Living related adult-to-adult liver transplantation : which patient should benefit from this technique ?

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Key words : living related, liver, transplantation, adult.

The only life-saving treatment for end-stage liver disease is liver transplantation. However, despite legislative and social efforts, there is still a shortage of cadaveric organ supply (1,2,3). This leads to an increased death rate and morbidity among potential recipients waiting on the transplantation list (2,4,5,6). To satisfy the increased demand, several alternatives, amongst which living-related liver transplant programs, were installed. Initially performed for children, it is now more and more accepted for adults (3,7,8,9,10).

For children, the donors are almost always intra-familial members. In the study of Otte *et al.*, including 63 patients transplanted, 60 donors were the father or the mother and in 3 cases the grandmother, aunt or uncle (10). However, in adult patients, where the parents are often too old to undergo a major liver resection, one can discuss whether or not the intrafamilial group can be enlarged by non-genetically emotionally-related persons, such as spouses, boyfriend or – girl in non-married couples or even good friends (2,6,11,12,13). In these circumstances it will be more difficult to ensure the psychological and legal protection of donor and recipient (14). The medical team must always assess the presence of volunteerism and altruistic motifs of the possible donor (11,12,14,15). The possibility of renumeration of organ donation (especially for non-related donors) and coercion (familial or medical pressure) on the donor must be excluded (12,13,14). Additionally, it is very important to persist in using the same criteria to decide whether a patient is suitable for liver transplantation. One could raise the question on whether the selection criteria could be broadened when a living related donor is available, for instance in the case of hepatic tumours.

As we have to act along the Hippocratic principle of non-maleficence, "above all, do not harm", one can wonder if the use of living donors is an exception rather than a rule. So the major role of the transplantation team is to decide whether the transplantation is justified on the basis of the lowest risk to the potential donor and a reasonable probability of success for the recipient (12, 16).

To reduce the operative risk of the donor, it is imperative to perform a medical, surgical and psychological work-up (1,2,17,18). For this purpose it is proposed to perform ABO blood typing, HLA determination and lymphocytotoxic cross match, complete blood biochemistry, virological serologies (CMV, HIV, EBV, toxoplasmosis, hepatitis B and C virus, HTLV, varicella), chest X-ray, echocardiography, lung function tests, helicoidal computed tomography scan of the abdomen with hepatic volumetry (19,20) and gynaecological examination with mammography in female donors. Preoperative banking of the donors own blood and plasma is necessary for autologous transfusion (17). Some centres still use an invasive procedure as arteriography of the celiac trunk and mesenteric arteries to assess possible anatomical variants or contra-indications (6,21). However, the possibility of angio- and cholangio- magnetic resonance imaging (MRI), as non-invasive and quickly performed examinations instead of arteriography and endoscopic retrograde cholangiography, have more and more proven their efficacy but have to be optimised (22,23). Another advantage of MRI is the absence of X-rays. Endoscopic retrograde cholangiography should only be a routine examination in living-related donors for children with Alagille's syndrome (24). Alagille's syndrome is a congenital autosomal dominant disease with variable penetration. The parents can have a subclinical form of the disease without liver tests abnormalities but with a paucity of the interlobular bile ducts and a reduction of the extrahepatic biliary ducts which makes liver donation impossible.

Liver biopsy is required when abnormal liver tests are present or when liver steatosis is suggested on CT or MRI (25,26). Biopsy should also be performed in donors with a history of alcohol abuse, with overweight and/or hyperlipidemia and in those whose liver volume appears large to body size (26).

The use of intraoperative Doppler ultrasound to localise the intrahepatic main blood vessels and biliary structures can diminish blood loss in the donor (6,17). The Cell-saver, to recuperate peroperative blood loss, can prevent blood transfusion in the donor (6,17).

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During the work-up, potential treatable diseases can be detected in the donor candidate, such as viral hepatitis and sarcoidosis, but results in a contraindication for living-donorship (11,25,27).

Post-operative morbidity of right lobectomy in donors ranges from 15%-25% (6,9). Especially biliary leakage, wound infection and bleeding were mentioned as major complications (2,11,17,18,28). The hospital stay is significantly longer in donors who underwent right liver lobe resection compared to those who had left lateral segmentectomy, extended left lateral segmentectomy or left lobectomy (29).

