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wjg@wjgnet.com
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CLINICAL RESEARCH

Analysis of surgical and perioperative complications in seventy-five right hepatectomies for living donor liver transplantation

Salvatore Gruttadauria, James Wallis Marsh, Giovan Battista Vizzini, Fabrizio di Francesco, Angelo Luca, Riccardo Volpes, Amadeo Marcos, Bruno Gridelli

Salvatore Gruttadauria, Giovan Battista Vizzini, Fabrizio di Francesco, Angelo Luca, Riccardo Volpes, Bruno Gridelli, Department of Abdominal Transplant Surgery, Istituto Mediterraneo Trapianti e Terapie ad Alta Specializzazione, Palermo 90127, Italy
Salvatore Gruttadauria, James Wallis Marsh, Amadeo Marcos, Bruno Gridelli, Department of Abdominal Transplant Surgery, University of Pittsburgh Medical Center, Palermo 90127, Italy
Author contributions: Gruttadauria S, Marsh JW, Marcos A and Gridelli B contributed equally to perform all surgical cases; Gruttadauria S, Vizzini GB, di Francesco F, Volpes R and Luca A designed research; Gruttadauria S and di Francesco F performed research; Gruttadauria S, Marsh JW, Marcos A and Gridelli B analyzed data; Gruttadauria S and di Francesco F wrote the paper.
Correspondence to: Salvatore Gruttadauria, MD, Department of Abdominal Transplant Surgery, Istituto Mediterraneo Trapianti e Terapie ad Alta Specializzazione, Palermo 90127, Italy. sgruttadauria@ismett.edu
Telephone: +39-91-2192111 Fax: +39-91-2192400
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Abstract

AIM: To present an analysis of the surgical and perioperative complications in a series of seventy-five right hepatectomies for living-donation (RHLD) performed in our center.

METHODS: From January 2002 to September 2007, we performed 75 RHLD, defined as removal of a portion of the liver corresponding to Couinaud segments 5-8, in order to obtain a graft for adult to adult living-related liver transplantation (ALRLT). Surgical complications were stratified according to the most recent version of the Clavien classification of postoperative surgical complications. The perioperative period was defined as within 90 d of surgery.

RESULTS: No living donor mortality was present in this series, no donor operation was aborted and no donors received any blood transfusion. Twenty-three (30.6%) living donors presented one or more episodes of complication in the perioperative period. Seven patients (9.33%) out of 75 developed biliary complications, which were the most common complications in our series.

CONCLUSION: The need to define, categorize and record complications when healthy individuals, such as living donors, undergo a major surgical procedure, such as a right hepatectomy, reflects the need for prompt and detailed reports of complications arising in this particular category of patient. Perioperative complications and post resection liver regeneration are not influenced by anatomic variations or patient demographic.

Key words: Right hepatectomy; Surgery; Living-related liver transplantation; Surgical complications

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INTRODUCTION

Lortat-Jacob reported the first anatomic right hepatectomy in 1952[1]. Since then, and particularly in the past two decades, hepatic surgery has achieved important technical breakthroughs, such as intermittent portal triad clamping, total vascular exclusion, preoperative portal vein embolization with two-stage hepatectomy, and sophisticated methods of parenchymal transection.

An increased interest in the outcomes of right hepatectomy for adult to adult living-related liver transplantation (ALRLT) has likely contributed to these breakthroughs[2].

Although surgical techniques of excellence and major improvements in perioperative management are now a

reality in referral centers for liver surgery, there are still several issues that make this major surgical procedure extremely worrisome when performed in healthy individuals, such as living donors.

In particular, there is still no definite consensus regarding the amount of liver that can be safely resected[3], a crucial point for the recipient and perhaps more important for the healthy donor.

Recent studies have emphasized that in living-related liver transplantation, results and survival appear to correlate with stratification in the volume of the liver allograft transplanted, expressed either as a graft-to-body weight ratio or as a percentage of the standard liver volume of the recipient[4].

