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Patterns of Care Quality and Prognosis Among Hospitalized Ischemic Stroke Patients With Chronic Kidney Disease

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Background—Relatively little is known about the quality of care and outcomes for hospitalized ischemic stroke patients with chronic kidney disease (CKD). We examined quality of care and in-hospital prognoses among patients with CKD in the Get With The Guidelines—Stroke (GWTG-Stroke) program.

Methods and Results—We analyzed 679,827 patients hospitalized with ischemic stroke from 1564 US centers participating in the GWTG-Stroke program between January 2009 and December 2012. Use of 7 predefined ischemic stroke performance measures, composite “defect-free” care compliance, and in-hospital mortality were examined based on glomerular filtration rate (GFR) categorized as a dichotomous (+CKD as <60) or rank-ordered variable: normal (≥90), mild (60 to <90), moderate (30 to <60), severe (15 to <30), and kidney failure (<15 or dialysis). There were 236,662 (35%) ischemic stroke patients with CKD. Patients with severe renal dysfunction or failure were significantly less likely to receive guideline-based therapies. Compared with patients with normal kidney function (≥90), those with CKD (adjusted OR 0.91 [95% CI: 0.89 to 0.92]), moderate dysfunction (adjusted OR 0.94 [95% CI: 0.92 to 0.97]), severe dysfunction (adjusted OR 0.80 [95% CI: 0.77 to 0.84]), or failure (adjusted OR 0.72 [95% CI: 0.68 to 0.76]), were less likely to receive 100% defect-free care measure compliance. Inpatient mortality was higher for patients with CKD (adjusted odds ratio 1.44 [95% CI: 1.40 to 1.47]), and progressively rose with more severe renal dysfunction.

Conclusions—Despite higher in-hospital mortality rates, ischemic stroke patients with CKD, especially those with greater severity of renal dysfunction, were less likely to receive important guideline-recommended therapies. (J Am Heart Assoc. 2014;3:e000905 doi: 10.1161/JAHA.114.000905)

Key Words: chronic kidney disease • glomerular Filtration Rate • guidelines • ischemic stroke • outcomes • prognosis • quality indicators • renal

Chronic kidney disease (CKD) is a frequent comorbidity among patients with symptomatic cerebrovascular disease,1 which has been independently linked with poorer prognoses among stroke patients including greater short- and long-term risk of death.2–6 Because most patients with CKD die of vascular causes, not progression to end-stage renal disease, more precise quantification of the co-morbid presence and effects of CKD among patients hospitalized with acute vascular events may be insightful.1 Moreover, it is conceivable that optimal evidence-based treatment of hospitalized patients with both symptomatic vascular disease and CKD may improve clinical outcomes.1 Recognizing this, the American Heart Association issued an expert advisory recommending that healthcare providers aggressively manage their vascular disease patients with CKD in order to sever potential causal pathways between the kidney and the heart.7 However, little if anything is known about the quality of evidence-based care provided to hospitalized stroke patients with CKD, and whether such care may differ by level of kidney dysfunction.

The objective of this study was 3-fold: (1) properly quantify the prevalence of CKD among hospitalized ischemic stroke patients and its association with in-hospital outcomes; (2) compare the quality of stroke-related care (ie, interventions addressing the management of stroke) among ischemic stroke patients with and without CKD; (3) assess whether care quality and in-hospital outcomes vary among ischemic stroke patients by CKD stage.
Methods

Patient Population

We used data from the Get With The Guidelines-Stroke (GWTG-Stroke) program database. Details of the design and conduct of the program have been previously described. Briefly, the program is a voluntary, national, quality-improvement initiative sponsored by the American Heart Association and American Stroke Association, geared at fostering improved adherence to guideline-based care in patients hospitalized with stroke and TIA. Briefly, participating hospitals use an Internet-based Patient Management Tool (Outcome Sciences Inc, a Quintiles Company) to enter data, receive decision support, and obtain feedback through on-demand reports of performance on quality measures. GWTG-Stroke participating hospitals record data from consecutive stroke and TIA hospital admissions. Case ascertainment is done via clinical identification during the hospital encounter, retrospective surveillance of International Classification of Diseases, ninth Revision codes, or both. Trained hospital personnel extract data on demographics, medical history, neuroimaging, in-hospital treatment, and discharge characteristics. While the GWTG-Stroke program is overrepresented with larger academic teaching hospitals, the patient demographics and comorbidites are similar to those described in other stroke registries and administrative databases. Outcome Sciences serves as the data collection and coordination center for GWTG. The Duke Clinical Research Institute serves as the data analysis center and has an agreement to analyze the aggregate de-identified data for research purposes. Each participating hospital received either human research approval to enroll cases without individual patient consent under the common rule or a waiver of authorization and exemption from subsequent review by their Institutional Review Board.

Performance Measures

Seven performance measures, pre-selected by the GWTG-Stroke program as primary targets for stroke quality-improvement efforts based on prevailing expert consensus treatment guidelines, were used to compare the quality of stroke-related care between ischemic stroke admissions with and without CKD. Acute ischemic stroke performance measures were: (1) intravenous tissue plasminogen activator in patients who arrive <2 hours after symptom onset and with no contraindications to treatment; (2) antithrombotic medication (includes any aspirin, aspirin/dipyridamole, ticlopidine, clopidogrel, unfractionated heparin, low-molecular-weight heparin, and warfarin) administered within 48 hours of admission; and (3) deep vein thrombosis prophylaxis (includes heparins, heparinoids, other anticoagulants, or pneumatic compression devices) within 48 hours of admission in non-ambulatory patients. Discharge ischemic stroke performance measures were: (1) antithrombotic (includes any aspirin, aspirin/dipyridamole, ticlodipine, clopidogrel, unfractionated heparin, low-molecular-weight heparin, and warfarin) medication; (2) anti-coagulation (includes therapeutic doses of warfarin, heparinoid), or other anticoagulants such as direct thrombin inhibitors) for patients with a diagnosis of atrial fibrillation or flutter (paroxysmal, persistent, or permanent); (3) cholesterol treatment (includes statins, fibrates niacin, binding resins, or selective cholesterol absorption inhibitors) if low-density lipoprotein cholesterol (LDL-C) >100 mg/dL or if LDL-C is not documented; and (4) counseling or medication for smoking cessation for patients who are current smokers (any cigarettes in past year, “smoking cessation”). The GTWG-Stroke assessment tool allows clinicians to check a box indicating a contraindication to a given performance measure and in such cases, compliance with the performance measure is seen as being met. To summarize the overall quality of stroke-related care, we calculated a defect-free measure of care, which is a binary variable calculated as the proportion of patients who received all of the interventions for which they were eligible.

