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Can eGFR be a prognostic factor for endovascular therapy for acute ischemic stroke?

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Abstract

Background & Objective: Chronic kidney disease (CKD) is associated with increased mortality risk in acute stroke patients. This study aims to investigate potential association between CKD and the prognosis of endovascular treated acute ischemic stroke patients. *Methods:* Patients with endovascular treatment (EVT) for acute ischemic stroke were studied retrospectively in a comprehensive stroke center. Patients were classified as pre-procedural CKD and non-CKD. The groups were compared regarding demographic data, procedural data, and outcomes. *Results:* A total of 140 patients (69 male, 49.3%) with a mean age of 66.51±11.8 were involved in the study. Symptomatic intracranial hemorrhage in the first 24 hours and mortality in three months were increased in the CKD group (50% vs. 19.8; p=0.001). Excellent and good outcomes were decreased in the CKD group (25% vs. 53.4; p=0.01 and 41.6% vs. 56.9%; p=0.03). Multiple logistic regression adjusted for potential confounders demonstrated that CKD was associated with lower rates of excellent outcome (odds ratio [OR] = 0.50, 95% confidence interval [CI], 0.25 to 0.80, p = 0.01), higher mRS scores (common OR = 1.82, 95% CI, 1.2 to 2.9, p = 0.01), and increased mortality (OR = 2.1, 95% CI, 1.2 to 4.2, p = 0.01) and sICH (OR = 1.15, 95% CI, 1.03 to 3.4, P = 0.04)
Conclusion: There is an association between CKD and poorer results in patients with acute ischemic stroke treated with EVT. The presence of CKD should not prohibit patients from undergoing EVT, but taking baseline eGFR into account may improve estimation of prognosis and help decision-making in treatment modality.

Keywords: Chronic kidney disease, ischemic stroke, endovascular treatment

INTRODUCTION

Chronic kidney disease (CKD) with an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73m2, increases the risk of ischemic stroke, and it is present in 20% to 35% of individuals who have experienced an acute ischemic stroke.[1] In CKD patients on dialysis, the risk of stroke is five times higher than in the general population. Stroke-related death rates are also high in CKD patients, and stroke is the third most common cause of death.[2] Up to half of stroke patients with CKD are unaware of their disease, which is a neglected factor of morbidity.[3]

Vertebrobasilar steal syndrome with the use of AV access in dialysis, decrease in intravascular blood volume secondary to hemodialysis, autonomic neuropathy, and hyperhomocysteinemia play a role in increasing the frequency of strokes associated with large artery disease in CKD and dialysis patients.[4] At the same time, CKD and atrial fibrillation (AF) comorbidities are also common. Studies show that 30% of patients with AF have CKD Stage III, IV or V. Antithrombotic drugs used for stroke prophylaxis in these patients with the risk of complications are also less used in the presence

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of CKD. This is especially for the non-vitamin K oral anticoagulants, which are not used in stage IV and V CKD.[5]

Studies show that there is a strong association between elevated serum creatinine and increased risk and outcome after stroke; and may be a biomarker for vascular disease risk.[3] In the case of proximal large artery occlusion strokes, endovascular treatment (EVT) is strongly recommended. One study that examined CKD patients undergoing EVT, found that CKD was associated with increased mortality risk in these patients. There was however, no association with functional outcome or symptomatic intracranial bleeding.[6]

The aim of this study is to investigate whether there is an association between the prognosis of stroke patients who has CKD, who is treated with EVT, which is a very critical treatment option in case of large artery occlusion.

METHODS

Patients who had EVT for acute ischemic stroke in a comprehensive stroke center between December 2019-June 2022 were retrospectively analyzed. Patients were included in the study if they had baseline creatinine levels and follow-up data available. Patients' files covering data on patient demographics, medical comorbidities, clinical and imaging aspects of the stroke, treatment information, and patient outcomes were accessed. The local ethics committee approved the study. The attending stroke team assessed baseline and 24-hour stroke severity using the National Institutes of Health Stroke Scale (NIHSS).[7] The size of the baseline infarct was determined using the Early CT Score as in the Alberta Stroke Program.[8] Successful recanalization was characterized as a Thrombolysis in Cerebral Infarction (TICI) score of 2b to 3.[9] The Chronic Kidney Disease Epidemiology Collaboration equation was used to compute the estimated glomerular filtration rate (eGFR).[10] Patients were classified as having CKD if their eGFR was less than 60 mL/min/1.73 m2.[11]

The primary outcome measure was 3-month mortality after EVT. Secondary outcomes were symptomatic intracerebral hemorrhage in 24 hours, good functional independence at three months (mRS-good), defined as an mRS score of 0, 1, or 2, and excellent functional independence at three months (mRS- excellent), defined as an mRS score of 0 or 1.[12]

IBM SPSS Statistics version 25.0 was used for statistical analysis (New York) to investigate potential clinical predictors of outcome measures, preliminary univariate logistic or ordinal regression, and Fisher's exact tests were utilized. The association between CKD (defined as an eGFR of 60 mL/min/1.73 m2) and outcome measures was examined using multiple logistic or ordinal regression, which included important factors with $P<0.05$ from the univariate analysis. Multiple logistic regression analysis was adjusted for age, atherosclerosis history, diabetes, and hypertension. To avoid overfitting, the number of variables utilized in the multivariable regression analysis was roughly limited to the number of adverse events divided by 10. All tests were two-tailed, and a p 0.05 level of significance was considered statistically significant.

