



ORIGINAL RESEARCH PAPER

General Medicine

ASSOCIATION OF KIDNEY FUNCTIONS WITH 30 DAY POST STROKE MORTALITY

KEY WORDS: Stroke, Glomerular Filtration Rate, Proteinuria, Renal Dysfunction

Ismail M. Haji	Department Of Critical Care Medicine, Yenepoya Medical College, Mangaluru
Ashrith Ma*	Department Of General Medicine, Yenepoya Medical College, Mangaluru *Corresponding Author
Shaheen B	Department Of Biochemistry, Yenepoya Medical College, Mangaluru
Mukhtarahamed B	Department Of General Medicine, Yenepoya Medical College, Mangaluru

ABSTRACT

BACKGROUND: Renal impairment most witnessed in hospitalized stroke patients, affecting the outcome of patients, as well as causing difficulties in their management. Association of renal dysfunction in post stroke mortality is important in outcome studies and risk standardization in hospital readmission rates. This study was designed and conducted with aim to evaluate the prevalence of renal dysfunction in patients after stroke and the 30 day mortality impact in post stroke patients.

MATERIALS AND METHODS: This was a retrospective study where data was collected from medical records of 40 patients admitted to ICU with a diagnosis of stroke dated from January 2018 to December 2019. The data were analyzed in the terms of demographic details, risk factors for stroke, pulse rate, mean arterial pressure, pulse pressure, plasma glucose and renal function tests at the admission. Estimated glomerular filtration rate was calculated by Chronic Kidney Disease Epidemiology Collaboration. All patients records were traced upto 30 days post stroke.

RESULTS: The statistical analysis were done with SPSS version 24.0. Time of survival was evaluated with multivariate Cox proportional hazard analysis. Results were expressed as hazard ratio (HR) and its 95% confidence interval (95% CI). A total of 23 patients expired during 30 day period of time following stroke. The independent predictors of death remained: age, eGFR <60 ml/min/1.73 m², proteinuria and glucose at a concentration >100 mg/dl.

CONCLUSION: In patients with stroke, the impaired kidney function expressed by low eGFR with or without the presence of proteinuria is a powerful and an independent prognostic factor for short-term survival.

INTRODUCTION

Stroke is the third leading cause of mortality after cancer and cardiovascular events. It is also the most important cause for morbidity and long-term disability. Studies suggest that reduced eGFR independent risk factor for stroke outcome.^{1,2} ARIC committee demonstrated that the prevalence of mortality on the 30 day period after a stroke was around 10 % (approximately 14,000 individuals).^{3,4}

Dysfunction of renal function is a strong risk factor for cardiovascular diseases and worsens a patient's prognosis with an overall prevalence around 11.6%.⁵ Renal dysfunction predicts mortality after acute stroke in the long term. On the other hand, in-hospital mortality after acute stroke is strongly associated with disorders of consciousness at the onset of stroke, severity of stroke, body temperature, blood glucose and some other comorbidities. The presence of renal dysfunction has been associated to higher mortality risk both in the short- and long-term after an ischemic stroke.^{6,7}

Considering the morbidity and mortality of kidney dysfunction after stroke, the present study aimed to evaluate the prevalence of renal dysfunction in patients after stroke and the 30 day mortality impact in post stroke patients.

MATERIALS AND METHODS

With level IV evidence, a retrospective study was conducted from 2018 January to 2019 December in the department of Critical Care Medicine, General Medicine and Biochemistry, Yenepoya Medical College with 40 patients of acute stroke to determine the effect of renal dysfunction measured at the admission.

After obtaining IEC approval, the case details were retrospectively retrieved from MRD section and analyzed for patients' demographic details, h/o arterial hypertension (AH), congestive heart failure (CHF), transient ischaemic attack (TIA), presence of diabetes mellitus (DM), atrial fibrillation (AF),

pulse rate (PR), mean arterial blood pressure (MAP), pulse pressure (PP), plasma glucose and renal function tests at the admission. Estimated glomerular filtration rate was calculated by Chronic Kidney Disease Epidemiology Collaboration. All patients records were traced up to 30 days post stroke.

