Evaluation of the candidates for kidney transplantation, special population

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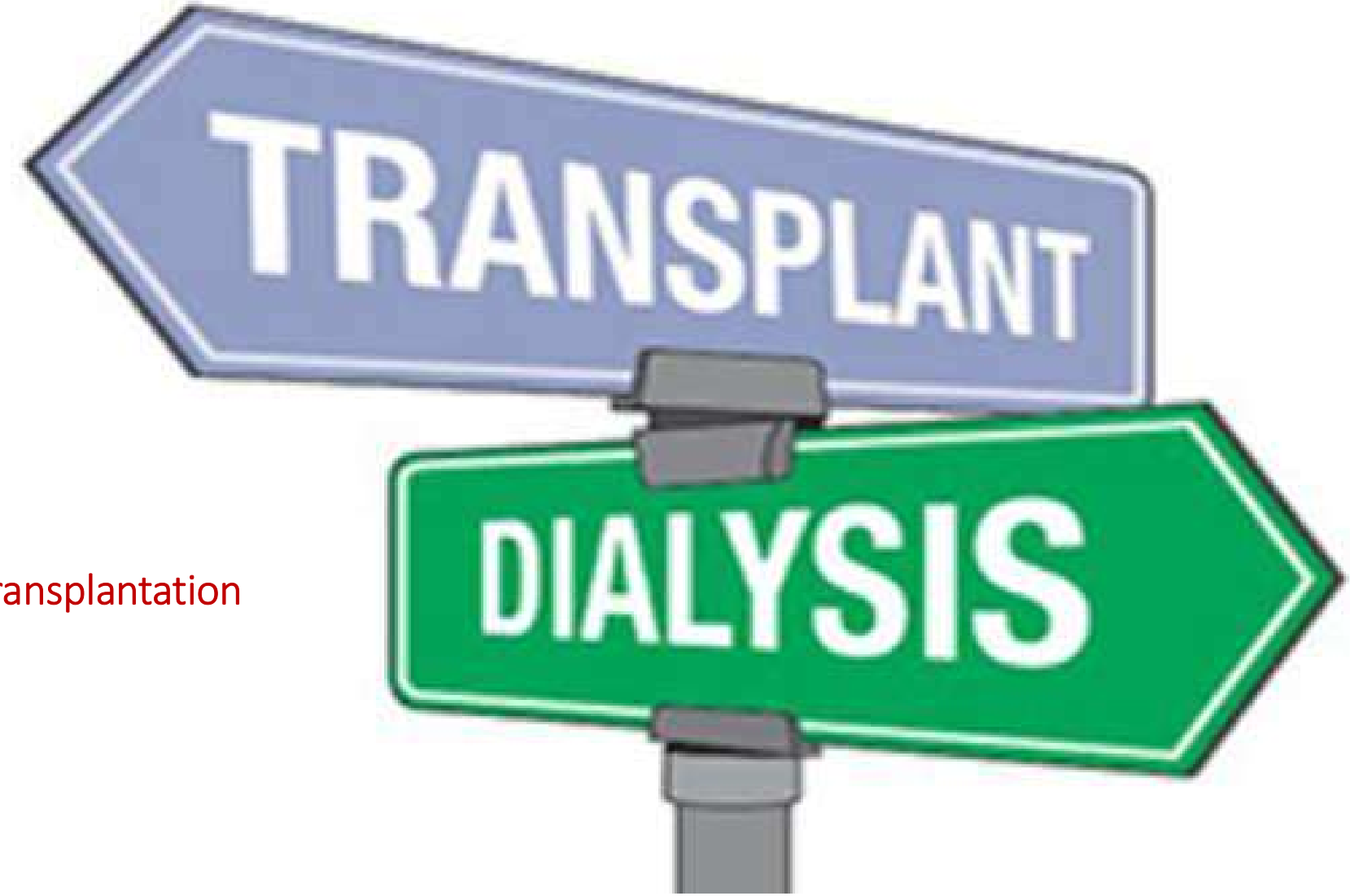

pre-emptive transplantation

- Preemptive kidney transplant is considered the preferred treatment for end-stage kidney disease, but only about 10-20% of kidney transplants are performed preemptively in the U.S.
- In 2019, 11% of all adult deceased donor kidney transplants (1,859) were preemptive.

Am J Transplant. 2021;00:1–10.

