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POINT OF VIEW

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Reduced size liver transplantation, split liver transplantation, and living related liver transplantation in relation to the donor organ shortage

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Abstract Because of the shortage of cadaveric donors, three techniques of partial liver grafting have been developed. These techniques are placed in perspective in relation to the organ shortage. Reduced size liver transplantation (RSLTx) is widely used and has results comparable to those from whole liver grafting. However, this technique, while benefitting pediatric patients, reduces the adult donor liver pool. It also makes inefficient use of an available adult donor liver. In split liver transplantation (SPLTx), the whole liver is used after bipartition for two recipients. The results are comparable to those of RSLTx. The problem with SPLTx is that it is a very demanding technique applied only in centers with extensive experience with liver resection and reduction. Living related liver transplantation (LRLTx) yields excellent results; however, it places an otherwise healthy person at risk. It is argued that instead of performing risky operations on healthy persons, the health authorities should take specific measures to alleviate the organ shortage. In the meantime, SPLTx should be developed further because of its optimal use of donor tissue. As for LRLTx, its excellent results and the present shortage of size-matched pediatric liver donors justify its use, at least for now.

Key words Liver transplantation, reduced size · Split liver transplantation · Living related liver transplantation

The present shortage of cadaveric donor organs is one of the main factors limiting the expansion of liver transplantation. Potential recipients continue to die while waiting for a suitable graft. Very often it is children who are the victims since pediatric donors are scarce [1, 7, 29]. In order to solve this problem, several centers have developed new techniques such as reduced size liver transplantation (RSLTx) [3, 24, 28, 31], split liver transplantation (SPLTx) [9, 15, 23, 26], and living related liver transplantation (LRLTx) [6]. With these three options available, the question arises of just what each technique contributes to reducing the organ shortage.

RSLTx has been performed by several centers for many years now. Thus far, its overall results are good (Table 1). One-year patient and graft survival vary from 62 % to 78 % and from 47 % to 62 %, [2, 10, 24]. As indicated by Otte et al., survival is dependent up on the condition of the recipient. RSLTx performed in urgent cases has a 1-year patient and graft survival of 43 % and 35 %, respectively, compared to 77 % and 68 % in elective patients [24]. Since the routine performance of RSLTx some centers have been able to report a reduction in the death rate on their waiting list [18, 34]. However, RSLTx only partially solves the problem posed by the organ shortage. In RSLTx, parts of adult donor livers – mostly the left liver lobe or left lateral segments – are used for pediatric recipients. The rest of the donor liver is discarded. These partially used livers are withdrawn from the pool of adult donor livers, thereby placing adult recipients at a disadvantage. This fact, plus the fact that potentially usable liver tissue is discarded, stimulated the emergence of the concept of

Table 1 Results of reduced size liver transplantation

Series	No. of patients	No. of grafts	1-year survival	
			Patient	Graft
Badger [2]	24	30	62 %	47
Emond [10]	23	27	78 %	61 %
Otte [24]	42	54	68 %	54 %
Groningen	38	45	77 %	62 %

Table 2 Results of split liver transplantation

Series	No. of patients	No. of grafts	1-year survival	
			Patient	Graft
Emond [9]	18	18	60 %	52 %
Houssin [15]	16	16	75 %	69 %
Shaw [30]	10	10	50 %	50 %
De Ville de Goyet [35]	23	25	78 %	68 %
Groningen	15	15	73 %	67 %

Table 3 Results of living related transplantation

Series	No. of patients	1-year survival		Morbidity donor	Mortality donor
		Patient	Graft		
Broelsch [6]	29	82 %	75 %	3/20 (15 %)	None
Emond [8]	20	95 %	85 %	3/20 (15 %)	None
Emond [11]	18	94 %	83 %	3/18 (17 %)	None
Tanaka [32]	33	82 %	–	1/33 (3 %)	None

