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Original Article

PRE-dialysis survey on anaemia management

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Abstract

Background. The PRE-dialysis survey on anaemia management (PRESAM) was designed to assess the care given to pre-dialysis patients in the 12 months before haemodialysis or peritoneal dialysis, with emphasis on anaemia management.

Methods. For this epidemiological study, a retrospective chart review was conducted for patients who started haemodialysis or peritoneal dialysis between 1 August, 1999 and 6 April, 2000. All adult patients who entered one of the 779 participating centres in 21 European countries, Israel or South Africa were included, except for patients who underwent dialysis only during an acute episode. In addition to demographic characteristics, the study examined the prevalence of anaemia, anaemia management including the use of iron supplementation and epoetin, source of referral to the dialysis centre, comorbidities and major clinical events.

Results. A total of 4333 new dialysis patients were included in the survey. At the first visit to the dialysis centre, 68% of the patients had a haemoglobin (Hb) concentration $\leqslant$11.0 g/dl; Hb concentration was positively correlated with creatinine clearance rate ($r=0.43$, $P<0.01$). Patients who received epoetin had a mean Hb concentration of 8.8 g/dl at the start of epoetin treatment, and 96% of these patients had an Hb concentration $\leqslant$11.0 g/dl. Only 26.5% of the patients received epoetin before dialysis. The length of time under the care of a nephrologist was associated with meeting the European Best Practice Guidelines (EBPG) target Hb concentration, as well as receiving epoetin.

Conclusions. Few pre-dialysis patients met the EBPG target for Hb concentration, despite regular nephrology care.

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Keywords: anaemia management; best practice guidelines; epidemiology; epoetin; pre-dialysis

Introduction

The treatment of patients with chronic renal failure with recombinant human erythropoietin (rHuEPO/epoetin) before starting or during dialysis can improve the patient's functional state, quality of life and probably the risk of morbidity and death [1–3]. In 1997, the National Kidney Foundation published the Dialysis Outcomes Quality Initiative Clinical Practice Guidelines for the Treatment of Anaemia of Chronic Renal Failure [4]. These evidence-based guidelines provide criteria on how to make best use of diagnostic and therapeutic procedures for the treatment of patients with anaemia before starting and during dialysis treatment.

In 1999, the European Dialysis and Transplantation Association (EDTA) published the European Best Practice Guidelines (EBPG) for the treatment of renal patients with anaemia [5]. These guidelines reviewed 200 additional publications and, based on three levels of evidence in accordance with the criteria of the US Agency for Health Care Policy and Research, updated the recommendations for the diagnosis and treatment of patients with anaemia from a European point of view. The EBPG aim to achieve haemoglobin (Hb) concentrations $>$11.0 g/dl in 85% of renal patients.

The European Survey on Anaemia Management (ESAM) [6] was published in 2000. This survey compiled prospective epidemiological data relating to the treatment of anaemia in a selected group of patients ($n=14\,527$) on haemodialysis or peritoneal dialysis from 14 European countries. The results of this survey emphasized the small percentage of patients who began epoetin treatment pre-dialysis (only 11% of the patients on haemodialysis), and the low Hb concentration in

patients at the start (mean <9.0 g/dl) and at the end of treatment.

The PRE-dialysis Survey on Anaemia Management (PRESAM) has been designed with the aim of evaluating the nephrological and anaemia management of pre-dialysis patients during the 12 months before dialysis. In this survey, the participating centres were asked to include all patients who started dialysis between 1 August, 1999 and 6 April, 2000. Retrospective data on the patients, and the diagnosis and treatment of anaemia were requested for the 12 months pre-dialysis. This survey fulfilled two objectives: to reveal the diagnostic and therapeutic patterns of anaemia in these patients and to document the pattern of referral of patients with chronic renal disease to a nephrologist before the start of dialysis in Europe, Israel and South Africa. A detailed analysis of the patient referral pattern will be presented elsewhere [7].

Subjects and methods

Study design

The PRESAM used a retrospective chart review to evaluate the management of anaemia in patients with chronic renal failure during the year before the start of dialysis. The inclusion criteria specified the enrolment of all patients aged 16–99 years who started haemodialysis or peritoneal dialysis in a participating dialysis centre between 1 August, 1999 and 6 April, 2000. Selection bias was prevented by the inclusion of all dialysis patients, except those patients who started dialysis for acute reasons and did not remain on dialysis after the acute episode. This epidemiological observational survey did not require any deviation from routine medical practice. Therefore, Institutional Review Board approval was either waived or expedited in participating institutions and informed consent was not required. The survey included patients from 779 dialysis centres from 21 European countries, as well as Israel and South Africa (Table 1). All physicians at dialysis centres in these countries were invited to participate in the survey. Participation was on a voluntary basis, without restrictions.

Table 1. Sample size by country and region

Western Europe	Sample size	Number of participating centres
Austria	182	31
Belgium	158	13
Denmark	70	8
Finland	58	4
France	432	156
Greece	129	42
Italy	360	80
Netherlands	146	13
Portugal	202	28
Spain	639	24
Switzerland	80	28
UK	425	38
Subtotal	2881	465
Central and eastern Europe		
Bulgaria	43	5
Croatia	85	20
Czech Republic	212	61
Hungary	271	39
Lithuania	32	10
Poland	438	95
Russia	89	12
Slovakia	142	29
Slovenia	32	10
Subtotal	1344	281
Other countries		
Israel	74	16
South Africa	34	17
Subtotal	108	33
Total	4333	779

Data collection and management

Collected data included: start date of dialysis, date of the first visit to a nephrologist, aetiology of chronic renal failure, source of referral to dialysis centre, date of the first consultation in the dialysis centre where the patient is currently dialysed, clinical data on the first visit to dialysis centre (including body weight, blood pressure, Hb and serum creatinine concentrations), and data related to comorbidity (such as diabetes type 1 or 2, hypertension, haemoglobinopathy, coronary heart disease, neoplasia, chronic hepatitis, cardiac failure, bronchopneumopathy, infectious disease, arrhythmia and inflammatory disease). Data were also collected on drug treatments, iron supplementation, major clinical events in the year as well as the month before dialysis (including angina pectoris, cardiac failure, myocardial infarction, infectious disease, inflammatory disease, bleeding, transfusion, surgery other than dialysis access and renal transplantation), and the type of vascular access (native fistula, synthetic fistula or catheter) when starting haemodialysis. Finally, the use of epoetin (including the physician who started epoetin treatment, epoetin dose, route and frequency of administration, and reasons for starting epoetin treatment), iron supplementation, Hb concentration, serum ferritin and serum creatinine concentrations, and transferrin saturation at the start of epoetin treatment were documented. Reasons for starting epoetin treatment could be low Hb concentration, cardiac failure, coronary heart disease, symptoms of anaemia (i.e. tiredness and dyspnoea), patient complaint or other. In addition, the target Hb concentration (the concentration aimed for in the individual patient, which was decided at the start of epoetin treatment and at the start of dialysis) was recorded [8].

