The Association between Glomerular Filtration Rate Estimated on Admission and Acute Stroke Outcome: The Shiga Stroke Registry

Aim: Although renal dysfunction has been identified as a novel risk factor affecting stroke prognosis, few have analyzed the association within large-scale population-based setting, using wide-range estimated glomerular filtration rate (eGFR) category. We aimed to determine the association of admission eGFR with acute stroke outcomes using data from a registry established in Shiga Prefecture, Japan.

Methods: Following exclusion of patients younger than 18 years, with missing serum creatinine data, and with onset more than 7 days prior to admission, 2,813 acute stroke patients registered in the Shiga Stroke Registry year 2011 were included in the final analysis. The Japanese Society of Nephrology equation was used to estimate GFR. Multivariable logistic regression was performed to analyze the association of eGFR with all-cause in-hospital death (modified Rankin Scale [mRS] 6), and at-discharge death/disability (mRS 2–6). Separate analyses were conducted within stroke subtypes.

Results: Compared to eGFR 60–89 mL/min/1.73 m², adjusted odds ratios (ORs) and 95% confidence interval [95% CI] for in-hospital death (in the order of eGFR ≤ 45, 45 – 59, and ≥ 90 mL/min/1.73 m²) were 1.54 [1.04 – 2.27], 1.07 [0.72 – 1.58], and 1.04 [0.67 – 1.59]. Likewise, adjusted ORs [95% CI] for at-discharge death/disability were 1.54 [1.02– 2.32], 0.97 [0.73–1.31], and 1.48 [1.06– 2.05]. Similar pattern was further evident in the eGFR ≤ 45 mL/min/1.73 m² group for both outcomes within acute ischemic stroke patients.

Conclusions: Our study has ascertained that in acute stroke, particularly ischemic stroke, low eGFR was significantly associated with in-hospital death and at-discharge death/disability. Additionally, high eGFR was found to be associated with at-discharge death/disability.

Key words: Stroke, Glomerular filtration rate, Mortality, Morbidity

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killer in the past\textsuperscript{4, 5}). Although being a developed country, Japan still suffers from immense healthcare cost for its stroke survivors\textsuperscript{6}. Improvement of stroke outcome by refined detection of high-risk patients with poor prognosis is thus mandatory to alleviate the situation. In the past few years, renal dysfunction has been identified as a novel risk factor affecting stroke prognosis, and estimated glomerular filtration rate (eGFR) is one of the parameters used as its proxy\textsuperscript{7-17}. Few, however, have analyzed the association within large-scale population-based setting, using wide-range eGFR category. It is therefore necessary to ascertain it using bigger and more comprehensive data. We aimed to determine the association of on-admission eGFR with in-hospital death and at-discharge death/disability in acute stroke patients using data from a registry established in Shiga Prefecture, Japan.

Methods

Subjects

The Shiga Stroke Registry (SSR) is a multicenter population-based stroke registry developed to provide comprehensive information on acute ischemic and non-traumatic hemorrhagic stroke in Shiga Prefecture, a region populated by 1.4 million people and located in the middle of Honshu Island, Japan\textsuperscript{18}. Of 41 acute care hospitals inside the prefecture with neurology/neurosurgery facilities, as well as smaller hospitals with rehabilitation facilities, data of all stroke cases were obtained retrospectively from medical records by trained investigators and put together in an encrypted database in the Shiga University of Medical Science. Civil registration death certificates were also used to identify stroke cases leading to death outside the hospital. The current study focused on 2,956 stroke patients registered from 1 January to 31 December 2011. Following exclusion of patients younger than 18 years (n = 5), with missing admission serum creatinine data (n = 65), and with onset more than 7 days prior to admission (n = 73), 2,813 acute stroke patients were included in the final analysis. The Institutional Review Board of Shiga University of Medical Science has approved the study protocol.

Determination of Stroke

Stroke was defined as rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 h or leading to mortality, with no apparent cause other than that of vascular origin\textsuperscript{19}. Stroke was further categorized as ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage, with the latter two grouped into hemorrhagic stroke. All cases were confirmed both clinically and radiologically, and the final diagnosis was made by more than 2 independent investigators.

