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Association of Kidney Function with 30-day and 1-year Post-Stroke Mortality and Hospital Readmission: GWTG-Stroke

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Abstract

Background and Purpose: Kidney dysfunction is common among patients hospitalized for ischemic stroke. Understanding the association of kidney disease with post-stroke outcomes is important to properly adjust for case mix in outcome studies, payment models and risk-standardized hospital readmission rates.

Methods: In this cohort study of fee-for-service Medicare patients admitted with ischemic stroke to 1579 Get With the Guidelines (GWTG)-Stroke participating hospitals between 2009 and 2014, adjusted multivariable Cox proportional hazards models were used to determine the independent associations of estimated glomerular filtration rate (eGFR) and dialysis status with 30-day and 1-year post-discharge mortality and re-hospitalizations.

Results: Of 204,652 patients discharged alive (median age [25th-75th Percentile] 80 years [73.0–86.0], 57.6% women, 79.8% White), 48.8% had an eGFR≥60, 26.5% an eGFR 45–59, 16.3% an eGFR 30–44, 5.1% an eGFR 15–29, 0.6% an eGFR<15 without dialysis, and 2.8% were receiving dialysis. Compared to eGFR≥60, and after adjusting for relevant variables, eGFR<45 was

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associated with increased 30-day mortality with the risk highest among those with eGFR<15 without dialysis (HR 2.09, 95% CI 1.66–2.63). An eGFR<60 was associated with increased 1-year post-stroke mortality that was highest among patients on dialysis (HR 2.65, 95% CI 2.49–2.81). Dialysis was also associated with the highest 30-day and 1-year re-hospitalization rates (HR 2.10, 95% CI 1.95–2.26; HR 2.55, 95% CI 2.44–2.66, respectively) and 30-day and 1-year composite of mortality and re-hospitalization (HR 2.04, 95%CI 1.90–2.18; HR 2.46, 95% CI 2.36–2.56, respectively).

Conclusions: Within the first year after index hospitalization for ischemic stroke, eGFR and dialysis status on admission are associated with post-stroke mortality and hospital readmissions. Kidney function should be included in risk-stratification models for post-stroke outcomes.

Keywords

Stroke; Kidney disease; Outcomes

Introduction

Kidney disease is prevalent among stroke patients and may be associated with increased risk for recurrent stroke and poorer long-term outcomes.[1, 2, 3] eGFR, a measure of renal function, is routinely assessed at the time of admission in patients with acute ischemic stroke. We previously found that a decreased eGFR on admission following acute ischemic stroke is associated with a lower odds of being discharged home and higher in-patient mortality.[4] Studies evaluating the association of admission eGFR with post-discharge mortality within the first year after stroke are inconsistent, possibly because of differences in eGFR categorization, dialysis status assessment, or sample size.[5–8] In addition, although risk-standardized hospital readmission rates are publicly reported measures intended to reflect quality of care[9], only limited data are available regarding the association of kidney disease with re-hospitalizations and its interaction with other demographic and clinical variables. Addressing these gaps is important to properly risk stratify patients with stroke and adjust for case mix in outcome studies and payment models.

We used data from a large Get With The Guidelines (GWTG)-Stroke cohort of patients, who were enrolled in fee-for-service Medicare at the time of the index acute ischemic stroke admission, to evaluate the independent associations of different levels of eGFR and being on dialysis, with 30-day and 1-year mortality and re-hospitalizations. We also studied the relationships of other patient and hospital characteristics with these outcomes stratified by the level of kidney dysfunction.

Methods

Supporting data are available within the article and its online supplementary files.

Patient population:

We used data on Medicare fee-for-service patients admitted with ischemic stroke between 2009– 2014 from GWTG-Stroke that were linked to Centers for Medicare and Medicaid Services (CMS) claims for long-term outcomes. Details of the GWTG-Stroke program have

been previously published.[10] Medicare-aged GWTG-Stroke ischemic stroke patients are generally representative of the national fee-for-service Medicare ischemic stroke population.[11] Quintiles Real-World & Late Phase Research (Cambridge, MA) served as the data collection and coordination center for GWTG. The Duke Clinical Research Institute (Durham, NC) served as the data analysis center.[10] Each participating hospital received either human research approval to enroll patients without individual patient consent under the Common Rule or a waiver of authorization and exemption from subsequent review by their institutional review board. Institutional review board approval was obtained for this study. A total of 300,768 patients with ischemic stroke who were discharged alive and who had records linked to CMS claims data were identified. From the 249,586 patients eligible for the study, 44,934 were excluded because of missing race, creatinine or extreme creatinine values that were not medically plausible. After relevant exclusions, 204,652 patients aged 65 years and older with ischemic stroke from 1579 GWTG-Stroke fully participating sites who were discharged alive were included in the analysis (Figure 1).

