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ORIGINAL RESEARCH

Association of Renal Impairment with Clinical Outcomes Following Endovascular Therapy in Acute Basilar Artery Occlusion

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Purpose: Renal impairment (RI) is associated with unfavourable outcome after acute ischaemic stroke with anterior circulation large vessel occlusion. We assessed the association of RI with clinical outcomes in patients with acute basilar artery occlusion (ABAO), and the impact of RI on the effects of endovascular therapy (EVT) versus standard medical treatment (SMT).

Patients and Methods: We used data from the BASILAR registry, an observational, prospective, nationwide study of patients with ABAO in routine clinical practice in China. Baseline estimated glomerular filtration rate (eGFR) was recorded at admission. The primary outcome was the modified Rankin Scale (mRS) score at 90 days. Secondary outcomes included favourable outcome (mRS score 0–3), mortality, and symptomatic intracranial haemorrhage (sICH). Multivariate logistic regression was used to assess the association of RI with mortality and functional improvement at 90 days.

Results: Among 829 patients enrolled, 747 patients were analysed. The median baseline eGFR was 89 mL/min/1.73m^2 (IQR, 71–100), and 350 (46.8%), 297 (39.8%), and 100 (13.4%) patients had baseline eGFR values of ≥90, 60–89, and <60 mL/min/1.73m^2, respectively. RI was associated with increased mortality (adjusted odds ratio [aOR], 1.97; 95% CI, 1.15–3.67) at 90 days and decreased survival probability (aOR 1.74; 95% CI, 1.30–2.33) within 1 year. EVT was associated with better functional improvement (common aOR, 2.50; 95% CI, 1.43–4.35), favourable outcome (aOR 5.42; 95% CI, 1.92–15.29) and lower mortality (aOR 0.47; 95% CI, 0.25–0.88) in ABAO patients with eGFR ≥90 mL/min/1.73m^2. However, RI was not modified the relationship of EVT with functional improvement (common aOR, 3.03; 95% CI, 0.81–11.11), favourable outcome (aOR 2.10; 95% CI, 0.45–9.79), and mortality (aOR 0.56; 95% CI, 0.15–2.06) by eGFR categories.

Conclusion: RI is associated with reduced efficacy of EVT and worse functional outcome and higher mortality at 3 months and lower survival probability at 1 year in patients with ABAO.

Keywords: ischemia stroke, basilar artery occlusion, renal impairment, endovascular therapy, glomerular filtration rate

Introduction

Renal impairment (RI), mainly characterised by a lower estimated glomerular filtration rate (eGFR) in chronic kidney disease, is common among patients with acute ischaemic stroke.[1] A growing number of studies have assessed the association of RI with clinical outcomes after acute ischaemic stroke following endovascular therapy (EVT) or intravenous thrombolysis (IVT).[2,3] In-hospital medical complications, such as vascular, urinary, and infectious, are relevant factors influencing the length of hospitalization after acute stroke.[4] Xiao et al reported that RI was independently associated with poor functional outcome at 90 days[5,6] and Laible et al found that RI was associated with higher mortality

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following endovascular therapy (EVT).[7] Similarly, the post hoc analysis of ENCHANTED trial[8] and a multicentre cohort study[9] showed that RI was associated with increased mortality. However, the bulk of the evidence is mostly based on studies in patients with anterior circulation large vessel occlusion.

Acute basilar artery occlusion (ABAO) is a rare ischaemic stroke, accounting for a very small proportion (approximately 1%) of all ischaemic strokes and 5–10% of strokes resulting from large vessel occlusion (LVO) strokes,[10,11] and it usually represents a major neurological disastrous disease as severe disability and mortality rates of ABAO affecting 85–95% of patients.[10–12] In contrast to anterior circulation stroke, patients with acute basilar artery occlusion (ABAO) have worse clinical outcomes, and patients with RI are prone to posterior circulation strokes due to the individual anatomical structure and functional characteristics of the vertebrobasilar arteries.[13,14] Laible and Rhim et al[15,16] reported that approximately one-fifth of patients with ABAO were found to have RI on admission. However, recent studies on the impact of RI on clinical outcomes after EVT have been relatively limited and conflicting for ABAO, and the current clinical guidelines for contraindications of RI in ABAO therapy are still unclear. A single centre study reported that RI was associated with higher intracranial haemorrhage but not with worse functional outcome at 3 months in patients with vertebrobasilar stroke.[15] A multicentre study[16] reported that RI was associated with unfavourable outcomes, but not with intracranial haemorrhage and mortality. Recently, Xiao et al reported that RI was associated with higher symptomatic intracranial haemorrhage and worse functional outcome at 3 months and 1 year.[6] However, these studies have many limitations, and it is difficult to generalise about the association between RI and ABAO due to the lack of a control group, the limited number of patients with RI, and the simplistic stratification.

Therefore, we sought to evaluate the association of RI with clinical outcomes and its interaction with different treatment modalities in patients with ABAO using the Endovascular Treatment for Acute Basilar Artery Occlusion Study (BASILAR) dataset, a multicentre, prospective registry programme in China.

Methods

Study Population

This cohort study used the BASILAR registry dataset (http://www.chictr.org.cn; ChiCTR1800014759), which recruited 829 consecutive patients with acute symptomatic and radiological BAO in 47 senior stroke centres covering 15 provinces and municipalities across China. Patients with missing serum creatinine values were excluded from this analysis. The study was approved by the institutional review board or the ethics committee at each participating centre, and written informed consent was taken from all study participants before entering the study, and other details of the study protocol have been published previously.[17] Patients with missing serum creatinine values were excluded in this analysis. We obtained the written informed consent from patients or their legal authorizes representatives in accordance with the Declaration of Helsinki. Data are available from the corresponding author upon reasonable requests.

