Split-Liver Transplantation Using the Left Lateral Segment: A Collaborative Sharing Experience Between Two Distant Centers

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Split-liver transplantation (SLT) increases the pool of organs for pediatric orthotopic liver transplantation (pOLT). With increased collaboration and organ sharing, transplant centers can fully maximize the use of all split donor allografts. Herein, we report the collaborative results between two distant centers involved in a sharing alliance.

The current study consists of a retrospective review of 56 pediatric LLS transplants performed at two collaborating centers between 9/1997 and 10/2003. Fifty-three patients (41% Status 1) were transplanted using 56 left lateral segment (LLS) grafts. Sixteen percent of LLS grafts were shared between the two institutions. Overall patient survival at both 1 and 3 years was 90% and 90%, respectively. Overall graft survival at both 1 and 3 years was 82% and 82%, respectively. Shared patient and graft survival was 89% and 89%, respectively. There was an 11% biliary complication and 18% vascular complication rate. Five patients required retransplantation. In conclusion, SLT increases the number of available allografts for pOLT. While SLT is technically demanding, with a significant learning curve, patient and graft survival rates compare favorably with United Network Organ Sharing (UNOS) averages. Sharing of grafts between centers is a safe and effective way to maximize organ usage and should be actively pursued through collaborative networks.

Key words: Left lateral segment, pediatric transplantation, split-liver transplantation

Abbreviations: SLT, Split liver transplantation; RTS, Right trisegmental; LLS, Left lateral segment; UNOS, United Network Organ Sharing; HAT, Hepatic artery thrombosis; pOLT, Pediatric orthotopic liver transplantation; PVT, Portal vein thrombosis; POD, Post-operative day; PNF, Primary non-function

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Introduction

The first split-liver transplantation (SLT) was performed by Pichlmayer et al. (1) in 1988. In that operation, the right trisegmental (RTS) graft went to a 63-year-old woman with biliary cirrhosis while the left lateral segment (LLS) graft went to a child with biliary atresia. Since that first operation there have been a number of series that have reported the results of LLS transplants (2–7) and have shown that patient and graft survival rates are comparable to whole organ and living related donor (LRD) pediatric transplant outcomes. The benefit of SLT is the ability to increase the donor organ pool by creating two allografts from a single donor. Previous reports have calculated that if all suitable donor organs were split, there would be enough allografts to transplant every pediatric patient on the United Network Organ Sharing (UNOS) waiting list (8,9). Furthermore, the same studies reported that waiting time for pediatric patients decreased from 128 days to 24 days (patients <1-year old) and 192 days to 30 days (patients >1-year old) after implementation of a policy to split all suitable organs. The increasing use of SLT has brought into question whether there is a need for LRD transplantation (3,6). Even though LRD transplantation has been safely performed, there has been a reported donor complication rate of 14–21% and a mortality rate of 0.5% (10–12). These results represent a significant complication and mortality rate for a donor who is otherwise completely healthy. The increased use of SLT and organ sharing between centers would decrease the need for LRD transplantation and the associated risks to donors of LRD transplantation.

For the full potential of SLT to be realized, transplant centers must institute collaborative sharing networks whereby each split allograft would be properly placed to two recipients. Instituting an SLT program requires effort and coordination between different centers for proper utilization of split allografts. The European model of cadaver allocation...
has allowed multiple centers to share split-liver grafts and maximize organ allocation (13). Unfortunately, organ sharing is still uncommon in the United States. Yersiz et al. (2) reported sharing 25 of 190 allografts (3 LLS and 22 RTS) between eight transplant centers while the recent American Society of Transplant Surgeons (ASTS)-commissioned survey (14) reported only a 5% incidence of organ sharing between five centers.

Since 1997, we have established a collaborative SLT network with a geographically distant transplant center and have shared over 15% of our LLS grafts. Our goal with this collaboration has been to maximize the use and allocation of split organs. With the use of SLT and our sharing alliance, we have been able to decrease the waiting time for transplantation in our pediatric population. This paper represents one of the first comprehensive descriptions of an intercenter split allograft utilization agreement between two institutions that have an impetus to maximize utilization of cadaveric donor organs. Herein, we report our combined experience of sharing the LLS for a pediatric transplant population at two geographically distant centers.