Variables

Renal dysfunction definitions:

eGFR was estimated based on the Isotope Dilution Mass Spectrometry (IDMS) traceable Modification of Diet in Renal Disease (MDRD) equation [eGFR = 175 × (serum creatinine)$^{-1.154}$ × (Age)$^{-0.203}$ × [1.210 if race=black] x [0.742 if sex=female] using creatinine on admission.[12] The eGFR levels were selected based on Chronic Kidney Disease (CKD) classification by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF KDOQI): eGFR 45 to 59 mL/min per 1.73 m^2 (CKD stage 3a); eGFR 30 to 44 mL/min per 1.73 m^2 (CKD stage 3b); eGFR 15 to 29 mL/min per 1.73 m^2 (CKD stage 4); eGFR<15mL/min per 1.73 m^2 without dialysis (CKD stage 5 without dialysis) and; treatment by dialysis. In this study, eGFR≥ 60 mL/min per 1.73 m^2 was categorized as no kidney dysfunction. Because the definition of CKD requires longitudinal eGFR data for at least 3 months, and because follow-up eGFR was not available, the data were analyzed by eGFR level rather than CKD stage.

Because dialysis status was not available in GWTG data, the GWTG database was linked with CMS data with dialysis patients identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes V45.11 (renal dialysis status), 585.6 (End stage renal diseases), V56.X (Encounter for dialysis and dialysis catheter care). Patients receiving dialysis were analyzed separately from those not receiving dialysis who had an eGFR<15 mL/min/1.73 m^2.

Outcomes:

Post stroke mortality and re-hospitalization were ascertained from information available from CMS data.

Covariates:

The GWTG standard covariates for the adjusted analysis of the association of admission eGFR with 30-day and 1-year mortality and re-hospitalizations included: 1) demographics:

age, sex, race; 2) medical history: atrial fibrillation/flutter, previous stroke/Transient Ischemic Attack (TIA), Coronary artery disease (CAD)/prior myocardial infarction (MI), carotid stenosis, diabetes mellitus, peripheral vascular disease (PVD), hypertension, dyslipidemia, smoking; 3) other patient characteristics: arrival on vs. off hours (Regular hours: 7AM-6PM, Monday-Friday), initial NIH Stroke Scale (NIHSS) score, 4) hospital characteristics such as region, hospital type (teaching/non-teaching), number of beds, annual ischemic stroke volume, annual Intravenous tissue Plasminogen Activator (IV- tPA) volume, rural location and Joint Commission stroke center status.

Variables that were included in the interaction analysis with admission eGFR were selected *a priori* based on their possible association with stroke outcomes and included, in addition to the above variables, initial systolic blood pressure, glucose level, LDL-cholesterol, independent ambulatory status at admission, medications at discharge, in-hospital procedures and complications, IV-tPA administration, and symptomatic intracranial hemorrhage (sICH)<36 hours from IV-tPA administration for patients who received IV-tPA, discharge location, smoking cessation advice or counseling, stroke education, stroke rehabilitation, and weight recommendation.

Statistical analysis:

Patient and hospital characteristics were summarized and compared by eGFR groups and dialysis status using proportions for categorical variables and medians with 25^{th} and 75^{th} percentiles for continuous variables. Differences across eGFR/dialysis groups were compared using Pearson chi-square tests, Fisher's Exact Test or Kruskal-Wallis tests as appropriate. Kaplan-Meier estimates and log-rank tests describe and compare unadjusted rates across groups. The relationship between eGFR groups and patient outcomes was assessed with Cox proportional hazards models starting at patient discharge alive. Robust sandwich estimates of the covariance were used to account for potential clustering of patients within hospitals. Multivariable adjustment was performed with the standard GWTG-Stroke adjustment list and potential confounders. Patients were administratively censored at 30 days or 1 year for applicable models or if there was a change in Medicare fee-for-service status. Non-mortality outcomes were censored at the time of mortality to estimate cause-specific hazard ratios. Results are reported for an overall test across eGFR groups (global p-value) and, with pairwise group comparisons as hazard ratios (HR) with 95% confidence intervals (CI) and p-values with the eGFR≥60 group as reference.

