Title

Renal Dysfunction Is Associated With Poststroke Discharge Disposition and In-Hospital Mortality

Journal

Stroke, 48(2)

ISSN

0039-2499

Authors

El Husseini, Nada
Fonarow, Gregg C
Smith, Eric E
et al.

Publication Date

2017-02-01

DOI

10.1161/strokeaha.116.014601

Peer reviewed

HHS Public Access

Author manuscript

Stroke. Author manuscript; available in PMC 2018 February 01.

Published in final edited form as:

Stroke. 2017 February ; 48(2): 327–334. doi:10.1161/STROKEAHA.116.014601.

Renal Dysfunction is Associated with Post-Stroke Discharge Disposition and In-Hospital Mortality: Findings from GWTG

Nada El Husseini, MD, MHSc.[1,6], **Gregg C. Fonarow, MD**[3], **Eric E. Smith, MD, MPH**[4], **Christine Ju, MS**[2], **Lee H. Schwamm, MD**[5], **Adrian F. Hernandez, MD, MHS**[2], **Phillip J. Schulte, Ph.D.**[2], **Ying Xian, M.D., Ph.D.**[2,6], and **Larry B. Goldstein, MD**[7]

[1]Department of Neurology, Wake Forest Baptist University Health Sciences, Winston-Salem, NC

[2]Duke Clinical Research Institute, Duke University Medical Center, Durham, NC

[3]UCLA Division of Cardiology, Ronald Reagan-UCLA Medical Center, Los Angeles, CA

[4]Hotchkiss Brain Institute, University of Calgary, Calgary, Canada

[5]Massachusetts General Hospital, Boston, MA

[6]Department of Neurology, Duke University Medical Center, Durham, NC

[7]Department of Neurology, University of Kentucky, Lexington KY

Abstract

Background and Purpose—Kidney disease is a frequent comorbidity in patients presenting with acute ischemic stroke. We evaluated whether the estimated glomerular filtration rate (eGFR) on admission is associated with post-stroke in-hospital mortality or discharge disposition.

Methods—In this cohort study, data from ischemic stroke patients in GWTG Stroke linked to fee for service Medicare data were analyzed. The Modification of Diet in Renal Disease (MDRD) study equation was used to calculate the eGFR (mL/min/1.73 m^2). Dialysis was identified by ICD-9 codes. Adjusted multivariable Cox proportional hazards models were used to determine the independent associations of eGFR with discharge disposition and in-hospital mortality. Adjusted individual models also examined whether the association of clinical and demographic factors with outcomes varied by eGFR level.

Results—Of 232, 236 patients, 47.3% had an eGFR≥60, 26.6% an eGFR 45–59, 16.8% an eGFR 30–44, 5.6% an eGFR 15–29, 0.7% an eGFR<15 without dialysis, and 2.8% were receiving dialysis. Of the total cohort, 11.8% died during the hospitalization or were discharged to hospice and 38.6% were discharged home. After adjusting for other relevant variables, renal dysfunction

Corresponding author: Nada El Husseini, MD, MHS, Wake Forest Baptist Medical Center, Department of Neurology, Division of Vascular Neurology, 6th Floor Janeway tower, Medical Center Boulevard, Winston Salem NC 27157, nelhusse@wakehealth.edu, Fax: 336-716-7794, Tel: 336-716-7548.

Conflicts of interest/Disclosures:
Christine Ju: Nothing to disclose
Dr. Schwamm: Nothing to disclose
Dr. Schulte: Nothing to disclose
Dr. Xian: Nothing to disclose
Dr. Goldstein: Nothing to disclose

was independently associated with an increased risk of in-hospital mortality which was highest among those with eGFR <15 without dialysis (OR 2.52, 95%CI 2.07–3.07). An eGFR 15–29 (OR 0.82, 95% CI 0.78–0.87), eGFR<15 (OR 0.72, 95%CI 0.61–0.86) and dialysis (OR 0.86, 95% CI 0.79–0.94) remained associated with lower odds of being discharged home. In addition, the associations of several clinical and demographic factors with outcomes varied by eGFR level.

Conclusions—eGFR on admission is an important predictor of post-stroke short-term outcomes.

Keywords

Stroke; Kidney disease; Outcomes

Introduction

Renal disease is prevalent among stroke patients and is associated with worse stroke outcomes.[1,2,3] Elevated eGFR on admission for stroke may reflect acute kidney injury or chronic kidney disease (CKD), which may in turn worsen the outcome following acute stroke. Data regarding the association of eGFR on admission with post-stroke outcomes is inconsistent. For example, in one study, an eGFR of 15–44 during hospitalization for acute stroke was associated with increased 1-year mortality.[4] Several other studies, however, find that proteinuria rather than eGFR was associated with in-hospital mortality.[3, 5] These studies were limited by the way eGFR was categorized and patients on dialysis were not analyzed separately. Furthermore, it is uncertain if the effect of patient or hospital-level characteristics on post-stroke outcomes varies by the level of kidney dysfunction.