Variables and Outcome

Data gathered included age, gender, comorbidities (hypertension, diabetes, myocardial infarction, atrial fibrillation, dyslipidemia), previous stroke, smoking status, admission details (systolic and diastolic blood pressure, modified Rankin Scale (mRS), Japan Coma Scale (JCS))\textsuperscript{20}, interventional/surgical therapy performed, tissue plasminogen activator administered, days from onset until death/hospital discharge, and discharge mRS score. Interventional therapy consisted of endovascular recanalization and coil embolization, whereas surgical therapy involved decompression, hematoma evacuation, cerebrospinal fluid diversion, thrombectomy, and aneurysm clipping by means of endoscopic and/or conventional craniectomy/ectomy. The outcomes of this study were all-cause in-hospital death (mRS of 6) and at-discharge death/disability (mRS 2-6).

Renal Function Evaluation

Admission serum creatinine was measured using enzymatic method in local laboratories and used to estimate GFR based on the Japanese Society of Nephrology equation: eGFR (mL/min/1.73 m\textsuperscript{2}) = 194 × (serum creatinine [mg/dL])\textsuperscript{\textsuperscript{-1.094}} × (age [year])\textsuperscript{-0.287} × 0.739 (for female)\textsuperscript{21}. The estimated GFR was then categorized as <45, 45–59, 60–89, and ≥90 mL/min/1.73 m\textsuperscript{2}, with eGFR 60–89 mL/min/1.73 m\textsuperscript{2} being the reference group\textsuperscript{22}. Patients with eGFR <45 mL/min/1.73 m\textsuperscript{2} were pooled together due to small number, whereas patients on renal replacement therapy (RRT) were gathered into a separate group due to their particular feature.

Statistical Analysis

Continuous variables were presented as mean (standard deviation) or median (interquartile range) as appropriate, and categorical variables as proportions. Differences in means or medians between two groups were analyzed using Student’s t-test or Mann–Whitney U test, respectively, while x\textsuperscript{2} or Fisher exact test was conducted to find differences in proportions as appropriate. Probability trends were determined by treating eGFR in its continuous nature and fitting it into linear/logistic regression models with variables of interest. Next, multivariable logistic regression analyses, adjusting for covariates regarded and/or identified from literatures to
be significantly associated with stroke outcomes, were performed to determine the association of eGFR with both outcomes. Separate analyses were done within stroke subtypes. Finally, sensitivity analyses were conducted for the outcome of at-discharge death/dependency (mRS 3-6) on all stroke subtypes. All analyses were conducted using SAS Version 9.4 software (SAS Institute). Differences with two-tailed p-value < 0.05

|                                | Non-RRT (n = 2743) | RRT (n = 70) | p       |
|--------------------------------|--------------------|--------------|---------|
| Age, mean years ± SD           | 74.1 ± 13.3        | 70.1 ± 13.4  | 0.04    |
| Female, n (%)                  | 1276 (46.5)        | 27 (38.6)    | 0.19    |
| Comorbidities, n (%)           |                    |              |         |
| Hypertension                   | 1973 (72.7)        | 59 (85.5)    | 0.02    |
| Diabetes                       | 726 (26.7)         | 30 (43.5)    | 0.002   |
| Myocardial infarction          | 165 (6.1)          | 3 (4.4)      | 0.79    |
| Atrial fibrillation            | 559 (20.6)         | 15 (22.1)    | 0.76    |
| Dyslipidemia                   | 951 (36.7)         | 20 (30.8)    | 0.32    |
| Previous stroke, n (%)         | 706 (25.8)         | 30 (42.9)    | 0.001   |
| Smoking status, n (%)          |                    |              | 0.54    |
| Never                          | 1634 (65.6)        | 38 (63.3)    |         |
| Ex                             | 325 (12)           | 6 (10)       |         |
| Current                        | 532 (21.4)         | 16 (26.7)    |         |
| SBP, mean mmHg ± SD            | 161.8 ± 33         | 166.7 ± 41   | 0.32    |
| DBP, mean mmHg ± SD            | 88.7 ± 20.4        | 85.8 ± 22.5  | 0.26    |
| Japan Coma Scale, n (%)        |                    |              | 0.03    |
| 0                              | 1241 (45.4)        | 32 (46.4)    |         |
| 1-3 (1-digit)                  | 693 (25.3)         | 9 (13)       |         |
| 10-30 (2-digit)                | 357 (13.1)         | 9 (13)       |         |
| 100-300 (3-digit)              | 444 (16.2)         | 19 (27.6)    |         |
| eGFR, mL/min/1.73 m², median (IQR) | 67.5 (52.9-82.7)   | 6.2 (4.7-10.1) | <.0001  |
| Admission mRS, n (%)           | 1703 (62.1)        | 17 (24.3)    | <.0001  |
| 0                              | 322 (11.7)         | 17 (24.3)    |         |
| 1                              | 173 (6.3)          | 8 (11.4)     |         |
| 3                              | 212 (7.7)          | 11 (15.7)    |         |
| 4                              | 243 (8.9)          | 11 (15.7)    |         |
| 5                              | 90 (3.3)           | 6 (8.6)      |         |
| Intervention/surgery, n (%)    | 296 (10.8)         | 9 (12.9)     | 0.59    |
| r-tPA, n (%)                   | 77 (2.8)           | 1 (1.5)      | 0.99    |
| Onset-death/discharge days, median (IQR) | 25 (13-46)     | 19.5 (10-39) | 0.09    |
| Final diagnosis, n (%)         | 1803 (65.7)        | 45 (64.3)    | 0.83    |
| Ischemic                       | 935 (34.1)         | 25 (35.7)    |         |
| Haemorrhagic                   | 1703 (62.1)        | 17 (24.3)    |         |
| Discharge mRS, n (%)           | 202 (7.4)          | 4 (5.7)      | 0.09    |
| 0                              | 509 (18.6)         | 11 (15.7)    |         |
| 1                              | 318 (11.6)         | 8 (11.4)     |         |
| 2                              | 287 (10.5)         | 8 (11.4)     |         |
| 4                              | 628 (22.9)         | 11 (15.7)    |         |
| 5                              | 390 (14.2)         | 8 (11.4)     |         |
| In-hospital death, n (%)       | 409 (14.9)         | 20 (28.6)    | 0.002   |

