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KDIGO Controversies Conference on Coronary Artery & Valvular Diseases in Chronic Kidney Disease

**June 28 - July 1, 2018
Vienna, Austria**

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. The current Controversies Conference is the third in a series related to cardiovascular disease (CVD) and kidney disease sponsored by KDIGO. The first dealt with management of arrhythmias in chronic kidney disease (CKD) and the second, management of heart failure in CKD.

Background

CVD is the leading cause of morbidity and mortality in patients with CKD. The increased risk of CVD begins during the earlier stages of CKD before the onset of kidney failure. Patients with CKD have a high prevalence of traditional coronary artery disease (CAD) risk factors such as diabetes and hypertension but they are also exposed to other non-traditional, uremia-related CVD risk factors such as inflammation, oxidative stress and abnormal calcium-phosphorus metabolism. Mitral annular calcification and aortic calcification are also highly prevalent in CKD and lead to conduction system abnormalities, endocarditis, embolism, as well as valvular stenosis and regurgitation.

Relevance of the Conference and Topic

Coronary artery disease and valvular disease are leading causes of hospitalizations in most developed countries and CKD is a major risk factor for both these conditions. The prevalence of CKD is expected



to increase in the future because of its close relationship to diabetes, hypertension and obesity. Data from the general population cannot be extrapolated to CKD because the pathophysiology of the CVD in CKD is different, the prevalence of comorbid conditions in CKD is high, and the potential side effects of interventions in CKD are higher still. We therefore need a better understanding of the epidemiology of CAD and valvular disease in CKD. We also need an improved appreciation of the pathophysiology, diagnosis, and treatment of CAD and valvular disease in CKD.

Conference Overview

The conference will be led by Mark J. Sarnak MD MS, nephrologist from Tufts Medical Center, Boston USA and Thomas H. Marwick, MBBS, PhD, MPH, cardiologist from Baker Heart and Diabetes Institute, Melbourne, Australia. This interactive conference will invite key thought leaders from cardiology, nephrology, cardiac surgery and other related disciplines who will comprehensively review the literature, and summarize what is known and what is not known in this field. Key areas of controversy will be focused upon and research and clinical recommendations will be provided so as to move the field forward. There will be four breakout groups that will focus on CKD and dialysis patients and one breakout group that will focus on kidney transplant recipients (see table below).

	Population	Focus
Breakout Group 1	CKD and Dialysis	Epidemiology, Screening & Diagnosis of CAD and Valvular Disease
Breakout Group 2	CKD and Dialysis	Pathology & Pathophysiology of CAD and Valvular Disease
Breakout Group 3	CKD and Dialysis	Diagnosis & Treatment of Prevalent CAD
Breakout Group 4	CKD and Dialysis	Diagnosis & Treatment of Prevalent Valvular Disease
Breakout Group 5	Transplant	CAD and Valvular Disease in Kidney Transplant Recipients



APPENDIX: SCOPE OF COVERAGE

GROUP 1: EPIDEMIOLOGY, SCREENING, AND DIAGNOSIS OF CAD AND VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

EPIDEMIOLOGY OF CAD

1. What is the incidence and prevalence of CAD in CKD or ESKD? How does this compare with the general population?
2. What is the clinical presentation of CAD in patients with CKD or end-stage kidney disease (ESKD)? Does the presentation of CAD differ between CKD and ESKD?
3. Are standard atherosclerotic CVD (ASCVD) risk equations accurate in patients with CKD or ESKD? Is there any evidence that conventional risk markers (e.g., hypertension, diabetes) affect ASCVD risk differently in patients with CKD? Are there risk markers that improve risk prediction specifically in patients with CKD or ESKD?

SCREENING & RISK ASSESSMENT FOR CAD

4. How often and with what methods should the risk of CAD be assessed?
5. Are standard guideline-directed medical therapies for prevention of CAD effective in patients with CKD?
6. Should dialysis patients (both pre-transplant as well as non-transplant candidates) be evaluated with stress testing? Coronary imaging?
7. How should cardiac troponin elevations be interpreted in patients with CKD or ESKD?

VALVULAR HEART DISEASE

8. What is the incidence and prevalence of valvular disease in CKD or ESKD? How does this compare with the general population?
9. Should patients with CKD or ESKD be screened for valvular disease?
10. Are any medical interventions effective in preventing the progression of valvular heart disease?



GROUP 2: PATHOLOGY AND PATHOPHYSIOLOGY OF CAD AND VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

PATHOLOGY

1. Pathology of CAD and valvular disease
 - a. What are the specific pathological characteristics of CAD and valvular heart disease in CKD patients (e.g., coronary media calcification, severity of disease and others)? How do these characteristics modify the course of the disease or specifically add to the increased risk (i.e., plaque rupture)?
 - b. What role does the cause of CKD play?
 - c. What are potential implications for assessment and treatment of CAD in CKD?

2. Differences in comparison with the general population
 - a. What are the main cardiovascular risks at different stages of CKD compared to the general population?
 - b. Are there differences in the outcomes of cardiovascular complications in CKD versus the general population due to these differences in pathology? (e.g., myocardial infarction in CKD compared to the general population?)