Understanding the impact of admission eGFR on short-term outcomes as well as its interaction with clinical and demographic factors is important as it may inform targeted interventions for high risk patients. Addressing this gap is also important to properly adjust for case mix in outcome studies and payment models.

The objectives of this study were to: (1) Examine the independent associations of the different levels of renal dysfunction, including being on dialysis, with discharge disposition and in-hospital mortality in a large Get With The Guidelines (GWTG)-Stroke cohort of patients who were eligible for fee-for-service Medicare at the time of the index acute ischemic stroke admission, (2) Assess the relationships of patient and hospital characteristics with short-term outcomes (discharge home, inpatient mortality) stratified by eGFR levels.

Methods

Patient population

We used data on patients admitted with ischemic stroke between 2009–2012 from fully participating sites from the GWTG-Stroke program database that was linked to CMS claims data. Details of the GWTG-Stroke program have been previously published.[1, 6] GWTG is a voluntary, national, quality-improvement initiative sponsored by the American Heart Association and American Stroke Association designed to improve adherence to the guideline-based care of patients hospitalized with stroke and TIA. GWTG-Stroke participating hospitals record data from all stroke and TIA admissions. Case ascertainment is

based on clinical identification during the hospitalization, retrospective surveillance of International Classification of Diseases, ninth Revision codes, or both. Trained personnel extract data on demographics, medical history, in-hospital treatment, and discharge characteristics.[6] Quintiles Real-World & Late Phase Research (Cambridge, MA) serves as the data collection and coordination center for GWTG. The Duke Clinical Research Institute (Durham, NC) serves as the data analysis center.[1, 6] Institutional review board approval was obtained for this study.

A total of 341,602 patients from 1,679 GWTG -Stroke fully participating sites who were admitted between 2009 and October 2014 and who had records linked to CMS claims data were identified. From this cohort, 603 were missing race information, 59,378 patients had missing serum creatinine (Cr), 1,471 had Cr < 0.5 mg/dL, and 856 had Cr> 15 mg/dL (these values were considered less likely to be physiologic), 13,650 were not eligible for fee-for-service Medicare at time of index stroke hospitalization admission and discharge, 27,935 were transfer inpatients or patients who received IV-tPA at an outside hospital, 5,473 had discharge status missing, left against medical advice, not documented or unable to determine, or were transferred to another acute care facility. The remaining 232,236 patients with ischemic stroke aged 65 years and older who were admitted from 1,581 sites were included in the analysis.

Variables

Renal dysfunction definitions

eGFR was estimated based on the MDRD equation [eGFR = 175 × serum creatinine-1.154 × Age-0.203 × [1.210 if race=black] × [0.742 if sex=female] using creatinine on admission.[7] The eGFR groups were mutually exclusive. Dialysis patients were identified based on ICD-9 codes and the remaining groups were defined based on calculated eGFRs.

The eGFR levels were selected based on CKD classification by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative: 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 <15 mL/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 was analyzed by eGFR level rather than CKD stage.

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

Outcomes

In-hospital mortality included any death prior to discharge or being discharged to hospice. Discharge disposition was dichotomized into discharge home vs. other.

Covariates

The covariates for the adjusted analysis of the association of admission eGFR with inpatient mortality/hospice and discharge disposition included the standard GWTG stroke adjustment variable list: 1) demographics: age, sex, race; 2) medical history: atrial fibrillation/flutter, previous stroke/TIA, CAD/prior MI, carotid stenosis, diabetes mellitus, peripheral vascular disease, hypertension, dyslipidemia, smoking; 3) other patient characteristics: arrival on vs. off hours, initial NIHSS score, 4) hospital characteristics such as region, hospital type (teaching/non-teaching), number of beds, annual ischemic stroke volume, annual IV- tPA volume, rural location and JC primary stroke center status.

The 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, and independent ambulatory status at admission. For each variable of interest, individual models for each eGFR stage were created with the standard GWTG Stroke adjustment variable list.

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 were compared using Pearson chi-square tests, Fisher's Exact Test or Kruskal-Wallis tests as appropriate.

The relationship between eGFR groups and patient outcomes were quantified using multivariable logistic regression with generalized estimating equations (GEEs). GEE methods were used to account for potential correlation and clustering of patients within hospitals. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs) with the eGFR≥60 group as reference.

To assess whether eGFR levels interacted with patient and hospital factors, adjusted and unadjusted logistic regression models with GEE were run for each factor of interest. Adjustment variables were based on the standard GWTG Stroke list (described under covariates). 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 OR and 95%CI between the factor and outcome is provided for each eGFR category.

Lack-of-fit tests were used to compare linear fit and non-linear fit models. If non-linearity was found, appropriate transformations were used to achieve linearity. Linear splines were used for glucose (knots at 100 and 150 mg/dL), LDL (knot at 65 mg/dL), and systolic blood pressure (knot at 150 mmHg) in the in-hospital mortality/hospice model. In addition to these variables, linear splines for hospital size (knot at 250 beds), and annual IV-tPA volume (knot

at 15) were used in the discharged home model. Co-linearity between covariates was assed using variance inflation factors (VIF). Large VIF values (VIF>5) between variables were examined. If there was evidence of strong correlation between two covariates, one was excluded from the model.