RESULTS

A total of 140 patients (69 male, 49.3%) with a mean age of 66.51±11.8 were included in this study. Thirty-three of the patients (23.6%) had diabetes mellitus (DM), and 101 had hypertension (HT, 72.1%). Ninety-four patients had dyslipidemia (68.6%), while 67 (47.9%) had atrial fibrillation; 24(17.1%) patients had CKD. Baseline NIHSS score was 18(4-38) and ASPECTS score was 9(6-10). Seventy-three patients (52%) had thrombolytic treatment. Successful recanalization (TICI 2b-3) was achieved in 131 (93.6%) patients. The mean admission creatinine level was 0.9(0.3-7) mg/dl and the mean eGFR was 85(8-90) mL/min/1.73 m2. Intracerebral hemorrhage in the first 24 hours occurred in 14 (10 %) patients. At three months, 76 (54.3%) patients achieved functional independence, and 35 (25.2%) had died. Excellent mRS was achieved in 68(48.6%) patients.

The study population was grouped into two in respect to the presence of CKD group 1[CKD (+), 24 patients] and group 2[CKD (-), 116 patients. Patients with CKD were more likely to be older and have DM and coronary artery disease (Table 1). Male predominance was apparent in group 2. The baseline NIHSS score and ASPECTS score were similar between groups, and the ratio of iv-tPA administration was also similar. Symptomatic intracranial hemorrhage in the first 24 hours was significantly higher in the CKD (+) group (16.6 % vs. 8.6%; $p< 0.002$). Three months mortality was also significantly higher in the CKD (+) group (50% vs. 19.8; $p<0.001$). Excellent and good outcome were significantly lower in the CKD (+) group (25% vs. 53.4; p=0.01 and 41.6% vs. 56.9%; $p<0.03$) (Table 1).

Table 1: Comparision of patients according to eGFR

Parameters	CKD(+) groupeGFR<60 (n = 24)	CKD (-) group eGFR≥60 (n = 116)	P
Age, year, mean±SD	67.9±12.5	65.4±11.7	***0.01***
M, n (%)	11(45.8%)	58(50%)	0.312
Risk factors			
Diabetes, n (%)	10 (41.7%)	23(19.8%)	***0.022***
Hypertension, n (%)	19 (79.2%)	82(70.7%)	0.06
Dyslipidemia, n (%)	15(65.2%)	79(69.3%)	0.700
Smoking, n (%)	7 (29.2%)	33(28.4%)	0.943
Coronary artery disease, n (%)	11 (45.8%)	39(33.6%)	***0.04***
Atrial fibrillation, n (%)	12(53.3%)	55(46.2%)	0.817
Baseline			
Systolic blood pressure, mmHg, mean±SD	154.2 ± 26.5	157.2 ± 30	0.06
NIHSS, median(IQR)	19(4-23)	17(6-38)	0.09
ASPECTS, median(IQR)	8(7-10)	9(6-10)	0.412
Creatinine, mg/dl, median(IQR)	1.6(1.2-7)	0.8(0.3-1.1)	***0.001***
eGFR, mL/min/1.73 m^2, median(IQR)	45(8-59)	85(61-90)	***0.001***
iv thrombolytic, n (%)	12(50%)	61(53%)	0.812
Procedure			
TICI 2b-3 recanalisation, n (%)	21(87.5%)	110(94.8%)	0.112
LKN to procedure completion, median (IQR)	72(0-300)	74(0-395)	0.824
Outcomes			
sICH, n (%)	4 (16.6%)	10(8.6%)	***0.002***
3-mon mRS, median (IQR)	3(1-5)	2(0-6)	0.07
3-mon mortality, n (%)	12(50%)	23(19.8%)	***0.001***
3-mon mRS excellent, n (%)	6(25%)	62(53.4%)	***0.01***
3-mon mRS good, n (%)	10(41.6%)	66(56.9%)	***0.03***

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; eGFR, estimated glomerular filtration rate; LKN, last known normal; mRS, modified Rankin Score; TICI, Thrombolysis in Cerebral Infarction; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracerebral hemorrhage

Unadjusted univariate and multivariable-adjusted odds ratios of outcome measures by renal admission function are presented in Table 2.Multiple logistic regression adjusted for potential confounders like diabetes mellitus, presence of atherosclerosis, age and presence of hypertension demonstrated that CKD was associated with lower rates of excellent outcome(odds ratio [OR] = 0.50 , 95% confidence interval [CI], 0.25 to .80, *p <0.01*), higher mRS scores (common OR = 1.82, 95% CI, 1.2 to 2.9, *p<0.01*), and increased mortality (OR = 2.1, 95% CI, 1.2 to 4.2, *p < 0.01*) and sICH (OR = 1.15, 95% CI, 1.03 to 3.4, *p <0.04*) (Table 2).

