

Table S1. The proportional hazards assumption for the models

Outcomes	Hcy (N=2650) ≤12.9μmol/L	Hcy (N=2790) >12.9μmol/L
New stroke	0.90	0.26
Stroke within 30 days	0.49	0.32
Composite vascular events	0.61	0.26
Ischemic stroke	0.91	0.31
Disabling stroke	0.10	0.26
Severe or moderate bleeding	0.15	0.24
Any bleeding	0.93	0.10
Fatal bleeding	NA	0.09
Intracranial hemorrhage	NA	0.09
Mild bleeding	0.71	0.09
Mortality	0.91	0.70

Hcy denotes homocysteine.

The proportional hazards assumption was tested by Schoenfeld residuals

Table S2. Baseline Characteristics of Included and Excluded Patients

Characteristics	Excluded (n=972)	Included (n=5440)	P value
Median age (IQR) -yr	65.7(58.3-72.7)	64.5(56.7-71.2)	<0.001
Female sex - no. (%)	358 (36.8)	1812 (33.3)	0.03
Han ethnicity - no. (%)	955 (98.3)	5327 (97.9)	0.50
Median blood pressure (IQR) - mm Hg			
Systolic	148(134-163)	148(136-161)	0.94
Diastolic	86(79-95)	86(80-95)	0.46
Medical history - no. (%)			
Hypertension	588 (60.5)	3367 (61.9)	0.41
Diabetes mellitus	239 (24.6)	1324 (24.3)	0.87
Dyslipidemia	82 (8.4)	532 (9.8)	0.19
Previous ischemic stroke	177 (18.2)	1173 (21.6)	0.02
Previous TIA	13 (1.3)	75 (1.4)	0.92
Myocardial infarction	15 (1.5)	81 (1.5)	0.90
Current smoking - no. (%)	254 (26.1)	1727 (31.7)	<0.001
CYP2C19 LOF allele carriers - no. (%)			
Intermediate metabolizers	759 (78.1)	4242 (78.0)	0.94
Poor metabolizers	213 (21.9)	1198 (22.0)	
Median time from symptom onset to randomization, n (%)			
<12 h	432 (44.4)	2194 (40.3)	0.02
≥12 h	540 (55.6)	3246 (59.7)	
Qualifying event - no. (%)			
Ischemic stroke	810 (83.3)	4348 (79.9)	0.01
TIA	162 (16.7)	1092 (20.1)	
Median NIHSS score in patients with qualifying ischemic stroke (IQR) *	2(1-3)	2(1-3)	0.10

Appendix 1, as supplied by the authors. Appendix to: Wang A, Tian X, Xie X, et al. Differential effect of ticagrelor versus clopidogrel by homocysteine levels on risk of recurrent stroke: a post hoc analysis of the CHANCE-2 trial. *CMAJ* 2024. doi: 10.1503/cmaj.231262. Copyright © 2024 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca.

Median ABCD ² score in patients with qualifying TIA (IQR) [†]	5(4-5)	4(4-5)	0.42
Previous antiplatelet therapy - no. (%) [‡]	91 (9.4)	657 (12.1)	0.02
Previous lipid-lowering therapy - no. (%) [‡]	64 (6.6)	435 (8.0)	0.13
Symptomatic ICAS, n (%)	353 (40.5)	2032 (40.2)	0.88
Symptomatic ECAS, n (%)	79 (9.1)	445 (8.8)	0.81
Stroke within 90 days	68 (7.0)	366 (6.7)	0.76

ECAS denotes extracranial artery stenosis. ICAS denotes intracranial artery stenosis.

IQR denotes interquartile range. LOF denotes loss-of-function. TIA denotes transient ischemic attack.

* National Institutes of Health Stroke Scale (NIHSS) scores range from 0 to 42, with higher scores indicating more severe stroke.

