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KDIGO Controversies Conference on Challenges in Management of the Kidney Allograft: From Decline to Failure

Discussion Questions

Breakout Group 1: Prognosis and Kidney Failure Trajectory

1. What should be the definition of a "failing kidney allograft"? Also, should we be using KDIGO nomenclature and definitions: e.g. GFR rather than "kidney function" or "allograft function"?

2. How often should serum creatinine be measured in stable patients more than one year after transplant? Does more frequent monitoring increase adherence to immunosuppressive medications?

3. Does the eGFR formula used affect management of a transplant recipient? Are current eGFR formulas adequate in kidney transplant patients and if not why not?

4. What is the accuracy of 2021 new eGFR formula derived from native kidneys and is there any evidence on how they perform in transplanted kidneys?

5. Anti-HLA DSA screening is the currently most predictive and used "biomarker" used for screening patients for de novo DSA appearance. Is monitoring of any biomarker more effective than monitoring serum creatinine? What is the role of cell-free DNA? Gene expression profiling? Protocol biopsy?

6. Which transplanted populations should be screened for subclinical rejection?

7. What is the evidence that treating chronic active AMR is safe and effective? What is the evidence that treating chronic TCMR and/or subclinical TCMR is safe and effective?

8. Is “death with function” a premature death with stable kidney function?

9. What is the role of proteinuria for prognostication?

10. Is AI-based multimodality combination of functional, structural, immunological parameters able to achieve high performance for allograft outcome prognostication?

11. Strategies for preserving residual kidney function: What is the evidence that novel therapies that slow CKD progression (e.g., SGLT2i, MRAs) are safe and effective in kidney transplant recipients? Role of metformin?

12. What should be the role of iBox and other pronosticators?

Breakout Group 2: Immunosuppression Strategies

1. What are the critical overarching considerations regarding immunosuppressive (IS) treatment in this patient population?
    a. What are the considerations for a patient with a failing allograft in terms of IS management?
        - Residual allograft function? Side effects and toxicities such as infection and malignancy? Development of chronic inflammation and need for nephrectomy? Risks of nephrectomy? Candidacy for next transplant? Availability of a living donor? Sensitization status?
    b. Should the timing of detection of failure be a major consideration?
        - Early versus late, or as defined by an eGFR threshold
    c. Does age play a role: Should there be different considerations for pediatrics vs adults vs elderly adults?

2. How do we consider specific immunosuppression management?
    a. Can we prevent HLA sensitization and/or nephrectomy by continuing IS?
        - What IS (type, dosage, and level) is needed to prevent sensitization?

b. Is it safe to maintain IS after graft failure? Is there an increased frequency of infection and malignancy?
c. What are the risks of IS withdrawal? Is there an increased frequency of rejection, chronic inflammation or need for nephrectomy?
    - How should IS treatment decisions affected by transplant nephrectomy?
d. Are there specific agents that may be more harmful (or more effective) in failing allografts?
e. What criteria (e.g., age, transplant history, presence of donor specific antibodies, re-transplant candidacy, availability of living donor, residual function, diuresis, timing after return to dialysis, type of dialysis modality) can guide risk stratification for maintaining IS?
f. What criteria (eGFR, diuresis, transplant history, can guide order and timing of immunosuppressive withdrawal?
g. Are patients adherent to IS treatment after graft failure?
h. What monitoring strategies are needed to guide and adjust IS (drug levels, lab values, side effects, diuresis, inflammation, PRA, biomarkers)?

3. How may clinical IS management in this patient population be facilitated?
    a. Who should be taking the lead for management?
    b. How is integration with community physician or general nephrologist managing CKD occur?
    c. How is this management plan integrated into their health care?
    d. How frequently should the visits be for IS management? When should drug levels be checked?
    e. Can care be expedited/integrated using telehealth approaches?