Clinical Variables and Outcome Assessment

Baseline characteristics of demographics, medical history, stroke etiology, admission National Institutes of Health Stroke Scale (NIHSS) score, admission posterior circulation Acute Stroke Prognosis Early Computed Tomography Score (pc-ASPECTS), pretreatment with IVT, occlusion site, and admission serum creatinine were collected by trained investigators (neurologists from participating hospitals). eGFR was calculated by measuring the serum creatinine level on admission using the Chronic Kidney Disease Epidemiology Collaboration China equation with an adjusted coefficient of 1.1 for the Asian population.[18,19] Patients were categorised into three groups according to their baseline eGFR: eGFR≥ 90, 60–89, and <60mL/min/1.73m^2, respectively.[20] Renal impairment was defined as an eGFR <60mL/min/1.73m^2.[21] After enrollment, all patients were followed up to 1 year through hospitalization registration and video telephony or telephone interview, until the endpoint or the latest followed up until March 2020. Followed-up was centralised and performed by trained interviewers who were unaware of baseline eGFR values and was based on a standardized interview protocol, supplemented by medical record review.

The primary outcome was a functional improvement as an mRS shift (mRS, score range from 0 [no symptoms] to 6 [death]) at 90 days.[22] The secondary outcomes included symptomatic intracranial hemorrhage (sICH) within 48 hours,

mortality, favourable outcome at 90 days, and mortality at 12 months. Mortality included all-cause mortality, and favourable outcome was defined as score of 0 to 3 for mRS.

Statistical Analysis

Categorical variables were presented as numbers (percentages) and compared using χ^2 or Fisher exact tests. Continuous variables were expressed as the median (interquartile range [IQR]) and compared using the Mann–Whitney *U*-test for variables without a normal distribution. The association between eGFR and clinical outcomes (functional improvement, favourable functional outcome, and mortality) was assessed by univariable and multivariable ordinal or binary logistic regression, and the outcomes were presented as odds ratios (OR) with 95% confidence intervals (CI) with patients with eGFR≥90mL/min/1.73m^2 as the reference.

The potential nonlinear relationship between eGFR and the adjusted OR of the outcomes was further evaluated using a multivariable logistic regression with restricted cubic spline curve with 3 knots for eGFR adjusting for all potential covariates. The effect of eGFR on the outcome of endovascular therapy (EVT vs SMT) was investigated by adding interaction terms in the multivariable logistic regression. The statistical significance of eGFR stratification for treatment modality (EVT vs SMT or direct EVT vs bridging therapy) was examined by adding interaction terms to multivariable logistic/ordinal regression. Multivariate Cox regression analyses were performed to investigate the effect of RI on the probability of survival at 1 year.

For propensity score-matched (PSM) analysis, we performed 1:2 matching based on the nearest-neighbor matching algorithm with a caliper width of 0.2 the propensity score with age, sex, NIHSS, pc-ASPECTS, stroke etiology, occlusion site and intravenous thrombolysis status as covariables.

All the potential covariates were adjusted for the following confounders in multivariable logistic regression: age (continuous), sex (categorical), hyperlipidemia (categorical), atrial fibrillation (AF, categorical), stroke etiology (categorical), occlusion site (categorical), baseline NIHSS score (ordinal, adjusted odds ratios [OR] per point increase), baseline pc-ASPECTS (ordinal, adjusted OR per point increase).

Statistical analysis was performed using SPSS statistical software version 26 (IBM Corp, Armonk, NY, USA), and R version 4.1.0 (R Core Team, China). Two-sided values of $P < 0.05$ were considered statistically significant. We excluded the missing essential data from our analysis, so we did not impute for missing data.

Results

Baseline Characteristic

Of the 829 patients with ABAO enrolled in the BASILAR, 82 (9.9%) had missing data on serum creatinine data. The flowchart of this study is presented in Figure 1. Of the 747 patients eligible for this analysis, the median (IQR) age was 65 (57–74) years, baseline eGFR was 89 (71–100) mL/min/1.73m^2, and 190 (25.4%) patients were female. Among these patients, 350 (46.8%), 297 (39.8%), and 100 (13.4%) had baseline eGFR values of ≥90, 60–89, and <60mL/min/1.73m^2, respectively (Table S1). Within the eGFR categories, baseline demographic and clinical outcome characteristics of patients by treatment modality in the unmatched and matched subgroups are summarised in Tables 1 and S2. Patients with decreased eGFR were older, had worse collateral status, and had higher rates of hypertension, atrial fibrillation, and coronary artery disease, but there were no significant differences between EVT and SMT among the 3 categories of eGFR (Table 1).

Association of RI with Clinical Outcomes at 3 Months

Regardless of treatment modality, the proportion of favourable outcomes was not significantly different, but the rate of mortality rate was significantly higher in the RI group than in the others. Using a multivariate logistic regression model with restricted cubic splines, the linear relationship was found between baseline eGFR and clinical outcomes. Here, if we set eGFR=60mL/min/1.73m^2 as the reference, and the OR of mortality significantly decreased with increasing of eGFR (Figure 2A), but the OR of favourable outcome was not statistically significant (P = 0.11; Figure S1A). Among the 3 categories of eGFR, RI was associated with increased mortality (adjusted OR[aOR], 1.97 [95% CI, 1.15–3.67; p = 0.01]), but

