Pediatric Organ Donation and Transplantation

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KEY WORDS
- brain death
- circulatory death
- end of life
- ethics
- organ donation
- pediatric
- transplantation

ABBREVIATIONS
- DCDD—donation after circulatory determination of death
- DNDD—donation after neurologic determination of death
- UNOS—United Network for Organ Sharing

Dr Workman conceptualized and designed the study, carried out the analyses, and drafted the initial manuscript; Mr Myrick assisted with study design and obtained the data sets; Dr Meyers assisted with study design and revised the manuscript; Dr Bratton conceptualized and designed the study, coordinated and supervised data collection and analysis, and critically reviewed and revised the manuscript; Dr Nakagawa assisted study design and concept, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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WHAT’S KNOWN ON THIS SUBJECT: The gap between organ availability and need continues to grow, and infants are among the most vulnerable candidates on the wait-list. The scarcity of donor organs has led the transplant community to look for alternative donor sources.

WHAT THIS STUDY ADDS: Children are receiving more grafts from pediatric donors, but they also continue to receive adult donor grafts. Donation after circulatory determination of death increases organ availability. Allocation changes have also helped increase pediatric transplantation and decrease wait-list deaths.

abstract

BACKGROUND AND OBJECTIVES: There is increasing unmet need for solid organ donation. Alternative donor sources, such as donation after circulatory determination of death (DCDD), are needed. The objective of this study was to examine the impact of DCDD on trends in pediatric organ donation and transplantation.

METHODS: Data were obtained from the Organ Procurement and Transplantation Network for US organ recipients and donors from 2001 to 2010 stratified according to age, organ, and deceased donor type (DCDD or donation after neurologic determination of death). Additional data included transplant wait-list removals due to death.

RESULTS: From 2001 to 2010, pediatric organ transplant recipients increased from 1170 to 1475. Organs from DCDD donors were transplanted into children infrequently but increased from 1 to 31. Pediatric donation after neurologic determination of death decreased by 13% whereas DCDD increased by 174% (50 to 137). Recipients of pediatric grafts decreased from 3042 to 2751. Adults receiving grafts from pediatric donors decreased from 2243 to 1780; children receiving pediatric grafts increased from 799 to 971. Organs from DCDD donors were transplanted into children infrequently but increased from 50 to 128 adults and 0 to 9 children. Pediatric candidates dying waiting for an organ decreased from 262 to 110.

CONCLUSIONS: From 2001 to 2010, children received more solid organ transplants and fewer children died waiting. Organ recovery from pediatric and adult DCDD donors increased. The number of pediatric recipients of DCDD grafts remains small. Adults primarily receive the direct benefit from pediatric DCDD but other changes in organ allocation have directly benefited children. Pediatrics 2013;131:e1723–e1730
The US organ transplant waiting list currently exceeds 117,000 people. In 2011, a total of 28,500 transplants were performed, yet during this same year, ~7000 people died waiting for a life-saving organ transplant.1 Despite success increasing national organ donation rates,2–4 efforts are needed to close the growing gap between available organs and transplant recipients. To that end, the Institute of Medicine published several consensus reports, most recently in 2006, recommending strategies to increase organ donation.5–7 Paramount among the recommendations was the development and implementation of organ donation after circulatory determination of death (DCDD).

