

Ethical Challenges for Kidney Transplant in Children with Multiple Co-morbidities

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1

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2

Case Vignette

- A 5-year-old girl with Jeune syndrome and ESRD secondary to NPH comes for TX evaluation
- On HD for 3 years, HD catheter in left femoral for ~ one year which is her last access
- Doing well without any major problems
- PD not an option:
 - Respiratory status may worsen due to PD
 - Psychosocial concerns

3

Other Co-morbidities

- **Ventilator Dependence:** For 3-1/2 years
 - On significant vent support
 - Rib expansion surgery refused by family as it could not guarantee withdrawal of vent support
 - Possible increase in vent settings with growth
 - Long-term survival unclear
- Not a lung Tx candidate



4

Other Co-morbidities

- **G tube Dependence:** For caloric needs
- **Physical /Cognitive Development:** Interactive, understands most commands, can speak few words, able to sit but not stand or walk, very limited vision
- **Social Support:**
 - Lives at home with her mother and younger healthy brother
 - Family is here illegally but child born here
 - Mother does not speak English or drive and uses medical transportation
 - Father not involved in care, but part of all major decision making
 - Live in public housing with limited space. No other help available
- **Life expectancy:** Prognosis variable, little long term data
- No patients reported living beyond 20 years of age

Am J Med Genet A. 2011 May;155A(5):1021-32.

5

Ethical Dilemmas

- Family does not request TX & fearful of surgeries
- Is chronic vent dependence a contraindication to TX?
- Is limited life expectancy a reason to decline TX?
- Given shortage of DD, is it ethical to give her a TX?
- Should the family pursue LD?
- If she receives TX now, would she be a candidate for re-TX?
- Should thoracic expansion be mandatory prior to TX?

6

Current Challenges

- Children with extreme prematurity, genetic syndromes, and multiple comorbidities (including neurodevelopmental delay) are surviving with improved technologies
- Some develop ESRD
- ~16% of these have some intellectual disability*
- The optimal approach to Tx in children with comorbidities is unknown since no consensus guidelines
 - *Wightman et al. Pediatr Transplant. 2014 Nov;18(7):714-9

7

What are the Challenges?

- Children with isolated intellectual disabilities (ID)
 - Mild, Moderate-severe MR
 - Persistent vegetative state or minimal consciousness state
- Children with ID and physical/developmental disabilities
 - A 12 year old with MR, who can't sit and is blind
 - A 14 year old who has CP, moderate-severe MR, GT and CIC dependent
- Children with multiple comorbidities and shortened life-expectancy
 - A child who is chronic vent. dependent
 - A child with liver, intestinal and or heart failure
 - ESKD a part of genetic syndrome affecting multiple organs
 - High risk of recurrent cancer- in remission

8

Why is it Challenging?

- Uncertain outcomes:
 - Constant advances in technology and medicine whereas knowledge is based on retrospective data
- Severe shortage of organs:
 - If there were an ample supply of organs, everybody could be a TX candidate
 - Small risk to LD in case of questionable benefit to recipient

9

Historical Context

- Children with intellectual disability were denied access to TX
 - Reduced life expectancy and lack of improvement in QOL
 - Lack of cognitive ability to comply with complex post-TX therapy
- **Low IQ as a contraindication to TX**
 - **1993 survey of 411 Tx centers:**
 - 54% centers considered IQ <70
 - 76% centers considered IQ <50
 - **2005 survey of pediatric TX centers:**
 - 56% centers considered IQ <35: relative contraindication
 - 40% considered an absolute contraindication
 - Some centers considered organ TX only if there was a LD

10

Ethical Concepts

- Futility
- Equity
- Utility

11

Futility: Story of Sisyphus



12

Medical Futility

- Therapy considered futile because it would not improve patient's condition according to existing data
- Medical futility is ethically controversial and poorly defined
- No statistical threshold for a treatment to be considered futile
- Often serious disagreement regarding the benefits of a therapy
- Conceptualized as a power struggle for decisional authority

13

Addressing Futility Disputes

- Optimize communication
- Provide frequent prognostic estimates
- Address emotional needs and understand family's perspective and reasons behind futile requests
- Assure that patient will not be abandoned
- Doing nothing is **NOT** an option and simply being there is an option
- Facilitate excellent palliative care
- Offer a time limited treatment trial with a mutually agreed-upon endpoint

14

Is Transplant Futile?