Multiple imputation with 25 imputations was used to estimate missing data in the models. 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. Hospital characteristics were not imputed.

Sensitivity analysis

Because admission eGFR may reflect acute renal dysfunction and not always reflect CKD, sensitivity analyses were performed to examine the association of outcomes and patient and hospital factors classified by eGFR but confined to patients who also have ICD-9-CM codes reflecting CKD. CKD was 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 232,236 patients with ischemic stroke ≥65-years, 109,913 (47.3%) had an eGFR≥60; 61,719 (26.6%) an eGFR 45–59; 39,201 (16.8%) an eGFR 30–44; 13,118 (5.6%) an eGFR 15–29; 1700 (0.7%) an eGFR <15 without dialysis and, 6,585 (2.8%) patients were receiving dialysis. Characteristics of the cohort and hospital characteristics by eGFR levels are described in Tables 1 and supplemental table I, respectively. The median age of the cohort was 81 years (25^{th}–75^{th} percentile [P]: 74–87 years). Compared to subjects with eGFR≥60 (median age 78, 25^{th}–75^{th} P: 71–85 years), those with eGFR<60 were older, except for those on dialysis (median age 76, 25^{th}–75^{th} P: 70–82 years). About 59% of the entire cohort were women and 80% were White. There were fewer Whites (58.1%) and more Blacks (27.6%) among those on dialysis compared to the other groups. History of previous stroke/TIA, CAD/MI, carotid stenosis, diabetes, peripheral vascular disease, hypertension, dyslipidemia, and heart failure were more common in those on dialysis; patients on dialysis were more likely to be taking antiplatelet or anticoagulant drugs, antihypertensive medications, lipid-lowering medications and diabetic medications prior to admission. The highest median NIHSS was among those with eGFR<15 without dialysis (NIHSS=8, 25th–75th P: 3–17). The percentage of receiving IV-tpa was lowest among those with GFR<15 not on dialysis.

In-hospital mortality or hospice

Of the total cohort, 27,409 (11.8%) died in the hospital or were discharged to hospice. Inpatient mortality or discharge to hospice was most common in those with an eGFR<15 without dialysis (N=497; 29.2%) and least common among those with eGFR≥60 (N=10,054; 9.1%). In-hospital mortality or discharge to hospice occurred in 12.1% (N=7,512) of patients with an eGFR 45–59, 14.8% (N=5,807) with an eGFR 30–44, 20.3% with an eGFR 15–29 (N=2,664), and 13.2% (N=875) with patients on dialysis. After adjusting for other relevant

variables, when compared to those with GFR≥60, all other eGFR levels were independently associated with increased odds of in-hospital mortality or discharge to hospice, with the highest risk among those with GFR<15 without dialysis (eGFR<15 vs eGFR>60; OR 2.52, 95% CI 2.07–3.07), p<0.0001 (Table 2).

Discharge disposition

Of the total cohort, 89,696 (38.6%) were discharged home. Discharge home was most common among those with an eGFR≥60 (N=47,051; 42.8% of those with eGFR≥60) and least common in those with an eGFR<15 without dialysis (N=400; 23.5% of those with eGFR<15 without dialysis). The frequency of discharge home was 37.3% in those with an eGFR 45–59 (N=23,037), 33.6% with an eGFR 30–44 (N=13,185), 27.5% with an eGFR 15–29 (N=3,617), and 36.5% in those receiving dialysis (N=2,406). After adjusting for other relevant variables, advanced kidney dysfunction including having an eGFR 15–29, eGFR< 15 without dialysis, and dialysis were each associated with a lower odds of being discharged home, with the greatest association in those with eGFR<15 without dialysis (eGFR<15 vs eGFR>60; OR 0.72, 95%CI 0.61–0.86, p=0.0002) (Table 3).

Association of clinical and demographic factors with in-hospital mortality by eGFR level

After covariate adjustment, the associations of age, previous stroke/TIA, systolic blood pressure on admission, glucose on admission, NIHSS, and teaching versus non- teaching hospital with in-hospital mortality varied by eGFR level (supplementary table II). For example, the interaction between eGFR and glucose level on admission was significant, but was only reflected by a decreased odds of in-hospital mortality/hospice per 5 mg/dL increase of glucose in patients on dialysis who presented with a blood glucose ≤ 100 mg/dL (OR=0.88, 95% CI 0.82–0.94, p=0.0003). An increase in NIHSS was associated with a worse outcome across all GFR levels, but the association was highest among those with an eGFR≥60 (OR=1.99, 95% CI 1.96–2.03, p<0.0001) and lowest in those with an eGFR<15 without dialysis (OR 1.70, 95% CI 1.54–1.87, p<0.0001). Being treated at a teaching versus non- teaching hospital was associated with decreased mortality/hospice only in those on dialysis (OR 0.77, 95% CI 0.61–0.97, p=0.0265). No interaction was found with history of atrial fibrillation.

