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## **KDIGO Controversies Conference on Central & Peripheral Arterial Diseases in CKD - Breakout Group Questions -**

### **Group 1: Cerebrovascular Disease (atherosclerotic disease as primary focus)**

1. What is the epidemiology in the context of CKD/dialysis?
  - a) What is the incident risk of stroke with CKD, proteinuria, kidney failure (i.e., ESKD), and in kidney transplant recipients?
  - b) Are eGFR, proteinuria, dialysis type independent risk factors for stroke?
  - c) What are the most frequently occurring stroke subtypes by eGFR, proteinuria, dialysis modality and in kidney transplant recipients?
  - d) Do patients with CKD get more severe strokes? Is stroke mortality higher with CKD/dialysis? Are there predictors of severity or mortality in this setting?
  
2. Can we predict stroke in CKD/dialysis?
  - a) Are there valid risk prediction tools that can be applied to CKD, dialysis populations?
  - b) Are novel population-specific prediction tools required?
  - c) What is the utility of the addition of kidney function to CHA<sub>2</sub>DS<sub>2</sub>-VASc scores (e.g., CHA<sub>2</sub>DS<sub>2</sub>-VASc-R and CHA<sub>2</sub>DS<sub>2</sub>-VAK scores)?
  - d) Should we routinely screen patients with CKD for AF?
  - e) Is there a timepoint in the course of their disease (or dialysis) that patients are most vulnerable to cerebrovascular events e.g., starting dialysis for the first time, with long interdialytic gaps?
  
3. What are the key pathophysiology and CKD/dialysis-related risk factors compared with non-CKD patients? (e.g., mineral metabolism/vascular calcification, dialysis procedure, etc.)
  - a) Do the mechanisms differ between those with and without proteinuria, and between those who are and aren't dialysis-dependent?
  - b) What is the role of hypertension?
  - c) How important are 'non-traditional' risk factors?



- d) Are there hemodialysis-specific factors in related to cerebral hypoperfusion/altered vasoregulation?
4. How best to diagnose and evaluate stroke in CKD/dialysis?
  - a) Role of imaging and biomarkers? Is there a tendency to suboptimally investigate these patients, particularly with regard to vascular or MR imaging because of concerns regarding contrast/gadolinium, or because of limiting co-morbidities/frailty (e.g., preventing the patient from lying flat for MRI etc.)?
  - b) Challenges in ascertainment of outcomes, especially in dialysis patients
  - c) How should we manage silent/incidental infarcts? What are their implications in terms of predictive ability for future symptomatic stroke risk (ischemic/hemorrhage/both), association with cognitive complaints/dementia, gait and balance abnormalities, and falls?
5. Therapies and prevention:
  - a) Is there equity in stroke care delivery in CKD?
  - b) Pharmacotherapies in acute stroke: BP management; role of thrombolysis, access to acute stroke unit
  - c) What is the safety and efficacy of endovascular and surgical interventions for ischemic and hemorrhage strokes respectively?
  - d) How should dialysis prescription be altered in the acute phase?
  - e) What are the key tenets of primary and secondary prevention?
  - f) What progress has been made since the 2016 KDIGO Arrhythmias Conference in terms of anticoagulation challenges and what is the role of a left atrial appendage occlusion device in CKD patients with AF? Are reversal agents safe in CKD and should they influence the choice of anticoagulant?
  - g) Are the outcomes of carotid interventions in advanced CKD/kidney failure (i.e., ESKD) improving?
6. What are the functional/neuropsychiatric outcomes after stroke?
  - a) Physical and functional recovery, return to independence
  - b) Neurocognitive changes
  - c) Psychiatric concerns

7. What are the short and long-term medical complications after stroke and how to mitigate
  - a) short and long-term (e.g., pneumonia, ACS)
  - b) dialysis considerations

### Group 2: Central Aortic Disease

1. What is the epidemiology of AAA in the context of CKD/dialysis?
  - a) What is the evidence for CKD as a risk factor for AAA development?
  - b) Is there any effect of pre-surgery GFR on post-surgery outcomes?
  - c) What is the association of AAA and AAA treatment with various techniques for CKD development/ eGFR loss or cardiovascular outcomes/mortality?
2. Association of central aortic disease and renovascular disease: What is the evidence of prevalence of renal artery stenosis in patients with AAA?
3. Acute kidney injury and AAA
  - a) What is the incidence of AKI after AAA? Is there a difference according to different management (open vs endovascular types? Are there other pre-disposing factors?)
  - b) What is the impact of AKI post-treatment of AAA on kidney and cardiovascular outcomes?
4. What are the potential differences in pathophysiology, natural history and risk of rupture of AAA between patients with and without CKD and between CKD stages?
5.
  - a) What are the means for diagnosis and optimal initial evaluation in CKD, including the value of duplex ultrasound, CT, MRI and angiography?
  - b) What is the optimal follow-up algorithm for post-procedure evaluation in patients with CKD?
6. What is the optimal management, indication for treatment of AAA including prevention of periprocedural acute kidney injury?
  - a) Is there a difference between modes of treatment (e.g., open surgery vs endovascular vs supra- or infrarenal graft fixation)