April 2020 ■ Volume 104 ■ Number 4S

Official Journal of
The Transplantation Society &
International Liver Transplantation Society

Transplantation®

KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation

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SECTION 1: ACCESS TO TRANSPLANTATION

1.1: We recommend that all patients with chronic kidney disease (CKD) G4-G5 (glomerular filtration rate [GFR] < 30 ml/min/1.73 m^2) who are expected to reach end-stage kidney disease (ESKD) (excluding those listed in Rec 1.1.3) be informed of, educated about, and *considered* for kidney transplantation regardless of socioeconomic status, sex, gender identity, or race/ethnicity *(1D)*.

1.1.1: Refer potential kidney transplant candidates for evaluation at least 6 to 12 months before anticipated dialysis initiation to facilitate identification/work-up of living donors and plan for possible pre-emptive transplantation *(Not Graded)*.

1.4: We recommend pre-emptive transplantation with a living kidney donor as the preferred treatment for transplant-eligible CKD patients *(1A)*.

1.4.1: We recommend pre-emptive transplantation (living or deceased donor) in adults when the estimated glomerular filtration rate (eGFR) is < 10 ml/min/1.73 m^2 or earlier with symptoms *(1D)*.

1.4.2: We recommend pre-emptive transplantation (living or deceased donor) in children when the eGFR is < 15 ml/min/1.73 m^2 or earlier with symptoms *(1D)*.

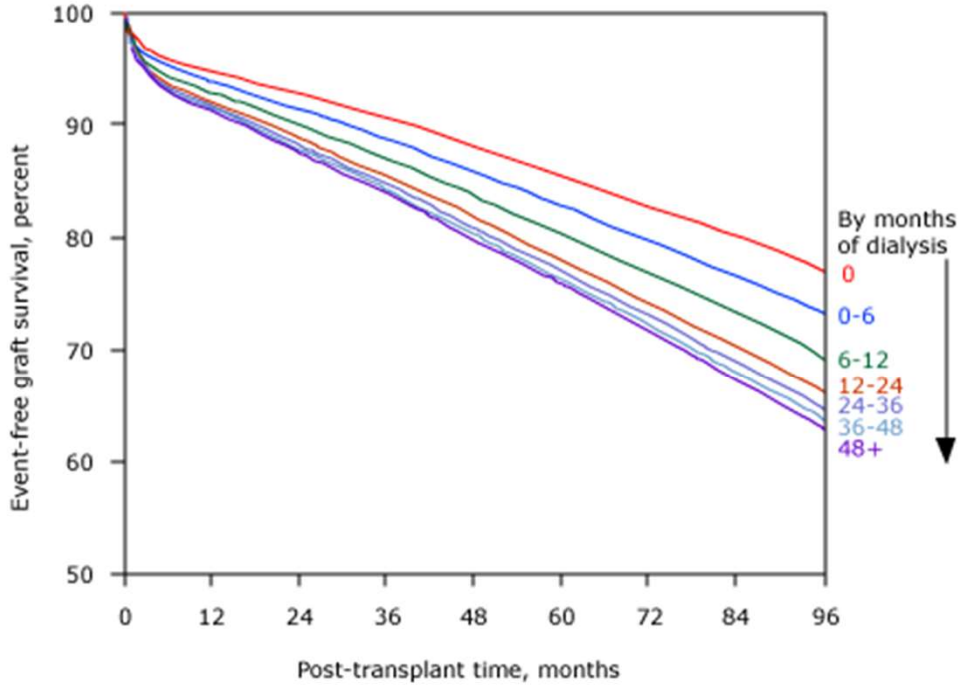
- Pre-emptive transplantation is the preferred treatment option but requires sufficient time to ensure a complete evaluation, and in many regions is restricted to those with a suitable living donor.
- The timing of pre-emptive living donor transplantation needs individual decision making depending on patient's symptoms and estimated GFR (eGFR).

  Candidacy assessment is to some extent subjective; those declined should have the right to seek a second opinion.

- Potential candidates should begin the evaluation process at least 6 to 12 months before the anticipated start of kidney replacement therapy.
- Earlier evaluation may render some of the diagnostic tests outdated while a delay might lead to an incomplete work-up and miss the opportunity for pre-emptive transplantation.
- When a live donor is available or where pre-emptive deceased donor transplantation is possible, cases should proceed when the eGFR is <10ml/min/1.73 m^2 (10 to 15ml/min/1.73 m^2 in pediatrics).
- Optimal timing, however, depends on factors other than GFR such as the pace of renal decline, presence of symptoms and living donor preferences

- Educate When GFR<30
- Modality Selection When GFR<20

Comparison of renal allograft survival according to months on dialysis



Data from: Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: A paired donor kidney analysis. Transplantation 2002; 74:1377.