† ABCD² score assesses the risk of stroke on the basis of age, blood pressure, clinical features, duration of TIA, and presence or absence of diabetes, with scores ranging from 0 to 7 and higher scores indicating greater risk.

‡ Medication within 1 month before symptom onset.

Table S3. Efficacy and Safety Outcomes of Patients With Different Antiplatelet Therapies Stratified by Hcy Adjusted for Renal Function

Outcomes	Hcy ≤12.9μmol/L (n=2650)				Hcy ≥12.9μmol/L (n=2790)				P _{int}	
	Ticagrelor -Aspirin Event rate (%)* (n=1349)	Clopidogrel -Aspirin Event rate (%)* (n=1301)	HR (95%CI)	P value	Ticagrelor -Aspirin Event rate (%)* (n=1391)	Clopidogrel -Aspirin Event rate (%)* (1399)	HR (95%CI)	P value		
Primary outcome										
Stroke	86 (6.4)	87 (6.7)	1.05(0.72-1.53)	0.80	74 (5.3)	119 (8.5)	0.60(0.42-0.85)	<0.001	0.04	
Secondary outcome										
Stroke within 30 days	72 (5.3)	74 (5.7)	0.98(0.65-1.47)	0.92	58 (4.2)	98 (7.0)	0.55(0.37-0.82)	<0.001	0.06	
Composite vascular events†	96 (7.1)	114 (8.8)	0.99(0.69-1.41)	0.96	95 (6.8)	134 (9.6)	0.61(0.43-0.85)	<0.001	0.07	
Ischemic stroke	86 (6.4)	85 (6.5)	1.09(0.74-1.60)	0.67	72 (5.2)	116 (8.3)	0.58(0.41-0.84)	<0.001	0.02	
Disabling stroke‡	44 (3.3)	33 (2.5)	1.31(0.74-2.33)	0.35	36 (2.6)	43 (3.1)	0.99(0.57-1.74)	0.98	0.55	
Ordinal stroke or TIA§			0.81(0.61-1.08)	0.15			0.71(0.54-0.93)	0.01	0.20	
Fatal stroke (mRS 6)	2 (0.2)	3 (0.2)			1 (0.1)	3 (0.2)				
Severe stroke	14 (1.0)	7 (0.5)			11 (0.8)	8 (0.6)				

(mRS 4-5)										
Moderate stroke	28 (2.1)	23 (1.8)			24 (1.7)	32 (2.3)				
(mRS 2-3)										
Mild stroke	42 (3.1)	54 (4.2)			38 (2.7)	76 (5.4)				
(mRS 0-1)										
TIA	9 (0.6)	25 (1.9)			20 (1.4)	11 (0.8)				
No stroke or TIA	1255 (93.0)	1189 (91.4)			1297 (93.2)	1269 (90.7)				
Primary safety outcome										
Severe or moderate bleeding¶	3 (0.2)	2 (0.2)	1.72(0.28-10.49)	0.56	6 (0.4)	6 (0.4)	0.74(0.12-4.47)	0.74	0.72	
Fatal bleeding	1 (0.1)	0 (0.0)	NA	NA	2 (0.1)	3 (0.2)	0.51(0.05-5.71)	0.59	1.00	
Intracranial hemorrhage	0 (0.0)	2 (0.2)	NA	NA	3 (0.2)	4 (0.3)	1.13(0.16-8.07)	0.90	0.99	
Secondary safety outcome										
Any bleeding	76 (5.6)	34 (2.6)	2.33(1.36-3.99)	<0.001	77 (5.5)	32 (2.3)	2.59(1.51-4.43)	<0.001	0.78	
Mild bleeding ¶	73 (5.4)	32 (2.5)	2.43(1.38-4.27)	<0.001	71 (5.1)	26 (1.9)	2.92(1.65-5.18)	<0.001	0.68	
Mortality	3 (0.2)	4 (0.3)	0.40(0.04-4.63)	0.47	4 (0.3)	10 (0.7)	0.42(0.08-2.17)	0.30	0.87	

CI denotes confidence interval. Hcy denotes homocysteine. HR denotes hazard ratio. mRS denotes modified Rankin Scale. NA denotes not

applicable. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ A stroke defined as disabling if the patient had a subsequent score on the modified Rankin scale of greater than 1 (indicating death or any degree of disability).

