Split-liver transplantation in two adult recipients
Evaluation of feasibility in 100 consecutive cadaver liver grafts

Gilles PONCET (1), Jérôme DUMORTIER (1), Antoine CHOUCAIR (1), Marwan DAWAHRA (1), Catherine BOUCAUD (1), Jean-Yves SCOAZEC (2), Olivier BOILLOT (1)

(1) Unité de Transplantation Hépatique, Fédération des Spécialités Digestives, Hôpital Edouard Herriot, Lyon ; (2) Service Central d'Anatomie et Cytologie Pathologiques, Hôpital Edouard Herriot, Lyon.


RÉSUMÉ
Objectif — Évaluer la faisabilité de la bipartition d'un greffon hépatique pour transplantation chez deux adultes.

Malades et méthodes — Les informations concernant 100 prélèvements hépatiques consécutifs ont été colligées. En fonction du déroulement chronologique du prélèvement, 4 groupes de critères de faisabilité de la bipartition pour deux adultes ont été définis : 1) critères initiaux du donneur : âge, poids, tests biologiques hépatiques ; 2) critères de prélèvement et de préparation du greffon : aspect macroscopique, poids, stabilité hémodynamique ; 3) critères anatomiques et 4) critères histologiques.

Résultats — L’application des critères de faisabilité de la bipartition pour deux adultes aurait conduit à écarter 47 greffons selon les critères initiaux, 34 au moment du prélèvement, 6 selon des critères anatomiques et histologiques. Finalement, 13 greffons hépatiques auraient pu être utilisés pour une bipartition pour deux adultes.

Conclusions — La bipartition d’un greffon hépatique pour deux adultes pourrait augmenter le nombre de greffon de 13 %. Elle nécessite la maîtrise de nombreux éléments techniques et logistiques qui devront être évalués.

SUMMARY
Aim — To evaluate the feasibility of splitting a liver graft for transplantation in two adult patients.

Patients and methods — We retrospectively collected data on the harvesting of 100 consecutive liver grafts. Data were separated into 4 groups to establish feasibility criteria, according to the chronological steps of harvesting: 1) initial criteria about the donor (age, weight, biological tests), 2) criteria concerning the liver graft at the time of harvesting (macroscopic appearance, graft weight, hemodynamic state of donor), (3) anatomical criteria and (4) histological criteria.

Results — If our criteria for the feasibility of splitting a liver graft for transplantation in two adults had been applied, 47 grafts would have been rejected based on initial criteria, 34 at the time of harvesting and 6 because of anatomical or histological evaluation. Finally, 13 liver grafts would have been accepted for splitting and then transplantation in two adults.

Conclusions — Split-liver transplantation for two adult recipients could increase the graft pool by 13%. This procedure requires technical changes in organ harvesting and coordination among centers.

Technical advances and progress in drug treatments have enabled good results after orthotopic liver transplantation, widening indications and consequently creating a shortage in available donor organs. Several solutions have been proposed to increase the number of donor organs for liver transplantation: optimization of the donor pool, acceptance of grafts from marginal or living donors, or obtaining two grafts from a single organ by splitting it between two adults or an adult and a child.

In 1984, Bismuth and Housin [1] announced the concept of split-liver transplantation, applying the technique used to reduce the size of adult organs for transplantation in children. The major drawback of this reduction technique is that 70 to 75% of the liver mass has to be sacrificed. This technique was progressively replaced by organ splitting allowing transplantation in an adult and in a child starting with a single liver [2-4]. In well-trained hands, this technique has provided good results [5-7]. It has led to shorter waiting lists for children, but has had no effect on waiting lists for adults. Split-liver transplants have recently been proposed for two adults [8, 9]. Prerequisites for this new technique include sufficient graft size for each adult recipient, currently estimated to be at least 1% of the recipient’s body weight [10]. The right liver is generally large enough for most adult recipients, but not the left liver. To overcome this inconvenience, it would be logical to select low-body-weight adult recipients.

The purpose of this retrospective study was to assess the feasibility of split-liver transplantation in two adults in 100 consecutive cadaver liver transplants.

Material and methods

This retrospective analysis was designed to assess the theoretical feasibility of split-liver transplantation in two adults. We collected data on
100 consecutive liver harvestings performed by the same transplantation team using the same harvesting technique.

**Graft harvesting technique**

The rapid harvesting technique was used in all cases by in situ aortic cannulation according to the method, slightly modified, described by Sartzi et al. in 1987 [1]. The preliminary dissection was limited to the minimum necessary associating: ligation of the cystic duct, section of the retroduodenal portion of the common bile duct prior to rinsing with about 100 ml saline solution and marker identification of the celiac aorta. The intra-abdominal organs were perfused exclusively via the aorta after completion of its distal portion and clamping the celiac aorta. The portal system was rinsed with the splenic and mesenteric venous flow. The perfusate was recovered in an overflow positioned in the lower part of the inferior vena cava. Immediately after harvesting, the graft was placed in a plastic box for preparation and perfused via the portal system. The graft was held in contact with the perfusion fluid during transportation.