CKD Definitions

The serum creatinine level obtained at the time of hospital admission was used to determine the estimated glomerular filtration rate. Estimated glomerular filtration rate per the Modification of Diet in Renal Disease Study Group equation was calculated for each patient using the abbreviated Modification of Diet in Renal Disease formula: estimated GFR (mL/min per 1.73 m²)=186×[serum creatinine]−1.15×age−0.203×[0.742 if female]×[1.21 if black].11 CKD was defined as eGFR<60 mL/min per 1.73 m². GWTG-Stroke patients without CKD (controls) were the referent group for purposes of comparison. We then categorized patients by kidney function (GFR in mL/min per 1.73 m²) using modified definitions from the National Kidney Foundation—Kidney Disease Outcomes Quality Initiative clinical practice guidelines: normal (GFR>90), mild (60≤GFR<90), moderate (30≤GFR<60), severe (15≤GFR<30), and kidney failure (GFR<15).

Statistical Analysis

Patient demographic and clinical variables, hospital-level characteristics, and compliance with the individual and summary quality-of-care measures were compared between patients with and without CKD. Percentages and means±SD were reported for categorical and continuous variables, respectively. Pearson χ² test and Wilcoxon rank-sum tests
were used to compare the categorical and continuous variables, respectively, between patients with and without CKD. To compare variables among CKD stages we used Pearson χ² test and Kruskal Wallis tests, respectively. The relationship between CKD status (yes versus no) and different levels of renal function versus compliance with individual performance measures, as well as the defect-free summary measure of care were further examined using multivariable logistic regression models. To account for within-hospital clustering, generalized estimating equations were used to generate unadjusted and adjusted models. Confidence intervals and P values were computed using Wald tests. The adjusted models included the following pre-specified potential confounders: age, sex, race, medical history (including atrial fibrillation, prosthetic heart valve, previous stroke/TIA, coronary heart disease, or previous myocardial infarction [coronary artery disease/previous MI], carotid stenosis, peripheral vascular disease, hypertension, diabetes, dyslipidemia, heart failure, and current smoking), systolic blood pressure (SBP) at admission, hospital size, region, teaching status, primary stroke center status and the number of annual stroke discharges from each hospital. Missing values for medical history (0.22%) were imputed to no history and for SBP (2.62%) to the median value. Patients with missing information in 1 or more hospitals characteristics were excluded from the models (less than 0.25%).

Similar multivariable logistic regression analyses were performed to explore the relationship between CKD status and 2 other binary outcome measures (ie, in-hospital mortality and discharge status [home versus other]). We included the same set of pre-specified potential confounders in all 3 of these outcomes-based models, and we chose not to adjust for differences in performance measures because of the inherent problem of confounding by indication (ie, the tendency for patients with inherently poorer prognosis to receive less care). Only eligible patients for each outcome with complete data are included in each model. We also conducted sensitivity analyses by generating models that included all of the aforementioned variables and the measure of stroke severity (NIH Stroke Scale Score) in the subgroup of patients in which this measure of stroke severity was documented (NIHSS missing in 36.1% of study population). NIHSS was analyzed as a continuous variable. All tests are 2-tailed with \( P<0.05 \) considered as the level of statistical significance. All statistical analyses were performed using SAS software (version X SAS Institute Inc).

**Results**

Of 858 124 ischemic stroke admissions at 1624 hospitals during the study period, after excluding patients with serum creatinine values missing (n=151 634), reported serum creatinine value out of range (ie, 0 or >20 mg/dL, n=2195), sex or race variable missing (n=979), and patient transferred out/left against medical advice/discharge status missing/ (n=23 489), there were 679 827 ischemic stroke admissions. An analysis of just those patients with serum creatinine values available versus missing revealed generally similar demographic and clinical characteristics, and where differences existed they were small and unlikely to be of major relevance (Table 1).

Among these ischemic stroke admissions (n=679 827), over one-third (34.8%; n=236 662) met the definition of CKD. Patients with CKD were older (mean, 76.2 versus 68 years), more likely to be female or white, and more likely to have a medical history of stroke/TIA, carotid stenosis, coronary artery disease/previous MI, hypertension, dyslipidemia, diabetes, atrial fibrillation/flutter, peripheral arterial disease, and heart failure, but they were less likely to be current smokers. Patients with CKD had more severe strokes (mean NIH stroke scale score 8.0 versus 6.7). Table 2 compares the demographic and clinical characteristics of ischemic stroke patients by presence of CKD and stage of kidney dysfunction. Compared with patients with earlier stages of kidney dysfunction (mild or moderate), those with more advanced stages of dysfunction (severe or failure) were older, more likely to be of black race, and much more likely to have a medical history of diabetes, peripheral arterial disease, and heart failure, but less likely to be of independent ambulatory status prior to admission. Patients with more advanced stages of kidney dysfunction (versus earlier stages) were more likely to present with altered level of consciousness or lower admission systolic blood pressure levels, but less likely to have strokes of mild severity.

There were significantly higher rates of compliance with all 7 performance measures and defect-free care among those without CKD compared with those with CKD. However, for some of the measures these differences were numerically rather modest. In-hospital outcomes were much worse for those with CKD versus without CKD across all 3 endpoints studied including in-hospital case fatality (Table 3). Table 4 shows a comparison of frequencies among ischemic stroke patients with various stages of kidney dysfunction. Significantly lower rates of compliance were observed with all 7 performance measures and defect-free care among those patients with more advanced stages of kidney dysfunction (versus earlier stages), but these differences were numerically very modest with the exception of patients presenting within 2 hours of ictus receiving IV tPA, for which there was a lower compliance rate ranging from 4 to 10 percentage points in those in advanced versus earlier stages of dysfunction (Table 4). In-hospital outcomes were much worse for advanced versus earlier stages of renal dysfunction including in-hospital case fatality (Table 4).
Table 5 displays unadjusted and adjusted odds ratios comparing ischemic stroke patients with various stages of kidney disease to those with normal renal function for the pre-specified stroke hospitalization performance measures and the summary defect-free care measure. Compared with patients with normal kidney function, those with CKD were significantly less likely to receive smoking cessation counseling at discharge (adjusted OR 0.86, 95% CI: 0.80 to 0.93), antithrombotic prescribed within 48 hours of admission (adjusted OR 0.82, 95% CI: 0.79 to 0.85), antithrombotic at discharge (adjusted OR 0.87, 95% CI: 0.83 to 0.91), anticoagulation at discharge if there was a diagnosis of atrial fibrillation or atrial flutter (adjusted OR 0.90, 95% CI: 0.85 to 0.95), lipid modifier at discharge (adjusted OR 0.96, 95% CI: 0.93 to 0.99), and defect-free care (adjusted OR 0.91, 95% CI: 0.89 to 0.92).