§ Severity measured using a six-level ordered categorical scale that incorporates subsequent stroke or TIA events and mRS score at 3 months.

The common odds ratio is shown rather than the hazard ratio.

¶ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.

Table S4. Efficacy and Safety Outcomes of Patients With Different Antiplatelet Therapies Stratified by Hcy and Sex

Outcomes	Sex	Hcy levels	Ticagrelor -Aspirin Event rate (%)*	Clopidogrel -Aspirin Event rate (%)*	HR (95%CI)	<i>P</i> _{int}
Stroke	Female	Hcy≤12.9μmol/L	44 (7.4)	36 (6.0)	1.29(0.80-2.09)	0.007
		Hcy>12.9μmol/L	16 (4.9)	30 (10.2)	0.45(0.22-0.90)	
	Male	Hcy≤12.9μmol/L	42 (5.6)	51 (7.3)	0.77(0.50-1.19)	0.75
		Hcy>12.9μmol/L	58 (5.4)	89 (8.1)	0.64(0.45-0.89)	
Stroke within 30 days	Female	Hcy≤12.9μmol/L	37 (6.2)	32 (5.4)	1.25(0.75-2.08)	0.02
		Hcy>12.9μmol/L	13 (4.0)	27 (9.2)	0.47(0.22-0.99)	
	Male	Hcy≤12.9μmol/L	35 (4.6)	42 (6.0)	0.79(0.49-1.27)	0.66
		Hcy>12.9μmol/L	45 (4.2)	71 (6.4)	0.61(0.42-0.90)	
Composite vascular events†	Female	Hcy≤12.9μmol/L	49 (8.2)	53 (8.9)	0.98(0.65-1.50)	0.04
		Hcy>12.9μmol/L	22 (6.7)	37 (12.6)	0.55(0.30-1.01)	

Ischemic stroke	Male	Hcy \leq 12.9 μ mol/L	47 (6.2)	61 (8.7)	0.74(0.49-1.11)	0.61	
		Hcy $>$ 12.9 μ mol/L	73 (6.9)	97 (8.8)	0.73(0.53-1.00)		
	Female	Hcy \leq 12.9 μ mol/L	44 (7.4)	35 (5.9)	1.33(0.82-2.16)	0.006	
		Hcy $>$ 12.9 μ mol/L	16 (4.9)	30 (10.2)	0.45(0.22-0.90)		
Disabling stroke \ddagger	Male	Hcy \leq 12.9 μ mol/L	42 (5.6)	50 (7.1)	0.79(0.51-1.21)	0.69	
		Hcy $>$ 12.9 μ mol/L	56 (5.3)	86 (7.8)	0.63(0.45-0.89)		
	Female	Hcy \leq 12.9 μ mol/L	19 (3.2)	10 (1.7)	1.87(0.83-4.23)	0.02	
		Hcy $>$ 12.9 μ mol/L	7 (2.1)	16 (5.4)	0.47(0.18-1.22)		
Ordinal stroke or TIA \S	Male	Hcy \leq 12.9 μ mol/L	25 (3.3)	23 (3.3)	0.99(0.55-1.81)	0.64	
		Hcy $>$ 12.9 μ mol/L	29 (2.7)	27 (2.4)	1.02(0.60-1.74)		
	Fatal stroke (mRS 6)	Female	Hcy \leq 12.9 μ mol/L	0 (0.0)	1 (0.2)	0.93(0.62-1.41)	0.15
			Hcy $>$ 12.9 μ mol/L	4 (1.2)	3 (1.0)	0.56 (0.32-0.99)	

