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Abstract

INTRODUCTION AND AIMS: Patients with renal impairment have risk of not only end-stage kidney diseases but also cardiovascular diseases (CVD). Though renal function is strongly dependent on ageing, the current staging of chronic kidney disease (CKD) do not include the age of patients. We have few evidences to show CVD mortality in with long-term follow-up for determination of nephrology referral policy according to the age of CKD patients.

METHODS: To examine age-dependency in CVD mortality among renal impaired patients, we observed the general population included a total of 97,043 persons (33,131 men and 63,912 women) aged 40-80 years living in Ibaraki prefecture that participated in annual community-based health checkups in 1993, and followed-up for 17.1 years.

RESULTS: The number of all-causes death was 15,172 (8,718 for men and 6,454 for women) and those of CVD death were 4,153 (2,189 for men and 1,964 for women). Hazard ratio (95% confidence interval) for death from CVD events according to estimated glomerular filtration rate (eGFR) categorization is; in male elders (age over 70 years), eGFR 50-59: 1.15 (0.98-1.35), eGFR 40-49: 1.01 (0.74-1.40), eGFR 30-39: 1.75 (1.09-2.19), eGFR <30: 0.97 (0.24-3.96); in female elders, eGFR 50-59: 1.10 (0.98-1.21), eGFR 40-49: 1.42 (1.17-1.72), eGFR 30-39: 1.83 (1.28-2.59), eGFR <30: 3.83 (1.89-7.73); in male non-elders (age 40 to 69 years), eGFR 50-59: 1.09 (0.93-1.28), eGFR 40-49: 1.70 (1.23-2.36), eGFR 30-39: 2.03 (0.95-4.29), eGFR <30: 3.31 (1.35-8.11); in female non-elders, eGFR 50-59: 1.04 (0.93-1.16), eGFR 40-49: 1.55 (1.20-2.01), eGFR 30-39: 2.13 (1.23-3.70), eGFR <30: 2.99 (1.40-6.41).

CONCLUSIONS: In 2012, the Japanese Societies of Nephrology (JSN) addressed non-elders with eGFR over 50 ml/min/1.73m² and elders with eGFR over 40 ml/min/1.73m² were not essentially referred to nephrologists unless they have significant proteinuria. Our results support the statement from JSN that eGFR- and age-dependent risk-management in persons with moderately decreased renal function (CKD G3).

Objectives

To clarify CVD mortality and risk in advanced CKD patients (G3).

Methods

Recruit; 97,043 persons (33,131 men and 63,912 women) aged 40-80 years living in Ibaraki prefecture in 1993
Follow-up; 17.1 years (the end of 2013)
Death causes; ICD-9 or ICD-10 based

