Retrospective analysis of the causes of rejection of potential donors for living related liver transplantation

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Abstract

Background A major prerequisite for living related liver transplantation is to ensure both donor safety and optimal graft quality. Therefore, excluding unsuitable donor candidates should be an important priority of the transplant team.

Purpose To analyze the criteria for exclusion of potential living related liver donors.

Patients and methods From November 2000 to March 2005, 327 potential living related donors for 136 potential recipients for liver transplantation were screened and worked up at the Liver Transplant Center, King Abdul Aziz Medical City. They were evaluated in a stepwise manner, including medical, physical, laboratory, psychosocial, and imaging assessment. Data regarding potential donors were retrospectively reviewed. Reasons for rejection of disqualified donors were analyzed.

Results Out of the 327 potential donors, 223 (68.2%) were rejected at an early stage. A total of 104 cases (31.8%) had computed tomographic (CT) volumetry and/or magnetic resonance cholangiography (MRCP). While 44 (42.3% of those who had CT volumetry and/or MRCP) had their workup completed and proved to be suitable candidates, 24 (23%) went for surgery. Causes for donor rejection were classified as donor-related factors (inadequate volume, unsafe anatomy, abnormal liver function tests, medical/psychiatric, fatty liver, etc.; $n = 191$) and recipient-related factors (too ill, died, received cadaveric transplant, etc.; $n = 112$).

Conclusion In our experience, as well as in those from other centers, a small proportion of potential donors prove to

be satisfactory candidates. Therefore, strict adherence to a stepwise evaluation process is of utmost importance, so unsuitable potential donors can be disqualified, as early as possible during workup.

Keywords Donor · Living related · Liver transplantation

Introduction

Preoperative evaluation of potential donors for living-donor liver transplantation enables selecting a suitable donor with optimal graft quality and ensuring donor safety. There are minor variations in the donor selection process among different centers, but the safety of the donor remains central to the process in all. By definition, a live donor is a completely healthy person. Therefore, the most serious ethical concern of living related liver transplantation (LRLT) is the risk to the healthy donor who will undergo a major operation without any potential health benefit. There should not be any compromise in the acceptance of living related donors. Thus, preserving the health of the donors and excluding persons from donation if they are not suitable candidates, for either medical or anatomic reasons, should be of utmost priority for the transplant team [1]. These concerns stimulated us to present this study aiming at exploring the reasons for disqualifying potential donors for LRLT at our institution.

Patients and methods

In response to the shortage of cadaveric organs and a continually growing waiting list, LRLT was initiated at King Abdul Aziz Medical City in November 2000. A total of 327

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potential living related donors for 136 potential recipients for liver transplantation were screened and worked up during the period from November 2000 to March 2005.

Data regarding potential donors were retrospectively reviewed. Reasons for rejection of disqualified donors were analyzed.

Donor selection

When a potential donor comes to our center with willingness to donate, the transplant team first explains to the donor the risks he or she will be taking and the implications of his or her decision on the recipient. The donor should make the decision voluntarily; they are advised that they can withdraw without explanation up to the moment of anesthesia. The basic requirements that the donor volunteer must fulfill include age between 18 and 55 years and relationship within the third degree of consanguinity with the recipient or spouse. The donor–recipient pair must be blood group identical or compatible. Since liver transplant recipients in our region face donor scarcity, it has become our practice to systematically inform all candidates for liver transplantation of the possibility of LRLT.

The donor evaluation process that we followed has been reported previously [2]. In summary:

Stage 1 begins with a complete medical history and physical examination, and preliminary laboratory and serologic tests.

Stage 2 consists of detailed laboratory and serologic testing, abdominal ultrasonography, chest radiography, electrocardiography, and psychosocial evaluation. The psychosocial evaluation is performed by a psychiatrist and a social worker to assess the social and family support system, present and past working status, and psychological fitness of the donor, including the ability to understand and accept the risks and benefits of donation.

Stage 3 consists of special imaging modalities that will aid in planning the operation. Including computed tomographic (CT) volumetry, CT angiography, and magnetic resonance cholangiography (MRCP).