Severe stroke (mRS 4-5)	Male	Hcy \leq 12.9 μ mol/L	2 (0.3)	2 (0.3)	0.72 (0.49-1.07)	0.85
		Hcy $>$ 12.9 μ mol/L	1 (0.1)	3 (0.3)	0.76 (0.55-1.04)	
	Female	Hcy \leq 12.9 μ mol/L	7 (1.2)	2 (0.3)		
		Hcy $>$ 12.9 μ mol/L	3 (0.9)	13 (4.4)		
Moderate stroke (mRS 2-3)	Male	Hcy \leq 12.9 μ mol/L	7 (0.7)	5 (0.7)		
		Hcy $>$ 12.9 μ mol/L	7 (0.7)	5 (0.5)		
	Female	Hcy \leq 12.9 μ mol/L	12 (2.0)	7 (1.2)		
		Hcy $>$ 12.9 μ mol/L	9 (2.8)	14 (4.8)		
Mild stroke (mRS 0-1)	Male	Hcy \leq 12.9 μ mol/L	16 (2.1)	16 (2.3)		
		Hcy $>$ 12.9 μ mol/L	21 (2.0)	19 (1.7)		
	Female	Hcy \leq 12.9 μ mol/L	25 (4.2)	26 (4.4)		
		Hcy $>$ 12.9 μ mol/L	9 (2.8)	14 (4.8)		
	Male	Hcy \leq 12.9 μ mol/L	17 (2.2)	28 (4.0)		

		Hcy>12.9μmol/L	29 (2.7)	62 (5.6)		
TIA	Female	Hcy≤12.9μmol/L	3 (0.5)	16 (2.7)		
		Hcy>12.9μmol/L	6 (1.8)	3 (1.0)		
	Male	Hcy≤12.9μmol/L	5 (0.7)	9 (1.3)		
		Hcy>12.9μmol/L	14 (1.3)	8 (0.7)		
No stroke or TIA	Female	Hcy≤12.9μmol/L	547 (92.1)	546 (91.3)		
		Hcy>12.9μmol/L	304 (93.3)	261 (88.8)		
	Male	Hcy≤12.9μmol/L	708 (93.4)	643 (91.5)		
		Hcy>12.9μmol/L	993 (93.2)	1008 (91.2)		
Severe or moderate bleeding¶	Female	Hcy≤12.9μmol/L	1 (0.2)	1 (0.2)	1.18(0.07-18.99)	1.00
		Hcy>12.9μmol/L	0 (0.0)	0 (0.0)	NA	
	Male	Hcy≤12.9μmol/L	2 (0.3)	1 (0.1)	1.84(0.17-20.40)	0.67
		Hcy>12.9μmol/L	6 (0.6)	6 (0.5)	0.87(0.26-2.88)	

Fatal bleeding	Female	Hcy \leq 12.9 μ mol/L	0 (0.0)	1 (0.2)	NA	NA
		Hcy $>$ 12.9 μ mol/L	0 (0.0)	0 (0.0)	NA	
	Male	Hcy \leq 12.9 μ mol/L	1 (0.1)	0 (0.0)	NA	1.00
		Hcy $>$ 12.9 μ mol/L	2 (0.2)	3 (0.3)	0.81(0.14-4.88)	
Intracranial hemorrhage	Female	Hcy \leq 12.9 μ mol/L	0 (0.0)	0 (0.0)	NA	NA
		Hcy $>$ 12.9 μ mol/L	1 (0.2)	0 (0.0)	NA	
	Male	Hcy \leq 12.9 μ mol/L	0 (0.0)	1 (0.1)	0.00(0.00-.)	1.00
		Hcy $>$ 12.9 μ mol/L	3 (0.3)	4 (0.4)	0.75(0.16-3.42)	
Any bleeding¶	Female	Hcy \leq 12.9 μ mol/L	41 (6.9)	15 (2.5)	2.59(1.35-4.96)	0.64
		Hcy $>$ 12.9 μ mol/L	20 (6.1)	6 (2.0)	5.76(1.63-20.37)	
	Male	Hcy \leq 12.9 μ mol/L	35 (4.6)	19 (2.7)	2.13(1.16-3.91)	0.88
		Hcy $>$ 12.9 μ mol/L	57 (5.4)	26 (2.4)	2.26(1.39-3.68)	
Mild bleeding¶	Female	Hcy \leq 12.9 μ mol/L	40 (6.7)	14 (2.3)	2.74(1.40-5.36)	0.71