Data were collected using a three-page pre-printed data collection tool (DCT). Each participating centre received DCTs and detailed instructions for their completion. The DCTs were scanned electronically using TELEform® scanning software. The scanned DCTs were reviewed and validated, and added to an SPSS® database. Data were then edited against a previously established series of domain and consistency edits. These established criteria-specified mandatory fields including the year of birth, start date of dialysis and serum creatinine concentration at the first visit to the dialysis centre. Of the 4729 original DCTs, 396 (8%) lacked data in one or more of these outlined areas and were therefore excluded from the database. The resulting analytical database therefore consisted of 4333 valid cases for which the mandatory data were available. Some of the non-mandatory data, however, were not available for all 4333 cases because of values outside the predefined boundaries,

logical inconsistencies with other data, or questionable or missing units.

Data transformations included the calculation of creatinine clearance using the Cockcroft–Gault formula as follows:

for men: ([140 – age] × weight in kg)/(72 × serum creatinine in mg/dl);
for women: {0.85 × ([140 – age] × weight in kg)}/(72 × serum creatinine in mg/dl) [9].

Iron status was also calculated using the following criteria: adequate iron status = serum ferritin $\geqslant$100 μg/l + transferrin saturation $\geqslant$20%; functional iron deficiency = serum ferritin 100 μg/l + transferrin saturation $<$20%; absolute iron deficiency = serum ferritin $<$100 μg/l.

Statistical analysis

Standard descriptive statistics were calculated for all study variables. Bivariate and multivariate distributions were examined by plotting distributions and stratification. Difference testing between groups was performed using the two-tailed *t*-test, analysis of variance, χ^2 or their non-parametric equivalent where appropriate. Significance for main effects was tested at the $\alpha = 0.05$ level.

Results

Epidemiology

The sample consisted of 4333 patients who had recently started dialysis (Table 2). Data for several variables were not recorded for all these patients. Fifty-nine percent of patients were male (total $n = 4265$). The mean age of all enrolled patients at the start of dialysis was 59.1 ± 15.6 years, with a median age of 62 years (total $n = 4333$). Approximately 16% of the patients started dialysis at age 75 years or older.

The two most common aetiologies of renal failure in the survey sample were diabetic nephropathy (23%) and chronic glomerulonephritis (19%) (total $n = 4289$). Vascular nephropathy (including hypertensive nephrosclerosis) and tubulo-interstitial nephropathy occurred in 10–13% of the patients.

Four of the five most prevalent comorbidities at a patient's first visit to a dialysis centre were cardiac-related: hypertension (78%), coronary heart disease (23%), cardiac failure (15%) and arrhythmia (8%). Eighty-four percent of patients had at least one cardiovascular comorbidity, including hypertension (total $n = 4333$). Excluding hypertension, 34% of the patients had at least one of the following conditions: coronary heart disease, cardiac failure or arrhythmia. Diabetic patients comprised 30.8% (1336/4333) of the total survey sample and they had a significantly higher rate of hypertension compared with non-diabetic patients ($n = 2997$) (84 versus 76%, $P < 0.01$). Similarly, 36% of the diabetic patients had coronary heart disease and 22% had cardiac failure compared with 18 and 12%, respectively, of non-diabetic patients ($P < 0.01$).

At their first visit to the dialysis centre, 57.3% of the patients (total $n = 3918$) had been under the care of a nephrologist for >1 year, 31.4% had been under the

Table 2. Demographic and clinical data

Variable	*n*[a]	Percent[b]	Mean	SD	Median
Gender	4265				
Male	2511	58.9			
Female	1754	41.1			
Type of dialysis	4190				
Haemodialysis	3659	87.3			
Peritoneal dialysis	531	12.7			
Type of vascular access	3582				
Native fistula	1976	55.2			
Synthetic fistula	82	2.3			
Catheter	1524	42.5			
Age at first visit to a nephrologist (years)	4267		55.7	17.2	59.0
Parameters at first visit to dialysis centre					
Age (years)	4317		57.3	16.2	60.0
Hb concentration (g/dl)	4020		10.0	2.1	9.9
Serum creatinine concentration (μmol/l)	4333		528.2	289.5	495.0
Creatinine clearance rate (ml/min)	3903		18.2	16.7	12.3
Length of time under care of nephrologist (months)	3918				
$\leqslant$1	554	14.1			
1–6	679	17.3			
6–12	439	11.2			
$>$12	2246	57.3			
Parameters at start of dialysis					
Age (years)	4333		59.1	15.6	62.0
Hb concentration (g/dl)	3629		9.5	1.7	9.4
Serum creatinine concentration (μmol/l)	3611		720.2	221.2	702.0
Creatinine clearance rate (ml/min)	3276		9.8	3.9	9.1
Iron supplementation	4187	42.4			

[a]Number of patients from the total population of 4333 for whom data were available.
[b]Calculated from the patients for whom data were available.