Adjusted Sensitivity analysis restricted to patients who had CKD identified by ICD-9-CM codes revealed that only the associations of sex and dyslipidemia with outcome varied by eGFR levels. Women were less likely to die in the hospital if they had eGFR 15–29 (OR 0.79, 95% CI 0.66–0.94, p=0.0096) and eGFR<15 without dialysis (OR 0.56, 95% CI 0.32–0.97, p=0.0387) whereas the association was not significant for other eGFR levels. Medical history of dyslipidemia was only associated with in-hospital mortality among those with an eGFR 30–44 (OR=0.73, 95% CI 0.64–0.83, p<0.0001).

Association of demographic and clinical factors with discharge home by eGFR level

After covariate adjustment, the association of age, sex, race, history of hypertension, history of dyslipidemia, NIHSS and independent ambulatory status on admission with discharge home varied by eGFR levels (Supplementary Table III). For example, NIHSS was inversely associated with discharge home among those with eGFR≥60 (OR 0.42, 95% CI 0.41–0.43,

p<0.0001) and in those with kidney dysfunction but had the lowest effect size among those on dialysis (OR 0.51, 95% CI 0.47–0.56, p<0.0001). Independent ambulatory status on admission was associated with discharge home in those with eGFR≥60 (OR 3.33, 95% CI 3.17–3.51, p<0.0001) as well as those with kidney dysfunction but the effect size was lowest in those on dialysis (OR 2.66, 95% CI 2.19–3.23, p<0.0001).

Adjusted sensitivity analysis restricted to those who also had an ICD-9-CM code consistent with CKD revealed that only the association of sex and hospital location (rural vs. urban) with discharge home varied by eGFR level. Women were less likely to be discharged home if they had eGFR 45–59 (OR 0.74, 95% CI 0.65–0.84, p <0.0001), eGFR 30–44 (OR 0.86, 95% CI 0.78–0.94, p=0.001) or eGFR 15–29 (OR 0.72, 95% CI 0.63–0.82, p<0.0001) but the association was not significant for other eGFR levels. Being treated in a rural vs. urban location increased the odds of discharge home if eGFR was 45–59 (OR 1.35, 95% CI 1.03–1.77, p=0.0291) and dialysis (OR 1.79, 95% CI 1.06–3.03, p=0.030) but was not significant in other eGFR levels.

Discussion

In this large nationwide study of Medicare beneficiaries aged ≥65-years with acute ischemic stroke, and after adjusting for relevant clinical and demographic factors, eGFR on admission was a strong predictor of outcome and modified the relationship of other clinical and demographic factors with in-hospital mortality and discharge disposition. Regardless of the eGFR level, patients with eGFR <60 were more likely to die in the hospital. In-hospital mortality following acute ischemic stroke was highest among patients with eGFR<15 without dialysis with about 2.5 times higher odds than those with eGFR ≥60 after adjusting for relevant variables. Patients with eGFR<15 without dialysis were also the least likely to be discharged home compared to those with eGFR ≥60. Compared to those with eGFR ≥60, patients with eGFR <15 without dialysis did worse than those on dialysis, reflecting either a beneficial effect of dialysis in patients with ESRD on stroke outcomes or, potentially reflecting the underlying severity of the comorbidities in this group that may have precluded eligibility for dialysis. Those with eGFR<15 not on dialysis tended to have more severe strokes. In our study, we adjusted for comorbidities and NIHSS, and despite this, those with eGFR<15 still fared poorly, likely from underlying unmeasured confounders related to their vascular risk factors and poor health status at baseline.

Previous reports evaluating the association of renal dysfunction on admission with acute post-stroke outcomes were inconsistent. For example, two studies found an association between in-hospital mortality and proteinuria, but no association with admission eGFR.[3, 5] One of these studies also did not find an association between the admission GFR and discharge home.[5] The lack of association between admission GFR and post-stroke outcomes in these studies could be due to the way GFR was categorized (classified into 3 groups in the one study and dichotomized as GFR≥60 or <60 in the other). In addition, one of the studies excluded patients with known CKD.[5] In contrast, GFR on admission independently predicted in-hospital mortality after acute myocardial infarction.[8] CKD defined by ICD-9-CM codes was associated in one study with in-hospital mortality.[9] The eGFR cut-offs in our study may better reflect the underlying severity of renal dysfunction. We also separately

analyzed patients using dialysis in contrast to previous studies.[1] In addition, because of the large sample, we were able to adjust for multiple relevant covariates.