SPLTx. In this procedure the adult donor liver is split on a back table into a segmental graft (mostly the left liver lobe or the left lateral segments) and a right lobe, each with their vascular and biliary pedicles, which are subsequently transplanted. In most cases the left lobe or lateral segments are used in a pediatric recipient and the right lobe in an adult. In SPLTx the available donor liver is thus used in an optimal way, placing neither the pediatric nor the adult recipient at a disadvantage. In fact, an extra graft is gained. The major drawback of this technique is that it is very demanding and requires both extensive knowledge of the hepatic anatomy and experience with liver resections. Despite these requirements, the results of SPLTx procedures are quite rewarding, as shown in Table 2. One-year patient survival ranges from 50 % to 78 % and 1-year graft survival from 50 % to 69 % [9, 15, 30, 35].

Recently, another possible technique for alleviating the donor shortage, especially in children, emerged: LRLTx. During this procedure, a part of the liver (left lobe or left lateral segments) is resected from a healthy family member, in most cases one of the parents, and transplanted in to their diseased child. The results of LRLTx reported so far are excellent (Table 3). One-year patient survival ranges from 82 % to 95 % and graft survival varies from 75 % to 85 % [6, 8, 10, 32]. With LRLTx, no liver tissue is removed from the donor pool. The major drawback of this new procedure, however, is that it places a healthy person at risk, as a liver resection is, indeed, a risky operation. Thus, the living donor operation introduces another, rather unique, risk factor into the whole transplant procedure.

How should the results of these three different procedures be judged? The most extensive experience with RSLTx thus far comes from the Brussels group [24]. They were able to show in a large series of 117 patients and 141 grafts that no difference could be observed in either patient or graft survival between reduced size grafts and whole organ grafts. Nor did morbidity differ between groups of patients who underwent these procedures. Therefore, one might argue that the results of the already established and routinely used RSLTx are the gold standard against which the newer techniques such as LRLTx and SPLTx should be compared. As can be seen from Tables 1 and 2, the results in terms of patient and graft survival between RSLTx and SPLTx are not much different. These findings have been confirmed by several groups [2, 10, 18, 34]. Patient and graft survival rates after LRLTx are superior to those after RSLTx and SPLTx. One must realize, however, that the patients transplanted with these various techniques are not really comparable. In the Brussels, Groningen, and Nebraska RSLTx and SPLTx series, the majority of the patients are UNOS code IV or urgent patients (Eurotransplant code). The outcome of transplantation in this type of patient is known to be inferior to that in elective patients [18, 24]. LRLTx recipients are, for the most part, elective patients. After the first European meeting on SPLTx, this fact was acknowledged and the decision was made to explore SPLTx further in nonurgent patients. The technique of SPLTx is, in itself, probably more difficult to learn than that of LRLTx. A learning curve can, therefore, be expected, whereas a left lobectomy or left lateral segmentectomy in a healthy person with only minor adaptations for preservation of the vessels and bile ducts is a routine procedure and, thus, comparatively easier.

The price one must pay for the superior results of LRLTx is the newly introduced risk of living related donation. What exactly are the risks for living related liver donation in a healthy person? Even in experienced hands, liver resections have a mortality ranging from 0 % to 4 % in elective patients with noncirrotic livers. Morbidity in such patients is higher and varies between 10 % and 20 % [5, 16, 25]. The results of living related donation have been reported by several centers. Apart from one perioperative death (1 out of 33 donors, 3 %) in the Hamburg series, recently reported during the ESOT Congress, thus far no additional mortality from living related liver donation has officially been report-

ed [6, 8, 11, 32]. Thus, mortality from living donation varies from 0 % zero to 3 % in different series. This is a figure that seems realistic, given the abovementioned mortality from left hepatectomies.

An appraisal of morbidity is more difficult because it is often underestimated. However, careful analysis of the reports reveals percentages varying between 3 % and 17 % [6, 8, 11, 32]; in a recent report by Marimoto et al., even higher figures were mentioned [21]. Of 34 parental donors, 20 had no symptoms, whereas the other 14 (41 %) had complaints ranging from fatigue and wound pain to gastritis and duodenal ulcers. These figures indicate that even in this elective situation in experienced centers, liver resections for living donation remain major operations that should only be performed on strict indication.

