The History and Evolution of Ethics in Living Organ Donation

Second Annual Islamic Bioethics Workshop
June 6, 2014
Mark Siegler, MD

Outline

- Part I: The history of living donor kidney transplantation
- Part II: The ethics of living donor kidney transplantation: then and now
- Part III: The origins of living donor liver transplant
- Part IV: The evolution of living donor kidney transplantation: a proposal
Alexis Carrell
(1873-1944)

Hull Court and Biological Laboratory
Carrel’s Achievements at Chicago 1904-1906

- Vascular anastomoses
- Organ transplantation
- Reattaching severed limbs
- Organ preservation ex vivo

250 yards
Alexis Carrel, 1905

“The problem of organ transplantation in man has been solved.”

Carrel’s Achievements at Chicago, 1904-1906

- “From a clinical standpoint, the transplantation of organs may become important...and may open new fields in therapy and biology.” (Carrel 1905)
Alexis Carrel received the 1912 Nobel Prize in Physiology or Medicine for “his work on vascular suture and the transplantation of blood vessels and organs.”

Carrel’s great work at Chicago and later at the Rockefeller Institute clearly established the experimental foundation for human transplants that were started 40 years later by Dr. Francis Moore.
Dr. Francis Moore

1913-2001

Transplant

THE GIVE AND TAKE OF TISSUE TRANSPLANTATION

FRANCIS D. MOORE, M.D.
David Hume, MD
University of Chicago, 1943
David Hume and Charles Hufnagel
Surgical Residents
1st successful kidney transplant (1)

- In 1947, during his surgical residency at the Brigham, Hume and a fellow resident performed the first successful human kidney transplant on a 29 year old post-partum patient who was dying of acute renal failure.

David Hume and Charles Hufnagel
Surgical Residents
1st successful kidney transplant (2)

- Hume attached the cadaveric donor kidney to the woman’s forearm so it rested outside the skin. The primitive transplant lasted only four days, but that was long enough to allow the woman’s own kidneys to recover and she survived to be discharged.
David M. Hume (1917-1973)  
University of Chicago, MD, 1943  
“The Father of Renal Transplantation”

David Hume  
“Father of Renal Transplantation”

- Hume conducted the first series of kidney transplants (1951-1953), performing for Dr. Francis Moore at the Brigham’s 11 transplants using cadaver kidneys.
- Because immunosuppressive drugs did not exist, there was only one “long” survival in Hume’s series (175 days).
The first successful, long-term kidney transplant by Dr. Joseph Murray (1954) was based on Dr. Hume’s earlier work.

Dr. Joseph Murray’s Operating Room at The Brigham

Richard Herrick (left) received a kidney from his identical twin, Ronald (right) in the world’s first successful kidney transplant, which took place at Peter Bent Brigham Hospital in Boston.
Joseph E. Murray, left, receiving the Nobel Prize for Physiology or Medicine from King Carl XVI Gustaf of Sweden, 1990

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Ethical issues in living donor kidney transplantation in 1954 (1)

1. End stage kidney disease was uniformly fatal. Dialysis treatments, still in their infancy, were available for only a few patients and could prolong life for a month or two.

2. There were no effective immunosuppressive drugs and therefore deceased donor transplants between strangers were uniformly unsuccessful.

Ethical issues in living donor kidney transplantation in 1954 (2)

3. The absence of immunosuppressive medications made it necessary to use identical twins, and this of course required a living donor transplant.

4. Dr. Moore’s group’s ethical justification for using living volunteer donors was their view that the recipient would die without a transplant and that the Brigham team was the best one in the world to try the transplant experiment.
Ethical issues in living donor kidney transplantation in 2015 (1)

• The current ethical justification for using living donors is different from what it was in 1954.
  – We now have long-term dialysis available so end-stage renal disease is not uniformly fatal.
  – We now have an organized system through UNOS for obtaining and distributing deceased donor organs.
  – We have very effective immunosuppressive medications.

Ethical issues in living donor kidney transplantation in 2015 (2)

• However, one ethical justification, perhaps the crucial one, for using living donors, remains as powerful today as it was for Dr. Moore in 1954.
• The key justification is that the supply of organs needed to save lives remains insufficient.
Shortage of Adult Organs in the U.S.

Data from optn.transplant.hrsa.gov and OPTN/SRTR Annual Report. Data include deceased and living donors.
http://www.organdonor.gov/about/data.html

A Long Wait for a Kidney

Since 1990, the number of people on the waiting list for a kidney transplant has grown sharply, while the number of transplants has increased only slightly.

Source: The Organ Procurement and Transplantation Network
The Wall Street Journal
https://econ411w14.lsa.umich.edu/tag/organ-market/
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Christoph Broelsch
University of Chicago, 1984-1991

The Ethics of Surgical Innovation

“There is no FDA for surgeons.”
- Anonymous
The Chicago Model

1. Proven need for the procedure
2. Approval by institutional leaders
3. Preclinical and clinical scientific data
4. “Field Strength” of the team
5. Maximum protection of living donors (risk/benefit; informed consent; donor advocate)
6. Public disclosure, review and approval before the 1st operation

ETHICS OF LIVER TRANSPLANTATION WITH LIVING DONORS

Peter A. Singer, M.D., F.R.C.P.C.
Mark Siegler, M.D.
John D. Lantos, M.D.
Jean C. Emond, M.D.
Peter F. Whittington, M.D.
J. Richard Thistlethwaite, M.D., Ph.D.
Christoph E. Broelsch, M.D., Ph.D.