Study populations

		Estimated glomerular filtration rate (ml/min/1.73m ²)					P for trend
		60≤	50-59	40-49	30-39	30>	
Men							
Number	(persons)	26904	2870	456	96	39	
Age	(years)	59.5	65.3	67.9	70.1	66.5	<0.001
Body mass index	(kg/m ²)	23.2	23.8	24.0	23.8	22.6	<0.001
Systolic blood pressure	(mmHg)	135.9	139.7	141.5	143.2	144.2	<0.001
Diastolic blood pressure	(mmHg)	80.8	82.2	82.4	82.7	83.0	<0.001
Blood glucose	(mg/dl)	116.3	122.5	124.0	129.0	118.6	<0.001
Total cholesterol	(mg/dl)	192.5	196.4	196.3	192.4	184.5	<0.001
High-density lipoprotein	(mg/dl)	52.9	49.5	47.6	47.4	47.8	<0.001
Triglycerides	(mg/dl)	148.3	159.5	165.5	155.2	148.5	<0.001
Antihypertensive drug use	(%)	17.6	33.1	45.6	56.3	59.0	<0.001
Diabetic Treatment	(%)	3.4	5.4	7.9	10.4	12.8	<0.001
Lipid-lowering drug use	(%)	1.1	2.2	1.8	6.3	2.6	<0.001
Current smoker	(%)	52.4	42.6	38.2	40.7	56.4	<0.001
Daily alcohol consumption	(%)	54.0	39.3	32.9	37.5	28.2	<0.001
Women							
Number	(persons)	47639	10104	1165	204	70	
Age	(years)	55.8	65.7	66.4	69.1	65.8	<0.001
Body mass index	(kg/m ²)	23.5	24.0	24.3	24.4	23.8	<0.001
Systolic blood pressure	(mmHg)	130.5	137.4	137.9	141.1	144.4	<0.001
Diastolic blood pressure	(mmHg)	77.4	79.1	79.3	80.0	79.8	<0.001
Blood glucose	(mg/dl)	106.4	115.3	118.7	126.4	117.5	<0.001
Total cholesterol	(mg/dl)	206.1	214.5	213.9	215.0	207.5	<0.001
High-density lipoprotein	(mg/dl)	57.3	55.0	53.5	51.2	48.5	<0.001
Triglycerides	(mg/dl)	130.4	151.3	155.8	171.4	167.5	<0.001
Antihypertensive drug use	(%)	17.6	33.1	45.6	56.3	59.0	<0.001
Diabetic Treatment	(%)	1.8	3.6	4.3	5.9	8.6	<0.001
Lipid-lowering drug use	(%)	2.7	5.1	5.3	3.9	8.6	<0.001
Current smoker	(%)	5.0	4.1	5.9	5.4	8.5	<0.001
Daily alcohol consumption	(%)	3.8	2.6	2.5	1.5	0.0	<0.001

Discussion

In 2012, the Japanese Societies of Nephrology (JSN) addressed non-elders (<69 years-old) with eGFR over 50 ml/min/1.73m² and elders (>70 years-old) with eGFR over 40 ml/min/1.73m² were not essentially referred to nephrologists unless they have significant proteinuria. It seems to be reasonable in light of CVD risk analyses in this study.

Conclusions;

Advanced CKD (namely CKD G3b and a part of G3a) is a risk of CVD mortality in Japan.

COI disclosure: None

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Background

"The relationships of proteinuria, serum creatinine, glomerular filtration rate with cardiovascular disease mortality in Japanese general population"

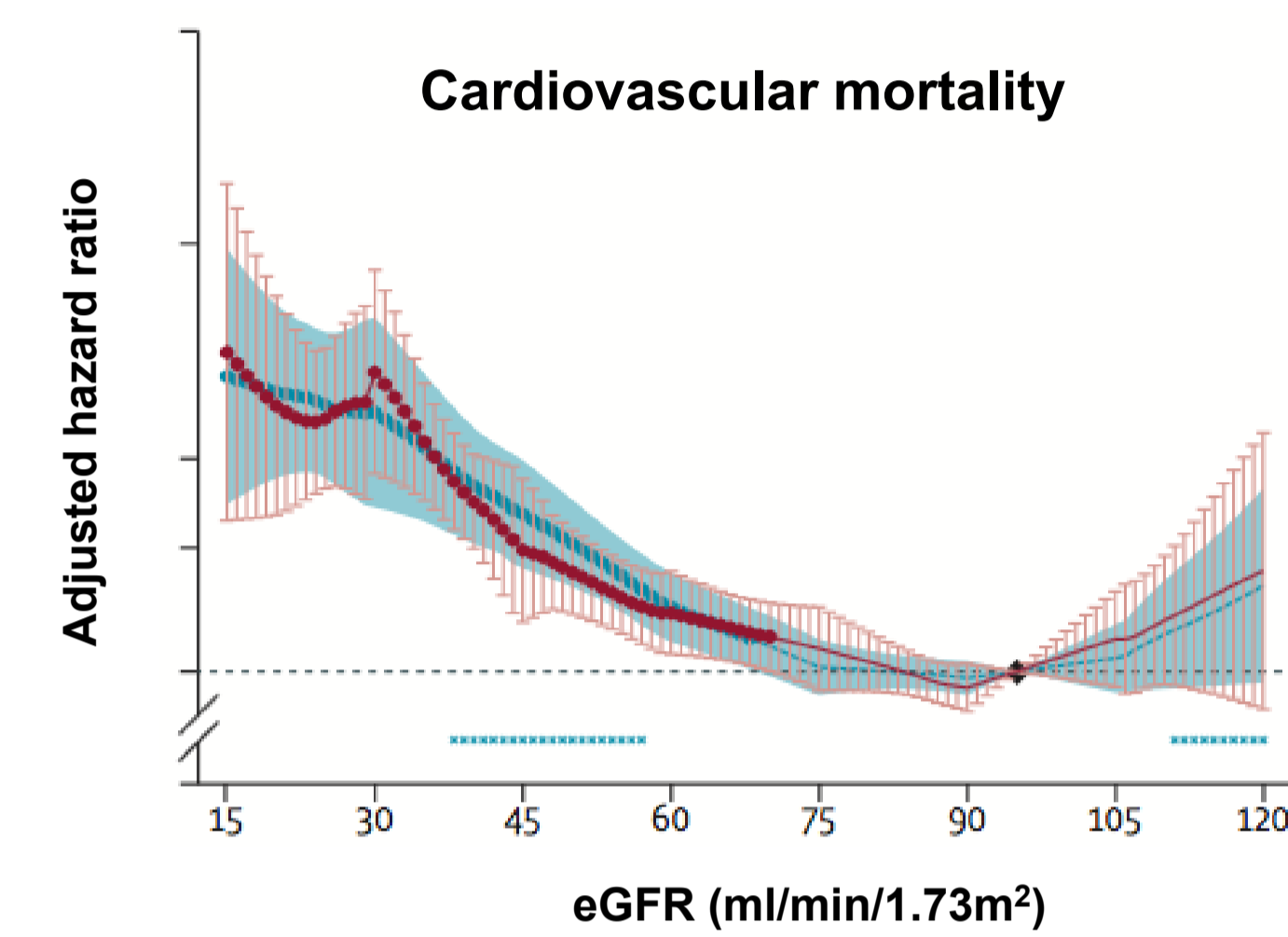
F Irie et al. *Kidney Int* 69:1264-1271.2006