- ESKD is a life-long condition and TX is not a cure
- TX does not often cure/improve other problems
- *Medical professionals have moral obligations to extend life and relieve suffering*
- *Recognize limitations of TX in meeting these ends in everyone*
- Therefore, TX not a universal option

15

Equity

- "The individual right approach"
 - Each individual should have equal access to health care and equal outcome
- What does equal access mean?
 - Does it mean that everyone gets a fair shot at TX?
 - Does it mean you have same waiting time with same medical info. if you live in DC vs. California?
 - Does it mean everyone gets an organ X amount of time regardless of blood type and PRA?

There are different perspectives about what is fair and some are just not feasible.

16

Utility

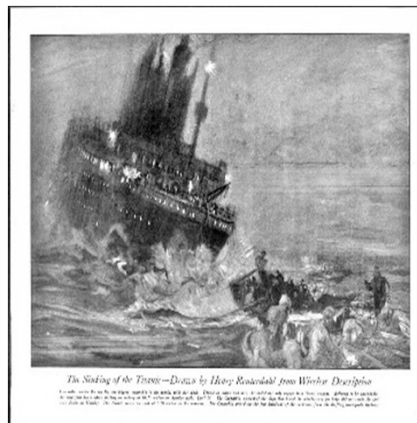
- Ethical theory proposed by Jeremy Bentham and James Mill
- UNOS definition: “the net medical benefit to all transplant patients as a group”

“All action should be directed toward achieving the greatest benefit for the greatest number of people.”

17

Lifeboat Ethics

- There are 50 people in a lifeboat with a room for 10 more
- 100 others swimming in water outside, begging for admission
- Options are:
 - Equity: Take everyone in, making a total of 150 in a boat designed for 60. The boat swamps; everyone drowns. Complete justice, complete catastrophe.
 - Utility: Make a rule and take 10 people by that rule.



18

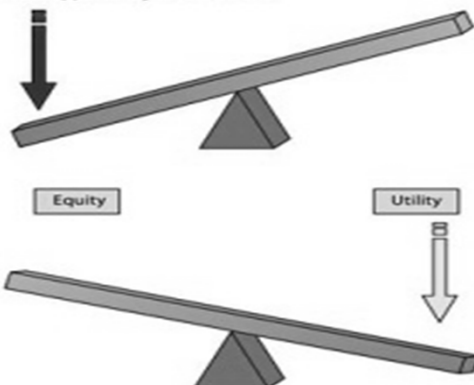
Current Wait-List

- 121,139 patients waiting for a TX
- 1 patient is added to the transplant list every 10 minutes
- 22 patients die each day waiting for TX

19

Equipoise in Transplant

Justice: each individual who would benefit from a transplant should have comparable opportunity to receive one



Each kidney should be transplanted into the recipient in whom it will survive the longest

20

Equity and Utility in Current Allocations

- Equity: Wait-list
- Utility:
 - HLA-matching
 - Allocation according to KDPI
 - Better kidneys for children
 - Extended criteria list

21

Transplant Decision

- How should transplant decision in a child with multiple comorbidities be made?

22

Important Questions to Consider

- What are extra-renal problems and how will TX affect these?
- What is the estimated life expectancy, how accurate is this and impact of TX on this?
- Would multi-organ TX be an option?
- What supports can be provided to improve chances of success?
- Who will be the medical guardian?
- What are long-term care plans (ability to provide self care, reside with parents, in a group or foster home, health insurance and provisions for medications and life-long monitoring)?
- If TX is inappropriate:
 - What conditions need to be met to reassess for TX,
 - Does the family want to continue with dialysis and
 - Has palliative care been offered?