In a separate analysis, we assessed whether eGFR modified the association of patient and hospital factors with outcomes using Cox proportional hazards models. For each factor, we report the interaction p-value; a significant interaction ($p<0.05$) suggests that eGFR level modifies the relationship between the factor and outcome. In such situations, the HR and 95% CI between the factor and outcome is provided for each eGFR category, estimated from the model with fitted interactions.

Functional forms of continuous variables were assessed using lack-of-fit tests comparing a linear fit with a restricted cubic spline fit. If non-linearity was found, appropriate transformations were used, including piecewise linear splines to approximate the non-linearity while balancing interpretability. Proportional hazards assumptions were assessed by

plotting the cumulative martingale residuals and appropriate transformations made when applicable. Co-linearity between covariates was assessed using variance inflation factors (VIF); no co-linearity of the variables was suggested. Multiple imputation (25 imputations) was used to estimate missing data except for initial NIHSS and hospital characteristics where a complete case analysis was performed. The missing rates for most patient characteristics were less than 1%, except NIHSS, which was missing 38% of cases. Baseline characteristics of those with NIHSS documented were compared to those of missing NIHSS. Most hospital characteristics were available, except for hospital type (0.28% missing) and number of beds (0.30% missing). If a patient had missing medical history, it was assumed that the medical conditions did not occur as abstractors were likely to skip the section when none applied. The characteristics of subjects included in the study were compared to patients who were excluded based on missing race, creatinine or creatinine values that are not medically plausible. Data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC). All tests were two-sided with p-values <0.05 indicating statistical significance, unadjusted for multiple comparisons.

Sensitivity analyses:

To determine whether the findings would be similar using other equations for the calculation of eGFR, a sensitivity analysis of the association of eGFR with mortality and rehospitalization was performed using another commonly used method for estimating eGFR, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation in which eGFR = 141 × min (Scr /κ, 1)α × max(Scr /κ, 1)-1.209 × 0.993Age × 1.018 [if female] × 1.159 [if black];Scr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males,α is −0.329 for females and −0.411 for males,min indicates the minimum of Scr /κ or 1, and max indicates the maximum of Scr /κ or 1.

Because admission eGFR may be caused by acute renal dysfunction and not always reflect CKD, sensitivity analyses were performed to determine the association of eGFR and dialysis with outcomes limited to patients who also have ICD-9-CM codes reflecting CKD identified by the following codes: 585.3 (CKD stage 3), 585.4 (CKD stage 4), 585.5 (CKD stage 5 excluding patients requiring chronic dialysis), 585.6 (end-stage renal disease requiring chronic dialysis), 585.9 (CKD unknown/unspecified).

Results

Of 204,652 patients discharged alive, 48.8% had an eGFR≥60, 26.5% eGFR 45–59, 16.3% eGFR 30–44, 5.1% eGFR 15–29, 0.6% eGFR<15 without dialysis, and 2.8% were receiving dialysis. Of the total cohort, 5% died within 30-days, 23% died within 1-year, 14 % were re-hospitalized within 30-days and 48% were re-hospitalized within 1-year. Characteristics of the initial cohort and hospital characteristics are described by eGFR categories in Table1, TableI and TableII. Subjects on dialysis were more likely than other eGFR groups to be non-white, to have previous stroke/TIA, CAD/prior MI, carotid stenosis, diabetes, PVD, hypertension, dyslipidemia, heart failure, and to be on antiplatelet, lipid-lowering, or diabetes medication. The characteristics of subjects excluded based on missing race, creatinine or extreme creatinine values are described in Table III. Compared to subjects

without missing NIHSS, those with missing NIHSS had longer stroke onset to ED arrival, lower rates of smoking cessation counseling, stroke education or weight recommendation (Table IV). A higher percentage of missing NIHSS was noted in smaller hospitals with lower numbers of strokes admissions and annual IV-tPA administration, in the South or Northeast, rural and without primary stroke center status (Table V).

The cumulative incidence of mortality within 1-year of discharge was higher as the eGFR decreased (eFigureI, Table 2). On multivariable analysis, eGFR<15 without dialysis was associated with the highest 30-day mortality (HR 2.09, 95% CI 1.66–2.63, p<0.0001). Being on dialysis was associated with the highest 1-year mortality (HR 2.65, 95%CI 2.49–2.81; Table 2).

The rate of re-hospitalization within 1-year after discharge was higher as the eGFR decreased (eFigureII, Table 3). On multivariable analysis, dialysis was associated with the highest 30-day and 1-year re-hospitalization rates (HR 2.10, 95% CI 1.95–2.26; HR 2.55, 95% CI 2.44–2.66, respectively; Table 3).

