The combination of kidney function and kidney size in relation to kidney function decline and risk of cardiovascular events and all-cause mortality in patients with clinical manifest vascular disease

Nicolette G.C. van der Sande[1,2], Frank F.L. Visseren[1], Peter J. Blankestijn[2]

On behalf of the SMART Study Group
[1] Department of Vascular Medicine, University Medical Centre Utrecht, the Netherlands
[2] Department of Nephrology and Hypertension, University Medical Centre Utrecht, the Netherlands

Correspondence: n.g.c.vandersande-4@umcutrecht.nl

Introduction

Estimated glomerular filtration rate (eGFR) is related to cardiovascular events and all-cause mortality.[1,2] However interpretation of eGFR can be challenging due to physiological decline with age. The combination of eGFR and kidney size reflects the capacity to filtrate per kidney volume or length, providing more insight on the health of the kidney. Therefore the ratio of eGFR to kidney size in relation to kidney function decline and the risk of cardiovascular events and all-cause mortality was evaluated in patients with clinical manifest vascular disease.

Methods

A prospective cohort study in 6904 patients enrolled in the SMART study with symptomatic arterial disease was performed. In 1469 patients with follow up measurements of kidney function linear regression analysis was used to quantify the relation between $eGFR/cm^3$, $eGFR/cm$ and annual kidney function decline. Cox proportional hazard models were used to determine the relation between $eGFR/cm^3$, $eGFR/cm$ and cardiovascular events and all-cause mortality.

Table | Sex pooled baseline characteristics by quartiles of $eGFR/cm^3$

eGFR/mean kidney volume	Quartile 1 (n = 1667)	Quartile 2 (n = 1666)	Quartile 3 (n= 1665)	Quartile 4 (n= 1667)
Men, range ($eGFR/cm^3$)	0.08-0.36	0.36-0.44	0.44-0.53	0.53-1.09
Women, range ($eGFR/cm^3$)	0.11-0.45	0.44-0.54	0.54-0.65	0.65-1.46
Age (years)	64 (9)	61 (10)	59 (10)	56 (11)
Male, n	1228 (74)	1228 (74)	1227 (74)	1228 (74)
History of cardiovascular disease				
Cerebrovasculair disease, n (%)	493 (30)	497 (30)	483 (29)	491 (29)
Coronary heart disease, n (%)	1036 (62)	1001 (60)	1021 (61)	946 (57)
Abdominal aortic aneurysm, n (%)	230 (14)	137 (8)	95 (6)	100 (6)
Peripheral arterial disease, n (%)	320 (19)	313 (19)	311 (19)	344 (21)
Smoking current or past, n (%)	1349 (81)	1309 (79)	1331 (80)	1308 (78)
Diabetes mellitus, n (%)	419 (25)	289 (17)	249 (15)	204 (12)
Body mass index (kg/m^2)	28 (4)	27 (4)	27 (4)	25.1 (4)
Systolic blood pressure (mmHg)	144 (22)	141 (20)	139 (21)	138 (20)
Diastolic blood pressure (mmHg)	82 (12)	81 (11)	81 (11)	81 (11)
eGFR (mL/min/1.73m^2)	63 (17)	75 (14)	80 (14)	87 (13)
Albuminuria, n (%)	421 (25)	260 (16)	243 (15)	189 (11)
LDL-cholesterol (mmol/L)	2.8 (1.0)	3.0 (1.1)	2.9 (1.0)	2.9 (1.1)
HDL-cholesterol (mmol/L)	1.2 (0.3)	1.2 (0.4)	1.2 (0.4)	1.3 (0.4)
Use of blood pressure-lowering agents	1387 (83)	1222 (73)	1186 (71)	1074 (64)
ACE-inhibitor, n (%)	614 (37)	464 (28)	448 (27)	384 (23)
Angiotensin II receptor blockers, n (%)	238 (14)	162 (10)	137 (8)	92 (6)
Use of glucose-lowering agents, n (%)	261 (16)	180 (11)	154 (9)	125 (8)
Use of lipid-lowering-drugs, n (%)	1154 (69)	1076 (65)	1108 (67)	1057 (63)
Left kidney length (cm)	11.5 (1.2)	11.4 (1.0)	11.2 (1.0)	10.9 (0.9)
Right kidney length (cm)	11.4 (1.2)	11.3 (1.0)	11.1 (1.0)	10.8 (0.9)
Left kidney volume (cm^3)	199 (59)	179 (43)	160 (37)	136 (31)
Right kidney volume (cm^3)	199 (60)	176 (45)	157 (37)	133 (32)

Values are presented as mean (standard deviation), median (interquartile range), or count (percentage)