23

Important Challenges

- Expected survival: often unsure
- QOL for the child and the family: Family is the best judge

“One who has never known the pleasures of mental operation, ambulation and social interaction does not suffer from their loss as much as one who has. While one who has known these capacities may prefer death to a life without them, we have no assurance that the handicapped person, with no point of comparison would agree”

The Ends of Human Life: Ezekiel. J Emanuel
- Resource allocation: A national level decision

24

Benefits/Burdens of TX

- Benefits: Improved longevity, QOL, cognition and neurodevelopment
- Burdens:
 - Risk for surgery and anesthesia
 - Infections
 - Malignancy
 - Need for frequent monitoring/biopsies
 - Need for immunosuppression for life of TX
 - Finite life

25

Transplant Societies Guidance

- Transplant societies do not consider reduced mental capacity as an absolute contraindication
- ASTP emphasizes importance of psychosocial assessment to determine candidacy but do admit that this can be very subjective
- “Recipient selection should not be unduly influenced by outcome predictors of questionable value”

26

ASTP Guideline

- “Cognitive disability should only pose a contraindication to transplantation when the disability is so severe that it precludes treatment compliance which cannot be compensated for with family or caregiver support.”

27

Disability and Transplant Outcomes

- Compared outcomes in 25 children with varying degrees of intellectual and motor disabilities to general TX recipient group
- Median follow up of 20 (1–187) months
- TX outcomes similar to those of the general population (100 % patient & graft survival in the disabled group versus 87 % graft survival and 98 % patient survival at 5 years in the general group)
 - [Am J Kidney Dis.](#) 2006 Mar;47(3):518-27

28

Decision Based on QOL

- A few studies including UNOS data suggest that outcomes of TX recipients with disabilities are similar to general TX population
- Caveat: these studies only included children who were actually transplanted and not reflective of eligible pool
- Decisions can't be based on QOL alone

29

Role of Life Expectancy

- "UNOS ethics committee recommends that transplantation should be carefully considered if the candidate's reasonable life expectancy with a functioning graft, based on factors such as age or co-morbid conditions, is significantly shorter than the reasonably expected "life span" of the transplanted organ."

30

Legal Considerations

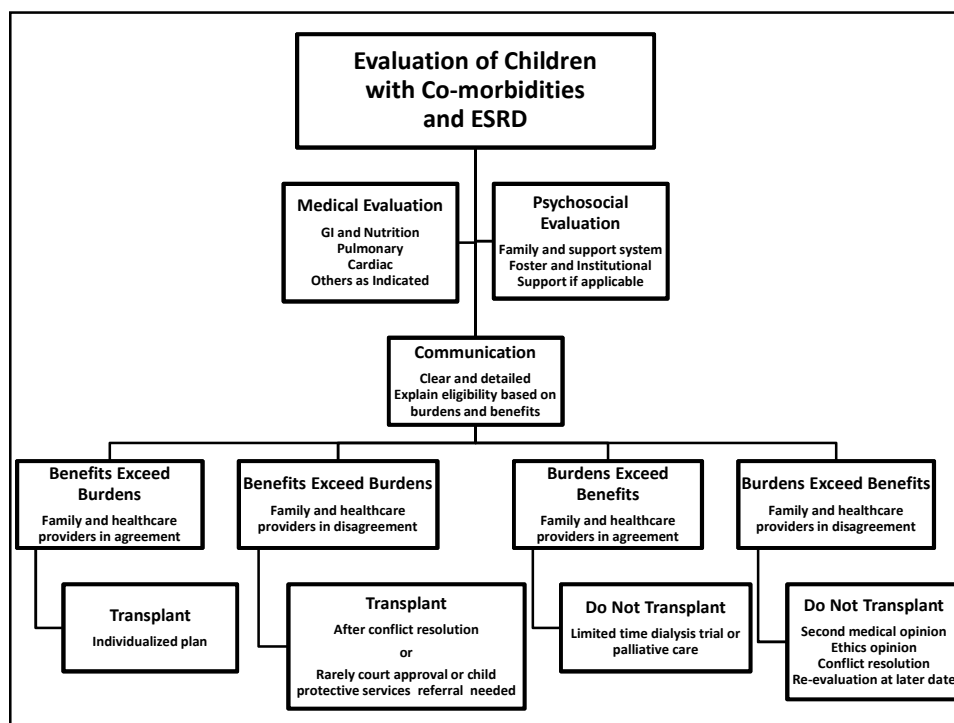
- ADA: disability can only be considered in allocation decisions if it compromises ability to derive benefit.
- The CMS COP (482.90) mandates that TX centers must have a fair and nondiscriminatory selection process including those with complexities and disabilities.
- In New Jersey, recent legislation explicitly prohibits TX eligibility discrimination for those with disabilities and provides an expedited court review for those who feel that law's provisions were not upheld