The composite of mortality and re-hospitalization within 1-year after discharge among ischemic stroke patients was also higher as the eGFR decreased (Figure III, Table 4). On multivariable analysis, dialysis was associated with the highest 30-day and 1-year composite of mortality and re-hospitalization (HR 2.04, 95% CI 1.90–2.18; HR 2.46, 95% CI 2.36–2.56, respectively; Table 4).

Adjusted sensitivity analysis using the CKD-EPI equation resulted in reclassification of 0.9% of the cohort to an eGFR<60 (eGFR>60,47.9%; eGFR 45–59, 25.2%; eGFR 30–44 , 17.1%; eGFR 15–29 ,6.3%; eGFR <15, 0.8%; Dialysis, 2.8%) and revealed similar association of eGFR with mortality and re-hospitalizations (Tables VI and VII).

An adjusted sensitivity analysis restricted to patients who also had CKD identified by ICD-9-CM codes revealed that compared to eGFR≥60 with ICD-9-CM suggestive of CKD, an eGFR<30 remained associated with increased 30-day and 1-year mortality, 30-day and 1-year re-hospitalization, and, 30-day and 1-year composite mortality and re-hospitalizations (Tables VIII, IX, X). An eGFR <15 was associated with the highest 30-days composite of mortality and re-hospitalization (HR 1.63, 95% CI 1.34–1.98) and dialysis was associated with the highest 1-year composite of mortality and re-hospitalization (HR 1.74, 95% CI 1.62–1.85) (Table X).

The associations of several demographic and clinical factors with 30-day and 1-year composite of mortality and re-hospitalization varied by the level of kidney dysfunction (Figures IV and V). The effects of most of the included factors on outcomes were weakened with advanced kidney dysfunction. For example, age and an increase in the NIHSS score were associated with an increase in composite 30-day and 1-year mortality and re-hospitalization regardless of eGFR, but the association was lowest among those on dialysis. The association of atrial fibrillation/flutter did not vary by the level of kidney function for 30-day outcomes, but was highest in those with eGFR>15 for 1-year outcomes. The association of anticoagulation with 30-day or 1-year outcomes did not vary by the level of kidney function. In contrast, a history of smoking in patients on dialysis was associated with

increased risk of mortality and rehospitalization at 1-year whereas the effect of smoking in other eGFR categories was less significant. Being a woman was associated with worse post-stroke outcomes only in dialysis patients. Compared to other levels of kidney dysfunction, patients on dialysis who had a symptomatic intracranial hemorrhage within 36-hours of treatment with IV-tPA had the highest 1-year mortality and re-hospitalizations (HR 7.51, 95%CI 2.79–20.22, p<.0001).

Discussion:

In this nationwide study of Medicare beneficiaries aged ≥65 years with acute ischemic stroke, after adjusting for relevant clinical and demographic factors, eGFR and dialysis status on admission were strong predictors of outcomes and modified the relationship of other clinical and demographic factors with 30-day and 1-year mortality and re-hospitalizations. In adjusted models, 30-day mortality was highest among patients with eGFR<15 without dialysis with about 2-times higher odds compared to those with eGFR≥60. In contrast, 1-year mortality, 30-day and 1-year re-hospitalizations, and 30-day and 1-year combined mortality and re-hospitalizations were highest among those on dialysis with at least 2-times higher odds for any of these outcomes.

These findings further extend and strengthen previous studies suggesting that renal dysfunction may be associated with increased post-stroke mortality.[8, 13, 14] Reduced admission creatinine clearance, high serum creatinine, and higher urea concentrations post-stroke were associated with a higher risk of all-cause mortality during a 7-year follow-up period.[15] In a study of a Chinese cohort with type 2 diabetes, low eGFR<45 ml/min/1.73m^2 was a predictor of 1-year post-stroke all-cause mortality.[6] In another study, acute kidney injury following acute ischemic stroke was an independent predictor of 10-year mortality.[16] In contrast, albuminuria but not eGFR were found in some studies to be associated with post-stroke mortality.[3, 5] None of these studies separately analyzed those on dialysis or based classifications according to the NKF KDOQI.

Data regarding the association of kidney dysfunction and re-hospitalizations is scarce. In some studies, renal disease was included in models for hospital readmissions in stroke patients and was found to be associated with higher readmissions; however these studies did not analyze the level of renal dysfunction and dialysis status.[9, 17, 18] In contrast, we found a strong, graded association of impaired renal function with 30-day and 1-year all-cause re-hospitalizations that was independent of other factors. Patients receiving dialysis had the highest risk of re-hospitalization at both 30-days and 1-year.

