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Organ allocation and utilization in pediatric transplantation

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ABSTRACT

Pediatric transplant candidates include heart, lung, liver, pancreas, small intestine, and kidney. The purpose of this article is to review the history and current methods for determining priority of the above-mentioned transplantable organs. The methods used by the authors involved the review of historical and current manuscripts and UNOS policy documents. We summarized the findings in order to create a concise review of the current policies and wait times for transplantation in pediatric transplant patients.

Despite multiple attempts and reports of transplantation, the first successful transplant did not occur until 1954, when a kidney from one identical twin was transplanted into his sibling. Due to lack of immunosuppression, long-term graft survival was a challenge. As immunosuppression improved, with the introduction of cyclosporine (in 1983) organ transplantation with heart, lung, kidney, pancreas, and small intestine experienced improved patient and graft survival. In 1984, Congress passed the National Organ Transplant Act (NOTA) and established the Organ Procurement and Transplantation Network (OPTN) to maintain a national registry for organ matching. Also in 1984, United Network of Organ Sharing (UNOS) was established as an independent, non-profit organization, committed to saving lives by uniting and supporting the efforts of donation and transplantation professionals (UNOS.org). Since then there have been several policy changes and a tremendous amount of research and analysis that has been devoted to maximizing the number of deceased donor organs available to recipients on the waiting list. More specifically, children have usually enjoyed special consideration and had the benefit of multiple policy changes that were designed to provide them with the shortest possible wait times. We will review the history of heart, liver, kidney, pancreas, lung and small intestine organ allocation, utilization and transplantation for children.

As of February 2017 there are 118,340 individuals who are listed for an organ transplant and within this group there are 1926 (1.6%) children (less than 18 years). In 2016 there were a total of 33,600 solid-organ transplants and children received 1880 (5.6%) of these organs (based on OPTN data as of February 20, 2017). It is obvious that children are a small part of the transplant equation, however, they represent the population that has the most long-term life to gain after a successful transplant. Historically, children have enjoyed preferred positions on the allocation algorithms for all the different solid organs. However, due to recipient size and weight limitations, it continues to be a challenge to find an organ for a sick child at the right time.

Liver transplantation

Currently there are 491 children (less than 18 years of age) waiting for a liver transplant (3.3% of the total waiting list). Of these, 52 are less than 1 year of age and 193 are 1–5 years of age. Currently there are about 700–750 new children added to the wait list each year and we are currently transplanting about 500–550 children per year (based on OPTN data as of February 20, 2017). Since 2006 there has been a significant decrease in the number of children who die waiting on the list; however, every year 25–30 children still die waiting for a liver. The goal of pediatric liver transplantation has always been to eliminate deaths on the wait list and for that reason the techniques and types of liver transplantation have evolved in an attempt to meet this target.

Dr. Tom Starzl performed the first successful pediatric liver transplant in 1968.[1] In the early years, pediatric transplantation was performed with whole organs only. Children less than 10 kg were immediately disadvantaged because of the difficulty in finding weight-matched livers. Also, as liver transplantation expanded, the need for pediatric liver transplants rapidly outstripped the availability of whole livers. In 1984 Bismuth, drawing from Couinaud's description of the anatomic divisions of the liver, described a technique for reducing an adult-sized liver into its

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smaller components (left lobe and left lateral segments).[2] This produced organs that could then be used in children and more importantly could be used to transplant children less than 10 kg. Later Drs. Otte and Broelsch, in 1988 reported a series of children transplanted with reduced-sized livers.[3,4] This technique expanded the donor to recipient weight ratio up to 5:1 to 10:1. Size reduction, however, brought its own problems including bleeding from the cut surface, bile leaks and an increased rate of hepatic artery thrombosis, all of which (to some degree) still continue to the present.

The major down side to liver reduction is that a portion of the adult liver is discarded. Both Pichlmayr and Bismuth (1988/1989) reported on the concept of split liver transplantation: the left lateral segment goes to a child and the remaining liver is distributed to an adult.[5] The early reports of this technique[6] showed an inferior patient and graft survival (67% and 50%, respectively) due to complications with the right-sided graft including bleeding from the cut surface, bile leak and necrosis of segment 4. Over time, these complications were addressed by using both in situ and ex situ techniques for the splitting of the liver. It also was recognized that appropriate donor selection was important to graft survival. It is now accepted that a donor considered for splitting should be less than 50 years old, liver function studies less than 2–3 times upper limit of normal, and should not be on any blood pressure support medications. In addition, the recipient should not be severely ill. When these donor and recipient factors are taken into account, current patient and graft survivals have been reported as high as 96% and 96%, respectively.[7]

However, despite these improvements, split liver transplantation continues to be a challenge for many centers. On the adult side, the right lobe graft does have the potential for increased complications over a whole organ and on the pediatric side, there can be disputes between centers over the allocation of the vessels to the left lobe/left lateral segment graft, especially how the hepatic artery is to be split. These dilemmas can often result in a graft not being split or if a graft is split, the right side is not ultimately transplanted.