Breakout Group 3: Management of Medical and Psychological Complications in Kidney Transplant Recipients

1) What is the preferred model of care to manage these complex patients? Refer to general nephrology multidisciplinary (MDC) clinics, routine transplant care or create special MDC transplant clinics for failing transplant recipients?
    a) Are patients managed by the transplant team until graft loss and beyond?

b) Do transplant teams have the expertise and time to reach recommended CKD/CVD and diabetes care targets?
c) Do they refer patients to back to primary nephrologist/dialysis center before graft loss?
d) What level of renal function (who should be referred) trigger referral to an MDC? What disciplines are required for an effective MDC?

2) Scope of Care for an MDC
   a) Would an increase in clinic patient visits/frequent nurse contact help prevent AKI/hospitalizations and reduce mortality and improve psychologic wellbeing?
   b) Would increase patient contact help facilitate patient decision making for transition to dialysis/modality choice/conservative care/palliative care?
   c) Can telehealth or other platforms help deliver care to these complex patients?

3) What are the different potential MDC models?
   a) What are their benefits and limitations?
   b) Should there be a shared coordinated care with other specialty clinics in selected patients (for example heart failure clinics, diabetes clinics) or should these MDCs broaden their scope of practice?

4) What types of psychological problems are experienced by this cohort and what types of interventions should be considered?

5) Are there unique challenges facing patients and physicians with a failing transplant compared to a cohort with progressive native kidney disease?

6) Is there a role for additional training to the providers on how to take care of patients with a failing graft?
   a) How should peer support interactions be facilitated by the MDC?
   b) What type of care should be included? Role of ancillary testing? What would routine screening for depression, frailty, and cognitive decline in performance provide for these patients and their health care team?

7) Goals of Care

a) Is there new evidence to challenge standard guidelines recommendations for the management of CKD (anemia, blood pressure, cardiovascular disease) in the general population?

8) How do you measure performance of MDCs in transplantation?

Breakout Group 4: Recognizing Graft Loss: Patient Factors and Kidney Replacement Therapy

1. How do we define the "failing graft"?
    a. Is this defined as a specific percentage rise in creatinine alone or is there a better marker to define when to increase follow-up?
    b. If a graft is defined as failing, should the patient return to the transplant center if in the community or how does the patient transfer back to the original referring nephrologist?
    c. What is optimal schedule for follow-up and what specific tests should be ordered? Biopsy, imaging, CKD labs?
    d. Are there ways to delay the onset of failure or to slow the progress to failure?

2. How do we prepare the patient for a relisting and/or return to dialysis?
    a. Should there be ongoing education about the potential for graft loss even immediately after transplant?
    b. What should patients be told about saving dialysis access sites after transplant?
    c. Are there services to assist patients with their loss? Social workers, healthcare navigators, emotional support staff, insurance and financial coordinators? How are patients put in touch with these resources? Who will pay for these services?
    d. Who should initiate the conversations about the need to return to dialysis? Is CrCl of 20 an appropriate marker for listing for re-transplant?

3. What are the ways to assess patients for retransplant in a fair, transparent and uniform way?
    a. With the legalization of marijuana, is it appropriate to list or relist patients with significant marijuana use? What defines "significant"?

b. Are there different ways to address patients who recognize the role of non-adherence vs those that do not?
c. Prior studies have shown high failure rates in patients who are re-transplanted who had documented non-adherence. Should the transplant centers have special requirements and how would they be applied fairly?
d. Should there be uniform standards considered for re-transplantation?
e. Should patients be encouraged to seek out a living donor or be required to find a living donor for retransplant?

4. What are the considerations for optimal KRT planning? Factors to consider include: re-transplant listing criteria or return to dialysis (e.g., timing of initiation, modality selection; optimal dialysis access and fistula creation; role of residual kidney function?

5. When do we consider conservative care as the appropriate option? How can we optimize the provision of supportive care, social care (e.g., workplace, etc.)?

6. Should transplant nephrologists be involved in monitoring graft function after return to dialysis, or are we "giving up" on the graft at that point? How often should the graft be monitored after return to dialysis? Should dialysis prescription be altered based on degree of graft function?

7. Are there specialized needs required in specific populations such as older adults, pediatrics, women?