We also evaluated the interaction between renal dysfunction and patient and hospital-level characteristics that may affect post-stroke outcomes. We found that the association with outcomes of several patient and hospital-level characteristics varied by eGFR level. For example, the association of sex with inpatient mortality varied by eGFR level only when the analysis was restricted to those who also had an ICD-9 diagnosis of CKD. In this group, women were about 20% less likely than men to die in the hospital if the eGFR was 15–29 and 45% less likely if <15 without dialysis, but there was otherwise no difference in in-hospital mortality between women and men. These results are consistent with previous findings of slightly lower mortality in women compared to men with CKD.[10] Also, lower post-stroke mortality was noted in women aged 35 to 54 years compared to men.[11] In contrast, another study found that in-hospital mortality in women with CKD hospitalized for stroke was higher compared to men, but a test for interaction with different levels of renal dysfunction was not performed.[12]

The association of sex with discharge disposition also varied by eGFR level. Women were as likely as men to be discharged home only if they had an eGFR<15 or were on dialysis but were otherwise less likely to be discharged home. This may be because eGFR<15 and dialysis are strong predictors of discharge outcomes, thus reducing the association with sex. These findings are consistent with previous studies that found an association between sex and post-stroke outcomes. In one study, older women had a higher risk than men of poor functional outcome at discharge after acute ischemic stroke.[13]

The presence of advanced renal dysfunction reduced the associations of several demographic/clinical factors with outcomes. The associations of increased age, systolic blood pressure on admission, and initial NIHSS score were reduced in the setting of advanced renal dysfunction. In contrast, glucose on admission was associated with outcome only in patients receiving dialysis. Mortality decreased for each 5 mg/dL increase in glucose in patients receiving dialysis who presented with blood glucose ≤100 mg/dL suggesting that hypoglycemia may play an even greater role in in-hospital mortality in dialysis patients. Interestingly, being treated at a teaching hospital was associated with lower mortality only in those on dialysis, possibly owing to the more complex care of these patients.

Similar patterns were found with factors associated with discharge home. Increased age played a smaller role in the association with discharge disposition among patients on dialysis compared to those not on dialysis. Admission NIHSS score and independent ambulatory status on admission were associated with outcome in all groups of patients including those with and without kidney dysfunction, but the effect size was lowest in those receiving dialysis.

Fewer interactions between eGFR and demographic and clinical factors were noted when restricting the analysis to those who also had ICD-9 indicating CKD. This may be because CKD ICD-9 codes may be insensitive and underestimated the prevalence of CKD.[14] Alternatively, the interaction of GFR on admission, which could reflect acute renal

impairment but not chronic renal disease, with clinical and demographic factors may be different in those who already have established CKD.

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 a younger population. GWTG–Stroke hospitals do tend to be larger, urban and teaching centers. GWTG–Stroke registry data, however, are generally representative of national fee-for-service Medicare ischemic stroke populations.[15] In addition, the majority of individuals ≥65-years use Medicare in the US.[16] Although generally valid, dialysis was identified based on ICD-9-CM codes, which may underestimate its true prevalence.[17] Residual measures and unmeasured confounding cannot be excluded. Admission creatinine was not uniformly obtained introducing a possible selection bias. The MDRD formula used for the analysis may not be an entirely accurate measure of eGFR in the setting of acute ischemic stroke. Multiple testing was done in a large database which may increase the likelihood of finding statistically significant results by chance. Also, because of the large sample size, differences that are not clinically important may be statistically significant.

Among Medicare beneficiaries with acute ischemic stroke, in-hospital mortality increased across all levels of renal dysfunction and was highest in those with an eGFR<15 not receiving dialysis. Discharge home was less frequent in those with advanced renal dysfunction. The association of other factors with outcomes varied by the level of renal dysfunction, confirming that admission eGFR identifies a group of patients at risk for poor outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: The Get With The Guidelines (GWTG)-Stroke program is supported in part by a charitable contribution from Bristol-Myers Squibb/Sanofi Pharmaceutical Partnership and the American Heart Association Pharmaceutical Roundtable. GWTG-Stroke has been funded in the past through support from Boehringer-Ingelheim and Merck. These funding agencies did not participate in study design or analysis, manuscript preparation, or approval of this study.

This work was supported by the National Institute of Diabetes and Digestive and Kidney Diseases (P30DK096493). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Dr. El Husseini: Research support from the Mini Grant award from the Duke O'Brien Center for Kidney Research. The mini grant award is a sub-award under Duke University's primary award from the NIH, award number 1P30DK096493–01.

Dr. Fonarow: Other research support from the Patient Centered Outcome Research Institute, NIH/AHRQ, GWTG Steering Committee, and employee of University of California which has a patent on an endovascular device.

Dr. Smith: Member of the American Heart Association -GWTG Steering Committee.

Dr. Hernandez: Other research support from Genentech, Daichi, Janssen and, AstraZeneca. Honoraria include AstraZeneca, Bayer and, Novartis