Methods

Between 9/1997 and 10/2003, there were 56 pediatric (<18 years of age) liver transplants in 53 patients using an LLS. Twenty-one LLS transplants were performed at Texas Children’s Hospital in Houston, Texas, and 35 LLS transplants were performed at the University of Texas Health Sciences Center at San Antonio. In the same time period, there were 80 pediatric whole-organ transplants between the two centers. All data for this study was analyzed retrospectively through a collaborative effort between Texas Children’s Hospital and The University of Texas Health Science Center at San Antonio. All RTS graft data and patient outcomes was reported by Washburn et al. (in submission). All study criteria and conditions were approved by the institutional review boards of both medical centers.

Donor selection

Cadaveric split-liver donor selection and criteria have been previously described (5,9). Each donor was selected through strict medical screening and only the optimal donor candidates were considered for SLT. In particular, the donors were young (age <40) without severe derangement in liver function, on no more than one vasopressor and with minimal steatotic liver disease by gross and histologic examination. Assessment of the donor organ and stability of the donor were performed by the organ procurement team. There was no use of volumetric CT scan imaging for assessment of graft size and appropriate liver mass. This assessment was solely made by visualization of the donor organ by the procuring team. If donors met all the previously listed criteria and a suitable recipient was identified at either institution, the liver was split into a LLS and RTS. Approximately 90% of donor split-livers were suitable for SLT. The LLS graft was inspected to assure that size and hepatocyte mass was appropriate for each recipient. There was available data for 52 donors. All donor demographics are presented in Table 1.

Recipient selection

Recipient demographics are outlined in Table 2. Fifty-six LLS transplants were performed in 53 pediatric (<18 years old) patients (three retransplants). Twenty-five males and 28 females received transplantation. The median recipient age was 14 months (range: 1 month to 18 years). Twenty-three (41%) patients were acutely ill and listed as a Status 1. The median PELD score was 16 (range: 6–39). As shown in Table 3, the most common indication for transplantation was that for extrahepatic biliary atresia patients while eight patients were transplanted for various metabolic diseases. In addition, nine patients were transplanted for fulminant hepatic failure. Recipients received full-informed consent for SLT. The SLT allograft and patient outcomes were explained in the context of center-specific results. Patients were also given the outcomes of complications, allograft dysfunction and patient survival from the results in the current SLT literature. No recipient refused to have an allocated organ split or refused to receive a split allograft. During this time period, no listed patient was transplanted at another institution.

Allograft allocation/arterial and biliary reconstruction

Fifty-six LLS allografts were created from 56 cadaveric donors. Allografts were generated through two organ procurement organizations. Seventy-five percent of the allografts were offered to the pediatric recipient. Sharing of grafts occurred through direct channels of communication after the

**Table 1: Donor demographics**

| Age (years) | 19 (range: 8–51) |
| Sex (M:F) | 37 males/15 females |
| Body mass index (BMI) | 23 (18–31) |
| Peak serum sodium | 153 (138–183) |
| Peak serum AST | 89 (19–550) |
| Peak serum ALT | 47 (6–267) |
| Creatinine | 1.3 (0.7–2.2) |
| Cause of death | 44 trauma/8 intracranial bleed |
| Donor arrest | 6 (12% total donors) |
| Vasopressor support | 45 (86%) |
| Length of stay (days) | 2 days (1–10) |

**Table 2: Recipient demographics**

| Age | 14 months (1 month to 18 years) |
| Gender | 25 males/28 females |
| UNOS status/PELD score | Status 1–23 pts/PELD—16 (6–39) |
| First transplant | 50 (94%) |
| Second transplant | 3 (6%) |
| Follow-up | 6 months to 6 years |

**Table 3: Indications for transplantation**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrahepatic biliary atresia</td>
<td>26</td>
</tr>
<tr>
<td>Fulminant hepatic failure</td>
<td>9</td>
</tr>
<tr>
<td>Ornithine transcarbamylase</td>
<td>4</td>
</tr>
<tr>
<td>Cryptogenic cirrhosis</td>
<td>2</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>2</td>
</tr>
<tr>
<td>Alagille syndrome</td>
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</tr>
<tr>
<td>Arteriovenous malformation</td>
<td>1</td>
</tr>
<tr>
<td>Acetaminophen toxicity</td>
<td>1</td>
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<tr>
<td>AIH</td>
<td>1</td>
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<tr>
<td>Cystic fibrosis</td>
<td>1</td>
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<tr>
<td>Galactosemia</td>
<td>1</td>
</tr>
<tr>
<td>PFIC</td>
<td>1</td>
</tr>
<tr>
<td>Propionic acidemia</td>
<td>1</td>
</tr>
<tr>
<td>Tyrosinemia</td>
<td>1</td>
</tr>
<tr>
<td>Unknown metabolic disorder</td>
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</tr>
</tbody>
</table>
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decision to split the organ was made. If the procuring team was unable to identify a recipient at their institution, all efforts were made to identify a suitable pediatric recipient at the collaborating institution. Overall, nine allografts were shared between the two centers.