Statistical analysis: The descriptive analytical statistics were evaluated statistically with IBM SPSS Statistics for Windows, Version 24.0, IBM Corp, Chicago, IL. Student's t test and Mann-Whitney U test were used to compare variables as appropriate. Univariate survival analysis was applied using standard Cox proportional hazard regression methods. Time of survival was evaluated with multivariate Cox proportional hazard analysis. Results were expressed as hazard ratio (HR) and its 95% confidence interval (95% CI). p value less than 0.05 was considered as statistically significant.

RESULTS

In our study, a total of 40 patients' medical records were analyzed retrospectively to determine the effect of renal dysfunction accounting for mortality in patients admitted with stroke. Among 40 analyzed patients, 24 (60.00%) were men and 16 (40.00%) were females. The mean age of our study population was 69.28±7.03 years. The risk factors for stroke are arterial hypertension in 12 (30.00%) patients, congestive heart failure in 17 (42.50%) patients, TIA in 9 (22.50%) patients, diabetes mellitus in 11 (27.50%) patients and atrial fibrillation in 7 (17.50%) patients. The mean serum creatinine level among our study population was 1.35±0.72 mg/dl what contributed for 47.50% of patients (19 patients) with eGFR <60 ml/min/1.73 m². The clinical data along with 95% CI and p value are shown in table 1.

Out of 40 analyzed patients, a total of 23 patients expired during 30 day period of time following stroke. The overall 30 day survival probability was 0.72 (95% CI 0.68 – 0.77). Cox proportional hazard regression analysis was used to evaluate the independent predictors of 30 day renal mortality in stroke

patients (as shown in table 1). In multivariate Cox proportional hazard analysis, independent predictors of death remained: age, eGFR <60 ml/min/1.73 m², proteinuria and glucose at a concentration >100 mg/dl.

Table 1: Clinical data of study population with stroke

Parameters	Survivors (n=17)	Dead (n=23)	Hazard regression analysis	95% CI	P value
Mean age (years)	62.16±3.74	64.85±4.16	1.47	1.43 – 1.52	0.000*
Males (n=24)	13 (54.16%)	11 (45.83%)	1.12	0.93 – 1.25	NS
Females (n=16)	4 (25.00%)	12 (75.00%)	0.91	0.80 – 1.02	NS
Arterial hypertension (n=12)	5 (41.66%)	7 (58.33%)	1.53	1.33 – 1.75	0.05
Congestive heart failure (n=17)	8 (47.05%)	9 (52.94%)	2.12	2.09 – 2.15	NS
Stroke / TIA (n=9)	5 (55.55%)	4 (4.44%)	1.78	1.67 – 1.95	<0.001*
Diabetes mellitus (n=11)	6 (54.54%)	5 (45.45%)	2.27	1.83 – 2.46	<0.001*
Atrial fibrillation (n=7)	1 (14.28%)	6 (85.71%)	1.31	0.92 – 1.58	0.02*
Pulse rate (bpm)	87 ± 16	91 ± 13	1.07	1.01 – 1.13	NS
Mean arterial pressure (mm Hg)	121 ± 24	129 ± 19	2.69	2.56 – 2.82	0.05
Pulse pressure (mm Hg)	62 ± 26	67 ± 21	0.82	0.70 – 0.91	<0.001*
Glucose (mg/dl)	136 ± 48	139 ± 59	1.46	1.45 – 1.49	<0.001*
Urea (mg/dl)	35 ± 12	61 ± 34	2.58	2.31 – 2.86	<0.001*
Creatinine (mg/dl)	0.89 ± 0.91	1.08 ± 0.99	1.91	1.78 – 2.16	<0.001*
eGFR <60 ml/min/1.73 m ² (n=19)	7 (36.84%)	12 (63.15%)	1.29	1.09 – 1.45	<0.001*
Proteinuria (n=23)	9 (39.13)	14 (60.86)	2.78	2.33 – 3.17	<0.001*