**The liver splitting technique**

The liver was divided ex situ. The right liver was separated from the left liver with preservation of segment I, which implicated saving the inferior vena cava with the left liver.

**Graft preparation**

The inferior aspect of the graft was exposed to release the inferior vena cava and the portal vein up to the origin of the bifurcation. The celiac trunk and its branches were dissected to the origin of the gastroduodenal artery. The common bile duct was identified followed by cholecystectomy.

Arteriography and cholangiography were obtained on the preparation table to search for anatomical segment variations contraindicating organ splitting.

**Liver splitting**

The hepatic artery and the first centimeters of the right and left branches were dissected. On the right, the dissection was limited to the first two centimeters in order to avoid sectioning any branches to the biliary system. Dissection of the portal vein and its two branches was done progressively up to the intra-hilar level. If there were no segmentary anomalies, section was achieved without dissection of the left hepatic duct to at least 10mm from the convergence.

In order to preserve the entire liver parenchyma, the inferior vena cava was preserved with the left liver. Following dissection of its terminal portion, the right suprahepatic vein was sectioned at the point it entered the inferior vena cava.

The anterior line separating the two half livers was drawn from the space between the termination of the right and middle suprahepatic veins along the principal portal sulcus down to the anterior border of the vesicular fossa. The section line then followed the imprint of the bladder on the inferior aspect of the liver to the hilum, reaching the section of its distal portion and clamping the celiac aorta. The portal system was rinsed with the splenic and mesenteric venous flow. The perfusate was recovered in an overflow positioned in the lower part of the inferior vena cava. Immediately after harvesting, the graft was placed in a plastic box for preparation and perfused via the portal system. The graft was held in contact with the perfusion fluid during transportation.

**Definition of feasibility and graft splitting for two adults**

Three groups of criteria were defined from the chronological steps of harvesting.

**Initial criteria**

Donor characteristics retained by the transplantation team before setting-out for harvesting were age < 50 years, weight > 60 kg, and acceptable liver tests at the time of harvesting: aminotransferase level < 500 IU/l (normal < 50 IU/l) and gamma-GT < 2N.

**Harvesting and splitting criteria**

The following data were recorded during the graft harvesting and preparation procedures: normal gross aspect of the graft, hemodynamic stability, graft weight > 1500 g.

**Anatomic criteria**

Anatomic criteria incompatible with right/left splitting were identified, principally segmentary arterial or biliary duplications (segments II + III and segment IV) where the arterial or biliary elements of segment IV were dependent on the vascular or biliary elements of the right liver. According to Couinaud and Haussin [12], 15% of the graft organs present this type of variation and cannot undergo splitting.

**Criteria recognized after transplantation**

Histology criteria were identified in the immediate post-transplantation biopsy specimen. Grafts were considered to have been unfit for splitting if severe preservation lesions were identified. These lesions were defined as polymorphonuclear infiltration, hepatocyte balloonization and clarification, presence of anoxia vacuoles, and presence of acidophilic necrosis.

**Results**

**Study population**

Donor, harvesting, and graft data are presented in tables I, II, and III, respectively.
Analysis of graft harvesting and splitting feasibility for two-adult transplantations

We applied the different feasibility criteria in a stepwise manner to a population of 100 graft harvestings. Based on the decision algorithm established from the defined criteria, 13 of the 100 harvested donor organs could have been split, allowing transplantation of 26 adult recipients.

Application of the initial criteria

Before setting-out for harvesting, the transplantation team’s criteria were compatible with splitting procedures for two-adult transplantation in 53% of the cases (figure 2).

Table I. – Donor characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>71/29</td>
</tr>
<tr>
<td>Sex-ratio</td>
<td>2.44</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>33.15</td>
</tr>
<tr>
<td>Range</td>
<td>8-63</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>68.76</td>
</tr>
<tr>
<td>Range</td>
<td>30-101</td>
</tr>
<tr>
<td>Blood group</td>
<td></td>
</tr>
<tr>
<td>A−/A+</td>
<td>9/43 (52)</td>
</tr>
<tr>
<td>B−/B+</td>
<td>1/9 (10)</td>
</tr>
<tr>
<td>AB−/AB+</td>
<td>2/1 (3)</td>
</tr>
<tr>
<td>O−/O+</td>
<td>4/31 (35)</td>
</tr>
<tr>
<td>Mean duration of coma (hours)</td>
<td>27.97</td>
</tr>
<tr>
<td>Range</td>
<td>5-240</td>
</tr>
<tr>
<td>Liver tests</td>
<td></td>
</tr>
<tr>
<td>AST (IU/L) (mean)</td>
<td>101</td>
</tr>
<tr>
<td>Range</td>
<td>13-823</td>
</tr>
<tr>
<td>ALT (IU/L) (mean)</td>
<td>77</td>
</tr>
<tr>
<td>Range</td>
<td>7-710</td>
</tr>
<tr>
<td>Gamma-GT (IU/L) (mean)</td>
<td>29</td>
</tr>
<tr>
<td>Range</td>
<td>3-188</td>
</tr>
</tbody>
</table>

Application of secondary criteria

Among the 53 harvested organs compatible with splitting procedures for two-adult transplantation, 19 were retained for splitting after preparation (figure 2).