DISCUSSION

EVT has been proven to considerably improve the prognosis of individuals who have experienced an acute ischemic stroke due to a large vessel occlusion.[13] The present study showed that patients with acute ischemic stroke and CKD who were treated with EVT had higher rates of sICH, lower rates of a good or excellent outcome, and were more likely to die within three months.

CKD is a global health problem with a prevalence rate of 13.1% in the United States.[1] Neurological diseases, including cerebrovascular disease, are common in CKD patients. The annual incidence of stroke in patients on hemodialysis is 15.1%, and in patients with CKD, it is 9.6%,

Table 2: Logisticregressionoddsratios of outcomemeasuresby renal function

	Univariate logistic regression		Multiple logistic regression	
eGFR< 60	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
sICH[y]	1.33 (1.12 – 3.3)	***0.04***	1.15(1.03-3.4)	***0.04***
3-mon mRS[z]	1.8 (1.3-2.7)	***0.003***	1.82 (1.2 - 2.9)	***0.01***
3-mon mRS excellent	0.55 (0.3-0.77)	***0.008***	.5 (0.25-0.8)	***0.01***
3-mon mortality[||]	2.25 (1.3-3.9)	***0.007***	2.1 (1.2-4.2)	***0.01***

Abbreviations: 95% CI, 95% confidence interval; mRS, modified Rankin Score; OR, odds ratio; sICH, symptomatic intracerebral hemorrhage.

whereas, in patients without CKD, it is 2.6%.[2] In our study group, 17.1 % of the patients had CKD. This is higher than the previous studies.[2,3] This may be attributable to the fact that the patients who had EVT and involved in the study, had a more severe stroke with increased risk factors.

In the present study, lower GFR was associated with higher death rates and mRS scores. This was similar to previous studies.[6] In our study group, three-month mortality was 25%, which was compatible with the literature.[13] In addition, 24-hour sICH in CT was 10%, and this is similar to the literature.[14,15]

In our study, three months mortality and sICH at 24 hours were increased in CKD patients. Most of the reports of increased mortality were attributed to post-procedural sICH, which occurs in approximately 6% of patients treated with EVT.[16,17] After sICH, the likelihood of poor functional outcome is increased 6-fold, and the 3-month mortality rate is increased to 66%.[12] A large cerebral infarction has an association with the complication of sICH.[12,18,19] A significant inflammatory response and edema associated with the large cerebral infarct contribute to the elevated sICH risk.[20] In our study, sICH was found to be increased in CKD patients. This may be caused by increased inflammatory status, increased age, and additional risk factors in CKD patients. Also, these patients have functional abnormalities in the coagulation system that may be contributed to the increase sICH in these patients.[20]

In our study, CKD is an independent predictor of mortality and functional outcomes after three months. The mechanism through which CKD contributes to an elevated risk of a poor outcome in acute ischemic stroke patients treated with EVT is not well understood. Like the findings of this study, individuals who have CKD generally tend to be older and suffer from a multitude of comorbidities, including hypertension, AF, and ischemic heart disease.[21] A decreased eGFR is connected to an increased risk of atherosclerosis, vascular abnormalities, and abnormal coagulation. Each of these factors contributes to an increased risk of stroke and poorer outcomes following a stroke.[22,23] CKD leads to additional chronic microvascular damage, which may hinder the capacity of the brain to recover from an acute ischemic attack. Patients with EVT who also had brain atrophy or chronic hyperglycemia provided evidence for this observation. Patients with CKD showed a more significant number of white matter lesions that were more widespread. Deep white matter was reduced in these patients.[24-27] Finally, patients with CKD who also have AF have a decreased likelihood of receiving novel oral anticoagulants.[28]

We do not recommend delaying EVT even though acute ischemic stroke patients with CKD had lower rates of functional independence and higher mortality. Previous research has shown that EVT benefits CKD patients.[29] Patients with CKD had notably low rates of coronary angiography, a characteristic known in the cardiology literature as "renalism".[30] A low GFR is not an automatic exclusion criterion for EVT in acute ischemic stroke. We found no evidence that these patients are less likely to be given EVT.

This study has some limitations. This study's findings are based on a cohort of non-selected stroke patients who received EVT therapy over time. The small number of patients in the study is a significant limitation, this is partly from the study period between December 2019 and June 2022 due to intermittent constraints from the COVID-19 pandemic. Because of the retrospective, single-center design of the study, some selection bias might have occurred, so the results may not be generalized to the whole population. Even with multivariable-adjusted logistic regression, residual confounding due to unanalyzed factors cannot be avoided. Due to the small number of cases in the CKD group, we were unable to categorize patients by illness stage. Additional research is required to address these issues and verify our findings.

In conclusion, this study shows an association between CKD and poorer outcomes in patients with acute ischemic stroke treated with EVT. The presence of CKD should not prevent patients from undergoing EVT, but taking baseline eGFR into account may improve estimation of prognosis and shared decision-making among patients, families, and physicians.

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