Chapter 6
Comorbidities and current smoking status amongst patients starting Renal Replacement Therapy in England, Wales and Northern Ireland: national and centre-specific analyses

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Key Words
Comorbidity · Dialysis · Ethnicity · Mortality · Renal replacement therapy · Smoking · Transplant waiting list

Abstract
Introduction: The prevalence of 13 comorbid conditions and smoking status at the time of starting renal replacement therapy (RRT) in England, Wales and Northern Ireland are described. ***Methods:*** Adult patients starting RRT between 2002 and 2007 in centres reporting to the UK Renal Registry (UKRR) and with data on comorbidity (n = 13,293) were included. The association of comorbidity with patient demographics, treatment modality, haemoglobin, renal function at start of RRT and subsequent listing for kidney transplantation were studied. Association between comorbidities and mortality at 90 days and one year after 90 days from start of RRT was explored using Cox regression. ***Results:*** Completeness of data on comorbidity returned to the UKRR remained poor. Of patients with data, 52% had one or more comorbidities. Diabetes mellitus and ischaemic heart disease were the most common conditions seen in 28.9% and 22.5% of patients respectively. Comorbidities became more common with increasing age (up to the 65–74 age group), were more common amongst Whites and were associated with a lower likelihood of pre-emptive transplantation, a greater likelihood of starting on haemodialysis (rather than peritoneal dialysis) and a lower likelihood of being listed for kidney transplantation. In multivariable survival analysis, malignancy and ischaemic/neuropathic ulcers were the strongest predictors of poor survival at 1 year after 90 days from start of RRT. ***Conclusions:*** The majority of patients had at least one comorbid condition and comorbidity is an important predictor of early mortality on RRT.

Introduction

Recording and reporting of the extent of comorbidity amongst patients starting treatment for established renal failure (ERF) is important for a number of reasons.

1. Risk adjustment in reports of the outcomes of renal replacement therapy: comorbidity is associated with both early and long term mortality [1–11], poor quality of life [12, 13] and may also influence attainment of various clinical performance measures and choice of RRT modality [14]. Case mix adjustment is therefore essential to quality reporting as differences in patient populations that exist across centres may affect process and outcome measures.
2. Resource allocation: patients with significant comorbidity require more inpatient [15] and outpatient care [16] and their treatment costs more; information on comorbidity may therefore help policy-makers, commissioners and providers to plan services.
3. Management of individual patients: the National Kidney Foundation in the US and others have expanded clinical practice guidelines to include management of diabetes [17], dyslipidaemia [18] and cardiovascular disease [19] in patients with chronic kidney disease (CKD). It is therefore important as a first step, to document the presence of comorbid illness to facilitate attainment of these goals.
4. International comparisons: there are marked national and international variations in the number of patients per million population starting RRT with differences in the proportion of patients with diabetes mellitus and other comorbidities [20]. Comparisons of outcomes of ERF between countries require adjustment for the differences in comorbidities.

The prevalence of various comorbid conditions and smoking status at the time of starting RRT and the association of these comorbidities with patient demographics and early mortality are described in this chapter.

The term Established Renal Failure (ERF) used throughout this chapter is synonymous with the terms of End Stage Renal Failure (ESRF) and End Stage Renal Disease (ESRD) which are in more widespread international usage. Within the UK, patient groups have disliked the term 'End Stage' which formerly reflected the inevitable outcome of this disease.

Methods

Study population

Incident adult (⩾18 years) RRT patients (n = 29,755) between 2002 and 2007 in the centres submitting data to the UKRR during these years were considered. Of these, patients who had data on comorbidity were included (n = 13,293; 44.6%). Data on completeness of comorbidity returns from each centre and overall may differ from those in previous UKRR reports due to some centres retrospectively entering previously missing comorbidity data.

Centre exclusions

In the 10th Annual Report [21], Ipswich and other centres using the Mediqal eMed system (all six centres in Northern Ireland, Basildon, Chelmsford, Dorset and Norwich) were excluded following discovery of an error in the data extraction software affecting some of these centres. This extraction error has now been rectified and these centres are included in this year's report. The nine centres in Scotland do not provide comorbidity data to the UKRR and are not included in these analyses.

Definition of comorbidity and method of data collection

Clinical staff in each centre are responsible for recording (in yes/no format), on their renal information technology (IT) system, the presence or absence of 13 comorbid conditions and information on current tobacco smoking (Table 6.1) for each patient at the time of starting RRT. Definitions of each of these conditions are given elsewhere [22]. Complete data on comorbidity for a given patient was considered to have been provided if there was a non-missing entry (yes/no) for at least one of the comorbid conditions. For some analyses comorbidities have been collapsed into broader categories.

- 'Ischaemic heart disease' was defined as the presence of one or more of the following conditions: angina, myocardial infarction (MI) in the three months prior to starting RRT, MI more than three months prior to starting RRT or coronary artery bypass grafting (CABG)/angioplasty.

Table 6.1. Comorbid conditions listed in the UKRR dataset

Comorbidity
Angina
Previous myocardial infarction (MI) within 3 months prior to start of RRT
Previous MI more than 3 months prior to start of RRT
Previous coronary artery bypass graft (CABG) or coronary angioplasty
(in some analyses the above four variables are combined under the term 'ischaemic heart disease')
Cerebrovascular disease
Diabetes (when not listed as the primary renal disease)
Chronic obstructive pulmonary disease (COPD)
Liver disease
Claudication
Ischaemic or neuropathic ulcers
Non-coronary angioplasty, vascular graft, or aneurysm
Amputation for peripheral vascular disease
(in some analyses the above four variables are combined under the term 'peripheral vascular disease')
Smoking
Malignancy

- 'Peripheral vascular disease' was defined as the presence of one or more of the following conditions: claudication, ischaemic or neuropathic ulcers, non-coronary angioplasty, vascular graft, aneurysm or amputation for peripheral vascular disease.
- 'Non-coronary vascular disease' was defined as the presence of cerebrovascular disease or any of the data items that comprise 'peripheral vascular disease'.

Ethnicity data reporting

Some centres electronically upload ethnicity coding to their renal IT system from the hospital Patient Administration Systems (PAS). Ethnicity coding in these PAS systems is based on self-reported ethnicity and uses a different coding system [23]. For the remaining centres, ethnic coding is performed by clinical staff and recorded directly into the renal IT system (using a variety of coding systems). For all these analyses, data on ethnic origin were grouped into Whites, South Asians, Blacks, Chinese and Others. The details of regrouping of the PAS codes into the above ethnic categories are provided in appendix G.