The association of kidney dysfunction with post-stroke outcomes may be due to several possible factors. Renal impairment in patients with stroke may indicate end-organ damage from common risk factors such as uncontrolled hypertension or other comorbidities.[15] Alternatively, renal impairment may cause endothelial dysfunction, homocystenemia, coagulation disorders, impaired endothelial release of tissue plasminogen activator, extravascular coagulation and higher levels of inflammatory cytokines and oxidative stress.[19,20] Our findings suggest the importance of including kidney dysfunction and especially dialysis status as predictors of re-hospitalizations and mortality both at 30-days and 1-year.

Future studies should evaluate whether targeted interventions directed towards this high-risk group reduces mortality and re-hospitalizations.

We also found that the association of several patient and hospital-level characteristics with outcomes varied by eGFR. Overall, the association of multiple factors with outcomes tended to lessen among those on dialysis, potentially reflecting unmeasured confounders or a stronger association of outcomes with dialysis. Some of the interactions may be due to chance (multiple testing) or may not be clinically important. In contrast, the significant increased risk of 1-year mortality and re-hospitalization in dialysis patients who develop sICH may be related to unmeasured comorbidities, significant hemostatic dysfunction, or poorer functional outcomes. It is possible that the finding of increased risk of worse outcome in women on dialysis is due to poorer previous functional status and other comorbidities. We believe that these results are interesting in that they identify other important predictors of outcomes in the setting of kidney dysfunction. More studies are needed to duplicate these findings and determine the reasons behind these interactions.

Adjusted sensitivity analysis restricted to patients who also had CKD identified by ICD-9-CM codes revealed that eGFR<30 (but not ≥30) and being on dialysis remained associated with post-stroke outcomes. This may be due to ICD-9 codes underestimating the prevalence of CKD or because the comparator was eGFR≥60 with a diagnosis of CKD.[21] It is also possible that the effect of acute kidney injury on post-stroke outcomes is different than established kidney disease.

This study has limitations. The data are limited to GWTG-Stroke participating hospitals and the Medicare population (aged ≥65 years) and may not be generalizable to younger populations. GWTG–Stroke data, however, are generally representative of national fee-for-service Medicare ischemic stroke populations.[11] In addition, about 95% percent of individuals ≥65-years use Medicare in the US.[22] Although generally valid, dialysis was identified based on ICD-9-CM codes, which may underestimate its true prevalence.[23] Unmeasured confounding cannot be excluded. Admission creatinine was not obtained in all patients introducing a possible selection bias, however, the difference in the other baseline characteristics of those included vs. excluded from the study based on admission creatinine was small. A time dependent analysis was not performed because creatinine was only available during the hospital admission. The MDRD formula for calculating eGFR may not be entirely accurate in the setting of acute ischemic stroke. A sensitivity analysis using the CKD-EPI equation, however, yielded similar results. Albuminuria and proteinuria data are not available in the GWTG database, which may explain why some subjects with eGFR≥60 have a diagnosis of CKD. NIHSS was missing in 38% of the cases and not at random; however, the difference between baseline characteristics of those missing NIHSS vs. not was modest and possible confounding variables were adjusted for in multivariable analyses. There was no correction for multiple testing. Finally, cause- specific mortality was not available.

Among older patients hospitalized with acute ischemic stroke who survived to discharge, a lower eGFR and dialysis on admission was independently associated with a higher 30-day

