Risk of fracture in chronic kidney disease

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Background

Chronic kidney disease (CKD) is common and has many complications. One of these is renal bone disease. In those on renal replacement therapy (RRT) there is an increase in the risk of fracture[2]. Globally hip fractures are estimated to cost $25.3 billion by 2025 and have huge quality of life and mortality issues whether someone has CKD or otherwise. Common risk factors for hip fracture include older age and female sex.

However in those with CKD not yet requiring RRT the evidence regarding clinical impact (in terms of fractures rather than biochemical changes has not been so clear.

Objectives

We aimed to identify the risk of suffering a hip fracture in those with CKD and compare this to those with normal renal function. Thus to ascertain whether the effect of renal bone disease is a biochemical or sub-clinical one in those with less advanced CKD.

Methods

A large population based cohort (GLOMMS-II) was constructed using data linkage of patients' laboratory data to hospital episode and registry data.

GLOMMS-II contained all individuals with a low eGFR (<60ml/min/1.73m^2) measured in the Grampian health board region in 2003 (in 2/3 of these with "CKD" the low eGFR was present for at least 90 days, in 1/3 with "impaired eGFR" it was not); all those with raised PCR and ACR; all those receiving RRT and a 20,000 sample of those with only normal eGFR measurements in 2003. A sample of ~20,000 of those who had no measurement of renal function in 2003, but samples in both 1999-2002 and 2004-2009 were also available to allow assessment of the effect of a clinical indication for sampling or otherwise.

For those with stage 3a to stage 5 CKD in GLOMMS-II, data-linkage to hospital episode statistics from the index date in 2003 to 30th June 2009 for hip fractures (ICD-10 S72.x) and related procedures (OPCS-4 W19.1, W24.1, W37.1, W38.1 W39.1) allowed ascertainment of hip fracture rates. Poisson regression was used to calculate incidence rate ratios for first hip fracture post-index and the association with severity of CKD versus normal renal function were calculated, with adjustment for age and sex. Fracture-free survival was calculated.

Results

Demographics

As with CKD globally, those in this analysis with CKD were older and more likely to be female. Baseline characteristics shown below (Table 1).

Table 1

		Not CKD	All CKD 3-5 n(%)	CKD Stage 3a n(%)	Stage 3b n(%)	Stage 4 n(%)	Stage 5 n(%)
Number		19852	19523	12657	5275	1407	184
Sex	Males (%)	(47.1)	(35.2)	(36.0)	(32.9)	(35.1)	(45.1)
	Females (%)	(52.9)	(64.8)	(64.0)	(67.1)	(64.9)	(54.9)
Age (years)	Median (IQR)	53.1 (39.0- 65.5)	76.1 (68.7- 82.3)	74.4 (67.1- 80.8)	78.8 (72.2- 84.2)	80.5 (73.8- 86.2)	75.5 (64.0- 81.8)

Hip fracture

There were 1,078 individuals who sustained at least one hip fracture during follow-up. The cumulative fracture-free survival is shown in figure 1.

The number and rate of first-observed fracture during follow-up, and both unadjusted and adjusted rate ratios are shown in table 2, and these last in figure 2.