Application of the histological and anatomic criteria

We applied the histological criteria before the anatomic criteria because the histological criteria were proven while the anatomic variations were estimated. After application of these criteria, 13 graft organs were retained (figure 2).

Discussion

The good results obtained after liver transplantation have led to wider indications, and consequently a shortage of donor organs. The large number of therapeutic strategies and harvesting proposals — marginal donors, living donors, adult/child and adult/adult split-liver strategies all merit further development in a comprehensive effort to overcome the difficult problem of organ shortage. In the current situation, obtaining two grafts for two adults from a single donor organ is a reasonable alternative. The set of successive criteria we applied to the different harvesting and preparation procedures for split-liver transplantation were designed to obtain a graft: a) of the best possible quality, and b) of sufficient size to avoid severe and potentially irreversible dysfunction [10].

The in situ aortic cannulation harvesting technique [11, 13-15] has been used for over ten years in our unit without a single case of primary dysfunction in a series of 400 consecutive donors (personal data). The positive effect of exclusive in situ aortic perfusion can be observed at two levels: the portal system is exposed to a lower more regular perfusion pressure and the intra-abdominal organs are cooled more progressively. The

Table II. – Organ characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvesting at the same site as the transplantation</td>
<td>Yes: 18, No: 82</td>
</tr>
<tr>
<td>Gross aspect of the liver</td>
<td>Normal: 93, Steatosis: 7</td>
</tr>
<tr>
<td>Hemodynamic incidents during harvesting</td>
<td>Yes: 2, No: 98</td>
</tr>
</tbody>
</table>

Table III. – Graft characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean graft mass (g)</td>
<td>1448.85 (885-2770)</td>
</tr>
<tr>
<td>Graft /recipient match (w/w)</td>
<td>2.1 % (2-2.6 %)</td>
</tr>
<tr>
<td>Arterial supply:</td>
<td></td>
</tr>
<tr>
<td>— Modal</td>
<td>72</td>
</tr>
<tr>
<td>— Right hepatic artery</td>
<td>12</td>
</tr>
<tr>
<td>— Left hepatic artery</td>
<td>13</td>
</tr>
<tr>
<td>— Right and left hepatic artery</td>
<td>3</td>
</tr>
<tr>
<td>Preservation damage at defined by histology results on biopsy at end of transplantation</td>
<td></td>
</tr>
<tr>
<td>[Mean cold ischemia: 609 minutes range: 350 mn-960 mn]</td>
<td></td>
</tr>
<tr>
<td>— mild to moderate</td>
<td>79</td>
</tr>
<tr>
<td>— severe*</td>
<td>21</td>
</tr>
</tbody>
</table>

* No primary function observed.
deleterious effect of excessive venous pressure can thus be minimized and the risk of cell heat shock is much lower [16, 17].

Donor age has an effect on graft quality and this is well recognized by all transplantation teams. Graft survival decreases significantly when the donor is aged over 60 years [6, 18]. We retained the 50-year cutoff level for liver splitting to remain well below this physiological barrier. Among our 100 consecutive donors included in this study, 17% were not retained for splitting because of their age, a direct consequence of population aging.

Donor weight is also a crucial element for determining the feasibility of organ partition. In the normal individual, the liver accounts for 2 to 2.5% of total body weight [19]. Consequently, providing two recipients with a post-transplantation graft mass sufficient to guarantee optimal organ function is a reasonable goal if the donor weighs at least 60 kg (the estimated weight of the graft thus being about 1500 g). Our data on 100 consecutive donors (table III) shows that the 60-kg cutoff for splitting procedures is a quite realistic limit.

Graft quality is also guaranteed by normal liver tests [6, 20]. In our experience with 400 consecutive liver donors however, we have not observed any significant difference in initial poor function (IPF) when the aminotransferase and gamma-GT levels are above or below twice normal (personal data). In the present context of liver splitting, we arbitrarily set the cutoff level at 500 IU/l for aminotransferases and gamma-GT less than twice normal.

The harvesting surgeon’s assessment of the gross aspect of the graft, although subjective, is an important element for decision making. Evidence of macroscopic steatosis strongly suggests that graft quality will decline during the cold ischemia phase, contraindicating partition [21]. We felt that 20% steatosis was a reasonable upper limit. If the gross aspect of the graft is doubtful, a frozen-section examination may be useful before splitting.