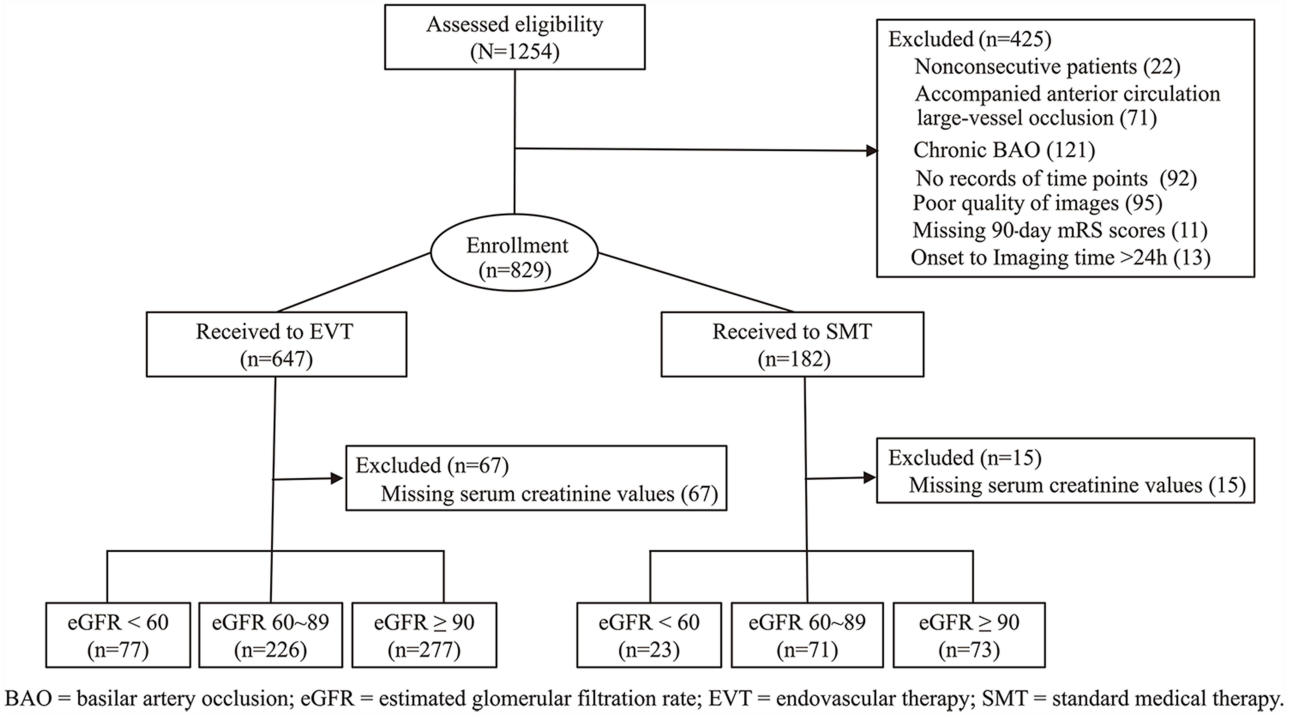

Figure 1 Flowchart of patient inclusion. This figure shows the enrollment information of patients in the present study.
Abbreviations: BAO, basilar artery occlusion; eGFR, estimated glomerular filtration rate; mRS, modified Rankin Scale; EVT, endovascular therapy; SMT, standard medical treatment.

RI was not associated with functional improvement (adjusted common OR[acOR], 1.61 [95% CI, 0.98–2.66; p = 0.06]) (Table 2).

Regarding treatment modality, the estimated marginal effect of EVT on favourable outcome gradually increases following the increase of eGFR, and the interaction effect of EVT on favourable outcome was significantly higher than SMT when eGFR ≥60mL/min/1.73m^2 (Figure 2B). The probability of a favourable outcome increased and the probability of mortality decreased with the increase of eGFR in the EVT and SMT cohorts (Figure 2C and D).

The distribution of 90-day mRS scores in both EVT and SMT for baseline eGFR categories is shown in Figure 3. There were significantly better trends towards favourable outcomes after EVT than SMT in patients with eGFR 60–89mL/min/1.73m^2 (31.0% vs 8.5%; P < 0.001) and patients with eGFR ≥90mL/min/1.73m^2 (33.6% vs 8.2%; P < 0.001 1) but not in the eGFR <60mL/min/1.73m^2 subgroups. Similarly, the rates of excellent outcomes and functional independence outcomes were higher, but mortality was lower in the EVT group compared with the SMT in the 2 upper eGFR sub-population. The rates of sICH were numerically higher with decreased eGFR in the EVT group, and only the difference in the eGFR ≥90mL/min/1.73m^2 subgroup was statistically significant (5.8% vs 0.0%, P = 0.03) between EVT and SMT (Table 1).

Multivariable logistic and ordinal regression analyses depicting the associations of baseline eGFR with clinical outcomes at 90 days in the subgroups of patients are shown in Figure 4. After adjustment, EVT was associated with shift analysis (acOR: 2.50 [95% CI, 1.43–4.35], p = 0.002 and 4.76 [95% CI, 2.44–9.09], p <0.001, respectively), mortality (0.47 [95% CI, 0.25–0.88], p = 0.02 and 0.19 [95% CI, 0.09–0.39], p <0.001, respectively), and favourable outcome (5.42 [95% CI, 1.92–15.29], p = 0.001 and 5.65 [95% CI, 1.91–16.73], p = 0.002, respectively) in the eGFR ≥90mL/min/1.73m^2 subgroups and eGFR 60–89mL/min/1.73m^2 subgroups but not in the eGFR <60mL/min/1.73m^2 subgroups. The treatment-by-eGFR category interaction for shift analysis (reference to eGFR ≥90mL/min/1.73m^2, p for interaction=0.80, and 0.09 in eGFR 60–89 and eGFR <60mL/min/1.73m^2, respectively), mortality (reference to eGFR ≥ 90mL/min/1.73m^2, p for interaction = 0.59 and 0.08 in eGFR 60–89 and eGFR <60mL/min/1.73m^2, respectively) were not statistically significant at 90 days.

Table 1 Baseline Characteristics of the Cohort by Treatment Modality and Estimated Glomerular Filtration Rate (eGFR) Category

