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ORIGINAL RENAL DISEASE IN A KIDNEY-TRANSPLANT POPULATION

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Abstract. Classification of the underlying renal disorder in kidney transplant patients involves some uncertainties. To allow evaluation of the risk of recurrence of renal disease in the transplanted kidney and other characteristics and risks inherent to the specific renal disorder we have investigated the basis for and reevaluated the diagnosis of 1000 consecutive patients who received transplants in Göteborg 1985–1993. In the original registry, 36% of patients had been given the diagnosis chronic glomerulonephritis but the diagnosis was confirmed by biopsy in only half of them, 18% of the total population. Systemic vasculitides and hereditary disorders other than adult polycystic kidney disease which constituted 3% and 6%, respectively, had frequently been overlooked. The term chronic pyelonephritis (15%) covered a variety of conditions including toxic tubulointerstitial disease, but was dominated by those caused by congenital urinary tract formations. Diabetic nephropathy (21%) was the consequence of Type 1 diabetes in 18% and Type 2 or other forms of diabetes in 3%. The proportion of patients with unknown cause of renal failure was 20%. The registry allows identification of small, distinct entities, which may be characterised as regards prerequisites for and consequences of kidney transplantation.

Key words: kidney transplantation, kidney disease, registry, classification

Presentations of kidney transplant patient populations often schematically state the original renal disease to be a certain proportion of chronic glomerulonephritis, chronic pyelonephritis, diabetic nephropathy, polycystic kidney disease (PCK), and hypertensive renal disease or nephrosclerosis. The conventional registry used in Göteborg is also based on such crude definition of the patients' original disease. Working with risks of recurrent disease or other risks specific to the renal diagnosis requires better definition of the basic disorder. In a region where renal transplantation is the preferred form of renal replacement therapy for all uraemic patients without complicating disorders strict classification also enables estimating the risk of developing terminal renal failure with defined renal diseases. We have therefore reevaluated the diagnosis in each of 1000 consecutive kidney transplant patients in Göteborg.

PATIENTS AND METHODS

The Transplant Unit in Göteborg serves 3.5 million (40%) of Sweden's inhabitants and the population of Iceland (0.3 millions). The population includes a proportion of immigrants mainly from Finland and the Middle East. In January 1985 to January 1993 1000 patients received 1095 kidney transplants in the Unit. Eight-hundred-seventy-four of these were first transplants, 160 second, 46 third, 13 fourth, and two were fifth transplants. Each patient occurs only once

Table I. *Demografic data of 1000 consecutive subjects transplanted in Göteborg in 1985–1993*

Age	
years, median (range)	44 (1–71)
Gender	
male/female, %	63.7/36.3
Ethnic origin, %	
Scandinavian	93.1
Finnish	2.0
German	0.7
South European	1.6
Middle East	1.7
Latin America	0.6
Other	0.3

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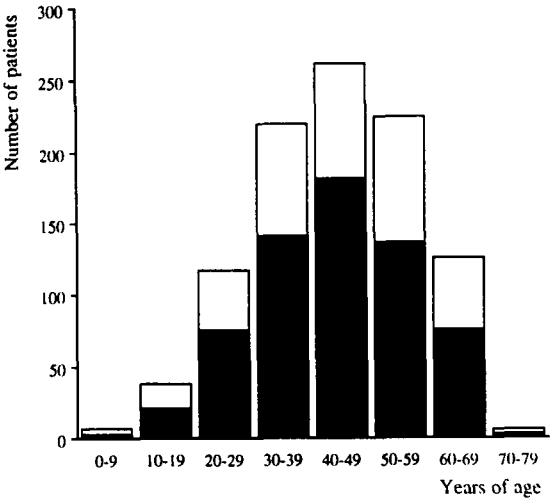

Fig. 1. Age at the time of kidney transplantation for 1000 consecutive patients. Open part of bars depict female patients.

in the following presentation. Demographic data are presented in Table I and Figure 1.

