Chapter 4
Comorbidities and Current Smoking Status amongst Patients starting Renal Replacement Therapy in England, Wales and Northern Ireland from 2008 to 2009

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Key Words
Comorbidity · Diabetes · Dialysis · eGFR · Ethnicity · Haemoglobin · Mortality · Renal replacement therapy · Smoking · Survival analysis

Summary

- Only 45.6% (n = 5,617) of the incident adult (⩾18 years) RRT patients reported to the UKRR between 2008 and 2009 had comorbidity data. In 2009, three centres provided data on 100% of new patients and 17 centres provided data for less than 5% of their new patients.
- In patients with comorbidity data, more than half had one or more comorbidities (56.5%) but in the subgroup of patients aged 65 years and over, 69.8% had one or more comorbidities.
- Diabetes mellitus and ischaemic heart disease were the most common conditions seen in 32.9% and 22.5% of patients respectively. Ischaemic heart disease, cerebrovascular disease, COPD, claudication and malignancy were more prevalent in patients 65 years and over.
- In 2008–2009, 12.4% of incident RRT patients were recorded as being smokers at the initiation of dialysis.
- Patients with peripheral vascular disease ($p = 0.0002$) and ischaemic heart disease ($p = 0.002$) were more likely to be referred to a nephrologist early and patients with malignancy ($p < 0.0001$) or liver disease ($p = 0.02$) were more likely to be referred late.
- In multivariable survival analysis, malignancy and the presence of ischaemic/neuropathic ulcers remained the strongest independent predictors of poor survival at 1 year after 90 days from the start of RRT in patients <65 years.

Introduction

The importance of adjusting for comorbidity in centre [1, 2] and international survival comparisons [3] is well recognised. As with all observational data, registry analyses exploring epidemiological issues, access to treatment or quality control, are subject to a number of selection biases. Such registry analyses can be significantly strengthened by adjustment for case-mix as differences in patient populations that exist across centres may affect process and outcome measures.

The aim of this work is to describe the prevalence of comorbid conditions and current smoking status in incident renal replacement therapy (RRT) patients reported to the UK Renal Registry (UKRR) and to examine the association between these comorbidities and early mortality.

Methods

Study population

Incident adult ($\geqslant$18 years) RRT patients (n = 12,322) between 2008 and 2009 in the centres submitting data to the UKRR were considered. Of these, patients who had data recorded on comorbidity were included (n = 5,617; 45.6%). 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

The nine centres in Scotland do not provide comorbidity data to the UKRR and are not included in these analyses. There was concern that data extraction in two centres (Stoke and Colchester) was inaccurate and these centres were excluded from this year's comorbidity 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 4.1) for each patient at the time of starting RRT. Definitions of each of these conditions are given in appendix B (http://www.renalreg.com/Report-area/Report2010/Appendix-B.pdf). Patients were classified as having complete comorbidity data if there was at least one entry (yes/no) for any one or more of the comorbid conditions. Comorbidities were grouped into broader categories for some analyses:

- '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.
- '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'.

Table 4.1. 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 these four variables are combined under the term 'peripheral vascular disease')
• Smoking • Malignancy

Ethnicity data reporting

Some centres electronically upload ethnicity coding to their renal IT system from the hospital Patient Administration Systems (PAS) [4]. Ethnicity coding in PAS is based on self-reported ethnicity and uses a different system [5] to the remaining centres where 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 and Others. Appendix H details the regrouping of the PAS codes into the above ethnic categories.

Statistical methods

The statistical methods for the three individual sections of this chapter are described separately. The number of patients with data on comorbidity and other variables included in the analyses are summarised in figure 4.1.

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.

