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Split Graft Liver Transplant for Paediatric Patients in Hong Kong

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Abstract There is a significant shortage of deceased liver grafts for paediatric patients worldwide. In Hong Kong, this problem is even more severe. In order to expand the donor pool, various methods have been used. Split-graft liver transplant is one of the potential ways to effectively increase the number of deceased donor grafts. Here, we present a review of our experience of using split-grafts for children in Hong Kong.

Key words Children; Split graft liver transplant

Introduction

Liver grafts can come either from living donor or deceased donor. For a living donor graft, the patient's parent or close relative (living-related donor) is usually the source. However, this practice is sometimes limited by the medical condition of the potential donor. Furthermore, there is a surgical risk to the healthy donors. Hence, the provision of a part of the liver by the living donor is always an act of altruism. One can therefore argue that the use of deceased donor grafts may be a better option. Nonetheless, the shortage of deceased donor has always been a major obstacle in our locality.

For the paediatric population, very few brain-dead donors are available and hence size-matching deceased donor graft is extremely limited. Therefore, various methods have been studied in order to improve the graft supply. Among them, splitting a deceased donor graft has become an alternative and viable choice for paediatric patients. The idea is to split up one deceased donor graft, using the larger portion for an adult patient and the smaller graft for a paediatric patient.

Splitting a liver graft is technically demanding and the initial results were not satisfactory. However, with more experience gained from performing living donor liver transplant, our technique has much maturation. The success of utilising split graft has reduced the demand for living donor graft and shortened the waiting time of patients.

From the liver transplantation experience since 1993, our center performed the first case of split-graft liver transplant for a paediatric patient in January 2003. Here, we review the outcomes of split-graft transplant and to compare the result with other organ sources.

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Materials and Methods

A retrospective study was carried out to review all paediatric patients, younger than 18 years, who had liver transplantation in Queen Mary Hospital, Hong Kong. Patient data and medical records were prospectively collected by the liver transplant research staff and retrospectively analysed. Demographic, operative and clinical data were collected. Outcomes analysis including occurrence of complications, graft and patient survivals (until the last follow up in March, 2009) are presented.

Results

A total of 93 cases of paediatric liver transplantation were performed in Queen Mary Hospital, Hong Kong between September 1993 and March 2009. The most common indication for transplant was biliary atresia (65.6%). This was followed by fulminant hepatitis, metabolic disease and retransplantation for graft failure (Figure 1). Regarding the type of graft, the majority (72.0%, n=67) had living donor grafts. For the remaining 26 cases, liver grafts were taken from deceased donors, with 10 cases of reduced-size grafts, 8 cases of whole grafts and 8 cases of split grafts.

Since 2003, eight cases of split graft liver transplant have been performed. Six of the split grafts were left lateral segment grafts and 2 were left lobe grafts. As the size of the graft limited the size of the recipient, all the patients were of young age with a median age of 10.5 months. The mean PELD score (Paediatric End-Stage Liver Disease Score) was 15.5 among the group. Biliary complications were seen in 2 patients. None of the patients developed vascular complication. However, there was one patient who suffered primary graft failure and required retransplantation. One patient died at 24 months after transplantation due to an unrelated cause. The median hospital stay is 24.3 days. Overall the graft survival rate is 75% and cumulative patient survival rate is 87.5% until our last follow up (Figure 2).

Living donor liver transplants were performed in 67 patients. While 15 recipients receiving living donor grafts had biliary complications including bile leakage and bile duct stricture, fourteen patients suffered from vascular complications. Five patients died of sepsis or lymphoproliferative disease. Patients stayed longer in hospital when compared with split graft recipients and the mean hospital stay is 36.5±16.8 days. Overall, the graft and patient survival rates are 86.6% and 89.6% respectively at the time of last follow up (Figure 2).

Since a whole graft is usually implanted in a larger size patient, the median age of the recipients who received this type of graft is older (154.0 months). As expected, cases of whole graft transplant are limited. However, the graft and patient survival rates are the best among different graft sources (100% for both survivals) (Figure 2). One patient developed bile leakage and one patient had hepatic vein thrombosis. Median hospital stay is 21.8 days.

