at December 31, 2000, information on cholesterol was obtained in 98.2% of the cases. The other parameters could not be analyzed due to the large number on which there was no information.

Hemodialysis

The women had higher levels of total cholesterol (Figure 1) and of LDL than the men. Despite this, the protecting effect of the HDL was higher in the women. Gender showed no influence in the concentration of triglycerides (Table 1).

The existence of diabetes mellitus in hemodialysis is not associated with a major hypercholesterolemia, the mean plasmatic cholesterol in the diabetic patients being 180.7 mg/dl and that of non-diabetic patients 179.6 mg/dl (p=0.5). When analyzed according to the type of nephropathy, it was found that the patients of the standard group had mean plasmatic cholesterol of 178.8 mg/dl, the patients with diabetic nephropathy 181.9 mg/dl and the group of the other nephropathies 179.8 mg/dl (p=0.48). There was a strong association between diabetes mellitus (whether as nephropathy or concomitant disease), hypertriglyceridemia and low levels of HDL. Thus it was found that in the diabetic patients (PRD or concomitant disease) the mean of triglycerides level was 160.9 mg/dl as against

that of the non-diabetics, in which it was 137.9 mg/dl (p<0.00001). The difference was maintained upon analysis of PRD only, where the patients of the standard nephropathies group had a mean of 140.2 mg/dl, the diabetics 161.4 mg/dl and the other nephropathies 139.3 mg/dl (p<0.00001).

Figure 1. Distribution of the plasmatic cholesterol in patients undergoing hemodialysis according to gender. Cases undergoing hemodialysis at 31.12.2000.

Table 1. Percentage distribution of the levels of cholesterol, LDL, HDL and triglycerides according to gender, of patients undergoing hemodialysis. Year 2000

As with the general population, age affects the total concentration of cholesterol, LDL and triglycerides. The levels are lower in the second and third decade of life, increase in the fourth and fifth decade and from the age of 65 years decrease steadily, the decrease being particularly notable in the case of the levels of triglycerides (Figure 2). The reduction of the levels in the over-65s may be due to the fact that these patients present a poorer nutritional state and that there is a higher proportion of persons treated. The HDL values were scarcely affected by age, and only in patients under 20 years were the values slightly higher than for the rest of the group (48.9 mg/dl versus 45.0 mg/dl).

Figure 2. Distribution of the level of triglycerides according to age. Cases undergoing hemodialysis at 31.12.2000.

Figure 3. Distribution of the level of cholesterol according to time in RRT. Cases under hemodialysis at 31.12.2000.

As the time remained in RRT increased, there was a reduction in the figures for cholesterol (Figure 3) and triglycerides (Figure 4).
A major increase in the levels of triglycerides was also observed with increase in the duration of HD sessions (Figure 5). That would surely be explicable by the fact that the patients dialyzed for a larger number of hours were more obese, had a higher body mass index (see Figure 20, page 28) and surely contained a higher percentage of diabetics.

Figure 4. Distribution of the level of triglycerides according to time in RRT. Cases under hemodialysis at 31.12.2000.

Figure 5. Distribution of the level of triglycerides according to number of hours of hemodialysis weekly. Cases under hemodialysis at 31.12.2000.

The presence of chronic liver disease was related with lower cholesterol figures (166.4 mg/dl versus 182.8 mg/dl, p<0.00001), LDL (92.7 mg/dl versus 110.0 mg/dl, p<0.00001) and trigylcerides (136.1 mg/dl versus 144.7 mg/dl, p=0.02), but not of HDL (46.0 mg/dl versus 44.9 mg/dl, p=0.2).