The indication for LRLTx is mainly determined by the shortage of cadaveric organs, as reported by several organ exchange organizations [33]. But does such an organ shortage really justify placing an otherwise healthy person at risk? Analysis of this situation reveals that the potential cadaveric organ pool can be extended substantially. Still, in most countries, a refusal rate of over 25 %–33 % for organ donation by relatives is reported [13]. Moreover, several publications reveal that the medical profession itself contributes to the shortage by not recognizing or reporting suitable donors [14, 17]. Also, logistical problems in either donor centers or transplantation centers are responsible for the nonuse of available donors [4]. Finally, many donor livers are not harvested for so-called medical reasons (i.e., for fear of transplanting nonviable livers).

To solve these problems, governmental support – adequate legislation and regulations in relation to organ donation and transplantation – is essential. Public education as to the benefits and results of transplantation should convince the public of the merits of organ donation. Support for individual donors and for transplantation centers in order to straighten out logistical problems may enable them to extend their possibilities. Also, professionals in the field of medicine should be trained to recognize potential donors and should be obliged to report them to the organ procurement organizations. The efficacy of such measures has already been proven in some countries and within some procurement organizations. In Belgium and Austria, for example, where adequate legislation does exist with regard to organ donation, the number of available donors per million inhabitants is higher than that in Germany or in the Netherlands, where such legislation is absent [12]. A rough calculation shows that the total number of livers available within Eurotransplant would double if the harvesting rate in Germany and the Netherlands was the same as that in Austria and Belgium. Within Eurotransplant, in a collaborative effort to optimize the use of available liver donors (Eurotransplant liver allocation program), the number of discarded livers due to organizational and logistical reasons has diminished substantially [4]. While a truly validated basis for judging the quality of donor livers is lacking [27], more and more evidence is emerging that most donor livers offered by experienced donor teams are suitable for transplantation. Therefore, one should realize that the potential cadaveric donor pool can be extended substantially, and all efforts should be concentrated on expanding the potential donor pool before undertaking risky operations in healthy persons.

In sum, it appears that RSLTx, in itself, does not diminish the organ shortage. It makes inefficient use of available liver tissue and places adult recipients on waiting lists at a disadvantage. SPLTx makes very efficient use of available liver tissue and does not harm any recipient pool. It is, however, a difficult procedure and centers performing SPLTx require additional organizational conditions. Good results, fully comparable to those after RSLTx, are obtained in experienced centers. LRLTx does not affect the cadaveric donor pool but rather provides an additional donor source. Results are excellent. Another argument put forward in favor of LRLTx is that because of the parent-child relationship, possible immunological advantages (e.g., better HLA-A, B, DR match and a negative cross-match) are present. However, the role of such a better immunological match in liver transplantation is not clearly defined [20]. Even in situations where there are complete HLA A, B, DR mismatches between donor and recipient and/or positive crossmatches, good results are reported [19, 22]. Therefore, it is debatable whether a better match obtained with living related donation warrants a major operation in a healthy subject. Logistical arguments are also used to support LRLTx. Both operations can be performed in an elective setting, which may have a positive influence on the quality of the procedure. The validity of this argument may, however, diminish in a well-trained and professional environment. The price one pays for these so-called advantages are morbidity and mortality in the living donor.

Measures to alleviate the donor shortage will take much time. In the meantime, and as a first step on the part of transplant surgeons, SPLTx should be developed further. It makes the most efficient use of available donor tissue. Experience should be expanded in order to improve its results and to spread the technique. SPLTx will expand the existing donor pool without endangering the integrity of healthy persons. Until the positive effects of improved donor programs are present, LRLTx is justified on the basis of its good results and the present shortage of cadaveric liver grafts. However, it should be performed cautiously in highly specialized centers with extensive experience with liver surgery, RSLTx, and SPLTx.

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