SUPPLEMENTAL MATERIAL

Etiology and outcome of ischemic stroke in patients with renal impairment including chronic kidney disease: Japan Stroke Data Bank

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sTable e-1. Subgroup analysis of renal impairment on the unfavorable outcome in cardioembolic stroke

	eGFR categories		**Proteinuria**	
	Odds ratio (95% confidence interval)	$P_{interaction}$	Odds ratio (95% confidence interval)	$P_{interaction}$
Age, years				
>75	1.37 (0.98 – 1.93)	0.635	3.20 (1.82 – 5.61)	0.710
≤75	1.17 (0.69 – 1.97)		3.74 (1.47 – 9.51)	
Sex				
Male	1.20 (0.85 – 1.68)	0.207	3.18 (1.79 – 5.65)	0.815
Female	1.67 (1.03 – 2.72)		3.38 (1.38 – 8.21)	
Hypertension				
Yes	1.19 (0.86 – 1.49)	0.425	3.01 (1.74 – 5.23)	0.355
No	1.41 (0.89 – 2.23)		4.19 (1.55 – 11.3)	
Diabetes				
Yes	1.15 (0.66 – 1.99)	0.206	1.71 (0.68 – 4.30)	0.120
No	1.41 (1.01 – 1.95)		4.05 (2.25 – 7.29)	
History of stroke				
Yes	1.33 (0.78 – 2.26)	0.926	3.05 (1.11 – 8.39)	0.355
No	1.29 (0.95 – 1.76)		3.68 (2.10 – 6.47)	
Previous antiplatelet use				
Yes	1.77 (1.07 – 2.93)	0.164	3.39 (1.26 – 9.09)	0.971
No	1.12 (0.80 – 1.57)		3.45 (1.96 – 6.07)	
Previous anticoagulant use				
Yes	1.18 (0.76 – 1.83)	0.813	2.43 (1.04 – 5.61)	0.540
No	1.41 (0.98 – 2.01)		4.13 (2.27 – 7.50)	
Previous statin use				
Yes	0.79 (0.46 – 1.36)	0.015	2.76 (1.23 – 6.21)	0.598
No	1.59 (1.14 – 2.18)		3.49 (1.93 – 6.31)	
Premorbid mRS				
>1	1.26 (0.73 – 2.17)	0.698	4.78 (0.98 – 23.4)	0.540
≤1	1.36 (0.99 – 1.86)		3.04 (1.83 – 5.03)	
NIHSS				

>4	1.26 (0.65 – 1.19)	0.748	4.25 (1.66 – 10.8)	0.960
≤4	1.39 (0.89 – 2.15)		3.01 (1.82 – 4.98)	

Abbreviations: eGFR, estimated glomerular filtration rate; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin scale

The model for unfavorable outcomes included age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid mRS, and initial NIHSS.

sTable e-2. Subgroup analysis of renal impairment on the unfavorable outcome in small vessel occlusion

	eGFR categories		**Proteinuria**	
	Odds ratio (95% confidence interval)	$P_{interaction}$	Odds ratio (95% confidence interval)	$P_{interaction}$
Age, years				
>75	1.33 (0.81 – 2.19)	0.247	1.74 (0.58 – 5.17)	0.994
≤75	1.22 (0.65 – 2.28)		1.37 (0.47 – 4.00)	
Sex				
Male	1.19 (0.76 – 1.86)	0.521	1.18 (0.49 – 2.82)	0.421
Female	1.64 (0.74 – 3.61)		4.94 (0.61 – 26.8)	
Hypertension				
Yes	1.26 (0.79 – 1.16)	0.731	1.38 (0.57 – 3.36)	0.937
No	1.30 (0.60 – 2.80)		1.88 (0.37 – 9.63)	
Diabetes				
Yes	1.86 (0.99 – 3.49)	0.021	2.24 (0.54 – 9.31)	0.964
No	0.95 (0.57 – 1.57)		1.69 (0.58 – 4.95)	
History of stroke				
Yes	1.26 (0.64 – 2.46)	0.800	4.34 (0.79 – 23.8)	0.112
No	1.31 (0.81 – 2.11)		1.07 (0.42 – 2.70)	
Previous antiplatelet use				
Yes	1.69 (0.91 – 3.17)	0.697	5.86 (1.27 – 27.1)	0.045
No	1.05 (0.63 – 1.74)		0.93 (0.34 – 2.55)	
Previous statin				
Yes	1.25 (0.56 – 2.78)	0.874	2.82 (0.53 – 15.1)	0.310
No	1.32 (0.85 – 2.05)		1.26 (0.52 – 3.07)	
Premorbid mRS				
>1	1.79 (0.98 – 3.30)	0.632	15.1 (1.79 – 128.4)	0.887
≤1	1.41 (0.93 – 2.15)		1.32 (0.62 – 2.79)	
NIHSS				
>4	1.35 (0.73 – 1.15)	0.362	1.39 (0.53 – 3.67)	0.233
≤4	1.58 (1.03 – 2.42)		1.97 (0.77 – 4.97)	