Analysis by stage of kidney dysfunction (Table 5), shows that compared with patients with normal kidney function, for patients presenting within 2 hours of stroke onset who received IV tPA or for lipid modifier medication prescribed at discharge, those with severe dysfunction or renal failure versus normal kidney function were less likely to be in...
### Table 2. Baseline Patient Characteristics by Chronic Kidney Disease Stage

| Variable Description | No CKD (GFR≥90) (N=163,772) | Mild CKD (60≤GFR<90) (N=279,393) | Moderate CKD (30≤GFR<60) (N=194,030) | Severe CKD (15≤GFR<30) (N=285,83) | Renal Failure (GFR<15) (N=14,049) | P Value
|----------------------|-----------------------------|----------------------------------|--------------------------------------|---------------------------------|---------------------------------|--------|
| **Demographics**     |                             |                                  |                                      |                                 |                                 |        |
| Age (18 to 110), y   | Mean 62.21 (14.9)           | 71.39 (13.8)                     | 76.81 (12.1)                         | 75.64 (13.3)                    | 68.10 (13.6)                    | <0.0001|
| Sex                  | Female 70,029 (42.76)       | 11,8221 (60.93)                  | 17,898 (62.62)                       | 8152 (58.03)                    |                                 |        |
| Ethnicity/race       | White 10,1145 (61.76)       | 18,431 (76.50)                   | 20,043 (70.12)                       | 7295 (51.93)                    |                                 | <0.0001|
|                      | Black 38,863 (23.73)        | 23,851 (12.29)                   | 5004 (17.51)                         | 4398 (31.30)                    |                                 |        |
|                      | Hispanic 13,043 (7.96)      | 11,041 (5.69)                    | 1958 (6.85)                          | 1416 (10.08)                    |                                 |        |
| **Arrival**          | EMS arrival EMS from home/scene 69,622 42.51 | 13,7306 (49.14) | 11,0803 (57.11) | 17,460 (61.09) | 7971 (56.74) | <0.0001 |
|                      | Last known well to arrival, minutes Mean 603.01 (988) | 510.11 (880.1) | 469.08 (836.8) | 498.07 (900.5) | 570.06 (956.9) | <0.0001 |
| **Past medical history** |                             |                                  |                                      |                                 |                                 |        |
| Atrial fib/flutter    | Yes 17,083 (10.46)          | 46,136 (23.83)                   | 6314 (22.12)                         | 2231 (15.91)                    |                                 | <0.0001|
| CAD/prior MI          | Yes 29,045 (17.78)          | 62,387 (32.22)                   | 10,698 (37.48)                       | 5040 (35.93)                    |                                 | <0.0001|
| Carotid stenosis      | Yes 42,14 (2.58)            | 9911 (5.12)                      | 1611 (5.64)                          | 607 (4.33)                      |                                 | <0.0001|
| Diabetes mellitus     | Yes 49,130 (30.08)          | 69,824 (36.06)                   | 14,195 (49.74)                       | 8249 (58.81)                    |                                 | <0.0001|
| Dyslipidemia          | Yes 58,684 (35.93)          | 91,530 (47.27)                   | 13,576 (47.57)                       | 6106 (43.53)                    |                                 | <0.0001|
| Hypertension          | Yes 109,599 (67.10)         | 162,084 (83.72)                  | 24,782 (86.83)                       | 12,126 (86.45)                  |                                 | <0.0001|
| Prosthetic heart valve| Yes 1,599 (0.96)            | 3,119 (1.61)                     | 452 (1.58)                           | 202 (1.44)                      |                                 | <0.0001|
| PVD                   | Yes 5,165 (3.16)            | 11,951 (5.99)                    | 2539 (8.90)                          | 1,483 (10.29)                   |                                 | <0.0001|
| Heart failure         | Yes 7,210 (4.41)            | 24,612 (12.71)                   | 5583 (19.56)                         | 2589 (18.46)                    |                                 | <0.0001|
| Smoker                | Yes 48,775 (29.86)          | 48,747 (17.49)                   | 3199 (11.21)                         | 1788 (12.75)                    |                                 | <0.0001|
| Previous stroke/TIA   | Yes 42,403 (25.96)          | 68,990 (35.63)                   | 10,848 (38.01)                       | 5140 (36.65)                    |                                 | <0.0001|
| **Premorbid medications** |                             |                                  |                                      |                                 |                                 |        |
| Anticoagulants        | Yes 13,432 (8.20)           | 26,062 (13.43)                   | 3695 (12.93)                         | 1643 (11.69)                    |                                 | <0.0001|
| Antiplatelets         | Yes 59,729 (36.47)          | 101,163 (52.14)                  | 15,393 (53.85)                       | 7303 (51.98)                    |                                 | <0.0001|
| Anti-Hypertensives    | Yes 91,530 (55.89)          | 158,375 (81.62)                  | 24,864 (86.99)                       | 11,746 (83.61)                  |                                 | <0.0001|
| Antilipemics          | Yes 53,597 (32.73)          | 94,150 (48.52)                   | 14,793 (51.75)                       | 7098 (50.52)                    |                                 | <0.0001|
| Anti-diabetics        | Yes 38,011 (23.21)          | 56,663 (29.20)                   | 11,321 (39.61)                       | 6168 (43.90)                    |                                 | <0.0001|