Clearly, living-related liver transplantation (LRLT) represents the natural evolution of other surgical procedures, namely reduced-size liver transplantation and split-liver transplantation[5], and is based on the segmental anatomy of the liver and on its peculiar capacity to regenerate.

This procedure represents a major challenge for the centers involved, though it has been widely reported that it is a valuable option for decreasing mortality rates and drop out from waiting lists[6,7].

However, potential risk for the donor makes this procedure unique, and when complications in the healthy donor arise, the implications for the medical community are potentially devastating[8]. A recent systematic review[9] that focused on adult donor outcomes concluded that there are small but real risks when using the right lobe for living donors, though it also claimed that nearly all donors returned to normal function within 6 mo. Moreover, due to the short history of ALRLT, the long-term risks for the living donor are still largely unknown.

Numerous single-institution series have reported their complications for liver living-related donors[10-15] and a recent large study from the U.S. reported an analysis of administrative data on a group of 433 right- and left-lobe living donors identified as those at risk for perioperative complications[16].

The ethical debate over the potential risk to the donor[17] renders this field of surgery controversial and, as a result, we believe, worthy of reports on all single center experiences.

The aim of this study is, in fact, to present an analysis of the surgical and perioperative complications in a series of seventy-five consecutive right hepatectomies for living related liver transplantation (RHLD) performed in our center.

MATERIALS AND METHODS

From January 2002 to September 2007, we performed 75 RHLD, defined as removal of a portion of liver corresponding to Couinaud segments 5-8, in order to obtain a graft for ALRLT. Two left-hepatectomies, corresponding to Couinaud segments 2-4, were performed for the same purpose during the initial phase of our experience, but are not reported in this study. The number of cases per year has been progressively increasing, with a peak reached in 2006, when 24 RHLD were performed. The trend has continued through this year (2007), with 17 RHLD performed so far. ALRLT represented the 20% of our total liver transplant activity over the last 2 years.

Donor selection and characteristics

All living donors went through a complete evaluation process, managed by a multidisciplinary team consisting of clinical psychologists, hepatologists, anesthesiologists, transplant surgeons, referring physicians and family doctors. The evaluation process was completed in 3 d, with blood work, ultrasound and consults on the first day; Volumetric Angio computed tomograghy (CT) Scan and Cholangio nuclear magnetic resonance imaging (MRI) on the second day; and liver biopsy on the third day.

Initially, the work-up included endoscopic retrograde cholangiography; this has since been replaced by Cholangio MRI.

Beginning in 2002, a total of 254 potential living donors were evaluated; 165 (65%) were excluded, and of those accepted for living donation, 12 (5%) are still undergoing work-up. At first we were more restrictive; as a result, all patients with aberrant vascular or biliary anatomy, or steatosis greater than 10%, were rejected. Then 20% macrovesicular steatosis was categorized as the upper limit.

Of the 75 living donors accepted, the ages ranged between 18 and 54, and all were biologically or emotionally related to the recipients. There were 46 ABO identical couples and 29 compatible couples (Table 1). These demographic data are quite similar to those reported online by the European Liver Transplant Registry concerning the activity of 135 institutions in 35 European countries in the period 1991-2005.

The CT-scan-calculated graft to recipient body-weight ratio was always above 0.8%, and all anatomic anomalies of the vascular and biliary system were detected by preoperative imaging (Table 1).

Two anti-hepatitis B core positive donors were immediately accepted[6] in accordance with the far-eastern experience, and were transplanted in two recipients with end stage liver disease secondary to hepatitis C virus, treated after transplant with lamivudine 100 mg/d.

Seven other donors were initially excluded because of their elevated body weight, which was a body mass index (BMI) of > 30. After nutritional assessment (nutritional and dietary past history, and life-style evaluation) the dietician arranged a personal diet, moderately hypocaloric (carbohydrates 55%-57%, proteins 17%-19%, and lipids 24%-27%) and encouraged the donor to perform physical activity. Acceptable monthly weight loss was considered approximately 2-4 kg, with a final BMI of < 30 kg/m^2. After 3 mo of a low calorie diet all seven living donors had a protocol liver biopsy that showed hepatic steatosis of < 20%, and were therefore considered eligible for donation.