The protective effect of HDL decreased in the presence of a smoking habit and of obesity. The percentage of patients with HDL values <40 mg/dl was higher in active smokers (48.3%) than in non-smokers (38.3%) (p=0.004), and in obese patients, with a body mass index (BMI) between 30 and 39, in whom HDL levels of <40 mg/dl presented in 56.2%, while in those for whom the BMI was less than 25% that percentage was 36.3% (p<0.00001). Cholesterol and triglycerides also increased in the obese patients (BMI 30-39), the mean for cholesterol being 184.8 mg/dl and for triglycerides 185.8 mg/dl, compared with 176.7 mg/dl and 130.5 mg/dl, respectively, in the patients with BMI <25 (both p<0.00001).

The patients with a history of ischemic heart disease had a higher percentage of hypertriglyceridemia (19.8% had levels exceeding 200 mg/dl versus 16.6%; p= 0.05) and lower levels of HDL (46.4% had levels lower than 40 mg/dl versus 40.8%; p= 0.05).

Peritoneal dialysis

The women had higher HDL levels than the men (Table 2). Moreover, only 26.8% of the women had non-protective HDL values, that is, values less than 40 mg/dl, in relation to 52.7% of the men. Gender had no influence on the total concentration of cholesterol, LDL and triglycerides (Table 2).

Table 2. Percentage distribution of levels of cholesterol, LDL, HDL and triglycerides according to gender, in patients under peritoneal dialysis. Year 2000.

Patients with a diabetic nephropathy had higher levels of cholesterol (32.6% over 239 mg/dl, while the percentage for those with a standard nephropathy was 12.2%, and the rest 25.6%; p=0.04). The absence of any effect of diabetes on the levels of triglycerides is probably related to the boosting effect of the glucose content of the peritoneal fluid on the lipoic metabolism.

Unlike in the case of hemodialysis, no age effect was observed on the concentration of cholesterol, triglycerides, LDL and HDL. This could be explained by the negative effect that the absorption of glucose from the peritoneal fluid had on the lipoic metabolism, for this would have a constant effect on all age groups.

Figure 6. Distribution of the level of triglycerides according to the presence of chronic liver disease. Cases under peritoneal dialysis at 31.12.2000.

Figure 7. Distribution of the level of triglycerides according to body mass index (BMI). Cases under peritoneal dialysis at 31.12.2000.

The existence of chronic liver disease did not affect the levels of cholesterol, LDL and HDL. It should nevertheless be stressed that all the patients undergoing peritoneal dialysis with chronic liver disease had levels of triglycerides lower than 200 mg/dl, while in the patients free from that disease that percentage was 79% (Figure 6).

Figure 8. Distribution of the level of triglycerides according to the presence of cerebrovascular disease. Cases under peritoneal dialysis at 31.12.2000.

The obese patients (BMI 30-39) had mean level of triglycerides higher than the other patients: the mean levels of triglycerides were 120.7 mg/dl in the group with BMI <25, 150 mg/dl in the BMI 25-29, 197.8 mg/dl in the BMI 30-39 and finally 94.5 mg/dl in the BMI >39 (p<0.00001) (Figure 7).

The patients with history of cerebrovascular accident (CVA) had a greater frequency of hypertriglyceridemia (46.2% had levels >200 mg/dl versus 17% of those with no history of CVA). While the patients with a peripheral vascular disease had lower levels of HDL (59.3% of those with peripheral vascular disease had levels of HDL <40 mg/dl versus 34.8% of those free from it) (Figure 8).

Transplant

The study of dyslipemia in kidney transplant was limited to 6 of the 7 kidney transplant units (KTU), and only the cholesterol figures were analyzed, due to the large number of cases on which no information was provided for the other lipoic parameters. That fact was due to most of the KTUs notifying the Register by exporting their databases and it not always being possible to adapt their applications to the new information requirements.

The women had higher cholesterol levels than the men, probably connected with higher levels of HDL (25.8% of the women had levels of >239 mg/dl, while in the men that percentage was 16.5%, p<0.00001).