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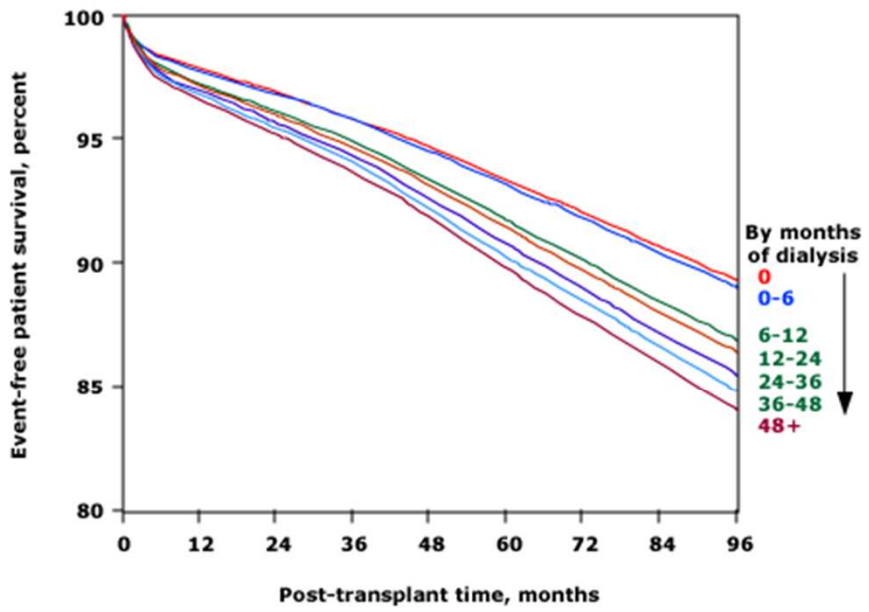
Comparison of renal transplant recipient survival according to months on dialysis



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Effects of pretransplant dialysis modality on outcomes early vs late after kidney transplantation

Posttransplant period	Relative risk (95 percent CI) PD:HD		
	Graft failure	Death-censored graft failure	Death
During the first three months	1.23 (1.09-1.39)*	1.33 (1.16-1.53)¶	1.03 (0.81-1.3)
Beyond the first three months	0.96 (0.87-1.05)	1.02 (0.89-1.16)	0.91 (0.8-1.04)

PD: peritoneal dialysis; HD: hemodialysis.
* $p<0.001$.
¶ $p<0.0001$.

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- Preemptive transplantation is generally preferred because it leads to substantial improvements in graft and patient survival when compared with transplantation after a period of dialysis therapy
- In a study of nearly 40,000 primary kidney transplant recipients, those undergoing preemptive transplantation had 25 and 27 percent reductions in the relative risk for graft loss for deceased- and live-donor transplants, respectively Corresponding risks for patient death were reduced by 16 and 31 percent.
- In an analysis of 7948 patients identified from the Dutch National Organ Transplant Registry, the 10-year survival was greater among patients who underwent a preemptive living-donor kidney transplant compared with patients who had a deceased-donor transplantation after a median time of three years on dialysis (73 versus 45 percent, respectively). Compared with wait-listing on dialysis, the patient survival benefit with preemptive transplantation was approximately 7.5 to 9.9 years for 40-year-old patients and 4.3 to 6 years for 70-year-old patients.

- The amount of time that a patient spends on dialysis prior to transplantation is directly related to increased mortality, suggesting a dose-dependent effect of dialysis.

- Improved graft and patient survival associated with preemptive transplantation may be related to decreased rates of delayed graft function and biopsy-confirmed acute rejection for both deceased-donor and living-donor transplants.
- In addition, relatively lower clearance provided by dialysis, compared with a transplanted kidney, may cause the accumulation of substances associated with atherosclerosis, malnutrition, and chronic inflammation.

- Despite its demonstrated benefit, only approximately 20 percent of living-donor and 5 percent of deceased-donor transplants are performed preemptively in the United States.
- This is primarily due to the rapid increase in the number of potential transplant candidates without a commensurate increase in the donor pool. As a result, the waiting time for a deceased-donor kidney has dramatically increased over the last 15 years.

Exemptions

- Patients with severe nephrotic syndrome may benefit from dialysis prior to transplantation with the expectation that residual kidney function, and thus nephrosis, will decline significantly.
- This is because severely nephrotic patients are hypercoagulable.
- Hypercoagulable patients who undergo transplantation are more likely to thrombose the transplanted kidney if they undergo preemptive transplantation.
- By contrast, dialysis tends to decrease the thrombotic tendency associated with nephrotic syndrome
- The optimal method to otherwise decrease severe nephrosis before kidney transplantation (eg, nephrectomy, embolization, or medical nephrectomy) remains unclear.
- Patients who are receiving their second transplant after the first transplanted kidney has failed within one year may also benefit from a short period of dialysis before the second transplantation.