Surgical complications were stratified according to the Clavien classification of postoperative surgical complications[18] (Table 2).

The perioperative period was defined as within 90 d

Table 1 Demographic, anatomic and surgical characteristics of 75 RHLD (mean ± SD)

Characteristics	*n*	Percent (%)
Age		32.27 ± 9.29
Range		[18;54]
Classes		
0-20	6	8
21-40	53	70.67
41-60	16	21.33
Sex		
Male	35	46.67
Female	40	53.33
Height (cm)		169.05 ± 8.86
Weight (kg)		68.19 ± 11.79
Donor relationship		
Biologically related	65	86.67
Sibling	10	13.33
Child	51	68.00
Parent	4	5.33
Not biologically related	10	13.33
Spouse	5	6.67
Other nonbiological	5	6.67
Donors		
ICU length of stay (d)		
Average		1.66
Range		[1;5]
Total length of stay (d)		
Average		8.26
Range		[6;14]
Length of donor surgery (h)		7.90 ± 1.75
Graft weight (g)		784.57 ± 158.15
GRBWR		1.43 ± 0.44
Bile ducts		
Double bile ducts	50	67
Single bile duct	25	33
Hepatic veins		
1	58	77
2	17	23
Hepatic arteries		
1	73	97
2	2	3
Portal veins		
1	65	87
2	10	13

GRBWR: Graft to recipient body weight ratio; ICU: Intensive care unit.

of surgery. Detailed descriptions of this surgical technique have been previously reported elsewhere[6,19].

Postoperative management and follow-up

After surgery, all donors were extubated before leaving the theater, and transferred to the intensive care unit (ICU) for at least 24-h monitoring. Deep venous thrombosis prophylaxis was based on early administration of low molecular heparin, started as soon as the prothrombin activity reached 50%, together with compression devices and early mobilization. Liver function tests were checked daily for at least 7 d, and then weekly for the first 2 mo. The subcutaneous administration of low molecular heparin was discontinued 14 d after surgery.

In order to guarantee optimal analgesia and early mobilization, all but two donors underwent epidural catheter placement immediately before surgery. Catheter removal was performed after 72 h, and after having normalized the coagulation parameters. Antimicrobial prophylaxis changed over time: the first 13 donors received piperacillin tazobactam for the first 72 h, after which prophylaxis consisted of ceftriaxone.

A CT scan of the abdomen was performed 2 mo after surgery, with volumetric analysis of the liver.

Three months after surgery all the donors were seen at the outpatient clinic for check up.

Statistical analysis

Data are expressed in mean ± SD for continuous variables and as percentage for categorical variables. Data were compared with chi-square test or Fisher's exact test 2 tailed for categorical variables and Student's *t*-test for continuous variables; $P < 0.05$ were considered significant.

All statistical analyses were performed using SPSS (SPSS Inc., Chicago, Ill, United States).

RESULTS

None of patients manifested any complications from pre-operative liver biopsy.

No living donor mortality was present in this series. No donor operation was aborted and no donors received any blood transfusion.

After the first 9 cases, we started to reinfuse the blood aspirated during surgery with the Cell Saver System (median: 250 mL; min: 0; max 1680).

Length of surgery, length of stay in the ICU, and total hospitalization are reported in Table 1, while all complications, codified according to the Clavien system, and their management, are reported in Table 2.

Twenty-three (30.6%) living donors presented one or more episodes of complication in the perioperative period. All these complications were resolved within the perioperative period.

Two donors (I.D. 1 and 12) had a small re-laparotomy because the intra-abdominal drain could not be removed.

One donor (I.D. 6) experienced a transient partial portal vein thrombosis, asymptomatically detected by ultrasound and completely resolved with low molecular heparin.