Figure 1 | Relation between $eGFR/cm^3$, $eGFR/cm$ and kidney function decline

	Annual kidney function decline	
	Absolute decline (mL/min/1.73m^2 per year)	Percentage decline (% per year)
$eGFR/cm^3$ per SD (n=1469)	-0.52 (-0.63 - -0.40)	-0.58 (-0.73 - -0.43)
$eGFR/cm^3$ < eGFR (n=466)	-0.97 (-1.29 - -0.65)	-0.95 (-1.32 - -0.58)
$eGFR/cm^3$ = eGFR (n=534)	-0.86 (-1.02 - -0.69)	-0.99 (-1.23 - -0.75)
$eGFR/cm^3$ > eGFR (n=469)	-0.47 (-0.68 - -0.26)	-0.56 (-0.87 - -0.26)
$eGFR/cm$ per SD (n=1469)	-0.81 (-0.91 - -0.70)	-0.85 (-0.99 - -0.71)
$eGFR/cm$ < eGFR (n=229)	-0.74 (-0.99 - -0.49)	-0.68 (-0.97 - -0.40)
$eGFR/cm$ = eGFR (n=1012)	-0.83 (-0.99 - -0.68)	-0.93 (-1.14 - -0.71)
$eGFR/cm$ > eGFR (n=228)	-0.67 (-0.90 - -0.45)	-0.78 (-1.10 - -0.46)

Results are adjusted for age, sex, diabetes, albuminuria, systolic blood pressure, body mass index and smoking. SD: standard deviation

Results

Mean annual change in eGFR was -0.79 mL/min/1.73m^2 per year, indicating a yearly decline. Compared to $eGFR/cm$, $eGFR/cm^3$ showed higher dispersion in relation to eGFR (figure 1). High $eGFR/cm^3$ and $eGFR/cm$, were significantly related to annual kidney function decline, -0.52 (CI -0.63 - -0.40) and -0.81 (CI -0.91 - -0.70) mL/min/1.73m^2 per year respectively. A total of 1012 cardiovascular events occurred and 1119 patients died. Overall, $eGFR/cm^3$, $eGFR/cm$ and all-cause mortality followed a U-shaped curve (figure 2). Low $eGFR/cm^3$ and $eGFR/cm$ were related to the occurrence of subsequent cardiovascular events.