Characteristic	eGFR<60 (n=100)			eGFR 60–89 (n=297)			eGFR ≥ 90 (n=350)		
	EVT (n=77)	SMT (n=23)	P value	EVT (n=226)	SMT (n=71)	P value	EVT (n=277)	SMT (n=73)	P value
Demographics									
Age (yrs), median (IQR)	71 (63–78)	75 (66–78)	0.39	70 (62–76)	73 (63–79)	0.08	60 (53–65)	61 (55–68)	0.17
Sex (female), n (%)	27 (35.1)	6 (26.1)	0.42	56 (24.8)	26 (36.6)	0.05	61 (22.0)	14 (19.2)	0.60
Clinical characteristics									
Baseline NIHSS score, median (IQR)	30 (18–35)	17 (10–30)	0.007	27 (16–33)	28 (15–33)	0.80	26 (18–32)	26 (16–33)	0.93
Baseline pc-ASPECTS, median (IQR)[a]	8 (7–9)	5 (7–9)	0.03	8 (7–9)	7 (6–8)	0.02	8 (7–9)	7 (6–8)	<0.001
Pc-CS score, median (IQR)[b]	4 (3–6)	4 (2–6)	0.47	5 (3–6)	4 (4–6)	0.70	4 (3–6)	5 (4–7)	0.05
BATMAN, median (IQR)[c]	4 (3–6)	1 (3–6)	0.42	4 (3–5)	5 (2–6)	0.16	4 (2–6)	5 (4–6)	0.001
Collateral status (ASITN/SIR), n (%)			0.70			0.35			0.61
0–1	56 (72.7)	18 (78.3)		135 (59.7)	47 (66.2)		162 (58.5)	43 (58.9)	
2	12 (15.6)	2 (8.7)		57 (25.2)	12 (16.9)		87 (31.4)	20 (27.4)	
3–4	9 (11.7)	3 (13.0)		34 (15.0)	12 (16.9)		28 (10.1)	10 (13.7)	
Intravenous thrombolysis, n (%)	15 (19.5)	2 (8.7)	0.35*	37 (16.4)	27 (38.0)	<0.001	55 (19.9)	16 (21.9)	0.70
Drinking	6 (7.8)	3 (13.0)	0.43*	36 (15.9)	17 (23.9)	0.12	84 (30.3)	20 (27.4)	0.63
Smoking current/past	21 (27.3)	5 (21.7)	0.60	69 (30.5)	13 (18.3)	0.05	121 (43.7)	24 (32.9)	0.10
Medical history, n (%)									
Hypertension	60 (77.9)	20 (87.0)	0.55*	159 (70.4)	50 (70.4)	0.99	180 (65.0)	52 (71.2)	0.32
Hyperlipidemia	22 (28.6)	7 (30.4)	0.86	76 (33.6)	23 (32.4)	0.85	98 (35.4)	38 (52.1)	0.009
Diabetes mellitus	20 (26.0)	6 (26.1)	0.99	41 (18.1)	14 (19.7)	0.77	66 (23.8)	16 (21.9)	0.73
Atrial fibrillation	32 (41.6)	2 (8.7)	0.004	61 (27.0)	17 (23.9)	0.61	30 (10.8)	5 (6.8)	0.31
Coronary artery disease	18 (23.4)	4 (17.4)	0.54	36 (15.9)	13 (18.3)	0.64	35 (12.6)	7 (9.6)	0.48
Cerebral infarction	18 (23.4)	9 (39.1)	0.14	50 (22.1)	17 (23.9)	0.75	55 (19.9)	16 (21.9)	0.70
Cause of stroke, n (%)			0.006			0.31			0.09
Large artery atherosclerosis	37 (48.1)	18 (78.3)		130 (57.5)	38 (53.5)		203 (73.3)	52 (71.2)	
Cardioembolism	35 (45.5)	2 (8.7)		78 (34.5)	23 (32.4)		44 (15.9)	7 (9.6)	
Other causes	5 (6.4)	3 (13.0)		18 (8.0)	10 (14.1)		30 (10.8)	14 (19.2)	
Occlusion sites, n (%)			0.01			0.04			<0.001
Distal basilar artery	35 (45.5)	4 (17.4)		88 (38.9)	24 (33.8)		73 (26.4)	13 (17.8)	
Middle basilar artery	22 (28.6)	15 (65.2)		66 (29.2)	33 (46.5)		92 (33.2)	44 (60.3)	
Proximal basilar artery	9 (11.7)	1 (4.3)		42 (18.6)	7 (9.9)		48 (17.3)	5 (6.8)	
Vertebral artery-V4	11 (14.3)	3 (13.0)		30 (13.3)	7 (9.9)		64 (23.1)	11 (15.1)	
OTT, median (IQR), min	221 (143–334)	268 (107–485)	0.46	247 (123–407)	210 (111–385)	0.53	248 (131–402)	234 (121–431)	0.78
OTI, median (IQR), min	180 (99–297)	240 (86–430)	0.45	210 (83–364)	176 (77–350)	0.53	215 (85–362)	185 (99–385)	0.70
Successful recanalization, n (%)	60 (77.9)	2 (8.7)	<0.001	184 (81.4)	7 (9.9)	<0.001	226 (99.1)	2 (0.9)	<0.001

(*Continued*)

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Table 1 (Continued).

Characteristic	eGFR<60 (n=100)			eGFR 60–89 (n=297)			eGFR ≥ 90 (n=350)		
	EVT (n=77)	SMT (n=23)	P value	EVT (n=226)	SMT (n=71)	P value	EVT (n=277)	SMT (n=73)	P value
Clinical outcomes									
mRS score 0–1 at 90 days, n (%)	13 (16.9)	2 (8.7)	0.51*	49 (21.7)	5 (7.0)	0.005	56 (20.2)	3 (4.1)	0.001
mRS score 0–2 at 90 days, n (%)	19 (24.7)	3 (13.0)	0.24	61 (27.0)	5 (7.0)	<0.001	77 (27.8)	5 (6.8)	<0.001
mRS score 0–3 at 90 days, n (%)	21 (27.3)	4 (17.4)	0.34	70 (31.0)	6 (8.5)	<0.001	93 (33.6)	6 (8.2)	<0.001
Mortality at 90 days, n (%)	47 (61.0)	16 (69.6)	0.46	101 (44.7)	55 (77.5)	<0.001	113 (40.8)	47 (64.4)	<0.001
sICH[d]	7 (9.2)	0	0.20*	14 (6.4)	1 (1.4)	0.13*	16 (5.8)	0	0.03*
Any ICH	13 (16.9)	0	0.04*	23 (10.2)	1 (1.4)	0.02	27 (9.7)	0	0.005
Severe adverse events									
Pulmonary infection	60 (77.9)	14 (60.9)	0.10	158 (69.9)	57 (80.3)	0.09	214 (77.3)	59 (80.8)	0.51
Hemicraniectomy	0	1 (4.3)	0.12*	2 (0.9)	0	0.71*	5 (1.8)	0	0.59*
Respiratory Failure	40 (51.9)	10 (43.5)	0.48	96 (42.5)	32 (45.1)	0.70	110 (39.7)	28 (38.4)	0.83
Circulatory Failure	32 (41.6)	7 (30.4)	0.34	58 (25.7)	23 (32.4)	0.27	49 (17.7)	14 (19.2)	0.77
Ulcer	17 (22.1)	7 (30.4)	0.41	40 (17.7)	15 (21.1)	0.52	46 (16.6)	15 (20.5)	0.43
Venous thrombosis	4 (5.4)	1 (4.3)	1.000*	12 (5.3)	4 (5.6)	1.000*	25 (9.0)	0	0.008

Notes: [a]Data were missing for 3 patients in eGFR 60–89 group and 2 patients eGFR≥90 group. [b]Data were missing for 1 patient in eGFR 60–89 group. [c]Data were missing for 1 patient in eGFR 60–89 group. [d]Data were missing for 1 patient in eGFR<60 group, 6 patients in eGFR 60–89 group and 3 patients eGFR≥90 group. *P values were calculated using the Fisher exact tests.