Statistical methods

The statistical methods for the four individual sections of this chapter are described separately.

The number of patients with data on comorbidity and other data variables included in the various analyses are summarised in figure 6.1.

1) Patient demographics

The proportion of patients starting RRT with various comorbidities was examined by age group (18–34, 35–44, 45–54, 55–64, 65–74 and $\geqslant$75 years), primary renal disease, ethnic origin and first modality of RRT. Chi-squared, Fischer's exact and Kruskal Wallis tests were used as appropriate to test for significant differences between groups.

2) Late presentation (referral), haemoglobin and renal function at start of RRT

The date of starting RRT and the date first seen by nephrologists were used to calculate the referral time. This was the number of days between first being seen and starting RRT. Referral times of 90 days or more were defined as early presentation. Referral times of less than 90 days were defined as late presentation. Data on referral time was incomplete and therefore only patients with data on comorbidity and referral time from centres with >75% data completeness for referral time were included in this analysis (n = 5,633; 18.9% of all patients starting RRT).

The association of various comorbidities with haemoglobin (Hb) concentration at start of RRT was studied amongst patients with comorbidity data and Hb data within 14 days before the start of RRT (n = 8,534; 28.7% of all patients starting RRT). Two-sample t-tests were used to compare the mean Hb at start of RRT amongst patients with a specific comorbidity with the mean for those with none of the comorbidities. As many tests were carried out, only p values <0.01 were considered statistically significant for these analyses.

The association of various comorbidities with estimated glomerular filtration rate (eGFR) at start of RRT was studied amongst patients with comorbidity data and eGFR data within 14 days before the start of RRT. The eGFR was calculated using the abbreviated 4 variable MDRD study equation [24]. For the purpose of eGFR calculation, patients who had missing ethnicity but a valid serum creatinine measurement were classed as Whites as the Black population only account for 3% of the total UK RRT population. The eGFR values were log transformed in order to normalise the data and then two-sample t-tests were used to compare the means of the log eGFR of those patients with the specific comorbidity against those with none of the comorbidities present. As many statistical tests were carried out, only p values <0.01 were considered statistically significant for these analyses.

There is no defined standard for a threshold eGFR at which patients should start RRT for ERF as the decision is based on clinical presentation, anticipated further deterioration and complications of uraemia as well as biochemistry. However, there are defined thresholds for pre-emptive listing for a kidney transplant. The European Best Practice Guidelines (EBPG) recommend that patients with progressive deterioration in renal function and a creatinine clearance of <15 ml/min/1.73 m^2 should be considered for pre-emptive transplantation; patients with ERF secondary to diabetes should

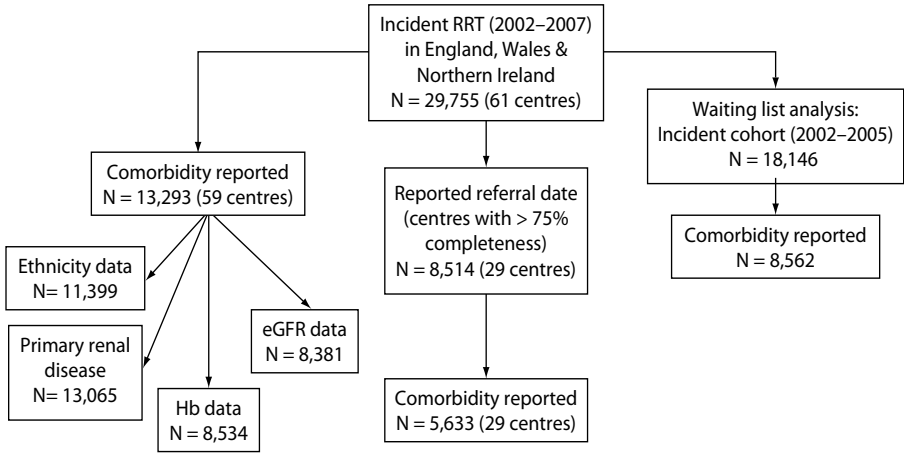

Fig. 6.1. Flow chart showing number of patients included in the various analyses

be considered for early and pre-emptive transplantation when their eGFR decreases to <20 ml/min/1.73 m^2 [25]. In the UK, the British Transplantation Society (www.bts.org.uk) endorse the EBPG and current UK Renal Association guidelines recommend that patients should be placed on the kidney transplant waiting list within six months of their anticipated dialysis start date [26]. There are no KDOQI guidelines for listing. It is therefore possible that patients could have started RRT with a transplant and an eGFR value as high as 20 ml/min/1.73 m^2. Patients with an eGFR >20 ml/min/1.73 m^2 were excluded from the eGFR analyses due to concerns on possible data extraction errors. Patients starting RRT between 2001 and 2005 from one centre (London West) were also excluded due to errors in the software data extraction process for this item. This extraction process was rectified in 2006. The eGFR analyses excluded 4,036 patients who had no data on eGFR within 14 days prior to start of RRT, 438 who had eGFR values >20 ml/min/1.73 m^2 and 438 patients from London West leaving 8,381 patients (28.2% of all patients starting RRT) in this analysis. Many UKRR analyses, including those presented here, rely on the accuracy of the date of start of RRT. A discussion of the issues around definition of the start date is included in chapter 7.

3) Activation on deceased donor kidney transplant waiting list

The association between comorbidity and activation on the deceased donor kidney transplant waiting list in 8,562 patients was examined. Date of first activation on the waiting list for all patients starting RRT between 2002 and 2005 on the UKRR database were obtained from NHS Blood and Transplant (formerly UK Transplant), the independent organisation responsible for maintaining the national organ donor register. Data on activation on the waiting list for patients starting RRT in the year 2006 were not available at the time of writing and therefore this analysis was restricted to the years 2002 to 2005. All patients were followed until 31st December 2006 to determine the date of activation on the waiting list. The prevalence of various comorbidities amongst patients activated on the waiting list within the first year of RRT was compared with those activated on the waiting list beyond the first year or never activated. Patients who died within the first year and were not on the active waiting list at the time of death were included under the 'non-waitlisted' group.

4) Patient survival

The Registry collected data with a 'timeline' entry on all patients who had started RRT for ERF. Patients who presented acutely and who were initially classified as acute renal failure requiring dialysis, but continued to require long-term dialysis can be re-classified by clinicians as having had ERF from the date of their first RRT. Many other national registries only collect data on patients who have survived the first 90 days of RRT. The UKRR, unlike these other registries, is able to collect and report data on factors affecting outcomes, including survival, in the first 90 days of RRT. However, the death rate is high in the first 90 days and highly variable between centres, due partly to individual clinical variation in the classification of patients with acute kidney injury who may be deemed from the start to be unlikely to recover renal function. To remove this centre variation and also allow comparison with results from other national registries, the association of comorbid conditions and survival 1 year after 90 days from start of RRT was also analysed.