The patients' records were reviewed for data on original renal disease, e.g. presenting symptoms, any renal biopsy obtained or histopathological investigation performed on removed kidneys, indications of a hereditary disorder, signs of a systemic disease. When a biopsy had been obtained, the original protocol was requested from the corresponding histopathological laboratory and/or renal unit and was received in 333/342 cases. The other 9 had been quoted in detail in the records.

RESULTS

Based on all available data, patients were allocated to more strictly defined groups of diagnoses. For "glomerulonephritis" a confirmation by histopathological investigation was required. Patients with diabetic nephropathy were separated according to type of diabetes, Type 1 defined as insulin-dependent diabetes with onset before the age of 31. Polycystic kidney disease (PCK) symptomatic during childhood was separated from the adult form and included in the group of other hereditary disorders. Patients presenting with hypertension and renal failure were classified as having "renovascular disease" if renal artery stenosis was demonstrated, otherwise only in the absence of proteinuria and haematuria. "Nephrosclerosis" was accepted as a diagnosis only if biopsy-verified. The proportion of patients without classified diagnosis was 20%. Some of these could be suspected on clinical grounds to have glomerulonephritis (nephrotic syndrome, recurrent haematuria in relation to infections etc.), while others had a truly unspecific course.

The original classification with corresponding data following reevaluation are presented in Table II. Table III shows age, gender and fraction of biopsy-verified diagnosis for each diagnostic group. Patients with hereditary disorders constitute the youngest group. Male patients dominate most groups, including adult PCK.

DISCUSSION

We could distinguish three types of problems associated with the conventional registry, namely 1. Disregard of known data, 2. Application of exact diagnoses on indistinct cases, and 3. Pooling of patients with separate diseases.

1. Disregard of known data

Hereditary disorders other than adult PCK were frequently overlooked. Family history was not taken or not taken into account when registrating. Twenty-eight additional cases of hereditary or congenital renal disease were "discovered" during the review. The total of 60 cases is certainly also an underestimation since we have not asked patients for additional information except when there was an indication of hereditary disease in the records (4).

Vasculitis was also frequently overlooked in the original registration, only 9 of 30 definite cases recorded as such. Furthermore, with newer serologic markers more cases without extra-renal manifestations are being recognized among patients with rapidly progressive glomerulonephritis. These could often not be identified in the registry because the tests were not available during the patients' active renal disease. About 25% of patients with biopsy-verified glomerulonephritis had some extent of crescent formation. This suggests that the 3.0% with vasculitides found in the registry is only a minor part of the true number.

Three patients with Type 1 diabetes had been registered as having diabetic nephropathy

Table II. *Original renal disease for 1000 consecutive subjects who received transplants in Göteborg in 1985–1993, according to the conventional registry and the revised diagnostic registry*

Conventional diagnosis	Percent patients	Revised diagnosis New criterion	Percent patients
Glomerulonephritis	35.7	Biopsy-verified	18.1
SLE	2.0		1.9
Systemic vasculitides	0.9		3.0
Chronic pyelonephritis	11.7		14.9
Diabetic nephropathy	20.9	Diabetes Type 1	17.5
		Other types of diabetes	3.1
Polycystic kidney disease	13.6	Adult form	12.9
Other hereditary disorders	2.0		6.0
Nephrosclerosis	4.0	Biopsy-verified	0.5
		Renovascular disease	0.9
Amyloidosis	0.8		0.8
Malignant renal tumor	0.1		0.4
Unspecified	8.3		20.0

Table III. *Original renal disease, age, gender and prevalence of renal biopsy for 1000 consecutive subjects who received transplants in Göteborg in 1985–1993, according to the revised registry*

