UK Renal Registry 16th Annual Report: Chapter 5 Comorbidities and Current Smoking Status amongst Patients starting Renal Replacement Therapy in England, Wales and Northern Ireland from 2011 to 2012

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

Summary

- Data on comorbidity at the time of start of renal replacement therapy (RRT) were submitted for only 7,085 (55.9%) of the incident adult (⩾18 years) RRT patients reported to the UK Renal Registry (UKRR) between 2011 and 2012. In 2012, nine centres provided data on 100% of new patients and 11 centres provided data for less than 5% of new patients.
- In patients with comorbidity data, more than half had one or more comorbidities (52.9%). In the subgroup of patients aged ⩾65 years, 64% had one or more comorbidities.
- Diabetes mellitus (primary renal disease and comorbidity) and ischaemic heart disease were the most common conditions, observed in 35% and 19% of patients respectively. Ischaemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), claudication and malignancy were more prevalent in patients aged >65 years.
- In 2011–2012, 14% of incident RRT patients were recorded as being smokers at the initiation of dialysis.
- There was a higher prevalence of ischaemic heart disease ($p < 0.02$) and peripheral vascular disease ($p < 0.0003$) in patients presenting early to a nephrologist than amongst those referred late. Malignancy ($p < 0.0001$) was more common in patients who were referred late.
- In the multivariable survival analysis (incident patients in 2007–2012), malignancy (hazard ratio (HR) 2.9) and liver disease (HR 2.2) were strongly associated with reduced survival at 1-year in individuals aged <65 years at start of RRT who survived more than 90 days.

Introduction

The number and extent of comorbid illnesses in patients initiating dialysis is increasing [1–3]. These comorbidities are significant predictors of mortality and other adverse outcomes [4]. It is therefore imperative to account for differences in the comorbid illness burden amongst the groups of dialysis patients being compared. The importance of adjusting for comorbidity when undertaking centre [5–7] and international survival comparisons [8] is well recognised. This also allows for fair comparisons to be made between treatment modalities and costs.

However, an important consideration in applying case-mix adjustment to analyses is data completeness. If individuals with comorbidity data differ systematically from those without data, entering variables into statistical models can further bias outcome measures and provide invalid associations [9, 10].

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

Methods

Study population

Incident adult ($\geqslant$18 years) RRT patients during 2011 and 2012 in the centres submitting data to the UKRR were considered. Of these, patients who had data recorded on comorbid conditions were included in statistical analyses. 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 four centres 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 the presence or absence of 13 comorbid conditions and information on current tobacco smoking (table 5.1) for each patient at the time of starting RRT on their renal information technology (IT) system. Definitions of each of these conditions are given in appendix B (www.renalreg.com).

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 5.1. Comorbid conditions listed in the UKRR dataset

- 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

Specific consideration needs to be made regarding diabetes coding. The UKRR also collect data on primary renal disease (PRD), and have used these data alongside the comorbidity data to determine which people had diabetes mellitus. The comorbidity screen is intended to capture those patients who have diabetes only when it is not the PRD, however some clinicians do enter 'yes' in the comorbidity field in such cases. Prior to statistical analyses, these fields were examined together to identify these cases and ensure diabetes is only counted as either the PRD or a comorbid condition for a certain individual.

Ethnicity data reporting

Some centres electronically upload ethnicity coding to their renal IT system from the hospital Patient Administration System (PAS) [11]. Ethnicity coding in PAS is based on self-reported ethnicity and uses a different system [11] to the remaining centres where coding of ethnicity 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 (www.renalreg.com) 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.

1) Patient demographics

The proportion of patients starting RRT with various co-morbidities 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 statistically significant differences between groups.

2) Late presentation (referral) and 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 90 or more 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 co-morbidity and referral time from centres with >75% data completeness for referral time were included 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 13 of the 2009 Report [12].

3) Patient survival

The UKRR collected data with a 'timeline' entry on all patients who had started RRT for established renal failure (ERF). Patients presenting acutely and initially classified as acute renal failure requiring dialysis who continued to require long-term dialysis, can subsequently be re-classified by clinicians as having had ERF from the date of their first RRT. The death rate is high in the first 90 days of commencing RRT with variability observed between centres. This between centre variation may in part be due to clinician variation in the classification of patients who present acutely requiring RRT and who may be deemed from the start to be unlikely to recover renal function. As mortality rate varies with time on RRT and to remove the influence of between centre variation in the classification of patients, the survival analysis was stratified into two time frames. This also enables comparison with results from other national registries. The association of comorbid conditions and survival within the first 90 days was analysed and subsequently the association of comorbid conditions and 1-year survival in the cohort who survived after 90 days from the start of RRT was also analysed.