Abbreviations: eGFR, estimated glomerular filtration rate; NIHSS, National Institute of Health

Stroke Scale; mRS, modified Rankin scale

The model for unfavorable outcomes included age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid mRS, and initial NIHSS.

sTable e-3. Associations with ischemic stroke subtypes, unfavorable outcome and mortality of patients receiving hemodialysis

	Ischemic stroke subtype	p	**Unfavorable outcome**	p	**In-hospital death**	p
	Odds ratio (95% confidence interval		Odds ratio (95% confidence interval		Odds ratio (95% confidence interval	
Cardioembolic stroke						
Crude model	1.46 (1.06 – 2.02)	0.019	2.07 (1.17 – 3.65)	0.012	1.60 (0.67 – 3.83)	0.283
Adjusted model	1.67 (1.14 – 2.45)	0.007	2.13 (1.06 – 4.28)	0.034	1.16 (0.43 – 3.15)	0.774
Large artery stroke						
Crude model	0.72 (0.51 – 1.02)	0.068	2.09 (1.12 – 3.91)	0.021	1.71 (0.23 – 12.9)	0.605
Adjusted model	0.64 (0.44 – 0.93)	0.019	1.96 (0.85 – 4.51)	0.115	2.16 (0.26 – 18.1)	0.476
Small vessel occlusion						
Crude model	0.94 (0.67 – 1.32)	0.720	2.47 (1.36 – 4.50)	0.003	NE	-
Adjusted model	0.94 (0.66 – 1.32)	0.704	1.87 (0.81 – 4.31)	0.141	NE	-
Other determined etiology stroke						
Crude model	0.86 (0.56 – 1.32)	0.498	2.41 (1.10 – 5.31)	0.028	NE	-
Adjusted model	0.93 (0.60 – 1.45)	0.744	1.04 (0.36 – 3.01)	0.939	NE	-
Undetermined etiology stroke						
Crude model	1.63 (0.69 – 3.86)	0.261	0.73 (0.21 – 2.58)	0.632	NE	-
Adjusted model	1.50 (0.62 – 3.66)	0.369	0.98 (0.16 – 5.88)	0.986	NE	-

An eGFR of 60 mL/min/1.73 m^2 was used as a reference.

The model for ischemic stroke subtypes was adjusted for age, sex, hypertension, diabetes, previous statin use, and atrial fibrillation. The model for

unfavorable functional outcomes was adjusted for age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid modified Rankin scale (mRS), and initial National Institutes of Health Stroke Scale (NIHSS).

NE = not evaluable

Figure legends

sFigure e-1. Patient flow chart

sFigure e-2. Associations between all eGFR levels and ischemic stroke subtypes (large artery stroke, other determined etiology stroke, and undetermined etiology stroke)

Odds ratios (OR) for the proportion of (A) large artery stroke, (B) other determined etiology stroke, and (C) undetermined etiology stroke by eGFR (per ml/min/1.73 m^2) using restricted cubic splines. Risk estimates were adjusted for age, sex, hypertension, diabetes, previous statin use, and atrial fibrillation. Solid lines represent the OR and dashed lines represent 95% CI. Knots were placed at 30, 45, and 60 mL/min/1.73 m^2 of eGFR. An eGFR of 60 mL/min/1.73 m^2 was used as a reference.

Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation.

sFigure e-3. Associations of joint eGFR and proteinuria with ischemic stroke subtypes

Odds ratio of renal impairment (eGFR [≥60/<60 mL/min/1.73 m^2] with/without proteinuria) for the proportion of ischemic stroke subtypes. The category of eGFR ≥60 mL/min/1.73 m^2 without proteinuria was set as a reference. Risk estimates were adjusted for age, sex, hypertension, diabetes, previous statin use, and atrial fibrillation

Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation.

sFigure e-4. Associations between renal impairment and unfavorable functional outcome in ischemic stroke subtypes in patients not receiving hemodialysis

Odds ratio of renal impairment (eGFR 45-59 mL/min/1.73 m^2, eGFR <45 mL/min/1.73 m^2, decreases in eGFR, or proteinuria) vs. eGFR ≥60 mL/min/1.73 m^2 or non-proteinuria for unfavorable functional outcomes in ischemic stroke subtypes

Risk estimates were adjusted for age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid mRS and initial NIHSS.

Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale

sFigure e-5. Associations between eGFR levels and unfavorable functional outcomes in ischemic stroke subtypes (large artery stroke, other determined etiology stroke, and undetermined etiology stroke)

Odds ratios (OR) for unfavorable functional outcomes after (A) large artery stroke, (B) other determined etiology stroke, and (C) undetermined etiology stroke by eGFR (per ml/min/1.73 m^2) using restricted cubic splines. Risk estimates were adjusted for age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and

endovascular treatment, premorbid mRS score, and initial NIHSS score. Solid lines represent the OR and dashed lines represent 95% CI. Knots were placed at 30, 45, and 60 mL/min/1.73 m^2 of eGFR. An eGFR of 60 mL/min/1.73 m^2 was used as a reference.
Abbreviations: eGFR, estimated glomerular filtration rate; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin scale.

sFigure-6. Associations between joint eGFR and proteinuria with unfavorable functional outcome

Odds ratio of renal impairment (eGFR [≥60/<60 mL/min/1.73 m^2] with/without proteinuria) for unfavorable functional outcomes in ischemic stroke subtypes. The category of eGFR ≥60 mL/min/1.73 m^2 without proteinuria was set as a reference. Risk estimates were adjusted for age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid mRS and initial NIHSS.
Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation.

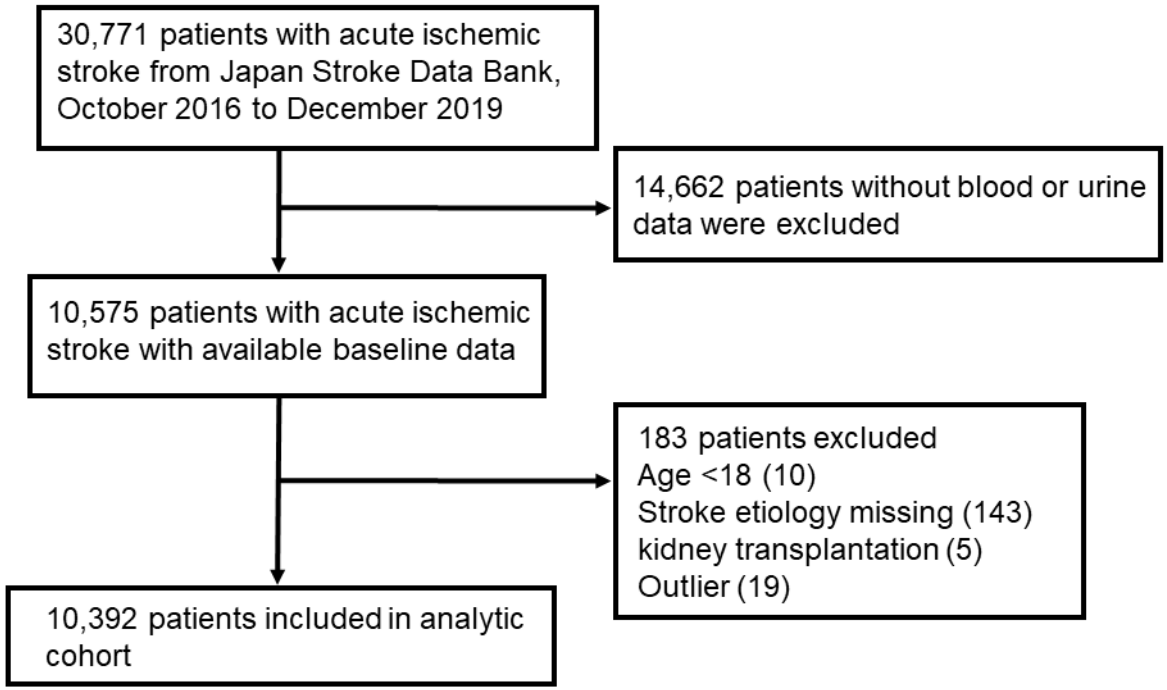
sFigure e-7. Proportions of in-hospital death in ischemic stroke etiologies according to the eGFR categories (eGFR <60, eGFR 45-59, eGFR <45, mL/min/1.73 m^2) or proteinuria