Abbreviations: ABAO, acute basilar artery occlusion; IQR, interquartile; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation-Alberta Stroke Program Early CT Score; PC-CS, posterior circulation collateral score; BATMAN, basilar artery on Tomography Angiography; sICH, OTT, onset-treatment time; OTI, onset-imaging time.

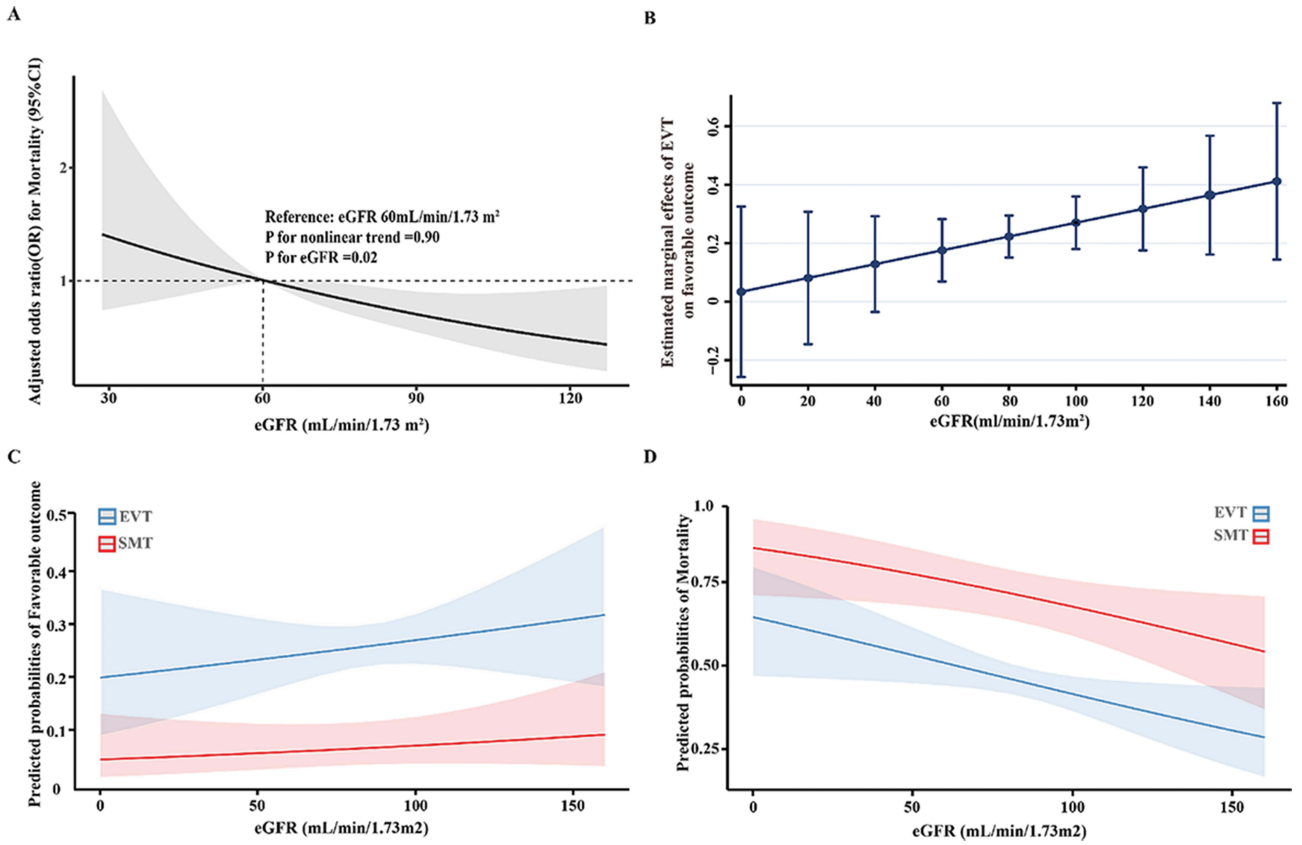

Figure 2 Association of eGFR with clinical outcomes. A restricted cubic splines curve with 3 knots illustrating the association of the baseline eGFR with mortality and favourable outcome in (**A**). The interaction effect of EVT on favourable outcome in (**B**). The estimated probabilities of a favourable outcome and mortality by treatment modality according to baseline eGFR are presented in (**C** and **D**). The EVT group had an increased estimated probability of favourable outcome and decreased estimated probability of mortality than the SMT group as the eGFR increases.

Association of RI and Clinical Outcome in Patients with Direct EVT and Bridging Therapy

The baseline characteristics of direct EVT and bridging therapy in the matched and unmatched subgroups with eGFR category are shown in Tables S3 and S4. After PSM, bridging therapy did not differ in the baseline demographics and clinical outcome compared with direct EVT, and it was independent of eGFR category. The distribution of 90-day mRS

Table 2 Associations Between Baseline Estimated Glomerular Filtration Rate Categories and Clinical Outcome at 3 Months