For each of the follow up periods, the association of baseline comorbidity with survival was studied using univariate and multivariate Cox regression models. For analyses of survival within the first 90 days, the cohort included patients starting RRT between 1st January 2002 and 30th September 2007 to allow a minimum of three months follow-up from the start of RRT. For the 1 year after 90 days survival analyses, the cohort included patients who survived at least 90 days on RRT and who started RRT between 1st January 2002 and 30th September 2006.

For each variable, the models estimated the hazard ratio of death comparing those with a particular comorbidity with those who did not have the comorbidity. In the univariate models, patients were first stratified by age group (<65 years and ⩾65 years) to account for the increasing incidence of certain comorbidities with age, which may otherwise obscure the analysis. The multivariate Cox models used a backward stepwise method that included all variables and then sequentially removed the variable with the largest p value (i.e. the one which added least to the model); the procedure was continued until all remaining variables were significant contributors to the model. The variables included in the multivariate model were: age (per 10 year increase), angina, MI within 3 months prior to starting RRT, MI more than 3 months prior to starting RRT, coronary artery bypass grafting (CABG) or coronary angioplasty, cerebrovascular disease, diabetes mellitus (whether as a cause of primary renal disease or as a comorbidity), chronic obstructive pulmonary disease (COPD), liver disease, malignancy, claudication, ischaemic/neuropathic ulcers, angioplasty/vascular graft, amputation and smoking.

All statistical analyses were performed using SAS version 9.1.3.

Results

Completeness of comorbidity returns from each participating centre

Table 6.2 shows that completeness of data returns still varies markedly between centres with four centres providing data on 100% of patients but 20 providing data for less than 5% of their new patients in 2007. There was no relationship between the size of the centre and the completeness of data returns. Amongst all incident patients, data on comorbidity declined from 46.9% of patients starting in 2002 to only 40.0% in 2007 (table 6.3). However, this decline in data completeness in recent years was more marked in new centres joining the UKRR in the later years that had not yet set up systems to collect these data. The data completeness amongst centres that have been submitting data since 2002 has shown a smaller decline from 46.9% in 2002 to 44.6% in 2007. After excluding centres that returned no comorbidity data, the average completeness of data

Table 6.2. Completeness of comorbidity data returns on incident patients from individual centres (2002–2007)

	2002		2003		2004		2005		2006		2007	
Centre	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return
Antrim							42	5	33	9	36	14
B Heart	66	2	103	0	102	0	116	1	115	0	95	1
B QEH					194	0	196	1	186	0	222	0
Bangor	29	66	33	48	36	64	40	55	41	61	36	44
Basldn			53	45	46	39	28	57	45	82	39	74
Belfast							131	15	112	14	91	24
Bradfd	62	100	74	85	61	92	66	95	50	100	87	99
Brightn					118	0	109	0	131	1	115	1
Bristol	124	82	163	85	164	79	175	78	177	89	154	73
Camb	74	4	96	1	110	1	111	1	157	2	127	0
Cardff	181	1	166	3	186	5	182	20	207	4	207	0
Carlis	26	23	31	23	29	72	31	94	27	93	25	80
Carsh	172	23	198	27	165	36	180	42	184	47	196	57
Chelms					52	50	38	47	49	84	52	54
Clwyd	20	0	12	0	14	0	27	0	18	0	23	0
Covnt	94	1	75	1	76	0	83	0	102	2	109	0
Derby			59	75	67	81	71	92	69	88	60	95
Derry									3	67	7	43
Donc											18	100
Dorset			65	98	59	100	45	98	53	100	58	95
Dudley	25	8	41	0	54	0	38	0	44	2	35	0
Exeter	82	51	97	54	110	46	110	31	104	28	122	6
Glouc	54	67	53	87	53	89	60	97	73	88	57	96
Hull	105	5	81	88	109	86	126	97	98	97	99	98
Ipswi	43	53	38	45	45	47	59	31	42	60	40	30
L Barts					185	76	184	87	187	80	200	74
L Guys	141	2	93	3	104	3	132	5	134	3	150	2
L Kings	115	88	108	100	114	98	136	99	113	99	128	100
L Rfree							132	2	209	1	182	0
L St.G											89	58
L West	250	72	254	62	295	67	290	52	283	67	334	47
Leeds	152	86	185	86	175	83	164	70	181	66	117	66
Leic	153	88	167	96	162	94	223	64	241	65	240	70
Liv Ain					3	0	29	3	34	0	34	3
Liv RI	152	49	114	62	130	61	139	63	140	51	114	44
M Hope			143	33	111	41	112	35	129	12	99	9
M RI											159	0
Middlbr	111	100	103	0	102	1	84	0	105	0	98	0
Newc	102	1	94	3	109	0	113	3	110	1	111	1
Newry							28	14	14	21	15	27
Norwch					95	4	119	6	109	11	108	6
Nottm	87	99	115	98	107	95	145	99	135	97	127	76
Oxford	170	30	188	60	171	65	156	51	162	14	139	86
Plymth	79	32	64	27	62	44	58	45	91	60	76	67
Ports	145	49	141	63	118	65	151	60	173	56	157	54
Prestn	110	1	98	1	79	0	118	0	121	1	128	0
Redng	40	3	63	0	59	0	74	0	77	1	91	0
Sheff	156	63	159	64	168	55	157	40	168	57	166	52
Shrew					55	0	42	0	54	0	55	2
Stevng	100	2	122	3	84	5	91	4	118	0	86	2
Sthend	34	59	42	67	40	80	34	74	47	96	34	94
Stoke											87	44
Sund	56	48	55	64	50	92	58	91	56	91	61	100

Table 6.2. Continued

Centre	2002		2003		2004		2005		2006		2007	
	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return	No. incident patients	% return
Swanse	113	82	125	97	93	91	98	97	113	96	123	93
Truro	59	66	53	83	67	81	32	88	50	78	45	93
Tyrone							23	30	30	47	22	32
Ulster							9	56	8	63	14	100
Wirral	43	16	53	13	66	14	58	7	55	0	53	0
Wolve	98	100	88	100	105	98	92	85	87	60	68	47
Wrexm	42	0	32	3	29	0	40	0	26	0	27	0
York	63	81	57	84	48	92	43	91	47	89	35	74
Totals	**3,728**		**4,154**		**4,836**		**5,428**		**5,727**		**5,882**	

