Table S1 Baseline Characteristics of Participants according to Treatment and eGFR

	eGFR≥90mL/min/1.73m^2			eGFR 60-89 mL/min/1.73m^2			eGFR＜60 mL/min/1.73m^2		
	Tenecteplase (n=465)	**Alteplase (n=486)**	***P* value**	**Tenecteplase (n=195)**	**Alteplase (n=171)**	***P* value**	**Tenecteplase (n=45)**	**Alteplase (n=50)**	***P* value**
Age, y	62.36±10.54	62.11±10.34	0.71	71.12±10.37	69.56±9.74	0.14	73.82±11.80	75.56±11.87	0.48
Females, n (%)	130(27.96)	144(29.63)	0.57	64(32.82)	64(37.43)	0.36	22(48.89)	20(40.00)	0.38
BMI, kg/m^2	23.99±3.45	24.31±3.44	0.15	23.65±3.63	23.95±3.58	0.43	22.50±3.77	23.46±3.39	0.20
NHISS	7.0(5.0,10.0)	7.0(6.0,10.0)	0.23	7.0(5.0,10.0)	8.0(6.0,11.0)	0.04	7.0(5.0,12.0)	6.0(5.0,10.0)	0.42
Medical history									
Hypertension, n (%)	315(67.74)	339(69.75)	0.5	152(77.95)	128(74.85)	0.49	39(86.67)	45(90.00)	0.61
Diabetes, n (%)	110(23.66)	137(28.19)	0.11	47(24.10)	55(32.16)	0.09	13(28.89)	15(30.00)	0.91
Hyperlipidemia, n (%)	90(19.35)	114(23.46)	0.12	34(17.44)	35(20.47)	0.46	5(11.11)	11(22.00)	0.16
Coronary heart disease, n (%)	97(20.86)	102(20.99)	0.96	53(27.18)	46(26.90)	0.95	16(35.56)	18(36.00)	0.96
Arrhythmia, n (%)	67(14.41)	79(16.26)	0.43	55(28.21)	48(28.07)	0.98	13(28.89)	19(38.00)	0.35
Current smoker, n (%)	196(42.24)	213(43.92)	0.83	54(27.69)	53(30.99)	0.61	14(31.11)	10(20.00)	0.43
History of medication use, n(%)									
Antiplatelet agents	53(11.40)	55(11.32)	0.97	31(15.90)	23(13.45)	0.51	6(13.33)	14(28.00)	0.08
Anticoagulant agents	1(0.22)	3(0.62)	0.34	4(2.05)	4(2.34)	0.85			0.08
Lipid –lowing drugs	32(6.88)	34(7.00)	0.94	28(14.36)	17(9.94)	0.2	7(15.56)	9(18.00)	0.75
Hypoglycaemic drugs	74(15.91)	77(15.84)	0.98	26(13.33)	34(19.88)	0.09	7(15.56)	7(14.00)	0.83
Antihypertensive drugs	181(38.92)	203(41.77)	0.37	94(48.21)	84(49.12)	0.86	19(42.22)	31(62.00)	0.05
mRS score before stroke			0.83			0.23			0.24
0	421(90.54)	438(90.12)		169(86.67)	155(90.64)		40(88.89)	40(80.00)	
1	44(9.46)	48(9.88)		26(13.33)	16(9.36)		5(11.11)	10(20.00)	

Onset-to-needle time, hours	179.05±55.96	182.80±56.72	0.31	176.65±55.68	171.17±56.95	0.45	163.02±45.55	181.10±58.53	0.10
Bridging thrombectomy, n (%)	19(4.09)	16(3.29)	0.52	6(3.08)	8(4.68)	0.43	2(4.44)	0(0.00)	0.13
eGFR,ml/min/1.73m^2	107.93±11.32	107.30±10.27	0.37	78.19±7.92	76.90±9.06	0.15	46.58±12.53	46.51±10.74	0.98
Serum creatinine, umol/L	63.12±11.21	63.79±11.94	0.38	87.17±13.57	88.42±14.67	0.40	139.91±67.71	135.95±46.45	0.74

