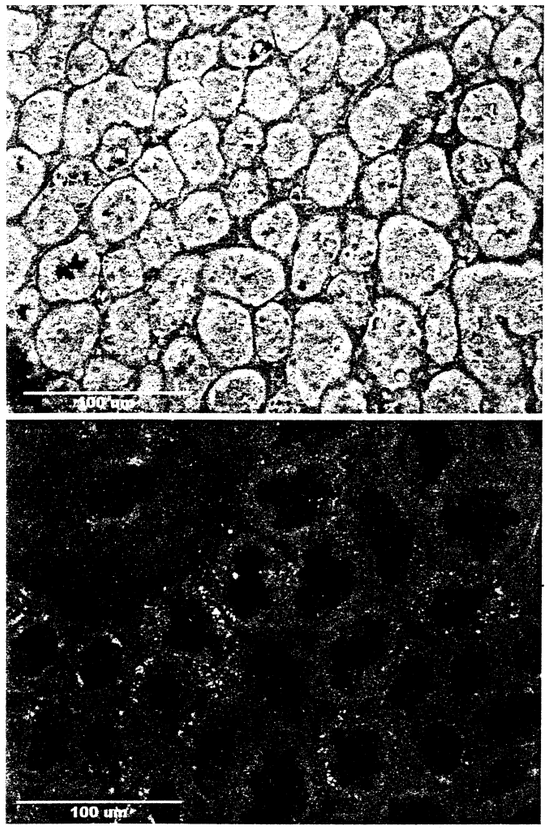

FIGURE 3. Immunofluorescence detection of active TGF-β_1 in transplant renal biopsy sections by scanning laser confocal microscopic method. (A) Representative section from patient treated with CsA. (B) Representative section from a patient treated with FK506.

cannot interact with TGF-β receptors because of noncovalent association of the LAP. TGF-β must be liberated from this complex before it can exert its actions (*26*). Conditions under which cells secrete TGF-β in a completely free form have not been described. The equilibrium between active TGF-β_1 and the TGF-β LAP is affected by a range of factors, but it is clear that active TGF-β_1 must always be derived from the latent form (*27*).

The increased expression of active TGF-β_1 in transplant renal biopsy specimens from patients receiving CsA, as opposed to FK506, is potentially an important finding, indicating that CsA may directly increase the expression of TGF-β_1 or might be involved in its activation. However, this observation must be interpreted with caution because, in this study, the biopsy specimens were taken for the diagnosis of clinical problems (most commonly acute rejection). Hence, the differences in expression of active TGF-β_1 could be secondary effects related to other events occurring within the graft at the time of the biopsy.

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IN SITU SPLIT LIVER TRANSPLANTATION FOR TWO ADULT RECIPIENTS

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Background. **Modifications of the in situ split liver technique are needed for safe transplantation in two adult recipients with a single donor.**

Methods. **The graft from a brain-dead donor, 187 cm tall and weighing 89 kg, was split in situ with a transection performed along the main portal fissure retaining the middle hepatic vein with the left graft. The right and left grafts, which weighed 985 and 760 g, respectively, were transplanted in two adult recipients weighing 70 and 56 kg, respectively.**

Results. **Both recipients had minor intraoperative blood loss and were discharged from intensive care on day 3. Both grafts were rapidly functional, and the two patients were in excellent condition with normal liver function tests 9 months after surgery.**

Conclusion. **In situ split liver transplantation can be performed with the middle hepatic vein retained in the left graft to obtain a sufficient volume of the two grafts suitable for two adult recipients. This modification of the technique could expand the donor pool for adult recipients.**

Ex situ split liver transplantation from cadaveric donors is an attractive concept allowing two recipients to receive transplants from a single liver (*1*). However, this technique did not gain wide acceptance because it was associated with increased morbidity and reduced graft survival (*2*). The main drawbacks were a risk of bleeding from the cut surface, a high incidence of biliary complications, and a prolonged cold ischemia time (*2*). To overcome these problems, Rogiers et al. described an in situ splitting procedure which was associated with reduced cold ischemia time, incidence of biliary complications and primary delayed function as well as with improved graft and patient survival rates compared with the ex-situ splitting (*3*). However, whether performed ex-situ or in-situ, splitting techniques generate left grafts of limited size as it is usually agreed that the middle hepatic vein belongs to the right liver (*4*). Transection is therefore either performed at the level of the falciform ligament (*5*, *6*) or in the middle of segment 4 but with the middle hepatic vein being retained with the right graft. With these techniques, it has very seldom been possible to obtain a left graft large enough for an adult recipient.

The aim of the present study is to describe a modification of the in-situ splitting technique consisting in a transection performed along the main portal fissure retaining the middle hepatic vein with the left graft. This modification generated two grafts of comparable size allowing for the first time the safe transplantation of two adult recipients.