Urinary protein	GFR and urinary protein categories					
	+ or more		-		+ or more	
	>60	<60	>60	<60	>60	<60
Creatinine	RR	95% CI	RR	95% CI	RR	95% CI
Men						
Number at risk	28812	804	680	122		
All causes						
No. of deaths	859	46	64	15		
Age-adjusted RR	1.00	1.74 (1.29-2.34)	1.66 (1.29-2.15)	2.79 (1.68-4.66)		
Multivariable RR*	1.00	1.39 (1.03-1.88)	1.53 (1.18-1.98)	2.15 (1.28-3.60)		
P for interaction			0.99			
All causes						
No. of deaths	3440	171	184	52		
Age-adjusted RR	1.00	1.66 (1.42-1.94)	1.32 (1.14-1.54)	2.64 (2.01-3.48)		
Multivariable RR*	1.00	1.50 (1.29-1.76)	1.33 (1.14-1.55)	2.44 (1.85-3.21)		
P for interaction			0.31			
Women						
Number at risk	57068	839	1874	164		
All causes						
No. of deaths	766	36	123	23		
Age-adjusted RR	1.00	2.45 (1.75-3.42)	1.72 (1.42-2.09)	3.34 (2.49-4.49)		
Multivariable RR*	1.00	2.02 (1.44-2.83)	1.58 (1.30-1.93)	4.00 (2.62-6.10)		
P for interaction			0.47			
All causes						
No. of deaths	2626	90	298	45		
Age-adjusted RR	1.00	1.91 (1.55-2.35)	1.47 (1.30-1.66)	3.24 (2.49-4.19)		
Multivariable RR*	1.00	1.74 (1.40-2.14)	1.40 (1.24-1.58)	2.89 (2.14-3.89)		
P for interaction			0.42			

Proteinuria, reduced GFR (<60 ml/min/1.73m²) and their combination were significant predictor of CVD mortality.

"Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis"

CKD-PC. *Lancet* 380:1662-1673.2012



Participants: 1,024,977 from 43 cohorts
Follow-up: 9.2 (S.D. 4.9) years
Reference: 95 ml/min/1.73m²

Adjusted for age, sex, race, smoking, history of CVD, serum cholesterol level, BMI, albuminuria

Advanced CKD was risk of CVD death.

