Ethics in Pediatric Kidney Transplantation

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Disclosures

I have no disclosures to report

Objectives

1. Review the principles of bioethics

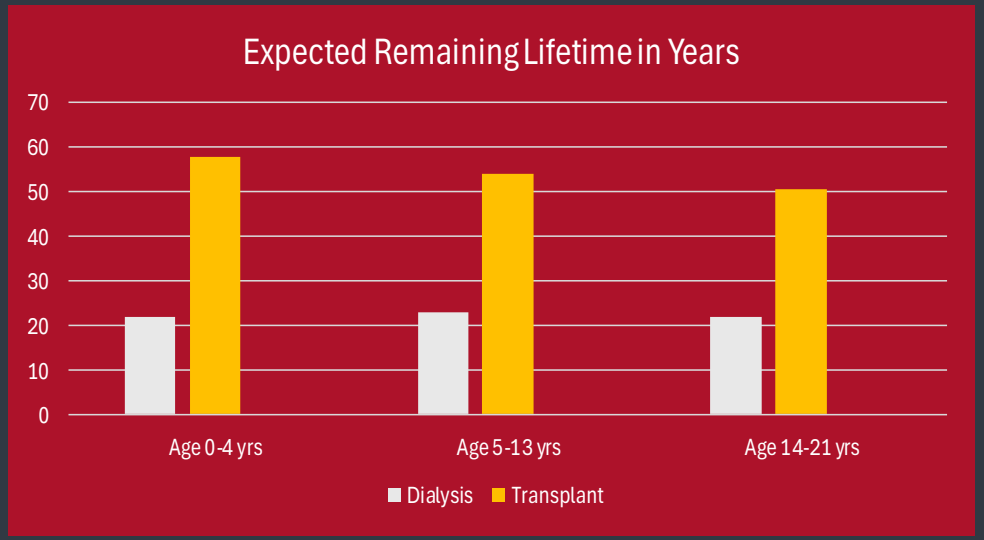
2. Discuss two ethically challenging cases involving pediatric kidney transplantation

3. Explore the evidence for if these challenges should limit transplant eligibility

Benefits of Kidney Transplantation for Children

Optimal therapy for children and adolescents with kidney failure

- Survival advantage of 25 to 35 years compared to dialysis
- Improved quality of life
- Improved linear growth
- Improved cognitive development
- Decreased cardiovascular disease
- Decreased overall medical cost compared to dialysis



Gap between supply and demand of kidney transplants is a chief contributor to many ethical debates in the field

USRDS Annual Data Report

PRINCIPLES OF ETHICS

AUTONOMY

Duty to respect a patient's right of self-governance

BENEFICENCE

Duty to maximize benefits and to enhance a patient's wellbeing

NONMALEFICENCE

Duty to avoid causing harm and to minimize harm to the patient

JUSTICE

Duty to treat patients fairly and equitably

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PRINCIPLES OF ETHICS

AUTONOMY

BENEFICENCE

NONMALEFICENCE

JUSTICE

UTILITY

Effort to maximize the good to the individual and society with each transplanted organ

BEST INTEREST

Prioritize the wellbeing of the child

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Case 1

Transplant

13 yo male with ESKD secondary to ANCA vasculitis managed with hemodialysis receives a deceased donor kidney transplant

First 6 months

Concerns for nonadherence

- Low tacrolimus levels
- Late labs
- Missed visits

Social concerns:

- Patient now living between two households
- Transportation issues
- Patient noted to have minimal adult supervision with medication
- Patient expresses desire for independence in medical care

Transplant

13 yo male with ESKD secondary to ANCA vasculitis managed with hemodialysis receives a deceased donor kidney transplant

First 6 months

Concerns for nonadherence
Social concerns

11 months

Creatinine 3mg/dl (baseline of 0.6mg/dl) & new strong class II DSAs

Biopsy: cellular rejection 1B and antibody mediated rejection

Transplant	13 yo male with ESKD secondary to ANCA vasculitis managed with hemodialysis receives a deceased donor kidney transplant
First 6 Months	Concerns for nonadherence Social concerns
11 Months	ACR & AMR
30 Months	Biopsy demonstrates transplant glomerulopathy with significant interstitial fibrosis/tubular atrophy
33 Months	Graft Failure

Transplant | Graft Failure | Dialysis | Transplant Referral

Given that kidneys are scarce resources, should this individual patient be offered transplant from the perspective of organ stewardship and justice?

Should transplant eligibility hinge on prior nonadherence?