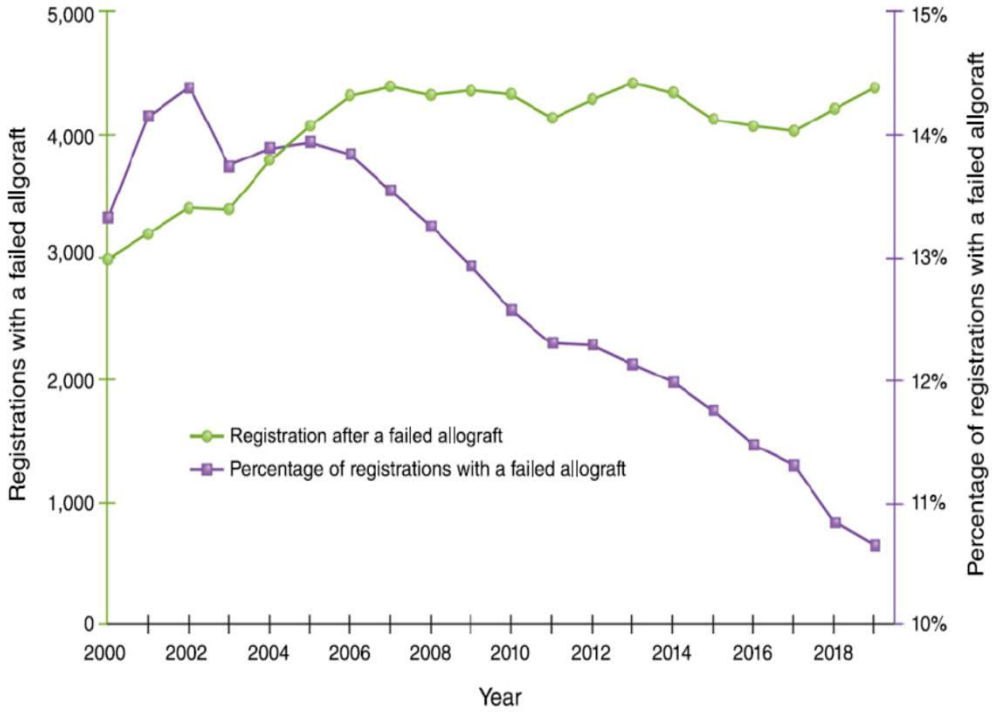

Figure 2. | Percentage of waitlist registrations for candidates with failed (or failing) allografts have decreased over time.

WHAT ARE THE CONSIDERATIONS FOR OPTIMAL KRT PLANNING? INTRODUCTION

- Kidney allograft failure is a period of higher risk of mortality compared with other transition periods for patients with ESRD.
- Patients with failing allograft experience irreversible and progressive decline in kidney function with anticipated allograft survival of less than 1 year, and return to renal replacement therapy or they already initiated RRT.
- Early recognition of kidney transplant recipients with failing allograft allows appropriately plan for transition of care, dialysis initiation, listing for re-transplantation or conservative/palliative treatment.

WHAT ARE THE CONSIDERATIONS FOR OPTIMAL KRT PLANNING? TRANSITION CONSIDERATION

Coordination between transplant and referring nephrologists is an integral part to managing the failing allograft and ensuring that both CKD management, initiation of dialysis and timely referral for re-transplantation are patient-centered and best address the needs of each individual patient.

Planning further renal replacement therapy they should consider the various issues, medical, surgical, psychological and social and it includes:

- Patient and family education about RRT methods (retransplantaion, HD, PD, palliative care/conservative)
- Timely preparation for kidney replacement therapy, dialysis access (fistula/ tunneled central venous catheter / Tenckhoff catheter)
- Referral to the transplant center for evaluation (pre-emptive re- transplantation / transplantaion after initiation of dialysis)

KIDNEY DISEASE · KDIGO · IMPROVING GLOBAL OUTCOMES

A. RE-TRANSPLANT LISTING CRITERIA - A CANDIDATE FOR RE-TRANSPLANT

Re-transplantation offers the most survival benefit to patients with failed transplants and pre-emptive renal re-transplantation is the best in order to minimize the morbidity associated with dialysis re-initiation. If patient already initiated dialysis he should undergo evaluation for transplantation*