RRT, renal replacement therapy; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; mRS, modified Rankin Scale; r-tPA, recombinant tissue plasminogen activator
Table 2. Characteristics of the study subjects not on renal replacement therapy

| eGFR (mL/min/1.73 m²) | ≤45 (n=431) | 45-59 (n=571) | 60-89 (n=1306) | ≥90 (n=435) | p-trend |
|------------------------|-------------|---------------|----------------|------------|---------|
| Age, mean years ± SD   | 80.9 ± 10.9 | 78 ± 10.4     | 72.5 ± 12.9    | 66.7 ± 15.4 | <.0001  |
| Female, n (%)          | 229 (53.1)  | 265 (46.4)    | 572 (43.8)     | 210 (48.3) | 0.25    |
| Comorbidities, n (%)   |             |               |                |            |         |
| Hypertension           | 351 (82.4)  | 433 (76.6)    | 917 (70.8)     | 272 (63.6) | <.0001  |
| Diabetes               | 152 (35.8)  | 141 (24.7)    | 329 (25.3)     | 104 (24.3) | 0.001   |
| Myocardial infarction  | 45 (10.6)   | 39 (6.9)      | 61 (4.7)       | 20 (4.6)   | <.0001  |
| Atrial fibrillation    | 135 (31.8)  | 145 (25.6)    | 226 (17.4)     | 53 (12.2)  | <.0001  |
| Dyslipidemia           | 136 (33.8)  | 210 (38.9)    | 462 (37.4)     | 143 (35)   | 0.67    |
| Previous stroke, n (%) | 126 (29.6)  | 176 (30.9)    | 322 (24.7)     | 82 (18.9)  | <.0001  |
| Smoking status, n (%)  |             |               |                |            | <.0001  |
| Never                  | 283 (74.3)  | 364 (70.8)    | 751 (62.7)     | 236 (59.2) |         |
| Ex                     | 52 (13.7)   | 74 (14.4)     | 153 (12.8)     | 46 (11.5)  |         |
| Current                | 46 (12.1)   | 76 (14.8)     | 293 (24.5)     | 117 (29.3) |         |
| SBP, mean mmHg ± SD    | 157.2 ± 35.1| 160.3 ± 32.8  | 163.7 ± 31.2   | 162.4 ± 33.4| 0.05    |
| DBP, mean mmHg ± SD    | 83.1 ± 20.9 | 86.9 ± 21.4   | 90.5 ± 19.8    | 90.9 ± 19.4| <.0001  |
| Japan Coma Scale, n (%)|             |               |                |            |         |
| 0                      | 140 (32.6)  | 258 (45.2)    | 651 (50)       | 192 (44.4) |         |
| 1-3 (1-digit)          | 127 (29.6)  | 158 (27.7)    | 314 (24.1)     | 94 (21.8)  |         |
| 10-30 (2-digit)        | 58 (13.5)   | 77 (13.5)     | 164 (12.6)     | 58 (13.4)  |         |
| 100-300 (3-digit)      | 104 (24.2)  | 78 (13.7)     | 174 (13.4)     | 88 (20.4)  |         |
| eGFR, mean mL/min/1.73 m² ± SD | 33.4 ± 9.5 | 53.4 ± 4.1 | 73.7 ± 8.4 | 108.5 ± 21.2 | <.0001 |
| Admission mRS, n (%)   |             |               |                |            | <.0001  |
| 0                      | 205 (47.6)  | 316 (55.3)    | 872 (66.8)     | 310 (71.3) |         |
| 1                      | 59 (13.7)   | 79 (13.8)     | 152 (11.6)     | 32 (7.4)   |         |
| 2                      | 36 (8.4)    | 41 (7.2)      | 79 (6.1)       | 17 (3.9)   |         |
| 3                      | 59 (13.7)   | 59 (10.3)     | 80 (6.1)       | 14 (3.2)   |         |
| 4                      | 58 (13.5)   | 60 (10.5)     | 93 (7.1)       | 32 (7.4)   |         |
| 5                      | 14 (3.3)    | 16 (2.8)      | 30 (2.3)       | 30 (6.9)   |         |
| Intervention/surgery, n (%) | 29 (6.8) | 44 (7.7) | 137 (10.5) | 86 (19.8) | <.0001 |
| tPA, n (%)             | 11 (2.6)    | 22 (3.9)      | 38 (2.9)       | 6 (1.4)    | 0.31    |
| Onset-death/discharge days, median (IQR) | 24 (12-51) | 27 (13-48) | 25 (13-45) | 25 (13-46) | 0.36 |
| Final diagnosis, n (%) |             |               |                |            | <.0001  |
| Ischemic               | 322 (74.7)  | 418 (73.2)    | 850 (65.1)     | 213 (49)   |         |
| Haemorrhagic           | 108 (25.1)  | 153 (26.8)    | 455 (34.8)     | 219 (50.3) |         |

SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; mRS, modified Rankin Scale; tPA, tissue plasminogen activator

is considered to be statistically significant.

Results

Characteristics of Patients by RRT Status

Table 1 shows basic characteristics of adult acute stroke patients by RRT status. Compared with non-RRT group, several significant differences were identified in RRT group: patients’ age was younger; hypertension, diabetes, previous stroke, and pre-admission significant disability were more prevalent; admission JCS score was worse; admission eGFR was extremely lower; and in-hospital death was higher.

Characteristics of Study Subjects by eGFR Category

Table 2 presents basic characteristics of study subjects by eGFR category. Of 2,743 non-RRT patients, 15.7% presented with eGFR of <45 mL/min/1.73 m², 20.8% with eGFR 45–59 mL/min/1.73 m², 47.6% with eGFR 60–89 mL/min/1.73 m², and 15.9% with
Prevalence of Outcomes by eGFR Category and the Association of eGFR with Outcomes in All Stroke

Table 3 shows prevalence of outcomes by eGFR category and the association of eGFR with outcomes in all stroke. Both in-hospital death and at-discharge death/disability display reverse relationship with eGFR. For multivariable adjustment, age, sex, hypertension, diabetes, myocardial infarction, atrial fibrillation, previous stroke, smoking status, diastolic blood pressure, admission JCS and mRS, intervention/surgery, and recombinant tissue plasminogen activator administration were selected as covariates. Compared to the reference group, only eGFR < 45 mL/min/1.73 m² group maintained its significant association with in-hospital death (from unadjusted OR [95% CI] of 1.48 [1.06–2.05]) to multivariable-adjusted OR [95% CI] of 1.48 [1.06–2.05]). RRT group, particularly, did not display any significant association with both outcomes after adjustments.

Prevalence of Outcomes by eGFR Category and the Association of eGFR with Outcomes in Ischemic and Hemorrhagic Strokes

Tables 4 and 5 show prevalence of outcomes by eGFR category and the association of eGFR with outcomes in ischemic and hemorrhagic strokes. In-hospital death and at-discharge death/disability had similar reverse relationship with eGFR in both stroke subtypes as in all stroke. In the same manner, eGFR < 45 mL/min/1.73 m² group in ischemic stroke displayed maintained significant association with in-hospital death (from unadjusted OR [95% CI] of 3.46 [2.37–5.05] to multivariable-adjusted OR [95% CI] of 1.60 [1.00–2.57]) and with at-discharge disability (from unadjusted OR [95% CI] of 3.53 [2.50–4.99] to multivariable-adjusted OR [95% CI] of 1.74 [1.10–2.76]). Still within the same stroke subtype, eGFR > 90 mL/min/1.73 m² group also showed maintained significant association with at-discharge disability (multivariable-adjusted OR [95% CI] of 1.52 [1.01–2.31]). As for hemorrhagic stroke, with the exception of RRT group that preserved its significant association with in-hospital death (from unadjusted OR [95% CI] of 3.64 [1.61–8.25] to multivariable-adjusted OR [95% CI] of 5.27 [1.43–19.50]), no other significant associations were identified.
Discussion