Another attempt to increase the donor pool for children has been the development of living-related transplantation. Broelsch et al.[8] first reported this procedure in 1990 taking the left lateral segment from an adult and transplanting it into an infant. In children, the left lateral segment is the most common segment that comes from a living donor. However, now that living-related transplantation is also used in adults, left lobes have also been transplanted into older children and adolescents. Unfortunately, due to the complex issues surrounding living-related donation both in the donor and the recipient, between 2012 and 2016 there have been only about 50–70 living-related liver transplants per year in children less than 18 years of age in the USA (based on OPTN data as of February 20, 2017).

Donation after cardiac death (DCD) liver transplantation has also been increasing over the last several years. Unfortunately, in 2016 there have been only a few DCD donors in children (3 donors <10 years of age, based on OPTN data as of February 20, 2017). The pediatric transplant community has been reluctant to embrace DCD transplantation due to the significant incidence of ischemic cholangiopathy that can require re-transplantation.[9] With the advent of machine perfusion of livers, more DCD donors may be considered for pediatric transplantation in the future.[10]

Most liver transplants are done with either ABO identical or compatible donors. However, ABO-incompatible (ABO-I) transplants can also be performed. ABO-I transplants in the United States are most frequently done when a recipient is severely ill and urgently requires an organ. Early results with ABO-I liver transplants had inferior patient and graft survival due to hepatic necrosis and the development of late biliary strictures.[11] It was then noted that children who were transplanted <1 year of age did well due to the fact that children of this age have low pre-transplant anti-ABO titers. In Japan, ABO-I liver transplantation is successfully performed using a combination of methods to lower anti-ABO titers including pre-operative and post-operative plasmapheresis along with post-operative intravenous immunoglobulin and rituximab.[12]

Over time, organ allocation methodology has also changed for children. Initially children were listed for transplant based on their degree of illness and they were ordered on the list by waiting time. Illness severity was divided into three broad groups as follows: Status 1—patients that required ICU care, Status 2—patients required continuous hospitalization, and Status 3—patients were at home. This system had several shortcomings: it was easy to manipulate and waiting time alone did not correlate with death on the waiting list. In 1998 CMS published the Final Rule stating that wait time alone could no longer be the major component of organ allocation. As a result UNOS in 2002 adopted the MELD (Model for End Stage Liver Disease) for adults and PELD (Pediatric End Stage Liver Disease) scores (children <12 years of age) as more objective ways to list patients (the higher the score the greater the chance of dying on the wait list). These scores were based on parameters that could be objectively measured (PELD—bilirubin, INR, serum albumin, age and growth failure). As in adults, these scores can be modified by applying for additional points by exception (UNOS review required) and the most critically ill patients can receive the highest designation—Status 1a and Status 1b. The implementation of PELD did slightly decrease the number of deaths on the wait list and slightly increased the number of transplants for children >2 years of age; however, deaths on the wait list in children <2 years of age still remained high.[13] Recently there has been concern over the disparity between the number of people awaiting a liver transplant in a given UNOS region versus the number of organs available to these patients. UNOS has been charged with the task of developing an organ distribution policy that will decrease this disparity. Multiple discussions have been held and proposals made but none as yet have been able to adequately solve this complex problem. It currently is unclear how organ distribution to children will be affected by any of the current proposals being evaluated.

In order to achieve the goal of no deaths on the pediatric wait list, currently the only two options are increasing split liver transplantation and living-related transplantation. The difficulty in increasing living-related transplantation is that it is only performed in a few centers and it is still limited by the availability of suitable donors. However, there is a real opportunity by increasing the number of split liver transplants. Currently in order to transplant all the children less than 5 years of age that were waiting and who were added to the wait list in 2016, there would be a need for 720 transplants. In 2016, in this group, there were 385 deceased donor transplants and there were 56 LRD transplants. That leaves 279 of these children still waiting for an organ. In 2016 there were 2721 liver donors between the ages of 18 and 34 years that potentially could have been a split liver donor. If only 10% of those donors had their liver split, all children less than 5 years of age would have been transplanted thereby removing the group of children who have the highest wait list mortality. All pediatric centers should develop a working relationship with an adult center regarding split liver transplants so that all the technical concerns can be addressed up front. This would facilitate donor planning and management between the centers. Currently UNOS is actively exploring ways to encourage the wider application of split liver transplantation.

Heart transplantation

In pediatric heart transplantation, there are currently 342 children (<18 years of age) awaiting a heart transplant (8.5% total