Table 3. Anaemia status: comparison between western Europe (WE) and central/eastern Europe (CEE) countries

Variable		n[a]	Percent[b]	Mean	SD	Median	P[c]
All patients	WE	2881					
	CEE	1334					
Target[d] Hb (g/dl) at start of dialysis	WE	2117		11.7	0.7	12.0	<0.01
	CEE	743		11.3	0.8	11.0	
Hb (g/dl) at start of dialysis	WE	2437		9.8	1.6	9.8	<0.01
	CEE	1105		8.7	1.8	8.6	
Hb (g/dl) at start of epoetin	WE	2104		9.0	1.2	9.0	<0.01
	CEE	747		8.2	1.3	8.3	
Iron supplementation	WE	2758[e]	42				<0.01
	CEE	1323[e]	39				
Iron status at start of dialysis							
Adequate iron stores	WE	534	36				<0.01
	CEE	234	53				
Functional iron deficiency	WE	333	22				
	CEE	81	18				
Absolute iron deficiency	WE	636	42				
	CEE	126	29				

[a]Number of patients, from total population of 4333, for whom data were available.
[b]Percent of patients from the number for whom data were available.
[c]*t*-test and Pearson's χ^2 were used where appropriate.
[d]Individually set target Hb.
[e]Sample size reflects all patients who responded yes/no to iron supplementation, while the percentage reflects those patients that responded yes.

care of a nephrologist for <6 months and 14.1% for <1 month (Table 2). Haemodialysis was started for 87.3% of the patients, whereas peritoneal dialysis was started for 12.7% (total $n=4190$). For more than half of the sample, dialysis was started because of fluid overload. Other reasons included severe acidosis and malnutrition. At the start of dialysis, 42.4% of the patients received iron supplementation (total $n=4187$).

Table 4. Epoetin treatment and anaemia status in the entire survey sample

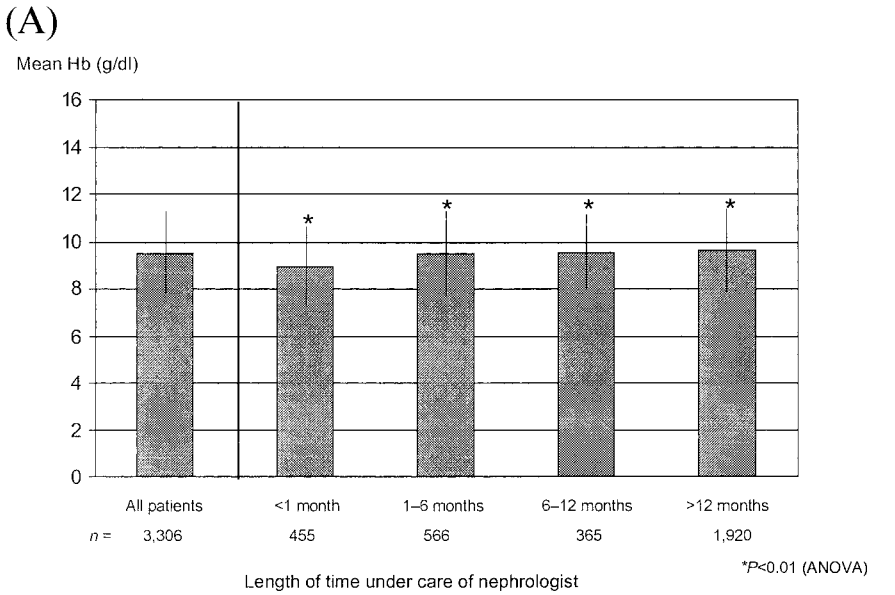
Variable	n[a]	Percent[b]	Mean	SD	Median
All patients ($n=4333$)					
Target[c] Hb (g/dl) at start of dialysis	2943		11.6	0.7	12.0
Hb (g/dl) at start of dialysis	3629		9.5	1.7	9.4
Hb (g/dl) at start of epoetin	2910		8.8	1.3	8.8
Iron supplementation	4187	42			
Iron status at start of dialysis:					
Adequate iron stores	794	40			
Functional iron deficiency	432	22			
Absolute iron deficiency	771	39			
Cohort: epoetin started before dialysis ($n=1085$)					
Target[c] Hb (g/dl) at start of dialysis	977		11.7	0.7	12.0
Hb (g/dl) at start of dialysis	1041		10.3	1.7	10.2
Hb (g/dl) at start of epoetin	1043		9.0	1.1	9.0
Iron supplementation	1060	67			
Cohort: epoetin and dialysis started simultaneously ($n=1332$)					
Target[c] Hb (g/dl) at start of dialysis	1088		11.5	0.8	12.0
Hb (g/dl) at start of dialysis	1187		8.9	1.5	8.8
Hb (g/dl) at start of epoetin	1254		8.6	1.3	8.6
Iron supplementation	1276	40			
Cohort: epoetin started after dialysis ($n=523$)					
Target[c] Hb (g/dl) at start of dialysis	308		11.5	0.7	11.5
Hb (g/dl) at start of dialysis	410		9.2	1.7	9.1
Hb (g/dl) at start of epoetin	489		8.7	1.3	8.7
Iron supplementation	506	32			
Cohort: no epoetin ($n=1155$)					
Target[d] Hb (g/dl) at start of dialysis	437		11.5	0.8	11.5
Hb (g/dl) at start of dialysis	842		9.4	1.8	9.5
Iron supplementation	1121	25			

[a]Number of patients, from total population of 4333, for whom data were available.
[b]Percent of patients from the number for whom data were available.
[c]Individually set target Hb concentration.

Haemoglobin values

At the patients' first visit to the dialysis centre, the mean Hb concentration was 10.0 ± 2.1 g/dl (total $n = 4020$) (Table 2), and 68% of the patients had an Hb concentration $\leqslant 11.0$ g/dl. The mean Hb concentration at the start of dialysis was 9.5 ± 1.7 g/dl, and 80% of the patients had an Hb concentration $\leqslant 11.0$ g/dl (total $n = 3629$). There was a significant difference in the mean Hb concentration between patients from western Europe (9.8 ± 1.6 g/dl) and those from central or eastern Europe (8.7 ± 1.8 g/dl) ($P < 0.01$) (Table 3). For patients who received epoetin, the mean Hb concentration at the start of epoetin was 8.8 g/dl, and 96% of these patients had Hb concentrations $\leqslant 11.0$ g/dl ($n = 2910$) (Table 4). The mean Hb concentration was 9.0 ± 1.2 g/dl for patients from western Europe and 8.2 ± 1.3 g/dl for patients from central or eastern Europe ($P < 0.01$) (Table 3).

The mean Hb concentration at the start of dialysis increased slightly but significantly with the length of time a patient had been under the care of the nephrologist ($P < 0.01$) (Figure 1). The mean Hb concentration for patients under the care of a nephrologist for < 1 month was 8.9 g/dl, for 1–6 months it was 9.5 g/dl, and for 6–12 months as well as for > 1 year it was 9.6 g/dl (total $n = 3306$). The same trend was observed when patient samples from western Europe or from central and eastern Europe were analysed separately (Figure 1B).