PATIENTS AND METHODS

In situ splitting was considered in a 27-year-old blood group B male 187 cm tall and weighing 89 kg, who had become brain-dead after drowning. This donor had been admitted at our institution and the duration of intensive care unit (ICU) stay before organ harvesting was 12 days. Liver harvesting was not part of a multiorgan procurement because the donor had renal insufficiency (creatinine, 720 μmol/L), cardiac failure, and pulmonary edema. The volumes of the left lateral segment, of the left liver, and of the right liver were 511, 890, and 1091 ml, respectively, as assessed by computed tomography. Angiography showed a normal arterial and portal supply to the liver. Intraoperative cholangiography showed a normal biliary distribution. The common trunk of the middle and left hepatic veins was controlled extraparenchymally as well as the origin of the right and left branches of the common hepatic artery and portal vein. A 2-mm large artery to segment 4 originating from the right branch of the hepatic artery was divided at that stage to favor the development of a collateral circulation during the transection phase. Parenchymal transection was performed using an ultrasonic dissector (Dissectron, Satelec, France) along the main portal fissure without clamping. The hepatic veins of segment 5 and 8, which were 1 cm in diameter, were divided close to their termination in the middle hepatic vein, but the main trunk of the middle hepatic vein was retained with the left graft. The left biliary duct was cut in the hilar plate without attempting to encircle it. The right and left grafts weighed 985 and 760 g, respectively.

The recipient of the right graft (comprising segments 5–8 and 1, the right hepatic vein, and the retrohepatic inferior vena cava [IVC]) was a 70-kg, 166-cm, 48-year-old blood group B man with Child C hepatitis C virus-related cirrhosis and a single 4-cm diameter hepatocellular carcinoma. The recipient of the left graft (comprising

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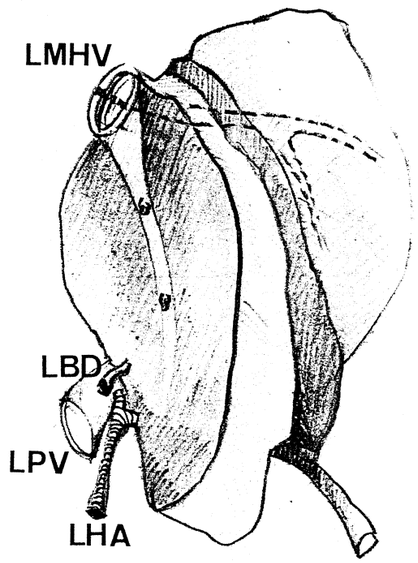

FIGURE 1. Schematic representation of the left graft. LBD, left biliary duct; LHA, left hepatic artery; LMHV, common trunk of the left and middle hepatic veins; LPV, left portal branch.

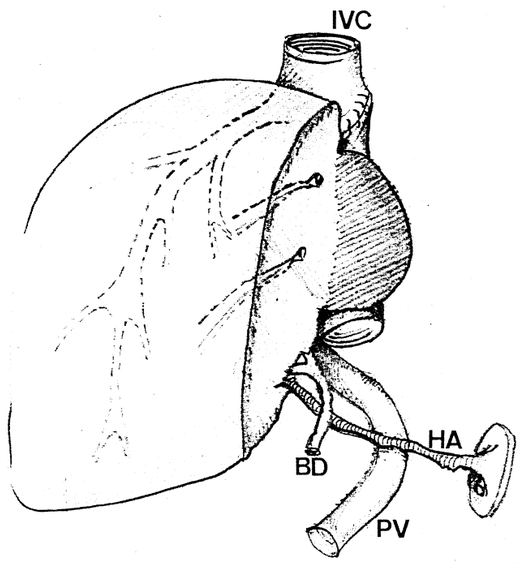

FIGURE 2. Schematic representation of the right graft. BD, biliary duct; HA, hepatic artery; IVC, inferior vena cava; PV, portal vein.

segments 2–4 and the middle and left hepatic veins) was a 56-kg, 165-cm tall, 46-year-old, blood group AB woman with Child B hepatitis C virus-related cirrhosis and a single 27-mm diameter hepatocellular carcinoma. Both patients were United Network for Organ Sharing status 3. Surgery in both recipients was initiated simultaneously and immediately after the cholangiography in the donor had confirmed that splitting was possible. Both patients underwent total hepatectomy with preservation of the portal and caval flows. The split liver was maintained perfused in situ until the two hepatectomies had been completed to minimize cold ischemia time. The left graft (Fig. 1) was immediately transplanted, whereas 20 min of back table preparation of the IVC (Fig. 2) were required before implantation of the right graft. In both recipients, vascular reconstruction was performed without interposition. Biliary reconstruction was performed by a Roux-en-Y anastomosis in the recipient of the left graft and by bilio-biliary anastomosis in the recipient of the right graft. Cold ischemia time was 93 and 72 min for the left and right grafts, respectively.

RESULTS

Surgery in the donor was uneventful with duration of parenchymal transection of 230 min and an intraoperative blood loss of 600 ml. A slight change in color of part of segment 4 was observed just after ligation of the small artery to segment 4 and improved rapidly. After transection of the hepatic veins of segments 5 and 8, a slight and reversible congestion of the adjacent parenchyma of the right liver was observed. The intraoperative course in the recipients of the right and left grafts was uneventful, and intraoperative blood losses were 1200 and 600 ml, respectively. No bleeding was observed from the cut surface after revascularization although neither fibrin glue nor mesh had been applied. Artificial ventilation was discontinued by postoperative day 2. Peak level of aspartate aminotransferase was 262 U/L on day 5 and 1104 U/L on day 1 for the recipient of the right and left graft, respectively.