For each of the follow up periods, the association of baseline comorbidity with survival was analysed using univariable and multivariable Cox regression models. For analyses of survival within the first 90 days, the cohort included patients starting RRT between 1st January 2007 and 30th September 2012 to allow a minimum of three months follow-up from the start of RRT. For the 1-year survival analyses on individual patients who survived at least 90 days after the start of RRT, the cohort included data on individuals who started RRT between 1st January 2007 and 30th September 2011.

For each variable, the models were used to estimate the hazard ratio of death, comparing the survival experience of patients with a particular comorbidity with those who did not have the co-morbidity (reference group). For both the univariable and multi-variable Cox models, patients were first stratified by age group (<65 years and $\geqslant$65 years) to account for the increasing incidence of certain comorbidities with age, which may otherwise confound the analyses. The multivariable 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 table 5.1. 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 these because, amongst other factors, 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 more robust analysis would make a considered judgement of which variables should be included (rather than an automatic one) and may require additional interaction terms.

For each model, a R^2 value was calculated using the Royston and Sauerbrei method [13]. The R^2 value is the percentage of the variation in mortality which is explained by the variables included in the final model.

All statistical analyses were performed using SAS version 9.3.

Results

Completeness of comorbidity returns from each participating centre

The number of patients with data on comorbidity and other variables included in the analyses are summarised in figure 5.1.

Of the 37,285 incident RRT patients starting RRT between 2007–2012, only 20,916 individuals had comorbidity reported to the UKRR. Of 12,677 incident RRT patients in 2011 and 2012, 7,085 individuals (55.8%) from 58 centres had data on comorbidity reported. In 2012, 6,344 patients commenced RRT in centres in England, Wales and Northern Ireland. Comorbidity data were provided for 3,479 (54.8%) of those patients (tables 5.2, 5.3). Table 5.2 highlights the continued wide variation in the completeness of data returns with nine centres providing data on 100% of patients, but 11 centres providing data for less than 5% of new patients in 2012.

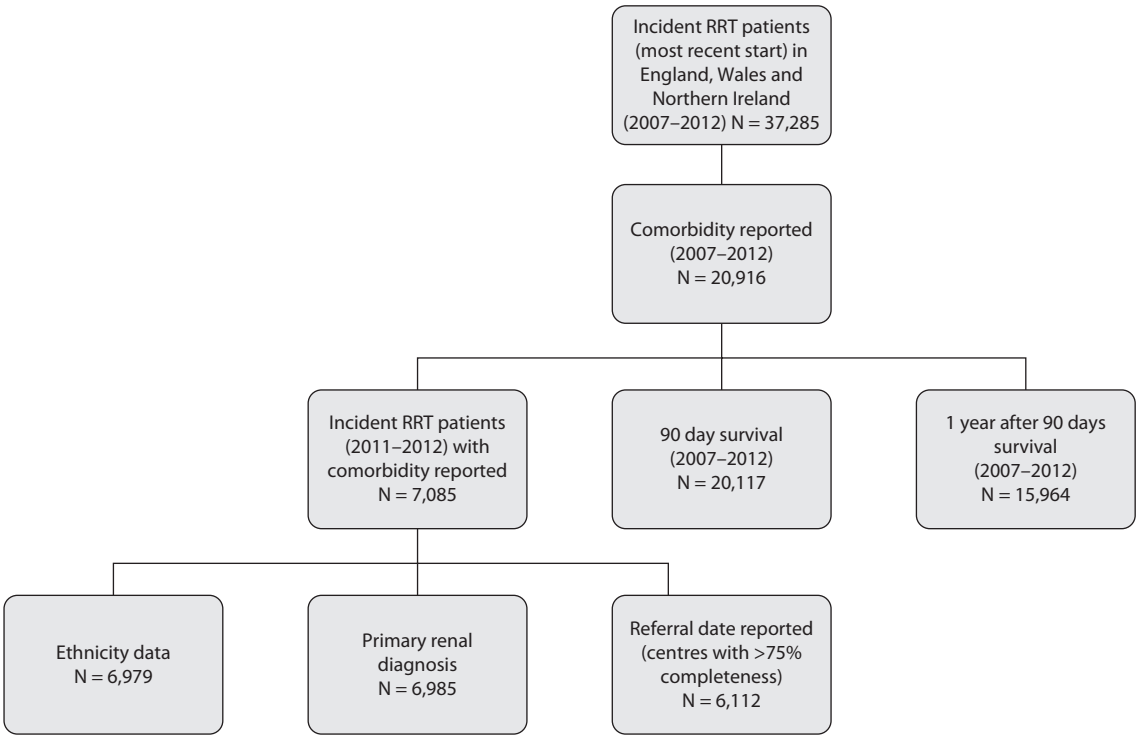

Fig. 5.1. Flow chart showing number of patients included in the various analyses

Limiting the comparison to the centres that reported in 2007, data completeness for comorbidity has dropped slightly. Completeness was 56.4% in 2007 and 55.1% in 2012 (table 5.3). When centres with 0% completeness for comorbidity were excluded, the median percentage of comorbidity returns in 2012 was 81.8%. For centres returning comorbidity data there has been an annual improvement in completeness since 2007 of 10% (table 5.3), albeit with a small decline in the most recent year.