Figure 2 | Relation between $eGFR/cm^3$, $eGFR/cm$ and all-cause mortality

Results are adjusted for age, sex, diabetes, albuminuria, systolic blood pressure, body mass index and smoking
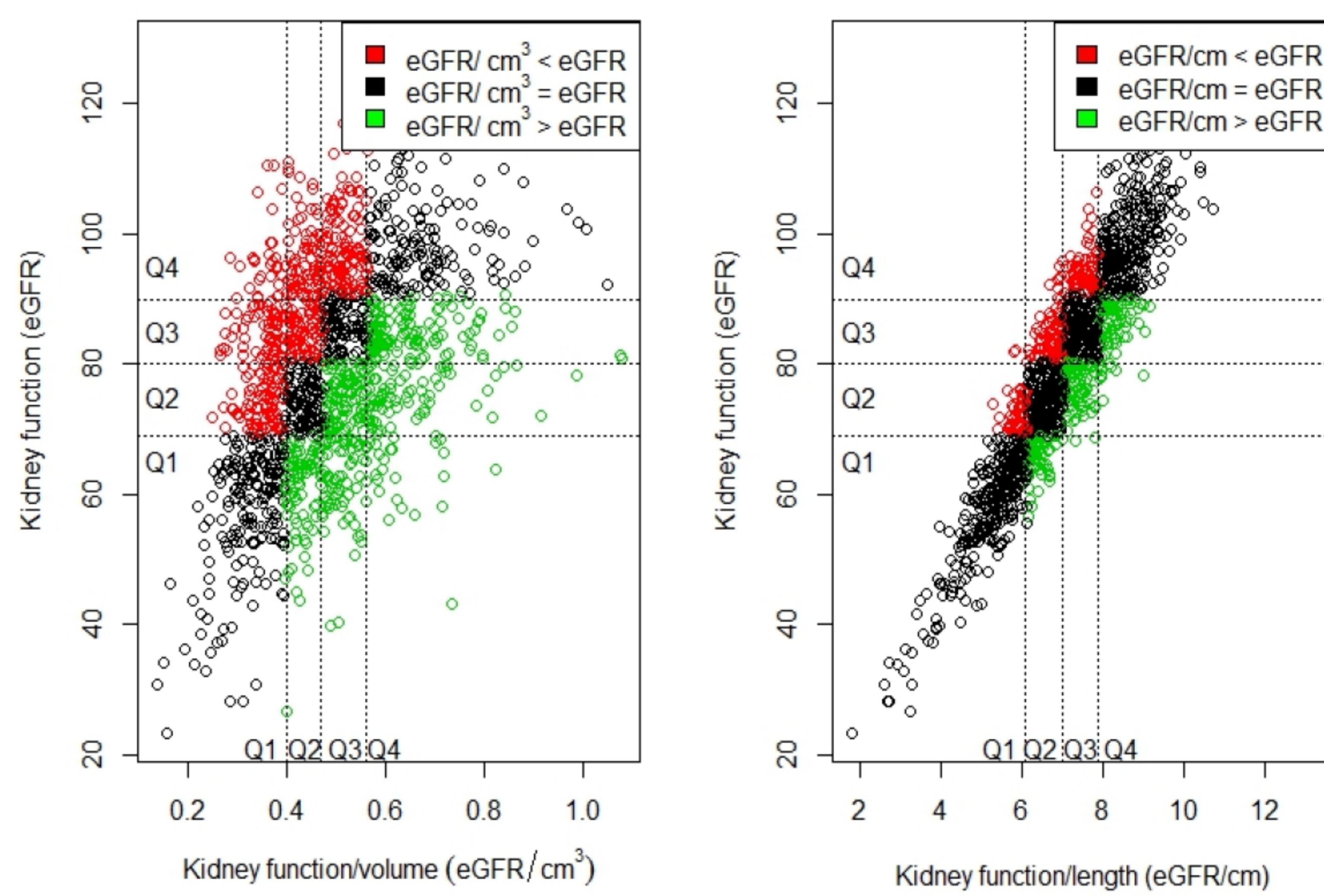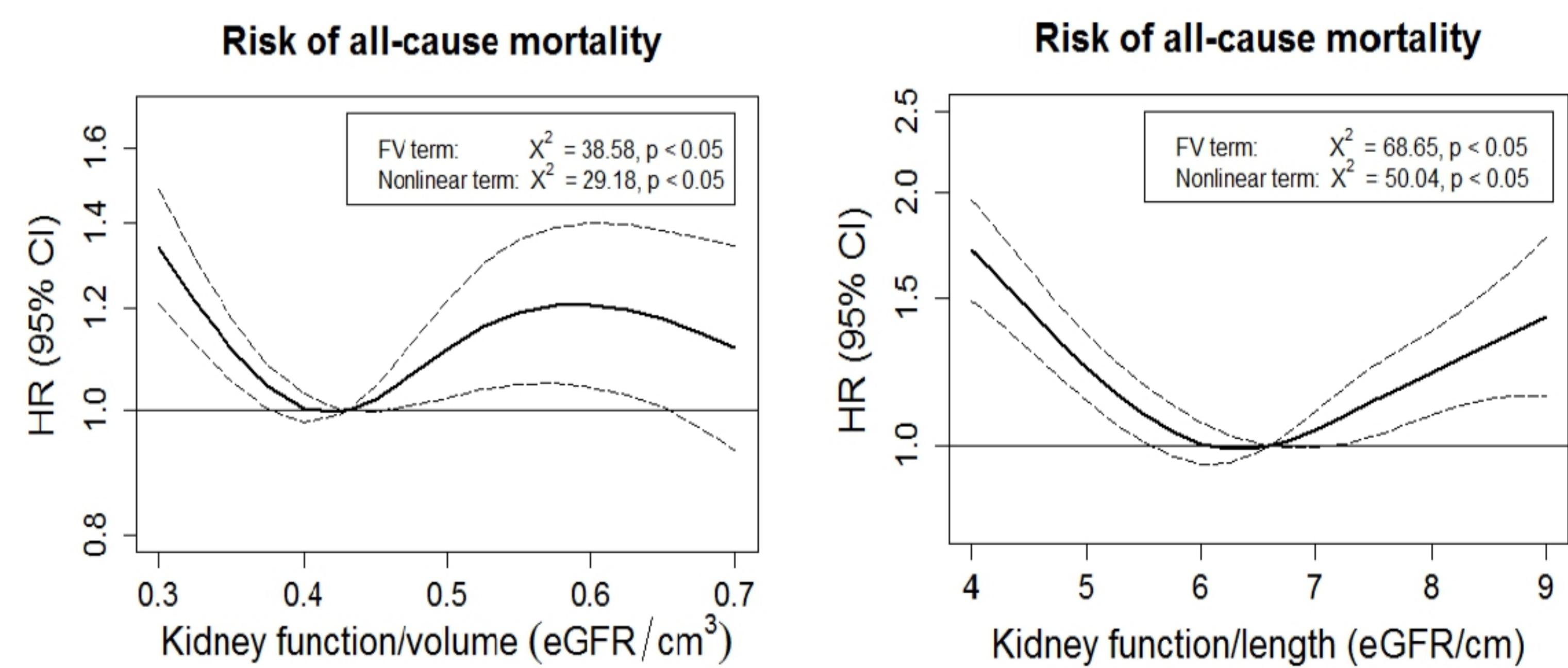
Conclusions

High $eGFR/cm^3$ and $eGFR/cm$, indications of glomerular hyperfiltration, are related to annual kidney function decline and all-cause mortality in patients with clinical manifest vascular disease. The combination of kidney function and size may be useful as an early marker of kidney deterioration and a risk factor for cardiovascular events and mortality.

References

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University Medical Center Utrecht

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Nicolette van der Sande

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