PATHOPHYSIOLOGY

3. Atherosclerosis
 - a. Dyslipidemia: What is the impact of CKD on lipid abnormalities? Impact of dyslipidemia on atherosclerosis mechanism in CKD?
 - b. Inflammation and oxidative stress: What impact does CKD have on inflammation and oxidative stress and in turn, on atherosclerosis?
 - c. What is the impact of CKD on plaque vulnerability?
4. Arteriosclerosis
 - a. What are the roles of mineral and bone disease (MBD), blood pressure, inflammation and hemodynamic factors in the development of arteriosclerosis?
 - b. What is the role of coronary microcirculation for cardiovascular risk in CKD?
5. Calcification
 - a. What does the role of MBD play in the pathology of coronary and valvular heart disease in CKD (e.g., in plaque and media calcification)? What are the potential therapeutic implications and effects on cardiovascular risk?
 - b. Arterial stiffness: What is the role of arterial stiffness on left ventricular hypertrophy in CKD?
 - c. Arterial calcification: What is the role of calcification in arterial stiffness and plaque stability?



GROUP 3: DIAGNOSIS AND TREATMENT OF PREVALENT CAD IN CKD AND DIALYSIS PATIENTS

DIAGNOSIS OF CAD

1. What is the preferred test for the diagnosis of prevalent CAD in individuals with CKD and ESKD?
 - a. Functional - Exercise stress testing without imaging vs stress imaging (exercise or pharmacological) e.g., echocardiography, SPECT, PET, MRI (non-gadolinium based)
 - b. Anatomic - coronary CTA, catheterization
2. How frequently should there be further evaluation for CAD in patients with a normal stress test awaiting kidney transplant?

TREATMENT OF CAD

3. Should CKD/ESKD be considered a CAD equivalent—should all patients with CKD or on dialysis be treated for secondary prevention of CAD?
4. How should patients with CKD/ESKD and CAD be treated with lipid-lowering therapies? (e.g., statins, ezetimibe plus statin or other lipid-lowering strategies?) Should there be a LDL treatment target in CKD and ESKD? Any role for non-statin medical therapies?
5. Is the risk of AKI and progression to ESKD a reason to withhold angiography and revascularization in otherwise suitable patients with CKD/ESKD? (e.g., PCI, CABG)
6. Are the indications for revascularization therapy in CKD different when compared with patients in whom kidney function is preserved? (e.g., elective for chronic CAD vs acute for ACS?)
7. Should multi-vessel CAD or high-risk CAD be preferentially treated with PCI in place of CABG in CKD or ESKD patients? (e.g., CABG vs PCI for left main CAD) Would treatment approach differ in patients with CKD vs. those being treated with dialysis?
8. What measures should be taken to reduce the risk of AKI in patients undergoing revascularization (e.g., PCI, CABG)?
9. Should duration of dual antiplatelet therapy be shortened in CKD patients?
10. Is coronary revascularization necessary prior to kidney transplantation in patients with prevalent CAD? If so, what is the preferred modality? (e.g., CABG, PCI)



GROUP 4: DIAGNOSIS AND TREATMENT OF PREVALENT VALVULAR DISEASE IN CKD AND DIALYSIS PATIENTS

Epidemiology

1. What are the morbidity and mortality rates for interventions in aortic stenosis (AS): TAVI vs., AVR vs., AVR + root? Compared to the general population?
2. What are the morbidity and mortality rates for interventions mitral valve disease: repair vs., MVR? Compared to the general population?

Mechanisms of Valvular Disease

3. What are the types and mechanisms of valvular disease and how do these differ in CKD/ESKD versus the general population?

Diagnosis of Valvular Disease (Including hemodynamic assessment)

4. How do we evaluate valve disease [aortic stenosis (AS)/aortic regurgitation/mitral stenosis/mitral regurgitation/ tricuspid valve disease (TR)] in the general population and are there differences that should be considered in CKD and ESKD?
5. In dialysis patients, is it important at what time in the dialysis cycle assessments are done?

Treatment of Valvular Disease

6. What are treatments of choice for patients with CKD and ESKD with valvular disease?
 - a. Medical therapy: What are the medical therapies for valvular disease and are there any differences in the general population versus CKD/ESKD?
 - b. Non-operative: What are the non-operative valve interventions for valvular disease including TAVR, mitral clip, mitral balloon valvuloplasty, tricuspid interventions and are there any differences in CKD/ESKD from the general population?
 - c. Surgical: What are the surgical therapies for valvular disease and are there differences in CKD/ESKD from the general population?
7. What are the implications for anticoagulation with choice of treatments for valvular disease?
8. What strategies should be used to prevent AKI and its sequelae during valve replacement surgery?

ENDOCARDITIS

9. What is the optimal diagnostic and therapeutic management for endocarditis in CKD/ESKD?



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GROUP 5: CAD AND VALVULAR DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

1. What are the objectives of screening for CAD prior to transplantation?
2. Which patient groups should be screened for CAD prior to transplantation?
3. What tools and research are needed to enable prediction of atherosclerotic plaque rupture in the perioperative period?
4. Should the approach to perioperative screening differ in deceased versus living donor candidates?
5. Which patients should be revascularized prior to transplantation?
6. How does delayed graft function modify perioperative risk?
7. What non-surgical therapies should be used to reduce perioperative CAD events?
8. How should patients be risk stratified after transplantation?
9. With regard to post-transplant risk, do we need to identify novel risk factors or should we simply treat patients with established risk factors better?