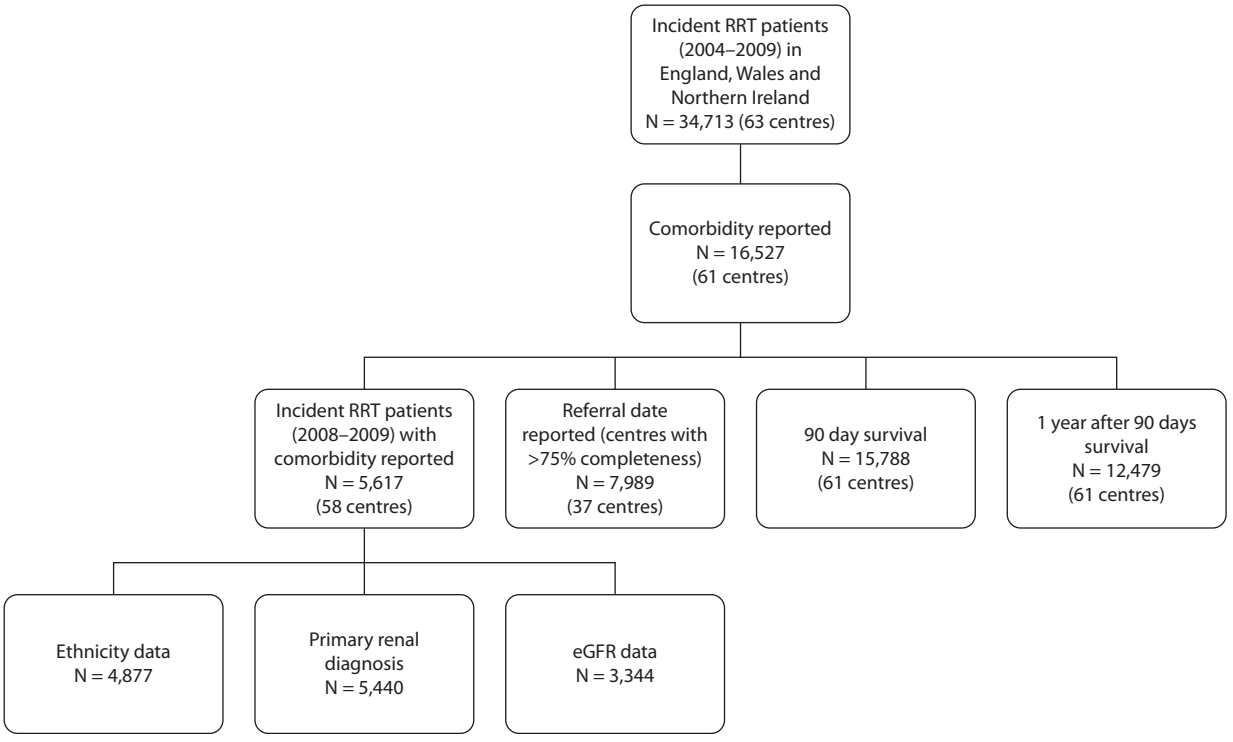

Fig. 4.1. Flow chart showing number of patients included in the various analyses

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

Referral time was defined as the number of days between the date first seen by a nephrologist and the date of starting RRT. Referral times of more than 90 days and less than 90 days define early and late presentation, respectively. Data on referral time were 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 = 7,989; 23.0% of all patients starting RRT between 2004 and 2009).

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 [6]. For the purpose of eGFR calculation, patients who had missing ethnicity but a valid serum creatinine measurement were classed as White as the Black population only account for 6% 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 each 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 eGFR at which patients should start RRT and a number of factors, including clinical presentation, symptoms, complications of uraemia and biochemistry, are used to determine dialysis initiation. However, there are defined eGFR thresholds for pre-emptive listing for a kidney transplant. The European Best Practice Guidelines (EBPG) recommend that patients with progressive irreversible 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 be considered for early and pre-emptive transplantation when their eGFR decreases to <20 ml/min/1.73 m^2 [7]. 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 [8]. 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.

For the eGFR analyses, incident RRT patients in 2008–2009 with comorbidity data were considered for inclusion (n = 5,617). Patients with no eGFR data (n = 1,443) were excluded, as were those with no eGFR data in the 14 days preceding RRT (n = 690). Patients with an eGFR >20 ml/min/1.73 m^2 (n = 140) were excluded from the eGFR analyses due to concerns about possible data extraction errors. This left 3,344 patients eligible for 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 13 of the 2009 report [9].

3) Patient survival

The Registry collected data with a 'timeline' entry on all patients who had started RRT for ERF. Patients presenting acutely and initially classified as acute renal failure requiring dialysis who continued to require long-term dialysis, can be re-classified by clinicians as having had ERF from the date of their first RRT. The death rate was high in the first 90 days and 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 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 2004 and 30th September 2009 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 2004 and 30th September 2008.

For each variable, the models were used to estimate the hazard ratio of death, comparing patients with a particular comorbidity with those who did not have the comorbidity. For both the univariate and multivariate Cox 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 analyses. The multivariate models used an automatic selection procedure to identify the variables most strongly related to survival. The potential variables to be included were: age (per 10 year increase), smoking status, diabetes (listed as PRD or not listed as PRD) and the other 12 comorbidities listed in figure 4.1. The automatic procedure starts by including only the variable most strongly related to survival. Then, with that variable included, it fits models adding each of the remaining variables in turn (singly) and chooses the variable that adds most to the model (in addition to the contribution made by the first variable included). The process continues in this way, adding variables that make a further significant contribution to the model, and removing any whose contribution becomes non-significant once other variables have been added. The final model only includes those variables selected by the process. These automatic methods have been used to give an indication of the variables most strongly related to survival but caution is needed in interpreting them because, amongst other things, when using correlated variables, a slight difference in the data (or in the algorithm chosen) could result in different variables being included in the final models. A better analysis would make a considered judgement of which variables should be included (rather than an automatic one) and would use interaction terms and/or adjustments other than age.