The recipient of the right graft was discharged from ICU on postoperative day 3, and his liver function tests normalized rapidly. He was discharged from hospital on postoperative day 21 with normal Doppler ultrasound. The recipient of the left graft was also discharged from ICU on postoperative day 3. The prothrombin time normalized somewhat later than in the recipient of the right graft (Fig. 3). She contemporary experienced a transient cholestasis at the time a biliary leakage was noted. Biliary leakage healed spontaneously. A control cholangiography on postoperative day 27 was normal, and the patient was discharged on day 35 with normal Doppler ultrasound. Nine months after transplantation, both patients were in excellent condition with normal liver function tests and Doppler ultrasound.

DISCUSSION

Initial reports of right liver procurement either by ex vivo or in situ splitting were all described with the middle hepatic vein being retained with the right graft (*2*, *3*, *6*) because it was feared that congestion would otherwise occur. This assumption was based on anatomical works showing that the middle hepatic vein predominantly drains the right liver and in particular segments 5 and 8, which have a separate drainage in this vein (*4*).

However, this assumption is not supported by what is observed when the right liver is not used as a graft but left in situ. During living-related transplantation, for example, we and others (*7*) deliberately frequently harvest the full left liver comprising segments 2–4 along with the middle and left hepatic veins without any obvious congestion in the remnant right liver (*7*). Conversely, we (unpublished data) and others (*8*) have recently performed successful living-related transplantations of right livers comprising segments 5–8 only drained by the right hepatic vein, with the middle hepatic vein being preserved in the donor. A possible interpretation of this apparent discrepancy is that an effective venous collateral circulation develops during in vivo liver transection, especially when it is performed without clamping of the hepatic pedicle, whereas it may not develop when transection is performed ex situ.

This observation is not unique to the venous drainage. Similar findings have been made with the arterio-portal supply to segment 4. When splitting is performed ex situ at the level of the falciform ligament, segment 4, which remains attached to the right graft, frequently becomes ischemic and may require primary or secondary removal (*3*). In contrast, devascularization of segment 4 is less frequent when the same splitting procedure is performed in situ or during living related harvesting of the left lateral segment (*3*). As experienced in the present case, a slight change in color is frequently observed just after ligation of the arterioportal pedicle to segment 4, but this change improves rapidly through the development of a collateral circulation.

The recipient of the right graft had an uneventful postoperative course. On postoperative day 1, prothrombin time was 70% of normal and the peak of serum transaminase levels was low. These findings suggest that there was no or minimal injury to the graft, which could have been a result of poor venous drainage or insufficient blood supply. To ensure an optimal outflow of the right graft, we also believe that the IVC should be harvested with this part of the liver, to allow an easy and large cavocaval anastomosis and to preserve the inferior and accessory hepatic veins that contribute to the venous drainage of the right liver through the dorsal sector. This technique may allow better venous drainage than that recently reported by Colledan et al. (*9*), who suggested retaining the donor's IVC with the left graft. For the left graft, we have found that the common trunk of the left and middle hepatic veins allowed a wide anastomosis to be performed.

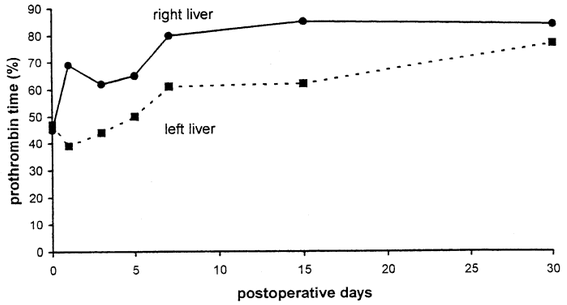

FIGURE 3. Postoperative kinetics of prothrombin time in the recipients of the right and left graft.

Besides these technical considerations, we feel that an ischemia time as short as possible is a necessary condition to achieve optimal function of the graft. This is why the in situ splitting and both transplantations were performed simultaneously in the same institution. This does not, however, rule out the possibility of using shipped grafts as in our collaborative program of living related liver transplantation to children (*10*) provided the recipient operation is initiated at the same time as the donor operation.

In addition, the graft should be of optimal quality with normal function tests. Finally, the recipients should be chosen so that the expected weight of the grafts may be no less than 1% of their body weight. Obviously, it can be anticipated that these conditions may only be associated occasionally, therefore limiting the feasibility of the technique.

In conclusion, we have shown that, by using a modified technique of in situ splitting, two adult patients can safely receive transplants from a single cadaveric graft. The basis of this modified technique is to preserve the middle hepatic vein with the left graft and the dorsal sector with the right graft and to perform splitting in situ, preferably without clamping of the hepatic pedicle. This approach is demanding, and requires the availability of three teams of experienced anesthesiologist and surgeons and increases the duration of the harvesting procedure but may be the only mean of extending the donor pool for adults.

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