Continued
Table 2. Continued

| Variable                          | Description | No CKD (GFR≥90) (N=163 772) | Mild CKD (60≤GFR<90) (N=279 393) | Moderate CKD (30≤GFR<60) (N=194 030) | Severe CKD (15≤GFR<30) (N=285 83) | Renal Failure (GFR<15) (N=14 049) | P Value    |
|-----------------------------------|-------------|-----------------------------|----------------------------------|--------------------------------------|----------------------------------|-----------------------------------|------------|
| **Pre-morbid status**             |             |                             |                                  |                                      |                                  |                                    |            |
| Ambulation                        | Independent | 136 608 83.41               | 229 396 82.11                   | 150 581 77.61                       | 20 245 70.83                     | 9764 69.50                         | <0.0001    |
| **Symptom type and severity**     |             |                             |                                  |                                      |                                  |                                    |            |
| Altered Consciousness             | Yes         | 24 012 14.66                | 47 998 17.18                    | 42 633 21.97                        | 7913 27.68                       | 3879 27.61                         | <0.0001    |
| NIHSS levels                      | 0-9         | 80 491 49.15                | 134 831 48.26                  | 85 084 43.85                        | 11 028 38.58                     | 5299 37.72                         | <0.0001    |
| **Admission care process**        |             |                             |                                  |                                      |                                  |                                    |            |
| Door to CT≤25 minutes              | Yes         | 26 861 16.40                | 54 149 19.38                   | 39 757 20.49                        | 5225 18.28                       | 2027 14.43                         | <0.0001    |
| **Admission biomarkers**          |             |                             |                                  |                                      |                                  |                                    |            |
| Body mass index, kg/m²             | Mean        | 28.47 (7.8)                 | 28.04 (7.2)                    | 27.89 (7.2)                         | 28.08 (7.6)                      | 28.13 (8.0)                        |            |
| Systolic blood pressure (50 to 250 mm Hg) | Mean      | 156.05 (29.2)               | 158.36 (29.3)                  | 156.45 (30.9)                       | 151.17 (34.2)                    | 151.66 (35.4)                      | <0.0001    |
| Serum Creatinine (0 to 20 mg/dL)   | Mean        | 0.72 (0.2)                  | 0.96 (0.2)                     | 1.38 (0.3)                         | 2.56 (0.6)                       | 6.55 (2.7)                         |            |
| **Hospital characteristics**       |             |                             |                                  |                                      |                                  |                                    |            |
| Number of beds                    | Mean        | 471.47 (309.4)              | 439.62 (297.0)                 | 423.15 (290.2)                      | 428.58 (296)                     | 452.77 (296.1)                     | <0.0001    |
| Region                            |             |                             |                                  |                                      |                                  |                                    |            |
| West                              | Mean        | 17.02 48 663                | 17.42 32 257                   | 16.62 4541                         | 15.89 2444                       | 17.40 2444                         | <0.0001    |
| South                             | Mean        | 36.45 99 676                | 35.68 70 335                   | 36.25 10 764                        | 37.66 5618                       | 39.99 5618                         |            |
| Midwest                           | Mean        | 20.20 56 647                | 20.28 40 035                   | 20.63 5849                         | 20.46 2736                       | 19.47 2736                         |            |
| Northeast                         | Mean        | 26.33 74 407                | 26.63 51 403                   | 26.49 7429                         | 25.99 3251                       | 23.14 3251                         |            |
| Hospital type                     |             |                             |                                  |                                      |                                  |                                    |            |
| Academic                          | Mean        | 107 151 65.43               | 65 986 59.14                   | 65 986 56.20                        | 65 986 56.88                     | 60.13 8448                          | <0.0001    |
| Rural location                    | Yes         | 6041 3.69                   | 11 169 4.00                    | 8592 4.43                         | 1316 4.60                        | 475 3.38                           | <0.0001    |
| Avg. annual ischemic stroke cases | Mean        | 240.20 (146.3)              | 229.79 (141.1)                 | 223.38 (139.4)                     | 223.40 (140.7)                   | 230.76 (141.7)                     |            |

CAD indicates coronary artery disease; CKD, chronic kidney disease; CT, computed tomography; GFR, glomerular filtration rate; MI, myocardial infarction; PVD, peripheral vascular disease; TIA, transient ischemic attack.
### Table 3. Frequencies Comparing Ischemic Stroke Patients With Chronic Kidney Disease (CKD) to Those Without CKD for 7 Performance Measures, a Summary Defect-Free Care Measure, and In-Hospital Outcomes

| Variable | Overall (N=679 827) | No CKD (GFR≥60) (N=443 165) | CKD (GFR<60) (N=236 662) | P Value |
|----------|----------------------|-----------------------------|--------------------------|---------|
| Performance measures | n, % | n, % | n, % | |
| Patients presenting within 2 hours of ictus receive IV tPA | 35 330, 78.03 | 23 039, 78.55 | 12 291, 77.08 | 0.0003 |
| Antithrombotic prescribed within 48 hours of admission | 414 672, 96.85 | 263 202, 97.12 | 151 470, 96.39 | <0.0001 |
| Deep venous thrombosis prophylaxis | 322 251, 97.50 | 211 230, 97.59 | 111 021, 97.34 | <0.0001 |
| Antithrombotic prescribed at discharge | 583 330, 98.60 | 390 884, 98.66 | 192 446, 98.49 | <0.0001 |
| Anticoagulation prescribed at discharge for AF patients | 86 199, 94.61 | 51 070, 95.05 | 35 129, 93.98 | <0.0001 |
| Smoking cessation intervention provided at discharge | 112 020, 97.12 | 88 739, 97.32 | 23 281, 96.35 | <0.0001 |
| Lipid-lowering agent prescribed at discharge | 315 999, 94.40 | 209 787, 94.60 | 106 212, 94.02 | <0.0001 |
| Composite measure | Defect-free: compliance 100% | 590 005, 90.81 | 390 431, 91.27 | 199 574, 89.93 | <0.0001 |
| In-hospital outcomes | | | | |
| In-hospital case fatality | 32 290, 4.75 | 16 786, 3.79 | 15 504, 6.55 | <0.0001 |
| In-hospital case fatality or discharged to hospice | 61 687, 9.07 | 31 580, 7.13 | 30 107, 12.72 | <0.0001 |
| Discharge destination other than directly home | 314 765, 8.61 | 190 252, 44.62 | 124 513, 56.30 | <0.0001 |

AF indicates atrial fibrillation; GFR, glomerular filtration rate.