The CVD mortality in each CKD category had been not clarified in Japan.

Results

Figure 1. Rate distribution of CVD and non-CVD mortality by eGFR categorization in men and women.

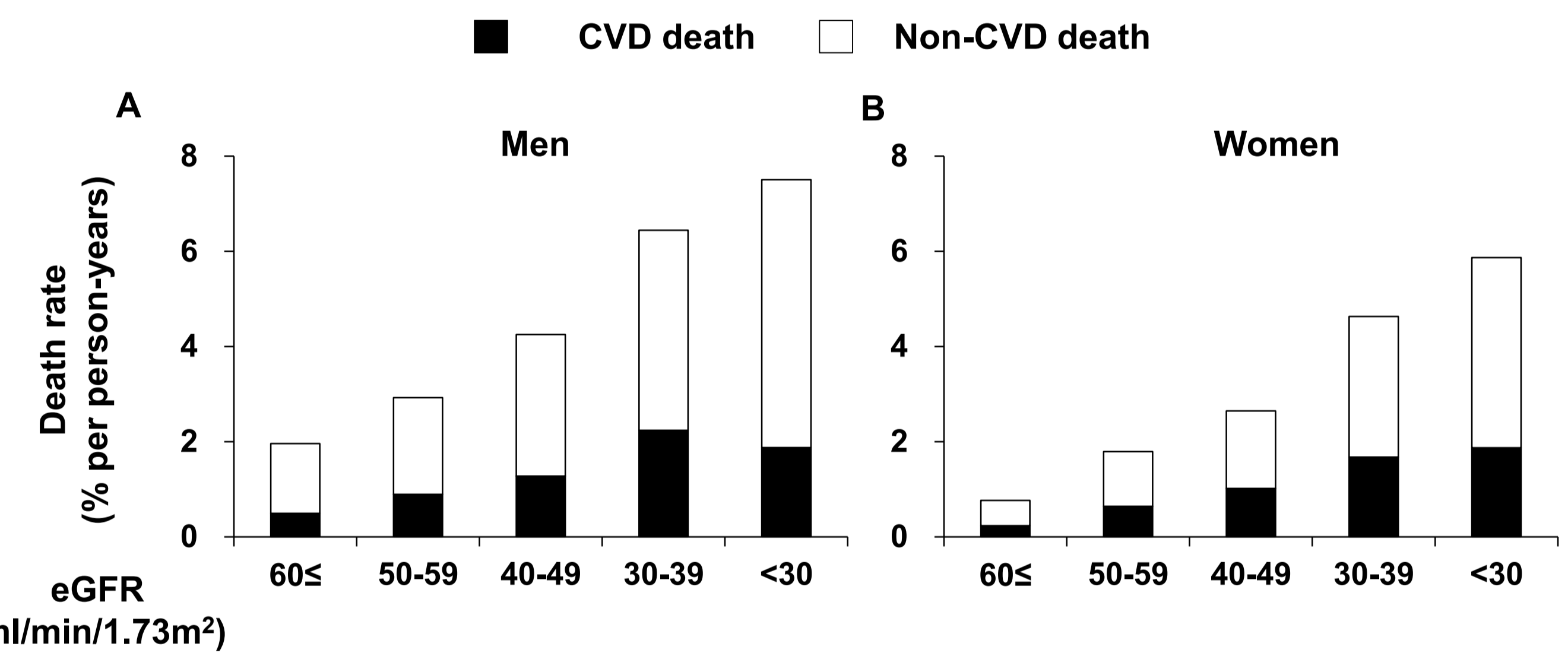
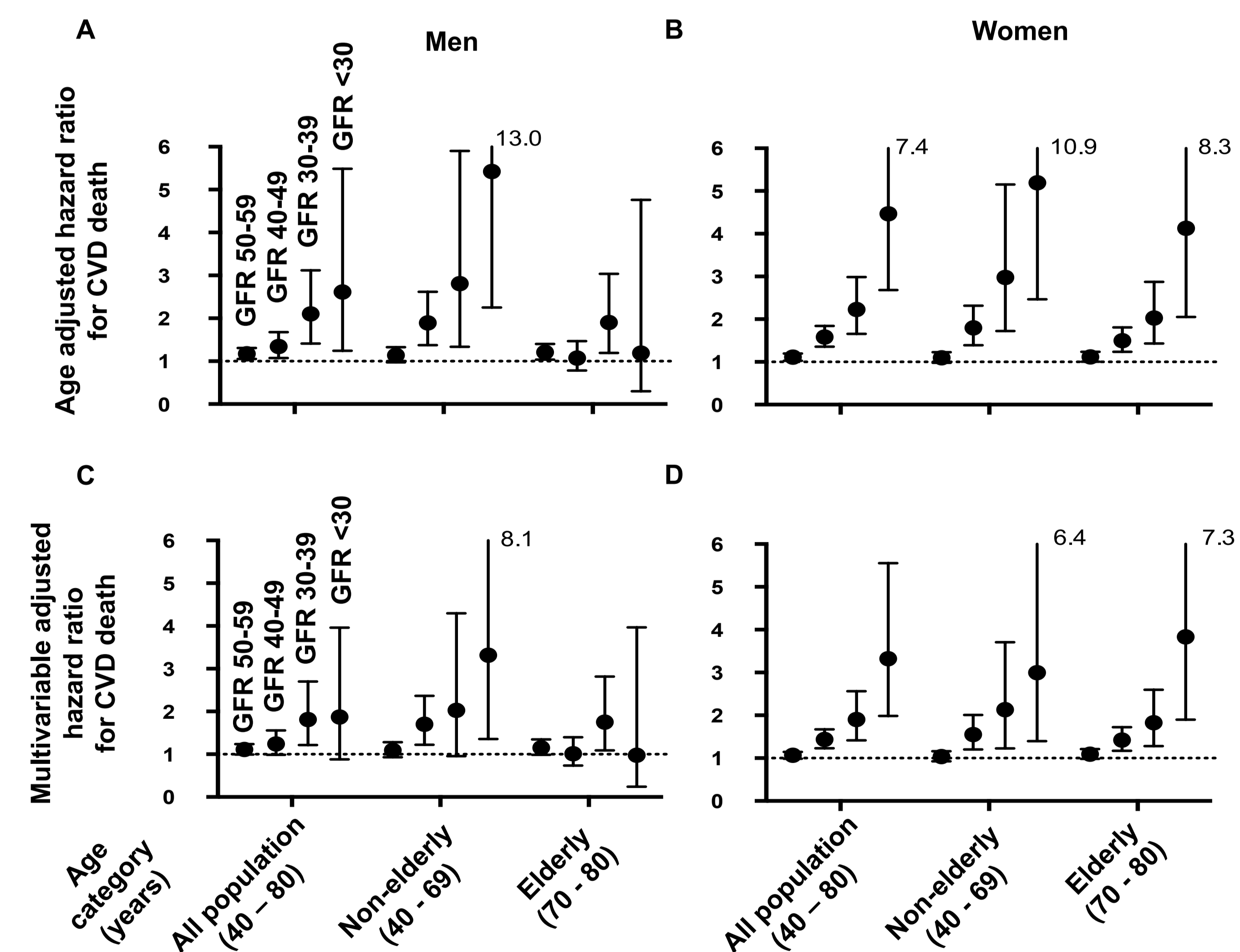


Figure 2. Risk of CVD mortality by eGFR- and age-categorization



Age-adjusted (A and B) and multivariable-adjusted hazard ratio (HR) (C and D) for CVD death was demonstrated with all ages, non-elders or elders in men and in women. Every HR was calculated by comparing to the subpopulation with eGFR≥60 ml/min/1.73m² as reference. Adjusted factors for CVD death are age, body mass index, urinary protein, blood pressure, use of anti-hypertensive drugs, triglyceride, high-density lipoprotein, total cholesterol, use of lipid lowering drugs, blood glucose, treatment for diabetes, smoking, alcohol consumption (C and D).