Two donors (I.D. 17 and 18) developed complications graded IV by the Clavien system. They were both admitted to the ICU: in one case for monitoring of an acute pancreatitis following an endoscopic retrograde cholangiopancreatography (ERCP) performed because of a biliary leak, and in the second case for monitoring of a pulmonary embolism with no cardiac derangements.

Five patients (I.D. 13, 14, 17, 20, 21) presented complications that required multiple treatments: i.e. percutaneous drainage and stent placement.

Two patients (I.D. 19 and 21) presented two discrete, unrelated complications each: pleural effusion plus intra abdominal collection in one case and pleural effusion plus biliary leak in the other case.

Seven patients (9.33%) (I.D. 5, 9, 13, 14, 17, 20, 21) out of 75 developed biliary complications, which were the most common complications in our series. However, all of them were successfully treated by interventional procedures with removal of all stents or catheters within 6 mo

Table 2 Classification of surgical complications in RHLD

Patients ID	Complications/Treatment	Classification of surgical complications Clavien annals of surgery 2004	Frequency (%) of complication for every classification grade
1	JP retained in the abdomen/Relaparotomy	Grade Ⅲb	13.04
2	Edema, ascites/None	Grade Ⅰ	21.74
3	Prolonged hyperbilirubinemia/None	Grade Ⅰ	
4	Fluid collection/Percutaneous drainage	Grade Ⅲa	17.39
5	Biliary leak /ERCP with stent placement	Grade Ⅲb, d	21.74
6	Transient portal vein thrombosis/Enoxaparin	Grade Ⅱ	13.04
7	Bilateral massive pleural effusion/Percutaneous drainage	Grade Ⅲa	
8	Colitis by CD/Metronidazole	Grade Ⅱ	
9	Biliary leak/ERCP (stent placement)	Grade Ⅲb, d	
10	Mild pleural effusion/None	Grade Ⅰ	
11	Intrabdominal fluid collection/Percutaneous drainage	Grade Ⅲa	
12	JP retained in the abdomen/Relaparotomy	Grade Ⅲb	
13	Intrabdominal fluid collection; biliary leak/Percutaneous drainage; ERCP (sphincterotomy)	Grade Ⅲb	
14	Intrabdominal fluid collection; biliary leak/Percutaneous drainage; ERCP (sphincterotomy and stent placement)	Grade Ⅲb, d	
15	Intrabdominal fluid collection/Percutaneous drainage	Grade Ⅲa	
16	Prolonged hyperbilirubinemia/None	Grade Ⅰ	
17	Intraabdominal fluid collection; Biliary leak/Percutaneous drainage, ERCP (sphincterotomy, stent placement X 3, acute pancreatitis, PTBD placement)	Grade Ⅲb, d/ Grade Ⅳ	4.35
18	Pulmonary embolism and iliac vein thrombosis/Anticoagulation	Grade Ⅳ	4.35
19	Moderate pleural effusion; intraabdominal fluid collection/Percutaneous drainage; percutaneous drainage	Grade Ⅲa- Grade Ⅲa, d	4.35
20	Biliary leak/ERCP (Sphincterotomy, endoscopic stent placement failure); PTBD	Grade Ⅲb, d	
21	Intraabdominal fluid collection; biliary leak, moderate pleural effusion/Percutaneous drainage; ERCP (sphincterotomy, endoscopic stent placement); percutaneous drainage	Grade Ⅲb, d	
22	Prolonged hyperbilirubinemia/None	Grade Ⅰ	
23	Fever/Antibiotic treatment	Grade Ⅱ	

Table 3 CT scan calculated donors mean liver volume (mean ± SD)

CT scan calculated		
Total liver volume	Right lobe volume	Remnant liver volume
1538.94 ± 277	954.67 ± 219.6	584.28 ± 121.67
	CT scan calculated right lobe volume 2 mo after surgery into the recipient	CT scan calculated remnant liver volume 2 mo after surgery
	1511.60 ± 257.88	1065.08 ± 195.24
	98% regeneration	69% regeneration

