Chapter 21: Co-morbidity in Incident Patients

Summary

- Adjustment for co-morbidity has been increasingly used in analyses throughout this years report (Chapters 16, 17, 18, 19 and 20).

- Co-morbidity adjustment was important for calculating survival. After adjusting for co-morbidity, social deprivation was no longer significant in the Cox model.

- The incidence of co-morbidity increased with age up to age 75. In patients aged over 75, the percentage starting RRT with cardiovascular and cerebrovascular disease appeared to reduce.

- Diabetic patients starting RRT had higher co-morbidity than non-diabetics despite their younger age (45% v 36%, $p<0.001$). Even after adjusting for co-morbidity in the Cox survival model, being diabetic was still a significant additional risk factor.

- Patients with co-morbidity tended to start RRT earlier with higher eGFRs.

- Co-morbidity returns are still poor and this is restricting survival analyses. Compared with the previous year, 4 centres had improved returns by more than 50% and 4 centres had worse returns.

- In 2003 co-morbidity, at start of RRT, was altered to include heart failure and non-coronary grafts and stents.

Co-morbidity data

The Registry has defined 15 'yes' (present) or 'no' questions relating to co-morbidity and asks clinicians to complete this record at the time of starting RRT. As an example, the screen made available to renal units using the CCL Proton system is shown in Figure 21.1. A patient may therefore have a fully completed screen, which has recorded that there are no co-morbid conditions present. Null entries are considered as missing data rather than a 'no'.

Beginning in 2003, the presence or absence of heart failure prior to the start of renal replacement therapy was also recordable. Definitions for each co-morbidity are given at the end of this chapter.

These data are used, together with age, ethnicity, primary diagnosis, etc., in survival and other analyses.

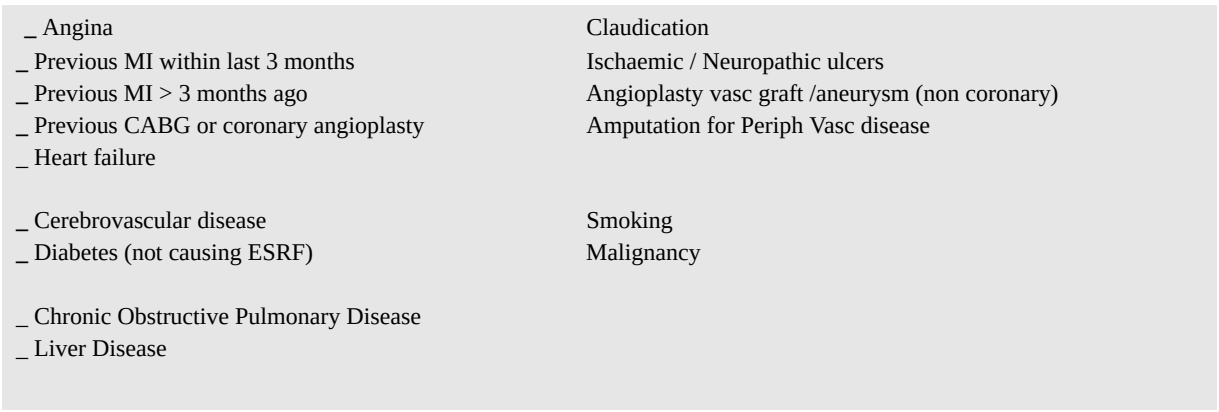

Figure 21.1. Co-morbidity entry screen for the CCL Proton system

Co-morbidity returns by renal units

The return of co-morbidity data for incident patients in 2002 remained very incomplete, although it had increased from previous years. Prior to 1999, co-morbidity data were rarely returned to the Registry. In 1999, at least one item of co-morbidity was reported for 20.8% of those patients registered as starting RRT that year. The returns by unit and year of starting RRT are shown in Table 21.1.