Data were expressed as median (IQR) or n (%). eGFR indicates estimated glomerular filtration rate; BMI, body mass index; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale

Table S2 Efficacy outcomes at 3 months according to 3 eGFR category

	eGFR(mL/min/1.73m^2)	Tenecteplase,%	Alteplase,%	Effect size	P value	Interaction P value
Primary outcome						
mRS score 0-1 at 90 days	≥90	302(65.5)	293(61.2)	1.07(0.97 to 1.18)	0.53	
	60-89	114(58.8)	86(51.5)	1.14(0.95 to 1.37)	0.13	0.55
	＜60	21(46.7)	26(52.0)	0.86(0.59 to 1.27)	0.74	
Secondary outcome						
mRS score 0-2 at 90 days	≥90	355(77.0)	363(75.8)	1.01(0.94 to 1.09)	0.79	
	60-89	132(68.0)	108(64.7)	1.04(0.90 to 1.21)	0.60	0.79
	＜60	26(57.8)	31(62.0)	0.94(0.69 to 1.30)	0.73	
mRS at 90 days	≥90	1(0 to 2)	1(0 to 2)	1.12(0.89 to 1.41)	0.34	
	60-89	1(0 to 3)	1(0 to 3)	1.16(0.81 to 1.68)	0.42	0.63
	＜60	2(1 to 4)	1(0 to 4)	0.82(0.40 to 1.68)	0.59	
European health-related	≥90	78.2±19.8	77.7±20.7	0.52(-2.12 to 3.17)	0.70	
quality of life at 90 days	60-89	77.6±20.5	71.9±23.4	5.75(0.99 to 10.51)	0.02	0.82
	＜60	71.9±22.9	78.4±18.3	-6.52(-16.09 to 3.04)	0.18	
Barthel Index score⩾95 at	≥90	325(73.0)	331(71.2)	1.02(0.94 to 1.11)	0.59	
90 days	60-89	114(65.2)	95(60.1)	1.07(0.91 to 1.26)	0.43	0.38
	＜60	21(60.0)	28(71.8)	0.86(0.60 to 1.22)	0.39	

Data are expressed as n/N (%), effect size (95% CI), median (IQR), or p value. mRS indicates modified Rankin Scale. NIHSS, National Institutes of Health Stroke Scale. Scores on the mRS range from 0 to 6, with 0 indicating no disability, 3 indicating moderate disability, and 6 indicating death.

The Cochran-Mantel-Haenszel χ^2 test adjusting for the pooled-site effect was used for comparison of primary endpoints between groups, and the 95% CI of risk rations (RR) was calculated. For secondary efficacy outcomes outcomes, a common odds risk with its 95% CI was calculated using ordinal logistic regression for the ordinal 90-day mRS score, and RRs with their 95% CIs were calculated using the Cochran-Mantel-Haenszel method considering the site effect of other outcomes.