and 1-year mortality and re-hospitalizations suggesting that kidney function should be included in risk-stratification models for post-stroke outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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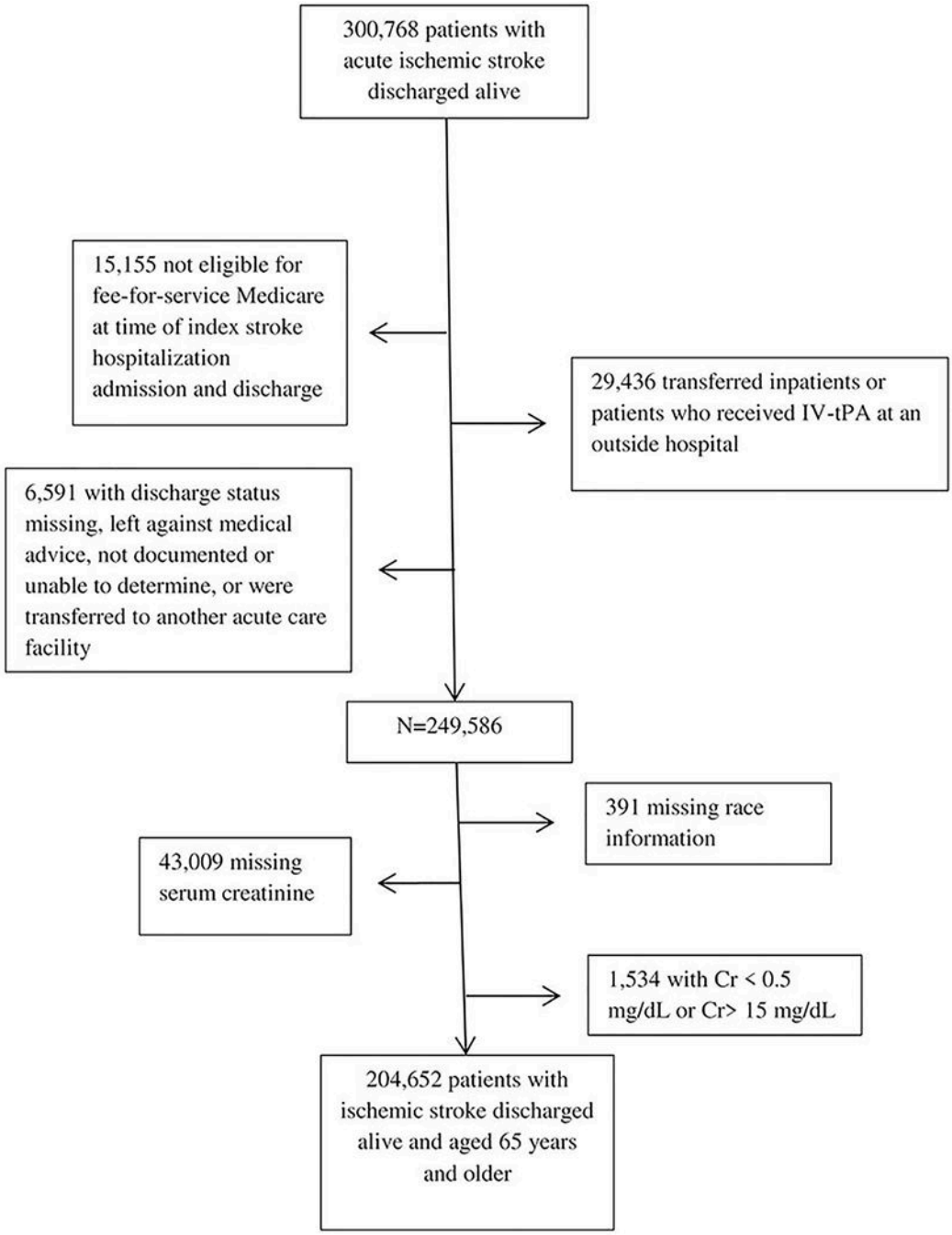

Figure 1.
Flowchart of Patient Selection

Table 1.