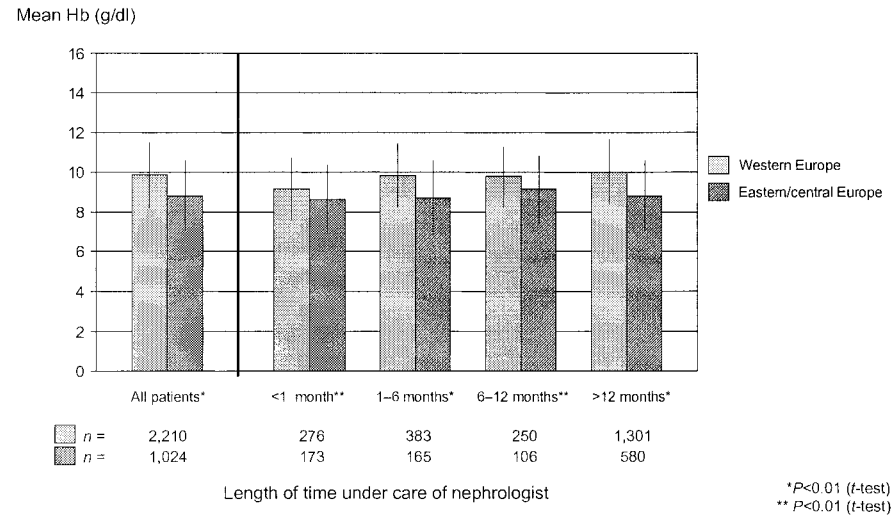


Fig. 1. Haemoglobin (Hb) concentration at start of dialysis by length of time under care of nephrologist. (**A**) Global analysis of all patients. Mean Hb concentration at start of dialysis significantly increased with length of time under care of a nephrologist ($P < 0.01$, ANOVA). (**B**) Separate analysis of patients from western Europe and of patients from central and eastern Europe.

The Hb concentration at the first visit to the dialysis centre was positively correlated with creatinine clearance rate ($r=0.43$; $P<0.01$), but there was considerable variability. For example, at a creatinine clearance rate of 20 ml/min, the Hb concentration ranged from 4.8 to 14.2 g/dl. At the first visit to the dialysis centre, patients with creatinine clearance rates >50 ml/min had a mean Hb concentration of 12.0 g/dl, those with rates of 40–50 ml/min had a mean Hb concentration of 12.3 g/dl, those with rates of 30–40 ml/min had a mean Hb concentration of 11.7 g/dl, those between 20 and 30 ml/min had a mean Hb concentration of 11.0 g/dl, those 10–20 ml/min had 9.8 g/dl, and those with a creatinine clearance of <10 ml/min had a mean Hb concentration of 9.0 g/dl. The association between Hb concentration and creatinine clearance rate was similar for diabetic and non-diabetic patients who were not treated with epoetin ($n=1777$) (Figure 2). The percentage of patients with a Hb concentration below the EBPG target of >11.0 g/dl was progressively smaller with improving creatinine clearance rates (Figure 3). Conversely, the percentage of patients maintaining an Hb concentration between 11.0 and 13.0 g/dl (Figure 3) increased with improving creatinine clearance rates. For both epoetin- and non-epoetin-treated patients, the mean creatinine clearance rates were low (12.4 and 12.0 ml/min, respectively) for those who had an Hb concentration <9.0 g/dl at the first visit to the dialysis centre. Creatinine clearance rate progressively increased with increasing

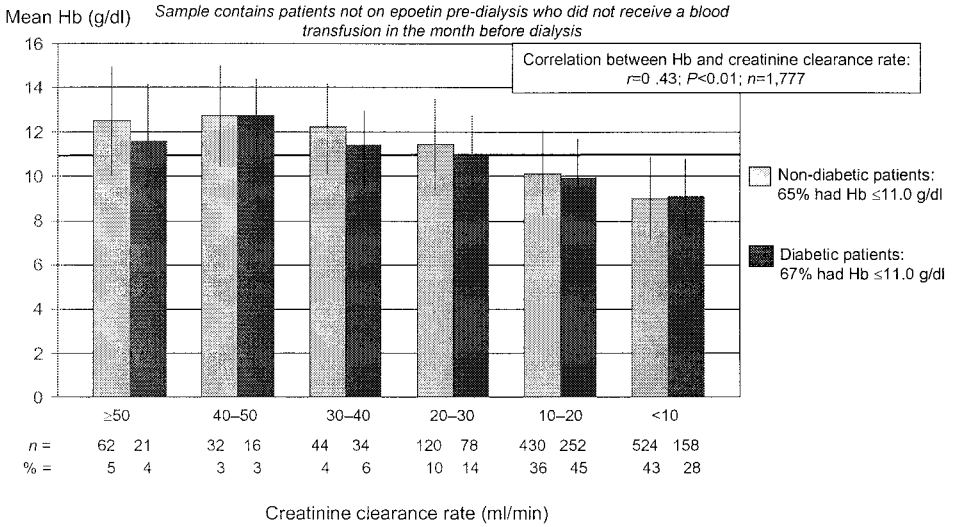


Fig. 2. Haemoglobin (Hb) concentration by creatinine clearance at first visit to dialysis centre, in patients with and without diabetes mellitus. There was a significant correlation between Hb concentration and estimated creatinine clearance ($r=0.43$; $P<0.01$; $n=1777$). For any estimated creatinine clearance, diabetic patients were not more severely anaemic than non-diabetic patients.