Prevalence of multiple comorbidity

Including all incident patients from the years 2011–2012 ($n = 12{,}677$), comorbidity data were available for 7,085 (55.8%). More than half of these patients had one or more comorbidities (52.9%) (table 5.4), but in the subgroup of patients aged $\geqslant$65 years, this increased to 64% for patients with one or more comorbidities recorded (table 5.5).

Frequency of each comorbid condition

Table 5.5 lists the prevalence of specific comorbidities and the percentage of the total number of incident patients for whom data were available for that item. Diabetes mellitus (either listed as the cause of PRD or as a comorbidity) was present in 35% of all patients. This is different to the sum of diabetes (not listed as PRD) and diabetes listed as PRD in table 5.5 and reflects some patients having both an entry in the comorbidity field for diabetes and having it recorded as their PRD as described in the methods section.

Prevalence of comorbidity by age group

Ischaemic heart disease, cerebrovascular disease, COPD, claudication, malignancy and non-coronary angioplasty 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 5.5). Smoking was also more common amongst patients under 65 years. With age categorised in 10 year age groups, prevalence of most comorbidities was seen to increase markedly from 18–65 years with some appearing to plateau beyond this (figures 5.2, 5.3). In those patients aged >75 years there was a slight reduction in several reported comorbidities apart from ischaemic heart disease (angina, MI, CABG), non-coronary angioplasty and cerebrovascular accidents.

Table 5.2. Percentage completeness of comorbidity data returns on incident patients from individual renal centres 2007–2012

	Percentage completeness of comorbidity data					
Centre	2007	2008	2009	2010	2011	2012
England						
B Heart	34.7	37.1	61.6	75.8	94.7	92.1
B QEH	33.3	32.8	39.6	39.1	50.7	66.7
Basldn	76.9	87.5	88.9	90.6	95.2	84.9
Bradfd	100.0	91.9	93.2	91.0	100.0	98.6
Brightn	36.7	34.5	12.0	6.6	9.2	14.0
Bristol	85.6	77.1	86.6	96.5	89.2	54.7
Camb	2.4	0.0	3.7	0.0	0.8	2.4
Carlis	92.3	96.7	85.7	63.6	67.9	52.6
Carsh	77.0	83.3	77.9	72.7	80.7	53.3
Chelms	54.9	36.1	35.3	26.7	19.2	11.1
Colchr		0.0	0.0	0.0	0.0	0.0
Covnt	0.0	0.9	0.9	3.5	2.7	9.8
Derby	85.5	91.8	93.5	84.8	82.5	91.4
Donc	90.0	26.9	42.5	60.0	62.8	82.5
Dorset	91.9	84.2	90.5	95.8	100.0	91.7
Dudley	0.0	2.2	4.4	0.0	2.3	0.0
Exeter	32.5	29.6	48.3	69.8	88.4	100.0
Glouc	94.9	89.1	67.1	44.3	51.7	37.8
Hull	98.0	92.7	84.9	87.4	97.3	96.9
Ipswi	50.0	34.2	10.5	12.1	0.0	2.3
Kent	76.0	81.3	89.1	100.0	100.0	100.0
L Barts	85.1	84.0	86.1	76.4	74.7	72.6
L Guys	7.2	3.1	3.5	2.8	5.0	1.6
L Kings	100.0	99.3	98.4	100.0	98.6	100.0
L Rfree	11.4	14.5	11.2	19.1	28.7	29.6
L St.G	68.9	70.7	60.0	59.3	51.4	36.3
L West	53.5	45.4	2.8	1.9	2.2	0.9
Leeds	82.3	79.1	90.2	91.3	98.1	98.1
Leic	77.1	76.9	69.7	65.5	49.1	64.3
Liv Ain	47.1	66.7	71.1	0.0	0.0	0.0
Liv RI	72.3	66.7	71.8	2.0	0.0	0.9
M RI	35.9	41.2	64.4	41.6	37.8	26.3
Middlbr	79.0	90.5	91.7	94.1	97.0	90.0
Newc	23.6	34.3	35.1	69.2	84.7	77.9
Norwch	18.0	21.4	23.6	41.9	46.0	37.8
Nottm	93.8	88.7	97.7	96.6	98.3	97.0
Oxford	86.7	82.4	92.5	96.4	98.9	99.4
Plymth	79.0	75.4	84.2	76.8	70.0	55.3
Ports	70.1	61.8	67.1	53.7	41.2	33.5
Prestn	43.9	42.5	50.0	44.4	20.0	9.5
Redng	57.6	66.0	66.0	66.3	78.6	84.9
Salford	10.9	2.2	0.8	0.7	0.0	0.0
Sheff	58.2	51.7	55.0	78.3	77.8	83.5
Shrew	67.2	88.1	85.4	100.0	100.0	100.0
Stevng	73.9	78.4	94.9	98.1	100.0	100.0
Sthend	88.2	80.6	95.7	75.0	86.2	100.0
Stoke	0.0	0.0	0.0	0.0	0.0	0.0
Sund	100.0	97.8	98.4	92.6	100.0	94.4
Truro	95.6	73.2	87.9	84.8	92.1	100.0
Wirral	15.1	15.4	17.5	11.3	6.5	2.0
Wolve	92.7	96.6	100.0	99.1	94.7	88.1
York	86.5	80.6	75.0	97.4	98.1	94.3