For each model, a R^2 value was calculated using the Royston and Sauerbrei method [10]. The R^2 value is the percentage of the variation in mortality which is explained by the variables included in the final model.

Results

Completeness of comorbidity returns from each participating centre

Of the 6,078 patients commencing RRT in centres in England, Wales and Northern Ireland in 2009, comorbidity data were provided for 2,697 (44.4%) (tables 4.2 and 4.3). Table 4.2 highlights the continued wide variation in the completeness of data returns with 3 centres providing data on 100% of patients, but 17 centres providing data for less than 5% of their new patients in 2009.

Limiting the analysis to only the centres that reported in 2004, data completeness for comorbidity has fallen from 52.1% in 2004 to 45.8% in 2009. When centres with 0% completeness for comorbidity were excluded, the median percentage of comorbidity returns in 2009 was 66.7%. This has shown an annual improvement since 2005, suggesting that once the renal information systems are set up to return comorbidity information, it is possible to improve data completeness.

Only patients in the UKRR database are included in table 4.2. Therefore for a small number of centres the numbers of new patients (N) shown for 2009 are different to those given in tables 1.1 and 1.3 in chapter 1 in which some manual corrections were made. As these additional patients are not in the database it was not appropriate to include them in the denominator for completeness calculations as, by definition, they could not have comorbidity data.

Prevalence of multiple comorbidity

Including all incident patients from the years 2008–2009 (n = 12,322), comorbidity data were available for 5,617 (45.6%). More than half of these patients had one or more comorbidities (56.5%) (table 4.4) but in the subgroup of patients aged 65 years and over, 69.8% had one or more comorbidities (table 4.5).

Frequency of each comorbid condition

Table 4.5 lists the prevalence of specific comorbidities and the percentage of the total number of incident patients for whom data was available for that item. Diabetes mellitus (either listed as cause of PRD or as a comorbidity) was present in 32.9% of all patients. Ischaemic heart disease, cerebrovascular disease, COPD, claudication and malignancy were more prevalent in patients 65 years and over. Liver disease, ischaemic/neuropathic ulcers and prior amputation were more frequently observed in younger patients; actual percentages, nevertheless, were quite small (table 4.5). Smoking was also more common amongst patients under 65 years. This broad stratification is quite misleading however, as prevalence of comorbidities increased markedly from 18–65 years and appeared to plateau beyond this (figures 4.2 and 4.3).

Table 4.2. Completeness of comorbidity data returns on incident patients from individual renal centres 2004–2009

	2004		2005		2006		2007		2008		2009	
Centre	N	% return	N	% return	N	% return	N	% return	N	% return	N	% return
Antrim			42	12	33	9	37	14	40	28	19	32
B Heart	106	0	121	2	115	0	101	2	106	1	99	16
B QEH	197	1	199	2	187	1	225	1	268	1	253	1
Bangor	36	64	40	55	42	60	36	69	41	68	30	77
Basldn	46	39	32	59	45	80	39	77	40	88	26	88
Belfast			130	25	119	25	89	34	69	32	53	38
Bradfd	61	92	67	96	50	100	88	99	63	90	54	96
Brightn	119	1	112	0	130	2	119	2	121	2	48	0
Bristol	164	82	175	81	176	98	157	83	176	74	157	80
Camb	107	1	111	0	155	2	127	1	113	0	138	1
Cardff	183	5	184	20	206	5	222	2	152	0	180	1
Carlis	29	79	31	84	27	85	26	88	30	77	24	83
Carsh	173	45	183	54	186	58	196	73	216	79	207	68
Chelms	50	48	40	50	49	84	52	54	34	38	38	45
Clwyd	13	23	26	19	18	22	22	36	15	40	17	53
Colchr									60	0	15	0
Covnt	80	0	85	0	105	2	112	0	115	0	119	0
Derby	67	75	72	74	69	67	63	84	92	90	78	91
Derry					3	67	8	50	6	50	16	56
Donc							18	94	26	27	40	43
Dorset	61	97	49	90	53	92	64	89	85	85	70	80
Dudley	54	0	38	0	45	2	39	0	47	0	66	0
Exeter	109	46	111	30	106	29	125	7	135	4	140	1
Glouc	54	85	61	97	72	89	58	95	47	85	79	65
Hull	108	87	127	98	105	91	99	97	113	91	102	72
Ipswi	46	46	59	29	42	62	41	46	38	34	38	3
Kent							175	62	140	66	128	60
L Barts	186	78	185	91	189	83	214	83	206	77	234	82
L Guys	122	7	146	12	153	12	165	7	166	3	179	3
L Kings	114	98	134	99	112	100	125	100	151	99	127	100
L Rfree			132	2	194	1	184	0	173	0	156	0
L St.G							96	68	100	67	108	55
L West	286	69	308	51	314	51	279	52	318	45	359	2
Leeds	185	82	171	74	180	77	129	81	161	79	156	87
Leic	163	93	226	66	243	68	245	77	242	76	222	67
Liv Ain	3	67	29	41	35	54	36	44	42	67	36	67
Liv RI	128	63	138	64	141	52	112	56	102	41	114	46
M Hope	112	43	112	34	131	12	121	12	141	1	118	0
M RI							161	27	134	36	150	44
Middlbr	101	91	84	90	109	72	99	63	93	90	95	85
Newc	107	1	112	4	106	1	106	1	98	1	100	0
Newry			28	14	13	23	15	27	21	86	20	100
Norwch	94	5	118	11	112	13	111	17	89	20	48	23
Nottm	107	95	145	99	137	97	129	93	116	89	124	94
Oxford	170	66	154	51	160	23	144	86	148	72	171	91
Plymth	63	43	60	47	93	67	76	79	69	70	60	77
Ports	119	67	149	64	175	63	157	66	170	54	151	40
Prestn	85	22	124	28	122	33	132	42	113	42	147	49
Redng	67	1	89	3	86	1	95	5	105	1	98	2
Sheff	167	59	158	42	168	57	166	56	180	51	142	52
Shrew	55	13	42	21	54	20	58	40	61	15	47	17
Stevng	84	37	92	42	122	48	89	70	103	76	97	74
Sthend	41	78	34	71	50	80	35	80	36	78	23	83
Stoke							87	0	82	0	109	0