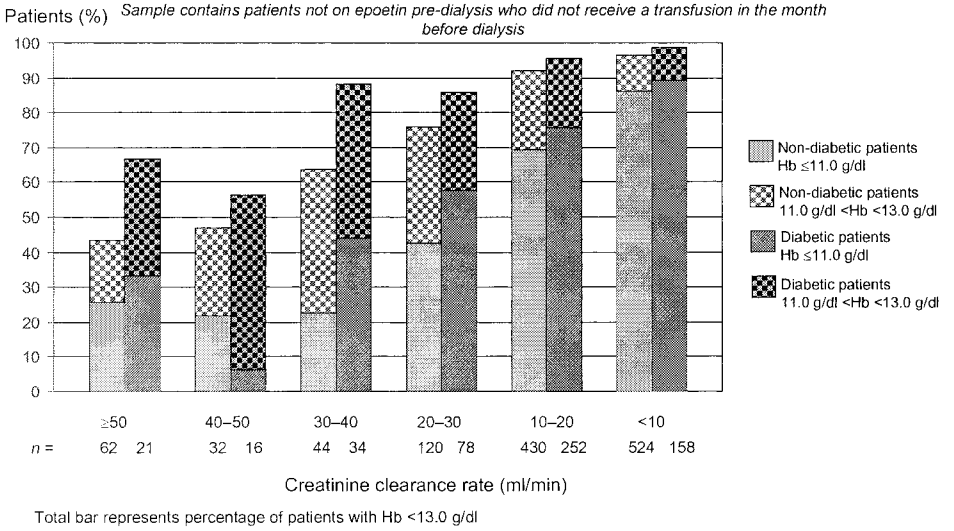


Fig. 3. Percentage of patients with haemoglobin (Hb) concentration $\leqslant 11.0$ g/dl or between 11.0 and 13.0 g/dl by creatinine clearance rate at first visit to dialysis centre. In diabetic as well as in non-diabetic patients, the percentage of patients with Hb concentrations $\leqslant 11.0$ g/dl was progressively smaller with improving estimated creatinine clearance rates.

Hb concentration, to a high mean of 33.0 ml/min (epoetin-treated) and 29.3 ml/min (non-epoetin-treated) in those with an Hb concentration $\geqslant$12.0 g/dl.

Epoetin treatment

Only 26.5% (1085/4095) of the patients started epoetin treatment before dialysis (Table 4). Dialysis was started before epoetin treatment in 12.8% (523/4095) of the patients, epoetin and dialysis were started simultaneously in 32.5% (1332/4095) of the patients, and 28.2% (1155/4095) did not receive epoetin at any time. The mean Hb concentration at the start of dialysis in patients who had received epoetin before starting dialysis was 10.3 g/dl compared with 9.2 g/dl in those who started epoetin after dialysis, 8.9 g/dl in those who started epoetin and dialysis simultaneously, and

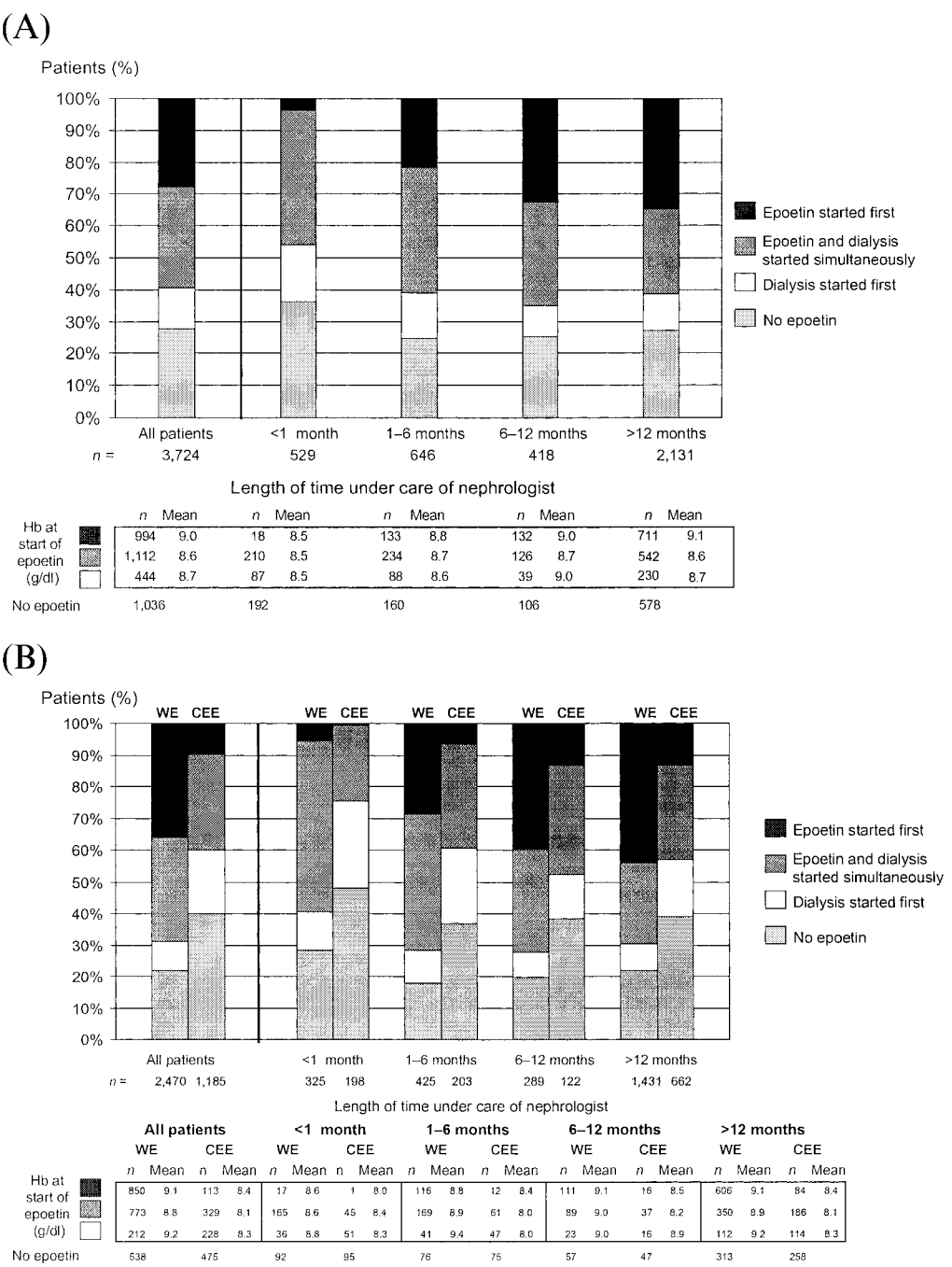
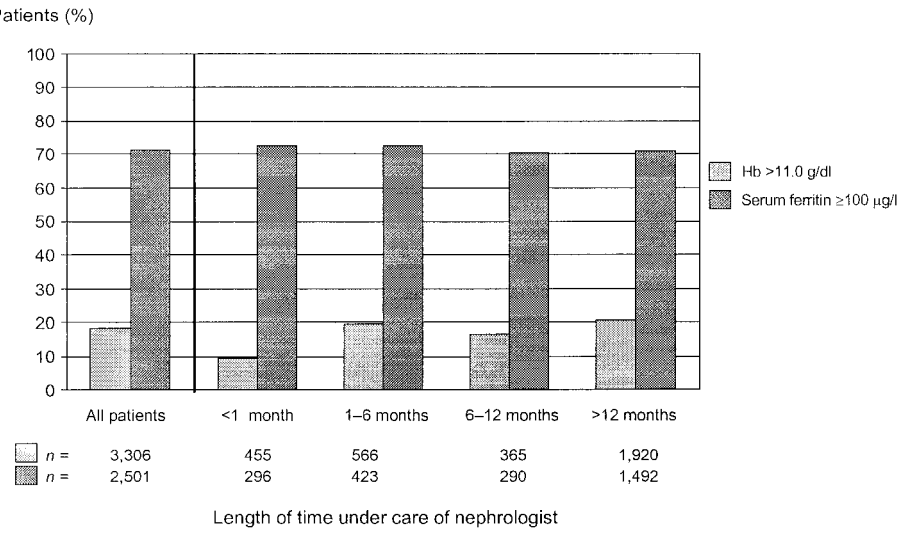
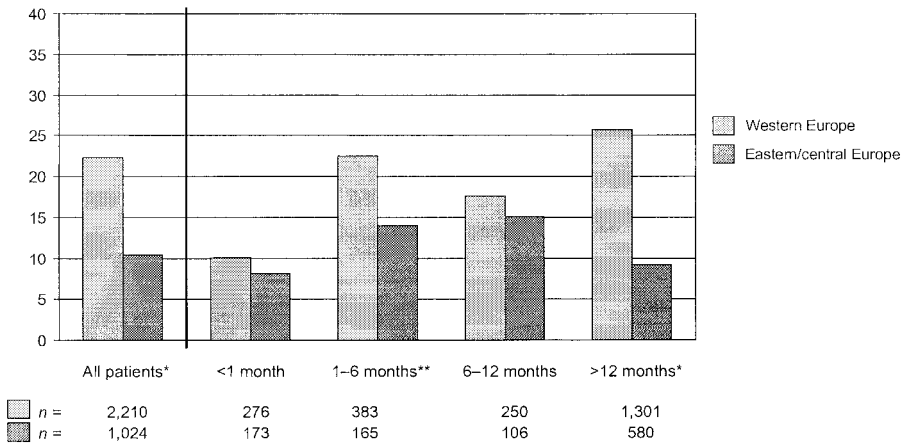