Table S3 Safety outcomes at 3 months according to 3 eGFR category

	eGFR(mL/min/1.73m²)	Tenecteplase,%	Alteplase,%	Effect size	P value	Interaction P value
Symptomatic intracranial haemorrhage within 36 h	≥90	7(1.5)	5(1.0)	1.41(0.45-4.42)	0.56	0.55
	60-89	7(3.6)	5(2.9)	1.41(0.49-4.08)	0.53	
	＜60	1(2.2)	3(6.0)	0.40(0.04-4.30)	0.43	
Symptomatic intracranial haemorrhage within 90 days	≥90	8(1.7)	6(1.2)	1.33(0.46-3.86)	0.60	0.82
	60-89	7(3.6)	6(3.5)	1.27(0.45-3.55)	0.66	
	＜60	2(4.4)	3(6.0)	0.87(0.14-5.29)	0.88	
Parenchymal haematoma 2 intracranial haemorrhage within 90 days	≥90	6(1.3)	3(0.6)	2.22(0.59-8.38)	0.23	0.99
	60-89	2(1.0)	0(0.0)	-	-	
	＜60	2(4.4)	0(0.0)	-	-	
Any intracranial haemorrhage within 90 days	≥90	23(4.9)	26(5.4)	0.95(0.55-1.65)	0.86	0.92
	60-89	15(7.7)	17(9.9)	0.84(0.43-1.64)	0.61	
	＜60	6(13.3)	7(14.0)	0.93(0.36-2.40)	0.87	
Other significant haemorrhage events within 90 days	≥90	1(0.2)	3(0.6)	0.34(0.03-3.33)	0.33	0.75
	60-89	2(1.0)	0(0.0)	-	-	
	＜60	2(4.4)	2(4.0)	0.4(0.02-9.26)	0.56	
Death within 90 days	≥90	16(3.4)	14(2.9)	1.18(0.58-2.4)	0.64	0.65
	60-89	19(9.8)	10(5.8)	1.86(0.87-3.98)	0.10	
	＜60	10(22.2)	11(22.0)	0.90(0.39-2.10)	0.81	
Adverse events within 90 days	≥90	384(82.2)	408(84.3)	0.98(0.93-1.03)	0.44	0.79
	60-89	177(91.2)	157(91.3)	1.01(0.95-1.07)	0.81	
	＜60	44(97.8)	48(96.0)	1.01(0.94-1.09)	0.76	
Serious Adverse events within	≥90	62(13.3)	55(11.4)	1.20(0.86-1.70)	0.29	0.33

90 days	60-89	36(18.6)	38(22.1)	0.90(0.60-1.35)	0.63
	＜60	17(37.8)	14(28.0)	1.10(0.58-2.08)	0.78

Data are expressed as n/N (%), effect size (95% CI) or p value. Risk ratios of the safety outcomes were calculated with their 95% CIs using binary logistic regression.

Table S4 Sensitivity analysis for efficacy outcomes excluding the patients with history of antiplatelet and anticoagulant drug use

	eGFR(mL/min/1.73m^2)	Event rate, %	Crude Effect Size (95% CI)	P value	Adjusted Effect Size (95% CI)*	P value
Primary outcome						
mRS score 0-1 at 90 days	≥90	531(63.98)	1	-	1	-
	60-89	164(54.67)	0.58(0.43-0.77)	＜0.01	0.75(0.54-1.06)	0.10
	＜60	36(48.00)	0.45(0.28-0.74)	＜0.01	0.71(0.39-1.29)	0.26
mRS score 0-2 at 90 days	≥90	638(76.87)	1	-	1	-
	60-89	197(65.67)	0.68(0.52-0.89)	0.005	0.88(0.65-1.2)	0.43
	＜60	45(60.00)	0.52(0.32-0.84)	0.007	0.76(0.44-1.31)	0.32
European health-related	≥90	80.00(70.00-90.00)	1	-	1	-
quality of life at 90 days	60-89	80.00(60.00-90.00)	-2.9(-5.69--0.12)	0.04	-1.35(-4.15-1.44)	0.34
	＜60	80.00(70.00-90.00)	-3.34(-8.79-2.1)	0.23	-1.75(-7.09-3.58)	0.52
Barthel Index score≥95 at	≥90	589(73.08)	1	-	1	-
90 days	60-89	174(63.04)	0.63(0.47-0.84)	0.002	0.9(0.64-1.26)	0.52
	＜60	38(66.67)	0.74(0.42-1.31)	0.30	1.23(0.63-2.41)	0.55

Data are expressed as n/N (%), effect size (95% CI), median (IQR), or p value. mRS indicates modified Rankin Scale. NIHSS, National Institutes of Health Stroke Scale. Scores on the mRS range from 0 to 6, with 0 indicating no disability, 3 indicating moderate disability, 6 indicating death.

The association between eGFR as a categorical variable and the efficacy and safety outcome was estimated by calculating the odds ratios (ORs) with 95% confidence intervals (CIs) using binary logistic regression models. β coefficient with its 95% CI was calculated using general linear model for the outcome of European quality of life visual analogue scale.