Table 5.2. Continued

Centre	Percentage completeness of comorbidity data					
	2007	2008	2009	2010	2011	2012
N Ireland						
Antrim	13.5	31.7	33.3	95.1	73.3	96.2
Belfast	33.3	32.9	46.6	52.8	42.0	50.6
Newry	26.7	90.5	100.0	95.2	100.0	88.9
Ulster	94.4	100.0	100.0	95.0	97.1	100.0
West NI	75.9	71.0	83.8	84.6	86.8	66.7
Wales						
Bangor	69.4	67.5	86.7	96.2	95.0	76.2
Cardff	10.9	16.0	23.2	28.5	32.8	21.8
Clwyd	47.6	53.3	60.0	57.1	76.5	81.8
Swanse	96.9	96.0	97.4	88.2	92.4	95.6
Wrexm	66.7	81.0	94.7	100.0	100.0	100.0
England	57.7	56.7	55.6	55.1	56.0	54.1
N Ireland	41.3	51.4	65.5	76.7	74.3	70.4
Wales	46.5	55.8	58.0	59.5	62.1	59.2
UK	56.4	56.5	56.0	56.0	56.9	54.8

Blank cell denotes no data returned for that year

Table 5.3. Summary of completeness of incident patient comorbidity returns (2007–2012)

	Years						Combined years
	2007	2008	2009	2010	2011	2012	
Renal centres included *N*	61	62	62	62	62	62	
New patients *N*	6,104	6,180	6,243	6,156	6,333	6,344	37,360
Patients with comorbid data entries *N*	3,445	3,490	3,493	3,450	3,606	3,479	20,963
Percentage of patients with comorbid data entries	56.4	56.5	56.0	56.0	56.9	54.8	56.1
Percentage restricted to centres reporting since 2007	56.4	57.0	56.1	56.3	57.3	55.1	56.4
Median percentage amongst only centres returning >0% comorbidity	71.2	71.0	71.4	75.8	81.6	81.8	75.8

Prevalence of comorbidity by ethnic origin

Figures 5.4 and 5.5 illustrate the presence of comorbidity by ethnic origin and age group. Figure 5.4 shows the prevalence of having at least one comorbidity recorded amongst patients of White origin was nearly 10% higher compared to incident patients from an ethnic minority. Figure 5.5 shows that this higher trend was observed across most age groups. However, diabetes mellitus specifically was much more frequently reported in South Asian patients (51.1%) than in White individuals (32.1%) (table 5.6). The reported prevalence of smoking was highest in individuals of White ethnicity (15%).

Table 5.4. Number of reported comorbidities in patients starting RRT, as a percentage of those for whom comorbidity data were available 2010–2012

Number of comorbidities	0	1	2	3	4	5+
Percentage	47.1	27.1	13.1	7.0	3.4	2.3

Prevalence of comorbidity amongst patients with diabetes mellitus

Table 5.7 describes comorbidity amongst patients with and without diabetes (as either primary renal disease or comorbidity). As would be expected, patients with diabetes mellitus had higher prevalence of peripheral vascular disease (20.9% compared to 7.0% in non-diabetic patients). Similarly, there was a statistically significant higher prevalence of ischaemic heart disease (27.7% and 14.4% respectively) and cerebrovascular disease (14.1% and 8.3% respectively) in the diabetic patients. Similar proportions of patients with diabetes and non-diabetic

Table 5.5. Frequency with which each condition was reported in incident RRT patients 2011–2012