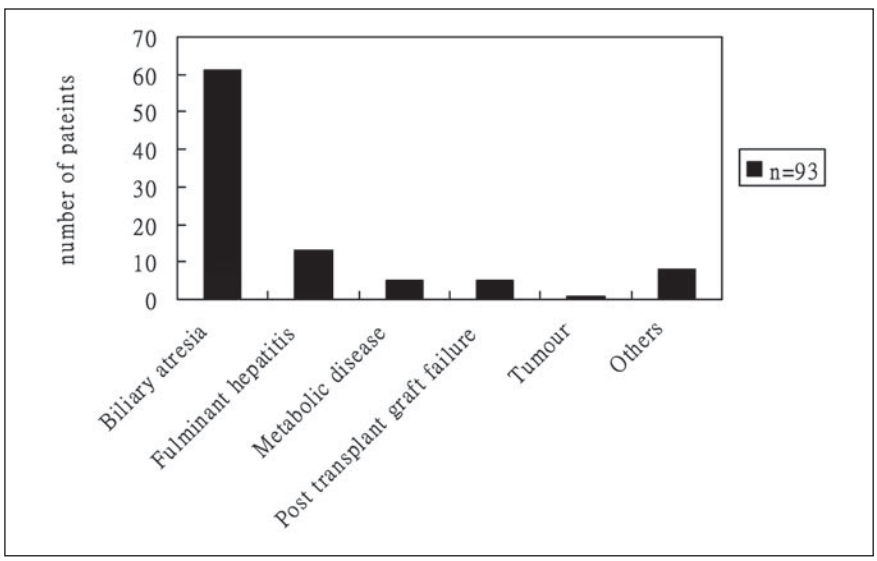

Figure 1 Indications for paediatric liver transplant in Queen Mary Hospital from 9/1993 to 3/2009.

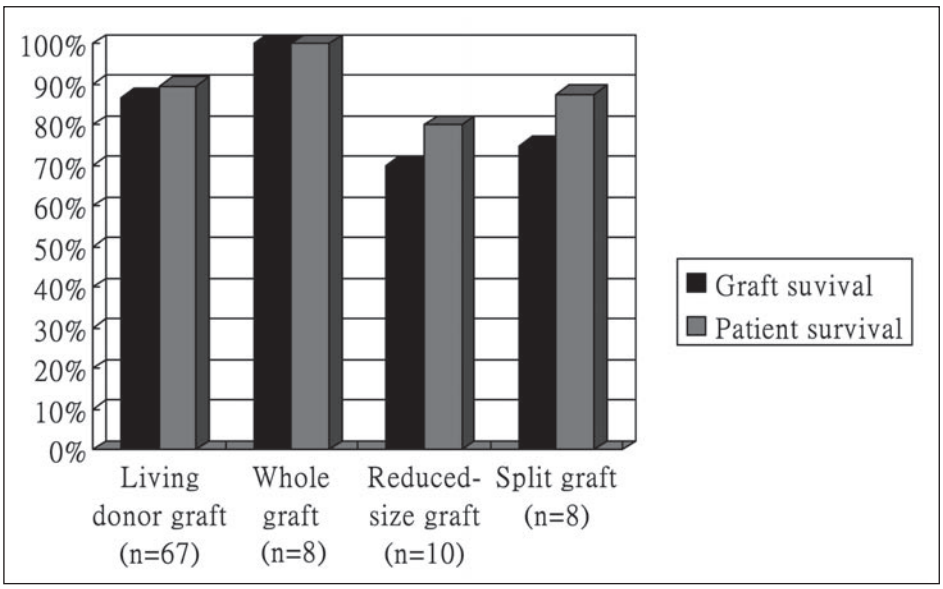

Figure 2 Graft and patient survival status until March, 2009.