Hemodynamic stability of the donor during harvesting also has an important effect on graft quality, a factor universally recognized [3, 18, 22]. Hemodynamic stability can generally be maintained, but a graft harvested from a hemodynamically unstable donor should not be used for splitting; we only had one graft in this situation.

Graft size is a crucial factor in deciding on whether liver splitting is feasible. It has been demonstrated that severe, sometimes irreversible, graft dysfunction, particularly cholestasis with secondary progression to ischemic damage, is frequent when the graft weighs less than 1% of the recipient’s body mass or less than 50% of the “ideal” graft [10, 23]. Setting the limit for size of the harvested graft at 1500 g would appear reasonable to meet this prerequisite for both adult recipients, assuming that the cumulative weight of the two recipients is about 150 kg. The graft size problem is directly affected by the right-left splitting scheme. Most splits produce a right liver with 60% of the original organ and a left liver with 40%. The right liver could thus be transplanted without risk of mismatch in a large number of recipients. The size of the left graft would however be a limiting factor to be carefully assessed before implantation in many recipients. Patients on the waiting list should be carefully selected, applying the 1% body weight rule. This could limit recipients to those weighing ≤ 55 kg. During the period of this study, we identified two potential recipients for each split graft, 71 recipients weighed 56 to 105 kg and 29 recipients weighed 38 to 55 kg.

Application of feasibility criteria at the time of harvesting would have yielded 19 livers compatible with splitting among the 100 harvested organs. Certain criteria cannot however be assessed at the time of harvesting. Preservation-related damage

Fig. 2 – Use of feasibility criteria for splitting a liver graft for transplantation in two adult patients.
is of course impossible to predict during the harvesting-splitting procedure since the histological criteria are defined on the basis of the biopsy taken at the end of the procedure. Among the 19 livers retained for splitting, we found three cases of severe preservation damage, which could have had a deleterious effect on graft function. Such damage could be recognized at histological examination in the operating room before graft transplantation. There is however a correlation between the duration of cold ischemia and histological damage, emphasizing the importance of shortening this period for grafts obtained from splitting procedures.

The exact incidence of anatomic variations cannot be identified without performing cholangiography and arteriography on all donor livers. According to Couinaud and Houssin [12] about 15% of the grafts present an arterial or biliary duplication of the type (II + III) and IV. This type of anatomic variation contraindicates right-left partition. Although liver splitting for two adult recipients has been proposed for several years, there is little data available on these variations. The largest reported series included 34 patients transplanted from July 1993 to December 1999 [9]. According to these authors, partition was only possible for 15% of the proposed grafts, in line with our own findings. These results can also be compared with a cohort of whole liver transplant recipients. Patient survival for whole liver, right liver, and left liver respectively was 88%, 74%, and 88% at one year and 85%, 74%, and 64% at two years. Graft survival was 88%, 74%, and 88% at one year and 74%, 74% and 43% at two years. Survival was significantly lower with steatotic grafts, poor clinical status of the recipient, and insufficient graft size (< 1% of recipient body weight). The three cases of primary non-function were observed after transplanting a left liver. These results clearly demonstrate that the left liver should be as large as possible, as well as the importance of graft-recipient size match. The “full-left full-right” splitting technique should be preferred, leaving the inferior vena cava with the left liver or splitting the inferior vena cava between the two halves.

A certain number of technical and logistic elements must be carefully controlled for successful harvesting-splitting procedures for two adult recipients. A reliable standardized method of splitting must be defined and accepted by all teams. In addition, all teams should accept the full-left procedure. In addition, splitting should be performed whenever feasible. These points require a clear declaration of intention from all liver transplantation teams since graft distribution rules currently penalize teams with the largest number of enrolled patients. The heart of the liver splitting issue is thus close collaboration between transplantation teams. In situ partition [8, 24, 25] would have the advantage of rapidly providing grafts for two teams, but does require more restrictive harvesting conditions and well-experimented harvesting teams. The chain of events necessitates three consecutive surgical procedures. The principal advantage of this technique is to reduce the duration of cold ischemia, and thus favor renewed graft function.

In conclusion, liver splitting for two adult recipients is, despite the difficulties developed above, an attractive technique that merits further study. Accepting the selection criteria described above, liver splitting could provide a 13% increase in the number of available grafts. Splitting livers for adult recipients will undoubtedly not resolve the problem of graft shortage but an increase in the number of available grafts to the order of 10% is significant. It is highly noteworthy that in France and in Europe in general close to 10% of the patients on the waiting lists die before a compatible graft becomes available (annual report of the French Liver Transplant Registry (Etablissement Français de Greffes), European Liver Transplant Registry).

References