Figure 1

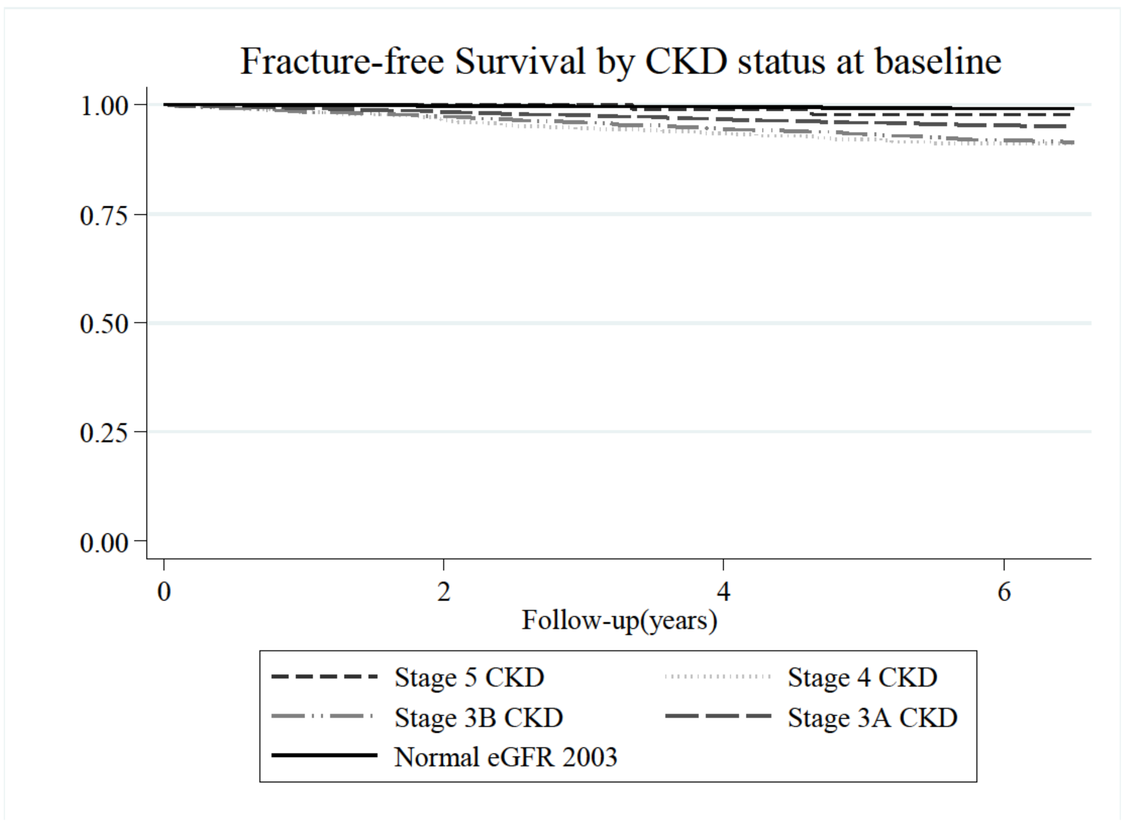
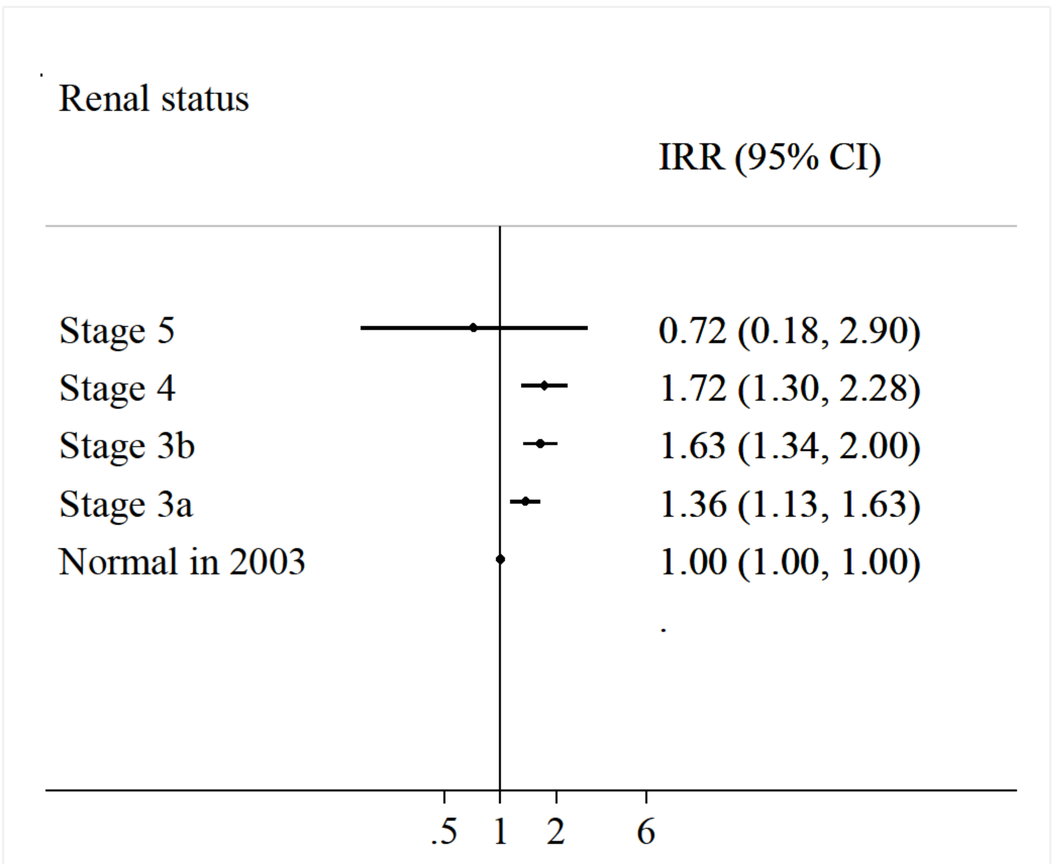


Table 2

CKD Stage	Fractures	Follow up (per person year)	Rate (per 100-person years)	Unadjusted Incidence Rate Ratio	95% CI	Adjusted: Sex,Age Incidence Rate Ratio	95% CI
Stage 5 CKD	2	606.8	0.330	2.22	(0.55- 8.96)	0.72	(0.18- 2.90)
Stage 4 CKD	77	4835.6	1.592	10.74	(8.20- 14.08)	1.72	(1.30- 2.28)
Stage 3B CKD	319	22632.8	1.409	9.51	(7.88- 11.47)	1.63	(1.34- 2.00)
Stage 3A CKD	515	63132.0	0.816	5.50	(4.62- 6.56)	1.36	(1.13- 1.63)
Normal	165	111303.7	0.148	1.00	Reference	1.00	Reference

Figure 2 Adjusted incidence rate ratios



Those with CKD had higher rates of hip fracture than those with normal renal function, this was partially confounded by the age and sex of those with CKD. However after correction for age and sex there still appeared to be a statistically significant increase in the risk of fractures even amongst those with stage 3a CKD.

Conclusions

As GLOMMS-II was a population based cohort with complete capture for a single health authority region, with complete follow-up for all still resident in Scotland, our findings are relevant to others practicing elsewhere in Europe.

Even those with less advanced CKD should be considered at increased risk of fractures. Future trials of fracture prevention should investigate how best to minimise this risk.

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