Blank cells – no data returned to the UKRR for that year

Table 6.3. Summary of completeness of incident patient comorbidity returns (2002–2007)

	Years						Combined years
	2002	2003	2004	2005	2006	2007	
Number of renal centres included	39	43	50	56	57	61	
Total number of new patients	3,728	4,154	4,836	5,428	5,727	5,882	29,755
Number of patients with comorbid data entries	1,749	2,120	2,338	2,355	2,381	2,350	13,293
Percentage	46.9	51.0	48.3	43.4	41.6	40.0	44.7
Percentage with comorbidity returns							
Median percentage amongst only centres returning >0% comorbidity	49.3	62.0	66.4	52.1	60.1	54.0	57.8

returns from centres ranged from 1–100% (mean 52.2%) for 2007, a moderate improvement on a mean of 46.0% in 2002.

As stated above, a return was considered to be 'complete' if there was at least one answer to the 14 questions on the comorbidity screen. However, most records that contained at least one answer contained answers to most or all of the other questions; only 0.7% had 10 or fewer questions answered, 1.0% contained 11 answers, 1.2% contained 12 answers, 7.5% contained 13 answers and 89.6% contained answers to all 14 questions.

Prevalence of multiple comorbidity

Of patients for whom comorbidity data were available, 52.4% had at least one comorbidity present and 26.3% had more than one comorbid condition (table 6.4).

Frequency of each comorbidity condition

Diabetes mellitus (either causing ERF or as a comorbidity) was present in 28.9% of all patients. Ischaemic heart disease was seen in 22.5% of all patients and as expected was more prevalent amongst those aged 65 years and above (32.1%) compared to those aged less than 65 years (13.4%). Peripheral vascular disease occurred in 11.3% of all patients being more common amongst those aged 65 years and above (15.0%) compared to those aged less than 65 years (7.8%). Table 6.5 gives the prevalence of each comorbidity and the percentage of the total number of incident patients for whom data was available for that item.

Table 6.4. Number of reported comorbidities in patients starting RRT, as a percentage of those for whom comorbidity data were available (2002–2007)

Number of comorbidities	0	1	2	3	4	5+
Percentage	47.6	26.2	13.0	7.1	3.7	2.5

Table 6.5. Frequency of each condition reported in incident RRT patients 2002–2007

Comorbidity	Age <65 years		Age ⩾65 years		p value*	% overall
	No. patients	(%)	No. patients	(%)		prevalence
Angina	581	(8.6)	1,434	(22.6)	<0.0001	15.3
MI in past 3 months	107	(1.6)	238	(3.7)	<0.0001	2.6
MI >3 months ago	391	(5.7)	987	(15.5)	<0.0001	10.4
CABG/angioplasty	333	(4.9)	565	(8.9)	<0.0001	6.9
Cerebrovascular disease	396	(5.8)	891	(14.0)	<0.0001	9.8
Diabetes (not cause of ERF)	331	(4.9)	682	(10.8)	<0.0001	7.8
Diabetes as primary disease	1,671	(24.4)	1,162	(18.1)	<0.0001	21.3
COPD	265	(3.9)	620	(9.8)	<0.0001	6.8
Liver disease	195	(2.9)	114	(1.8)	<0.0001	2.3
Malignancy	417	(6.1)	1,089	(17.0)	<0.0001	11.4
Claudication	301	(4.4)	705	(11.1)	<0.0001	7.6
Ischaemic/neuropathic ulcers	224	(3.3)	184	(2.9)	0.2	3.1
Angioplasty/vascular graft	111	(1.6)	319	(5.0)	<0.0001	3.3
Amputation	153	(2.3)	88	(1.4)	0.0002	1.8
Smoking	1,112	(17.7)	740	(12.3)	<0.0001	15.1
Some comorbidity present	2,811	(41.0)	4,159	(64.7)	<0.0001	52.4

* p values from Chi-squared tests for differences between age groups in the percentage with the comorbidities

Prevalence of comorbidity by age band

Figures 6.2 and 6.3 illustrate the increasing prevalence of comorbidity with increasing age up to the 65–74 year age group in incident patients with levelling off or slight reductions in reported comorbidity amongst patients aged over 75 years.

Prevalence of comorbidity by ethnic origin

Figure 6.4 illustrates the presence of comorbidity by ethnic origin, showing a higher prevalence of having at least one comorbidity amongst patients of White origin compared to the ethnic minorities. Figure 6.5 shows that the lower prevalence of comorbidity amongst patients of Black or South Asian origin is not entirely attributable to younger age amongst these groups, as the prevalence of comorbidity was lower than in the White population even in the 18–34 year age group. Table 6.6 shows the prevalence of major comorbidities in each group. Compared

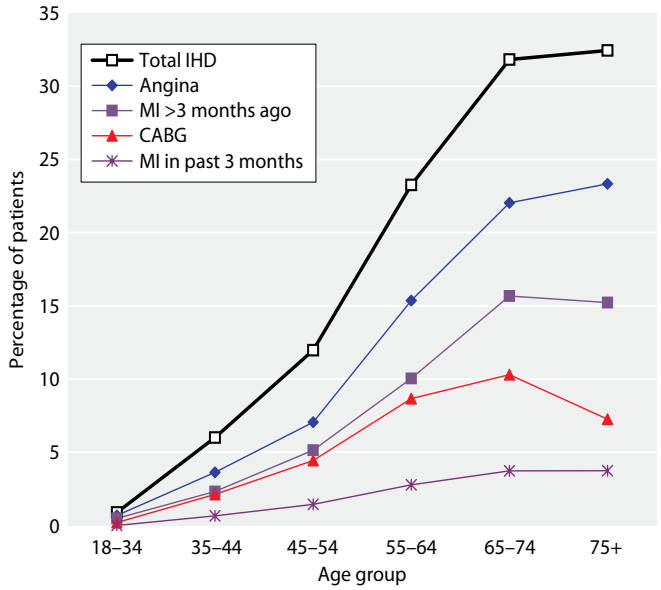

Fig. 6.2. Prevalence of ischaemic heart disease amongst incident patients 2002–2007 by age at start of RRT