* statistically significant

DISCUSSION

The retrospective analysis demonstrated the significance of renal dysfunction at the time of hospital admission on short-term outcome (30 day) in patients with stroke. The presence of renal dysfunction (as eGFR <60 ml/min/1.73 m²) and proteinuria were independent negative predictors of 30 day survival among patients hospitalized due to stroke. The presence arterial hypertension, congestive heart failure and atrial fibrillation as well as higher PR, MAP, serum glucose, urea and creatinine were also associated with significant mortality in patients with 30 day period of post stroke.^{8,9}

According to a meta-analysis with 12 studies, the prevalence of renal dysfunction with more than 5 million stroke patients was 11.6% (95% CI: 10.6-12.7%).⁵ Helbert et al found a lower prevalence of renal dysfunction even considering the same definition criteria for AKI from that meta-analysis. The renal dysfunction has been associated with more advanced age, congestive heart failure, diabetes mellitus, atrial fibrillation and stroke.¹⁰

Various studies demonstrated the presence of renal dysfunction was independently associated to a higher 30-day mortality after stroke,^{7,11,12} but our study found an inverse proportion between renal dysfunction and stroke. The NIHSS score is directly proportional to the short and long-term mortality after stroke.¹³ An NIHSS score more than 15 is associated to a high risk of death in post stroke.^{14,15} The advanced age of patients with stroke as well as renal dysfunction has shown a higher case fatality rate in 30 days post stroke.¹⁶

In our retrospective analytical study, the majority of patients that died had a NIHSS score above 14 and were above the median age of 68. We believe that the presence of arterial hypertension, congestive heart failure, diabetes mellitus, atrial fibrillation had higher mortality rate in patients with stroke within 30 day period. None of the patients in our study needed acute hemodialysis.

Meta-analysis showed the evidence that acute kidney injury is a common complication following both AIS and ICH and it is associated with increased mortality following AIS but not ICH. This highlights the need for early assessment of renal function in the acute phase of AIS, in particular, and avoidance of factors than may induce AKI in vulnerable patients.⁵

Patel et al. reported trends for a decreased mortality rate in

patients with AKI after stroke in the last few years;¹⁷ however, there is an increase in the need of hemodialysis in patients with AKI.¹⁸ In our study, the baseline creatinine values in dead individuals with stroke were higher than the normal which was inversely proportional to the study done by Tennankore et al.¹⁹ The limitations of the study were small sample size, need of randomized control trial and the baseline characteristics of renal function test before the onset of stroke episode to standardize the association of renal dysfunction leads to mortality in stroke individuals.

CONCLUSION

The assessment of renal function in stroke is the predictor for the survival outcome. In patients with stroke, the impaired kidney function expressed by low eGFR with or without the presence of proteinuria is a powerful and an independent prognostic factor for short-term survival.