### Table 4. Frequencies Comparing Ischemic Stroke Patients With Various Categories of Chronic Kidney Disease (CKD) to Those Without CKD for 7 Performance Measures, a Summary Defect-Free Care Measure, and In-Hospital Outcomes

| Variable | No CKD (GFR≥90) (N=163 772) | Mild CKD (60≤GFR<90) (N=279 393) | Moderate CKD (30≤GFR<60) (N=194 030) | Severe CKD (15≤GFR<30) (N=28 583) | Renal Failure (GFR<15) (N=14 049) | P Value |
|----------|-----------------------------|----------------------------------|--------------------------------------|----------------------------------|---------------------------------|---------|
| Performance measures | n, % | n, % | n, % | n, % | n, % | |
| Patients presenting within 2 hours of ictus receive IV tPA | 7480, 78.21 | 15 559, 78.72 | 10 678, 77.98 | 1185, 73.06 | 428, 67.94 | 0.0002 |
| Antithrombotic prescribed within 48 hours of admission | 96 901, 96.97 | 166 301, 97.21 | 122 656, 96.75 | 19 097, 95.22 | 9717, 94.21 | <0.0001 |
| Deep venous thrombosis prophylaxis | 80 105, 97.62 | 131 125, 97.57 | 91 000, 97.40 | 13 375, 97.17 | 6646, 96.82 | <0.0001 |
| Antithrombotic prescribed at discharge | 146 502, 94.74 | 244 382, 98.73 | 159 897, 98.62 | 21 645, 97.92 | 10 904, 97.78 | 0.0004 |
| Anticoagulation prescribed at discharge for AF patients | 13 457, 94.78 | 37 613, 95.15 | 30 423, 94.36 | 3432, 91.74 | 1274, 91.20 | <0.0001 |
| Smoking cessation intervention provided at discharge | 44 581, 97.47 | 44 158, 97.17 | 19 178, 96.53 | 2629, 95.81 | 1474, 95.04 | <0.0001 |
| Lipid-lowering agent prescribed at discharge | 76 542, 94.74 | 133 245, 94.51 | 88 724, 94.11 | 11 998, 93.57 | 5490, 93.51 | <0.0001 |
| Composite measure | Defect-free: compliance 100% | 145 339, 91.37 | 245 092, 91.21 | 164 938, 90.31 | 23 136, 88.42 | 11 500, 87.61 | <0.0001 |
| In-hospital outcomes | | | | | | |
| In-hospital case fatality | 5551, 3.39 | 11 235, 4.02 | 11 451, 5.90 | 2775, 9.71 | 1278, 9.10 | <0.0001 |
| In-hospital case fatality or discharged to hospice | 9842, 6.01 | 21 738, 7.78 | 23 035, 11.87 | 4950, 17.32 | 2122, 15.10 | <0.0001 |
| Discharge destination other than directly home | 65 560, 41.44 | 12 4692, 46.50 | 101 764, 55.74 | 15 811, 61.26 | 6938, 54.33 | <0.0001 |

AF indicates atrial fibrillation; GFR, glomerular filtration rate.
Table 5. Unadjusted and Adjusted Odds Ratios Comparing Ischemic Stroke Patients With Various Stages of Kidney Dysfunction to Those With Normal Kidney Function for 7 Performance Measures and a Summary Defect-Free Care Measure

| Process Measures                                      | Category of CKD                            | Unadjusted OR (95% CI)* | P Value | Adjusted OR (95% CI)* | P Value |
|--------------------------------------------------------|--------------------------------------------|-------------------------|---------|-----------------------|---------|
| Patients presenting within 2 hours of ictus            |                                            |                         |         |                       |         |
| receive IV tPA                                          |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 1.04 (1.00 to 1.08)     | 0.0571  | 1.06 (1.00 to 1.12)   | 0.0585  |
| Moderate kidney dysfunction (GFR ≥30 to <60)           |                                            | 1.02 (0.97 to 1.07)     | 0.4550  | 1.04 (0.97 to 1.11)   | 0.3105  |
| Severe kidney dysfunction (GFR ≥15 to <30)             |                                            | 0.86 (0.79 to 0.93)     | 0.0004  | 0.85 (0.76 to 0.96)   | 0.0088  |
| Renal failure (GFR<15)                                  |                                            | 0.74 (0.65 to 0.84)     | <0.0001 | 0.72 (0.61 to 0.85)   | 0.0001  |
| Deep venous thrombosis prophylaxis                      |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 1.00 (0.95 to 1.05)     | 0.9602  | 1.02 (0.96 to 1.07)   | 0.6040  |
| Moderate kidney dysfunction (GFR ≥30 to <60)           |                                            | 0.95 (0.90 to 1.00)     | 0.0480  | 0.98 (0.93 to 1.05)   | 0.6012  |
| Severe kidney dysfunction (GFR ≥15 to <30)             |                                            | 0.89 (0.80 to 0.98)     | 0.0146  | 0.94 (0.84 to 1.05)   | 0.2477  |
| Renal failure (GFR<15)                                  |                                            | 0.79 (0.70 to 0.90)     | 0.0003  | 0.83 (0.72 to 0.95)   | 0.0068  |
| Smoking cessation intervention provided at discharge    |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 0.89 (0.85 to 0.94)     | <0.0001 | 0.95 (0.88 to 1.02)   | 0.1604  |
| Moderate kidney dysfunction (GFR ≥30 to <60)           |                                            | 0.76 (0.71 to 0.81)     | <0.0001 | 0.87 (0.80 to 0.96)   | 0.0034  |
| Severe kidney dysfunction (GFR ≥15 to <30)             |                                            | 0.66 (0.58 to 0.74)     | <0.0001 | 0.76 (0.65 to 0.89)   | 0.0009  |
| Renal failure (GFR<15)                                  |                                            | 0.59 (0.48 to 0.71)     | <0.0001 | 0.62 (0.48 to 0.78)   | 0.0001  |
| Antithrombotic prescribed within 48 hours of admission |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 1.05 (1.01 to 1.10)     | 0.0075  | 1.08 (1.03 to 1.13)   | 0.0011  |
| Moderate kidney dysfunction (GFR ≥30 to <60)           |                                            | 0.91 (0.88 to 0.95)     | <0.0001 | 0.96 (0.91 to 1.01)   | 0.1164  |
| Severe kidney dysfunction (GFR ≥15 to <30)             |                                            | 0.64 (0.60 to 0.69)     | <0.0001 | 0.67 (0.62 to 0.73)   | <0.0001 |
| Renal failure (GFR<15)                                  |                                            | 0.54 (0.49 to 0.58)     | <0.0001 | 0.54 (0.49 to 0.59)   | <0.0001 |
| Antithrombotic prescribed at discharge                  |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 1.12 (1.07 to 1.17)     | <0.0001 | 1.08 (1.01 to 1.14)   | 0.0055  |
| Moderate kidney dysfunction (GFR ≥30 to <60)           |                                            | 1.06 (1.01 to 1.11)     | 0.0122  | 0.98 (0.92 to 1.05)   | 0.5877  |
| Severe kidney dysfunction (GFR ≥15 to <30)             |                                            | 0.76 (0.70 to 0.82)     | <0.0001 | 0.68 (0.61 to 0.76)   | <0.0001 |
| Renal failure (GFR<15)                                  |                                            | 0.72 (0.65 to 0.81)     | <0.0001 | 0.68 (0.59 to 0.78)   | <0.0001 |
| Antithrombotic prescribed at discharge for AF patients |                                            |                         |         |                       |         |
| Mild kidney dysfunction (GFR <60 to <90)                |                                            | 0.85 (0.81 to 0.89)     | <0.0001 | 0.90 (0.85 to 0.95)   | 0.0001  |
compliance; for antithrombotic agents prescribed within 48 hours of admission or at discharge, as well as anticoagulation prescribed at discharge in patients with atrial fibrillation or atrial flutter, those with severe dysfunction and renal failure were less likely to be in compliance, but those with mild dysfunction were more likely to be in compliance; and for defect-free care, those with moderate dysfunction, severe dysfunction, and renal failure were less likely to be in compliance.