The diabetic patients (PRD or concomitant diseases) had lower total levels of cholesterol (51% had cholesterol <200 mg/dl versus 43.4% of the rest, p=0.03). This is probably a reflection of the fact that these patients receive more treatment with hypolipemiants than the other patients, due to the fact that they are a population with greater cardiovascular risk.
The effect of age on cholesterol levels was similar to that observed in the patients under hemodialysis. The lowest levels were observed in patients under 35 years, after which they began to increase, only to fall again from the sixth decade of life (Figure 9).

Figure 9. Distribution of the level of cholesterol according to age group. Cases with functioning transplant at 31.12.2000.

Figure 10. Distribution of the level of cholesterol according to estimated creatinine clearance. Cases with functioning transplants at 31.12.2000.

There was a relationship between renal function and cholesterol levels. The patients with estimated creatinine clearance < 30 ml/min. had high levels of cholesterol. The percentage of patients with cholesterol levels <200 mg/dl was 49% in those with normal estimated creatinine clearance (>59 ml/min.), and 36% when the glomerular filtration was lower than 30 ml/min. (Figure 10).

Table 3. Percentage distribution of cholesterol levels according to treatment with certain immunosuppressants, in patients with functioning transplants. Year 2000.

Table 3 shows a preliminary analysis of the different plasmatic levels of cholesterol according to whether the patient was treated with certain immunosuppressants, independently of the associated combination. In general, the patients treated with cyclosporine A, steroids and rapamycine had higher levels of cholesterol than those not taking those drugs. In the case of patients who took azathioprine or did not do so, there were no statistically significant differences, while those who took tacrolimus had lower levels. This analysis did not include the effect of the associated treatment.

Hypolipemiant treatment

Figure 11. Hypolipemiant treatment according to type of dialysis. Cases under dialysis at 31.12.2000.

In general, the proportion of patients undergoing dialysis and receiving hypolipemiant treatment was low. Patients under peritoneal dialysis received pharmacological treatment more frequently than did those undergoing hemodialysis (28.7% versus 15.3%, p<0.00001). This fact was a consequence of the greater severity of the dyslipemia observed in peritoneal dialysis. The most widely used treatment was with statins (Figure 11).

Figure 12. Level of LDL according to cardiovascular risk and type of dialysis. Cases undergoing dialysis at 31.12.2000.

Figure 13. Level of cholesterol according to whether or not hypolipemiant treatment given, and the type of dialysis. Cases undergoing dialysis at 31.12.2000.

Upon analysis of the percentage of patients undergoing dialysis and following the recommendations of the National Cholesterol Education Program (NCEP-ATP-III for

2001), it was observed that among the population with high cardiovascular risk, 48.1% of the patients undergoing hemodialysis fulfilled the objective of maintaining an LDL level <100 mg/dl in comparison with 30.2% of the patients undergoing peritoneal dialysis ($p<0.03$). This worse control of dyslipemia in patients undergoing peritoneal dialysis was related to a greater influence of the pathogenic mechanisms involved (obesity, diabetes), which were in turn influenced by the glucose content of the peritoneal exchange fluid (Figure 12). Control of dyslipemia in patients undergoing peritoneal dialysis was, moreover, worse than in those undergoing hemodialysis, despite their having a higher percentage of treatment (Figure 13).

In peritoneal dialysis, patients with ischemic heart disease, AHT and diabetes received hypolipemiant treatment in 36.8%, 29.5% and 25.2% of cases, respectively, while in patients undergoing hemodialysis those percentages were lower: 20.2%, 15.9% and 20.9%, respectively (Figure 14).

Figure 14. Percentage of patients treated with hypolipemiants by concomitant disease and type of dialysis. Cases undergoing dialysis at 31.12.2000.

In hemodialysis, the frequency of hypolipemiant treatment increased with the BMI. In peritoneal dialysis, the largest proportion of patients treated were among those with a BMI between 25 and 29.

In short, hypolipemiant treatment has to be intensified in patients undergoing dialysis, especially in the group with high cardiovascular risk and in patients undergoing peritoneal dialysis. At present, assessment of dyslipemia and monitoring of the treatment would necessarily require the LDL and HDL levels to be available.