Outcome	eGFR	Number of events (%)	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
mRS shift, median (IQR)	≥90	5 (3–6)	1 [Reference]	NA	1 [Reference]	NA
	60–89	6 (3–6)	1.21 (0.91–1.61)	0.19	1.13 (0.80–1.58)	0.50
	<60	6 (3–6)	1.73 (1.11–2.69)	0.02	1.61 (0.98–2.66)	0.06
Favorable outcome (mRS 0–3)	≥90	99/350 (28.3)	1 [Reference]	NA	1 [Reference]	NA
	60–89	76/297 (25.6)	0.87 (0.62–1.24)	0.44	0.76 (0.48–1.19)	0.22
	<60	25/100 (25.0)	0.85 (0.51–1.41)	0.52	0.75 (0.41–1.40)	0.37
Mortality	≥90	160/350 (45.7)	1 [Reference]	NA	1 [Reference]	NA
	60–89	156/297 (52.5)	1.31 (0.96–1.79)	0.08	1.18 (0.81–1.74)	0.39
	<60	63/100 (63.0)	2.02 (1.28–3.19)	0.03	1.97 (1.15–3.67)	0.01
sICH	≥90	16/347 (4.6)	1 [Reference]	NA	1 [Reference]	NA
	60–89	15/291 (5.2)	1.12 (0.55–2.32)	0.75	1.38 (0.61–3.11)	0.44
	<60	7/99 (7.1)	1.57 (0.63–3.94)	0.33	1.69 (0.61–4.68)	0.31

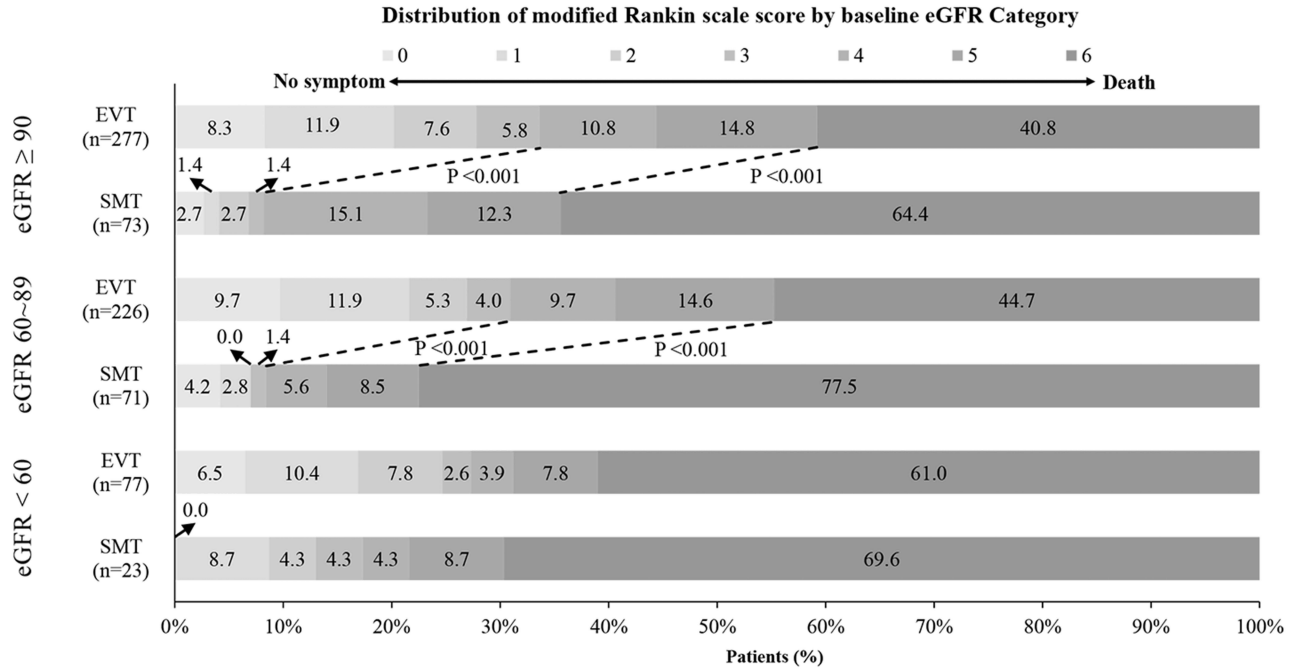

Figure 3 Distribution of the modified Rankin Scale (mRS) scores at 90 days. This figure shows the 90-day mRS scores distributions stratified by treatment modality in all patients according to the eGFR categories.

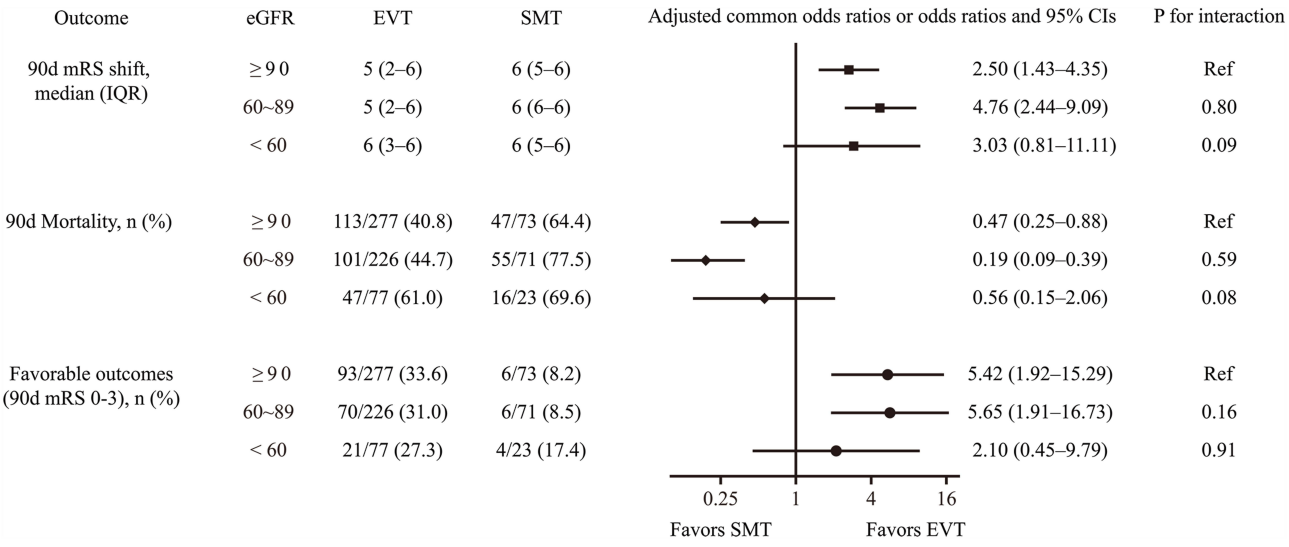

Figure 4 Effect of EVT according to baseline eGFR categories. Reported odds ratios are adjusted for age, sex, AF, baseline NIHSS, pc-ASPECTS, stroke etiology, and occlusion site.

