The burden and survival implications of comorbidity in people with chronic kidney disease stage 3

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Renal Risk in Derby RRID

1. Background

- Multimorbidity is a growing concern for health and social care systems due to demographic and epidemiological transition to older population profiles.
- Chronic kidney disease (CKD) is often considered in isolation but commonly occurs in conjunction with other chronic conditions.
- The extent, burden and prognostic significance of its comorbidities is not well understood.
- The majority of people with CKD in the UK have mild to moderate disease and are managed in primary care

2. Aim

To describe the prevalence, medication burden and survival implications of eleven comorbidities in a cohort of people with CKD stage 3 in a primary care setting.

3. Methods

- The Renal Risk in Derby (RRID) study is a prospective cohort study of people with CKD stage 3 in a primary care setting.
- People with eGFR 59-30ml/min/1.73m^2 on two occasions prior to inclusion were recruited between August 2008 and March 2010.
- Medical history was obtained (including medication history) and participants underwent clinical assessment, urine and serum biochemistry tests.
- Comorbidities included (defined as self-reported, doctor-diagnosed unless specified):
  - Hypertension
  - Diabetes
  - Ischaemic heart disease
  - Heart failure
  - Peripheral vascular disease
  - Cerebrovascular disease
  - Respiratory disorder (asthma or chronic obstructive pulmonary disease, defined by medication)
  - Depression (defined by taking selective serotonin reuptake inhibitors)
  - Painful condition (defined by chronic analgesia use)
  - Thyroid disorder (defined by taking thyroxine or carbimazole)
  - Anaemia (KDIGO-defined)
- Degree of comorbidity and medication burden were described.
- Multivariable logistic regression (adjusted for age, sex, education status, smoking, BMI and eGFR) was used to identify independent associations with greater treatment burden (taking more than five medications) and greater multimorbidity (two or more comorbidities)
- A Kaplan Meier plot and multivariable Cox proportional hazards models (adjusted for age, sex, smoking, BMI, eGFR and uACR) were used to investigate associations between comorbidity and all-cause mortality.

4. Results

- 1741 people with CKD were recruited. Mean age was 72.9 9 years. 67% were over 70
- Mean baseline eGFR was 52 10ml/min/1.73m^2.
- Isolated CKD was uncommon:
  - Only 78 (4%) had no comorbidities
  - 453 (26%) had one comorbidity
  - 508 (29%) had two comorbidities
  - 702 (40%)) had more than two comorbidities. (Figure 1)
- 1528 (88%) had hypertension as a comorbidity. The next commonest were painful condition 30%, anaemia 24%, ischaemic heart disease 23%, diabetes 17% and thyroid 12% respectively
- 1033/1741 (59%) were taking five or more medications and 198 (11%) were taking ten or more.
- On multivariable logistic regression, greater treatment burden (taking more than five medications) and greater multimorbidity (two or more comorbidities) were both independently associated with:
  - Increasing age
  - Smoking
  - Increasing BMI
  - Decreasing eGFR
- Greater treatment burden was also independently associated with lower education status.
- 175/1741 (10%) died after a median of 3.6 years of follow up, most commonly from cardiovascular disease (41%). (Figure 2)
- Higher number of comorbidities, older age, male sex, ex-smoking and lower eGFR were all independent predictors of all-cause mortality. (Table 1)

Figure 1. Proportion of people with different degrees of comorbidity who have each of the 11 conditions