For the 10 patients who had reduced-size grafts, they were all performed in young patients with a median age 20.2 months. Six patients received left lateral segment grafts and 4 patients received left lobe grafts. One patient developed portal vein stenosis. There was also one case of biliary stricture. Two patients died of respiratory failure and portopulmonary hypertension. One graft loss happened at 2 year after initial operation due to graft hepatitis. The hospital stay in this group is the longest (median=41.3 days). The graft and patient survival rates are 70% and 80% respectively (Figure 2).

Then, we analysed the percentage of living donor graft, transplantation rate, mean PELD score and mean waiting time before and after 2003 when the first case of split graft was carried out. Several difference have been noted (Table 1). Before that, living donor graft accounted for 76.5% of all liver transplants while this has reduced to 70.6% after 2003. The paediatric transplantation rate has risen from 4.5 cases per year to 8.7 cases per year. Furthermore, the mean PELD score of recipients dropped from 23.7±13.8 to 17.8±12.8 and a shorter waiting time (14.4±5.7 weeks vs 11.5±9.6 weeks) was seen after 2003 (Table 1).

Discussion

The most common indication for paediatric liver transplant in our locality is biliary atresia. The majority of our patients was very young at the time of transplantation. In our series, 61.2% patients were younger than 3 years when they underwent transplantation. Worse than other countries, the number of deceased donors is very limited in Hong Kong. Deceased donor transplant only accounts for 28.0% in our series. Although most parents are willing to donate organs for their children, this is sometimes limited by the medical condition of the donors. Besides, donors are subjected to the risk of complications, including 0.1% to 0.5% mortality, when undergoing hepatectomy.[1] Therefore, utilising deceased donor graft is still the best option if available.

Due to the shortage of deceased donor liver grafts for children, transplant surgeons have been actively looking for new methods to expand the donor pool. The first technique is reduced-size liver transplant.[2] However, this

Table 1 Difference observed before and after 2003 indicating the benefit brought about by introducing split graft transplant

	Before 2003	After 2003
Percentage of living donor	76.5	70.6
Transplantation rate	4.5 cases/year	8.7 cases/year
Mean PELD score*	23.7±13.8	17.8±12.8
Mean waiting time (weeks)	14.4±5.7	11.5±9.6

* 12 patients were excluded because their data were missing or age >12 years when PELD score is not applicable

method does not actually increase the number of grafts available but includes the paediatric candidates into the adult liver graft pool. In addition, the remaining portion of liver will be wasted. After the technique of liver resection in patient with liver tumour was mastered, the idea of splitting a liver graft for one adult and one paediatric patient was first reported by Pichlmayr[3] and Bismuth[4] in 1988. Their technique served as the fundamental principle for dividing the whole liver into two suitable grafts. In Asia, the first split graft liver transplant for adult and paediatric patients was done in Taiwan in 1997.[5] In Hong Kong, the history of split graft liver transplant for an adult and a paediatric patient started with an international sharing of organ in January 1999 when a liver graft from a 35-year old deceased donor in Taiwan was divided into a left lateral segment graft for a 3-year old girl in Taiwan and a right lobe graft for a 51-year old man in Hong Kong.[6] This initial experience of international sharing of split liver graft set up an encouraging example for the establishment of an organ-sharing network in the region with a hope that more transplant candidates can be saved. On 31st January 2003, Queen Mary Hospital performed the first split graft liver transplantation for an adult and a paediatric patient with three surgical teams operating simultaneously.

The selection of donor for liver splitting is highly restricted. It has been proposed that deceased donor must be hemodynamically stable and age younger than 55 years. Other parameters including body weight, past medical history, results of liver function test, electrolyte balance are also considered when deciding whether the donor graft is suitable for splitting.[7] In general, about 15% to 20% donors are eligible for split liver transplantation.[8] The requirements of organ quality are more demanding if full right and left split grafts are intended.