Table 6 shows unadjusted and adjusted odds ratios comparing ischemic stroke patients with various stages of kidney dysfunction to those with normal function for the 3 outcome measures. In-hospital case fatality was higher for patients with CKD versus no CKD (adjusted OR 1.44, 95% CI: 1.40 to 1.47), and progressively rose with more severe renal dysfunction to the extent that patients with renal failure had well over twice the odds of dying in the hospital compared to those without CKD (adjusted OR 2.39, 95% CI: 2.22 to 2.57). Presence of CKD (versus no CKD) was also associated with poorer outcomes with regard to the endpoints of in-hospital case fatality or discharged to hospice (adjusted OR 1.31, 95% CI: 1.28 to 1.33) and discharge destination other than directly home (adjusted OR 1.06, 95% CI: 1.04 to 1.07). However, analyses by stage of renal dysfunction showed that patients with earlier stages of dysfunction had better outcomes than those with normal function: patients with mild dysfunction had lower odds of experiencing in-hospital case fatality or being discharged to hospice (adjusted OR 0.88, 95% CI: 0.85 to 0.91), and those with mild dysfunction (adjusted OR 0.81, 95% CI: 0.80 to 0.83) or moderate dysfunction (adjusted OR 0.88, 95% CI: 0.86 to 0.90) had lower odds of discharge destination other than home. The more advanced stages of renal dysfunction (severe and failure) were both associated with higher odds of experiencing in-hospital case fatality/
being discharged to hospice and a discharge destination other than home (Table 6). Regression models that included the measure of stroke severity (NIH Stroke Scale Score) showed a similar pattern of results (not shown).

**Discussion**

In this large, contemporary nationwide study, we observed that 1 of every 3 hospitalized ischemic stroke patients had CKD, that the odds of dying in the hospital after adjusting for major confounders was 44% higher for those patients with CKD compared with those without CKD, and the independent relation of kidney dysfunction with in-hospital mortality rose progressively with worsening renal dysfunction. These results, based on >600,000 ischemic stroke admissions at >1500 hospitals, definitively confirm data from previously published analyses of small single-center studies that showed a high prevalence of CKD linked to poorer outcomes among hospitalized ischemic stroke patients. In addition, our study is the first as far as we are aware to evaluate the quality of stroke-related care among hospitalized ischemic stroke patients by CKD presence and stage of kidney dysfunction, finding that patients with evidence of renal dysfunction are significantly less likely to receive several effective therapies, which are currently included in ischemic stroke hospitalization performance and quality measures. This latter finding is in accord with studies among patients hospitalized with acute cardiovascular conditions that revealed greater underuse of medications for vascular risk reduction as kidney function declines.13–15

Table 6. Unadjusted and Adjusted Odds Ratios Comparing Ischemic Stroke Patients With Various Stages of Kidney Dysfunction to Those With Normal Kidney Function for 3 Outcome Measures

| Outcome Measures                              | Category of CKD                              | Unadjusted OR (95% CI)* | P Value | Adjusted OR (95% CI)* | P Value |
|-----------------------------------------------|----------------------------------------------|-------------------------|---------|-----------------------|---------|
| In-hospital case fatality                     | CKD (GFR<60)                                 | 1.90 (1.85 to 1.95)     | <0.0001 | 1.44 (1.40 to 1.47)   | <0.0001 |
| In-hospital case fatality                     | Mild kidney dysfunction (GFR ≥60 to <90)     | 1.28 (1.23 to 1.33)     | <0.0001 | 0.99 (0.95 to 1.03)   | 0.5626  |
| In-hospital case fatality                     | Moderate kidney dysfunction (GFR ≥30 to <60) | 1.99 (1.91 to 2.08)     | <0.0001 | 1.27 (1.22 to 1.32)   | <0.0001 |
| In-hospital case fatality                     | Severe kidney dysfunction (GFR ≥15 to <30)   | 3.45 (3.27 to 3.65)     | <0.0001 | 2.14 (2.03 to 2.26)   | <0.0001 |
| In-hospital case fatality                     | Renal failure (GFR<15)                       | 3.16 (2.94 to 3.41)     | <0.0001 | 2.39 (2.22 to 2.57)   | <0.0001 |
| In-hospital case fatality or discharged to hospice | CKD (GFR<60)                                 | 1.94 (1.91 to 1.98)     | <0.0001 | 1.31 (1.28 to 1.33)   | <0.0001 |
| In-hospital case fatality or discharged to hospice | Mild kidney dysfunction (GFR ≥60 to <90)     | 1.35 (1.31 to 1.38)     | <0.0001 | 0.88 (0.85 to 0.91)   | <0.0001 |
| In-hospital case fatality or discharged to hospice | Moderate kidney dysfunction (GFR ≥30 to <60) | 2.19 (2.12 to 2.25)     | <0.0001 | 1.07 (1.04 to 1.11)   | <0.0001 |
| In-hospital case fatality or discharged to hospice | Severe kidney dysfunction (GFR ≥15 to <30)   | 3.43 (3.30 to 3.56)     | <0.0001 | 1.70 (1.63 to 1.78)   | <0.0001 |
| In-hospital case fatality or discharged to hospice | Renal failure (GFR<15)                       | 2.91 (2.75 to 3.09)     | <0.0001 | 2.09 (1.96 to 2.23)   | <0.0001 |
| Discharge destination other than directly home | CKD (GFR<60)                                 | 1.60 (1.58 to 1.62)     | <0.0001 | 1.06 (1.04 to 1.07)   | <0.0001 |
| Discharge destination other than directly home | Mild kidney dysfunction (GFR ≥60 to <90)     | 1.23 (1.21 to 1.25)     | <0.0001 | 0.81 (0.80 to 0.83)   | <0.0001 |
| Discharge destination other than directly home | Moderate kidney dysfunction (GFR ≥30 to <60) | 1.78 (1.74 to 1.82)     | <0.0001 | 0.88 (0.86 to 0.90)   | <0.0001 |
| Discharge destination other than directly home | Severe kidney dysfunction (GFR ≥15 to <30)   | 2.24 (2.17 to 2.31)     | <0.0001 | 1.10 (1.07 to 1.14)   | <0.0001 |
| Discharge destination other than directly home | Renal failure (GFR<15)                       | 1.68 (1.61 to 1.75)     | <0.0001 | 1.11 (1.06 to 1.16)   | <0.0001 |