Comorbidity	Age <65 years		Age ⩾65 years		p value*	% overall prevalence
	N	(%)	*N*	(%)		
Any comorbidity present	1,459	(41.6)	2,291	(64.0)	<0.0001	52.9
Angina	194	(5.6)	536	(15.2)	<0.0001	10.4
MI in past 3 months	42	(1.2)	99	(2.8)	<0.0001	2.0
MI >3 months ago	208	(6.0)	467	(13.2)	<0.0001	9.7
CABG/angioplasty	176	(5.1)	385	(10.9)	<0.0001	8.0
Cerebrovascular disease	231	(6.7)	496	(14.0)	<0.0001	10.4
Diabetes (not listed as PRD)	182	(5.2)	476	(13.5)	<0.0001	9.4
Diabetes listed as PRD	1,008	(29.1)	765	(21.7)	<0.0001	25.4
COPD	155	(4.5)	345	(9.8)	<0.0001	7.1
Liver disease	154	(4.4)	68	(1.9)	<0.0001	3.2
Claudication	142	(4.1)	277	(7.9)	<0.0001	6.0
Ischaemic/neuropathic ulcers	147	(4.2)	123	(3.5)	0.0989	3.9
Angioplasty/vascular graft	77	(2.2)	208	(5.9)	<0.0001	4.1
Amputation	110	(3.2)	86	(2.4)	0.06	2.8
Smoking	516	(15.4)	431	(12.6)	0.0008	14.0
Malignancy	234	(6.8)	659	(18.6)	<0.0001	12.7

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

patients were smokers at the time of initiation of RRT (14.0% and 13.8% respectively). Malignancy was more common in non-diabetic patients ($p < 0.0001$) and may reflect 'competing risks', with diabetic patients tending to die at a younger age with cardiovascular disease, rather than developing malignancy in older age.

Late presentation and comorbidity

Table 5.8 shows the presentation time for patients with various comorbidities. In total, 6,112 individuals contributed data to this analysis. Patients referred to a nephrologist early had a higher prevalence of peripheral vascular disease, and ischaemic heart disease. There was a much higher proportion of patients with malignancy in the late referral group.

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

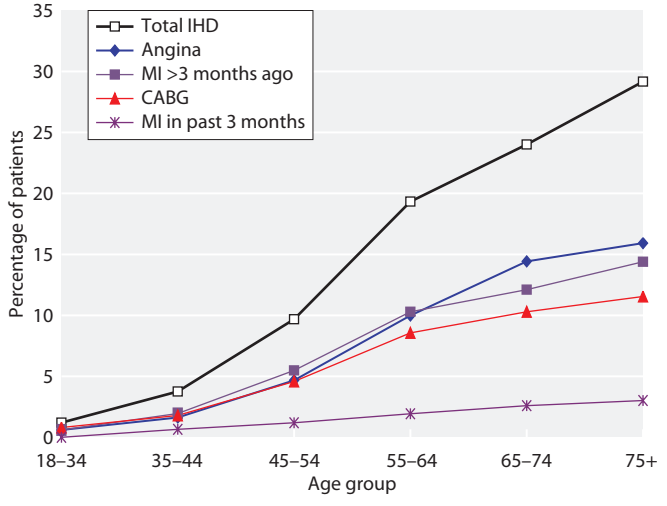

Fig. 5.2. Prevalence of ischaemic heart disease amongst incident patients 2011–2012 by age at start of RRT

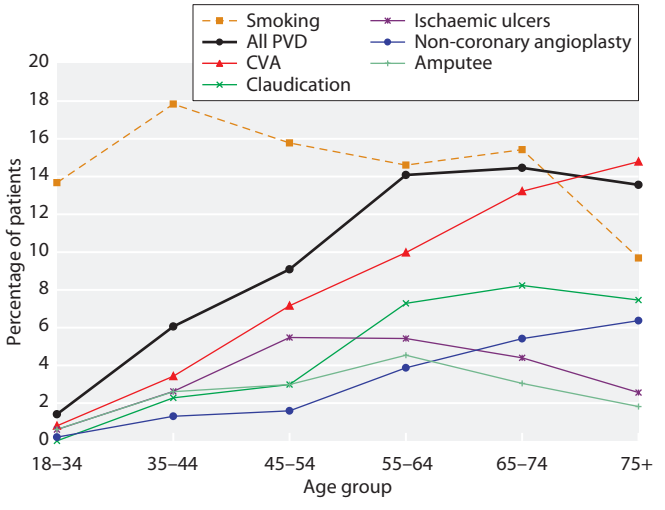

Fig. 5.3. Prevalence of non-coronary vascular disease amongst incident patients 2011–2012 by age at start of RRT