First Living Liver Donor (Teri Smith) and Recipient (Alyssa Smith)


Alyssa and her husband, Benjamin Riggan (2014)
Liver Transplantation in Children From Living Related Donors

Surgical Techniques and Results

CHRISTOPHE E. BREDLICH, M.D., Ph.D., PETER F. WHITTINGTON, M.D., JEAN C. EMOND, M.D., THOMAS G. HOFFRON, M.D., J. RICHARD THISTLETHWAITE, M.D., PH.D., LARRY STEVENS, M.D., JAMES PIPER, M.D., SUSAN H. WHITTINGTON, and J. LANCE LICKTON, M.D.

Pediatric liver transplantation with reduced size donor organs (RSO), has evolved into a standard clinical procedure increasing the choices of recipients for their treatment. Nevertheless organ availability remains a major problem. The authors therefore have proposed to study the use of hepatic segments from living related donors (LRD) in a group of 20 children less than 2 years of age weighing less than 35 kg, to whom standard indications for transplantation suited. Volunteer related donors were selected after medical and psychiatric evaluations, and the suitability of the donor's liver was established by functional and histologic criteria. A two-panel informed consent process ensured appropriate "voluntarism." Nineteen infants received LRD as first grafts and one as a second graft. Seventeen of the recipients are alive 3 to 18 months after LRD. Fifteen of 20 patients are currently at home with the original graft and normal liver function (bilirubin < 1.0 mg%) after a median hospital stay of 37 days (range, 14-95 days). Four patients underwent retransplantation, in all cases due to arterial thrombosis. The overall graft survival for 28 primary LRD’s is 95%, with follow-up between 3 and 18 months. A number of technical problems occurred during our initial trials, the most aggravating being vascular thromboses. As fluid approaches to vascular reconstruction should reduce the incidence of thromboses and improve the rate of survival in future cases. The donor group for the initial 29 LRD procedures consisted of 12 mothers, 7 fathers, and 1 grandmother. In addition, one father and one aunt, who was an identical twin of the recipient’s father, who did not qualify for anatomic reasons, were named as potential LRD donors. Two donors survived and are now in normal health between 3 and 18 months after LRD. Having returned to their usual employment and school responsibilities. The median hospital stay was 6 days (range, 2-18). Complications were minimal, and all were minor limited to four minor cases of upper gastrointestinal hemorrhage was performed. After alteration of the procedure

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Dr. Giuliano Testa and I have a simple but radical proposal to increase the supply of kidneys for transplantation. We believe that such an effort would save lives while also improving recipients’ quality of lives.

Here is the proposal:

We strongly encourage a wider utilization of living kidney donors.

Here is the radical part of the proposal:

We recommend that living kidney donors, rather than deceased donors, become the first and preferred choice of doctors and patients.
3 Key Questions

1. What is the best ethical justification for using living kidney donors?
2. Is it ethical to *promote* the use of living kidney donors?
3. Practically, how might we increase living kidney donors?

**Question 1:**
What is the best ethical justification for using living kidney donors?
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What is the best ethical justification for using living kidney donors?

Answer:
The potential supply of living donors is far, far greater than the potential supply of deceased donors (even including Donation after Cardiac Death, DCD, donors, who now account for 10% of deceased donors)

The potential supply of deceased organ donors


**Table 1. Estimates of the Donor Pool.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>1997</th>
<th>1998</th>
<th>1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate of national pool of potential deceased organ donors</td>
<td>13,565</td>
<td>13,728</td>
<td>13,317</td>
</tr>
</tbody>
</table>

* Data are from the United Network for Organ Sharing.


Data are from the United Network for Organ Sharing.
Number of potential deceased donors based on Sheenhy E, et al. estimate in 2003 NEJM paper. This may be a low estimate. It does not include an estimated number of DCD donors.

Number of potential deceased donors and living donors based on Sheenhy E, et al. estimate in 2003 NEJM paper. This may be a low estimate. It does not include an estimated number of DCD donors.
How Are We Actually Doing?

According to the U.S. OPTN National Data:

• In 2013,
  – 16,896 kidney transplants were performed in the U.S.
  – Of these kidney transplants, 12,273 used deceased donors and 5,733 used living donors (33.9% Living)

• By June 30, 2014,
  – 8,324 kidney transplants were performed in the U.S.
  – Of these kidney transplants, 2,673 were from living donors (32.1%)

OPTN: http://optn.transplant.hrsa.gov/latestData/rptData.asp
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Living Kidney Donors

Number of Living Donor Kidney Transplants (1998-2012)

Living Donation Around the World
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Japan

- Living donors account for 83.6% of kidney donations.


**Question 2:**
Is it ethical to *promote* the use of living kidney donors?
The Ethical Balance: Is living donor kidney transplantation ethical?