		Hcy>12.9μmol/L	20 (6.1)	6 (2.0)	5.76(1.63-20.37)	
	Male	Hcy≤12.9μmol/L	33 (4.4)	18 (2.6)	2.15(1.15-4.04)	0.95
		Hcy>12.9μmol/L	51 (4.8)	20 (1.8)	2.72(1.57-4.70)	
Morality	Female	Hcy≤12.9μmol/L	1 (0.2)	2 (0.3)	0.48(0.04-5.43)	1.00
		Hcy>12.9μmol/L	0 (0.0)	4 (1.4)	NA	
	Male	Hcy≤12.9μmol/L	2 (0.3)	2 (0.3)	1.14(0.15-8.70)	0.74
		Hcy>12.9μmol/L	4 (0.4)	6 (0.5)	0.67(0.19-2.40)	

CI denotes confidence interval. Hcy denotes homocysteine. HR denotes hazard ratio. mRS denotes modified Rankin Scale. NA denotes not applicable. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ A stroke defined as disabling if the patient had a subsequent score on the modified Rankin scale of greater than 1 (indicating death or any

degree of disability).

§ Severity measured using a six-level ordered categorical scale that incorporates subsequent stroke or TIA events and mRS score at 3 months.

The common odds ratio is shown rather than the hazard ratio.

¶ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.

Table S5. Efficacy and Safety Outcomes of Patients With Different Antiplatelet Therapies Stratified by Hcy and *CYP2C19* Loss-of-function Allele Carriers

Outcomes	<i>CYP2C19</i> metabolizers	Hcy levels	Ticagrelor -Aspirin Event rate (%)*	Clopidogrel -Aspirin Event rate (%)*	HR (95%CI)	<i>P</i> int
Stroke	Intermediate	Hcy≤12.9μmol/L	63 (6.0)	69 (6.8)	0.90(0.58-1.37)	0.10
		Hcy>12.9μmol/L	58 (5.4)	91 (8.3)	0.52(0.35-0.79)	
	Poor	Hcy≤12.9μmol/L	23 (7.8)	18 (6.5)	2.66(0.91-7.75)	0.10
		Hcy>12.9μmol/L	16(5.0)	28 (9.2)	0.79(0.35-1.78)	
Stroke within 30 days	Intermediate	Hcy≤12.9μmol/L	54(5.1)	57 (5.6)	0.89(0.56-1.41)	0.15
		Hcy>12.9μmol/L	47 (4.4)	73 (6.7)	0.51(0.32-0.80)	
	Poor	Hcy≤12.9μmol/L	18 (6.1)	17(6.1)	1.65(0.51-5.32)	0.21
		Hcy>12.9μmol/L	11 (3.4)	25 (8.2)	0.69(0.28-1.71)	
Composite vascular events†	Intermediate	Hcy≤12.9μmol/L	70 (6.6)	91 (8.9)	0.84(0.56-1.26)	0.16
		Hcy>12.9μmol/L	71 (6.6)	104(9.5)	0.52(0.35-0.77)	