Distribution of in-hospital death in ischemic stroke subtypes according to eGFR strata and proteinuria
Abbreviations: eGFR; estimated glomerular filtration rate

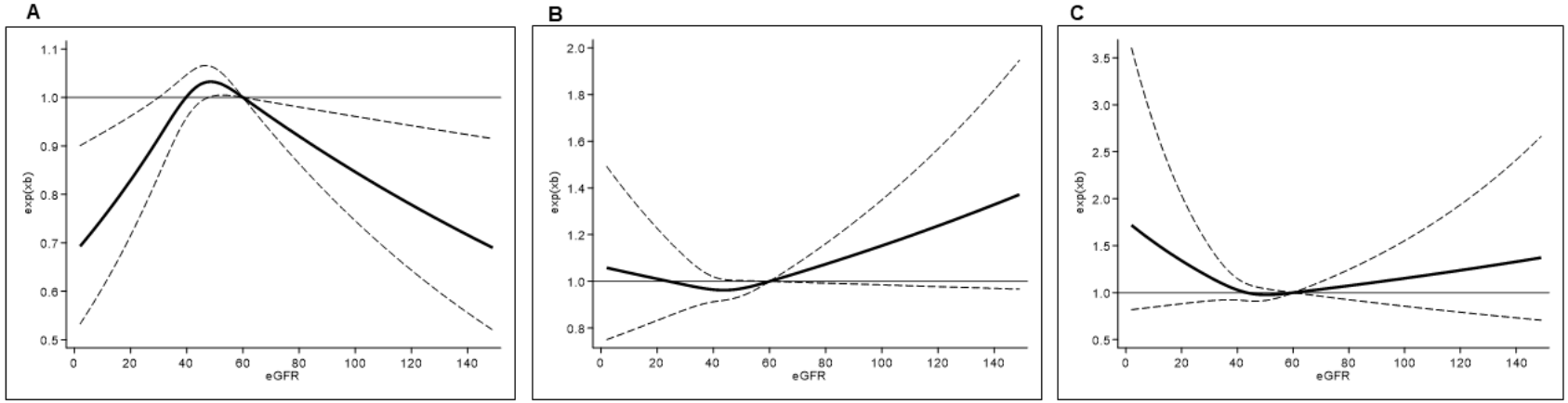
sFigure e-8. Associations between renal impairment and in-hospital death in ischemic stroke subtypes

Odds ratio of renal impairment (eGFR 45-59 mL/min/1.73 m^2, eGFR <45 mL/min/1.73 m^2, decreases in eGFR, or proteinuria) vs. eGFR ≥60 or non-proteinuria for in-hospital death in ischemic stroke subtypes
Risk estimates were adjusted for age, sex, hypertension, diabetes, history of stroke, previous statin use, previous antiplatelet, alteplase use or/and endovascular treatment, premorbid mRS and initial NIHSS.
Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; NE; not evaluable