31

Suggested Approach

- Individualized evaluation and plan
 - We are serving individual human beings with highly complex medical situations, a process of *individual* evaluation must be maintained within broad parameters

32



33

Definitions of Physical and Mental Disabilities

34

Developmental Disability: Definition

- Severe chronic disability attributed to physical impairment or combination of mental and physical impairments
- Manifested before 22 years of age
- Likely to continue indefinitely
- Results in substantial functional limitations, and the need for interdisciplinary services for an extended period of time
- Cerebral palsy, autism, epilepsy, deafness, blindness and global developmental delay
 - North Carolina Council on Developmental Disabilities. <http://nccdd.org>.

35

Minimally Conscious State

- A condition of severely altered consciousness
- Minimal but definite behavioral evidence of self- or environmental awareness
- Behaviors include following simple commands, yes/no responses, intelligible verbalization and purposeful behavior
 - Giacino JT et al. The minimally conscious state: Definition and diagnostic criteria. *Neurology* 2002; 58:349–353.

36

Persistent Vegetative State

- Complete unawareness of self and environment
- No purposeful, or voluntary responses to visual, auditory, tactile, or noxious stimuli
- No evidence of language comprehension or expression
- Presence of sleep-wake cycles, with complete /partial preservation of hypothalamic and brain-stem autonomic functions.
- Bowel and bladder incontinence; and variably preserved cranial-nerve and spinal reflexes.
- Persistent for 1 month after acute traumatic or non-traumatic brain injury
 - Recovery exceedingly rare 12 months after traumatic and 3 months after a non-traumatic injury.

• Medical aspects of the persistent vegetative state . The Multi-Society Task Force on PVS. N Engl J Med 1994; 330: 1499–1508.

37

Boston Children's Policy: DS Kamin et al. Am J of Transplantation 2016; 16: 767–772

- TLAC: Broad representation from medical and outside community to ensure listing criteria are fair and nondiscriminatory and patients declined for listing have been considered without bias
- Patients should not be excluded from listing solely on the basis of DD
- Minimum thresholds for organ/patient survival should not be different for patients with DD
- Having a conscious experience and not just biological survival is a minimum goal
- Children in MCS or a PVS should be evaluated by a neurologist to help team/family determine benefits of TX
- TX should not be offered to children in PVS

38

Boston Children's Policy

- Carefully educate families about risks and benefits of TX and collaboratively make the best decision possible
- Deference should be given to families for decision making if comorbidities do not impact post-TX survival.
- TX should not be offered to patients who WILL be harmed by this procedure
- Families should be told, in person and in writing, the reasons for not listing
- Alternatives to TX ought to be offered in a caring manner
- In case of discordance, offer families a second opinion for evaluation

39

Future Studies

- "Comorbidity score" and a "Frailty Index" linked to outcomes in adult TX candidates
- No such data for children
- Current studies are small with heterogeneous patients
- Need for better prediction of pt/graft survival based on objective measures of illness
- Aggregate data not a substitute for individualized assessment, but helpful in framing prognosis discussions

40

Future Studies

- Data collection in children who received TX and those who did not
- Regular debriefings about each case can help decision-making
- Publication and media bias focuses attention on exceptional successes of TX
- Lack of acknowledgement of positive outcomes in families who opted against TX
- Long-term outcomes for medically complex children are likely to improve and risk–benefit ratios may change
- Need to revisit eligibility criteria on an ongoing basis

41

Take Home Point

- Be on the same page with the patient and the family
- Our job is to help families make the right decisions for their children and for themselves
- Sometimes, waiting out helps clarify things for team and the families

42