Fig. 4. Start of epoetin treatment in relation to dialysis by length of time under care of nephrologist. **(A)** Global analysis of all patients. The percentage of patients starting epoetin treatment before dialysis increased with length of time under care of a nephrologist. **(B)** Separate analysis of patients from western Europe and of patients from eastern Europe. In both cases, the percentage of patients starting epoetin treatment before dialysis increased with length of time under care of a nephrologist, but this percentage was lower for patients from central and eastern Europe than for patients from western Europe.

(A)

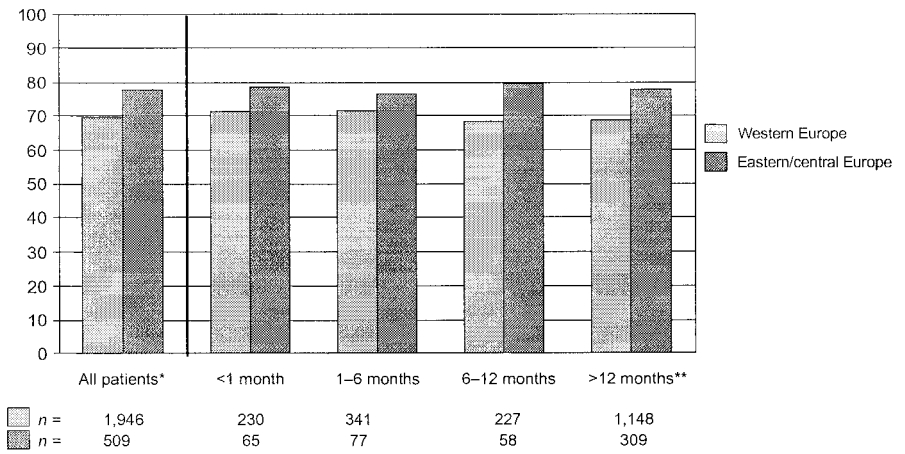


(B)



*P<0.01 (chi-square)
**P<0.05 (chi-square)

(C)



*P<0.01 (chi-square)
**P<0.01 (chi-square)

9.4 g/dl in those who received no epoetin (Table 4). The percentage of patients meeting the EBPG target Hb concentration of >11.0 g/dl at the start of dialysis was 31% of those who started epoetin first, 14% of those who started dialysis first, 8% of those who started dialysis and epoetin simultaneously, and 17% of those who were not treated with epoetin.

The percentage of patients who received epoetin before dialysis increased with the length of time under the care of a nephrologist (Figure 4A and B). There was also an increase in the mean Hb concentration at the start of epoetin treatment for patients who received epoetin before dialysis, from 8.5 g/dl in patients who were under the care of a nephrologist for <1 month ($n=18$) to 9.1 g/dl in patients under the care of a nephrologist for >1 year ($n=711$). When patients from western Europe were analysed separately, the mean Hb concentration increased from 8.6 g/dl in patients who were under the care of a nephrologist for <1 month ($n=17$) to 9.1 g/dl for those who were under the care of a nephrologist for >12 months ($n=606$) (Figure 4B). In the entire sample, patients who started epoetin pre-dialysis had a mean Hb concentration of 9.0 g/dl at the start of epoetin treatment ($n=994$). Those who started dialysis first had a mean Hb concentration of 8.7 g/dl at the start of epoetin treatment ($n=444$) and those who started epoetin and dialysis simultaneously had a mean Hb concentration of 8.6 g/dl ($n=1112$) (Figure 4A). For patients from western Europe, mean Hb concentrations at the start of epoetin were 9.2 g/dl ($n=212$) for those who started dialysis first and 8.8 g/dl ($n=773$) for those who started epoetin and dialysis simultaneously (Figure 4B). For patients from central and eastern Europe, these Hb concentrations were 8.3 g/dl ($n=228$) and 8.1 g/dl ($n=329$), respectively (Figure 4B).