In the current study, low eGFR (\(<45\) mL/min/1.73 m\(^2\)) was shown to be significantly and positively associated with all stroke outcome: its ORs for in-hospital death and at-discharge death/disability were 1.54 times higher than the reference group. Additionally, high eGFR (\(\geq90\) mL/min/1.73 m\(^2\)) was significantly associated with these outcomes.

**Table 6.** Sensitivity Analyses: The Association of eGFR With At-Discharge Death/Dependency in All Strokes and Its Subtypes

| eGFR (mL/min/1.73 m\(^2\)) | RRT | \(<45\) | 45-59 | 60-89 | \(\geq90\) |
|-----------------------------|-----|--------|------|------|--------|
| \((n=45)\)                  |     |        |      |      |        |
| \(\geq45\)                  | 8 (17.8) | 66 (20.5) | 46 (11) | 59 (6.9) | 18 (8.5) |
| Unadjusted                  | 2.90 (1.29-6.51) | 3.46 (2.37-5.05) | 1.66 (1.11-2.49) | 1.00 | 1.24 (0.71-2.15) |
| Model 1\(^a\)               | 2.97 (1.29-6.85) | 2.17 (1.46-3.23) | 1.26 (0.83-1.91) | 1.00 | 1.66 (0.94-2.92) |
| Model 2\(^b\)               | 0.91 (0.27-3.07) | 1.60 (1.00-2.57) | 1.20 (0.74-1.94) | 1.00 | 0.92 (0.45-1.86) |

Sensitivity Analyses: The Association of eGFR With At-Discharge Death/Dependency in All Strokes and Its Subtypes

Table 6 presents the association of eGFR with at-discharge death/dependency in all strokes and its subtypes as sensitivity analyses. Compared to the reference group, significant association was maintained only in eGFR \(<45\) mL/min/1.73 m\(^2\) in ischemic stroke (from unadjusted OR [95% CI] of 3.56 [2.50—4.99] to multivariable-adjusted OR [95% CI] of 1.74 [1.10—2.76]).
associated with at-discharge death/disability, its OR was 1.48 higher than the reference group. Further analyses within each stroke subtypes, as well as sensitivity analyses, discovered the same pattern to be strongly evident in the ischemic stroke. In regard to RRT patients, this group displayed a notable association with death only within hemorrhagic stroke.

Despite growing interest in similar subject, divulging the association either in overall stroke7,9, ischemic10-14; or hemorrhagic subtypes15-17); in-between study findings have been contradictory, for example, while Yahalom et al23 and Tsagalis et al33 showed significant and positive result between low eGFR and mortality and poor outcome after stroke, the opposite was identified in a study by Lin et al32. Result interpretations were complicated by small sample size7,9, 12-15, 17), non-population-based setting7,9, 11, 12, 14), narrow-range eGFR category7, 11, 13-15), or lack of control for stroke severity12, 15). The present study deals with these issues by employing data from a large-scale population-based setting registry, implementing wide-range eGFR category, and separating analyses between non-RRT and RRT patients. The latter, particularly, is paramount as serum creatinine level in RRT patients is unreliable; thus, its inclusion will confound the study results23).

The mechanism underlying the relationship between renal function and poor stroke outcome has not been clearly understood. In our study, low eGFR group exhibited the highest prevalence of traditional vascular risk factors linked to stroke, e.g. hypertension, diabetes, myocardial infarction, atrial fibrillation, previous stroke, smoking status, diastolic blood pressure, admission Japan Coma Scale and modified Rankin Scale, intervention/surgery, and recombinant tissue plasminogen activator administration. All regression analyses result are in odds ratio (95% confidence interval).