Cardiovascular risk factors

The study presented below was carried out using the criteria of the latest version (2001) of the National Cholesterol Education Program (NCEP ATP-III). The data from the dyslipemia study and the variables existing in the Register (existence of cardiovascular disease, obesity, diabetes, etc.) were used, and according to the classification criteria all that was missing was the family history of first-degree coronary disease.

Hemodialysis

Figure 15. NCEP (ATP-III-2001) cardiovascular risk factors. Cases undergoing hemodialysis at 31.12.2000.

Figure 16. Number of cardiovascular risk factors. Cases undergoing hemodialysis at 31.12.2000.

Patients undergoing hemodialysis are at high cardiovascular risk. An adaptation of the NCEP (Adult Treatment Panel III) criteria was used with the objective of determining a desirable LDL level for each group of patients. In the analyses presented below, patients with dyslipemia are taken to be those who have cholesterol figures of >199 mg/dl or triglycerides >1999 mg/dl and are under treatment with hypolipemiants to lower the level of cholesterol; the HDL was not taken into account in view of the high number of cases for whom no information was available. Obesity is taken to mean a body mass index of >30. High cardiovascular risk is taken to mean the presence of diabetes, ischemic heart disease, cerebrovascular disease or peripheral vascular disease. Moderate risk is taken to mean the existence of two or more of the following factors: age (an age of over 45 years in men and 55 in women is considered a risk factor), smoking habit, arterial hypertension (AHT) and dyslipemia. Finally, low risk is taken to mean persons who present only one of the above factors, at most.

Figure 17. Cardiovascular risk factors. Cases undergoing hemodialysis at 31.12.2000.

Figure 18. Frequency of the various cardiovascular risk factors. Cases undergoing hemodialysis at 31.12.2000.

Figure 15 shows that 87.5% of the patients had moderate to high risk. There was individual accumulation of the various risk factors (Figure 16), with 62.6% presenting three or more (between 3 and 7). Individual assessment of the various risk factors showed that age was the most important in that it affected 82.4% of the patients, followed by AHT which was suffered by 69.1% of the patients and, finally, the presence of cardiovascular disease, which affected 52.8% of the patients. Cardiovascular disease was taken to mean the existence of any of the following pathologies: ischemic heart disease, cerebrovascular disease or peripheral vascular disease (Figure 17).

Other risk factors studied are shown in Figure 18. The type of dyslipemia was variable in function of the parameter studied. Amongst those factors was the atherogenic index, which is the ratio between total cholesterol and HDL and is considered a cardiovascular risk factor when that ratio is >4, a situation in which 29.3% of patients were found. A decrease of HDL below 40 mg/dl was the most important factor, affecting 42.2% of the patients and being one of the lipoic alterations characteristic of patients undergoing dialysis. The prevalence of hypercholesterolemia was not high amongst the hemodialysis patients, as only 30.6% had levels of >199 mg/dl and less than 8% had levels of >139 mg/dl. Hypertriglyceridemia (triglycerides >139 mg/dl) was considered to be one of the lipoic alterations usual among patients undergoing dialysis, but in the population studied only arose in 17.4%. This fact is probably related to the characteristics of the patients, such as the fact that it is quite an aged population and therefore one in which other aspects could apply (malnutrition or effects of treatment).

Peritoneal dialysis

Figure 19. NECP (ATP-III-2001) cardiovascular risk factors. Cases undergoing peritoneal dialysis at 31.12.2000.

Figure 20. Number of cardiovascular risk factors. Cases undergoing peritoneal dialysis at 31.12.2000.

Figure 21. Cardiovascular risk factors. Cases undergoing peritoneal dialysis at 31.12.2000.