***** The models were adjusted for age，sex，baseline NIHSS，history of hypertension, onset-to-needle time and bridging thrombectomy.

Table S5 Sensitivity analysis for safety outcomes excluding the patients with history of antiplatelet and anticoagulant drug use

	eGFR(mL/min/1.73m^2)	Event rate,%	Crude OR (95% CI)	P value	Adjusted OR (5% CI)*	P value
Symptomatic intracranial haemorrhage within 36 h	≥90	10(1.19)	1	-	1	-
	60-89	12(3.93)	2.65(1.18-5.96)	0.018	2.41(0.99-5.87)	0.05
	＜60	3(4.00)	3.44(1.09-10.88)	0.036	3.01(0.79-11.42)	0.11
Symptomatic intracranial haemorrhage within 90 days	≥90	12(1.43)	1	-	1	-
	60-89	13(4.26)	2.47(1.15-5.3)	0.020	2.29(0.99-5.27)	0.05
	＜60	4(5.33)	3.72(1.31-10.56)	0.014	3.37(1.01-11.24)	0.048
Parenchymal haematoma 2 intracranial haemorrhage within 90 days	≥90	6(0.71)	1	-	1	-
	60-89	2(0.66)	0.58(0.12-2.67)	0.48	0.46(0.09-2.37)	0.35
	＜60	1(1.33)	2.25(0.48-10.57)	0.30	1.94(0.31-12)	0.48
Any intracranial haemorrhage within 90 days	≥90	38(4.52)	1	-	1	-
	60-89	30(9.84)	1.76(1.11-2.8)	0.016	1.41(0.85-2.36)	0.19
	＜60	10(13.33)	2.92(1.52-5.6)	0.001	2.13(0.99-4.56)	0.05
Death within 90 days	≥90	24(2.85)	1	-	1	-
	60-89	24(7.87)	2.64(1.56-4.47)	0.0003	1.95(1.08-3.53)	0.03
	＜60	18(24.00)	8.71(4.75-15.97)	<.0001	6.46(3-13.9)	<.0001
Adverse events within 90 days	≥90	702(83.47)	1	-	1	-
	60-89	282(92.46)	2.1(1.4-3.13)	0.0003	1.8(1.18-2.74)	0.006
	＜60	74(98.67)	6.16(1.93-19.68)	0.002	5.46(1.68-17.77)	0.005
Serious Adverse events within 90 days	≥90	97(11.53)	1	-	1	-
	60-89	60(19.67)	1.81(1.31-2.49)	0.0003	1.56(1.1-2.22)	0.013

	＜60	25(33.33)	3.45(2.16-5.53)	<.0001	2.85(1.68-4.82)	<.0001

Data are expressed as n/N (%), effect size (95% CI) or p value. Odds ratios of the safety outcomes were calculated with their 95% CIs using binary logistic regression.

***** The models were adjusted for age，sex，baseline NIHSS，history of hypertension, onset-to-needle time and bridging thrombectomy.

Table S6 Sensitivity analysis for efficacy outcomes excluding the patients with history of diuretics, dehydration agents and contrast agents use

	eGFR(mL/min/1.73m^2)	Event rate, %	Crude Effect Size (95% CI)	P value	Adjusted Effect Size (95% CI)*	P value
Primary outcome						
mRS score 0-1 at 90 days	≥90	594(63.46)	1	-	1	-
	60-89	197(55.49)	0.6(0.46-0.79)	0.0002	0.82(0.6-1.12)	0.21
	＜60	44(48.35)	0.45(0.29-0.7)	0.0004	0.65(0.38-1.12)	0.12
Secondary outcome						
mRS score 0-2 at 90 days	≥90	716(76.50)	1	-	1	-
	60-89	235(66.20)	0.72(0.56-0.92)	0.0088	0.98(0.73-1.3)	0.86
	＜60	54(59.34)	0.54(0.35-0.83)	0.0051	0.77(0.47-1.27)	0.31
European health-related	≥90	80.00(70.00-90.00)	1	-	1	-
quality of life at 90 days	60-89	80.00(60.00-90.00)	-3.03(-5.67--0.39)	0.0246	-1.2(-3.87-1.46)	0.38
	＜60	80.00(70.00-90.00)	-2.24(-7.3-2.82)	0.3859	-0.18(-5.17-4.81)	0.94
Barthel Index score⩾95 at	≥90	654(72.11)	1	-	1	-
90 days	60-89	206(63.00)	0.66(0.5-0.86)	0.0022	0.94(0.69-1.28)	0.69
	＜60	47(67.14)	0.79(0.47-1.33)	0.3751	1.33(0.73-2.44)	0.36