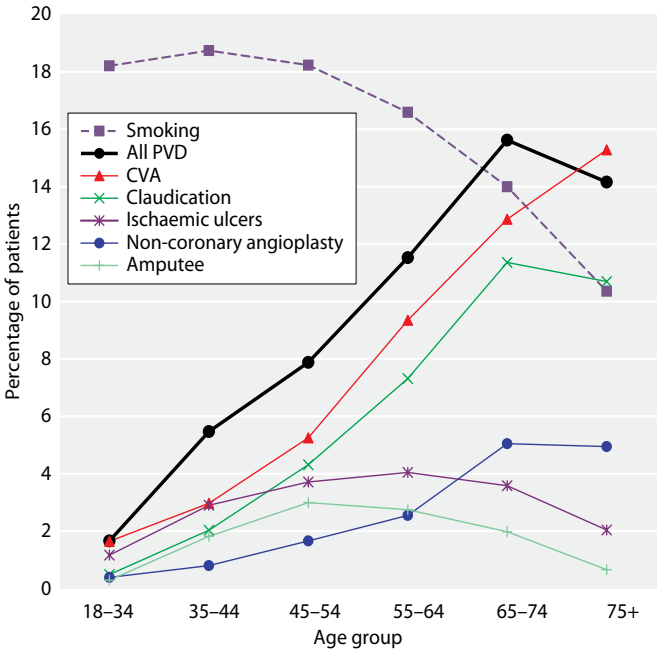

Fig. 6.3. Prevalence of non coronary vascular disease amongst incident patients 2002–2007 by age at start of RRT

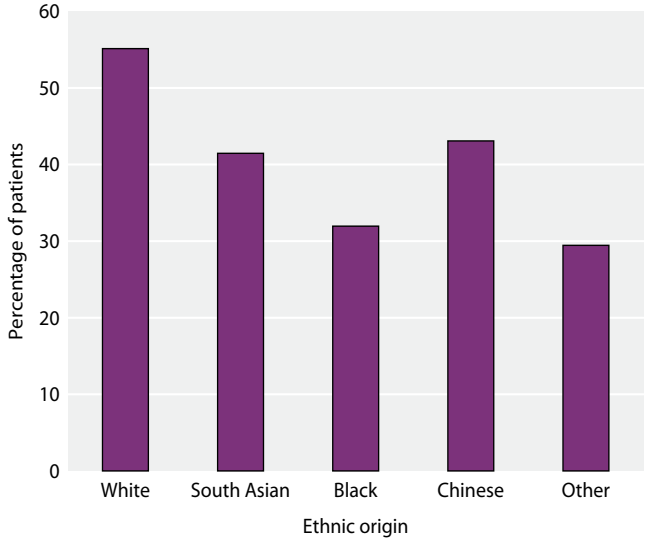

Fig. 6.4. Presence of comorbid conditions by ethnic origin at the start of RRT amongst patients starting RRT 2002–2007

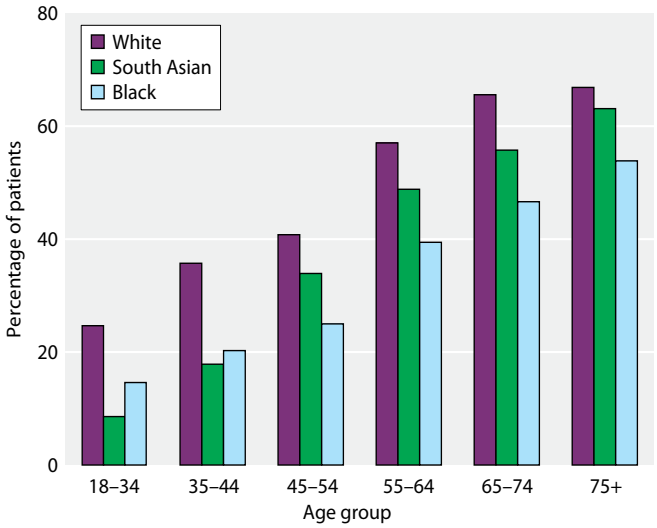

Fig. 6.5. Percentage of patients with comorbidity by ethnic origin in each age group at the start of RRT (2002–2007)

to Whites, Blacks and South Asians had lower prevalence of most comorbid conditions (with the exception of liver disease and diabetes mellitus).

Prevalence of comorbidity amongst patients with diabetes mellitus

Only 13,065 patients (43.9% of all patients starting RRT) who had data on comorbidity and primary renal disease were included in this analysis. Table 6.7 compares comorbidity amongst patients with and without diabetes (either as primary renal disease or comorbidity) who had at least one other comorbidity present, showing higher rates of ischaemic heart disease, cerebrovascular disease and peripheral vascular disease amongst diabetic patients.

Haemoglobin concentration at the time of starting RRT and comorbidity

The mean Hb prior to starting RRT in patients who were recorded as starting without any comorbidity present is 10.2 g/dl compared to 10.1 g/dl for those with some comorbidity. Of patients without any co-morbidity 55.7% achieved an Hb >10 g/dl compared to 52.8% with some comorbidity. Compared to those without any comorbidity, the mean Hb concentrations

Table 6.6. Prevalence of comorbidities amongst incident patients starting RRT 2002–2007 by ethnic group, as percentages of the total number of patients in that ethnic group for whom comorbidity data were available

	Patients with comorbidity										
	White		South Asian		Black		Chinese		Other		
Comorbidity	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	p value*
Smoking	1,452	(16.6)	52	(5.8)	32	(5.7)	4	(7.3)	14	(6.3)	<0.0001
Cerebrovascular disease	923	(10.0)	92	(8.6)	56	(8.6)	9	(14.3)	20	(6.5)	0.08
Peripheral vascular disease	1,105	(12.0)	83	(7.8)	28	(4.3)	7	(11.1)	23	(7.5)	<0.0001
Ischaemic heart disease	2,143	(23.4)	244	(23.4)	60	(9.3)	9	(14.5)	36	(11.9)	<0.0001
Liver disease	197	(2.1)	39	(3.7)	21	(3.2)	7	(10.9)	5	(1.6)	<0.0001
COPD	690	(7.5)	42	(4.0)	15	(2.3)	1	(1.6)	9	(2.9)	<0.0001
Malignancy	1,170	(12.6)	26	(2.4)	39	(6.0)	2	(3.2)	16	(5.2)	<0.0001
Diabetes of either category	2,419	(26.0)	525	(49.0)	227	(34.6)	18	(27.7)	121	(39.2)	<0.0001
Diabetes (not cause of ERF)	700	(7.7)	97	(9.4)	32	(4.9)	3	(4.8)	22	(7.2)	0.02
Diabetes as primary disease	1,719	(18.5)	428	(40.0)	195	(29.7)	15	(23.1)	99	(32.0)	<0.0001

