Global Action. Local Change.

KDIGO Controversies Conference on CKD & Arrhythmias

October 27-30, 2016
Berlin, Germany

Kidney Disease: Improving Global Outcomes (KDIGO) is an international organization whose mission is to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines. Periodically, KDIGO hosts conferences on topics of importance to patients with kidney disease. These conferences are designed to review the state of the art on a focused subject and to ask conference participants to determine what needs to be done in this area to improve patient care and outcomes. Sometimes the recommendations from these conferences lead to KDIGO guideline efforts and other times they highlight areas for which additional research is needed to produce evidence that might lead to guidelines in the future.

Background

It is well established that cardiovascular disease (CVD) is more frequent in chronic kidney disease (CKD).[1-3] Unfortunately, they may not be recognized and even if they are they may be undertreated. Additionally, the early stages of CKD or its progression may be underrecognized among patients with acute or chronic cardiovascular conditions. Because of the severity and progressive nature of both CKD and CVD, clinical decision-making in the presence of both conditions may also be complex, especially with respect to risk stratification, treatment selection, clinical effectiveness of therapies, and net clinical benefit in view of competing risks. Randomized trials have consistently excluded

patients with CKD and end-stage renal disease (ESRD), although the trial landscape in this area has improved.[4, 5]

In particular, patients with CKD are predisposed to heart rhythm disorders. CKD patients may present with a wide spectrum of arrhythmias ranging from supraventricular arrhythmias and ectopics, atrial fibrillation and flutter, ventricular ectopics and sustained and non-sustained ventricular tachycardia, and sudden cardiac death (SCD). Factors in CKD that may contribute to arrhythmogenesis include cardiac structural remodeling (e.g., hypertrophy, dilatation, fibrosis, left ventricular dysfunction), vascular changes (e.g., endothelial dysfunction, atherosclerosis, arteriosclerosis and calcification), changes to electrical milieu (e.g., electrolytes, autonomic tone, repolarization), and systemic factors (e.g., uremia, inflammatory processes, thrombosis).[6, 7]

Relevance of the topic and the conference

There is a strong public health and economic imperative to improve outcomes for people with kidney disease and heart rhythm disorders. Evidence gaps have been recently defined in professional society consensus documents.[6, 8] However, treatment guidelines that specifically address this population are limited. Although many arrhythmias have a variety of treatment options, their management in CKD is complex and often more limited. A notable example of a kidney-arrhythmia phenotype is atrial fibrillation (AF) in CKD. Pharmacokinetic alterations in CKD of membrane active compounds, such as antiarrhythmic drugs used in AF, may potentiate safety and efficacy. AF has a higher incidence and prevalence in CKD than in non-CKD patients. CKD increases risk of stroke among patients with AF, but it also increases bleeding risk

from anticoagulation, making it difficult to discern the net clinical benefit of anticoagulation in specific situations. Direct oral anticoagulants (DOACs) have variation in absorption, half-life, and renal elimination, which must be accounted for to maintain efficacy while minimizing bleeding risks in narrow therapeutic windows. There are also concerns that renin-angiotensin-aldosterone system (RAAS) blockade may not be effectively implemented in this vulnerable population due to hyperkalemia but new potassium-binding agents are now emerging which may allow the use of RAAS therapies to gain their cardio- and reno-protective benefits.

As with any drug therapy there are substantial evidence gaps and clinical challenges in the use of cardiovascular procedures and medical devices in CKD patients. Procedures to prevent arrhythmias (e.g., catheter ablation) may have differing safety and efficacy profiles in CKD patients than in trial populations. Studies of implantable defibrillators (ICDs) largely excluded patients with advanced CKD, but these therapies may still be effective to prevent SCD, including newer generation technologies which avoid hardware in the vascular space, that may be beneficial in ESRD.

CONFERENCE OVERVIEW

To this end, this KDIGO conference will gather a global panel of multidisciplinary clinical and scientific expertise (e.g., nephrology, cardiology & cardiac electrophysiology, pharmacology, neurology, etc.) who will identify key issues relevant to the optimal prevention, management and treatment of arrhythmias and their complications in patients with kidney disease. The objective of this conference is to assess our current state of knowledge related to the epidemiology of atrial fibrillation and stroke in kidney

disease; stroke prevention in atrial fibrillation and CKD; prognostication and prevention of SCD in CKD; maintenance of electrolyte homeostasis in CKD and dialysis, particularly hyperkalemia; and rate versus rhythm control in atrial fibrillation in CKD.

Drs. Mintu Turakhia, MD, MAS, FACC, FHRS, FAHA (Cardiac electrophysiology, Stanford University School of Medicine) and Christoph Wanner, MD, FERA (Nephrology, University of Würzburg Hospital, Germany) will co-chair this conference. The format of the conference will involve topical plenary session presentations followed by focused discussion groups that will report back to the full group for consensus building. Invited participants and speakers will include worldwide leading experts who will address key clinical issues as outlined in the **Appendix: Scope of Coverage**. The conference output will include publication of a position statement that will help guide KDIGO and others on therapeutic management and future research.