The operative mortality in living-related liver transplantation is estimated approximately 0.2% to 0.4% (26). Four deaths due to portal vein thrombosis, lung emboli and acute Budd-Chiari due to torsion of the left liver lobe on a series of 1400 living donor transplantation have been reported or communicated personally (27,30,31). Probably more deaths happened but are not reported for the moment. For this reason, a work-up for prothrombotic state has to be performed in donor candidates.

For the psychological work-up, the donor may not have major personality disorders or mental retardation (2). Drug and alcohol dependent donors are excluded (1,25,32).

On the medical, anatomical and psychological basis a potential candidate can be excluded or chosen to be the most suitable with lowest risk for partial liver donation (33). With such stringent criteria it is not surprising that about 50-70% of potential living liver donors are not accepted because of increased risk to the donor or because of liver unsuitability (6,25).

The recipient's benefits from living donation are multiple (1,2,12,16,27) : a) the waiting time is eliminated and deterioration and debilitating complications can be avoided ; b) the quality of the donor organ is higher because of a better work-up ; c) transplantation is performed in elective and ideal circumstances ; d) the cold-ischemia-time is short with minimal ischemic and reperfusion damage and e) there is a good size-matching of the graft (9).

The only benefit for the donor is a psychological one : more self-esteem and most of the time increased happiness, especially when the transplant was successful and the loved one is again in good health. However, depression and divorce have been mentioned after living related donation (1,14).

Apart from these stringent medico-psychological criteria, there remains an unresolved ethical point : do we have to propose living-related donation to all adult patients candidates for liver transplantation or only to patients with a good or on the contrary, with a bad prognosis ?

If we propose a living-related donation to a patient in quite good condition, we know that these patients have a better prognosis after liver transplantation than patients in poor condition. Because they are still in good condition, the transplantation is not very urgent and we have the time to do the work-up of the possible living donor, so transplantation can occur in the best conditions. On the other hand, if the patient is in good condition, he can wait for a cadaveric donor and perhaps it is unnecessary to expose a living-related donor to the surgical risks, even if they are estimated as minimal.

If the recipient has for example a hepatocellular carcinoma (1 tumour < 5cm or < 3 tumours, < 3cm), a long waiting time on the transplant list can lead to further progression of the tumour, so that at the time of transplantation the tumour is too far progressed or the patient's clinical state has deteriorated which decreases the recipient's post-transplant prognosis.

In case of patients with good condition, the donors have less the feeling that they are obliged or forced to be the life saver of their beloved.

For patients in poor condition, who will quickly die on the transplantation list, the living-related donor may be the only salvage. For the potential donor, the pressure will be clearly more important, and could be morally and psychologically more difficult to refuse donation. This will probably lead to a more forced donation. For this purpose an intensive psychological work-up by the physician and a psychologist is necessary (14,32). The transplant team must always be capable to excuse a potential donor or propose him an escape route, for example a current medical contraindication, in case the donor does not want to participate (32). On the other hand, living donation is the sole hope for the patient. The donor and recipient have to be aware that the outcome of the patient is worse because of the bad physical state and high morbidity associated with his pathology. As transplant team, it can sometimes be difficult to decide whether the donor operative risk, outweighs a possible poor recipient outcome (12,16).

Should we inform all transplant candidates that living-related donation is a possible option ? If there is a living-related donation available, there are more cadaveric donors left for patients who do not have suitable living-related donors. This allows other patients to receive a cadaveric organ at an earlier time point, than he should have had otherwise (16,34). But at least the patient and family can not accuse the physicians that they did not propose this possibility, for example when the patient dies on the waiting list or deteriorates fast.

In conclusion, the use of several transplantation programs such as cadaveric transplantation with whole livers, split-livers (18,34,35,36), domino-livers (37) and living-related transplantation, is probably the best way to manage the problem of organ shortage in liver transplantation (38). Also, still more efforts should be undertaken in all hospitals to recognise a potential cadaveric donor and to optimise his conditions for explantation. The use of marginal donor livers in elective low risk recipients should be encouraged (38,39).

We conclude that each case has to be examined separately and that the living donor candidates should be strictly selected according to basic guidelines, taking into account both results of preoperative and psychological screening and the wishes of the family. The possibility of living-related liver transplantation should be proposed to all transplant candidates and thus giving everyone the chance of having the best suitable donor.

In the near future, living-related liver donation should be stimulated to reduce the time on the waiting list. A prospective multicentric registry should be kept to evaluate risk-benefit and outcome of this procedure in donor and recipient.

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