* p values from Chi-squared tests for differences between ethnic groups in the percentage with the comorbidities

Table 6.7. Patients with and without diabetes (either as primary diagnosis or comorbidity) that have other comorbid conditions

	Non-diabetic patients		Diabetic patients		
Comorbidity	N	(%)	N	(%)	p value*
Ischaemic heart disease	1,648	(18.2)	1,214	(32.2)	<0.0001
Smoking	1,281	(15.1)	524	(15.0)	0.9
Malignancy	1,178	(13.0)	279	(7.3)	<0.0001
Cerebrovascular disease	734	(8.1)	527	(13.8)	<0.0001
Peripheral vascular disease	657	(7.3)	794	(20.8)	<0.0001
COPD	612	(6.8)	254	(6.7)	0.9
Liver disease	204	(2.3)	97	(2.5)	0.3

* p values from Chi-squared tests for differences in the percentage with the comorbidities between diabetic patients and non-diabetic patients

at the start of RRT were lower amongst those with malignancy (10.1 g/dl, $p = 0.005$), a history of claudication (10.0 g/dl, $p = 0.005$), ischaemic/neuropathic ulcers (9.8 g/dl, $p = 0.0002$) and amputation (9.8 g/dl, $p = 0.001$).

Late presentation (referral) and comorbidity

Table 6.8 shows the prevalence of various comorbidities by referral time. Peripheral vascular disease was more frequent amongst those who presented earlier than later; malignancy was more frequent amongst those presenting later than earlier. There was no association between time of presentation and any other comorbidity.

Renal function at the time of starting RRT and comorbidity

The geometric mean eGFR prior to starting RRT in patients with each of the individual comorbidities is shown in table 6.9. The (geometric) mean eGFR prior to starting RRT in patients who were recorded as starting without any comorbidity present was 7.4 ml/min/1.73 m^2. In each case, average eGFR was slightly higher amongst patients with comorbidity compared to patients without any comorbidity.

Age and comorbidity in patients by treatment modality at start of RRT

Amongst all patients with data on comorbidity, 2.2% started RRT with a pre-emptive transplant. The proportion of patients aged less than 65 years who had at least one comorbidity was 42% amongst those who started with either HD or PD compared to 17% amongst patients who had a pre-emptive transplant (Fischer's exact test, $p < 0.0001$). The number of pre-emptive transplants was too small to undertake comparisons for individual comorbidities.

The median age of all patients with comorbidity data on HD at the start of RRT was 66.3 years compared with 59.2 years for those starting PD (Kruskal Wallis test, $p < 0.0001$). For each of the comorbid conditions except for recent MI within 3 months prior

Table 6.8. Percentage prevalence of specific comorbidities amongst patients presented late (0–89 days) compared with those presented early (>89 days)

	Late referral		Early referral		
Comorbidity	N	(%)	N	(%)	p value*
Cerebrovascular disease	152	(10.6)	436	(10.4)	0.9
COPD	105	(7.3)	270	(6.5)	0.3
Diabetes (not a cause of ERF)	111	(7.8)	352	(8.6)	0.4
Ischaemic heart disease	332	(23.2)	1,010	(24.4)	0.4
Liver disease	35	(2.4)	82	(2.0)	0.3
Malignancy	263	(18.2)	424	(10.1)	<0.0001
Peripheral vascular disease	142	(9.9)	549	(13.1)	0.001
Smoking	222	(16.2)	646	(15.9)	0.8

* p values from Chi-squared tests for differences between referral groups in the percentage with the comorbidities

Table 6.9. eGFR within 2 weeks prior to the reported start of RRT (2002–2007) by comorbidity

Comorbidity	eGFR geometric mean (ml/min/1.73 m^2)	eGFR 95% CI	p value*
Without comorbidity	7.4	7.3–7.5	Ref
Some comorbidity present	8.2	8.1–8.2	<0.0001
Angina	8.6	8.4–8.7	<0.0001
MI in past 3 months	8.5	8.1–8.9	<0.0001
MI >3 months ago	8.6	8.4–8.8	<0.0001
CABG/angioplasty	8.9	8.7–9.2	<0.0001
Cerebrovascular disease	8.3	8.1–8.5	<0.0001
Diabetes (not cause of ERF)	8.4	8.2–8.6	<0.0001
Diabetes as primary disease	8.5	8.4–8.7	<0.0001
Diabetes of either category	8.5	8.4–8.6	<0.0001
COPD	8.3	8.1–8.6	<0.0001
Liver disease	8.0	7.6–8.6	0.006
Malignancy	7.7	7.5–7.9	0.002
Claudication	8.6	8.4–8.8	<0.0001
Ischaemic/neuropathic ulcers	8.6	8.3–9.0	<0.0001
Angioplasty/vascular graft	8.6	8.3–9.0	<0.0001
Amputation	8.8	8.3–9.3	<0.0001
Smoking	8.1	8.0–8.3	<0.0001

* Two-sample t-tests compare log (eGFR) for each comorbidity against those without comorbidity

to starting RRT, the median age of patients on HD was higher than those on PD (Table 6.10). Table 6.10 compares the prevalence of individual comorbidities in patients on HD and PD at the start of RRT, showing significantly higher prevalence amongst HD patients of all comorbid conditions other than previous CABG/coronary angioplasty. The percentages shown are out of the total population of patients on that modality at the start of RRT with data for that comorbidity.

Comorbidity and subsequent activation on deceased donor transplant waiting list (TWL)

Table 6.11 shows that patients starting dialysis as their first RRT modality and who were activated on the TWL

Table 6.10. Patients with comorbid conditions present in incident patients starting HD and PD 2002–2007

	HD			PD			
Comorbidity	N	(%)	Median age	N	(%)	Median age	p value*
Angina	1,635	(17.0)	71.8	370	(11.6)	68.3	<0.0001
MI >3 months ago	1,081	(11.2)	71.4	292	(9.1)	69.1	0.001
MI in past 3 months	302	(3.1)	70.3	43	(1.3)	70.6	<0.0001
CABG/angioplasty	663	(6.9)	69.1	227	(7.1)	67.7	0.8
Cerebrovascular disease	1,069	(11.0)	71.4	214	(6.7)	66.8	<0.0001
Diabetes (not cause of ERF)	842	(8.9)	70.6	166	(5.2)	67.0	<0.0001
COPD	761	(8.0)	71.2	122	(3.8)	66.9	<0.0001
Smoking	1,439	(15.9)	62.0	386	(13.0)	55.2	0.0001
Liver disease	267	(2.8)	60.1	38	(1.2)	58.2	<0.0001
Malignancy	1,290	(13.3)	72.0	208	(6.5)	70.0	<0.0001
Claudication	832	(8.6)	71.0	172	(5.4)	67.1	<0.0001
Ischaemic/neuropathic ulcers	353	(3.6)	64.1	54	(1.7)	61.4	<0.0001
Angioplasty/vascular graft	348	(3.6)	71.8	79	(2.5)	70.8	0.002
Amputation	202	(2.1)	61.9	38	(1.2)	56.7	0.001