Table 4 Distribution of anatomic variations in the complicated and uncomplicated groups of RHLD, *n* (%)

Anatomic variations	23 complicated RHLD	54 RHLD without complications	*P* value
Double bile ducts	15 (65.21)	36 (66.67)	
Single bile duct	8 (34.78)	18 (33.33)	0.78
Hepatic veins			
Single	21 (91.30)	39 (72.22)	
Double	2 (8.69)	15 (27.78)	0.09
Hepatic arteries			
Single	22 (95.65)	53 (98.15)	
Double	1 (4.34)	2 (1.85)	0.82
Portal veins			
Single	20 (86.95)	46 (85.19)	
Double	3 (13.04)	8 (14.81)	0.54

from surgery.

CT-scan-calculated donor mean total liver volume, mean right lobe volume, mean remnant liver volume, plus mean liver volume 2 mo after surgery in the donor and in the recipients, are reported in Table 3.

Mean value of donor liver volume was restored to 98% of the preoperative mean volume within 2 mo of surgery in the recipient and to 69% of the preoperative mean volume in the donor.

There was an 18% difference ($P = 0.0001$) between CT-scan-calculated right lobe donor mean volume (954.67) and right lobe weight mean value (784.56) on the back table.

There were no differences in distribution of anatomical variations in the groups of complicated and uncomplicated RHLD (Table 4). In addition, there were no differences between the complicated and uncomplicated RHLD regarding the baseline and post regeneration mean value of calculated liver volumes (Table 5).

All patients returned to their own activity after this perioperative period.

DISCUSSION

Donor safety has to be the first priority during the entire process of living-related transplantation, from the first day of evaluation through the entire follow-up period.

Therefore, an accurate and comprehensive step-by-step work-up protocol for donor evaluation has been designed in our center in order to ensure donor safety and, additionally, to confirm that the donor is capable of providing a suitable graft for the recipient.

In our experience, use of routine liver biopsy, though not generally accepted in all centers, allowed the exclu-

Table 5 CT scan calculated donors mean liver volume in the complicated and uncomplicated groups of RHLD (mean ± SD)

	23 complicated RHLD	54 RHLD without complications	*P* value
CT scan calculated total liver volume	1517.7 ± 292.4	1547.20 ± 292.43	0.68
CT scan calculated right lobe volume	957.67 ± 226.37	953.50 ± 219.16	0.94
CT scan calculated remnant liver volume	560.05 ± 89.19	593.70 ± 131.69	0.28
CT scan calculated remnant liver volume 2 mo after surgery	1078.6 ± 201.65	1059.57 ± 194.42	0.72

sion of potential donors who otherwise would have been considered fit to donate based on other tests[20].

On the other hand, the biopsy allowed us to enroll donors who were anti-hepatitis B core positive.

Moreover, the routine use of liver biopsy as a screening tool in the living donor work-up allowed us to explore more safely the very common problem of steatosis.

The usefulness of steatotic livers depends on the percentage of fat, as livers with moderate to severe steatosis decrease graft and patient survival (with an additional unpredictable risk for liver donor regeneration). A BMI of > 30 may reliably predict a higher degree of steatosis in most donors. In order to enlarge the pool of living donor livers, but also to improve post-transplant outcomes, we made an attempt to lower the percentage of steatosis, rather than to turn down such overweight donors, by applying a short-term treatment of diet and exercise in all living-donor candidates with hepatic steatosis. After RHLD, no such donors experienced life-threatening complications or died. No long-term clinical impairment of treated donors has been observed and, after donation, all of them have returned to previous activity.

A strategy of careful evaluation of the living donor performed by an interdisciplinary team cannot be overemphasized.

A wide range of living donor complication rates are reported in the literature, with an estimated risk of mortality and morbidity after RHLD of 0.4% and 35%, respectively.