ACKNOWLEDGEMENTS: Nil

CONFLICTS OF INTEREST: Nil

FUNDING SOURCES: Nil

REFERENCES

- Sato H, Ishimori N, Sakakibara M, Yamada S, Kawashima N, Urasawa K, et al. Decreased glomerular filtration rate is a significant and independent risk for in-hospital mortality in Japanese patients with acute myocardial infarction: report from the Hokkaido acute myocardial infarction registry Hypertension Research. 2012;35:463-469.
- Lee M, Saver JL, Chang KH, Liao HW, Chang SC, Ovbiagele B. Low glomerular filtration rate and risk of stroke: meta-analysis. *BMJ*. 2010;341:c4249-c4249.
- Cabral NL, Cougo-Pinto PT, Magalhaes PS, Longo AL, Moro CH, Amaral CH, et al. Trends of Stroke Incidence from 1995 to 2013 in Joinville, Brazil. *Neuroepidemiology* 2016;46:27381.
- Koton S, Schneider AL, Rosamond WD, Shahar E, Sang Y, Gottesman RF, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. *JAMA* 2014;312:259-68.
- Zorrilla-Vaca A, Ziai W, Connolly ES Jr, Geocadin R, Thompson R, Rivera-Lara L. Acute Kidney Injury Following Acute Ischemic Stroke and Intracerebral Hemorrhage: A Meta-Analysis of Prevalence Rate and Mortality Risk. *Cerebrovasc Dis* 2017;45:1-9.
- Covic A, Schiller A, Mardare NG, Petrica L, Petrica M, Mihaescu A, et al. The impact of acute kidney injury on short-term survival in an Eastern European population with stroke. *Nephrol Dial Transplant* 2008;23:2228-34.
- Khatri M, Himmelfarb J, Adams D, Becker K, Longstreth WT, Tirschwell DL. Acute kidney injury is associated with increased hospital mortality after stroke. *J Stroke Cerebrovasc Dis* 2014;23:25-30.
- Adams HP, Adams RJ, Brott T, Del Zoppo GJ, Furlan A, Goldstein LB, Grubb RJ, Higashida R, Kidwell C, Kwiatkowski TC, Marler JR, Hademenos GJ: Guidelines for the early management of patients with ischemic stroke. A scientific statement from the stroke council of the American Stroke Association. *Stroke* 2003;34:1056-1083.
- Adams H, Adams R, Del Zoppo G, Goldstein LB: Guidelines for the early management of patients with ischemic stroke. 2005 guidelines update. A

- scientific statement from the Stroke Council of the American Heart Association/American Stroke Association. *Stroke* 2005;36:916-921.
10. Helbert do Nascimento Lima, Tais Seibel, Gisele Colato, Norberto Luiz Cabral. The impact of acute kidney injury on fatality of ischemic stroke from a hospital-based population in Joinville, Brazil. *Braz. J. Nephrol.* 2019;1-7.
 11. Tsagalis G, Akrivos T, Alevizaki M, Manios E, Stamatellopoulos K, Laggouranis A, et al. Renal dysfunction in acute stroke: an independent predictor of long-term all combined vascular events and overall mortality. *Nephrol Dial Transplant* 2009;24:194-200.
 12. Kong FY, Tao WD, Hao ZL, Liu M. Predictors of one-year disability and death in Chinese hospitalized women after ischemic stroke. *Cerebrovasc Dis* 2010;29:255-62.
 13. Fonarow GC, Saver JL, Smith EE, Broderick JP, Kleindorfer DO, Sacco RL, et al. Relationship of national institutes of health stroke scale to 30-day mortality in medicare beneficiaries with acute ischemic stroke. *J Am Heart Assoc* 2012;1:42-50.
 14. Mittal SH, Goel D. Mortality in ischemic stroke score: A predictive score of mortality for acute ischemic stroke. *Brain Circ* 2017;3:29-34.
 15. Smith EE, Shobha N, Dai D, Olson DM, Reeves MJ, Saver JL, et al. A risk score for in-hospital death in patients admitted with ischemic or hemorrhagic stroke. *J Am Heart Assoc* 2013;2:e005207.
 16. Bonita R, Anderson CS, Broad JB, Jamrozik KD, StewartWynne EG, Anderson NE. Stroke incidence and case fatality in Australasia. A comparison of the Auckland and Perth population-based stroke registers. *Stroke* 1994;25:552-7.
 17. Patel A, Nadkarni G, Benjo A, Agarwal SK, Konstantinidis I, Simoes P, et al. Temporal trends of outcomes for acute kidney injury in acute ischemic stroke from 2002 to 2012: an analysis of nationwide inpatient sample data. *J Am Coll Cardiol* 2015;65:A2094.
 18. Nadkarni GN, Patel AA, Konstantinidis I, Mahajan A, Agarwal SK, Kamat S, et al. Dialysis Requiring Acute Kidney Injury in Acute Cerebrovascular Accident Hospitalizations. *Stroke* 2015;46:3226-31.
 19. Tennankore KK, Soroka SD, Kiberd BA. The impact of an "acute dialysis start" on the mortality attributed to the use of central venous catheters: a retrospective cohort study. *BMC Nephrol* 2012;13:72.