Considerations of patients with a failed allograft not yet on dialysis

- Refer pre-emptively for waiting list when eGFR approaches 20ml/min
- Identification of potential living donor
- Referral for dialysis (HD/PD) access creation if there is no living donor
- Consider reduction in immunosuppression to decrease side effects and complications

Patient already on dialysis

- Refer for waiting list if applicable
- Tapering of immunosuppression
- Identification of a potential donor

B. RETURN TO DIALYSIS – NOT A CANDIDATE FOR RE-TRANSPLANT

Stable transplant function, eGFR >20 ml/m^2

- Establish joint management nephrology unit
- Optimal CKD management including BP control, anemia, proteinuria, secondary hyperparathyroidism, cardiovascular issues, malignancy surveillance etc.
- Close monitoring of levels of immunosuppression and side effects

Failing transplant with declining function

- Establish dialysis method and create appropriate dialysis access
- Reduce immunosuppression over time
- Monitor graft function and lab/clinical symptoms in order to initiate dialysis at optimal time
- Consider conservative/palliative medical care if applicable

Patient already on dialysis

- Tapering of immunosuppression

Preparation for Retransplant Listing

- Education of Tx Nephrologists
- Early recognition/referral
- Maximize CKD care
- Consideration for dialysis modality

B. RETURN TO DIALYSIS - TIMING OF DIALYSIS INITIATION

- There are no specific guidelines to the timing of dialysis initiation based on eGFR after graft failure. Studies in transplant-naive patients with CKD might not be generalizable to patients with a failed renal allograft. \
- Unique factors associated with a failed allograft (i.e. immunosuppression, inflammation, sarcopenia) and long lasting RRT, means that the optimal timing of dialysis initiation in failed transplant patients might differ from that in transplant-naive patients.
- We recommend the timing of dialysis initiation based on clinical factors and symptoms related to CKD progression rather than eGFR evaluation alone.
- Filtration impairment and interstitial damage do not go parallel - uremia symptoms (anemia, overhydration, acidosis etc.) may appear at higher eGFR. eGFR may by higher as a result of low creatinine caused by sarcopenia.

B. RETURN TO DIALYSIS - **MODALITY SELECTION**

- There is no proven benefit of either HD or PD after failed allograft.
- Choice of dialysis modality after graft failure should be based on the clinical characteristics of kidney transplant patients since no clear and definitive evidence is available in the scientific literature.
- Patients with planned re-transplantation (particularly from a living donor) may benefit from PD treatment since it seems to be associated with better outcomes in the early period after graft failure.
- Patient should have a choice. Patients on PD before transplantation often chose the same modality after graft failure.

B. RETURN TO DIALYSIS - **OPTIMAL DIALYSIS ACCES AND FISTULA FORMATION 1**

- After establish dialysis modality, an appropriate dialysis access should be created and it could be either fistula or tunneled catheter.
- The current KDOQI 2020 (Kidney Disease Outcomes Quality Initiative) clinical practice guideline for vascular access recommends moving away from a "fistula first" approach in favor of a patient centered ("patient first") approach to vascular access planning and management.
- In patients with failed graft not a candidates for re- transplant age and frailty may determine type of vascular access.
- Candidates for transplant with estimated short waiting time may start on tunnelled catheter.

B. RETURN TO DIALYSIS - **OPTIMAL DIALYSIS ACCES AND FISTULA FORMATION 2**

- Delivering a more individualized approach to vascular access in the KDOQI-advocated "life plan" requires consideration of access options based on an individual's personal circumstances, needs, and preferences, as well as application of the best evidence to guide optimal outcomes.
- Age has been used as a guide to access choices, but applying frailty assessments may allow to even better identify individuals who may or may not benefit from a particular access creation type (high risk of failure to mature).
- Ultimately such an approach may show frailty to be a key component in individualizing vascular access planning and ultimately fulfilling the aspirations of the failing graft life plan.

B. RETURN TO DIALYSIS - RESIDUAL GRAFT FUNCTION

- Although residual renal function is known to be beneficial in dialysis patients, no such advantage has been demonstrated in those with failed allograft.
- There is no data to support the hypothesis that low-dose immunosuppression will prolong residual renal function in dialyzed patient.
- There is some weak evidence to support its continuation in patients returning to peritoneal dialysis.
- For patients with a failing allograft not yet requiring dialysis maintaining residual graft function is still essential because they avoid dialysis.

Candidacy and Residual Function

- Consider formal Frailty assessment prior to retransplantation
- Based on candidacy, determine immunosuppression management
- Role of alteration of dialysis prescription (??)

Considerations in re-Listing work-up

- Frailty
- Cardiac decline/CHF
- Adherence
- Outcome of previous allograft
- Cancer risk?