Liver biopsy is not routinely performed in our center. Echo-guided liver biopsy is done if there is radiographic evidence of fatty infiltration or parenchymal liver disease, even with normal liver function. Candidates with significant liver steatosis (over 30%) are advised to control their diet and exercise. Later, if repeated liver biopsy demonstrates a decrease or absence of fatty change, the potential donor is accepted.

Absolute exclusion criteria were any underlying medical condition placing the donor at undue risk for complications (diabetes, cardiopulmonary disease, etc.), ABO incompat-

ibility, positive hepatitis serology, active infectious disease, and history or laboratory results suggestive of underlying liver disease, inadequate graft size, or significant steatosis.

Results

Potential donor demographics

There were a total of 327 potential living related donors (177 male and 150 female) for 136 potential recipients for liver transplantation. Donor age, body weight, and body mass index (BMI) were 19–55 years (median 38), 39–108 kg (median 61.3), and 17.4–30.3 kg/m² (median 22.6), respectively. There were 5 parents, 180 siblings, 30 sisters, 25 brothers, 26 husbands, 34 wives, and 27 cousins (Table 1). The indications for liver transplantation are summarized in Table 2.

Stage of exclusion of disqualified donors

Whereas out of the 327 potential donors, 44 (14.5%) had their workup completed, 283 (85.5%) were excluded at different points of the workup (Table 3). A total of 145 exclusions (51% of all exclusions) occurred during stage 1 and 78 during stage 2 (27.5% of all exclusions). A total of 104 cases proceeded to stage 3, of whom 60 were excluded (21.5% of all exclusions). The remaining 44 cases (13.5% of the total number of potential donors) completed their workup and proved to be suitable donors. Out of these, only 24 cases went for surgery (Table 4).

Table 1 Potential donor demographics

Potential donors	Number
Gender (male/female)	177/150
Age (years)	19–55 (median 38)
Body weight (kg)	39–208 (median 61.3)
BMI (kg/m ²)	17.4–30.3 (median 22.6)
Relation	
Sibling	180
Parent	5
Husband	26
Wife	34
Brother	25
Sister	30
Cousin	27
Type of hepatectomy planned	
Right hepatectomy	292
Left hepatectomy	22
Left lateral segmentectomy	13
Total	327

Table 2 Primary diagnosis in recipients

Primary diagnosis	Number
Viral hepatitis	104
Hepatitis C	87
Hepatitis B	17
Hepatocellular carcinoma	12
Biliary atresia	6
Other chronic liver disease	14
Alcoholic liver disease	1
Primary biliary cirrhosis	3
Primary sclerosing cholangitis	2
Autoimmune hepatitis	3
Metabolic liver disease	2
Cryptogenic liver cirrhosis	3
Total	136

Table 3 Stages at which donors were excluded

Stage at exclusion	Number	Percentage (%)
Stage 1	145	51
Stage 2	78	27.5
Stage 3	60	21.5
Total	283	

Table 4 Fate of donors who completed workup and proved to be suitable donors

Potential donors who completed work up	Number
Underwent hepatectomy	24
Never came to surgery	20
Reason	
Deterioration of the intended recipients	8
Recipient death	5
Withdrawal of recipient consent	4
Cadaveric organ transplantation	3
Total	44

Multiple potential donors

Multiple candidates existed in 52 cases. There were two donor candidates in 46 cases, three candidates in 5, four candidates in 1, and strangely enough one case had 11 candidates (Tables 5, 6).

Reasons for rejection of disqualified donors

Causes for donor rejection were classified as donor-related factors ($n = 191$) and recipient-related factors ($n = 112$);

Table 5 Multiple potential donors

Multiple potential donors	Number of recipients
2	46
3	5
4	1
11	1

Table 6 Reasons for selecting a donor among multiple candidates in the family ($n = 53$)

Reason for selection	Number of potential donors
Discussion among the family	8
Better graft volume	27
Strong desire to be donor	5
Other donors failed to fulfill selection criteria	13

Table 7 Recipient reasons for exclusion of potential donors

Reason for exclusion	Number	Percentage (%)
Too sick	28	25
Withdrawal of consent	22	19.6
Diagnosed with portal vein thrombosis	19	17
Died	15	13.4
Received cadaveric organ	12	10.7
Traveled abroad seeking transplantation elsewhere	12	10.7
China	8	
Germany	2	
USA	2	
Progression of hepatocellular carcinoma detected	4	3.6
Total number of donors excluded	112	100
Before completion of donor evaluation	92	82
After completing full donor evaluation	20	18

these include 20 potential donors who completed their workup and proved to be good candidates but never came to surgery. This will result in a total of 303 disqualified donors, with 283 having been rejected before completing their workup (Tables 7, 8).