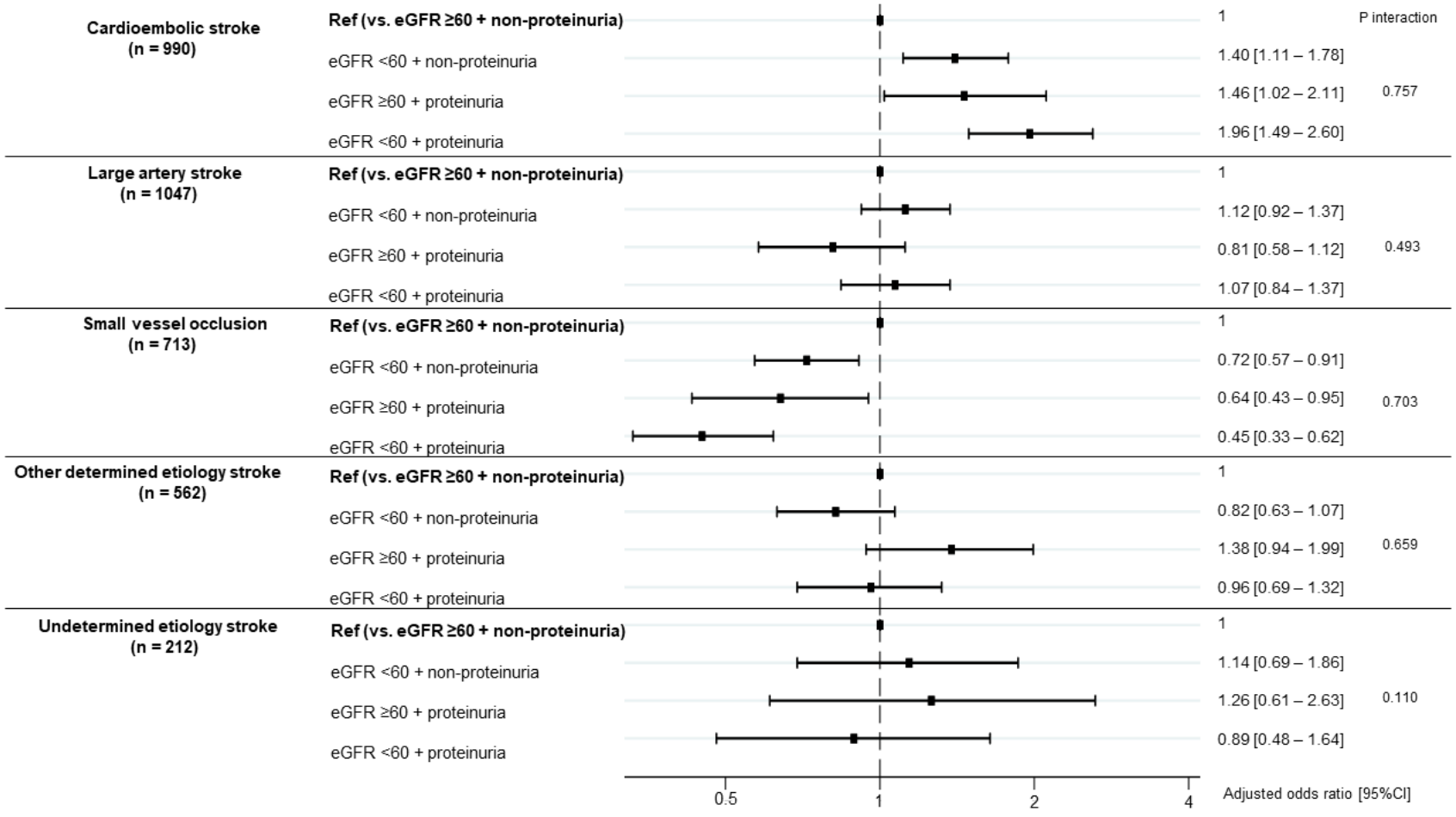
sFigure e-1. Patient flow chart



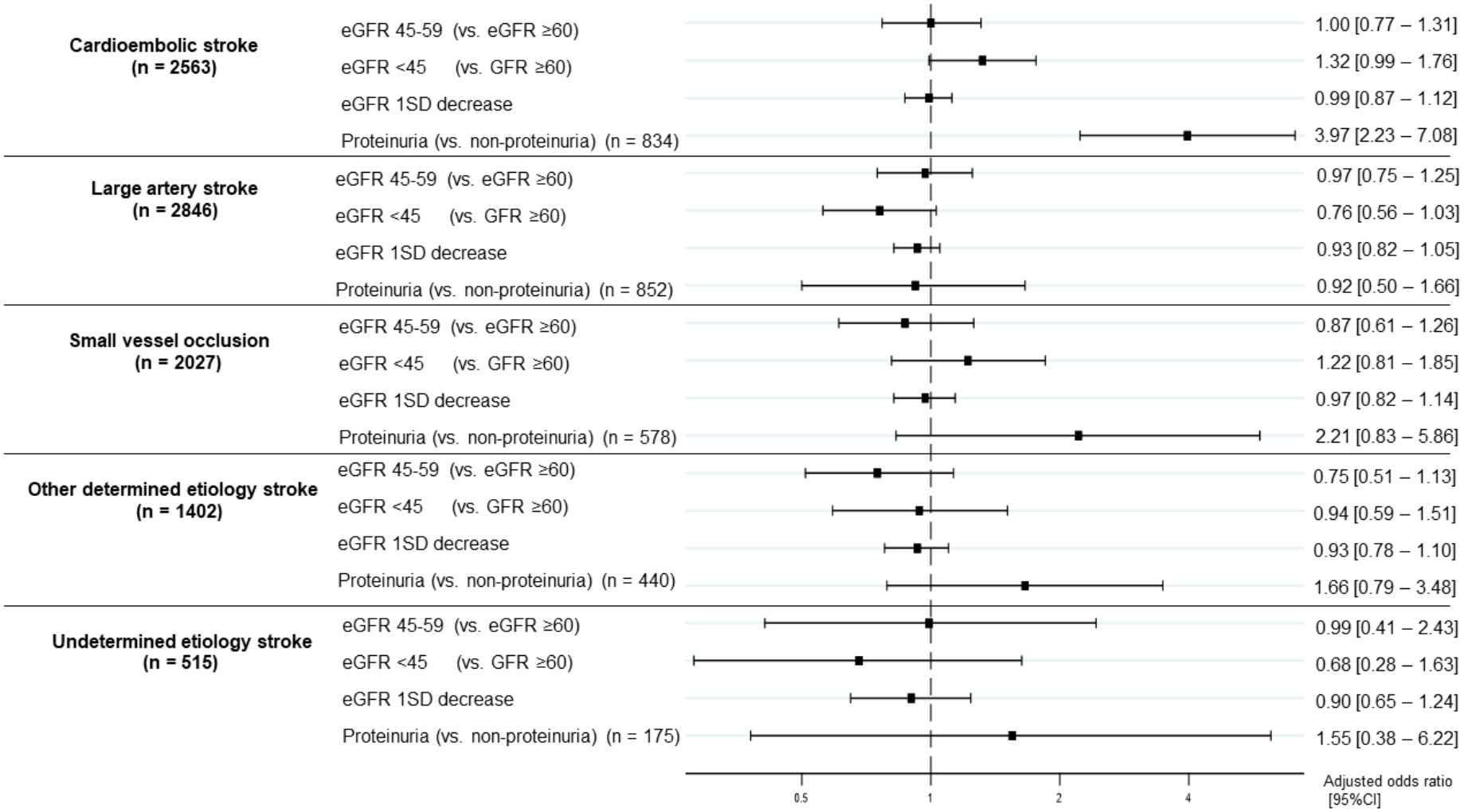
sFigure e-2. Associations between all eGFR levels and ischemic stroke subtypes (large artery stroke, other determined etiology stroke, and undetermined etiology stroke)



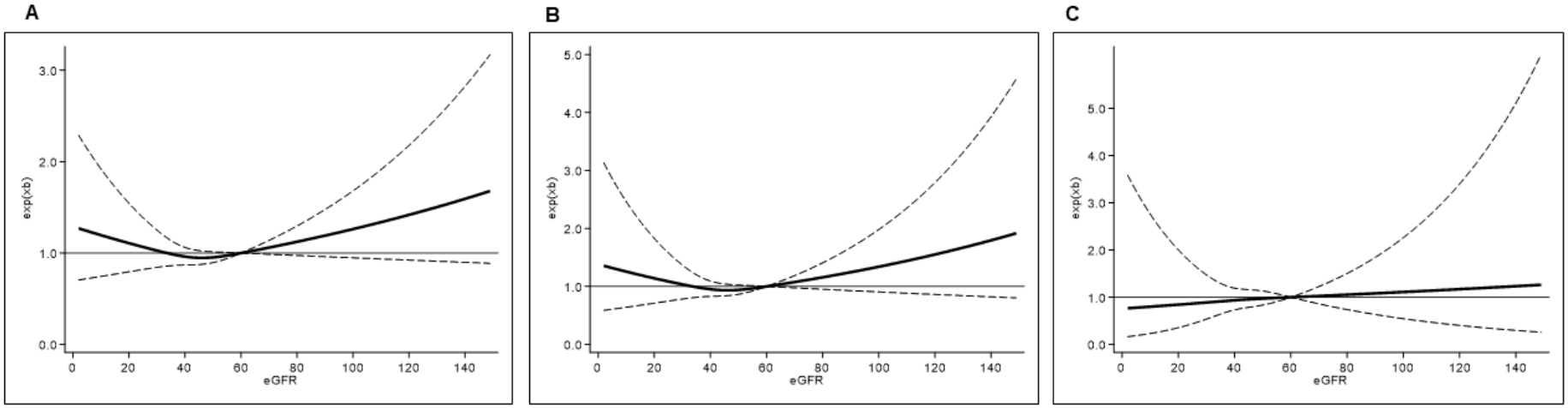
sFigure e-3. Associations of joint eGFR and proteinuria with ischemic stroke subtypes



sFigure e-4. Associations between renal impairment and unfavorable functional outcome in ischemic stroke subtypes in patients not receiving hemodialysis



sFigure e-5. Associations between eGFR levels and unfavorable functional outcomes in ischemic stroke subtypes (large artery stroke, other determined etiology stroke, and undetermined etiology stroke)