Clinicians were more likely to start epoetin treatment if patients had both a low Hb concentration and symptoms of anaemia (tiredness, dyspnoea) (41%, total $n=3013$). Hb concentration alone was the reason for starting treatment in 25% of the patients (total $n=3018$).

The mean dose at the start of epoetin treatment was 6302 ± 3944 IU/week. For patients who received epoetin pre-dialysis ($n=1031$), the mean dose was 5832 ± 3429 IU/week. This was similar to the mean dose for patients who received epoetin after the start of dialysis (5660 ± 3542 IU/week) ($n=488$). These mean doses were significantly lower than those for patients in whom dialysis and epoetin were started simultaneously (6852 ± 4208 IU/week; $F=28.9$, $P<0.01$) ($n=1244$). The association between Hb concentration and epoetin dose was weak for all patients regardless of when epoetin was started in relation to dialysis.

Iron supplementation

At the start of dialysis, 40% had adequate iron status and 60% had iron deficiency (39% had absolute deficiency and 22% functional deficiency) (total $n=1997$). Two-thirds of the patients who received epoetin pre-dialysis also received iron supplementation (total $n=1060$) (Table 4). Of the patients who started epoetin and dialysis simultaneously ($n=1276$), only 40% received iron supplementation, although 59% were iron deficient. In the patients who started epoetin treatment after dialysis ($n=506$), 32% received iron supplementation, although 62% were iron-deficient. In the patients treated with epoetin, there were no significant differences in iron status (i.e. adequate, functional deficiency, or absolute deficiency) between those who started epoetin before, after or simultaneously with dialysis. Of the patients who were not treated with epoetin, 56% were iron-deficient (37% absolutely and 19% functionally).

No iron supplementation was given to 74.6% of the patients who did not receive epoetin, whereas only 51.0% of the patients who were treated with epoetin were not supplemented. Additionally, of the patients who were treated with epoetin pre-dialysis, only 33% did not receive iron supplementation. Of the patients who received epoetin pre-dialysis and also iron supplementation, the majority (67%) were treated with oral iron only, 16% were treated with intravenous (i.v.) iron only and 10% were given both i.v. and oral therapy.

Patients without iron supplementation received the highest mean epoetin dose of 6591 IU/week ($n=4187$). Patients with both i.v. and oral iron supplementation received a mean epoetin dose of 5940 IU/week, those with only oral iron received a mean dose of 5861 IU/week, and those given i.v. iron alone were treated with the lowest epoetin dose with a mean of 5278 IU/week.

Attainment of EBPG targets

The EBPG for the management of anaemia in renal patients recommends an individual target Hb concentration of >11.0 g/dl, and aims for an Hb concentration of >11.0 g/dl in 85% of all patients. The mean individual target Hb concentration in the overall PRESAM sample at the start of dialysis was 11.6 ± 0.7 g/dl (total $n=2943$) (Table 4). Nevertheless, only 18% of the patients had an actual Hb concentration >11.0 g/dl at the start of dialysis (Figure 5A). This percentage was 22% for patients from western Europe, and 10% for patients from eastern or central Europe (Figure 5B). Overall, the lowest incidence of

Fig. 5. EBPG on anaemia management: attainment of Hb and ferritin targets at start of dialysis by length of time under care of nephrologist. **(A)** Global analysis of all patients. **(B)** Analysis of the percentage of patients reaching Hb concentrations >11.0 g/dl at start of dialysis by length of time under care of a nephrologist, according to the country of origin (western Europe *vs* central and eastern Europe). **(C)** Analysis of the percentage of patients reaching ferritin concentrations ⩾100 μg/l at start of dialysis by length of time under care of a nephrologist, according to the country of origin (western Europe *vs* central and eastern Europe).

patients who met the EBPG target Hb concentration of >11.0 g/dl was in the cohort who had been under the care of a nephrologist for <1 month ($n=455$) (Figure 5A). This was also observed when patients from western Europe or from eastern and central Europe were analysed separately (Figure 5B). In the cohort who had been under the care of a nephrologist for >12 months, both EBPG targets for Hb and ferritin concentrations were met by 26% of all patients in the sample who received both epoetin and iron, compared with only 18% of the patients who received epoetin only, 11% who received iron only, or 11% who received neither treatment. A comparison of patients from western Europe and from central and eastern Europe showed that a greater proportion of patients from western Europe were iron-deficient ($P<0.01$) (Figure 5C).

Comorbidity

Patients treated with epoetin pre-dialysis had significantly lower rates of cardiac failure in the year before dialysis than patients not treated with epoetin pre-dialysis (20 *vs* 24%, $P<0.05$). They also had significantly lower incidences of ischaemic heart disease (either angina or myocardial infarction) (17 *vs* 21%, $P<0.05$) and lower rates of blood transfusion (17 *vs* 21%, $P<0.05$). Furthermore, 11% required blood transfusions in the month before dialysis, compared with 19% of those who did not receive epoetin pre-dialysis ($P<0.001$). Similarly, patients treated with epoetin pre-dialysis also had lower rates of clinical events in the month before dialysis compared with those who did not receive epoetin pre-dialysis (cardiac failure 20 *vs* 23%, $P<0.05$; ischaemic heart disease 12 *vs* 16%, $P<0.001$).

Discussion

The PRESAM survey provided an opportunity to study a sample of 4333 incident patients in various countries. The epidemiological value of this sample is that all patients starting dialysis at any of the participating centres have been included. The mean age at the start of dialysis was 59.1 years (median 62 years), which is negligibly lower than in the ESAM [6] (mean 61 years and median 64 years). This is because the study population in the ESAM consisted of prevalent patients, whereas in the PRESAM it consisted of incident patients. In this survey, we found that the most common cause of chronic renal failure was diabetic nephropathy (23%), followed by chronic glomerulonephritis (19%) and vascular nephropathy, including hypertensive nephropathy (13%). In the ESAM [6], the second most common prevalent disease was diabetic nephropathy (18%). In the USA, analysis of data from the United States Renal Data System (USRDS) showed that diabetic nephropathy was also by far the most frequent cause of end-stage renal failure, followed by hypertensive nephropathy and chronic glomerulonephritis [10]. In addition to the advanced age of patients and frequency of diabetes, there were also frequent, significant comorbidities documented during the first visit to a dialysis centre. Hypertension, coronary heart disease, heart failure and arrhythmia were frequently recorded during the first visit and diabetic patients showed these comorbidities more often than non-diabetic patients.