Should the rules for a second transplant be stricter if the initial graft was lost due to nonadherence?

Is it in the best interest of the patient to receive a second transplant in adolescence or wait until adulthood?

Nonadherence

- Adolescents have the highest rates of nonadherence among kidney transplant recipients at 40%[1]
- Barriers to adherence are reported by 43% pKTR and 34% caregivers[2]
- Medication nonadherence has consistently been associated with higher rates and faster progression of graft failure
- Adherence is difficult to measure

Multifactorial Contributors to Nonadherence

Risk factors in adolescence

- Lower parental supervision
- Peer pressure
- Increased propensity to risk taking
- Immature cognitive reasoning
- Feeling of invincibility
- Presence of neurocognitive dysfunction from CKD

1.Dobbels et al, Ped Transplant 2012; 2. Varnell et al, Ped Transplant 2017; Figure: Nevins et al, J AM Soc Nephrol 2017

Argument against re-transplantation	Arguments in favor of re-transplantation
Organ scarcity	Retransplant in kidney transplant is more cost-effective and has better outcomes than dialysis
Principles of justice and utilitarianism in patient care	Principles of non-maleficence, benevolence, and equity
Past non-adherent behavior is a predictor of future behavior[1,2]	Evidence shows that behavioral change is possible[5,6]
Outcomes after re-transplantation are inferior to outcomes after primary transplant[2,3]	Patients admitting to be non-adherent cannot be punished for their honest
Adolescence and transition to adult care is a high-risk period.[4]	Risk factors for non-adherence can be addressed[7]

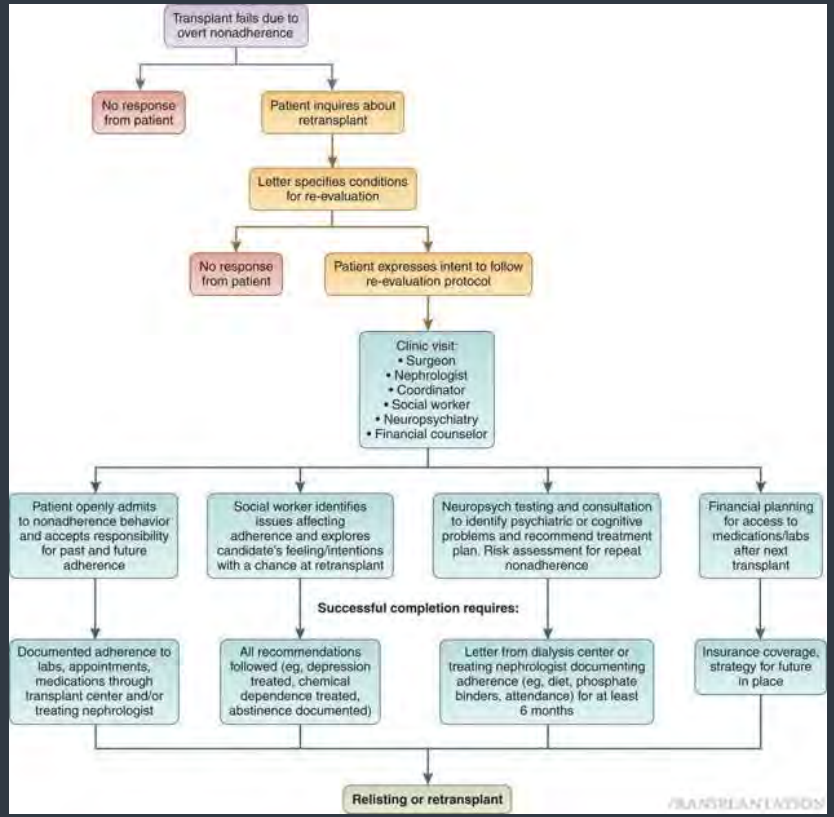
1. Dunn (Am J Transplant 2009); 2. Akpinar (Transplant 2009), 3. (Marcen (Transplant Rev 2008), 4. Kindem (Transplant 2023), 5. Haynes (Coch Data Syst Rev 2008), 6. De Bleser (Transpl Int 2009), 7. Foster (AJKD 2018)

KDIGO: Candidates with a history of nonadherence should be considered for transplant unless ongoing, health –compromising behavior

AST: considering delaying transplant for patients who continue to demonstrate poor adherence despite intervention

Recommendations

- A pre-transplant assessment aimed at identifying risk factors
- Patients receive adherence education and counselling
- All modifiable risk factors resulting in nonadherence be addressed prior to relisting



KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation
(Chadban etal, Transplantation 2020)

Transplant → Graft Failure → Dialysis → Transplant Referral

2.7 years

Social: CPS report filed, placed in foster care
Psychosocial: Assessment completed, education and behavioral interventions applied
Mental health: Depression addressed, attends weekly psychotherapy sessions
Medical: Demonstration of dialysis and medication adherence
Developmental health: 11th grade, cognitive testing performed

As behavior can be improved with focused intervention and risk-factors can be addressed, denying re-transplant to a child based on non-adherence may not be appropriate

Denying transplant on the basis of possible future challenges is not ethically supported

Decision Made to List for Transplant

Case 2

2 year old male with ESKD secondary to congenital cystic dysplasia is referred for kidney transplant.

Patient has been on chronic peritoneal dialysis since DOL 7 with multiple complications including:

- Peritonitis and line associated infections
- Ischemic brain injury and seizures
- Mild-moderate developmental delay
- Growth delay

Patient received initial hepatitis B vaccine but since then has not received any additional immunizations due to family's personal objections

Should we proceed with transplant listing if vaccine schedule is not complete?

Is the risk of the child remaining on dialysis greater than the risk of a vaccine preventable illness?

Should the child be punished with dialysis for their parent's choices?

If the parents refuse medical recommendations for immunization, will they not follow other medical advice following transplant?

Vaccines

- Vaccination prior to transplant offers the best change of developing immunity
- Transplant recipients are at greater risk for acquiring vaccine-preventable illnesses and their sequelae
- Live virus vaccines are safest to give prior to transplant

- Current state of vaccination
  - Childhood vaccination rates remain below pre-pandemic levels
  - Rising rates of vaccine hesitancy
  - Hesitancy linked to ideas about bodily autonomy, parental authority, and mistrust of science

Risks Associated with Vaccine Refusal

Recipient

- Increased risk for vaccine-preventable illnesses and sequelae
- Risk of non-adherence to other therapies and sequelae

Other patients

- Risk of transmission to other transplant recipients in clinic

Institution

- Risk of transmission to medical staff
- High cost and limited availability of post-exposure treatments for staff

Graft

- Risk of graft failure or dysfunction from vaccine-preventable illnesses or nonadherence to other therapies
- Missed opportunity to allocate to another recipient with potentially better risk profile

Risks Associated with Dialysis

Cardiovascular disease

Neurocognitive deficits

Poor growth

Higher cost

Decreased survival

Kates et al, Curr Opinion Organ Trans 2022

Is it appropriate to deny solid organ transplantation on the basis of vaccine refusal?

Arguments in Support	Arguments in opposition
Beneficence: Benefits the patient by protecting the patient and their graft from complications of vaccine-preventable illness	**Non-maleficence**: Inability to access a transplant causes immediate, severe, and irreversible harm to patients who refuse vaccination
Beneficence: Maximally protects others in the clinical environment, including transplant patients, other patients, and healthcare staff. Avoids negative impact on performance metrics and transplant center liability	**Autonomy**: Achieving vaccination through coercion risks damaging the provider–patient relationship, the family unit, and the public perception of vaccination
Utility: Maximizes the benefits of organ transplantation, gives a scarce resource to who have maximized their health	**Justice**: Creates additional barriers to transplantation for patients from marginalized groups
Justice: Is consistent with OPTN recommendations that “serious, consistent, and documented non-compliance” be considered in listing decisions	**Respect**: Assumptions about adherence to other recommendations apart from vaccination, and fails to respect patients’ reporting of their intentions

Guidance

American Society of Transplantation (AST) and American Society of Transplant Surgeons (ASTS) recommend vaccinating pediatric transplant candidates

- Not endorsed vaccine mandates or dismissing children whose parents refuse to vaccinate

American Academy of Pediatrics (AAP): recommend vaccinating transplant candidates

- Pediatricians may consider dismissal of families who refuse vaccination

Other pediatric transplant centers

Recommendations for Transplant Evaluation

- Perform a detailed immunization history and serologic evaluation
- Candidates should be evaluated by an infectious disease physician
- Counsel candidates on importance of vaccination and added benefits of competing vaccination before transplant
- Educational materials should be provided and available in multiple languages
- Transplant centers seek to understand reasons for vaccine refusal
- Correct any misinformation or misperceptions
- Approach with compassion and interest in education over punishment
- Use non-coercive measures
- Reduce other barriers to vaccination
- Collaboration with dialysis team and pediatrician

Outcome: family agreed to vaccines

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