Regarding the technical aspect, there are two ways of splitting the liver. The procedure can be broadly divided into in-situ and ex-situ splitting of the liver. In-situ splitting procedure results in a shorter cold ischaemic time at the expense of a longer duration of the donor procedure. For the ex-situ splitting, the surgeons can have a bloodless operating filed during the splitting procedure but post-implantation bleeding can be a potential problem.[9] In case one of the recipients is a small-sized paediatric patient, the liver is splitted into a left lateral segment graft (LLS) including Couinaud segments 2 & 3 for a child and a right trisegment graft (RTS) including Couinaud segments 1, 4 to 8 for an adult. This is usually the case for paediatric liver transplant. Subsequently, this method is modified to provide two liver grafts for two adult patients or one adult and one large-sized paediatric patient. In such case, the liver is splitted along the Cantlie's line resulting into a right lobe (Couinaud segments 5-8) and a left lobe (Couinaud segments 1-4) grafts.[10]

Broering et al has reviewed the outcomes of split liver transplant from various centers.[7] From 1990 to 2002, 20 centers have performed this procedure and the total number of cases is 915. While the graft survival ranges from 50% to 88%, the patient survival ranges from 50% to 92%. Yersiz et al from the UCLA Transplant Center published their experience of 100 in-situ split liver transplantations in 2003.[9] In their series, 100 livers were divided into left lateral segment and right trisegment grafts resulting in 190 allografts. They were transplanted into 105 children and 60 adults with the remaining 25 shared by other centers. For paediatric transplantation using the left lateral segment, the 3-year graft survival rate was 64% which was slightly inferior to 73% in whole graft transplantation and 71% in living donor using left lateral graft ($p= 0.12$). The recipient 3-year survival rate was 75%, whereas the 3-year recipient survival rates in the whole graft transplantation group and living donor group were 81% and 84%, respectively ($p=0.01$). They concluded that split-liver transplantation is an effective way for immediate expansion of the deceased donor pool and helps to reduce the dependence upon living donation.

The complication rate of utilising splitted left lateral segment graft has been reported to be similar as that of living donor-left lateral segment and whole graft with respect to biliary and vascular complications.[11-13] However, primary non-function has been reported to be more commonly seen in patients receiving split graft.[9]

When compared with living donor transplantation, the occurrence of biliary complications is comparable in our series. However, the fact that no patient receiving split graft developed vascular complication has made itself prominent in terms of complication rate (Figure 3). From our cumulative survival graph, one can appreciate that both the graft and patient survivals achieve similar results as other types of liver grafts (Figure 2). Although the limited case number forbids an accurate statistical conclusion, these results are encouraging. Furthermore, as the number of split graft is still far less than living donor graft, it is expected that an even better survival can be achieved in the coming future with more experience accumulated.

On the other hand, the benefit of utilising split grafts is obvious when looking at the difference before and after 2003 when the first case was performed (Table 1). First,