Data are expressed as n/N (%), effect size (95% CI), median (IQR), or p value. mRS indicates modified Rankin Scale. NIHSS, National Institutes of Health Stroke Scale. Scores on the mRS range from 0 to 6, with 0 indicating no disability, 3 indicating moderate disability, an 6 indicating death.

The association between eGFR as a categorical variable and the efficacy and safety outcome was estimated by calculating the odds ratios (ORs) with 95% confidence intervals (CIs) using binary logistic regression models. β coefficient with its 95% CI was calculated using general linear model for the outcome of European quality of life visual analogue scale.

* The models were adjusted for age，sex，baseline NIHSS，history of hypertension, history of antiplatelet and anticoagulant drug use, onset-to-needle time and bridging thrombectomy.

Table S7 Sensitivity analysis for safety outcomes excluding the patients with history of diuretics, dehydration agents and contrast agents use

	eGFR(mL/min/1.73m^2)	Event rate,%	Crude OR (95% CI)	P value	Adjusted OR (5% CI)*	P value
Symptomatic intracranial haemorrhage within 36 h	≥90	12(1.27)	1	-	1	-
	60-89	12(3.33)	2.65(1.18-5.96)	0.02	2.41(0.99-5.87)	0.05
	＜60	4(4.40)	3.44(1.09-10.88)	0.04	3.01(0.79-11.42)	0.11
Symptomatic intracranial haemorrhage within 90 days	≥90	14(1.48)	1	-	1	-
	60-89	13(3.61)	2.47(1.15-5.3)	0.02	2.29(0.99-5.27)	0.05
	＜60	5(5.49)	3.72(1.31-10.56)	0.01	3.37(1.01-11.24)	0.048
Parenchymal haematoma 2 intracranial haemorrhage within 90 days	≥90	8(0.84)	1	-	1	-
	60-89	2(0.56)	0.58(0.12-2.67)	0.48	0.46(0.09-2.37)	0.35
	＜60	2(2.20)	2.25(0.48-10.57)	0.30	1.94(0.31-12)	0.48
Any intracranial haemorrhage within 90 days	≥90	48(5.07)	1	-	1	-
	60-89	32(8.89)	1.76(1.11-2.8)	0.016	1.41(0.85-2.36)	0.19
	＜60	13(14.29)	2.92(1.52-5.6)	0.001	2.13(0.99-4.56)	0.05
Death within 90 days	≥90	29(3.06)	1	-	1	-
	60-89	28(7.78)	2.64(1.56-4.47)	0.0003	1.95(1.08-3.53)	0.028
	＜60	21(23.08)	8.71(4.75-15.97)	<.0001	6.46(3-13.9)	<.0001
Adverse events within 90 days	≥90	788(83.21)	1	-	1	-
	60-89	329(91.39)	2.1(1.4-3.13)	0.0003	1.8(1.18-2.74)	0.006
	＜60	89(97.80)	6.16(1.93-19.68)	0.0022	5.46(1.68-17.77)	0.005