References

1. Ovbiagele B, Schwamm LH, Smith EE, Grau-Sepulveda MV, Saver JL, Bhatt DL, et al. Patterns of care quality and prognosis among hospitalized ischemic stroke patients with chronic kidney disease. Journal of the American Heart Association. 2014; 3:e000905. [PubMed: 24904017]
2. Holzmann MJ, Aastveit A, Hammar N, Jungner I, Walldius G, Holme I. Renal dysfunction increases the risk of ischemic and hemorrhagic stroke in the general population. Annals of medicine. 2012; 44:607–615. [PubMed: 21612332]
3. Kumai Y, Kamouchi M, Hata J, Ago T, Kitayama J, Nakane H, et al. Proteinuria and clinical outcomes after ischemic stroke. Neurology. 2012; 78:1909–1915. [PubMed: 22592359]
4. Yahalom G, Schwartz R, Schwammenthal Y, Merzeliak O, Toashi M, Orion D, et al. Chronic kidney disease and clinical outcome in patients with acute stroke. Stroke; a journal of cerebral circulation. 2009; 40:1296–1303.
5. Ovbiagele B, Sanossian N, Liebeskind DS, Kim D, Ali LK, Pineda S, et al. Indices of kidney dysfunction and discharge outcomes in hospitalized stroke patients without known renal disease. Cerebrovascular diseases. 2009; 28:582–588. [PubMed: 19844098]
6. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, et al. Get with the guidelines-stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. Circulation. 2009; 119:107–115. [PubMed: 19075103]
7. Stevens LA, Coresh J, Feldman HI, Greene T, Lash JP, Nelson RG, et al. Evaluation of the modification of diet in renal disease study equation in a large diverse population. Journal of the American Society of Nephrology : JASN. 2007; 18:2749–2757. [PubMed: 17855641]
8. Afshinnia F, Ayazi P, Chadow HL. Glomerular filtration rate on admission independently predicts short-term in-hospital mortality after acute myocardial infarction. American journal of nephrology. 2006; 26:408–414. [PubMed: 16926535]
9. Fabbian F, Gallerani M, Pala M, De Giorgi A, Salmi R, Dentali F, et al. Association between in-hospital mortality and renal dysfunction in 186,219 patients hospitalized for acute stroke in the emilia-romagna region of italy. Angiology. 2014; 65:906–910. [PubMed: 24277911]
10. Roderick PJ, Atkins RJ, Smeeth L, Mylne A, Nitsch DD, Hubbard RB, et al. Ckd and mortality risk in older people: A community-based population study in the united kingdom. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2009; 53:950–960. [PubMed: 19394727]
11. Towfighi A, Tai W, Markovic D, Ovbiagele B. Sex-specific temporal trends in in-hospital mortality after stroke among middle-age individuals in the united states. Stroke; a journal of cerebral circulation. 2011; 42:2740–2745.
12. Ovbiagele B. Chronic kidney disease and risk of death during hospitalization for stroke. Journal of the neurological sciences. 2011; 301:46–50. [PubMed: 21094955]
13. Irie F, Kamouchi M, Hata J, Matsuo R, Wakisaka Y, Kuroda J, et al. Sex differences in short-term outcomes after acute ischemic stroke: The fukuoka stroke registry. Stroke; a journal of cerebral circulation. 2015; 46:471–476.
14. Kern EF, Maney M, Miller DR, Tseng CL, Tiwari A, Rajan M, et al. Failure of icd-9-cm codes to identify patients with comorbid chronic kidney disease in diabetes. Health services research. 2006; 41:564–580. [PubMed: 16584465]
15. Reeves MJ, Fonarow GC, Smith EE, Pan W, Olson D, Hernandez AF, et al. Representativeness of the get with the guidelines-stroke registry: Comparison of patient and hospital characteristics among medicare beneficiaries hospitalized with ischemic stroke. Stroke; a journal of cerebral circulation. 2012; 43:44–49.
16. Collins AJ, Foley RN, Herzog C, Chavers B, Gilbertson D, Herzog C, et al. Us renal data system 2012 annual data report. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2013; 61:A7, e1–e476. [PubMed: 23253259]
17. Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayer WC, Liangos O, et al. Validity of international classification of diseases, ninth revision, clinical modification codes for acute renal failure. Journal of the American Society of Nephrology : JASN. 2006; 17:1688–1694. [PubMed: 16641149]

Table 1

Baseline patient characteristics and discharge disposition by eGFR level

Variable	Overall (N=232236)	GFR≥60 (N=109913)	GFR 45–59 (N=61719)	GFR 30–44 (N=39201)	GFR 15–29 (N=13118)	GFR<15 (N=1700)	on Dialysis (N=6585)	P-value
Demographics								
Age Median (25th–75th P)	81.0 (74.0–87.0)	78 (71.0–85.0)	83 (76.0–88.0)	83.0 (77.0–88.0)	83.0 (77.0–89.0)	82.0 (75.0–87.0)	76.0 (70.0–82.0)	<0.0001
Sex %								
Female	58.6	52.8	62.4	66.0	69.3	69.2	53.6	<.0001
Race %								
Other	2.6	2.7	2.4	2.7	2.4	2.7	3.1	<.0001
Asian	1.8	2.0	1.6	1.6	1.8	2.2	2.4	
Hispanic	4.3	4.4	3.7	3.9	4.4	4.2	8.6	
Black	10.7	12.2	8.1	8.0	9.8	14.1	27.6	
White	80.3	78.4	83.9	83.6	81.3	76.5	58.1	
Arrival and Admission Information								
Arrival Mode %								
Unknown	1.5	1.6	1.4	1.4	1.3	1.4	1.6	<.0001
Private transport/taxi/other from home/scene	34.0	37.5	32.6	29.6	26.9	23.7	30.8	
EMS from home/scene	64.4	60.7	65.8	68.9	71.6	74.8	67.4	
Arrival during Off Hours (Regular hours: 7 AM – 6 PM, M–F)	42.7	42.0	43.0	44.0	43.3	41.2	41.0	<.0001

