Endocarditis Is a Common Stroke Mechanism in Hemodialysis Patients

Koto Ishida, MD; Mesha Gay Brown, MD; Mark Weiner, MD; Sidney Kobrin, MD; Scott E. Kasner, MD; Steven R. Messé, MD

Background and Purpose—Hemodialysis patients are at high risk for ischemic stroke, and previous studies have noted a high rate of cardioembolism in this population. The aim of this study was to determine ischemic stroke causes among hemodialysis patients and elucidate specific cardioembolic stroke mechanisms.

Methods—This study is a retrospective cross-sectional study of hemodialysis patients admitted with acute stroke to the University of Pennsylvania Health System between 2003 and 2010. Strokes were classified using modified Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria as large vessel, cardioembolism, small vessel, atypical, multiple causes, or cryptogenic. Cardioembolic strokes were further characterized for specific mechanism.

Results—We identified 52 patients hospitalized with acute stroke while receiving hemodialysis. Mean age was 64±13 years, 56% were female, and 67% were black. Stroke subtypes included 3 (6%) large vessel, 20 (38%) cardioembolism, 6 (11%) small vessel, 3 (6%) other, 4 (8%) with multiple causes, and 16 (31%) were unknown. Among patients who had an echocardiogram performed, 5 of 52 (10%; 95% confidence interval, 1%–18%) had a patent foramen ovale. Cardioembolic stroke mechanisms included 6 with infective endocarditis (accounting for 12% of all strokes).

Conclusions—Cardioembolism and cryptogenic stroke are the predominant stroke mechanisms among hemodialysis patients. Infective endocarditis was identified frequently relative to other stroke cohorts, and a raised index of suspicion is warranted in the hemodialysis population. (Stroke. 2014;45:00-00.)

Key Words: endocarditis ■ renal dialysis ■ stroke

Patients with end-stage renal disease receiving hemodialysis have a high risk of ischemic stroke. Potential explanations include prevalence of traditional vascular risk factors in this population, malnutrition, and possibly even hemodialysis itself attributable to volume shifts and blood pressure lability, although other unidentified factors may also play a role. A large prospective study of stroke in hemodialysis patients reported that cardioembolism was the most common stroke cause, though specific mechanisms were not reported. Patients on hemodialysis may be at greater risk to develop atrial fibrillation, presumed attributable to electrolyte shifts and structural cardiac changes. The incidence of bacteremia is also elevated in patients receiving hemodialysis, increasing the risk for infective endocarditis. In addition, venous thrombi are common in hemodialysis patients which may lead to paradoxical embolization in patients with a patent foramen ovale (PFO). We undertook this study to better characterize stroke causes among patients receiving hemodialysis and to specifically evaluate cardioembolic mechanisms.