Table 21.1. Co-morbidity data returns, by centre, at the start of RRT

Treatment centre	1999		2000		2001		2002	
	No. incident	% Return co-morbidity	No. incident	% Return co-morbidity	No. incident	% Return co-morbidity	No. incident	% Return co-morbidity
Bradford	–	–	39	48.7	61	91.8	61	100
Bristol	117	88.9	147	93.2	149	83.2	151	75
Cambridge	–	–	64	0	48	0	104	4
Cardiff	135	0	134	0	136	0	155	0
Carlisle	26	46.2	28	35.7	25	4.0	26	20.7
Carshalton	108	10.2	116	10.3	118	12.7	119	0.6
Coventry	91	0	88	0	101	0	104	0
Derby	25	0	40	0	49	0	-	-
Exeter	82	28.0	72	34.7	99	18.2	98	39
Gloucester	59	1.7	46	97.8	49	87.8	50	64.9
Guys	119	0	120	0	103	0	109	0
Heartlands	82	0	86	0	64	0	85	0
Hull	64	1.6	81	2.5	75	0	75	3.8
Leeds LGI	62	25.8	68	85.3	74	70.3	76	50.8
Leicester	158	80.4	171	76.6	174	86.8	183	76.2
Liverpool	–	–	154	31.2	182	35.2	183	8.7
Notts	128	24.2	113	71.7	121	64.5	121	98.9
Oxford	134	0	132	1.5	163	0	170	0
Plymouth	67	0	60	0	63	0	64	0
Portsmouth	–	–	104	0	141	39.7	144	36.4
Preston	104	0	116	0	134	0	137	0
Reading	45	0	54	0	72	0	65	0
S Cleveland	90	0	87	70.1	81	90.1	82	0
Sheffield	133	17.3	134	78.4	150	84.7	152	57.1
Stevenage	–	–	103	0	126	0	125	1.0
Southend	43	2.3	39	2.6	35	20.0	37	31.4
St James	79	86.1	91	93.4	86	76.7	87	76.3
Sunderland	45	0	45	0	35	0	40	46.4
Swansea	83	26.5	90	58.9	110	40.0	111	74.8
Truro	–	–	38	7.9	35	37.1	38	63.8
Wolverhmtn	75	0	77	0	77	0	76	0
Wordsley	43	0	40	0	34	0	34	0
Wrexham	51	0	55	0	36	0	36	0
York	51	74.5	40	92.5	36	77.8	38	68.7
Totals	2299		2872		3042		3136	

Frequency of co-morbidity returned

Table 21.2. Frequency of co-morbidity at the time of starting RRT

Co-morbidity	Age <65 years		Age >65 years		Total %
	No. pts	%	No. pts	%	incidence
Angina	57	10.1	169	26.7	18.8
MI in past 3 months	13	2.3	28	4.4	3.4
MI >3 months ago	29	5.1	103	16.3	11.0
CABG/angioplasty	23	4.1	33	5.2	4.7
Cerebrovascular disease	40	7.0	105	16.6	12.1
Diabetes (not as cause of ERF)	25	4.5	68	10.8	7.8
Diabetes as primary disease	350	20.4	259	14.5	17.6
Diabetes of either category	55	23.6	84	19.2	21.4
COPD	32	5.6	71	11.3	8.6
Liver disease	13	2.3	11	1.8	2.0
Malignancy	31	5.5	105	16.7	11.3
Claudication	25	4.4	85	13.5	19.2
Ischaemic/neuropathic ulcers	20	3.5	28	4.5	4.0
Angioplasty/vascular graft	4	0.7	27	4.3	2.6
Amputation	13	2.3	9	1.4	1.8
Smoking	105	19.1	85	13.9	16.4

Abbreviation: MI - myocardial infarction; CABG - coronary artery bypass grafting; ERF - established renal failure; COPD - chronic obstructive pulmonary disease

Total number of patients with data entered for each co-morbidity, and percentage of total incident patients with each co-morbidity present, are shown in Table 21.2.