Thirty-five (64%) of the 56 allografts were created with an in situ split and 21 allografts (36%) were created with an ex vivo split. Ex vivo allografts were used earlier in this study experience while the current preferred method has been in situ splitting of the allograft. The preference among procuring centers was to maintain the celiac axis with the LLS whenever possible, thereby decreasing the need for microsurgical anastomosis and arterial reconstruction. The celiac axis was kept with the LLS in 33 (59%) of the 56 allografts. The celiac axis was kept with the RTS allograft if there was a large left hepatic artery, a replaced left hepatic artery, or if the organ was initially allocated to an adult (RTS graft). Arterial reconstruction was required in 16 allografts. Biliary reconstruction consisted of 54 Roux-en-Y hepaticojejunostomy with placement of an internal stent. The biliary stent was a pediatric feeding tube, which was allowed to pass after suture dissolution. Two patients (3.6%) had a biliary reconstruction with a duct-to-duct anastomosis.

Statistics

Results are shown as median values within a range. Patient and graft survival was calculated with a Kaplan–Meier log-rank analysis. A chi-square test or Fisher exact test was performed for comparison of categorical data, and two-tailed Student’s t-test was used to compare ratio and interval variables. A p-value of less than 0.05 was considered statistically significant. All calculations were performed and compiled using Microsoft Excel (Microsoft Corp, Redmond, WA) or SPSS version 11.0 software (SPSS Corp, Chicago, IL).

Results

Patient and allograft survival

Overall, there were 56 LLS allografts created from 56 cadaveric donors. Out of the 56 allografts, nine grafts were shared between the two centers. The 56 grafts were transplanted into 53 patients (three retransplants with LLS). All patients were followed up for a minimum of 6 months, with the longest follow-up being 76 months. Kaplan–Meier survival log-rank analysis was calculated at 1-, 3- and 5-year intervals for patient survival (Figure 1). Patient survival rates at 1, 3 and 5 years were 90%, 90% and 90%, respectively. In comparison, pediatric whole-organ patient survival at 1, 3 and 5 years was 94%, 90% and 90%, respectively. UNOS (2000–2001) whole-organ and LRD data showed a 1-year survival rate of 86% and 87%, respectively. There were five overall deaths (10% mortality rate) in this study. Two patients died from multi-organ system failure (MOSF) on postoperative day (POD) 21 and POD 24, respectively. Another patient died from primary non-function (PNF) on POD 2. PNF was defined as death or retransplantation within 1 week of the initial transplant. The fourth patient expired from poor venous inflow on POD 1. The last patient expired from caval stenosis on POD 79 after his second transplant.

Graft survival at 1, 3 and 5 years was 82%, 82% and 75%, respectively (Figure 1). Pediatric whole-organ graft survival at 1, 3 and 5 years was 91%, 88% and 71%, respectively.

Figure 1: Kaplan–Meier patient and graft survival curves for pediatric patients undergoing LLS transplantation at Texas Children’s Hospital and the University of Texas Health Science Center at San Antonio (1997–2003).

UNOS (2000–2001) whole-organ graft survival and LRD graft survival at 1 year was 81% and 80%, respectively. Overall, 10 of 56 grafts failed (18%). The 10 grafts were lost from the following causes: one poor venous inflow, two HAT, two PNF, one PVT, one caval stenosis, two MOSF and one biliary stricture. Five patients who developed graft failure were retransplanted (three with LLS).

Complications

Vascular complications included five HAT and five PVT. The vascular complication rate was 18%. There was an 11% biliary complication rate. Biliary complications were three bile leaks, two biliary strictures and one missed bile duct. Vascular complications were responsible for a total of five graft failures. Biliary complications resulted in one graft failure.

Status 1 patients

There were 23 patients listed as UNOS Status 1 in this study. There were 10 total complications in this group (43%). Patient and graft survival analysis can be viewed in Figure 2. The 1- and 3-year patient survival rate was 89% and 89%, respectively. The 1- and 3-year graft survival rate was 85% and 85%, respectively. When comparing complications between Status 1 patients versus non-Status 1 patients, there was no statistical significance in complication rates (p < 0.20).

Ex vivo versus in situ split results

Thirty-five grafts were split in situ while 21 grafts were split ex vivo. Complete graft data was not available for four grafts. In the in situ group, there were two deaths, three
HAT, three PVT and five biliary complications. The ex vivo group had three deaths, two HAT, two PVT and one biliary complication. In the two grafts that had PNF, one was split in situ and the other ex vivo. When comparing biliary complications between the two groups, the difference did not reach statistical significance (p = 0.20). All other variables showed no difference when compared between ex vivo and in situ groups.