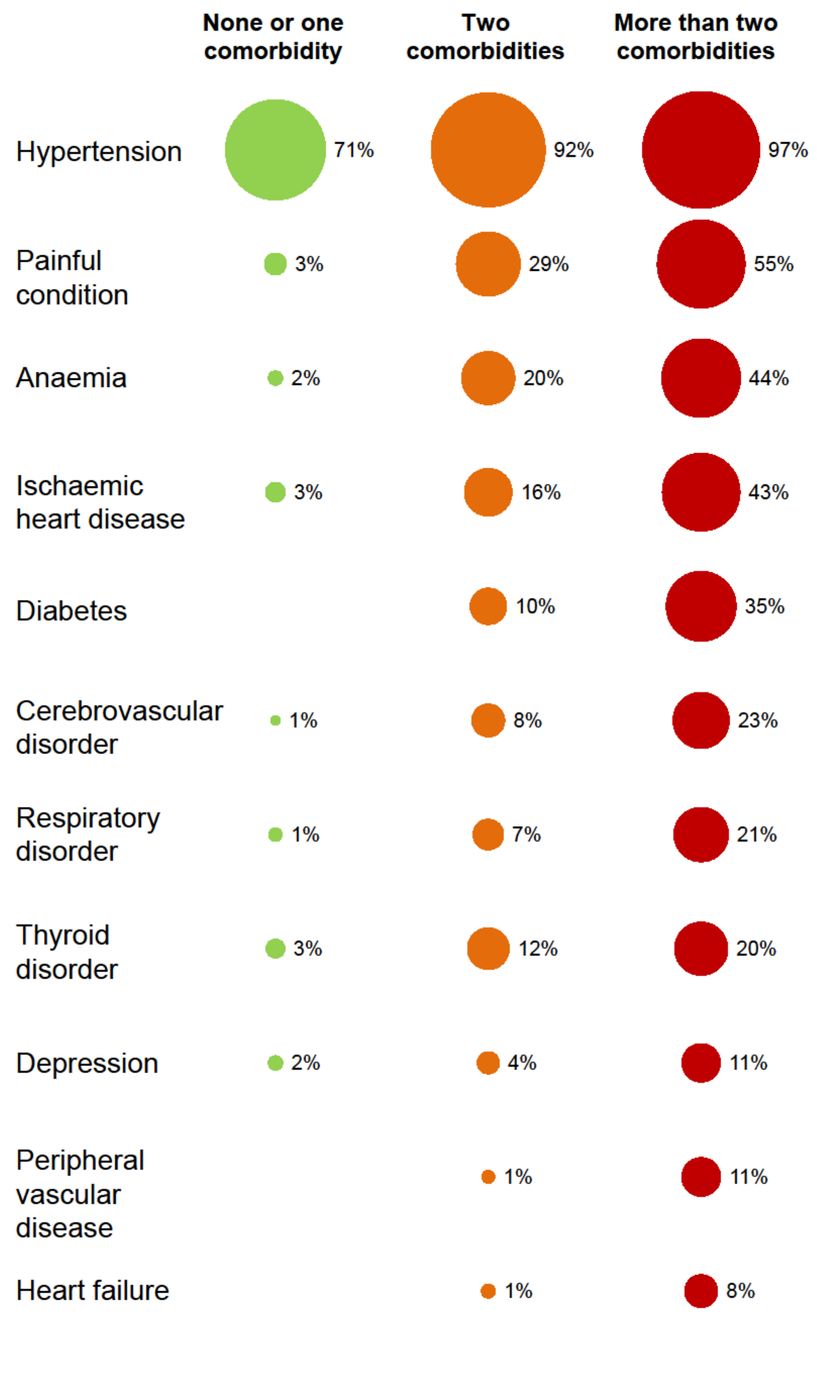

Figure 2. Kaplan Meier plot showing survival by extent of comorbidity

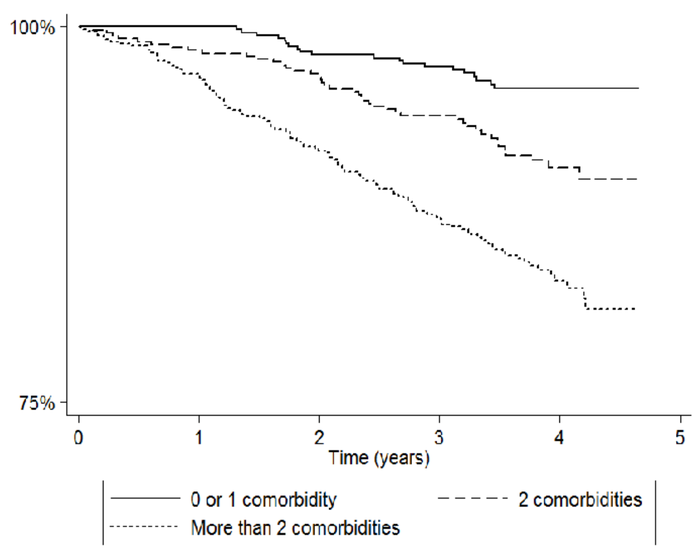

Table 1. Multivariable Cox proportional hazards model of comorbidity and survival

	Hazard ratio (95% CI) *	p value
CKD + 2 or more comorbidities (vs CKD + 0 or 1)	2.81 (1.72-4.58)	<0.001
Age (years)	1.07 (1.05-1.09)	<0.001
Sex (male vs. female)	1.45 (1.06-1.97)	0.020
Ex smoker (vs never smokers)	2.07 (1.01-4.25)	0.049
BMI (kg/m2, continuous)	0.98 (0.95-1.02)	0.319
eGFR (continuous, ml/min/1.73m^2)	0.96 (0.94-0.97)	<0.001
Log average uACR (mg/mmol, continuous)	0.99 (0.99-1.00)	0.885

*Adjusted for age, sex, smoking, BMI, eGFR and uACR

5. Conclusions

1. Isolated CKD was rare even in this cohort recruited from primary care.
2. The presence of more comorbidities was independently associated with all-cause mortality.
3. Integrated care for people with CKD should recognise this complexity and consider treatment burden and patient capacity (including quality of life, function and balancing the overall benefit of interventions).

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52 ERA 351--FP

J3) Chronic Kidney Disease. Clinical Epidemiology.

Simon Fraser

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.