- b) What is the evidence on optimal peri-procedural management (including isotonic fluid administration) for AKI prevention?
7. How may management differ in special populations? (e.g., in cases of acute ruptures; care of the older adults >75 yrs)
8. What is the evidence on aortic dissection epidemiology and natural course in patients with CKD? Are there differences in optimal treatment of aortic dissection between patients with or without CKD?

### Group 3: Renovascular Disease

1. What is the epidemiology in the context of CKD/dialysis? What are the determinants of good and bad outcomes (e.g., proteinuria; kidney size)
2. What is the pathophysiology? (e.g., role of hypoxia, inflammation, etc.; novel biomarkers?)
3. What are the clinical signs associated with atherosclerotic renovascular disease (ARVD)?
4. What are the means for diagnosis and optimal evaluation, including value of duplex ultrasound, CT, MRI (non-contrast and contrast studies) and angiography?
5. Which patients should be investigated for ARVD?
6. What standard medical therapy should be given to all patients with ARVD? Is there evidence on optimal treatment in patients with both AAA and critical RAS?
7. In particular, what are the risks and benefits of renin angiotensin blockade (ACE-I or ARB) in ARVD?
8. Which cases should be selected for surgical revascularization (e.g., unilateral vs. bilateral disease, progressive CKD, etc)?

- a) What are the indications for renal revascularization treatment with angioplasty/stenting?
  - b) What are the indications for surgical revascularization?
9. How may management differ in special populations? (e.g., dialysis patients; stenoses in kidney transplants, renovascular fibromuscular dysplasia in patients with atherosclerotic disease)

#### Group 4: Peripheral Arterial Diseases

1. What are key gaps in the epidemiology of PAD in CKD/dialysis/transplant?
  - a) How to define and measure PAD in CKD for reliable epidemiological estimates? Potential of underestimating the burden of PAD in CKD.
  - b) Lacking data on PAD epidemiology in transplant?
  - c) Lacking data on patient-reported outcomes?
  - d) What are important outcomes for patients with PAD and CKD to be explored in future epidemiological studies
  - e) Sparse data on cost-effectiveness
  - f) Limited data on acute limb ischemia (ALI)?
2. What are the key pathophysiological mechanisms behind disproportionately high burden of PAD in CKD with implications on PAD diagnosis and management?
  - a) Vascular calcification
  - b) Uremic toxins
  - c) Others like inflammation, oxidative stress
3. What are the optimal approaches to diagnose PAD in CKD?
  - a) Ankle-brachial index (ABI), toe-brachial index (TBI), waveforms
  - b) Imaging
    - Modalities
    - Contrast (e.g., angiography, CT, MRI, etc.)
  - c) Who should get screened? All CKD or subpopulations (e.g., diabetes)
  - d) Should approaches differ by CKD types (e.g., dialysis or transplant)?
  - e) What is the role of biomarkers/prediction models?
4. What are key challenges in the management and treatment of PAD in CKD?
  - a) Level of evidence base for treatment of PAD in CKD/dialysis/transplant



- Statin
  - Antiplatelet
  - Revascularization
  - PCSK9 inhibitors
  - Diabetic therapy (regular foot care, a concern of SGLT2 inhibitors)
  - Lifestyle (smoking cessation)
  - Supervised exercise therapy
- b) Compliance of evidence-based treatments of PAD in CKD
- c) Amputation-related issues
- Eligibility
  - Post-amputation care
  - Role of palliative care
  - Any new treatments?
  - Podiatrists/multidisciplinary team care
- d) Any specific treatments to specific populations?
- Specific discussion about diabetes
  - Diagnostic approach
  - Regular footcare
  - SGLT2 inhibitors
  - Amputation
- e) Impact of PAD on CKD management
- Prognosis
  - Transplantability
  - Vascular access
  - Upper-extremity PAD (probably most relevant to dialysis)
  - Impact of CKD on PAD management
  - Contrast for revascularization