**Shared graft results**

Nine allografts (16%) were shared between the two centers. The median cold ischemia time for the shared allograft group was 6.5 h compared to 7.3 h for the nonsnared allograft group. The patient and graft survival in this subset of patients was 89% and 89%, respectively. The median follow-up for this subgroup of patients is 17 months (range: 1–46 months). These results compare favorably to UNOS whole-organ and LRD results as previously mentioned. There was one mortality in the shared group. There were two complications in this group. One patient required a second operation for bleeding, while the second patient developed poor venous outflow, necessitating venous outflow reconstruction. There were no biliary or arterial complications in this group.

Since instituting SLT and the sharing alliance between our two centers, we have been able to meet the needs of our pediatric population without instituting an LRD transplantation program. Furthermore, the SLT patients have seen a decrease in waiting time in comparison to whole-organ patients. The median wait time for SLT patients at center 1 and center 2 were 51 and 101 days, respectively. The median wait time for whole-organ allograft patients at center 1 and center 2 were 244 and 130 days, respectively.

**Discussion**

Split liver transplantation (SLT) has allowed for maximization of donor organs by creating two allografts from a single organ. The use of SLT mainly involves use of a RTS graft for adults and the LLS in children. Even though SLT can increase the number of donor organs, SLT has not been fully embraced by the transplantation community. The recent ASTS national survey (14) demonstrated that of the 83 responding transplant centers, only 45% had any experience with SLT. Of the centers with SLT experience, 67% had performed less than five transplants and over 50% of SLT was being performed by only 13 centers. In our current study, both surgical centers have a dedicated commitment to using SLT. To maximize organ usage, we have established a collaborative network to increase organ sharing and data collection in hopes of improving SLT outcomes and maximizing split organ placement.

In our study, the patient and graft survival rates were excellent. Previously published studies have reported 1-year patient survival ranging from 76% to 100% (2–7) and 1-year graft survival from 71% to 100%. Our results also compared favorably to UNOS data (15) for cadaveric whole-organ transplantation from 2000 to 2001, where the 1-year patient and graft survival rates were 86% and 81%, respectively. These results would suggest that the use of a LLS graft did not pose any greater risk to patient or graft survival when compared to previously published data. On comparison with whole-organ pediatric grafts at each center, there was no significant difference between LLS graft outcomes versus whole-organ outcomes. The study results also demonstrated that patient and graft survival did not decrease in an acutely ill population. Approximately 43% of the patients in this study were listed as Status 1, comprising just under half of the total recipient population. This population was comparable to the UCLA series of in situ splits (8) where 41.5% of their SLT recipients were Status 1. In that study, the total recipient survival was 96% and the LLS graft survival was 75%. Looking at our Status 1 population, the 3-year patient and graft survival was 89% and 85%, respectively. Our results and those of previous studies reaffirmed the safety and efficacy of using the LLS in critically ill pediatric patients.

At both of our centers, the use of the SLT has decreased the emphasis for an LRD transplantation program. Previous studies have shown that LRD can increase the donor organ pool with acceptable results (15,16). Roberts et al. (17) recently reported that use of living donors in pediatric patients (<2 years old) showed better 1-year graft survival and lower 1-year mortality risk than cadaveric donor transplantation. However, the survival advantage of LRD transplantation was not present after 1 year and was even lower than that of SLT for patients 2 years or older. Abt et al. (18) expanded on the analysis of pediatric liver transplant recipients by identifying that the LRD allografts had
improved graft survival when compared to split-liver allografts for patients less than 2 years of age; however, there was no statistically significant difference in patient survival between the two graft types. A recent survey (11) was sent to all transplantation programs concerning living donor outcomes and the respondents of this survey, reported a donor complication rate of 14.5% and one donor death. Furthermore, there was a significant number of serious complications: biliary leak (6%), reoperation (4.5%) and major postoperative infection (1.1%). Lee et al. (12) also recently published a series concerning donor complications after LRD transplantation. They found that 14% of donors had complications such as bile leak, intraperitoneal abscesses, active bleeding and portal vein stenosis. Another large analysis by The European Transplant Registry concluded that that the LRD mortality and morbidity rate in Europe was 0.5% and 21%, respectively (10). Finally, a recent case report by the Japanese on a living related donor death has further highlighted the current dilemma of LRD (19). With these previous studies, donor complications have been shown to be very common and donor mortality was reported in three of the above-mentioned studies. Our belief is that SLT, with implementation of a sharing network, would reduce or alleviate the need for an LRD, thereby providing the necessary organs without risking the life of a healthy donor.