References

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APPENDIX: SCOPE OF COVERAGE

GROUP 1. Epidemiology of Atrial Fibrillation (AF) and Stroke in Kidney Disease

- What is the global disease burden of AF, stroke and CKD? What is the overlap among them?
- What are the risks for, and what is the significance of developing a new AF or a stroke in the presence of CKD?
- What is the significance of developing CKD in the presence of established AF or stroke?
- Are there interactions between these conditions? For example, does AF or stroke cause CKD incidence/progression? Does CKD increase stroke occurrence/ recurrence? Do they exacerbate other adverse outcomes (death)?
- Should screening for AF be performed in patients with CKD? How do prior and ongoing AF screening studies apply to patients with CKD? What is the best method of screening? (e.g., opportunistic, short- and long-term non-invasive ECG monitoring, implantable loop recorder, mobile app).
- Should stroke risk scores be estimated in patients with CKD to guide therapy? Do existing risk scores apply to patients with CKD? What is the best risk score to assess in these patients?

GROUP 2. Stroke Prevention in Atrial Fibrillation and CKD

Pathogenesis of AF in CKD

- What is the relation between AF and cardioembolic stroke in CKD? Is it causal or a marker of vascular risk/non-embolic stroke risk?

Assessment of trade-offs regarding anticoagulation

- CKD increases both risk of ischemic stroke in AF and risk of major bleeding (and intracranial hemorrhage) with oral anticoagulation. Is risk stratification for thromboprophylaxis in AF different for CKD populations (i.e., do CHA_2DS_2-VASc and the various bleeding scores apply)?

Thromboprophylaxis

- What are the stroke prevention options in CKD 3/4 vs CKD 5D patients? What is the state of evidence in clinical trials for stroke prevention with direct oral anticoagulants in CKD and ESRD?
- How should clinicians choose among the various options: warfarin, direct oral anticoagulants, and left atrial appendage occlusion among CKD patients?

Special factors in CKD

- Since albuminuria is a risk factor for stroke in CKD populations, how does it affect the benefits and risks of antithrombotic therapies for AF?
- How does erythropoietin therapy interact with antithrombotic therapy for AF?

Pharmacokinetics of anticoagulants

- What are the implications for perioperative management of anticoagulation in patients with CKD?
- What are the implications regarding reversal?
- How can we address safety signals regarding anticoagulation with novel oral anticoagulants (NOACs) among CKD patients? Data on NOACs vs warfarin in CKD?

Future directions

- What are the important evidence gaps and what do the ongoing trials address?
- What are most important endpoints for trials in patients with AF and CKD?

GROUP 3. Risk Prediction and Prevention of Sudden Cardiac Death (SCD) in CKD

- What are the incidence and etiologies of SCD in CKD and ESRD populations?
- What are the CKD-related risk factors for SCD? (e.g., electrolytes, autonomic imbalance, left ventricular hypertrophy and fibrosis, atherosclerosis, endothelial dysfunction, acidosis, uremia, etc.)
- What are the roles of cardiac biomarkers (e.g., troponins) as risk predictors for SCD?
- What is the prognostic significance of incidentally detected arrhythmias in CKD and ESRD? (e.g., non-sustained ventricular tachycardia, premature ventricular complexes, bradyarrhythmias)
- What is the prognostic significance of syncope and the appropriate work-up?

- Balancing risk of SCD and competing risks in ESRD: What is the role of ICDs for primary prevention and secondary prevention of SCD in ESRD?
- What are the treatment options for primary prevention of SCD with implantable defibrillators in CKD and ESRD? (Discuss transvenous ICDs, subcutaneous ICDs, and wearable cardioverter defibrillators)

GROUP 4. Potassium Homeostasis and Handling in CKD and Dialysis

- Do electrolyte abnormalities increase risk of cardiovascular or arrhythmic events? In addition to potassium, what is the role of phosphorus in contributing to arrhythmia risk in dialysis patients?
- What is the role and treatment options for potassium homeostasis (particularly hyperkalemia)? How do new treatments for hyperkalemia enable the use of RAAS blockers in patients with CKD or CKD and CVD?
- What is the role of dialysate and dialysis parameters for prevention of arrhythmic events in ESRD?
- Should dialysis patients be monitored via cardiac telemetry during dialysis?
- Does intradialytic hypotension play a role in predisposing patients to cardiac arrhythmias?
- Should there be guidelines regarding dialysis characteristics in patients with arrhythmias?

GROUP 5. Rate versus Rhythm Control in Atrial Fibrillation in CKD

- What is the current evidence regarding rate vs. rhythm control in general? What recommendations are available for the general population?
- What is the specific evidence for rate vs. rhythm control in CKD?
- What are the considerations in deciding on rate versus rhythm control for an initial AF treatment strategy?
- What are the considerations for anti-arrhythmic drug selection in CKD?
- What is the role of catheter ablation for AF in CKD and what are the data on its safety and effectiveness?
- How effective is risk factor modification (e.g., weight loss, exercise, sleep apnea treatment) for reduction of AF severity in CKD?