CAD indicates coronary artery disease; CKD, chronic kidney disease; GFR, glomerular filtration rate; LDL, low-density lipoprotein; MI, myocardial infarction.

*Compared to normal defined as a glomerular filtration rate ≥90. All models are adjusted for age, race, gender, medical history (atrial fibrillation, prosthetic heart valve, previous stroke/TIA, CAD/previous MI, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, heart failure, and current smoking), systolic blood pressure (SBP) at admission, hospital size, region, teaching status, and the number of annual stroke discharges from each hospital.
A major strength of our study was the ability to also examine the relationships of specific stages of kidney dysfunction to various stroke hospitalization performance measures and in-hospital outcome types. For instance, while the overriding message from our results is that presence of CKD is associated with lesser compliance with benchmarks of stroke care and poorer outcomes, these results were primarily driven by the more advanced stages of dysfunction, ie, severe and failure. Indeed, hospitalized ischemic stroke patients with mild dysfunction actually had similar or better in-hospital outcomes when compared with those patients with normal function. On the surface, this may seem counterintuitive since proposed explanations for why vascular disease patients with CKD may have poorer clinical outcomes than those without CKD, is the frequent co-presence in the former patient group of deleterious conditions like anemia, oxidative stress, electrolyte imbalances, hyperhomocysteinemia, and chronic inflammation. However, in our study we observed that patients with mild dysfunction versus normal function were significantly more likely to receive an antithrombotic prescription within 48 hours of admission, be discharged on an antithrombotic, receive anticoagulation at discharge if they had a diagnosis of atrial fibrillation or flutter; showed a strong trend towards being more likely to receive intravenous thrombolysis; showed a non-significant pattern of being more likely to receive a lipid-lowering agent at discharge; and were no less likely to receive smoking cessation counseling at discharge, deep venous thrombosis prophylaxis, or overall stroke hospitalization defect-free care. Although given the nature of our study, we could not establish causality, it is not inconceivable that better in-hospital care and perhaps significantly higher frequency of pre-morbid cardiovascular medications in patients with mild CKD versus normal function may have led to similar or better outcomes among the former patient group.

Underutilization of evidence-based treatments has similarly been seen in other patient subgroups with chronic conditions that place them at high vascular risk such as diabetes mellitus and peripheral artery disease. While the specific reasons for why there is an underuse of evidence-based therapies among hospitalized ischemic patients with CKD are not exactly known, it stands to reason that potential contributors to this evidence-practice treatment gap may include the facts that the randomized trial evidence upon which several expert-consensus recommendations for stroke treatment are based typically excluded patients with major renal dysfunction, patients with CKD are generally more likely to experience adverse effects of many medications, given the effect of renal azotemia on platelet function patients with kidney disease are at an increased risk for bleeding and questionable therapeutic efficacy. All of the aforementioned factors may be leading clinicians caring for hospitalized ischemic stroke patients to be more cautious about prescribing these therapies, despite the greater risk for cardiovascular events and poor clinical outcomes in these patients. However, emerging evidence suggests that the benefits of many secondary prevention drugs used in the treatment of known vascular disease may be of equal or greater benefit to those with renal dysfunction when compared with those without, and a published analysis of the GWTG-Stroke dataset that looked at predictors of tPA-related sICH did not find any association between serum creatinine levels and risk for tPA-related sICH.

This study has limitations. First, data were derived from the medical record and depended on the accuracy and completeness of clinical documentation (eg, it is conceivable that some patients reported to be eligible for treatment were not treated due to contraindications or intolerance that was not documented; or very ill patients with advanced CKD in the process of being discharged to hospice for terminal care were not candidates for certain treatments). Second, although hospitals are instructed to include all consecutive admissions or to take a random sample, these processes are not audited so the potential for selection bias exists. Third, while we controlled for known confounders, unmeasured confounding could have affected our results. Fourth, our findings may not necessarily apply to hospitals that differ in patient characteristics or care patterns from GWTG-Stroke hospitals. Fifth, we only examined in-hospital outcomes, therefore, the longer-term impact of CKD or of the differences in quality of care identified in this study on stroke-related outcomes were not determined. Next, although the MDRD formula is the preferred method for estimating renal function, it generally should be applied when renal function is stable, and this may not be the case for many patients admitted with acute ischemic stroke, potentially limiting its usefulness in this population. However, our intent was not to determine precise renal function but to estimate the degree of renal impairment in a large cohort of patients hospitalized with acute ischemic stroke. In addition, admission creatinine was not available in all patients, which may have introduced bias into the findings. Finally, we were unable to definitively establish an association between hospital care performance measures and outcomes or pinpoint the mechanisms by which renal dysfunction may affect mortality.

In conclusion, in this sizeable multi-site study we confirmed that renal dysfunction prevalence is high and associated with poor clinical outcomes among patients hospitalized with an ischemic stroke. Furthermore, we found that despite higher rates of in-hospital mortality linked to worsening renal dysfunction, ischemic stroke patients with advanced stages of dysfunction were significantly less likely to receive evidence-based pharmacologic and non-pharmacologic management strategies during their index hospitalization.
Intensified quality improvement efforts are warranted to enhance the care of hospitalized patients with ischemic stroke and kidney dysfunction.