Table 4.2. Continued

	2004		2005		2006		2007		2008		2009	
Centre	N	% return	N	% return	N	% return	N	% return	N	% return	N	% return
Sund	52	96	59	93	58	90	62	95	45	87	64	95
Swanse	95	93	100	96	116	97	126	98	124	97	113	97
Truro	68	79	32	88	52	79	45	91	40	35	51	45
Tyrone			24	33	29	52	22	55	25	48	19	68
Ulster			9	56	8	63	16	100	14	100	13	100
Wirral	67	15	60	7	52	0	53	0	42	2	62	0
Wolve	105	98	95	85	85	88	68	91	88	95	66	98
Wrexm	29	10	42	5	26	8	27	26	21	67	19	79
York	50	90	45	87	48	90	38	84	37	70	46	67
Totals	**4,888**		**5,531**		**5,811**		**6,161**		**6,244**		**6,078**	

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

Table 4.3. Summary of completeness of incident patient comorbidity returns (2004–2009)

	Years						Combined years
	2004	2005	2006	2007	2008	2009	
Number of renal centres included	50	56	57	62	63	63	
Total number of new patients	4,888	5,531	5,811	6,161	6,244	6,078	34,713
Number of patients with comorbid data entries	2,549	2,634	2,717	3,010	2,920	2,697	16,527
Percentage of patients with comorbid data entries	52.1	47.6	46.8	48.9	46.8	44.4	47.6
Percentage restricted to centres in since 2004	52.1	49.9	49.1	51.5	49.0	45.8	49.5
Median percentage amongst only centres returning >0% comorbidity	63.9	51.1	58.1	62.6	66.7	66.7	61.9

Prevalence of comorbidity by age band

Figures 4.2 and 4.3 illustrate the increasing prevalence of comorbidity with increasing age up to the 65–74 year age group in incident RRT patients. In those patients aged >75 years there was a slight reduction of most reported comorbidities.

Prevalence of comorbidity by ethnic origin

Figures 4.4 and 4.5 illustrate the presence of comorbidity by ethnic origin and age group. Figure 4.4 shows a higher prevalence of having at least one comorbidity amongst patients of White origin compared to the ethnic minority. Diabetes mellitus is much more frequently observed in South Asian patients (49.6%) than in White individuals (30.3%) (table 4.6).

Table 4.4. Number of reported comorbidities in patients starting RRT, as a percentage of those for whom comorbidity data were available 2008–2009

Number of comorbidities	0	1	2	3	4	5+
Percentage	43.5	29.2	13.4	7.8	3.7	2.5

Prevalence of comorbidity amongst patients with diabetes mellitus

Table 4.7 compares comorbidity amongst patients with and without diabetes (as either primary renal disease or comorbidity). As would be expected, patients with diabetes mellitus had higher rates of vascular disease (20.7% compared to 8.0% in non-diabetics). Similarly, ischaemic heart disease and cerebrovascular disease were more common in diabetics. Smoking at the time of initiation of RRT was the same for diabetics and non-diabetics (12.4%).