Ischemic stroke	Poor	Hcy \leq 12.9 μ mol/L	26 (8.8)	23 (8.2)	2.10(0.81-5.47)	0.26
		Hcy>12.9 μ mol/L	24 (7.5)	30 (9.9)	0.93(0.44-1.97)	
	Intermediate	Hcy \leq 12.9 μ mol/L	63 (6.0)	68 (6.7)	0.91(0.59-1.40)	0.08
		Hcy>12.9 μ mol/L	56 (5.2)	88 (8.0)	0.51(0.33-0.77)	
Disabling stroke‡	Poor	Hcy \leq 12.9 μ mol/L	23 (7.8)	17(6.1)	3.43(1.07-10.97)	0.07
		Hcy>12.9 μ mol/L	16(5.0)	28 (9.2)	0.79(0.35-1.78)	
	Intermediate	Hcy \leq 12.9 μ mol/L	28 (2.7)	27 (2.6)	0.98(0.51-1.90)	0.76
		Hcy>12.9 μ mol/L	29 (2.7)	29 (2.6)	1.02(0.53-1.95)	
Ordinal stroke or TIA§	Poor	Hcy \leq 12.9 μ mol/L	16(5.4)	6(2.2)	4.63(0.96-22.42)	0.09
		Hcy>12.9 μ mol/L	7(2.2)	14 (4.6)	0.70(0.21-2.38)	
Fatal stroke(mRS 6)	Intermediate	Hcy \leq 12.9 μ mol/L	1 (0.1)	3 (0.3)	0.76(0.55-1.05)	0.69
		Hcy>12.9 μ mol/L	1 (0.1)	3 (0.3)	0.69(0.50-0.95)	

Stroke severity	Stratification	Hcy level	Events (n)	Events (%)	HR (95% CI)	P-value
Severe stroke (mRS 4-5)	Poor	Hcy ≤ 12.9 μmol/L	1 (0.3)	0 (0.0)	1.02 (0.56-1.86)	0.46
		Hcy > 12.9 μmol/L	0 (0.0)	0 (0.0)	0.75 (0.42-1.32)	
	Intermediate	Hcy ≤ 12.9 μmol/L	9 (0.9)	5 (0.5)		
		Hcy > 12.9 μmol/L	10 (0.9)	5 (0.5)		
Moderate stroke (mRS 2-3)	Poor	Hcy ≤ 12.9 μmol/L	5 (1.7)	2 (0.7)		
		Hcy > 12.9 μmol/L	1 (0.3)	3 (1.0)		
	Intermediate	Hcy ≤ 12.9 μmol/L	18 (1.7)	19 (1.9)		
		Hcy > 12.9 μmol/L	18 (1.7)	21 (1.9)		
Mild stroke (mRS 0-1)	Poor	Hcy ≤ 12.9 μmol/L	10 (3.4)	4 (1.4)		
		Hcy > 12.9 μmol/L	6 (1.9)	11 (0.6)		
	Intermediate	Hcy ≤ 12.9 μmol/L	35 (3.3)	42 (4.1)		
		Hcy > 12.9 μmol/L	29 (2.7)	62 (5.7)		
	Poor	Hcy ≤ 12.9 μmol/L	7 (2.4)	12 (4.3)		

			Number of events (%)	Number of events (%)	HR (95% CI)	P
TIA	Intermediate	Hcy>12.9µmol/L	9(2.8)	14 (4.6)		
		Hcy≤12.9µmol/L	7(0.7)	20 (2.0)		
	Poor	Hcy>12.9µmol/L	12(1.1)	10(0.9)		
		Hcy≤12.9µmol/L	1 (0.3)	5(1.8)		
No stroke or TIA	Intermediate	Hcy>12.9µmol/L	8(2.5)	1 (0.3)		
		Hcy≤12.9µmol/L	983 (93.4)	933(91.3)		
	Poor	Hcy>12.9µmol/L	1002(93.5)	994 (90.8)		
		Hcy≤12.9µmol/L	272(91.9)	256(91.8)		
Severe or moderate bleeding¶	Intermediate	Hcy>12.9µmol/L	295 (92.5)	275 (90.5)		
		Hcy≤12.9µmol/L	2 (0.2)	1 (0.1)	2.03(0.18-23.13)	0.70
	Poor	Hcy>12.9µmol/L	5 (0.5)	6 (0.5)	0.71(0.12-4.36)	
		Hcy≤12.9µmol/L	1 (0.3)	1 (0.4)	5.06(0.08-337.28)	NA
		Hcy>12.9µmol/L	1 (0.3)	0 (0.0)	NA	NA