Baseline Patient Clinical Characteristics by eGFR level

Variable	Overall (N=204652)	eGFR ≥60 (N=99789)	eGFR 45–59 (54158)	eGFR 30–44 (N=33369)	eGFR 15–29 (N=10433)	eGFR <15 (N=1201)	Dialysis (N=5702)	p-value
Age								
Median (25th-75th P*)	80.0 (73.0–86.0)	78.0 (71.0–84.0)	82.0 (76.0–87.0)	83.0 (76.0–88.0)	83.0 (76.0–88.0)	80.0 (74.0–86.0)	75.0 (70.0–82.0)	<.0001
Sex%								
Women	57.6	52.1	61.2	65.3	69.0	68.7	53.3	<.0001
Race								
Other	2.6	2.7	2.4	2.6	2.4	2.5	3.1	<.0001
Asian	1.9	2.0	1.6	1.6	1.9	2.3	2.4	
Hispanic (any race)	4.3	4.5	3.8	3.9	4.5	4.5	8.6	
Black	11.2	12.6	8.5	8.5	10.4	14.9	28.2	
White	79.8	78.0	83.4	83.1	80.6	75.5	57.5	
Labs/Vitals at Admission								
Glucose (mg/dL) Median (25th-75th P)	117.0 (100.0–147.0)	115.0 (100.0–143.0)	117.0 (101.0–145.0)	120.0 (102.0–153.0)	124.0 (103.0–162.0)	121.0 (103.0–154.0)	126.0 (101.0–171.0)	<.0001
Creatinine (mg/dL) Median (25th-75th P)	1.0 (0.8–1.3)	0.8 (0.7–1.0)	1.1 (1.0–1.3)	1.5 (1.3–1.6)	2.2 (1.8–2.5)	4.6 (3.7–7.0)	3.6 (2.1–5.5)	<.0001
Heart rate (bpm) Median (25th-75th P)	77.0 (67.0–88.0)	77.0 (67.0–89.0)	76.0 (67.0–88.0)	76.0 (66.0–88.0)	76.0 (66.0–88.0)	77.0 (67.0–91.0)	77.0 (67.0–88.0)	<.0001
BMI (kg/m^2) Median (25th-75th P)	26.1 (22.9–29.9)	26.0 (22.9–29.9)	26.0 (22.8–29.7)	26.3 (23.0–30.2)	26.4 (22.0–30.6)	26.2 (22.6–30.3)	26.4 (22.9–30.7)	<.0001
INR Median (25th-75th P)	1.0 (1.0–1.1)	1.0 (1.0–1.1)	1.0 (1.0–1.1)	1.0 (1.0–1.1)	1.0 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	<.0001
NIHSS score* Median (25th-75th P)	4.0 (2.0–9.0)	4.0 (1.0–8.0)	4.0 (2.0–9.0)	4.0 (2.0–10.0)	5.0 (2.0–11.0)	5.0 (2.0–12.0)	4.0 (2.0–10.0)	<.0001
Labs/Vitals at Discharge								
Systolic blood pressure (mmHg) Median (25th-75th P)	137.0 (122.0–150.0)	136.0 (122.0–150.0)	137.0 (122.0–150.0)	137.00 (122.0–151.0)	138.0 (123.0–153.0)	138.0 (124.0–151.0)	138.0 (121.0–152.0)	<.0001
Diastolic blood pressure (mmHg) Median (25th-75th P)	71.0 (63.0–79.0)	72.0 (64.0–80.0)	70.0 (63.0–79.0)	70.0 (62.0–78.0)	69.0 (61.0–78.0)	70.0 (62.0–79.0)	67.0 (59.0–76.0)	<.0001
Medical History %								
Atrial fibrillation / Flutter	22.7	20.0	25.4	25.7	25.1	19.9	21.5	<.0001

Variable	Overall (N=204652)	eGFR ≥60 (N=99789)	eGFR 45–59 (54158)	eGFR 30–44 (N=33369)	eGFR 15–29 (N=10433)	eGFR <15 (N=1201)	Dialysis (N=5702)	p-value
Prosthetic heart valve	1.4	1.3	1.4	1.6	1.8	0.8	1.79	<.0001
Previous stroke / TIA	27.7	25.9	28.3	30.4	30.9	27.1	33.0	<.0001
CAD/ prior MI	30.4	26.2	31.5	35.6	39.6	32.8	45.4	<.0001
Carotid stenosis	4.4	3.6	4.5	5.5	6.1	5.33	6.1	<.0001
Diabetes	30.7	27.6	28.3	34.8	41.3	40.0	60.9	<.0001
PVD	5.50	4.36	5.39	6.73	8.90	6.42	12.84	<.0001
Hypertension	80.0	76.1	81.6	85.3	86.6	84.0	88.4	<.0001
Smoker	9.4	11.8	7.2	7.0	7.1	7.4	8.2	<.0001
Dyslipidemia	45.4	43.5	46.3	48.1	47.9	44.8	48.6	<.0001
Heart failure	10.2	6.8	10.5	14.4	19.4	15.0	23.4	<.0001

Table 2.

Association of eGFR group and mortality within 30-days and 1-year from discharge for patients admitted with ischemic stroke.

eGFR Group (ref=eGFR≥60*)	30 days Mortality rate	30 days unadjusted Hazard Ratio 95% CI p-value	30 days Adjusted Hazard Ratio 95% CI p-value	Global P	1 year mortality rate	1 year unadjusted Hazard Ratio 95% CI p-value	1 year Adjusted Hazard Ratio 95% CI p-value	Global P
eGFR 45–59	5%	1.34 (1.27–1.40) <.0001	1.0 (0.94–1.06) 0.9786	<.0001	22%	1.30 (1.27–1.34) <.0001	1.05 (1.01–1.08) 0.0053	<.0001
eGFR 30–44	7%	1.76 (1.67–1.85) <.0001	1.22 (1.14–1.30) <.0001		28%	1.70 (1.66–1.74) <.0001	1.30 (1.25–1.34) <.0001	
eGFR15–29	9%	2.55 (2.38–2.73) <.0001	1.65 (1.51–1.81) <.0001		38%	2.51 (2.42–2.60) <.0001	1.82 (1.73–1.91) <.0001	
eGFR<15	12%	2.98 (2.51–3.53) <.0001	2.09 (1.66–2.63) <.0001		40%	2.76 (2.51–3.03) <.0001	2.05 (1.80–2.34) <.0001	
Dialysis	7%	1.77 (1.60–1.96) <.0001	1.80 (1.57–2.07) <.0001		40%	2.52 (2.41–2.64) <.0001	2.65 (2.49–2.81) <.0001	