The first kidney transplant occurred in 1954 from a donor after circulatory death. This transplant was followed by a lung transplant in 1963 and liver and heart transplants in 1967.8,9 However, as medical technology advanced and patients with devastating brain injuries could be supported with mechanical ventilation, ethical concerns about the definition of death emerged. An expanded definition of death, including loss of circulatory and respiratory function or loss of all function of the entire brain including the brain stem became medically accepted.10,11 Transplanting organs from donors after formal declaration of brain death, donation after neurologic determination of death (DNDD), lead to better outcomes and readily became the standard source of organs for several decades.12,13 However, the growing need for donor organs not met by traditional “brain-dead” donors and the desire of dying patients and families to donate organs renewed interest in DCDD, which was reintroduced in 1993 when DeVita and Snyder published the Pittsburgh protocol.14 Ongoing efforts by the Institute of Medicine and refinements in DCDD protocols at several institutions helped with the reemergence of DCDD, particularly in adults. Although it remains a secondary pathway to donation, DCDD has become an accepted way of recovering more organs for transplantation and is contributing to the national pool of donor organs. Advances in DCDD have been challenging for potential pediatric donors for several reasons, including: limited health professional experience and comfort; lack of standardized protocols15; concern for potential compromised DCDD graft survival16,17; and amplified ethical concerns, including parental emotions surrounding unanticipated, often traumatic, death that create a highly charged and potentially conflicted environment, which can be a burden to grieving families.18,19

Although most national standards for DDGD programs and protocols were developed for adults, children comprise a critical percentage of those waiting and dying on the transplant list, and potential pediatric donors are often lost to the donor pool.20 Infants in particular have the highest wait-list mortality due to size limitations and organ availability.21 A 2007 review of US national data from the United Network for Organ Sharing (UNOS) questioned the benefit of pediatric DCDD donation despite modestly increasing donation.22 Conversely, the development of a DCDD protocol at a single pediatric transplant center increased donor rates by >50%,23 In addition, recent data suggest that long-term recipient and graft survival for both pediatric kidney and liver transplants with the use of DCDD donors may be equivalent to DNDD organs.24,25 Pediatric DCDD donors are an important component to increasing the donor pool, but it is unclear how these organs are being used on a national level. Therefore, the current review critically examined the recent impact of pediatric DCDD by evaluating trends in pediatric organ donation and comparing organ utilization patterns among pediatric and adult transplant recipients.

METHODS

Publicly available data were obtained from the Organ Procurement and Transplantation Network from 2001 to 2010.26 These data are universally de-identified and thus exempt from human subject regulation by the University of Utah Institutional Review Board. The data were stratified according to age groups (pediatric [aged 0–17 years] versus adult [aged >17 years]), organ donated or received (kidney, liver, heart, lung, pancreas, and small bowel), and type of donation (DCDD or DNDD). We also obtained the total number of organ- and age-specific waiting list candidates per year and transplants performed per year, as well as age-specific removals from the transplant candidate list due to death. SPSS version 18.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) was used for descriptive statistics and to generate figures.

RESULTS

From 2001 to 2010, a total of 14,221 children received solid organ transplants from deceased donors. The number of children undergoing transplantation each year increased from 1170 in 2001 to a peak of 1628 in 2009, and decreased slightly in 2010 to 1475. Pediatric donors provided the majority of organs for pediatric transplant patients; however, this decreased from 68% to 66% over the study period (Fig 1). DCDD donor organs were transplanted into children infrequently but increased steadily from 1 in 2001 to 31 in 2010. The total number of pediatric donor organs used for transplantation decreased during the study period from 3042 to 2751; however, children receiving pediatric grafts increased from 799 to 971 while adults receiving pediatric grafts decreased from 2243 to 1780 (Fig 2). This decrease in pediatric donor organs mirrors a 15% decrease
in pediatric donors: 987 in 2001 to 841 in 2010. There was a 13% decrease (2992 to 2614) in recipients of pediatric DNDD grafts while recipients of pediatric DCDD grafts increased 174% (from 50 to 137). In 2010, pediatric DCDD graft recipients included 128 adults (1 lung, 27 livers, and 100 kidneys) and 9 children (3 livers, 5 kidneys, and 1 heart) (Fig 3). Table 1 provides a list of organs transplanted into pediatric and adult recipients from pediatric DCDD.