scores in both direct EVT and bridging therapy for baseline eGFR categories is shown in Figure S2. Multivariable ordinal and logistic regression analyses indicated that the functional improvement did not differ between the direct EVT and bridging therapy group nor did favourable outcome or mortality at 3 months. In addition, the treatment-by-eGFR category interaction for shift analysis (reference to eGFR ≥ 90mL/min/1.73m^2, p for interaction=0.46, and 0.01 in eGFR 60–89 and eGFR < 60mL/min/1.73m^2, respectively), mortality (reference to eGFR ≥ 90 mL/min/1.73m^2, p for interaction = 0.95 and 0.16 in eGFR 60–89 and eGFR < 60mL/min/1.73m^2, respectively), and sICH (reference to eGFR ≥ 90mL/min/1.73m^2, p for interaction = 0.33 and 0.79 in eGFR 60–89 and eGFR < 60mL/min/1.73m^2, respectively) were not statistically significant at 3 months (Table S5). When restricting the analysis to the patients receiving direct EVT, RI

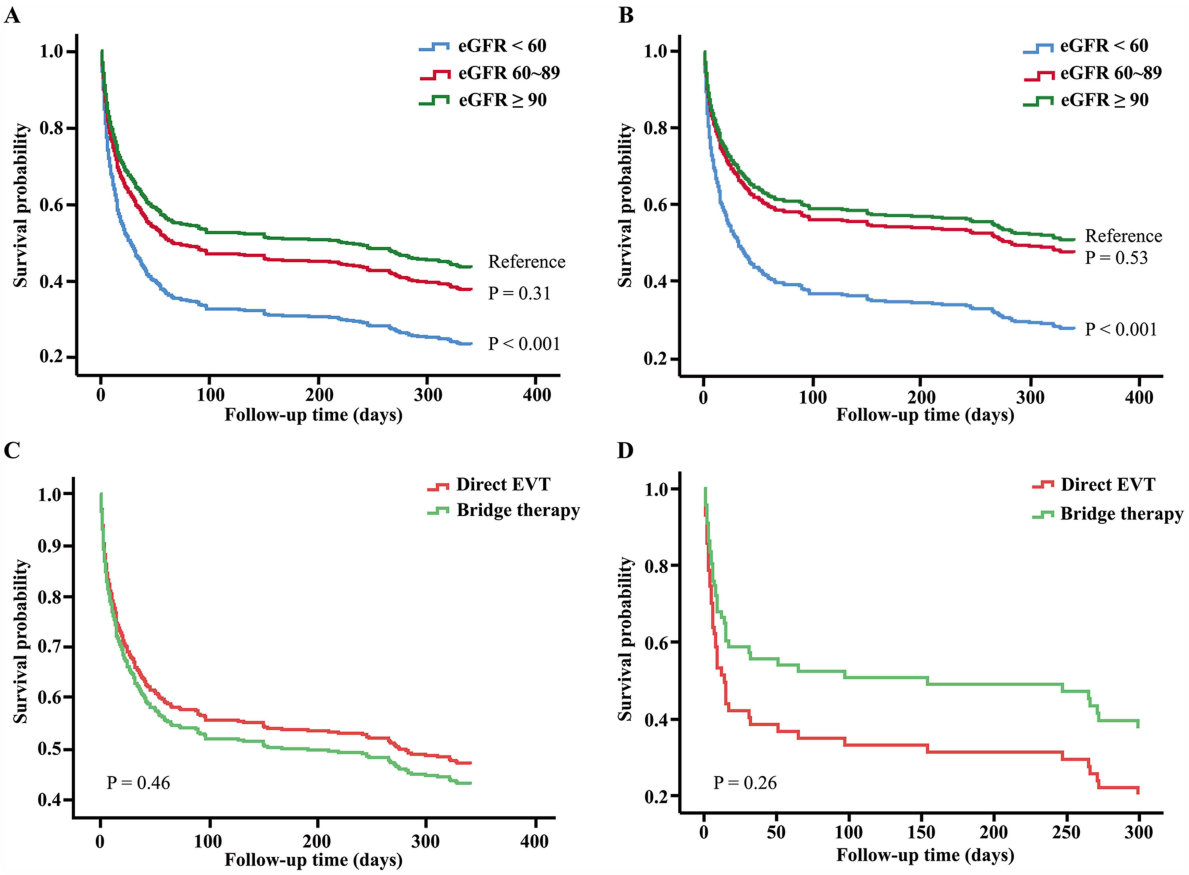

Figure 5 Cumulative survival probability for patients. Cumulative survival curves were plotted according to baseline eGFR categories in all patients (**A**) and patients with EVT (**B**). Cumulative survival curves were plotted according to IVT in all patients (**C**) and patients with RI (**D**).

was significantly associated with worse functional improvement (0.47 [95% CI, 0.23–0.85], p = 0.02) and the increased risk of mortality (2.43 [95% CI, 1.27–4.64], p = 0.001) at 90 days (Table S6).

Long-Term Survival According to Renal Impairment

In the study population, 195 patients died during hospitalization period and 46 patients had missing data, leaving 506 patients were followed up to 1 year, including 62 patients with RI. Multivariate Cox regression analysis indicated that RI remained significantly associated with the decreased survival probability at 1 year both in the overall population and in patients receiving EVT (1.62 [95% CI, 1.08–2.43], p=0.02, and 1.86 [95% CI, 1.14–3.02], p = 0.01) compared to patients with eGFR ≥ 90mL/min/1.73m^2. However, the cumulative survival probability did not differ between the direct EVT group and the bridging therapy group in all patients (0.82 [95% CI, 0.58–1.15], p = 0.24) or in the subgroup of patients with RI (0.51 [95% CI, 0.11–2.37], p = 0.39) (Figure 5).