Diagnosis (revised)	Percent patients	Males %	Age at transplant median (range)	Biopsy-verified, %
Glomerulonephritis	18.1	73	39 (9–64)	100
SLE	1.9	26	41 (26–57)	79
Systemic vasculitides	3.0	53	40 (15–67)	70
Tubulointerstitial disease	14.9	52	45 (11–69)	20
Diabetes type 1	17.5	55	39 (19–66)	14
Other types of diabetes	3.1	84	54 (40–64)	10
Adult PCK	12.9	64	52 (33–71)	0
Other hereditary disorders	6.0	70	26 (1–66)	57
Nephrosclerosis	0.5	80	48 (36–66)	100
Renovascular disease	0.9	67	51 (36–60)	0
Amyloidosis (hereditary form excluded)	0.8	63	55 (39–66)	75
Malignant renal tumor	0.4	50	58 (16–62)	–
Others	20.0	70	51 (12–71)	12

although two had biopsy-verified glomerulonephritis and one had a hereditary disorder.

2. Application of exact diagnoses on indistinct cases

Originally, about one third of the patients had the diagnosis chronic glomerulonephritis, which is in accordance with reports from most transplant units (1). The diagnosis was based on renal biopsy in only half of the patients. In the remaining cases the diagnosis rested on more or less unspecific criteria, often just proteinuria with declining renal function.

Nephrosclerosis or hypertensive renal disease is another diagnosis often used in less clearcut cases (10). In a strict sense it means arteriolo- or arterio-sclerosis with ischaemic glomerular and interstitial changes. In a loose sense it is applied on patients with renal failure and hypertension, especially when elderly. In addition, it was found to be used for unspecific end-stage kidney disease on biopsy. Restricted use of this term is one of the major causes of the increase in the number of patients with unclassified renal disease. The choice of a dignosis in unclear cases appears to be based to some extent on tradition, chronic glomerulonephritis being preferred in some regions and

nephrosclerosis for similar cases in others. Chronic interstitial nephritis seems to be more frequently used in India (2).

The proportion of biopsy-verification of what is considered to be chronic glomerulonephritis has previously been reported to be about 50% in German, Irish, Indian, and British series of patients with endstage renal failure (2, 3, 5, 6) and 28% in an Italian study (9). This is one fact which makes estimation of the risk of recurrence of glomerulonephritis in transplanted kidneys unreliable (5, 8, 9).

3. Pooling of patients with separate diseases

This problem remains to some extent in the revised registry. The protocol of the histopathological investigation was obtained in almost all cases allowing sub-classification according to type of glomerulonephritis. However, even the selected, biopsy-verified group is heterogeneous with regard to diagnostic accuracy. In some patients the lesions were too pronounced, the tissue available too scarce or the techniques applied insufficient. Retrieval from the registry of patients with certain forms of glomerulonephritis will therefore inevitably result in under-estimation of the prevalence.

Patients with "chronic pyelonephritis" constitute about a fifth of patients transplanted. This is also a normal figure for transplant registries (1). The term covers a wide range of tubulo-interstitial diseases, such as congenital urinary tract malformations, bacterial infections, effects of nephrotoxic agents. The total number of such diseases is of little value but the contribution of each fraction is important e.g. for estimation of various environmental risks and evaluation of treatment policies. In the revised registry, distinct entities may be identified. For instance, three (independent) patients had become uraemic after ingestion of a nephrotoxic mushroom, and four as a consequence of hyperplasia of the prostate.

Type 1 diabetes is the most common form of diabetes causing renal failure in Scandinavia. In reports on RRT in patients with diabetic nephropathy those with Type 2 diabetes have either been included in the total, excluded, or separated on unspecified criteria (7). In this series of patients with diabetic nephropathy we found 31 diabetic patients (15% of patients with diabetic nephropathy) not fulfilling the criteria of Type 1. Fifteen other patients with Type 2 diabetes had a separate or additional renal diagnosis. This is a minimum since we cannot be sure that we have detected all patients treated only with diet.

The large unclassified group is also very heterogeneous. In fact, all diagnostic groups except Type 1 diabetes and polycystic kidney disease are probably represented there. In many of these cases the patients' history and investigations that were performed allow educated guesses on the true diagnosis. In a series of reports on kidney transplantation to patients with various diseases, based on the revised registry, and focusing on risks of recurrence and other hazards specific to the condition, we will include relevant data from this group.

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