Late presentation and comorbidity

Table 4.8 shows the referral time for patients with and without various comorbidities. Patients with peripheral vascular disease and ischaemic heart disease were more likely to be referred to a nephrologist early and patients with malignancy or liver disease were more likely to be referred late.

Table 4.5. Frequency with which each condition was reported in incident RRT patients 2008–2009

Comorbidity	Age <65 years		Age ⩾65 years		p value*	% overall prevalence
	N	(%)	N	(%)		
Any comorbidity present	1,293	(44.2)	1,880	(69.8)	<0.0001	56.5
Angina	241	(8.3)	498	(18.6)	<0.0001	13.2
MI in past 3 months	54	(1.9)	88	(3.3)	0.0007	2.6
MI > 3 months ago	212	(7.3)	434	(16.3)	<0.0001	11.6
CABG/angioplasty	195	(6.7)	316	(11.8)	<0.0001	9.2
Cerebrovascular disease	187	(6.4)	395	(14.8)	<0.0001	10.4
Diabetes (not listed as PRD)	172	(6.0)	338	(12.7)	<0.0001	9.2
Diabetes listed as PRD	785	(26.9)	549	(20.4)	<0.0001	23.8
COPD	130	(4.5)	275	(10.3)	<0.0001	7.3
Liver disease	107	(3.7)	53	(2.0)	0.0001	2.9
Claudication	151	(5.2)	265	(9.9)	<0.0001	7.5
Ischaemic/neuropathic ulcers	126	(4.3)	76	(2.8)	0.0028	3.6
Angioplasty/vascular graft	67	(2.3)	146	(5.5)	<0.0001	3.8
Amputation	73	(2.5)	59	(2.2)	0.45	2.4
Smoking	406	(14.6)	256	(10.0)	<0.0001	12.4
Malignancy	200	(6.9)	528	(19.8)	<0.0001	13.1

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

Renal function at the time of starting RRT and comorbidity

Table 4.9 shows the geometric mean eGFR prior to starting RRT in patients with each of the individual comorbidities. The (geometric) mean eGFR prior to starting RRT in patients who were recorded as starting without any comorbidity present was 8.0 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

All comorbidities were more prevalent in patients receiving haemodialysis as their initial modality of treatment rather than peritoneal dialysis (table 4.10). This difference was statistically significant for all comorbid conditions other than previous CABG/coronary angioplasty. The median age of patients with comorbidity data starting RRT on HD was 66.6 years compared

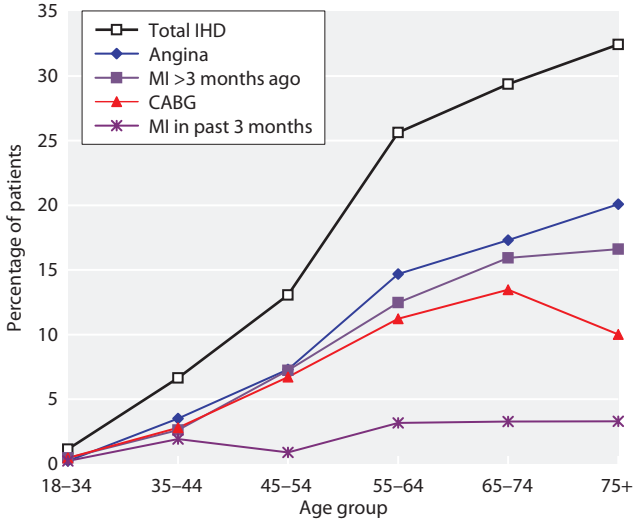

Fig. 4.2. Prevalence of ischaemic heart disease amongst incident patients 2008–2009 by age at start of RRT

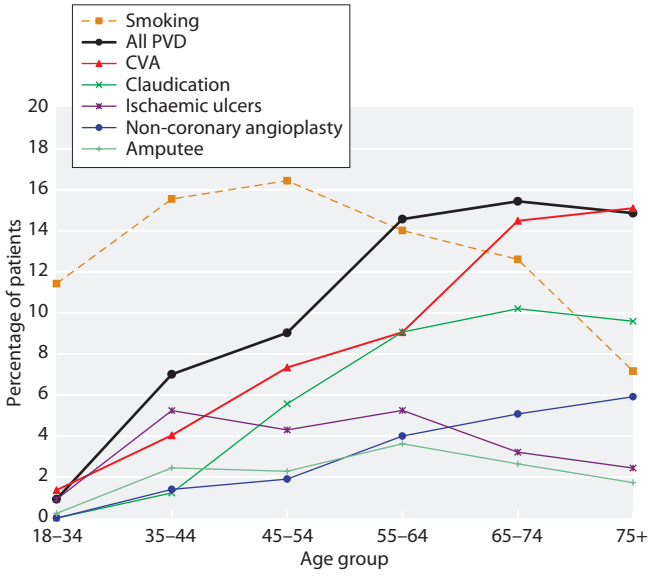

Fig. 4.3. Prevalence of non-coronary vascular disease amongst incident patients 2008–2009 by age at start of RRT