Frequency of co-morbidity by age band

In Figure 21.2 there is an increase in the presence of cardiac and cerebrovascular co-morbidity with age although in patients over 75 this appears to reduce. Within the general population co-morbidity would be expected to increase with age. Whether this reduction is due to these patients either dying prior to starting renal replacement therapy, or not being referred or accepted for renal replacement therapy is unknown.

Figure 21.3 demonstrates the increased incidence of diabetes and malignancy with age of patients starting renal replacement therapy. The incidence of smoking in patients starting renal replacement therapy reduces from the age of 45, while peripheral vascular disease follows a similar pattern to cardiac co-morbidity, decreasing in patients aged 75 or more years.

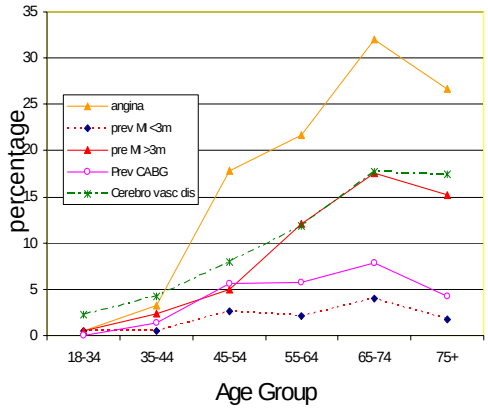

Figure 21.2. Frequency of cardiac and cerebrovascular co-morbidity in incident patients

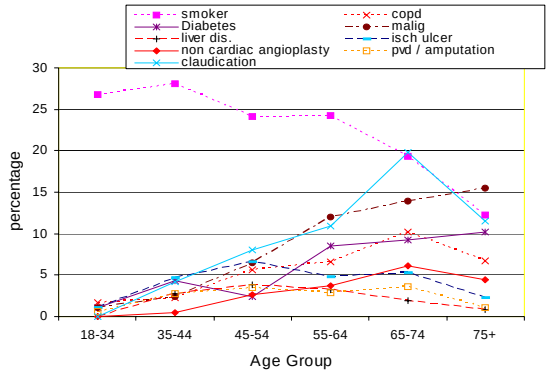

Figure 21.3. Frequency of co-morbidity in incident patients

Frequency of co-morbidity by modality at day 90

The frequency of co-morbidity within the different dialysis modalities varies (Figure 21.4). Interpretation of these differences is difficult, as not only is the median age of PD patients less than that of HD patients, those starting RRT aged over 75 (who are more likely to be on HD) have less co-morbidity than those aged 65 – 75 years (see Figures 21.2 and 21.3).

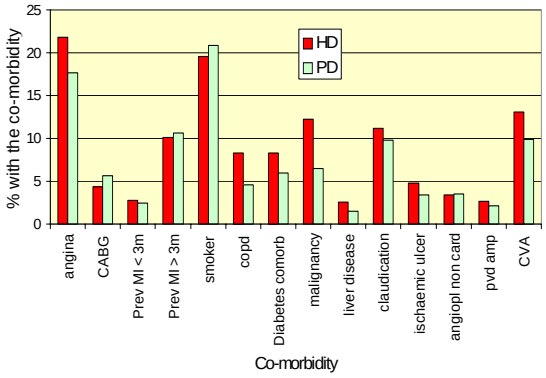

Figure 21.4. Frequency of co-morbidity by modality at day 90

Frequency of co-morbidity in diabetics and non-diabetics

Figure 21.5 shows that diabetic patients have significantly more co-morbidity than non-diabetics, despite having a younger median age.