* p values from Chi-squared tests for differences between modalities in the percentage with the comorbidities

Table 6.11. Comorbidity amongst incident patients 2002–2005 who were activated on the transplant waiting list within the first year compared to those who were not activated within the first year of RRT

	Not activated on waiting list in first year			Activated on waiting list in first year			
Comorbidity	N	(%)	Median age	N	(%)	Median age	p value*
Angina	1,300	(19.4)	71.3	58	(3.5)	56.6	<0.0001
MI >3 months ago	857	(12.7)	70.9	28	(1.7)	56.7	<0.0001
MI in past 3 months	219	(3.2)	70.3	8	(0.5)	56.0	<0.0001
CABG/angioplasty	513	(7.7)	69.0	35	(2.2)	58.3	<0.0001
Cerebrovascular disease	791	(11.7)	71.5	47	(2.8)	57.9	<0.0001
Diabetes (not cause of ERF)	584	(8.8)	71.0	32	(2.0)	54.4	<0.0001
COPD	541	(8.1)	71.5	31	(1.9)	56.7	<0.0001
Smoking	1,044	(16.6)	64.8	217	(14.1)	43.3	0.02
Liver disease	170	(2.5)	62.1	15	(0.9)	55.0	<0.0001
Malignancy	957	(14.2)	71.9	30	(1.8)	57.4	<0.0001
Claudication	679	(10.1)	70.3	20	(1.2)	49.2	<0.0001
Ischaemic/neuropathic ulcers	246	(3.7)	64.1	12	(0.7)	47.1	<0.0001
Angioplasty/vascular graft	275	(4.1)	71.3	7	(0.4)	47.6	<0.0001
Amputation	126	(1.9)	58.9	5	(0.3)	51.7	<0.0001

* p values from Chi-squared tests for differences between transplant waiting list groups in the percentage with the comorbidities

within the first year, were younger and had significantly less comorbidity at the start of RRT than those who were not activated within the first year.

Comorbidity and survival within 90 days of starting RRT

On univariate analysis stratified for age, most comorbidities were associated with an increased risk of death in the first 90 days when compared with a patient in the same age group without that comorbidity. This was true amongst patients aged <65 years and those aged ⩾65 years, the associations being more profound for those aged <65 years (data not shown). Multivariable stepwise Cox regression analyses stratified by age group (<65 and ⩾65) are shown in table 6.12 and table 6.13 respectively. Comorbidities when present in younger patients were a more important pointer to earlier death than when present in older patients. Diabetes did not emerge as an independent predictor, probably due to the close association between diabetes and ischaemic heart disease and peripheral vascular disease. Some comorbidities may appear not to be associated with an increased risk of death, partly because of the low number of patients in these groups and partly because those who had severe disease and were thought likely not to survive 90 days may not be started on RRT (for instance, liver disease in those aged 65 or over).

Comorbidity and survival 1 year after 90 days of commencing RRT

Multivariable analyses using the stepwise Cox proportional hazards model and stratified by age group (<65 and ⩾65) are shown in table 6.14 and table 6.15

Table 6.12. Multivariate Cox proportional hazards model for predictors of death within the first 90 days of starting RRT during 01/01/02–30/09/07 amongst patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	5.5	3.5–8.5	<0.0001
Liver disease	5.0	2.7–9.1	<0.0001
Amputation	3.8	1.8–8.1	0.000
Angina	1.9	1.2–3.2	0.009
Age (per 10 yrs)	1.4	1.2–1.8	0.001

Table 6.13. Multivariate Cox proportional hazards model for predictors of death within the first 90 days of starting RRT during 01/01/02–30/09/07 amongst patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
MI in past 3 months	1.8	1.3–2.7	0.002
Ischaemic/neuropathic ulcers	1.6	1.0–2.6	0.031
Malignancy	1.6	1.2–2.0	0.000
Age (per 10 yrs)	1.5	1.3–1.7	<0.0001
COPD	1.5	1.1–1.9	0.006
MI >3 months ago	1.4	1.1–1.8	0.006
Angina	1.3	1.0–1.7	0.019

Table 6.14. Multivariate Cox proportional hazards model for predictors of death in the first year after completion of 90 days of starting RRT during 01/01/02–30/09/06 amongst patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	4.4	3.3–6.0	<0.0001
Ischaemic/neuropathic ulcers	2.1	1.3–3.5	0.002
Diabetes of either category	1.9	1.5–2.5	<0.0001
Amputation	1.8	1.1–3.1	0.032
COPD	1.6	1.0–2.5	0.037
Age (per 10 yrs)	1.4	1.2–1.6	<0.0001

respectively. Malignancy and ischaemic/neuropathic ulcers were the strongest predictors of death in the first year after completion of 90 days of starting RRT amongst those aged less than 65 years. Recent MI was no longer significantly associated with an increased risk of death, possibly because the prognostic importance of this marker is time-dependent and so would not be any more powerful a predictor than other markers of atherosclerotic vascular disease a year later.

Discussion

Data completeness remained poor in many centres. Unlike many data items that are transferred electronically from the local laboratory systems to the renal IT systems, the recording of comorbidity on the renal IT system requires clinical staff to be motivated to record these data, preferably at the point of care and at the time of starting RRT. It is possible that the introduction in England of a system of tariff-based payment by results might act to encourage clinicians to improve the systematic recording of comorbidity. The approval of the national renal dataset will make reporting of these items mandatory (http://www.ic.nhs.uk/services/datasets/dataset-list/renal). Furthermore, the publication, from 2006 onwards, of de-anonymised survival statistics for each centre and demonstrating the centre effect on survival of adjusting for these comorbidities [27] may provide some stimulus to clinical directors to improve collection of comorbidity data. The UKRR is also exploring the possibility of linking to the Hospital Episode Statistics dataset within the Secondary Uses Service (http://www.connectingforhealth.nhs.uk/), which would provide an alternative way of sourcing some of these data from inpatient diagnosis discharge codes, along the lines of the approach used by the United States Renal Data System.