Overall, the complication rates range from 0% to 67%, with an overall crude complication rate of 31%[21]. The literature has reported 11 deaths, and 2 liver transplants in donors who have undergone RHLD. Additionally, one donor is in a persistent vegetative state after donation[22].

Organ shortage is a dramatic problem which can be limited by the rational use of ALRLT. So, based on our previous experience with liver resection[2] and use of partial livers from deceased donors[23], we began the living-related liver transplant program. Moreover, our partnership with one of the most active living-related liver transplant programs in the world[24] has allowed us to gain experience rapidly in this controversial field of surgery.

In our series, 30.6% of living donors developed a complication in the perioperative period, this not different from data recently reported in the literature[24]. In this group, RHLD with complications, there was no major incidence of anatomic variants, or difference in terms of liver regeneration after surgery, when compared with patients who did not develop any complications.

Additionally, our data regarding CT-scan-calculated liver volume confirmed that volumetric imaging may overestimate the actual liver volume[24].

Biliary complications (9.33%) were the most common complications after RHLD in our series, though no patients had to undergo repeated laparotomy for this reason. In two cases, after the failure of the endoscopic treatment, we were able to resolve the biliary leak due to a combined "rendezvous" procedure between endoscopist and interventional radiologist, who were able to pass an internal external transhepatic biliary drainage.

None of the 75 live donors in this series, regardless of their post-operative course, manifested any regrets about live donation.

In conclusion, this study reports the largest Italian experience with RHLD, focused on perioperative complications and on donor safety, which must be the first priority in right-lobe living-related donation.

Strict donor selection, detailed informed consent validated by the Italian law, together with a growing volume of cases performed every year, have allowed us to safely perform right hepatectomies for living donation in our center.

The need to define, categorize and record complications when healthy individuals, such as living donors, undergo a major surgical procedure like a right hepatectomy, reflects the need for prompt and detailed reports of complications arising in this particular category of patient.

Perioperative complications and post resection liver regeneration are not influenced by anatomic variations or patient demographic.

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COMMENTS

Background

Adult to Adult living related liver donors play an essential role in filling the gap of transplants needed due to a heavy shortage of cadaveric donations. Considering that living related donors are healthy individuals at baseline, it is imperative to ensure good outcomes and return to quality of life.

Research frontiers

The study improved measures to assure safety in the healthy donor, improved overall diagnostic capability by non-invasive tools in the donor work-up, and provided possibility of expanding Milan Criteria for recipient of living-related liver transplantation (LRLT). It indicated improvements in prevention of biliary complications and small-for-size syndrome.

Innovations and breakthroughs

Authors designed an accurate, comprehensive step-by-step work-up protocol for donor evaluation to ensure donor safety and to confirm that the donor is capable of providing a suitable graft. Their research has proven the necessity of evaluat-

ing the overall health of both the donor and recipient at many different levels from biopsy to body mass index. It indicated liver biopsy in the exclusion of potential donors otherwise considered fit to donate. These biopsies assess the quality of the donation to ensure the likelihood of success of the transplant and the health of both the donor and the recipient. These biopsies also confirm the true donor status of Hepatitis B, thereby allowing us to enroll donors who had false positive serum tests. They also test body mass index in order to prescribe a diet and exercise program to heavier donors to allow their inclusion. Their experience shows that heavier donors, when subjected to an exercise and diet program, all return to previous activity. In fact, no life threatening complications, long term impairments, or deaths have occurred in these donors. It indicated improvements in prevention of biliary complications and small-for-size syndrome.

Applications

It would be applied in improving in prevention of biliary complications and measures to assure safety in the healthy donor.

Peer review

This is an important issue that needs reporting. The authors performed a single institution series-report study of 75 patients stratifying them into two groups, complicated (23) and uncomplicated resections (54) to try to identify factors that might have influenced outcome. For this purposed, they analyzed anatomical variations and the liver remnant volume. With high wait list mortality and rather static donor levels, ALRLT is an option that needs serious consideration and historically the high rate of donor complications has held units back from moving forward with this procedure.

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