Smoking was the most frequent co-morbidity in both diabetic and non-diabetic patients (22% and 20% respectively). Malignancy was more common at the start of renal replacement treatment in non-diabetic than in diabetic patients (12% v 3%, p<0.0001). In diabetic ERF patients, cerebrovascular disease, peripheral vascular disease and cardiac disease were all significantly more common at the start of treatment than in non-diabetic patients. For this analysis cardiac disease included 'angina', 'previous myocardial infarction' (MI) and previous cardiac by-pass grafts. When analysed separately, angina was present in 30% of diabetics at start of RRT compared with 20% of non-diabetics (p<0.0001) and 'MI more than 3 months prior to start of treatment' was significantly more common in diabetics (14% v 11%, p=0.02). There was no difference in the proportion of diabetics and non-diabetics who had an 'MI less than 3 months before the start of renal replacement therapy' (4% v 3%, p=0.17); similarly, previous coronary angioplasty was uncommon in both

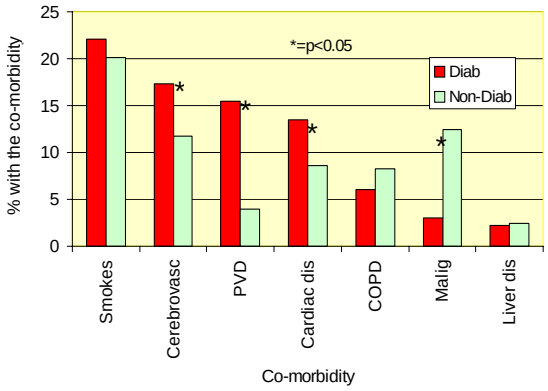

Figure 21.5. Frequency of co-morbidity in diabetics and non-diabetics

diabetics and non-diabetics (6% v 5% respectively, p=0.22). Peripheral vascular disease (PVD), which included 'claudication', 'ischaemic and neuropathic ulcers', 'non-cardiac angioplasty' and 'amputations due to ischaemia', was significantly more common in diabetic patients (p<0.001).

A Cox proportional hazards model, which included age (as a linear variable), ethnicity, primary diagnosis (including diabetes) and co-morbid diagnoses, was constructed to analyse incident patient survival, excluding the first 90 day period. In the first model, centres were excluded if they had less than 80% co-morbidity returns (n= 1,139). In the second model all patients from centres returning co-morbidity were included (n = 3,206). In both these models diabetes remained a significant variable in the model after adjusting for other co-morbidity (p= 0.02 and p = <0.0001 respectively). Diabetes also remained significant in the second model as a co-morbidity (i.e. not as the primary diagnosis for renal failure) (p= 0.0054).

Social deprivation and Co-morbidity

The Townsend index was used as a measure of social deprivation (calculated for the Registry from the patients' postcode from the 2001 census data, by Hannah Jordan of Southampton University). It is a composite measure of social deprivation based on total unemployment rate, no car households, overcrowded households and not owner-occupier households, based on the electoral ward as at the 2001 Census. The higher the Townsend index, the greater is the social deprivation. A full analysis is included in Chapter 17 of this years report.

The analysis used an incident cohort which was analysed by dividing the UK general population according to quintiles of social deprivation. The results showed that the more socially deprived groups were younger and had higher rates of co-morbid illnesses (more diabetes, cardiovascular disease, peripheral vascular disease, and COPD) than the more affluent groups. They were also significantly more likely to be current smokers (21.5% v 14.8% p<0.0001). The incidence of malignancy was reduced in the more socially deprived groups.

In the univariate analyses, increasing social deprivation was correlated with reduced patient survival (after adjusting for age). After including the co-morbidity data (which remained an independent predictor of survival) in the Cox proportional hazards model, social deprivation was no longer an independent predictor of survival (p= 0.97). These analyses showed the importance of being able to adjust each centre's survival for the presence of co-morbidity.

Estimated GFR prior to RRT and co-morbidity

Using the abbreviated MDRD calculation, the eGFR prior to starting renal replacement therapy is shown in Table 21.3.

Patients with co-morbidity generally started renal replacement therapy earlier than those without co-morbidity and appeared to have a higher median eGFR, although these differences may be smaller than might have been expected clinically.