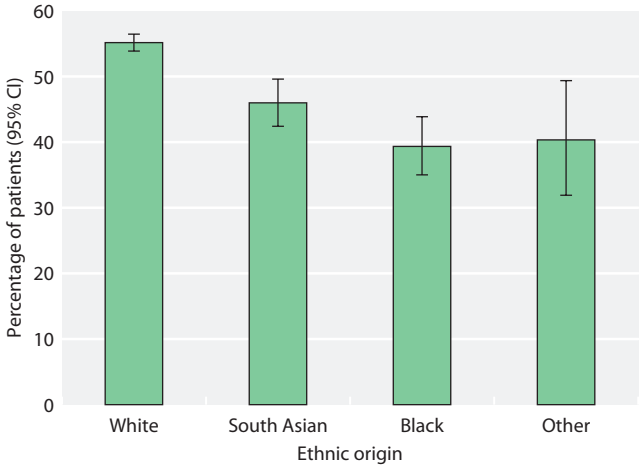

Fig. 5.4. Presence of comorbid conditions at the start of RRT by ethnic origin amongst patients starting RRT 2011–2012

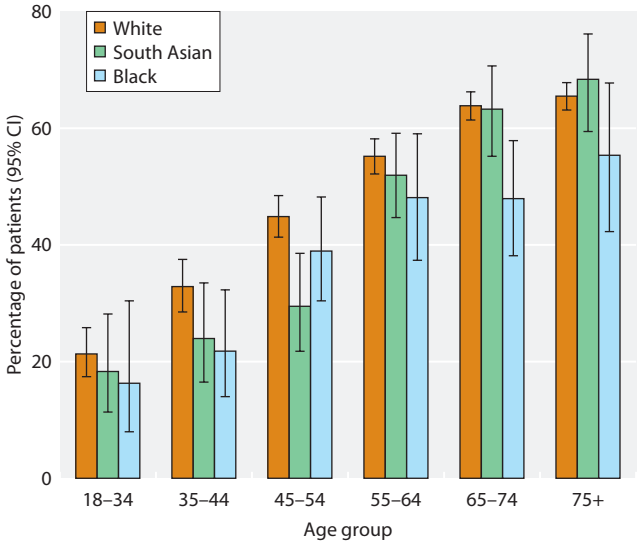

Fig. 5.5. Percentage of patients with comorbidity by ethnic origin in each age group at the start of RRT 2011–2012

Table 5.6. Prevalence of comorbidities amongst incident patients starting RRT 2011–2012 by ethnic group, as percentages of the total number of patients in that ethnic group for whom comorbidity data were available

	White		South Asian		Black		Other		
Comorbidity	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)	p value*
Ischaemic heart disease	1,082	(19.4)	166	(22.9)	42	(9.2)	15	(12.8)	<0.0001
Cerebrovascular disease	562	(10.0)	80	(11.0)	64	(14.0)	6	(5.1)	0.01
Diabetes (not listed as PRD)	538	(9.6)	70	(9.6)	29	(6.3)	8	(6.8)	0.09
Diabetes listed as PRD	1,257	(22.5)	302	(41.5)	147	(32.2)	43	(36.1)	<0.0001
COPD	456	(8.2)	30	(4.1)	8	(1.7)	3	(2.6)	<0.0001
Liver disease	155	(2.8)	23	(3.2)	26	(5.7)	11	(9.4)	<0.0001
Peripheral vascular disease	723	(13.0)	43	(5.9)	28	(6.2)	8	(6.8)	<0.0001
Smoking	817	(15.0)	59	(8.4)	41	(9.4)	13	(11.5)	<0.0001
Malignancy	806	(14.4)	40	(5.5)	31	(6.8)	8	(6.8)	<0.0001

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

Table 5.7. 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	635	(14.4)	650	(27.7)	<0.0001
Cerebrovascular disease	366	(8.3)	331	(14.1)	<0.0001
COPD	312	(7.1)	170	(7.2)	0.79
Liver disease	135	(3.1)	79	(3.4)	0.50
Peripheral vascular disease	309	(7.0)	489	(20.9)	<0.0001
Smoking	592	(13.8)	320	(14.0)	0.78
Malignancy	635	(14.4)	218	(9.3)	<0.0001

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

Table 5.8. Percentage prevalence of specific comorbidities amongst patients presenting late (<90 days) compared with those presenting early (⩾90 days) (2011–2012 incident patients)

	Late referral		Early referral		
Comorbidity	*N*	(%)	*N*	(%)	p value*
Ischaemic heart disease	176	(16.3)	970	(19.5)	0.02
Cerebrovascular disease	105	(9.7)	500	(10.0)	0.7
Diabetes (not listed as PRD)	110	(10.2)	477	(9.6)	0.5
COPD	97	(9.0)	365	(7.3)	0.1
Liver disease	45	(4.2)	138	(2.8)	0.02
Peripheral vascular disease	95	(8.8)	633	(12.7)	0.0003
Malignancy	217	(19.9)	554	(11.1)	<0.0001
Smoking	158	(15.4)	690	(14.2)	0.3