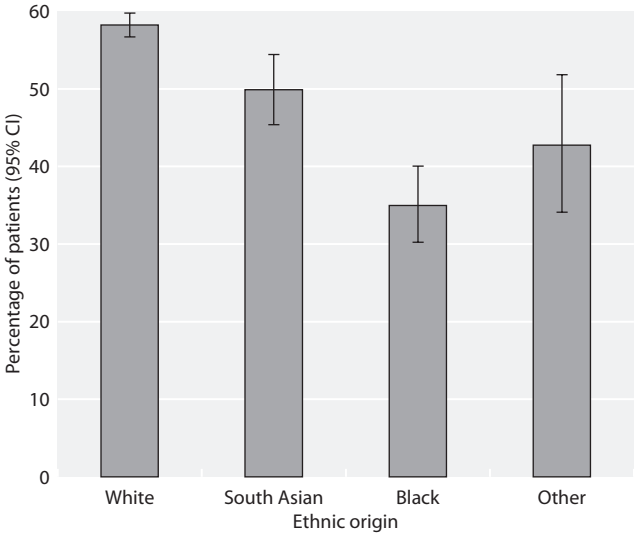

Fig. 4.4. Presence of comorbid conditions at the start of RRT by ethnic origin amongst patients starting RRT 2008–2009

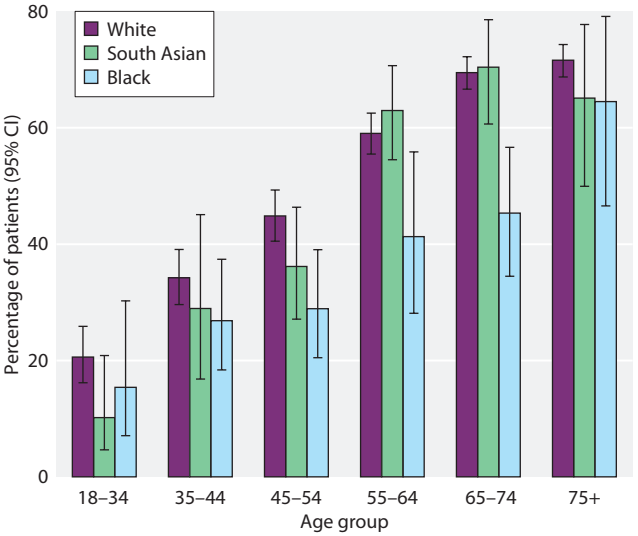

Fig. 4.5. Percentage of patients with comorbidity by ethnic origin in each age group at the start of RRT 2008–2009

Table 4.6. Prevalence of comorbidities amongst incident patients starting RRT 2008–2009 by ethnic group, as percentages of the total number of patients in that ethnic group for whom comorbidity data was available

	No. of patients (%) with comorbidity								
	White		South Asian		Black		Other		p value*
Ischaemic heart disease	883	(22.6)	135	(29.2)	31	(8.6)	13	(11.1)	<0.0001
Cerebrovascular disease	409	(10.5)	46	(10.0)	32	(8.9)	9	(7.7)	0.61
Diabetes (not listed as PRD)	334	(8.6)	45	(9.8)	25	(6.9)	5	(4.3)	0.18
Diabetes listed as PRD	856	(21.8)	186	(39.8)	103	(28.4)	30	(25.6)	<0.0001
COPD	308	(7.9)	16	(3.5)	9	(2.5)	3	(2.6)	<0.0001
Liver disease	103	(2.6)	17	(3.7)	16	(4.4)	7	(6.1)	0.031
Peripheral vascular disease	511	(13.1)	52	(11.3)	19	(5.3)	9	(7.8)	<0.0001
Smoking	512	(13.7)	28	(6.2)	20	(5.7)	13	(11.5)	<0.0001
Malignancy	556	(14.2)	20	(4.4)	21	(5.8)	9	(7.7)	<0.0001

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

Table 4.7. Number and percentage of patients with and without diabetes (either as primary diagnosis or comorbidity) who have other comorbid conditions