Another alternative approach to case-mix adjustment for variations between centres in outcomes would be to use information on the levels of comorbidity or life expectancy in the general population from which the centre draws its patients, given that most renal centres in the UK have relatively well-defined catchment areas. Such an approach has been suggested for analyses comparing different regions or countries [28, 29]. However, adjustment for general population mortality as well as individual patient comorbidity might risk over-adjustment and the catchment areas of many centres would not show uniform levels of general population life expectancy.

These analyses demonstrate that comorbidities are common amongst UK patients starting RRT, with over 52% of patients with comorbidity data having at least one recorded comorbidity. Diabetes mellitus (either causing ERF or as a comorbidity) was the most common condition seen in 28.9% of patients compared to 52.2% reported in the USA [30]. Ischaemic heart disease was seen in 22.5% of all patients and this proportion was similar to that reported in the USA [30]. The prevalence of most comorbid conditions increased with increasing age up to 65–74 age group and the levelling off or slight reductions in reported comorbidity amongst patients aged over 75 years may reflect a 'healthy survivor effect' or decisions made by nephrologists and/or patients aged over 75 years with cardiovascular comorbidity not to embark on RRT.

Comorbidities were more prevalent amongst patients with diabetes mellitus; but non-Whites, who had more diabetes, had lower prevalence of most other comorbid conditions compared to Whites. This may once again reflect a 'healthy survivor effect' in that non-White

Table 6.15. Multivariate Cox proportional hazards model for predictors of death in the first year after completion of 90 days of starting RRT during 01/01/02–30/09/06 amongst patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
Ischaemic/neuropathic ulcers	2.0	1.5–2.9	<0.0001
Liver disease	1.9	1.2–2.9	0.005
Age (per 10 yrs)	1.7	1.5–1.9	<0.0001
Malignancy	1.6	1.3–1.9	<0.0001
Angina	1.6	1.3–1.8	<0.0001
COPD	1.5	1.2–1.9	0.000
Cerebrovascular disease	1.3	1.1–1.5	0.01
CABG/angioplasty	0.7	0.5–0.9	0.008

patients with significant comorbidity die prematurely before reaching ERF as suggested by a recent study [31]. The lower prevalence of comorbidity amongst those healthy survivors reaching ERF also explains some of the survival advantage on RRT reported amongst non-Whites compared to Whites [32, 33]. This survival advantage in Blacks is still seen after adjusting for comorbidity and one new theory is that this group of patients has demonstrated a more rapid decline through the stages of CKD (resulting in lead time CKD bias) and start RRT with a reduced arteriosclerotic load when compared with the White population.

In these analyses, patients with comorbidity started RRT at a higher eGFR compared to patients without comorbidity and this could suggest that patients with more comorbidity tend to be advised to start dialysis earlier or become symptomatic of their kidney failure earlier compared to those without comorbidity. Previous reports had suggested that an earlier start may be associated with better survival [34, 35]. However, Traynor *et al.* have subsequently shown that the better survival associated with earlier start could be due to lead time bias [36]. More recent studies have shown that greater kidney function at the start of RRT was associated with poor survival [37, 38] and this could be partly explained by high prevalence of comorbidity amongst those starting RRT at a higher GFR. Another study however reported that earlier start was associated with poor survival even after adjusting for comorbidity [39].

Late presentation for nephrology services and RRT commencement is reducing and the insight from this analysis is perhaps relevant. In the report covering a similar analysis for the years 1999–2004 there were some centres included who had sent incorrect comorbidity data returns [40]. The corrected data has been re-analysed for these years (data not shown) and there has been little change in the pattern of comorbidity with late presentation. Malignancy remained as the condition with the largest absolute difference in prevalence between early (10.1%) and late presentation (18.2%). A further analysis of the type of malignant diseases would be useful to better understand this. Peripheral vascular disease remained more common in those presenting earlier.

The lower Hb concentrations at start of RRT associated with peripheral vascular disease and malignancies could be due to diminished erythropoietin (EPO) responsiveness or varying centre prescribing patterns for EPO amongst patients with these comorbidities. The lower Hb concentration associated with peripheral vascular disease does not seem to be explained by late referral or presentation, as these patients were referred earlier compared to those without this comorbidity.

Patients who started HD were older and had more comorbidity compared to those starting PD. These findings probably reflect a perception amongst UK nephrologists, nurses and patients that PD is in general more suitable for younger and fitter patients. In addition, the presence of certain comorbid conditions such as cerebrovascular disease, liver disease and COPD that adversely affect the ability of patients to perform PD exchanges or to tolerate large volumes of dialysate in the peritoneum could have favoured the choice of HD in these patients. Some centres in the UK are starting to provide assisted PD (by a carer) which may alter this patient distribution in future.

The proportion of patients who subsequently get activated on the deceased donor transplant waiting list and receive a transplant was much less amongst those with comorbidity compared to those without. Hence, when time taken to activate patients on the transplant waiting list is used as a marker of quality of care provided by the centres, adjustments for differences in comorbidity should be made for meaningful comparisons of the performance of each centre in listing patients for a transplant.

The analyses also demonstrate that comorbidity was associated with increased mortality in patients on RRT in the UK. This is consistent with the findings of many other studies elsewhere using a variety of comorbidity scores [1–11]. The prevalence and severity of comorbidity increases with time on RRT and this change in comorbidity over time has been reported to be associated with mortality [3]. The UKRR, in addition to collecting baseline comorbidity data, is therefore hoping to stimulate collection of annual comorbidity data on RRT patients. Further research using baseline and annual comorbidity is needed to develop risk scores to predict mortality on RRT. The development of these risk scores would help clinicians to provide prognostic advice to patients and guide them in making decisions on initiation of RRT and when assessing patients for a kidney transplant.

Renal registries are an integral part of national quality control processes and provide a tool for benchmarking of clinical outcomes. Adequate case mix adjustment is essential in order to compare survival and other intermediate outcomes amongst patients on RRT within and between countries. Currently such an exercise is not feasible due to differences in definitions of comorbidity, poor data completeness and variation in methods

of data collection between registries. Standardised data collection methods, including those for recording comorbid conditions and their severity, have long been recognised as important and are central to the EU-funded QUEST initiative of the ERA-EDTA Registry [41]. The UKRR is currently undertaking a collaborative study with other registries such as the USRDS, ANZDATA and CORR to identify and share good practice in the collection of comorbidity data between these four registries with a view to improving data completeness rates for countries already collecting such data and giving guidance to those considering doing so.

Conflict of interest: none

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