**NO**

1) A “misuse” of surgical techniques to benefit a third party


**YES**

1) Increases organ supply

2) Better quality organs and better patient outcomes

3) In 60 years, more than 250,000 living donors in 40+ countries have said **YES** to living donation. No country has prohibited living donation. Many lives have been saved.

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**Question 2A:** What are the ethical arguments in favor of promoting living kidney donation?
Quality of kidneys from living donors and patient outcomes are better

• Compared to patients receiving deceased donor organs, patients receiving living donor organs have:
  – Decreased waiting time
  – Better graft quality
  – Lower risk of disease transmission
  – Better survival

• For example, the half-life of a kidney from a living donor is, on average, longer than that of a kidney from a deceased donor.

Scientific Registry of Transplant Recipients. www.srtr.org
Question 2B: What are the ethical arguments against using and promoting living kidney donation?

The two major ethical concerns about living kidney donation:

1. The surgery is used to benefit a third party and not the patient.
2. There are donor risks of morbidity and mortality.
“Is it ever morally right and ethically justifiable to injure one person to help another?”

Francis D. Moore, MD, 1964

The two major ethical concerns about living donation:

1. The surgery is used to benefit a third party and not the patient.
2. There are donor risks of morbidity and mortality.
Dr. Thomas Starzl, 1987

"The most compelling argument against living donation is that it is not completely safe for the donor."

Is “completely safe” the correct ethical standard or is “safe enough” a reasonable ethical standard?

Donor Risks

- The minor risks to donors are pain, temporary disability, loss of income, etc. (100%)
- The major risks to donors:
  - short term: perioperative death (3/10000 = 0.03%)
  - long term: increased risk for renal failure but absolute risk remains small
Short Term, Major Risk:
Perioperative Mortality Risk

- Mortality 0.03% in a population of 80,347 individuals (approx. 1/3300, median follow-up 6.3 years)
- Similar mortality to a matched cohort of 9,364 healthy individuals.


Long term risk of kidney failure?

Donation increases the risk of renal failure when donors are compared to a healthy, matched cohort. However, the magnitude of the absolute risk was small.

Muzaale, et al. 2014

Estimated lifetime risk of ESRD:

- 326 per 10,000 unscreened nondonors (general population)
- 90 per 10,000 donors
- 14 per 10,000 healthy nondonors

Once again, here is our proposal:

1. We strongly encourage a wider utilization of living donors, especially living kidney donors.
2. We recommend that living donors, rather than deceased donors, become the first and preferred choice of doctors and patients.
The justification for our proposal:

1. Many lives could be saved and recipients would have improved the quality of life.
2. By giving recipients a living donor kidney, we would be offering them a better standard of transplantation treatment than they would get from a deceased donor kidney.
3. Donor risks exist of perioperative mortality and long-term end-stage renal disease, but they are relatively small.

Question 3:
Practically, how might we increase the supply of living kidney donors?

7 suggestions
1. Change the ambivalent attitude in the transplant community about the ethics of living organ donation.

   After 60 years, it is clear:
   Living kidney donation IS ETHICAL.

2. Modify government and UNOS policies to make living kidney donation, rather than deceased donation especially of kidneys and pediatric livers, the preferred and encouraged donation.
3. Don’t be shy: Discuss potential benefits to donors.

**Donor Benefit:**

- Psychological benefit of altruistic behavior
- Increased feelings of self esteem and self worth
- The opportunity to save another person’s life with a relatively small amount of additional risk to one’s self
- Probably donors derive a greater benefit when they help a relative, but altruistic donation to strangers also provides donor benefits

4. Expand paired exchanges and donor chains.
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- In 1997, my colleagues and I analyzed the ethical issues associated with the idea of a paired-kidney-exchange program.
- The idea for such a program was first proposed by Felix Rapaport in 1986. It had not been acted on until after our *NEJM* paper in 1997.
Feb 2012: Nonsimultaneous Extended Altruistic Donor (NEAD) chain of length 60 (30 transplants)

5. Develop marketing campaigns similar to those that have been used to encourage deceased donation
6. To ensure public confidence and trust, maintain the highest standards of voluntary informed consent, including donor advocates

7. Consider decreasing financial disincentives or introducing financial incentives

**Decrease disincentives:**
- Help ensure job security
- Cover all donation-related expenses
- For a defined period, make available health, disability, and life insurance for donors

**Introduce incentives:**
- Consider offering tax credit, college tuition benefits, early access to Medicare, contribution to a retirement fund
- Allow living donors and their loved ones to jump to the top of the waiting list if they unexpectedly need a kidney transplant.

Consider a regulated market for kidneys (a discussion for another time)
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Some ways to correct disincentives:
• Government agencies pay all costs living donors face
• Donors and loved ones jump to the top of the transplant list if they need a kidney transplant

Conclusion
• Wide variation in different countries on the use of living donors
• I propose that we address the worsening shortage of kidneys for transplantation worldwide by working to increase the number of living kidney donors.
• If we are successful, our success will be measured in the number of lives saved and in the improvement of quality of life for kidney transplant patients.
Thank you very much.

END