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

treatment than in those starting on peritoneal dialysis (table 5.9). The median age for all patients starting dialysis in England, Wales and Northern Ireland in 2011–2012 was 67.3 years (IQR 54.5–76.4) for haemodialysis and 60.5 years (IQR 46.6–71.8) for peritoneal dialysis. In comparison, the median age of patients with comorbidity data starting RRT on HD was 67.6 years compared with 60.6 years for those starting on PD. For patients with pre-emptive transplant the median age of patients with comorbidity data was 49.5 years. For most of the comorbid conditions, the median age of patients on HD was higher than for patients on PD (table 5.9). As it would be expected a greater percentage of the transplanted patients had no comorbidities when compared to non-transplanted patients (77.4% vs. 43.4% respectively) (table 5.10).

Comorbidity and survival within 90 days of starting RRT

In univariable analysis stratified by age, most comorbidity was associated with an increased risk of death in the first 90 days after starting RRT 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). Results of the multivariable stepwise Cox regression analyses stratified by age group (<65 and ⩾65) are

Table 5.9. Number (and percentage) of incident patients with comorbid conditions starting PD and HD 2011–2012

	HD			PD			
Comorbidity	*N*	(%)	Median age	*N*	(%)	Median age	p value*
Angina	625	(12.3)	72.7	100	(6.5)	70.0	<0.0001
MI in past 3 months	132	(2.6)	71.3	9	(0.6)	73.2	<0.0001
MI >3 months ago	556	(10.9)	72.3	114	(7.4)	69.4	<0.0001
CABG/angioplasty	426	(8.4)	71.1	121	(7.8)	70.7	0.483
Cerebrovascular disease	613	(12.0)	72.2	108	(7.0)	69.6	<0.0001
Diabetes (not listed as PRD)	558	(10.9)	72.9	87	(5.6)	68.9	<0.0001
COPD	439	(8.6)	71.5	56	(3.6)	67.6	<0.0001
Liver disease	187	(3.7)	58.8	29	(1.9)	58.4	0.001
Claudication	354	(6.9)	71.1	62	(4.0)	64.7	<0.0001
Ischaemic/neuropathic ulcers	223	(4.4)	64.6	37	(2.4)	60.2	0.0004
Angioplasty/vascular graft	241	(4.7)	72.6	41	(2.7)	66.3	0.0004
Amputation	163	(3.2)	64.0	30	(1.9)	61.0	0.01
Smoking	715	(14.5)	65.4	210	(13.8)	55.5	0.47
Malignancy	757	(14.8)	73.4	126	(8.1)	71.3	<0.0001

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

Table 5.10. Comorbidity amongst incident patients (2011–2012) who underwent transplantation (by the end of 2012) compared to those who remained on dialysis or died

	Not transplanted		Transplanted		
Comorbidity	*N*	(%)	*N*	(%)	p value*
Patients with comorbidity data	6,315		770		
No comorbidity present	2,739	43.4	596	77.4	<0.0001
Ischaemic heart disease	1,288	20.7	36	4.7	<0.0001
Cerebrovascular disease	711	11.4	16	2.1	<0.0001
Diabetes (not cause of ERF)	638	10.2	20	2.6	<0.0001
COPD	488	7.8	12	1.6	<0.0001
Liver disease	206	3.3	16	2.1	0.0775
Peripheral vascular disease	790	12.7	28	3.7	<0.0001
Smoking	885	14.7	62	8.3	<0.0001
Malignancy	875	14.0	18	2.4	<0.0001

shown in tables 5.11 and 5.12. As identified in the univariable models, the relative magnitude of the hazard ratios associated with comorbidity in younger patients tended to be greater than in the older patient group. Diabetes did not emerge as an independent predictor of death, perhaps explained by its close association with, and mediation in the causal pathway by, cardiovascular diseases. Some comorbidities may appear not to be associated with an increased risk of death in this analysis because of the low number of patients in these groups or because of selection within the cohort. For example, individuals with severe comorbid disease, and whose prognosis on RRT was considered very poor, may not have been started on RRT (for instance, liver disease in those aged ⩾65 years).

The final four variables in the model examining death within the first 90 days of starting RRT in patients aged <65 (table 5.11) explain 31% of the variation in survival. For patients aged ⩾65, the final eight variables in the model explain 12% of the variation in survival (table 5.12).