Variable	Overall (N=232236)	GFR≥60 (N=109913)	GFR 45–59 (N=61719)	GFR 30–44 (N=39201)	GFR 15–29 (N=13118)	GFR<15 (N=1700)	on Dialysis (N=6585)	P-value
Patient location when stroke symptoms first discovered%								
Not determined	0.5	0.5	0.6	0.6	0.6	0.4	0.6	<.0001
Outpatient healthcare setting	1.4	1.3	1.1	1.2	1.1	1.4	6.3	
Inpatient in hospital	2.7	2.3	2.4	2.9	4.3	6.7	5.4	
Chronic health care facility	11.0	8.9	11.9	13.2	16.5	18.2	12.2	
Not in a healthcare setting	84.2	86.8	83.8	81.8	77.2	73.0	75.2	
Symptom location occurring in Chronic Health Care Facility (Among Patients Discharged to SNF) %	25.1	23.4	25.8	26.3	28.4	28.2	27.5	<0.0001
Onset to arrival time Median (25th–75th P)	178.0 (66.0–545.0)	194.0 (69.0–586.0)	167.0 (64.0–510.0)	158.0 (62.0–484.0)	168.0 (66.0–520.0)	234.0 (70.0–604.0)	162.5 (61.0–488.0)	<.0001
Medical History%								
Atrial fibrillation / Flutter	24.8	21.7	27.8	28.2	27.9	22.1	22.8	<.0001
Prosthetic heart valve	1.4	1.3	1.4	1.6	1.8	1.4	1.8	<.0001
Previous stroke / TIA	27.9	26.1	28.5	30.3	30.1	27.6	32.5	<.0001
CAD/ prior MI	30.8	26.5	31.8	35.9	39.5	32.7	45.7	<.0001
Carotid stenosis	4.3	3.6	4.4	5.5	5.7	5.2	6.2	<.0001
Diabetes (combined)	30.3	27.2	27.8	33.9	39.8	38.6	60.1	<.0001

Variable	Overall (N=232236)	GFR≥60 (N=109913)	GFR 45–59 (N=61719)	GFR 30–44 (N=39201)	GFR 15–29 (N=13118)	GFR<15 (N=1700)	on Dialysis (N=6585)	P-value
PVD	5.6	4.4	5.4	6.6	8.7	6.3	13.0	<.0001
Hypertension	79.9	76.0	81.4	84.9	85.7	83.1	87.7	<.0001
Smoker	8.9	11.3	6.9	6.6	6.6	6.8	7.7	<.0001
Dyslipidemia	44.4	42.8	45.3	46.7	46.1	41.7	48.0	<.0001
Heart failure	11.2	7.5	11.4	15.6	20.7	17.1	24.3	<.0001
Medical History Panel missing	0.1	0.1	0.1	0.1	0.1	0.06	0.06	0.2972
Medications Prior to Admission %								
Antiplatelet or Anticoagulation medications	58.7	55.6	60.5	62.8	62.7	54.4	63.8	<.0001
Antihypertensives	77.4	71.2	79.7	85.4	88.2	81.9	87.0	
Cholesterol reducer	44.3	41.3	44.8	48.3	49.3	44.0	55.5	
Diabetic medication	24.2	21.8	22.3	27.6	32.3	29.4	45.6	
Labs/Vitals at Admission								
Glucose (mg/dL) Median (25^{th}–75^{th} P)	118.0 (101.0–149.0)	116.0 (100.0–144.0)	118.0 (101.0–147.0)	122.0 (103.0–156.0)	127.0 (105.0–165.0)	127.0 (104.0–163.0)	126.0 (101.0–172.0)	<.0001
Creatinine (mg/dL) Median (25^{th}–75^{th} 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 (1.9–2.5)	4.5 (3.6–6.7)	3.7 (2.2–5.6)	<.0001
INR* Median (25^{th}–75^{th} 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)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	<.0001