From 2001 to 2010, as the number of pediatric transplants increased, pediatric candidates dying waiting for an organ dramatically decreased from 262 to 110. During this time, the number of children on the transplant candidate list remained relatively stable (Fig 4).
DISCUSSION

Analysis of pediatric solid organ donation and transplantation in the United States from 2001 to 2010 demonstrates an increase in transplant procedures, with the majority of deceased donor organs coming from pediatric donors. The increased utilization of pediatric grafts by pediatric recipients is likely a result of changes in UNOS allocation protocols and occurred despite an overall decrease in both pediatric donors and total organs recovered from children. During this time period, organs recovered from pediatric DNDD decreased and organs from pediatric DCDD increased. Even with preferential allocation of pediatric donor grafts to pediatric recipients, adults continue to receive the majority of pediatric organs, particularly from DCDD donors. Importantly, fewer children died on the transplant candidate list waiting for an organ, suggesting that children have been relatively spared from the escalating gap between needed organs and available donors.

Changes in donation and organ allocation for children are affected by many factors. UNOS made several organ allocation strategy changes for liver and kidney placement (those organs representing the greatest percentage of pediatric solid organ transplants) during the study period. In 2002, the model for end-stage liver disease and pediatric end-stage liver disease scoring systems were established, and in 2005, regional sharing of pediatric donor livers was implemented.27 Our analysis suggests that these liver allocation changes improved access to transplantation for children with liver failure and support earlier reports which investigated the effect of the model for end-stage liver disease/pediatric end-stage liver disease scoring systems on pediatric liver transplantation.28,29

Two major policy changes affected donor kidney allocation during the study period. In 2002, a policy defining use of expanded criteria kidney donors was implemented, and in 2005 “Share 35” gave pediatric recipients priority to kidneys from deceased donors aged <35 years. Before Share 35, approximately one-half of all children with end-stage renal disease received kidneys from living related donors.3 Despite this policy change, there has been a rapid rise in the total number of pediatric kidney transplants by an average of 61 per year.1 The kidney shortage remains an enormous problem for the transplant community, and allocation strategy changes to maximize donor kidney utilization are currently being assessed.30,31

Although children benefited from changes in organ allocation, pediatric donor organs continue to be necessary and important for adult recipients who far outnumber their pediatric counterparts. Adult donors are also far more numerous than pediatric donors,1 and thus even with preferential allocation of pediatric grafts to pediatric recipients, some adult organs should rightly be given to children. Although size matching is an important component of organ allocation for most organs, innovative techniques such as split, live donor, and reduced liver grafts have expanded the pediatric recipient pool from adult donors and helped decrease waiting times.32,33
Increased use of split livers is quantitatively the most important component of this equation. Liver splitting remains more common when the organ is offered initially to the child and the split is done primarily for size reduction; the remaining portion of the liver may then be used for a second recipient, usually an adult. When a liver is offered first to an adult, the adult recipient may be approached with an inquiry of willingness to split their organ with a child, although no regulations require such an inquiry. To increase the availability of split livers from organs offered primarily to adults, adult transplant teams need to place greater importance on this option. Policies making the split liver option mandatory rather than elective for primary adult recipients remain controversial but are being actively pursued in some UNOS regions.

Currently, the majority of organs for pediatric kidney transplants are from adult donors. This is in part due to the risk of vascular complications among small recipients. Infants must be at least 8 to 9 kg to accommodate a donor kidney, which usually is placed in the iliac fossa. Use of kidneys from young small donors (DNDD or DCDD) further increases rates of vascular thrombosis in small recipients, which most transplant surgeons will not accept for children. Policies making the split liver option mandatory rather than elective for primary adult recipients remain controversial but are being actively pursued in some UNOS regions.