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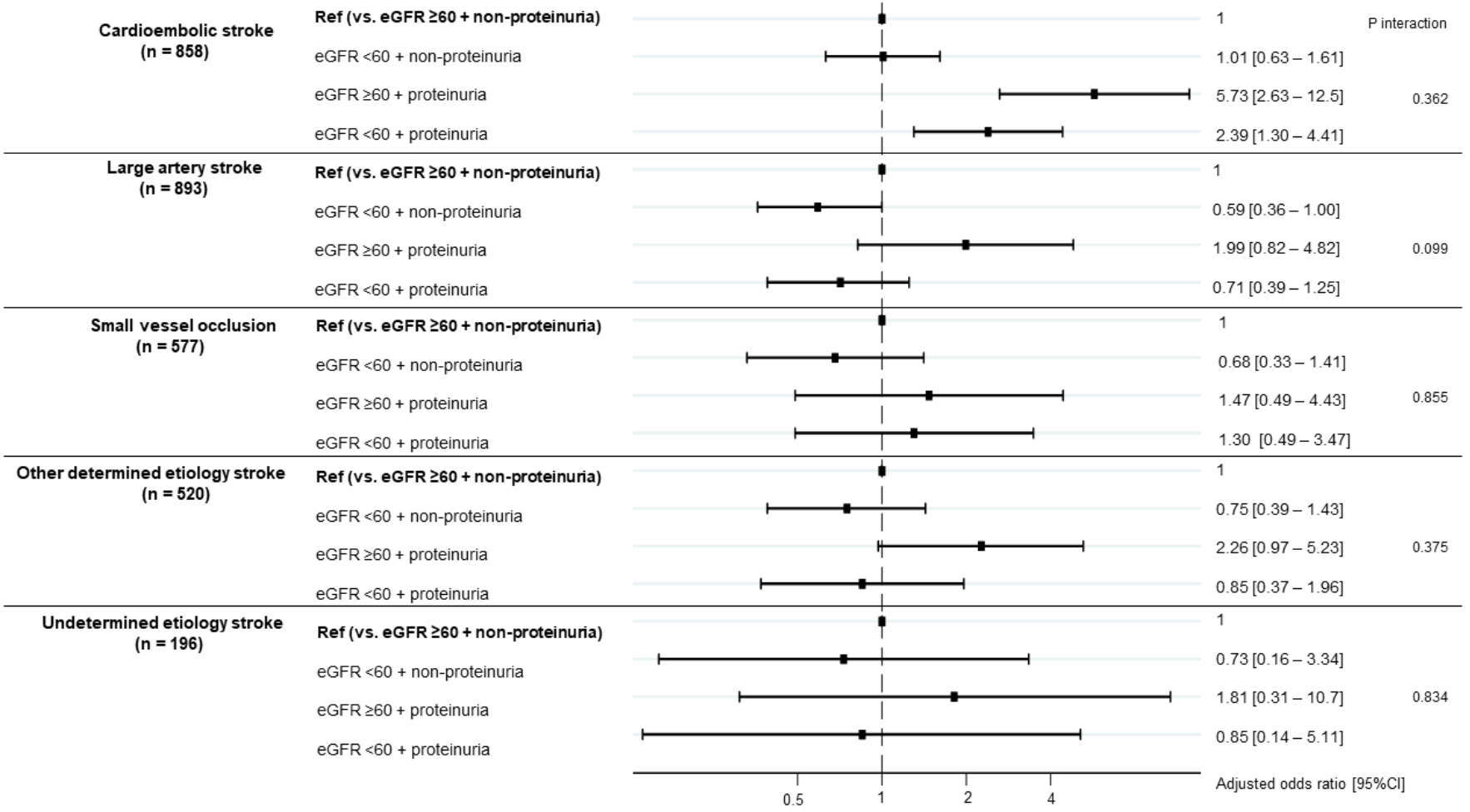
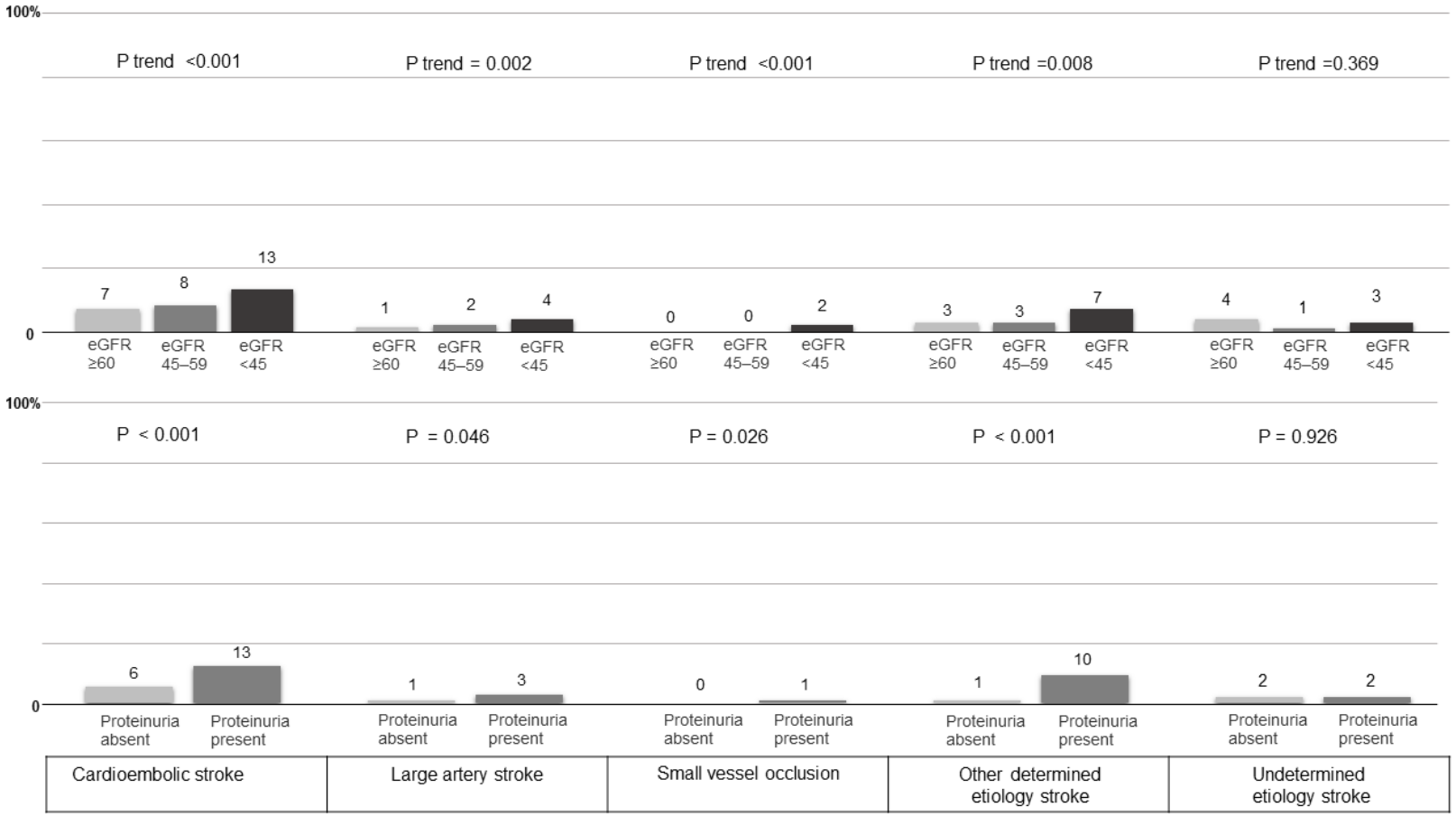


sFigure e-7. Proportions of in-hospital death in ischemic stroke etiologies according to the eGFR categories (eGFR <60, eGFR 45-59, eGFR <45, mL/min/1.73 m^2) or proteinuria



sFigure e-8. Associations between renal impairment and in-hospital death in ischemic stroke subtypes