	Non-diabetic patients		Diabetic patients		
Comorbidity	N	(%)	N	(%)	p value*
Ischaemic heart disease	626	(17.4)	585	(32.5)	<0.0001
Cerebrovascular disease	303	(8.4)	254	(14.1)	<0.0001
COPD	264	(7.3)	122	(6.8)	0.46
Liver disease	99	(2.8)	49	(2.7)	0.96
Peripheral vascular disease	287	(8.0)	371	(20.7)	<0.0001
Smoking	428	(12.4)	213	(12.4)	0.95
Malignancy	534	(14.8)	169	(9.4)	<0.0001

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

Table 4.8. Percentage prevalence of specific comorbidities amongst patients presenting late (0–89 days) compared with those presenting early (>89 days)

	Late referral		Early referral		
Comorbidity	N	(%)	N	(%)	p value*
Ischaemic heart disease	371	(21.3)	1,540	(24.9)	0.002
Cerebrovascular disease	167	(9.5)	670	(10.8)	0.1
Diabetes (not listed as PRD)	145	(8.4)	541	(8.8)	0.5
COPD	122	(7.0)	437	(7.1)	0.9
Liver disease	62	(3.5)	156	(2.5)	0.02
Peripheral vascular disease	180	(10.3)	847	(13.7)	0.0002
Malignancy	347	(19.8)	684	(11.0)	<0.0001
Smoking	275	(16.0)	853	(14.0)	0.03

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

with 59.1 years for those starting on PD (Kruskal Wallis test, $p < 0.0001$). For each of the comorbid conditions, the median age of patients on HD was higher than for patients on PD (table 4.10).

Comorbidity and survival within 90 days of starting RRT

On univariate analysis stratified for age, most comorbidity was 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 tables 4.11 and 4.12. As identified in the univariate models, comorbidities in younger patients were more indicative of early death than when present in older patients. Diabetes did not emerge as an independent predictor of death, probably due to its close association with 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

Table 4.9. eGFR within 2 weeks prior to the start of RRT by comorbidity 2008–2009

Comorbidity	eGFR geometric mean (ml/min/1.73 m^2)	eGFR 95% CI	p value*
No comorbidity present	8.0	7.9–8.2	Ref
Any comorbidity present	8.7	8.6–8.9	<0.0001
Angina	9.0	8.7–9.3	<0.0001
MI in past 3 months	9.0	8.3–9.8	0.013
MI > 3 months ago	9.2	8.9–9.5	<0.0001
CABG/angioplasty	9.4	9.0–9.8	<0.0001
Cerebrovascular disease	9.0	8.7–9.3	<0.0001
Diabetes (not listed as PRD)	8.7	8.4–9.0	0.001
Diabetes listed as PRD	9.1	8.9–9.4	<0.0001
COPD	9.1	8.8–9.5	<0.0001
Liver disease	8.4	7.8–9.1	0.304
Claudication	9.0	8.6–9.3	<0.0001
Ischaemic/neuropathic ulcers	9.1	8.5–9.6	0.001
Angioplasty/vascular graft	8.6	8.1–9.1	0.058
Amputation	9.3	8.7–10.0	0.001
Smoking	8.3	8.0–8.6	0.164
Malignancy	8.5	8.2–8.8	0.017

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

Table 4.10. Number (and percentage) of incident patients with comorbid conditions starting PD and HD 2008–2009

	HD			PD			
Comorbidity	N	(%)	Median age	N	(%)	Median age	p value*
Angina	626	(15.2)	71.2	111	(9.0)	67.8	<0.0001
MI in past 3 months	122	(3.0)	69.9	19	(1.6)	59.4	0.007
MI > 3 months ago	531	(12.9)	71.0	110	(9.0)	69.3	0.0002
CABG/angioplasty	403	(9.8)	69.3	103	(8.4)	67.6	0.15
Cerebrovascular disease	479	(11.6)	71.6	98	(8.0)	66.7	0.0004
Diabetes (not listed as PRD)	424	(10.3)	71.4	77	(6.3)	68.8	<0.0001
COPD	354	(8.6)	71.2	48	(3.9)	67.0	<0.0001
Liver disease	135	(3.3)	61.3	23	(1.9)	56.9	0.011
Claudication	351	(8.5)	70.6	61	(5.0)	65.4	<0.0001
Ischaemic/neuropathic ulcers	177	(4.3)	62.6	23	(1.9)	50.6	<0.0001
Angioplasty/vascular graft	177	(4.3)	72.0	35	(2.9)	65.4	0.024
Amputation	111	(2.7)	64.3	18	(1.5)	57.2	0.015
Smoking	506	(12.8)	61.9	141	(12.0)	56.4	0.46
Malignancy	621	(15.0)	72.6	102	(8.3)	68.7	<0.0001

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

Table 4.11. Multivariate Cox proportional hazards model* for predictors of death within the first 90 days of starting RRT during 01/01/2004–30/09/2009: patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	5.1	3.4–7.7	<0.0001
Amputation	4.7	2.6–8.4	<0.0001
Liver disease	3.7	2.1–6.5	<0.0001
Angina	1.9	1.2–3.0	0.005
Age (per 10 yrs)	1.6	1.3–2.0	<0.0001

* This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units), smoking and the 13 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'.