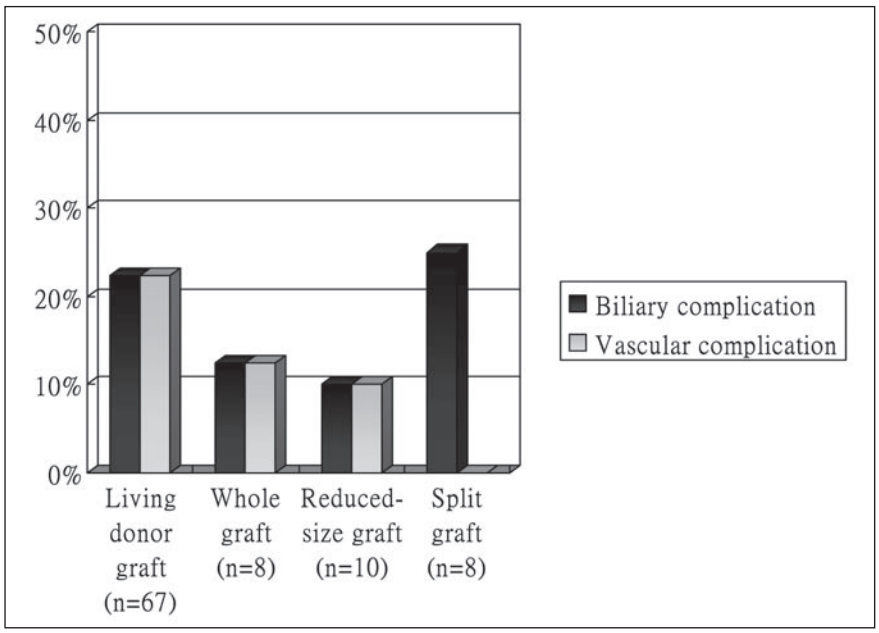

Figure 3 Biliary and vascular complication rates of various types of grafts.

living donor graft accounted for less percentage. This reflects that less living donor is required. Second, the paediatric transplantation rate has also risen from 4.5 cases per year to 8.7 cases per year after 2003. With a lower PELD score, more patients could receive a graft at an earlier stage. In fact, the mean PELD score for patients with split graft is only 15.5 which means that patients with lower score can also be benefit from split graft liver transplant. This is further evidenced by a shorter waiting time seen after 2003.

In conclusion, split graft liver transplant is an effective way to immediately expand the donor pool with a reduction in donors' risk. Improvement in transplantation rate and waiting time with less living donors subjected to operative risk are the associated advantages. Given the initial outcomes are promising, the technique of utilising split grafts for liver transplant deserves further development. With more experience, a better outcome is foreseeable. Together with an increasing number of deceased donors, it is hoped that more patients can benefit with less living donors required.

References

1. Chan SC, Fan ST, Lo CM, Liu CL, Wong J. Toward current standards of donor right hepatectomy for adult-to-adult live donor liver transplantation through the experience of 200 cases. Ann Surg 2007;245:110-7.
2. Broelsch CE, Emond JC, Thistlethwaite JR, Rouch DA, Whitington PF, Lichtor JL. Liver transplantation with reduced-size donor organs. Transplantation 1988;45:519-24.
3. Pichlmayr R, Ringe B, Gubernatis G, Hauss J, Bunzendahl H. Transplantation of a donor liver to 2 recipients (splitting transplantation)-a new method in the further development of segmental liver transplantation. Langenbecks Arch Chir 1988;373:127-30.
4. Bismuth H, Morino M, Castaing D, et al. Emergency orthotopic liver transplantation in two patients using one donor liver. Br J Surg 1989;76:722-4.
5. de Villa VH, Chen CL, Chen YS, et al. Split Liver Transplantation in Asia. Transplant Proc 2001;33:1501-2.
6. de Villa VH, Chen CL, Chen YS, et al. International sharing of split liver grafts in Asia: initial experience. Clin Transplant 2000;14(4 Pt 1):355-9.
7. Broering D, Schulte Am Esch J, Fischer L, Rogiers X. Split liver transplantation. HPB (Oxford) 2004;6:76-82.
8. Toso C, Ris F, Mentha G, Oberholzer J, Morel P, Majno P. Potential impact of in situ liver splitting on the number of available grafts. Transplantation 2002;74:222-6.
9. Yersiz H, Renz JF, Farmer DG, Hisatake GM, McDiarmid SV, Busuttil RW. One hundred in situ split-liver transplantations: a single-center experience. Ann Surg 2003; 238:496-505.
10. Azoulay D, Astarcioglu I, Bismuth H, et al. Split-liver transplantation. The Paul Brousse policy. Ann Surg 1996; 224:737-46.
11. Busttil RW, Goss JA. Split liver transplantation. Ann Surg 1999;229:313-21.
12. Mirza DF, Achilleos O, Pirenne J, Buckels JA, McMaster P, Mayer AD. Encouraging results of split-liver transplantation. Br J Surg 1998;85:494-7.
13. Broering DC, Mueller L, Ganschow R, et al. Is there still a need for living-related liver transplantation in children? Ann Surg 2001;234:713-21.