### Table 6. Prevalence and odds ratio (95% confidence interval) of each eGFR category for death/dependency (mRS 3-6) in all stroke and its subtypes

|                          | eGFR (mL/min/1.73 m²) |
|--------------------------|-----------------------|
|                          | RRT                  | <45       | 45-59     | 60-89    | ≥90      |
| **All stroke**           |                       |          |          |          |          |
| Unadjusted               | 1.48 (0.89-2.47)      | 2.75 (2.13-3.55) | 1.27 (1.03-1.55) | 1.00     | 1.01 (0.81-1.26) |
| Model 1a                 | 1.82 (1.05-3.15)      | 1.79 (1.36-2.36) | 0.92 (0.74-1.15) | 1.00     | 1.41 (1.10-1.80) |
| Model 2b                 | 1.02 (0.46-2.27)      | 1.23 (0.85-1.79) | 0.77 (0.57-1.03) | 1.00     | 1.32 (0.94-1.84) |
| **Ischemic stroke**      |                       |          |          |          |          |
| Unadjusted               | 1.89 (1.01-3.53)      | 3.56 (2.65-4.77) | 1.52 (1.20-1.93) | 1.00     | 0.98 (0.72-1.32) |
| Model 1a                 | 1.87 (0.95-3.71)      | 2.07 (1.50-2.86) | 1.01 (0.78-1.31) | 1.00     | 1.49 (1.05-2.11) |
| Model 2b                 | 1.18 (0.46-3.05)      | 1.54 (1.01-2.35) | 0.81 (0.57-1.14) | 1.00     | 1.56 (1.00-2.45) |
| **Hemorrhagic stroke**   |                       |          |          |          |          |
| Unadjusted               | 0.87 (0.35-2.14)      | 1.81 (1.04-3.17) | 1.02 (0.67-1.56) | 1.00     | 0.69 (0.49-0.98) |
| Model 1a                 | 1.39 (0.53-3.68)      | 1.27 (0.71-2.28) | 0.83 (0.53-1.30) | 1.00     | 0.94 (0.64-1.38) |
| Model 2b                 | 0.54 (0.13-2.29)      | 0.49 (0.22-1.10) | 0.63 (0.35-1.17) | 1.00     | 0.91 (0.54-1.52) |

eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy; mRS, modified Rankin Scale

aAdjusted for age and sex

bAdjusted for age, sex, hypertension, diabetes, myocardial infarction, atrial fibrillation, previous stroke, smoking status, diastolic blood pressure, admission Japan Coma Scale and modified Rankin Scale, intervention/surgery, and recombinant tissue plasminogen activator administration

All regression analyses result are in odds ratio (95% confidence interval).
Furthermore, admission NIHSS, a strong predictor of stroke outcome, is of no less importance. A recent study investigating lipid management targets in Japan showed inadequate attainment rates in the population, raising alarm for its improvement.

As a consequence of undesirable effects associated with renal dysfunction, a more vigilant management of acute stroke patients with this condition is warranted. Increased risk of intracerebral hemorrhage with thrombolysis administration, decreased responsiveness of antiplatelet agents, and limited use of anticoagulants are few of the limitations critical to be recognized in providing medical therapy to these high-risk patients. Should any indication for interventional/surgical therapy arise, cautious peri-, intra-, and postoperative management is imperative, covering aspects such as fluid and electrolytes therapy, anesthetic agent selection, and contrast agent use. Promotion and preventive measures to manage cardiovascular disease risk factors in community level, specifically in renal dysfunction patients, is of no less importance. A recent study investigating lipid management targets in Japan showed inadequate attainment rates in the population, raising alarm for its improvement.

Besides the aforementioned strength of this study, eGFR 60–89 mL/min/1.73 m² was selected as the reference group, considering the specific range of which to better represent the aging nature of stroke patients by taking into account study subjects’ mean eGFR and age. However, because only Japanese patients were studied, results may not be applicable to other populations. Serum creatinine was only measured on admission and in individual centers, thereby influencing its accuracy. Furthermore, admission NIHSS, a strong predictor of stroke outcome, was not incorporated due to its high rate of missing data. However, we perceive this issue to be overcome by using JCS, a Japanese-based consciousness level score developed in the same year as the Glasgow Coma Scale, which has been proven to have good predictability of stroke outcome.

In conclusion, our study has ascertained that in acute stroke, particularly in ischemic stroke, low eGFR was associated with in-hospital death and at-discharge death/disability. Additionally, high eGFR was found to be associated with at-discharge death/disability. These findings reemphasize the importance of having great awareness among clinicians managing these stroke patients with renal dysfunction.

**Acknowledgement and Notice**

None.

**Conflict of Interest**

None.

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