Author Contributions
All authors were involved in the final decision to submit the manuscript. **Study concept and design:** Ovbiagele, Fonarow. **Acquisition of data:** Get With The Guidelines Stroke Personnel. **Analysis and interpretation of data:** Ovbiagele, Schwamm, Smith, Grau-Sepulveda, Saver, Bhatt, Hernandez, Peterson, Fonarow. **Drafting of the manuscript:** Ovbiagele. **Critical revision of the manuscript for important intellectual content:** Ovbiagele, Schwamm, Smith, Grau-Sepulveda, Saver, Bhatt, Hernandez, Peterson, Fonarow. **Statistical analysis:** Grau-Sepulveda.

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References
1. Lee M, Ovbiagele B. Renocerebrovascular disease: linking the nephron and neuron. **Expert Rev Neurother.** 2011;11:241–249.
2. Ovbiagele B. Chronic kidney disease and risk of death during hospitalization for stroke. **J Neurol Sci.** 2011;301:46–50.
3. Ani C, Ovbiagele B. Relation of baseline presence and severity of renal disease to long-term mortality in persons with known stroke. **J Neurol Sci.** 2010;288:123–128.
4. Tsagalis G, Akrivos T, Alevizaki M, Manios E, Stamatelopoulos K, Laggouranis A, Vemmos KN. Renal dysfunction in acute stroke: an independent predictor of long-term all combined vascular events and overall mortality. **Nephrol Dial Transplant.** 2009;24:194–200.
5. Lee M, Markovic D, Ovbiagele B. Impact and interaction of low estimated GFR and B vitamin therapy on prognosis among ischemic stroke patients: the Vitamin Intervention for Stroke Prevention (VISP) trial. **Am J Kidney Dis.** 2013;62:52–57.
6. Ovbiagele B, Bath PM, Cotton D, Sha N, Diener HC, for the PROFESS Investigators. Low glomerular filtration rate, recurrent stroke risk, and effect of renin-angiotensin system modulation. **Stroke.** 2013;44:3223–3225.
7. Brosius FC III, Hostetter TH, Keleporius E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, Smith GL, Wilson PW; American Heart Association Kidney and Cardiovascular Disease Council; Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; Quality of Care and Outcomes Research Interdisciplinary Working Group; National Kidney Foundation. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease. **Circulation.** 2006;114:1083–1087.
8. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, Ellrodt G, Cannon CP, Liang L, Peterson E, Labresh KA. 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.
9. Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SG, Halperin JL, Johnston SG, Katsan I, Kernan WN, Mitchell PH, Ovbiagele B, Palesch YY, Sacco RL, Schwamm LH, Warrington-Smoller S, Turan TN, Worthen D; American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Cardiovascular and Interventional Cardiology, Council on Quality of Care and Outcomes Research. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. **Stroke.** 2013;44:2297–2304.
10. Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerchchalk BM, Khatri P, McMullan PW Jr, Qureshi AI, Rosenfield K, Scott PA, Summers DR, Wang DZ, Wintemark M, Jonas H; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. **Stroke.** 2013;44:970–987.
11. National Kidney Foundation Kidney Disease Outcome Quality Initiative Advisory Committee. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. **Am J Kidney Dis.** 2002;39:S1–S246.
12. Kleinbaum D, Klein M. Logistic Regression—A Self Learning Text, 2nd ed. New York, NY: Springer; 2002.
13. Patel UD, Ou FS, Ohman EM, GподобWO, Pollock CV Jr, Peterson ED, Roet M; Antithrombotic Therapy and Prevention of Thrombosis, 9th ed. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S–e436S.
14. Patel UD, Hernandez AF, Liang L, Peterson ED, LaBresh KA, Yancy CW, Albert M, Ellrodt G, Fonarow GC, Liang L, Peterson E, Labresh KA. 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.
15. Vasiwala S, Cannon CP, Fonarow GC, Peacock WF, Laskey W, Schwamm LH; Get With The Guidelines Steering Committee and Investigators. Quality of care and outcomes among patients with acute myocardial infarction by level of kidney function in the Get With The Guidelines-Myocardial Infarction program. **Am Heart J.** 2008;156:674–681.
16. Schiffrin EL, Lipman ML, Mann JP. Chronic kidney disease: effects on the cardiovascular system. **Circulation.** 2007;116:85–97.
17. Reeves MJ, Vaidya RS, Fonarow GC, Liang L, Smith EE, Matulonis R, Olson DM, Schwamm LH; Get With The Guidelines Steering Committee and Hospitals. Quality of care and outcomes in patients with diabetes hospitalized with ischemic stroke: findings from Get With The Guidelines-Stroke. **Stroke.** 2010;41:e409–e417.
18. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA. The quality of health care delivered to adults in the United States. *N Engl J Med*. 2003;348:2635–2645.

19. Ezekowitz J, McAlister FA, Humphries KH, Norris CM, Tonelli M, Ghali WA, Knudtson ML; APPROACH Investigators. The association among renal insufficiency, pharmacotherapy, and outcomes in 6,427 patients with heart failure and coronary artery disease. *J Am Coll Cardiol*. 2004;44:1587–1592.

20. Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, Copetti M, Graziano G, Tognoni G, Jardine M, Webster A, Nicolucci A, Zoungas S, Strippoli GF. Effects of antiplatelet therapy on mortality and cardiovascular and bleeding outcomes in persons with chronic kidney disease: a systematic review and meta-analysis. *Ann Intern Med*. 2012;156:445–459.

21. Power A, Epstein D, Cohen D, Bathula R, Devine J, Kar A, Taube D, Duncan N, Ames D. Renal impairment reduces the efficacy of thrombolytic therapy in acute ischemic stroke. *Cerebrovasc Dis*. 2013;35:45–52.

22. Agrawal V, Rai B, Fellows J, McCullough PA. In-hospital outcomes with thrombolytic therapy in patients with renal dysfunction presenting with acute ischaemic stroke. *Nephrol Dial Transplant*. 2010;25:1150–1157.

23. Menon BK, Saver JL, Prabhakaran S, Reeves M, Liang L, Olson DM, Peterson ED, Hernandez AF, Fonarow GC, Schwamm LH, Smith EE. Risk score for intracranial hemorrhage in patients with acute ischemic stroke treated with intravenous tissue-type plasminogen activator. *Stroke*. 2012;43:2293–2299.