

Dialysis Initiation in Patients with Chronic Coronary Artery Disease and Advanced Chronic Kidney Disease in the ISCHEMIA-CKD Trial

By Benjamin Lidgard and Nisha Bansal

In patients with advanced chronic kidney disease (CKD), the decision to pursue invasive strategies for treatment of coronary artery disease involves careful consideration. Data from the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA)-CKD trial may better inform these decisions. The National Heart, Lung, and Blood Institute (NHLBI)-funded ISCHEMIA-CKD trial was a randomized clinical trial that included 777 patients from 30 countries, predominantly in the United States, Russia, Poland, India, and China. Inclusion criteria included aged ≥ 21 years, kidney failure on maintenance dialysis or estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m², and at least moderate ischemia on a pharmacologic or exercise stress test (1). The trial found no difference in cardiovascular events with a strategy of coronary

angiography and revascularization versus conservative goal-directed medical therapy.

A post hoc analysis of a subset of 362 participants in the ISCHEMIA-CKD trial investigated risk of subsequent dialysis initiation in both treatment groups (2). Despite comparable eGFR at randomization, participants in the invasive arm had shorter times to dialysis initiation (6 versus 18 months in the conservative arm), although overall risk of dialysis initiation was equal between groups at a median follow-up of 23 months. There was no statistical difference in rates of post-procedure acute kidney injury (AKI) between the two treatment groups (7.8% vs. 5.4%; $p = 0.26$), so AKI is an unlikely explanation for these findings. Further work is needed to understand other factors that may explain this association.

The study had several strengths, including study of a

trial population. However, some limitations should be acknowledged. Several risk factors for CKD progression, including previous rate of progression, proteinuria, and CKD etiology, were unknown and potentially affected risk of dialysis initiation. Post-procedural follow-up and the decision to initiate dialysis were not protocolized; it is possible, given the non-blinded design, that providers were biased toward early dialysis initiation in participants in the invasive arm.

In summary, findings from the ISCHEMIA-CKD trial provide important new data on cardiovascular procedures in patients with advanced CKD. It will be interesting to see how these findings are translated into clinical care, including counseling patients on the risks versus benefits of cardiovascular procedures, as well as pre-kidney transplant evaluations. ■

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The authors report no conflicts of interest.

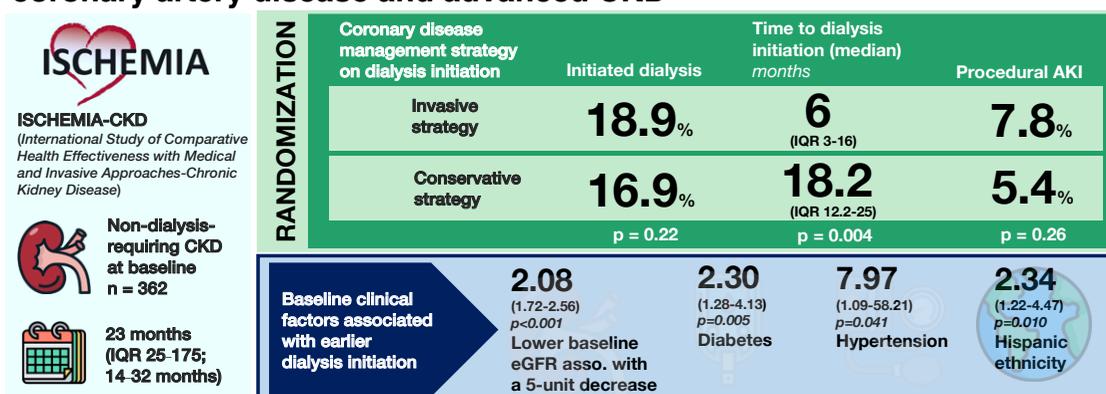
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Effect of treatment strategies on the timing of dialysis initiation in patients with chronic coronary artery disease and advanced CKD

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Conclusion: In participants with non-dialysis-requiring CKD in ISCHEMIA-CKD, randomization to an invasive chronic coronary artery disease management strategy (relative to a conservative chronic coronary artery disease management strategy) is associated with an accelerated time to initiation of maintenance dialysis for kidney failure. IQR, interquartile range.

Briguori C, et al. Dialysis initiation in patients with chronic coronary disease and advanced chronic kidney disease in ISCHEMIA-CKD. *J Am Heart Assoc* 2022; 11:e022003. doi: 10.1161/JAHA.121.022003

Visual Abstract by Edgar Lerma, MD, FASN

Findings

Apixaban Reduces Bleeding Risk in Dialysis Patients with Atrial Fibrillation

For dialysis patients with nonvalvular atrial fibrillation (AF), anti-coagulation with apixaban—at both standard and below-label doses—lowers the risk of bleeding events compared with warfarin, concludes a study in the *American Journal of Kidney Diseases*.

Using US Renal Data System data from 2013 to 2018, the researchers identified 17,156 Medicare beneficiaries with nonvalvular AF receiving maintenance hemodialysis. All patients (12,517) had a new prescription for warfarin, and 2382 patients had apixaban at a label-concordant dose of 5 mg twice daily, or 2257 patients had apixaban at a lower dose of 2.5 mg twice daily. Outcomes, including stroke or systemic embolism, major bleeding events, and death from any cause, were compared between apixaban groups. The mean age of patients was 66 years, and 38% of patients were women, 68% were White, and 28% were Black. The percentage receiving warfarin decreased from 86% in 2014 (the year apixaban was approved) to 42% in 2018.

Risk of stroke or systemic embolism was similar across treatment groups: approximately 2 per 100 patient-years with approaches designed to simulate intention-to-treat (ITT) analysis and to incorporate censoring at drug switch or discontinuation (CAS). However, apixaban was associated with a lower rate of major bleeding events. In the ITT analysis, hazard ratios (HRs) were 0.67 with label-concordant dosing and 0.68 with below-label dos-

ing. In the CAS analysis, HRs were 0.53 and 0.562, respectively. Label-concordant apixaban was also associated with lower all-cause mortality: HR was 0.85 with both ITT and CAS analyses. There was no difference in mortality with below-label apixaban versus warfarin.

Nonvalvular AF is common in dialysis patients, and anti-coagulants are prescribed to reduce the risk of stroke. In this group of patients, the direct oral anti-coagulant apixaban is sometimes given at below-label doses to reduce bleeding risks. There are limited data to guide anti-coagulant treatment in dialysis patients with AF.

This analysis suggests that apixaban reduces the risk of major bleeding, compared with warfarin, in dialysis patients with nonvalvular AF. Bleeding risk is similar for label-concordant and below-label dosing, whereas the standard dose appears to be associated with lower mortality. The investigators conclude, “Label-concordant apixaban dosing may therefore provide the best tradeoff of benefits and risks among the treatment approaches assessed” [Wetmore JB, et al. Apixaban dosing patterns versus warfarin in patients with nonvalvular atrial fibrillation receiving dialysis: A retrospective cohort study. *Am J Kidney Dis*, published online ahead of print April 22, 2022. doi: 10.1053/j.ajkd.2022.03.007; [https://www.ajkd.org/article/S0272-6386\(22\)00621-7/fulltext](https://www.ajkd.org/article/S0272-6386(22)00621-7/fulltext)]. ■