Methods
We performed a retrospective chart review of hemodialysis patients admitted with an acute ischemic stroke to 2 hospitals in the University of Pennsylvania Health System: the Hospital of the University of Pennsylvania and Penn Presbyterian Hospital. Both hospitals are located in West Philadelphia and together admit 700 patients with acute ischemic stroke annually. This project was approved by the institutional review board at the University of Pennsylvania. Using billing data collected between 2003 and 2010, we cross-referenced all inpatients with a diagnosis of stroke (discharge International Classification of Diseases, Ninth Revision, code between 430 and 436.99 or diagnosis related groups 14–17) with a list of hospital service charges for hemodialysis. Identified patients’ charts were reviewed to confirm acute ischemic stroke, that hemodialysis was ongoing before the stroke event, and also to extract demographic and clinical data. The available diagnostic stroke evaluation was reviewed including neuroimaging (head computed tomography or magnetic resonance imaging), vascular studies (carotid and transcranial Doppler ultrasound, magnetic resonance angiography, computed tomography angiography, or conventional angiogram), and echocardiographic studies (transthoracic or transesophageal). Stroke cause was categorized by 2 independent raters using modified Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. Stroke causes were categorized as large vessel, cardioembolic, small vessel, atypical nonatherosclerotic, multiple causes, or cryptogenic. Discordant ratings were resolved by consensus. Comparisons were made using χ², Fisher exact, and t tests as appropriate. Prevalence estimates and 95% confidence intervals for PFO were determined.
Results
The search query between 2003 and 2010 identified 171 patients, of which 52 patients were confirmed to have been receiving hemodialysis before hospitalization with acute stroke. Mean (±SD) age was 64±13 years, 29 (56%) were female, and 35 (67%) were black, 6 (12%) white, and 11 (21%) of unknown race. A history of hypertension was noted in 46 (88%), whereas 29 (56%) had a history of diabetes mellitus. Hemodialysis access included 9 (17%) with an arteriovenous graft, 23 (44%) with a tunneled catheter, and 20 (38%) with an arteriovenous fistula. Figure 1 displays the final determined stroke subtypes in this cohort. Cardioembolic mechanisms followed by cryptogenic mechanisms were most common. Among the 4 patients with multiple possible stroke mechanisms, all carried a diagnosis of atrial fibrillation. Figure 2 displays a Venn diagram of identified cardioembolic stroke mechanisms including 6 with acute infective endocarditis, accounting for 12% of the overall cohort. Excluding patients who were transferred to the University of Pennsylvania Health System, endocarditis accounted for 3 of 37 (8%) strokes. Overall, there were no statistical differences in demographic or vascular risk factors comparing patients with endocarditis to those without: age, 57 versus 65 years (P=0.14); hypertension, 100% versus 87% (P=1.00); and diabetes mellitus 67% versus 54% (P=0.68). There was also no association between endocarditis and type of hemodialysis access; endocarditis was seen in 3 of 21 (14%) patients with a fistula, 3 of 23 (13%) patients with a tunneled catheter, and 0 of 8 (0%) with a graft, P=0.72.

Transthoracic echocardiography only was performed in 36 patients (69%), and 16 (31%) received transesophageal echocardiography. Overall, PFO was identified in 5 of 52 patients (10%; 95% confidence interval, 1%–18%). Agitated saline contrast (bubble study) was performed in only 21 of 52 patients (40%), and PFO was identified in 3 of 21 patients (14%; 95% confidence interval, 0%–17%).

Discussion
This cohort of hemodialysis patients with stroke reveals that cardioembolic and cryptogenic stroke subtypes were most common. Among the 4 patients with multiple possible stroke mechanisms, all carried a diagnosis of atrial fibrillation. Figure 2 displays a Venn diagram of identified cardioembolic stroke mechanisms including 6 with acute infective endocarditis, accounting for 12% of the overall cohort. Excluding patients who were transferred to the University of Pennsylvania Health System, endocarditis accounted for 3 of 37 (8%) strokes. Overall, there were no statistical differences in demographic or vascular risk factors comparing patients with endocarditis to those without: age, 57 versus 65 years (P=0.14); hypertension, 100% versus 87% (P=1.00); and diabetes mellitus 67% versus 54% (P=0.68). There was also no association between endocarditis and type of hemodialysis access; endocarditis was seen in 3 of 21 (14%) patients with a fistula, 3 of 23 (13%) patients with a tunneled catheter, and 0 of 8 (0%) with a graft, P=0.72.

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We hypothesized that PFO would be prevalent among hemodialysis patients with stroke because PFO provides a right-to-left interatrial shunt and hemodialysis patients are at high risk for venous and right atrial thrombi. Despite this presumed risk for paradoxical embolization, the prevalence of PFO in this cohort was comparable with what has been described in population-based cohorts without stroke. There are important limitations to this study. As a retrospective case series, it is possible that there was systematic bias in patient acquisition. For example, critically ill patients with large strokes may not have continued hemodialysis if care was withdrawn or patients with mild stroke or transient ischemic attack may not have been hospitalized or not hospitalized long enough to require hemodialysis treatment. Finally, stroke evaluations were not systematic and many patients did not undergo a bubble study, the most sensitive means to identify a PFO, and thus we may have underestimated the prevalence of PFO in this cohort.

To conclude, this study of hemodialysis patients with acute stroke demonstrated that cardioembolic causes are the most common. Endocarditis was much more prevalent than in unselected stroke cohorts. Thus, a heightened index of suspicion for endocarditis is warranted in the hemodialysis population.

Disclosures
None.
References
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