Atrial Fibrillation and Chronic Kidney Disease

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, with a five-fold increased stroke risk. Patients with chronic kidney disease (CKD) have a higher stroke and bleeding risk compared to the general population. The prevalence of both these conditions is increasing with our aging population, and many such patients are not anticoagulated for fear of bleeding complications. Guidelines for treatment are not yet available. In this Heartbeat, we will outline a clinical management plan for this uniquely challenging complex scenario based on a state-of-the-art publication from the June Journal of the American College of Cardiology.1

Complex Clinical Situation

A bidirectional relationship exists between AF and CKD. A rapidly increasing elderly population with diabetes and hypertension is associated with an increasing incidence of CKD, which in turn is associated with a parallel increase in incident AF.2,3 Worsening CKD results in increasing incidence of AF,4,5,6 which in turn hastens the occurrence of more progressive CKD.7,8 Both conditions increase the propensity for thromboembolic risk and paradoxically hemorrhagic risk resulting in high-risk patients that are very difficult to treat. Several pathophysiological factors have been demonstrated to induce a prothrombotic state while increasing bleeding risk in such patients. The thromboembolic and hemorrhagic risks are particularly high among dialysis-dependent patients with end-stage kidney disease (ESKD).

Chronic Kidney Disease

CKD is defined as a reduction in renal function with a decreased glomerular filtration rate (GFR) < 60 ml/min/1.73 m2 and/or the presence of albuminuria.

Stage I > 90 ml/min/1.73 m2 (perfect:NL)
Stage II 60-89 ml/min/1.73 m2
Stage III 30-59 ml/min/1.73 m2 (CKD)
Stage IV 15-29 ml/min/1.73 m2 (severe)
Stage V < 15 ml/min/1.73 m2 (ESKD)

CKD has the potential for gradual progression to ESKD, which requires dialysis to correct the accompanying fluid and electrolyte imbalance.

Risk Assessment

Stroke/thromboembolism and bleeding risks can be assessed using clinical risk scores, such as the CHA2DS2-VASc and HAS-BLED.
**Stroke Risk: CHA2DS2-VASc Score**

- Congestive heart failure: 1 point
- Hypertension: 1 point
- Age: 65-74 = 1 point; >75 = 2 points
- Diabetes: 1 point
- Stroke or TIA: 2 points
- Vascular disease: 1 point *(PAD, CAD, carotid vasc dx, previous MI or aortic plaque)*
- Female sex: 1 point.

Oral anticoagulant (OAC) treatment should be considered for men with a risk score of 1 and strongly recommended for all with a score of 2.9

**Bleeding Risk: HAS-BLED Score**

- Abnormal renal function: dialysis; SCr > 2
- Hypertension: SBP > 160 mm Hg
- Abnormal liver function: cirrhosis or LFT > 3x ULN
- History of major bleed: any cause
- History of alcohol ingestion: > 8 drinks/week
- Currently taking NSAIDS or anti-platelet drug
- History of labile INR: < 60% TTR
- Age > 65; 2 points for age > 75
- Frequent falls

Two or more points indicates high risk.

If a CKD patient is high risk for stroke, in most cases we are going to recommend anticoagulation even if they are high bleeding risk; a stroke is much more catastrophic. Computing the scores will help us to be more aware and take steps to mitigate bleeding risk by correcting modifiable risk factors—hypertension, discontinuing alcohol, unneeded aspirin, non-steroidal anti-inflammatory drugs or adding a proton pump inhibitor—whichever is most appropriate.

It is important to emphasize that treatment should be individualized based on shared decision making after discussion of the absolute and relative risks of stroke and bleeding and the patient’s and family’s values and preferences. This is where using the SPARC (Stroke Prevention in Atrial Fibrillation Risk Calculator) with them becomes quite useful—especially in those very complex cases. The SPARC calculator is a combination of CHADS2, CHA2DS2-VASc and HAS-BLED scores, available on Cardiosource, and is based on the most recent guidelines—www.vhpharmsci.com/sparc
(available as a mobile app for your phone).

Watchman left atrial appendage occluding devices may be considered in patients with clear contraindications for OAC—the benefits and risks must be carefully considered for each individual case.

**Clinical Management**

Effective stroke prevention means OACs, whether as well-controlled vitamin K antagonist (VKA) therapy or one of the new oral anticoagulants (NOACs).

Unfortunately, there is limited data about OAC treatment in CKD as most of these patients were excluded from the large randomized trials. There is no data about NOACs in ESKD.

**ESKD/GFR < 15ml/min:** There is resistance to use of VKA (2% in Germany and 37% in Canada) because of uncertainty of benefit versus risk, especially in those patients on dialysis. If the CHA2DS2-VASc score is high and bleeding risk is low, VKA may be considered while closely following these patients to maintain INR time in therapeutic range (TTR) > 70% (quality management). Among non–dialysis-dependent ESKD patients with AF, there is more robust data favoring the use of quality dose-adjusted VKA. However, a just-released observational study noted that rates of stroke/thromboembolism were comparable in VKA recipients and non-recipients, but bleeding was higher.10

There is no data on NOACs, and the consensus is to avoid them because they have a high degree of renal excretion (25% for apixaban, 50% for edoxaban, 66% for rivaroxaban and 80% for dabigatran). In select patients, if the stroke risk is high and there is no history of bleeding, apixaban (2.5 or 5 mg Bid) may be considered, based on the dosing algorithm. (Apixaban...
dose should be reduced from 5 mg to 2.5 mg twice daily for patients with any two of these three conditions: 80 years old or greater, weight of 60 kg (132 lb.) or less, or a serum creatinine greater than 1.5 mg/dL).

**Severe CKD (GFR) 15-30ml/min:** The European Guidelines recommend that NOACs best not be used. For patients in the US, the FDA has approved the NOACs at reduced dosages (per table). These dosages are not approved on the basis of clinical trial outcome data, but on pharmacological modeling data (more efficacious).

**Mild-Moderate CKD:** When NOACs were introduced, namely the direct thrombin inhibitor (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban and edoxaban), they were considered viable alternatives to VKAs for patients with mild-to-moderate CKD requiring an oral anticoagulant for thromboprophylaxis with appropriate dose adjustment for renal function as per algorithm.

The Cockcroft-Gault method (in the Qx Calculate app on your phone) should be used for more accurate assessment of renal function (creatinine clearance [CrCl]), as this formula was used during various randomized trials of NOACs and does not result in overestimation of renal function in elderly patients or those with lower GFR, hence, allowing for better dose adjustment in this patient group—as per algorithm.

*“Chronic Kidney Disease”*

**Proposed algorithm/options for oral anticoagulant therapy in AF with CKD:**

**Pearls per Dr. Valentin Fuster Commentary:**

Concurrent AF and CKD increase thromboembolic and hemorrhagic risk, and these risks increase with progressive CKD, with both risks being especially high in ESKD patients on dialysis.

Quality management of VKA may be considered in ESKD, particularly if CHA2DS2-VASc score is high and bleeding risk is low.

NOACs should be avoided in ESKD with the exception of apixaban 2.5 to 5 mg Bid in select cases.

In moderate CKD, if planning to use a NOAC, first consider apixaban at half or full dose (better safety profile).
References

1. Yee C. Lau, MBChB; Marco Proietti, MD; Elisa Guiducci, MD; Andrew D. Blann, PhD; Gregory Y.H. Lip, MD. Atrial fibrillation and thromboembolism in patients with chronic kidney disease. *J Am Coll Cardiol.* June 2016; 68: 1452-1464