The finding that 57% of the patients who were referred to a dialysis centre had been under the care of a nephrologist for >1 year and only 14% for <1 month is promising. The latter are patients who, according to several authors [11,12], would have to be considered as being so-called 'late referrals'. However, the mean creatinine clearance rate at the first visit to a nephrologist was only 18.2 ml/min, with over 35% of the patients having rates below 10 ml/min. Therefore, despite more than half of the patients being under the care of a nephrologist for >1 year, most arrived at the dialysis centre with an extremely advanced degree of renal insufficiency.

It is of particular significance that in this survey 68% of the patients had an Hb concentration ⩽11.0 g/dl (mean Hb concentration, 10.0 g/dl) when they arrived at the dialysis centre for the first time, and should therefore, according to the EBPG, be considered for treatment with epoetin. Even when only patients from western Europe were considered, 78% had an Hb concentration ⩽11.0 g/dl (median Hb concentration, 9.8 g/dl). The mean Hb concentration at the start of the treatment with epoetin was only 8.8 g/dl. These values are very similar to those observed in the ESAM survey, despite the fact that the ESAM patients were on dialysis and had started treatment several years before. The patients who had been under the care of a nephrologist for >1 year had higher Hb concentrations than those who had been referred later. Nevertheless, these patients started haemodialysis with a mean Hb concentration of 9.6 g/dl, which is still much lower than the recommended concentration. Even when only patients from western Europe were considered, this latter group of patients started dialysis with a mean Hb concentration of 9.8 g/dl. In other words, as in the ESAM survey, the inadequate treatment of patients with anaemia cannot be attributed exclusively to the late referral of the patients. It may also be attributed to the fact that some nephrologists do not follow the recommendations in the EBPG. Comparisons between patients from western and from eastern/central Europe show that patients from eastern/central Europe are less likely to receive epoetin treatment before starting dialysis, and have lower Hb concentrations at the start of epoetin treatment as well as at the start of dialysis. This probably reflects differences in funding available to the health care systems in the respective regions.

For patients who were not treated with epoetin and who had not received blood transfusions in previous months, there was a clear correlation between the degree of renal insufficiency (creatinine clearance rate) and the degree of anaemia (Hb concentration).

However, there was great variability, and patients with creatinine clearance rates as low as 20 ml/min had a range of Hb concentrations from severe anaemia to normal (from 4.8 to 14.2 g/dl). In patients with creatinine clearance rates >50 ml/min, the mean Hb concentration was only 12.0 g/dl, indicating that there was a large proportion of anaemic patients in this group. Another notable finding is that no significant differences were observed in the relationship between Hb concentration and creatinine clearance rate in diabetic patients compared with non-diabetic patients. This is in contrast to other studies, which showed that diabetic patients are more affected by anaemia with declining renal function [13].

In this survey we observed that 26.5% of all patients in the sample received treatment with epoetin before starting dialysis (36% of the patients from western Europe and 10% of the patients from central or eastern Europe). In a review of more than 150 000 patients on dialysis in the USA, Obrador *et al*. [14] found that only 23% of the sample had received treatment with epoetin before starting dialysis. It is also of interest to emphasize that in our survey patients who start dialysis when they already receive epoetin have a higher Hb concentration than those not being treated (10.3 versus 9.2 g/dl), though the concentration is still much lower than that recommended in the EBPG. In addition, the mean Hb concentration was 9.2 g/dl in patients who started treatment with epoetin after dialysis. This study showed that the patients who had been under the care of a nephrologist for >1 year have received treatment with epoetin more often. When the reasons for starting treatment with epoetin were analysed, Hb concentration alone was only responsible for 25% of the cases. It appears that doctors postponed treatment with epoetin until patients showed symptoms of anaemia. The mean initial dose was slightly >6000 IU/week (but this varied greatly), and the mean dose was lower in patients who were treated with epoetin before dialysis.

A total of 60% of the patients were iron-deficient (39% absolutely and 22% functionally), and two-thirds of the patients treated with epoetin pre-dialysis also received iron supplementation. The iron status of the patients did not improve with length of time under the care of a nephrologist. Iron supplementation continued to be insufficient, perhaps because only 26% of the patients received i.v. iron supplementation, and some nephrologists probably do not follow the recommendations in the EBPG. As observed in the ESAM, in patients who did not receive iron supplementation, doses of epoetin were the highest.

The EBPG recommend an individual target Hb concentration of >11.0 g/dl with the aim of achieving this in 85% of the patients in the unit. For the patients studied in the PRESAM, however, the mean individual target was 11.6 g/dl (median value: 12.0 g/dl for patients in western Europe and 11.0 g/dl for patients in central or eastern Europe), but only 18% of the patients (22% of the patients from western Europe and 10% of the patients from central or eastern Europe) had an Hb concentration >11.0 g/dl when starting dialysis. The percentage of patients whose Hb concentration reached 11.0 g/dl was correlated with the length of time under the care of a nephrologist. One significant observation was that a lower incidence of heart failure and ischaemic heart disease is observed in the patients undergoing treatment with epoetin before dialysis than in patients who were not treated with epoetin before the start of dialysis. The cohort treated with epoetin before dialysis also had significantly lower rates of blood transfusions than those not treated with epoetin.

In summary, this pre-dialysis survey serves to draw attention to the following points. More than 30% of the patients had been followed by a nephrologist for <6 months when they started dialysis, which probably invalidated or reduced the effectiveness of measures taken to delay the progression of chronic renal insufficiency and control comorbidity. Cardiovascular comorbidities are extremely common, particularly in diabetic patients and, in this survey, diabetes was the most common cause of chronic renal insufficiency. Although being under the care of a nephrologist for >1 year is associated with less frequent (predominantly heart-related) complications, only a small proportion of patients receive treatment with epoetin before starting dialysis. Patients start dialysis with severe anaemia, and treatment with epoetin is started at Hb concentrations far below those recommended by the EBPG.

It is to be hoped that the data reported in this survey may draw attention to the risks of late treatment of anaemia and help to improve the management of anaemia during the initial stages of chronic renal insufficiency. Such improvements in practice may positively impact quality of life and cardiac status, and may even delay the progression of chronic renal insufficiency [15].

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