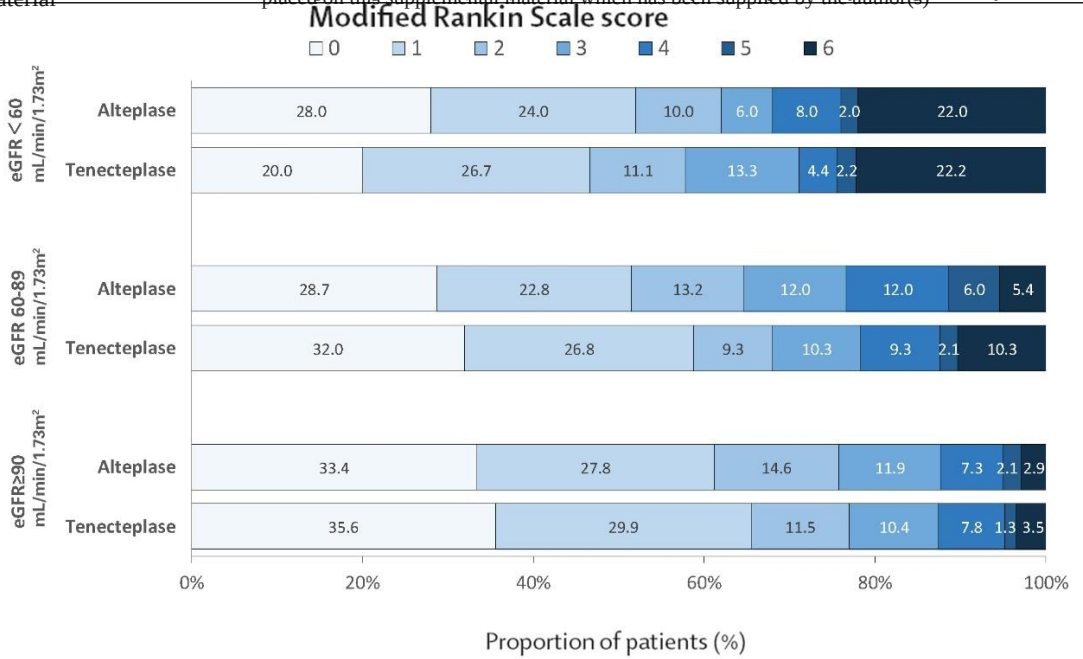
Serious Adverse events within 90 days	≥90	116(12.25)	1	-	1	-
	60-89	73(20.28)	1.81(1.31-2.49)	0.0003	1.56(1.1-2.22)	0.0127
	＜60	31(34.07)	3.45(2.16-5.53)	<.0001	2.85(1.68-4.82)	<.0001

Data are expressed as n/N (%), effect size (95% CI) or p value. Odds ratios of the safety outcomes were calculated with their 95% CIs using binary logistic regression.

***** The models were adjusted for age，sex，baseline NIHSS，history of hypertension, history of antiplatelet and anticoagulant drug use, onset-to-needle time and bridging thrombectomy.

Figure S1 Distribution of modified Rankin Scale scores at 90 days in the participants according to eGFR and assigned treatment

Figure S2. Odds ratios with 95% confidence intervals of estimated glomerular filtration rate (eGFR) with the mRS 0-1 outcome (A), symptomatic intracranial haemorrhage within 36 h (B), and all-cause mortality (C), adjusted for age, sex, baseline NIHSS, history of hypertension, history of antiplatelet and anticoagulant drug use. onset-to-needle time, bridging thrombectomy,
eGFR knots at 30, 60, 90 and 120 mL/min/1.73 m^2. Reference group is eGFR of 90 mL/min/1.73 m^2.


Modified Rankin Scale score
0
1
2
3
4
5
6
eGFR < 60 mL/min/1.73m²
Alteplase
28.0
24.0
10.0
6.0
8.0
2.0
22.0
Tenecteplase
20.0
26.7
11.1
13.3
4.4
2.2
22.2
eGFR 60-89 mL/min/1.73m²
Alteplase
28.7
22.8
13.2
12.0
12.0
6.0
5.4
Tenecteplase
32.0
26.8
9.3
10.3
9.3
2.1
10.3
eGFR≥90 mL/min/1.73m²
Alteplase
33.4
27.8
14.6
11.9
7.3
2.1
2.9
Tenecteplase
35.6
29.9
11.5
10.4
7.8
1.3
3.5
0%
20%
40%
60%
80%
100%
Proportion of patients (%)