Variable	Overall (N=232236)	GFR≥60 (N=109913)	GFR 45–59 (N=61719)	GFR 30–44 (N=39201)	GFR 15–29 (N=13118)	GFR<15 (N=1700)	on Dialysis (N=6585)	P-value
Systolic blood pressure (mmHg) Median (25^{th}–75^{th} P)	155.0 (137.0–178.0)	157.0 (140.0–179.0)	156.0 (138.0–178.0)	153.0 (134.0–175.0)	148.0 (127.0–171.0)	145.0 (121.0–169.0)	151.5 (129.5–177.0)	<.0001
Diastolic blood pressure (mmHg) Median (25^{th}–75^{th} P)	79.0 (68.0–91.0)	81.0 (70.0–92.0)	79.0 (68.0–91.0)	77.0 (66.0–89.0)	73.0 (62.0–86.0)	72.0 (60.0–87.0)	73.0 (62.0–86.0)	<.0001
Heart rate (bpm) Median (25^{th}–75^{th} P)	77.0 (67.0–89.0)	78.0 (68.0–89.0)	77.0 (67.0–89.0)	77.0 (67.0–90.0)	77.0 (66.0–90.0)	79.0 (68.0–94.0)	78.0 (68.0–90.0)	<.0001
BMI (kg/m^2) Median (25^{th}–75^{th} P)	25.9 (22.7–29.7)	25.8 (22.7–29.7)	25.8 (22.6–29.5)	26.0 (22.8–30.0)	26.1 (22.7–30.2)	25.6 (22.1–29.8)	26.2 (22.8–30.5)	<.0001
NIHSS score Median (25^{th}–75^{th} P)	5.0 (2.0–12.0)	4.0 (2.0–10.0)	5.0 (2.0–12.0)	5.0 (2.0–13.0)	6.0 (2.0–15.0)	8.0 (3.0–17.0)	5.0 (2.0–12.0)	<.0001
Received IV tPA (Regardless of Contraindications or Warnings) %	7.7	7.6	8.3	7.6	7.0	5.6	6.4	<.0001
Received IV tPA (Excluding Contraindications and Warnings for Both 0–3 Hours and 3–4.5 Hours) %	10.0	9.7	10.8	10.0	9.1	6.9	8.3	<.0001
IV rt-PA Arrive by 2 Hour, Treat by 3 Hour %	78.1	78.8	78.9	76.9	74.6	79.7	71.3	0.0002
IV rt-PA Arrive by 3.5 Hour, Treat by 4.5 Hour %	53.1	53.3	54.3	51.6	53.0	50.9	46.3	0.0001
Door to IV tPA within	32.8	34.3	32.0	31.1	32.6	25.0	24.3	<0.0001

Variable	Overall (N=232236)	GFR≥60 (N=109913)	GFR 45–59 (N=61719)	GFR 30–44 (N=39201)	GFR 15–29 (N=13118)	GFR<15 (N=1700)	on Dialysis (N=6585)	P-value
60 minutes %								
Discharge Disposition								
% Home	38.6	42.8	37.3	33.6	27.5	23.5	36.5	<.0001
Hospice - Home	1.6	1.4	1.7	1.9	2.5	3.3	1.7	
Hospice - Health Care Facility	4.5	3.4	4.9	5.9	7.3	9.9	3.6	
Skilled Nursing Facility	24.0	21.4	25.4	27.0	29.7	29.1	25.0	
Inpatient rehab facility	23.1	24.5	22.7	21.8	19.5	15.7	21.3	
Long-term care facility	1.6	1.4	1.6	1.8	2.1	1.7	3.3	
Intermediate Care facility	0.1	0.1	0.2	0.2	0.2	0.1	0.1	
Other/Other Unspecified	0.4	0.4	0.5	0.4	0.4	0.5	0.3	
Expired	5.5	4.2	5.5	6.9	10.4	15.9	7.8	

* P: percentile

Percentages are based on non-missing data

Table 2

Association of eGFR level and in-hospital mortality or hospice for patients admitted with ischemic stroke-reference group is eGFR≥60 mL/min/1.73 m^2

CKD Group (ref=eGFR≥60)	Unadjusted Odds Ratio 95% CI	P-value	Global P	Adjusted Odds Ratio 95%CI	P-value	Global P
eGFR 45–59	1.38 (1.34–1.43)	<.0001	<.0001	1.06(1.01–1.10)	0.0162	<.0001
eGFR 30–44	1.74 (1.68–1.80)	<.0001		1.23(1.17–1.29)	<.0001	
eGFR 15–29	2.56(2.44–2.67)	<.0001		1.71(1.58–1.85)	<.0001	
eGFR<15	4.09(3.66–4.56)	<.0001		2.52(2.07–3.07)	<.0001	
Dialysis	1.54(1.43–1.67)	<.0001		1.56(1.39–1.76)	<.0001	

Table 3

Association of eGFR level and discharge home for patients admitted with ischemic stroke. Reference group is eGFR ≥60 mL/min/1.73 m^2

eGFR Group (ref=eGFR≥60)	Unadjusted Odds Ratio 95% CI	P-value	Global P	Adjusted Odds Ratio 95% CI	P-value	Global P
eGFR 45–59	0.80 (0.780.82)	<.0001	<.0001	1.04(1.01–1.07)	0.0065	<.0001
eGFR 30–44	0.68(0.66–0.70)	<.0001		0.98(0.94–1.01)	0.2302	
eGFR 15–29	0.51(0.49–0.53)	<.0001		0.82(0.78–0.87)	<.0001	
eGFR<15	0.42(0.37–0.47)	<.0001		0.72(0.61–0.86)	0.0002	
Dialysis	0.78(0.74–0.82)	<.0001		0.86(0.79–0.94)	0.0005	