Patients undergoing peritoneal dialysis are also a population with high cardiovascular risk and, according to the NCEP (ATP-III) criteria they showed a distribution similar to that of the population undergoing hemodialysis (Figure 9), though they did show a greater individual accumulation of the various risk factors (Figure 20), with 70.1% having three or more risk factors and 46.7% having four or more (between 4 and 7).
Hypertension was the most frequent risk factor, affecting 83% of the patients, followed by age, a risk factor affecting nearly 70% of cases. In general, the patients undergoing peritoneal dialysis were younger, and there was a higher percentage of diabetes and obese patients, than among those undergoing hemodialysis (Figure 21).

In addition, as Figure 22 shows, the simultaneous coexistence of dyslipemia-diabetes-hypertension was to be found in double the number of peritoneal dialysis patients in relation to those undergoing hemodialysis (17.7% versus 6.3%, $p<0.00001$).

Dyslipemia was more prevalent in this group of patients, and showed some particular features when compared with the hemodialysis group. The decrease of HDL was similar

to that of the hemodialysis patients, but the peritoneal dialysis group had a higher percentage of hypercholesterolemia (52.6% versus 30.6%, p<0.00001) and a tendency towards greater hypertriglyceridemia. There was also a higher percentage of patients with an atherogenic index of >4 (37.5% versus 29.3%, though it was not statistically significant), showing the severity of the dyslipemia.

Diabetes and obesity were factors responsible for the severity of the dyslipemia in patients undergoing peritoneal dialysis. The prevalence of diabetes was 34.6% in peritoneal dialysis as against 22.3% in hemodialysis, while obesity affected 25.2% and 9.4%, respectively (in both cases the p was <0.0001). These patients also had a higher percentage of AHT (83% versus 69.1%).

Figure 22. Frequency of the various cardiovascular risk factors. Cases undergoing peritoneal dialysis at 31.12.2000.

Transplant

73.4% of the patients with functioning transplants were at moderate or high cardiovascular risk (NCEP-2001), though the proportion of patients at high risk was lower (37.3%) than in patients undergoing hemodialysis and peritoneal dialysis (58.4% and 51.6%, respectively, p<0.0001) (Figure 23).

Moreover, there was a lower accumulation of risk factors when compared with the patients undergoing dialysis, as in transplant patients only 35% of the patients presented three or more risk factors simultaneously.

Figure 23. NCEP (ATP-III-2001) cardiovascular risk factors. Cases with functioning transplants at 31.12.2000.

Figure 24. Cardiovascular risk factors. Cases with functioning transplants at 31.12.2000.

Age, arterial hypertension and dyslipemia were the most important risk factors (Figure 24).

Age was a risk factor that affected a smaller percentage (60.6%) than in the case of patients undergoing dialysis (82.4% in hemodialysis and 69.2% in peritoneal dialysis (p<0.00001).

Hypercholesterolemia (??200 mg/dl) was frequent in patients with transplant (55.9%), with a prevalence similar to that of patients undergoing peritoneal dialysis (52.6%) but higher than that observed in the patients undergoing hemodialysis (30.6%) (p<0.0001). It was not possible to analyze the levels of triglycerides, LDL or HDL, due to the high percentage with no reply in this group of patients.

The percentage of hypertense patients was also different according to the type of treatment, affecting 60.5% of patients with functioning transplants, compared with 69.1% in hemodialysis patients and 83.0% in peritoneal dialysis patients (p<0.00001).

The prevalence of cardiovascular disease also showed considerable differences according to the treatment (p<0.00001), being presented by 29.9% of the patients with functioning transplants, as against 53.0% of the hemodialysis patients and 40.9% of the peritoneal dialysis patients. Of the patients with transplants 9% were diabetic, a percentage which rose to 22.3% in the hemodialysis patients and 34.6% in the peritoneal dialysis patients (p<0.00001).

Finally, there were differences in the percentage of obese patients ($p<0.00001$), with 13.0% for patients with functioning transplants, 9.4% for patients undergoing hemodialysis and 25.2% for patients undergoing peritoneal dialysis. No statistically significant differences were found in relation to the smoking habit.