

[EDITORIAL]

Atrial Fibrillation in Patients with End-stage Kidney Disease on Dialysis

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Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice, with a lifetime risk of 1 in 6 for subjects ≥ 40 years, even in the absence of structural heart disease. The prevalence of AF in patients with chronic kidney disease is notably high. The incidence of AF increases with decreases in the kidney function, and the prevalence of AF reaches 32% in older patients on hemodialysis.

AF is a major cause of ischemic stroke, and nonvalvular AF increases the risk of ischemic stroke about five-fold. However, whether or not AF increases the risk of stroke in patients with end-stage kidney disease remains controversial. AF increases the risk of stroke in some studies, but not to a staggering degree (hazard ratio, 1.26-1.79) (1). In studies from Western countries and Japan, AF is not associated with an increased risk of stroke in patients on hemodialysis (2). Similarly, in the study by Mitsuma et al. on this issue, among patients on hemodialysis, the risk of stroke was not markedly different between patients with and without AF (hazard ratio, 1.68) (3). Taken together, these findings suggest that the impact of AF on the risk of stroke is low in patients on dialysis compared with those who do not have chronic kidney disease.

Patients with end-stage kidney disease often have several conventional risk factors for atherosclerosis, such as hypertension, dyslipidemia, diabetes, and proteinuria. Furthermore, they also have characteristic risk factors for atherosclerosis, such as uremic toxins, vascular calcification, and hypercoagulability. Therefore, in patients on dialysis, the risk of stroke is 6 to 10 times higher than in the general population, and the incidence of stroke is 10 to 36 per 1,000 patient years (4). The study by Mitsuma et al. showed similar results, noting an incidence of stroke and systemic embolism of 21 per 1,000 patient years (3). Because patients on dialysis are already at a high risk of developing stroke, the additional increase in the stroke risk due to AF may be negligible.

Oral anticoagulation therapy is useful for preventing stroke in patients with AF. However, several studies, including a meta-analysis, have shown that warfarin is not associated with a decrease in the rates of mortality and ischemic stroke but is associated with an increase in the risk of major bleeding in patients on dialysis who have AF (5). According to the guideline established by the Japanese Society for Dialysis Therapy, the use of warfarin to prevent stroke is generally not recommended in patients on dialysis, and cautious use of warfarin with tight control of International Normalized Ratio (INR) < 2.0 is only considerable in patients whose risk of stroke is estimated to be decreased by the drug.

In the last decade, direct non-vitamin K-dependent oral anticoagulants (DOACs) have become available for the prevention of stroke in patients with AF. However, phase III studies for DOACs have not included patients with end-stage kidney disease, and DOACs are not recommended in patients on dialysis under the current guidelines. Still, some studies have examined the efficacy of DOACs in patients with end-stage kidney disease (6, 7). In a meta-analysis, the incidence of ischemic stroke was found to be similar between DOACs and warfarin, and the incidence of major bleeding was slightly lower with DOACs than with warfarin in patients with [a reduced?] creatinine clearance or an estimated glomerular filtration rate between 15 and 60 mL/min (6). In other studies, the incidences of both stroke and bleeding were similar between apixaban and warfarin in patients with severe kidney dysfunction (7). DOACs may be useful in patients with end-stage kidney disease, although further studies are needed to determine their efficacy and safety.

Although AF has little to no impact on the risk of stroke in patients on dialysis, AF is associated with adverse events (8). AF is associated with all-cause mortality (hazard ratio, 1.32-1.82) and cardiovascular events (hazard ratio, 1.39-2.15) in patients on dialysis (8). Interestingly, in a

study on this issue, the incidence of non-cardiovascular death has seemed higher in patients with AF (103.0 per 1,000 patient years) than in those without AF (37.9 per 1,000 patient years), although AF was found to not be associated with the risk of non-cardiovascular death in another study (3, 8). The presence of AF may indicate a poor prognosis in patients on dialysis.

The authors state that they have no Conflict of Interest (COI).

References

1. Wizemann V, Tong L, Satayathum S, et al. Atrial fibrillation in hemodialysis patients: clinical features and associations with anti-coagulant therapy. *Kidney Int* **77**: 1098-1106, 2010.
2. Wiesholzer M, Harm F, Tomasec G, Barbieri G, Putz D, Balcke P. Incidence of stroke among chronic hemodialysis patients with nonrheumatic atrial fibrillation. *Am J Nephrol* **21**: 35-39, 2001.
3. Mitsuma W, Matsubara T, Hatada K, et al. Atrial fibrillation had less impact on the risk of ischemic stroke in non-anticoagulated patients undergoing hemodialysis: insight from the RAKUEN study. *Intern Med* **57**: 2295-2300, 2018.
4. Nayak-Rao S, Shenoy MP. Stroke in patients with chronic kidney disease...: how do we approach and manage it? *Indian J Nephrol* **27**: 167-171, 2017.
5. Shah M, Avgil Tsadok M, Jackevicius CA, et al. Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation* **129**: 1196-1203, 2014.
6. Kimachi M, Furukawa TA, Kimachi K, Goto Y, Fukuma S, Fukuhara S. Direct oral anticoagulants versus warfarin for preventing stroke and systemic embolic events among atrial fibrillation patients with chronic kidney disease. *Cochrane Database of Syst Rev* **11**: Cd011373, 2017.
7. Sarratt SC, Nesbit R, Moye R. Safety outcomes of apixaban compared with warfarin in patients with end-stage renal disease. *Annals of pharmacotherapy* **51**: 445-450, 2017.
8. Genovesi S, Vincenti A, Rossi E, et al. Atrial fibrillation and morbidity and mortality in a cohort of long-term hemodialysis patients. *Am J Kidney Dis* **51**: 255-262, 2008.

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