More widespread acceptance of DCDD kidneys for transplantation into children will require greater assessment of long-term function, which should be optimized for younger recipients. Both examples underscore how adult donors are mitigating organ shortage for children. At first glance, the allocation of DCDD organs seems to highlight how pediatric donation helps alleviate the organ shortage in the adult population. Although the total number of DCDD organs is increasing, our data demonstrate that the number of pediatric recipients using these organs remains very small. The reasons for this discrepancy are not entirely clear, although concern for decreased graft survival in the 1990s for adult DCDD liver transplant recipients has been noted. More recent studies suggest that for both pediatric and adult recipients, graft and patient survival for DCDD

<table>
<thead>
<tr>
<th>Year</th>
<th>Organ</th>
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<th>Adult Recipients</th>
<th>Total Organs Transplanted</th>
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<td>14 (63)</td>
<td>15 (63)</td>
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<td>14 (79)</td>
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<td>1 (100)</td>
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</tbody>
</table>

Numbers in parentheses represent percent transplanted that year for each organ.
kidney and liver transplants is equivalent to DNDD organs.\textsuperscript{23,24,43–46} Perhaps as DCDD becomes a more common practice, children will directly benefit from organs recovered by this method of donation.

Even without the direct receipt of DCDD organs, we argue that children benefit from this type of donation. By providing adults with available organs that are currently considered “expanded criteria” or less suitable for children, the total number of donor organs available for transplantation increases. Therefore, although we cannot directly ascribe the increase in pediatric transplants and decrease in wait-list deaths to increased organ availability from DCDD donors, this additional source of organs alleviates in part the pediatric organ shortage by making more organs available to candidates of all ages.

An unavoidable circumstance of pediatric organ donation is that parents have to consider donation at the same time they are grieving their child’s end of life. When considering organ donation, 1 of the key factors influencing parental consent is the altruistic desire to help another child live or help prevent or relieve the suffering of other parents.\textsuperscript{47,48} Although it would be misleading to let parents think that their child’s donated organs will definitely be transplanted into another sick child, it would be reasonable to inform parents that organ donation from children does help other children, even if not directly.

An additional concern regarding DCDD is that increased emphasis on this pathway to donation may alter end-of-life medical decisions, causing a decrease in DNDD and thus fewer available donor organs. It is conceivable that the option of DCDD may decrease the availability of donor organs because, on average, fewer organs are procured per DCDD donor compared with DNDD donor.\textsuperscript{49} Our data support the declining rate of DNDD as DCDD is increasing, in agreement with several other recent reports.\textsuperscript{50,51} However, when the question of altered medical decision-making was studied directly in children, the option of DCDD did not affect the number of patients who eventually donated organs after meeting neurologic criteria for death.\textsuperscript{25} Clearly, the decline in DNDD donors has been affected by major medical advances, preventive health measures, and traffic safety improvements, resulting in fewer patients progressing to brain death.\textsuperscript{50} With ongoing progress in critical care medicine and improved patient survival from brain injuries that previously were fatal, there are likely to be even fewer DNDD donors in the future; thus, the medical community will need to evaluate viable alternatives.

This study has several limitations. First, the data were not indexed for population growth. Some of the increased rates of donation and transplantation seen over the study period may be attributed in part to an increase in the population during this time period. Second, with respect to the donor data, the Organ Procurement and Transplantation Network database allows for identification of donor organs allocated, not individual patients who donated. The organs from a single donor can be placed in up to 8 individuals. Therefore, the data do not solely reflect the changing rates of donation as efforts to improve donor management have increased the number of organs recovered per donor. In addition, recipient status was not included in the data. Including this information in future studies might help further elucidate organ placement, particularly when an organ from a pediatric donor is transplanted into an adult. Finally, the
decrease in pediatric wait-list deaths may not be completely attributed to increased transplant rates and shortened waiting times. During the study period, advances in the medical management of patients have evolved, allowing some of these children to improve and either decrease in pediatric wait-list deaths.

CONCLUSIONS
Recovery and transplantation of organs to children from pediatric donors are increasing. This increase has occurred despite the decreasing number of pediatric donor organs recovered during the past 10 years, the majority of pediatric donor organs still transplanted into adults, and the DCDD organs being used almost exclusively for adult recipients. Although it is true that pediatric donation (both DCDD and DNDD) does not always directly benefit other children, improving the overall process of donation and increasing organ recovery allows for more pediatric transplants and fewer pediatric wait-list deaths.

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