The implementation of a collaborative network has allowed us to share organs with a geographically distant center and maximized the use of donor organs in our region. Organ sharing is infrequent between geographically distant transplant centers. Renz et al. (14) reported only a 5% sharing rate among transplant centers in the recent ASTS survey. Yersiz et al. (2) reported sharing of 3 LLS/22 RTS grafts in their recent report and Rela et al. (20) reported sharing of only 3 RTS out of 41 grafts. The most likely reason for minimal organ sharing was the substantial effort and coordination required between transplant groups for placement of organs. In our region, we attempted to share as many split organs as possible. As shown by Washburn et al. [in submission] data on RTS graft between our centers highlighted the point that 40% of RTS grafts were shared. In this LLS series, 16% of LLS allografts were shared between our two centers. The results from these grafts were excellent with a patient and graft survival rate of 89% and 89%, respectively, demonstrating that organ sharing was a safe and effective method for SLT transplantation. These results are comparable to the overall results from our study as well as UNOS pediatric whole-organ and LRD patient/graft survival. The European model of organ sharing has also produced similar results, where transplant centers have expressed a high degree of satisfaction with the outcomes from shared grafts (13).

The organ sharing agreement was initially established to maximize usage of all cadaveric donor grafts and to decrease the need for implementation of an LRD transplantation program at each institution. The sharing agreement included only two of the programs within the state since neither program had any previous experience with this type of sharing agreement. The goal of this agreement was to demonstrate that a sharing network would improve utilization of cadaveric organs and that the patient and graft outcomes would be comparable to whole-organ grafts, thereby providing a model for future SLT collaborative networks.

In implementing an SLT program, there needs to be a formal policy on the consent procedure for patients offered a split-liver allograft. We believe that, patients should be informed at either the time of listing or prior to ascension to the top of the transplant list that SLT is advocated at each institution. Furthermore, the patients should be informed that per UNOS policy, the use of split-liver allografts is an ethical responsibility of transplant centers to increase use of cadaveric allografts (21). Patients are also presented with data about the national outcomes of SLT as well as the center-specific allograft and patient outcomes. After the explanation of SLT, patients need to be made aware of their right to accept or refuse a split organ. Through this study period, there have been no recipients who refused to accept a split-liver allograft and also no recipients who refused to have an organ split.

We attributed the success of our organ-sharing agreement to a personal knowledge of the other transplant team, open channels of communication between the two groups, and also the expertise of each center in performing SLT. After identification of an acceptable split donor, the procuring team would contact the collaborating center to ascertain whether there was an acceptable recipient for the second allograft. In the majority of cases, the allograft was initially offered to the pediatric recipient. The RTS allograft was initially offered locally based on medical urgency for transplantation. Only if the local centers declined the RTS allograft, was it then allocated to centers within the sharing agreement. Recipients within the sharing agreement were selected on the basis of medical urgency. There were no concerns of the quality of the split graft because of our knowledge of the procuring team and previous experience with shared grafts. Furthermore, established technical policies (i.e. allocation of the celiac trunk) had been discussed and agreed on by both centers. With the implementation of a national UNOS sharing policy, we have found that this policy has decreased the flexibility that has been needed for an implementation of a successful collaborative agreement. The implementation of a mandatory UNOS sharing policy may possibly further hinder intercenter agreements by forcing centers that have no interest or expertise in SLT to use split-liver allografts. Currently, our agreement is a voluntary agreement and allows for full utilization of each split allograft, eliminating the need for LRD transplantation at each respective institution. Under the current allocation system, unless the organ is offered to a pediatric patient, there is no way to identify a pediatric recipient in need of an LLS graft. Our collaborative agreement between the

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two centers has allowed for identification of both adult and pediatric recipients for SLT. As our collaborative network may serve as the model, UNOS policy should allow for flexibility between centers, in particular to allow organ sharing between centers that have a strong impetus on use of SLT.

In conclusion, our results show that the use of the LLS allograft is a safe and effective means of increasing the cadaveric donor organ pool for pediatric patients. Furthermore, organ sharing should be pursued and encouraged among transplant centers with an expertise in SLT to maximize organ usage. The description of the intercenter agreement may serve as a model for further collaborative sharing networks. In future, modification of the current UNOS policy for organ sharing to allow increased flexibility could further the application of SLT to encompass the majority of pediatric liver transplantation.

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