Table 5.11. Multivariable Cox proportional hazards model* for predictors of death within the first 90 days of starting RRT during 01/01/2007–30/09/2012: patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	4.3	3.0–6.3	<0.0001
Ischaemic/ neuropathic ulcers	2.3	1.3–4.1	0.004
Angina	1.9	1.2–3.0	0.004
Age (per 10 years)	1.6	1.3–1.9	<0.0001

*This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units) and the 14 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'

Comorbidity and survival 1-year after 90 days of commencing RRT

Age, smoking and four other comorbidities were independently associated with an increased hazard of death within the first year after 90 days of commencing RRT for patients aged <65 years and three of these (age, malignancy and ischaemic/neuropathic ulcers) were among the nine variables independently associated with mortality beyond day 90 in patients ⩾65 years (tables 5.12, 5.13 and 5.14). Diabetes mellitus was independently associated with increased 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 10% of the variation in survival was explained by the nine variables included in the final model.

Table 5.12. Multivariable Cox proportional hazards model* for predictors of death within the first 90 days of starting RRT during 01/01/2007–30/09/2012: patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
MI in past 3 months	2.0	1.4–2.9	0.000
Amputation	1.8	1.1–2.9	0.030
Ischaemic/neuropathic ulcers	1.7	1.1–2.6	0.012
Malignancy	1.6	1.3–1.9	<0.0001
Angina	1.5	1.2–1.9	<0.0001
Age (per 10 years)	1.5	1.3–1.7	<0.0001
COPD	1.4	1.0–1.8	0.022
Diabetes of either category	0.8	0.6–1.0	0.018

*This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units), and the 14 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'

Table 5.13. Multivariable Cox proportional hazards model* for predictors of death in the year after the first 90 days of starting RRT during 01/01/2007–30/09/2012: patients aged <65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	2.9	2.2–3.8	<0.0001
Liver disease	2.2	1.6–3.1	<0.0001
Ischaemic/neuropathic ulcers	2.1	1.5–3.0	<0.0001
Diabetes of either category	1.8	1.5–2.2	<0.0001
Smoking	1.5	1.2–1.9	0.001
Age (per 10 years)	1.5	1.3–1.6	<0.0001

*This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units) and the 14 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'

Table 5.14. Multivariable Cox proportional hazards model* for predictors of death in the year after the first 90 days of starting RRT during 01/01/2007–30/09/2012: patients aged ⩾65 years

Comorbidity	Hazard ratio	95% CI	p value
Malignancy	1.7	1.5–1.9	<0.0001
COPD	1.6	1.4–1.9	<0.0001
Age (per 10 years)	1.5	1.4–1.7	<0.0001
Amputation	1.5	1.0–2.2	0.047
Ischaemic/neuropathic ulcers	1.5	1.1–2.0	0.024
MI in past 3 months	1.4	1.0–1.9	0.027
Cerebrovascular disease	1.4	1.2–1.7	<0.0001
Angioplasty/vascular graft	1.3	1.1–1.7	0.016
Angina	1.3	1.1–1.5	0.004

*This is the result of a stepwise procedure. The variables considered in the model were: age (in 10 year units) and the 14 comorbidity variables except that 'diabetes (not listed as PRD)' was replaced by 'diabetes of either category' which included 'diabetes listed as PRD'

Discussion

Case-mix adjustment is integral to quality reporting [14, 15], risk adjustment in clinical research [16, 17], resource allocation and management of patients with comorbid conditions in day to day practice [18].

Comorbidity data completeness continues to be a cause for concern with overall completeness of comorbidity reporting to the UKRR being fairly static. Missing data may hamper case-mix adjustment but also introduces the risk of selection bias, so caution must be used in interpreting the influence of comorbidity on patient outcomes.

The Multivariable Cox proportional hazards model for predictors of death within the first 90 days of starting RRT account for 31% and 12% of the variation in survival in patients aged <65 and ⩾65 years respectively. Whereas for predictors of death in the year after the first 90 days of starting RRT the model accounted for 26% and 10% of the variation in survival in patients aged <65 and ⩾65 years respectively. It is noteworthy that even in analyses 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.

A number of studies have demonstrated the association of various laboratory and physiological parameters, for example serum albumin, systolic blood pressure, body mass index, serum phosphate, and parathyroid hormone, with mortality and other outcomes in dialysis patients [19–22]. Future studies of survival should also consider other factors such as nutrition, mobility, cognition and socio-economic status in addition to centre level factors at the start of dialysis to better assess the risk factors and outcomes for RRT patients. Data completeness permitting, the UKRR is in a unique position to test the association of these parameters and account for the variation in survival.

A number of approaches are currently being explored by the UKRR to improve comorbidity data completeness, including collaboration with renal IT suppliers, linkage with other secondary data sources (e.g. Hospital Episode Statistics dataset) and statistical imputation techniques. Multiple imputation [23] is a statistical technique for estimating missing data. In multiple imputation, missing comorbidities for an individual patient are estimated dependent on available information that is correlated to the missing comorbidities or explains the reason for the missing data. In the future the UKRR is likely to use this combination of approaches to adjust for case-mix when exploring the variation in outcome between centres.

Conflicts of interest: none

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