*Mortality rate in the reference group (eGFR≥60) was 4% at 30 days and 18% at 1 year.

Table 3.

Association of eGFR group and re-hospitalization within 30-days and 1-year from discharge for patients admitted with ischemic stroke.

eGFR Group (ref=eGFR≥60*)	30 days re-hospitalization rate	unadjusted 30 days re-hospitalization Hazard Ratio (95% CI) p- value	Adjusted 30 days re-hospitalization Hazard Ratio (95% CI) p- value	Global P	1 year rehospitalization rate	unadjusted 1 year re-hospitalization Hazard Ratio (95% CI) p- value	Adjusted 1 year re-hospitalization Hazard Ratio (95% CI) p- value	Global P
eGFR 45–59	13%	1.12 (1.09–1.15) <.0001	1.04 (1.01–1.09) 0.0256	<.0001	48%	1.17 (1.15–1.19) <.0001	1.06 (1.04–1.08) <.0001	<.0001
eGFR 30–44	16%	1.37 (1.32–1.41) <.0001	1.22 (1.17–1.28) <.0001		54%	1.42 (1.39–1.44) <.0001	1.23 (1.20–1.26) <.0001	
eGFR15–29	21%	1.82 (1.74–1.91) <.0001	1.65 (1.56–1.76) <.0001		62%	1.80 (1.74–1.85) <.0001	1.53 (1.47–1.59) <.0001	
eGFR<15	23%	1.95 (1.73–2.21) <.0001	1.82 (1.55–2.13) <.0001		57%	1.66 (1.53–1.80) <.0001	1.47 (1.31–1.64) <.0001	
Dialysis	27%	2.38 (2.26–2.52) <.0001	2.10 (1.95–2.26) <.0001		81%	2.88 (2.79–2.97) <.0001	2.55 (2.44–2.66) <.0001	

*Re-hospitalization rate in the reference group (eGFR≥60) was 12 % at 30 days and 42% at 1 year.

Table 4.

Association of eGFR group and composite of mortality and re-hospitalization within 30 days and 1 year from discharge for patients admitted with ischemic stroke.

eGFR Group (ref=eGFR≥ 60*)	30 days composite of mortality and re-hospitalization rate	Unadjusted 30 days mortality and re-hospitalization Hazard Ratio (95%CI) P-value	Adjusted 30 days mortality and re-hospitalization Hazard Ratio (95%CI) P-value	Global P	1 year composite of mortality and re-hospitalization rate	Unadjusted 1 year mortality and re-hospitalization Hazard Ratio(95%CI) P-value	Adjusted 1 year mortality and re-hospitalization Hazard Ratio(95%CI) P-value	Global P
eGFR 45–59	17%	1.18 (1.15–1.21) <.0001	1.04 (1.01–1.08) <.0001	0.0224	53%	1.20 (1.18–1.22) <.0001	1.06 (1.04–1.08) <.0001	<.0001
eGFR 30–44	20%	1.45 (1.41–1.49) <.0001	1.22 (1.17–1.26) <.0001		60%	1.47 (1.45–1.50) <.0001	1.23 (1.20–1.26) <.0001	
eGFR15–29	26%	1.97 (1.89–2.05) <.0001	1.64 (1.55–1.73) <.0001		70%	1.91 (1.86–1.96) <.0001	1.55 (1.50–1.61) <.0001	
eGFR<15	29%	2.14 (1.92–2.38) <.0001	1.85 (1.60–2.13) <.0001		66%	1.85 (1.72–1.99) <.0001	1.58 (1.43–1.74) <.0001	
Dialysis	30%	2.24 (2.13–2.36) <.0001	2.04 (1.90–2.18) <.0001		84%	2.70 (2.62–2.78) <.0001	2.46 (2.36–2.56) <.0001	

*The composite of mortality and re-hospitalization rates in the reference group (eGFR≥60) was 14% at 30 days and 47% at 1 year.