Discussion

The undisputed disadvantage of LRLT is the potential risk of serious complications in or death of the donor and a greater incidence of technical complications in recipients. This means that donor morbidity and mortality should be

Table 8 Donor reasons for disqualification

Reason for exclusion	Number	Percentage (%)
Withdrawal of consent	43	22.5
Abnormal liver function tests	28	14.7
Small graft size	28	14.7
Medical	20	10.5
Asthma	4	
Diabetes mellitus	3	
Cardiac murmur	2	
Hypercoagulability	4	
Other	7	
Positive hepatitis serology	19	10
Unsafe anatomy	13	5.6
Portal vein variants (Figs. 1, 2)	8	
Biliary anomalies (Fig. 3)	5	
Psychosocial reasons	11	6.8
Fatty liver (Fig. 4)	10	5.2
Inadequate remnant liver	9	4.7
Abnormal liver biopsy	3	1.6
Too young to give legal consent	3	1.6
Substance abuse	3	1.6
Total number of donors excluded	191	100

reduced to a minimum. Mortality in living donors represents the gravest complication that can occur [1]. Ethical concerns have been raised too, and the success of this procedure ultimately depends on two critical issues: safety and efficiency. The safety of the donor undergoing a hepatectomy remains central to the entire process [3], and is primarily achieved with a thorough workup to exclude upfront overt risks. The success of adult-to-adult liver transplantation depends on many factors, of which donor

Fig. 1 Computed tomographic portogram of 32-year-old male potential donor showing a right anterior portal vein branch (arrow) joining the left portal vein

Fig. 2 Computed tomographic portogram of 44-year-old male potential living related liver donor showing trifurcation of portal vein (confluence of right posterior portal vein [RPPV], right anterior portal vein [RAPV], and left portal vein [LPV] to the main portal vein [MPV])

selection is probably the most critical. Selection criteria vary around the world, but most include initial screening, detailed medical workup, emotional/psychological evaluation, imaging, and multistage consent.

Taking into account the increasing frequency of adult-to-adult living-donor liver transplantation, the American Society of Transplant Surgeons' Ethics Committee has published a set of practice guidelines for donor selection and evaluation [3]. According to the guidelines, potential donors should be healthy individuals and should be carefully evaluated and approved by a multidisciplinary team,

Fig. 3 MRCP of 30-year-old male potential living related liver donor showing aberrant drainage of the right posterior duct (RPD) into the left hepatic duct (LHD)

Fig. 4 Computed tomographic scan of 43-year-old female potential living related liver donor showing a liver with markedly decreased attenuation, even lower than the attenuation of the hepatic vessels. Corresponding histology (not shown) from a liver biopsy demonstrates 80% macrovesicular hepatic steatosis

including hepatologists and surgeons, to ensure that these donors can tolerate the procedure.

At our institution, the donor evaluation protocol includes three stages. Evaluation proceeds from simple and noninvasive to more complex and invasive tests. We aim at identifying contraindications to donation as early as possible and with the least-invasive testing. We think that this protocol is an economical approach to donor selection that minimizes candidate risk and can be easily implemented in both emergent and elective settings. Stage 1 identifies the largest group of exclusions before proceeding to more costly and invasive testing. Stage 2 includes an extensive medical and psychosocial evaluation before proceeding to the final phases of donor evaluation, which involve anatomical assessment of the potential graft. Other advantages of this phased process include multiple opportunities for the donor candidates to reevaluate and reaffirm their decision to donate. Typically, living-donor selection at our institution occurs over a period of 1–2 months; however, this process can be shortened in emergent situations to less than 24 h.