Discussion

This study indicated that RI was the association between baseline eGFR levels and the functional outcomes at 3 months after ABAO. RI was associated with mortality at 90 days and 1 year follow-up, but RI was not associated with functional improvement, favourable outcome or sICH. Furthermore, the baseline eGFR was independently associated with functional improvement, favourable outcome and mortality when comparing treatment effects between EVT and SMT, but RI modified the relationship between EVT and outcomes in patients with ABAO. Stroke and chronic kidney disease are serious global health problems and 35% of patients with ischaemic stroke coexist with CKD because the human brain and kidney are low-resistance end organs with sharing a small vascular structure and continuous exposure to highly

pulsatile pressure and flow.[23,24] Previous studies have shown that reduced renal function is closely associated with unfavourable outcome after ischaemic stroke.[1,5] Large-scale evidence based on the anterior circulation stroke showed that RI is an independent risk factor for unfavourable outcomes as well as stroke development following EVT.[2,25,26] Recently, 3 randomised clinical trials (BEST, BASICS, and BAOCHE initiated a new era of EVT in patients with ABAO, although the eGFR data were not reported).[27–29] A multicentre observational study of 110 patients undergoing EVT suggests that RI is an independent risk factor for unfavourable outcomes at 90 days and survival probability in patients with ABAO.[6,16] Our results are consistent with those of previous studies both anterior circulation stroke and vertebrobasilar stroke. Our study shown a linear relationship between eGFR and functional outcomes, and the favourable outcomes were significantly decreased in patients with RI at 90 days, based on a reference value of eGFR≥90mL/min/1.73m^2 (Figure S1B). However, a single centre study[15] found that lower eGFR was associated with higher ICH but not with worse outcome after thrombectomy at 90 days in vertebrobasilar stroke, and a multicentre study[6] suggested that RI was associated with a higher risk of sICH in hospital and a decreased in survival, favourable outcome, and functional improvement at 90 days and 1-year follow-up in patients with vertebrobasilar artery occlusion who received EVT, which is not consistent with our study. The discrepancy between these studies may be attributable to the differences in limited numbers, different methods of grouping patients by eGFR, and prespecified power analysis.[15]

The important point of our study was the renal function-dependent association of EVT with clinical outcomes of ABAO because the influence of RI on clinical outcomes in patients who underwent EVT has not received sufficient attention. This study revealed that the correlation of EVT with clinical outcomes after ABAO was significant only in patients with an eGFR of ≥60mL/min/1.73m^2, whereas EVT had no significant association with clinical outcomes compared with SMT in patents with an eGFR of <60mL/min/1.73m^2. Consistent with thrombolytic therapy,[15] RI itself may modify the association of EVT with the clinical outcomes in patients with ABAO. Interestingly, we discovered that RI was associated with an increased proportion of mortality but not sICH at 90 days in all patients who underwent EVT but not in the subgroup of patients who received bridging therapy. Since mortality in patients with RI is largely attributable to cardiovascular and cerebrovascular disease,[30] the renal function-dependent association of EVT on mortality risk may indicate that the cumulative influence of RI on cardiovascular and cerebrovascular atherosclerosis cannot be rescued by EVT. Therefore, even after successful recanalization, neurointerventionists should pay attention to the comprehensive management of patients to improve patient outcomes. To investigate whether RI has an independent influence on survival after discharge in patients with ABAO, we followed up to 1 year for survival patients. Multivariable Cox regression analysis showed that RI was associated with a decreased likelihood of survival, which is consistent with the latest research in acute vertebrobasilar stroke.[6,16]

The underlying mechanism of unfavourable outcomes with RI is unknown. Previous studies have shown that haematological disease was the cause of the acute cerebrovascular disease.[31] This is a noteworthy aspect that should be emphasized because hematological disorders are a commonly unrecognized cause of acute stroke with a particular treatment depending on its etiology. In our study, the baseline NIHSS, pc-ASPECTS, and time from onset to treatment were similar among baseline eGFR categories (Table S1). There are several possible explanations for this. Firstly, renal function-dependent pathophysiological mechanisms, including coagulation disorders, endothelial damage, systemic inflammation, and oxidative stress, are the main reasons for unfavourable outcomes after ABAO.[14] Secondly, patients with RI are more likely to have aggravated cerebrovascular risk, including hypertension, hyperlipidemia, and platelet dysfunction.[14] Thirdly, RI affects neurohormonal communication resulting in sympathetic overflow and activation of the tissue renin–angiotensin system and mediating inflammation and inducing vascular fibrosis.[14,32] Finally, RI increases the risk of contrast-associated acute kidney injury due to heavy use of contrast agents during EVT, which in turn is associated with increased mortality.[33] These potential mechanisms may partly explain why a decreased eGFR is associated with unfavourable outcome and modify the relationship between EVT and clinical outcomes in patients with ABAO.

However, this study had several limitations. Firstly, the observational and nonrandomized control study may cause selection bias. The doctors, family members, or even patients themselves may be more inclined to choose conservative treatment other than EVT for patients with severe RI because of the lower life expectancy, so the results need to be further validated with more study data. Secondly, renal function was measured solely by baseline serum creatinine, which does not reflect the information on proteinuria. Additionally, data of acute kidney injury were not available in this study, and the eGFR data were not collected during follow-up after EVT. Thirdly, we did not completely exclude extremely low

or extremely high eGFR values, although a small number of studies excluded patients with eGFR <30mL/min/1.73m^2 or creatinine≥3mg/dl in their protocol. However, we simply divided RI into three groups based on baseline eGFR, and there was not perform detailed analysis of the relationship between different levels of RI and stroke prognosis due to the limited sample size of RI patients.

Conclusions

Our results revealed that RI was associated with increased mortality at 3 months and decreased survival probability within 1 year, but RI was not associated with functional improvement, favourable outcome, or sICH at 3 months. Furthermore, the association of EVT with clinical outcomes was dependent on eGFR in patients with ABAO, and. RI modified the relation of EVT with the outcomes. Further studies are necessary to validate these findings and optimize treatment methods to increase favourable outcome in patients with ABAO following EVT.

Data Sharing Statement

The data that support the findings of this study are available on reasonable request from the correspondence author after approval of the ethics committee and all participating centres.

Ethics Approval and Consent Participate

The methods of the trial were carried out in accordance with relevant guidelines and regulations. The trial protocol was approved by medical ethics committee of the Second Affiliated Hospital of the Army Medical University and all participating centres. All enrolled patients or their legally authorized representatives provided written informed consent before enrollment.

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Disclosure

The authors declare no competing interests in this work.

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