Table 21.3. Median eGFR and presence or absence of co-morbidity

	Present (95%CI)	Absent (95%CI)
Angina	7.7 (8.0 – 8.6)	6.8 (7.2 – 7.5)
MI in past 3 months	7.6 (7.3 – 9.5)	6.9 (7.4 – 7.7)
MI >3 months ago	7.3 (7.6 – 8.4)	6.9 (7.4 – 7.7)
CABG/angioplasty	7.8 (7.7 – 9.1)	6.9 (7.4 – 7.7)
Cerebrovascular disease	7.6 (7.9 – 8.8)	6.9 (7.3 – 7.6)
Diabetes (not as cause of ERF)	7.5 (7.4 – 8.7)	6.9 (7.4 – 7.7)
Diabetes as primary disease	8.0 (8.3 – 8.6)	6.9 (7.5 – 7.6)
Diabetes of either category	-	-
COPD	7.5 (7.7 – 8.8)	6.9 (7.4 – 7.7)
Liver disease	7.3 (7.2 – 8.9)	7.0 (7.4 – 7.7)
Malignancy	6.9 (7.1 – 8.1)	7.0 (7.4 – 7.7)
Claudication	7.8 (7.9 – 8.8)	6.9 (7.3 – 7.6)
Ischaemic/neuropathic ulcers	7.7 (7.7 – 9.2)	6.9 (7.4 – 7.7)
Angioplasty/vascular graft	7.8 (7.5 – 9.4)	7.0 (7.4 – 7.7)
Amputation	8.7 (8.5 – 10.8)	6.9 (7.4 – 7.7)
Smoking	7.1 (7.3 – 8.0)	6.9 (7.4 – 7.7)

Appendix to Chapter 21

Important changes to co-morbidity definitions in 2003

The non-coronary angioplasty group has been widened to include other vascular grafts and arterial stents. The new definitions are given below:

Angioplasty, stenting, vascular graft and aneurysm (all non-coronary)

This category now includes vascular grafts (e.g. aortic bifurcation grafts), vascular aneurysms and arterial stents.

Episode of heart failure (right or left) prior to RRT

This is whether or not it was only the result of fluid overload.

Co-morbidity definitions

Angina

A history of chest pain on exercise with or without ECG changes, exercise tolerance test, radionucleotide imaging or angiography.

Previous MI within the past 3 months

The rise and fall of a biomarker (CK, CK-MB or Troponin) together with one of either: ischaemic symptoms, pathologic Q waves, ischaemic ECG changes or a coronary intervention. This definition is from both the European Society of Cardiology and the American College of Cardiology.

Previous MI more than 3 months ago

From the time of the start of RRT.

Previous CABG or coronary angioplasty

Episode of heart failure (right or left)

This is whether or not it was only caused by fluid overload.

Cerebrovascular disease

Any history of strokes (of whatever cause) and including transient ischaemic attacks caused by carotid disease.

Diabetes (not causing established renal failure)

This includes diet-controlled diabetics.

Chronic obstructive pulmonary disease

This is defined as a slowly progressive airways disorder characterised by obstruction of the expiratory airflow, which does not change markedly over several months, may be accompanied by airway hyper-reactivity and may be partially reversible.

N.B. Chronic bronchitis and emphysema may occur in the absence of airflow obstruction. Asthma patients may rarely develop airflow obstruction that does not improve with steroids.

Liver disease

Persistent enzyme evidence of hepatic dysfunction *or* biopsy evidence *or* hepatitis B e antigen or hepatitis C antigen (polymerase chain reaction) positive serology.

Malignancy

Defined as any history of malignancy (even if curative), for example the removal of a melanoma; excludes basal cell carcinoma.

Claudication

Current claudication based on a history, with or without Doppler or angiographic evidence.

Ischaemic/neuropathic ulcers

The current presence of these ulcers.

Angioplasty, stenting, vascular graft, vascular aneurysm (all non-coronary)

This category now includes vascular grafts (e.g. aortic bifurcation grafts) and renal artery stents.

Amputation for peripheral vascular disease

Smoking

Being a current smoker or having a history of smoking within the previous year.