At the Medical College of Virginia [3], a four-step process was outlined. Step 1 included history and physical examination, basic blood testing, serologies, chest X-ray, and abdominal ultrasonography. Step 2 involved a psychological evaluation and informed consent, more detailed blood testing including HLA typing, magnetic resonance imaging (MRI), pulmonary function tests, two-dimensional gradient-echo imaging, electrocardiography, and liver biopsy. Step 3 was celiac/superior mesenteric artery angiography with portal venous phase. Step 4 involved planning the date of surgery, donating an autologous unit of blood, and signing a second informed consent.

In our series, out of the 327 potential donors evaluated, 223 (68.2%) were excluded early at the first and second stages of evaluation. The remaining 104 cases (31.8%) had CT volumetry and/or MRCP. Forty-four cases had their workup completed and proved to be good candidates; of these, 24 (23%) went for surgery. We classified the causes for donor exclusion as donor-related factors (191) and recipient-related factors (112). Donor reasons for rejection included withdrawal of consent ($n = 43$), abnormal liver function tests ($n = 28$), small graft size ($n = 28$), medical reasons ($n = 20$), and positive hepatitis serology ($n = 19$). Recipient reasons for rejection included being too sick ($n = 28$), withdrawal of consent ($n = 22$), portal vein thrombosis ($n = 19$), recipient death ($n = 15$), cadaveric organ ($n = 12$), having traveled abroad ($n = 12$), and progression of hepatocellular carcinoma ($n = 4$).

The determination of donor suitability, as a percentage of total potential donor candidates depends on what the denominator is. If one counts all individuals who present themselves voluntarily as potential donors, then this will form a much larger group than those who have, for example, been prescreened for blood type compatibility and hepatitis serology. It is also important to note the differences between the pediatric and adult living-donor literature [1]. Most donors for pediatric living-donor transplantation are the parents of the recipient. Blood group incompatibility is less common and motivation is seldom in question [3].

In a series from the Medical College of Virginia [3] that included 126 potential donors, 87 were rejected for the following reasons: incompatible blood type (40); liver biopsy showing fat that brought the corrected graft-to-recipient weight ratio (GRWR) to less than 0.8% (14); history and physical examination (5); hepatitis C virus-positive (5); substance abuse (5); Hb_c antibody-positive (3); GRWR less than 0.8% without steatosis (3); diabetes (2); psychologically unfit (2); cardiac complications (2); refused when asked for a second consent (2); chest X-ray (1), MRI (1), or angiography (1) indicating risk for unfavorable outcome; and pregnancy (1).

In a study by Sterneck et al. [4] out of 73 potential donors, 33% were rejected, 15% because of adverse risk factors. Morimoto et al. [5] evaluated 135 potential donors for 120 recipients of LRLT, 11% were not accepted. In an earlier series of 109 donors, the same authors found fatty liver in 10 and abnormal transaminases in another 10 [5]. In a third series, Renz [6] found only 10 (13%) of 75 potential donors for 38 recipients suitable. Contraindications included the following: significant medical history in 23% and psychosocial reasons in 20%; furthermore, 23% of the potential donors had declined assessment. Pomfret et al. [7] looked at the evaluation of 66 potential donors in a clinic where 15 right lobe transplants were performed.

They found that 32 of the 66 potential donors were rejected: 15 recipient related (too ill, died, received cadaveric transplant) and 17 donor related (inadequate volume, unsafe anatomy, abnormal liver function tests, medical/psychiatric, fatty liver $\geq 20\%$). Out of the 34 acceptable donors, 15 went to surgery, 9 were waiting, and 10 had aborted the donation process.

Conclusion

The donor evaluation process is meant to reveal conditions that will place the donor at an undue risk for complications and to identify factors that may adversely affect graft function. It should be done methodically. In our experience, as well as in those from other centers, only a small proportion of potential donors prove to be satisfactory candidates. Therefore, strict adherence to the stepwise evaluation process is of utmost importance, so unsuitable potential donors can be disqualified, as early as possible during workup.

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