Fatal bleeding	Intermediate	Hcy \leq 12.9 μ mol/L	1 (0.1)	0 (0.0)	NA	NA
		Hcy $>$ 12.9 μ mol/L	1 (0.1)	3 (0.3)	0.45(0.04-5.02)	
	Poor	Hcy \leq 12.9 μ mol/L	1 (0.3)	0 (0.0)	NA	NA
		Hcy $>$ 12.9 μ mol/L	0 (0.0)	0 (0.0)	NA	
Intracranial hemorrhage	Intermediate	Hcy \leq 12.9 μ mol/L	0 (0.0)	1 (0.1)	NA	1.00
		Hcy $>$ 12.9 μ mol/L	3 (0.3)	4 (0.4)	1.05(0.14-7.60)	
	Poor	Hcy \leq 12.9 μ mol/L	0 (0.0)	0 (0.0)	NA	NA
		Hcy $>$ 12.9 μ mol/L	0 (0.0)	1 (0.4)		
Any bleeding [¶]	Intermediate	Hcy \leq 12.9 μ mol/L	56 (5.3)	25 (2.4)	1.97(1.06-3.67)	0.63
		Hcy $>$ 12.9 μ mol/L	65 (6.1)	29 (2.6)	2.50(1.40-4.48)	
	Poor	Hcy \leq 12.9 μ mol/L	20 (6.8)	9(3-2)	3.64(1.11-11.96)	0.52
		Hcy $>$ 12.9 μ mol/L	12 (3.8)	3(1.0)	4.85(0.57-41.51)	
Mild bleeding [¶]	Intermediate	Hcy \leq 12.9 μ mol/L	54(5.1)	24 (2.3)	1.98(1.04-3.76)	0.50

		Hcy>12.9μmol/L	60 (5.6)	23(2.1)	2.89(1.55-5.42)	
	Poor	Hcy≤12.9μmol/L	19 (6.4)	8(2.9)	4.61(1.22-17.48)	0.59
		Hcy>12.9μmol/L	11 (0.4)	3(1.0)	4.85(0.57-41.51)	
Mortality	Intermediate	Hcy≤12.9μmol/L	1 (0.1)	4 (0.4)	0.45(0.04-5.06)	0.88
		Hcy>12.9μmol/L	3 (0.3)	9 (0.8)	0.47(0.09-2.56)	
	Poor	Hcy≤12.9μmol/L	2(0.7)	0 (0.0)	NA	NA
		Hcy>12.9μmol/L	1 (0.3)	1 (0.3)	NA	

CI denotes confidence interval. Hcy denotes homocysteine. HR denotes hazard ratio. mRS denotes modified Rankin Scale. NA denotes not applicable. TIA denotes transient ischemic attack.

* Event rates for ordinal stroke or TIA are raw estimates, whereas event rates for other outcomes are Kaplan-Meier estimates of the percentage of patients with events at 90 days.

† Composite vascular events include ischemic stroke, hemorrhagic stroke, TIA, myocardial infarction, vascular death.

‡ A stroke defined as disabling if the patient had a subsequent score on the modified Rankin scale of greater than 1 (indicating death or any

degree of disability).

§ Severity measured using a six-level ordered categorical scale that incorporates subsequent stroke or TIA events and mRS score at 3 months.

The common odds ratio is shown rather than the hazard ratio.

¶ Severe or moderate bleeding and mild bleeding were defined according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) criteria.