Table 4.12. Multivariate Cox proportional hazards model* for predictors of death within the first 90 days of starting RRT during 01/01/2004–30/09/2009: patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
MI in past 3 months	2.3	1.6–3.2	<0.0001
Ischaemic/neuropathic ulcers	2.0	1.3–3.0	0.001
Malignancy	1.8	1.5–2.2	<0.0001
COPD	1.6	1.3–2.1	0.0002
Angina	1.5	1.2–1.9	0.0004
Age (per 10 yrs)	1.5	1.3–1.7	<0.0001
Smoking	1.4	1.0–1.8	0.024
MI > 3 months ago	1.3	1.1–1.7	0.015

* This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units), smoking and the 13 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'.

days, may not be started on RRT (for instance, liver disease in those aged ⩾65 years).

The final five variables in the model examining death within the first 90 days of starting RRT in patients aged <65 (table 4.11) explain 40% of the variation in survival. For patients aged ⩾65, the final eight variables in the model explain 16% of the variation in survival (table 4.12).

Comorbidity and survival 1 year after 90 days of commencing RRT

Age, smoking and four comorbidities were independently associated with an increased hazard of death within the first year after 90 days for patients aged <65 years and four of these were among the eight variables independently associated with mortality beyond day 90 in patients ⩾65 years (tables 4.13 and 4.14). Diabetes mellitus was independently associated with increased

Table 4.13. Multivariate Cox proportional hazards model* for predictors of death in the year after the first 90 days of starting RRT during 01/01/2004–30/09/2008: patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	3.3	2.5–4.5	<0.0001
Ischaemic/neuropathic ulcers	2.6	1.8–3.7	<0.0001
Liver disease	2.1	1.4–3.2	0.0002
Diabetes of either category	1.9	1.5–2.4	<0.0001
Age (per 10 yrs)	1.4	1.2–1.5	<0.0001
Smoking	1.3	1.0–1.7	0.031

* This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units), smoking and the 13 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'.

Table 4.14. Multivariate Cox proportional hazards model* for predictors of death in the year after the first 90 days of starting RRT during 01/01/2004–30/09/2008: patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
Amputation	2.7	1.8–4.1	<0.0001
Liver disease	2.0	1.3–3.0	0.001
Malignancy	1.8	1.5–2.1	<0.0001
Age (per 10 yrs)	1.7	1.5–1.9	<0.0001
Cerebrovascular disease	1.3	1.1–1.6	0.001
COPD	1.3	1.0–1.6	0.03
Angina	1.3	1.1–1.5	0.003
Smoking	1.3	1.0–1.5	0.02

* This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units), smoking and the 13 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'.

mortality in patients <65 years but not in those aged ⩾65 years. Overall the final six variables in the model exploring death in the year after the first 90 days of starting RRT in patients <65 years explain 26% of the variation in survival. For patients ⩾65 years, only 12% of the variation in survival was explained by the eight variables included in the final model.

Discussion

Comorbidity data completeness has been a cause for concern since comorbidities were first reported by the UKRR in 1999 [11]. Overall rates of completeness are fairly static, though an improvement has been seen in those centres with an established mechanism for recording comorbidity information. The current rate of 44.4% in the UK compares with rates of 85% in Canada, 95–100% in Australia and New Zealand and 100% in the USA. Some work has recently been undertaken to learn from experience in these countries [12]. Comorbidity information should improve in the future through a combination of linkage with other secondary data sources (e.g. Hospital Episode Statistics dataset), statistical imputation techniques and local governance pressures now that comorbidity items form part of the National Renal Dataset.

Caution must be taken in interpreting the influence of comorbidity. In at least one study, patients with comorbidity recorded have significantly better health outcomes than those with missing comorbidity [13] so the generalisation of findings from the selected group of patients reported in this chapter cannot be assumed.

One further consideration is that even in analyses (both inside and outside the UK) with 100% comorbidity completeness, the proportion of variance in survival that can be explained by these major medical disorders generally remains below 50% when age, primary renal disease, ethnicity and comorbidities are included in the statistical model. Future studies of survival should consider other factors such as nutrition, mobility, cognition and socio-economic status at the start of dialysis to better assess the risk factors and outcomes for RRT patients. This is particularly important as we recognise that many older patients for instance, can be successfully transplanted with improved survival compared to matched wait-listed patients [14].

Conflicts of interest: none

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