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Complications of right lobe living donor liver transplantation☆

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***Background/Aims*: Right lobar living donor liver transplantation (LDLT) has been controversial because of donor deaths and widely variable reports of recipient and donor morbidity. Our aims were to ensure full disclosure to donors and recipients of the risks and benefits of this procedure in a large University center and to help explain reporting inconsistencies.**

***Methods*: The Clavien 5-tier grading system was applied retrospectively in 121 consecutive adult right lobe recipients and their donors. The incidence was determined of potentially (Grade III), actually (Grade IV), or ultimately fatal (Grade V) complications during the first post-transplant year. When patients had more than one complication, only the seminal one was counted, or the most serious one if complications occurred contemporaneously.**

***Results*: One year recipient/graft survival was 91%/84%. Within the year, 80 (66%) of the 121 recipients had Grade III ($n = 54$) Grade IV ($n = 16$), or Grade V ($n = 10$) complications. The complications involved the graft's biliary tract (42% incidence), graft vasculature (15%), or non-graft locations (9%). Complications during the first year did not decline with increased team experience, and adversely affected survival out to 5 years. All 121 donors survive. However, 13 donors (10.7%) had Grade III ($n = 9$) or IV ($n = 4$) complications of which five were graft-related.**

***Conclusions*: Despite the satisfactory recipient and graft survival at our and selected other institutions, and although we have not had a donor mortality to date, the role of right lobar LDLT is not clear because of the recipient morbidity and risk to the donors.**

***Keywords*: Liver transplantation; Complications; Biliary tract; Hepatic artery; Living donation; Right lobe**

1. Introduction

Successful transplantation to pediatric recipients of small portions of the left hepatic lobe of living adult donors was first reported in 1990 [1,2]. By the mid 1990s, removal began of larger hepatic fragments for adult-to-adult transplantation [3–6]. It was soon recognized that the risk of donor death with living donor liver transplantation (LDLT) exceeded that of live kidney donation and that the highest mortality was with right lobar LDLT [7,8]. Because of concern about the donor deaths, and uncertainty about recipient outcomes, a group of stakeholders agreed in 2005 that all LDLT cases should be entered into an international registry [9].

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Abbreviations: LDLT, living donor liver transplantation; UPMC, University of Pittsburgh Medical Center; UNOS, United Network for Organ Sharing; MELD, model for end-stage liver disease; IRB, Institutional Review Board; SFSS, small for size syndrome; NASH, non-alcoholic steatohepatitis; NIH, National Institute of Health; A2ALL, NIH-funded 9-center adult to adult living donor liver transplant consortium.

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It was further agreed that the rate and severity of recipient and donor complications would be determined with the multi-tier grading system developed by Clavien et al. [10,11] (Table 1). One of the high priorities was definitive assessment of the right lobar LDLT that had become the most commonly used living donor procedure for adult recipients in Western (non-Asian) countries. Instead, there have been striking disparities in the reported incidence and severity of complications in both right lobar donors and their recipients [12].

To help explain these inconsistencies and allow full disclosure to all interested parties of the risks and benefits of right lobar LDLT, we analyzed our nearly 4-year experience with 121 consecutive cases. The parallel purpose of this quality assurance study was to identify factors that potentially could be modified to improve results.

2. Patients and methods

2.1. Patient population(s), procedures, and immunosuppression

We retrospectively identified and analyzed the complications during the first post-transplant year of 121 right liver lobe recipients whose operations and follow-up were carried out at the Montefiore Hospital of the University of Pittsburgh Medical Center (UPMC) between March 2003 and November 2006. Recipient disease severity scores (model for end-stage liver disease, MELD) were calculated as of the time of transplantation with a UNOS formula based on the individual's bilirubin, creatinine, and a coagulation index. Data sets were compiled that included, but were not limited to, the donor and recipient demographic, anatomic, operative, and survival parameters shown in Fig. 1 and Table 2. Although the formal recipient complication analysis was limited to the first year, 2–5 year survival data also were obtained.

The donor work-up included liver function tests, liver biopsy, ultrasound examination, and psychological assessment [13]. Because of the medical insurance-driven policy mandating prompt donor return to primary healthcare providers, there often was a paucity of donor post-transplant information in our records after discharge from the primary hospitalization. Consequently, there may have been late donor complications or long-term disability of which we are unaware.

The donor operation [14] consisted of removal of 36–81% ($63 \pm 6.9\%$) of the CT-estimated liver volume. After complete removal of the recipient's diseased liver, the donor right lobe was transplanted to the vacated hepatic fossa, with technical variations that were dictated largely by anatomic variations in both the recipient and donor [14,15]. In addition to the hepatic allograft, 10 recipients during the last third of the experience (October 2005–October 2006) also were given an infusion of unmodified mononuclear cells obtained from the donor by leukopheresis [16].

Individualized immunosuppression for recipients was guided by the generic algorithm that has empowered the field of organ transplantation: i.e. sufficient initial treatment to prevent non-reversible acute rejection with subsequent reduction of immunosuppression to maintenance levels [17]. Baseline treatment was with tacrolimus to which prednisone, lymphoid depleting agents, or other drugs were added as described in the Section 3.

2.2. Clavien classification of complications

Clavien's modified 5-tier scoring system [11] was used for both recipients and donors (Table 1) in preference to his original version [10] which had only four grades [10]. When patients had more than one complication, only the seminal one was counted, or the most serious one if complications occurred contemporaneously. The onset of the complication was defined as the time when the resulting organ dysfunction began or the corrective treatment was started.

Because most of the Clavien I scores were trivial, these were grouped with those that had no Clavien grades. Some of the Clavien II complications that were not related to the allograft were potentially serious (e.g. atelectasis or pneumonia). If they were managed solely with antibiotics or other non-procedural means, however, they did not qualify for a grade higher than II. The same rules applied to graft-related complications: e.g. 11 bile leaks that ceased with external drainage under antibiotic coverage, but without corrective interventional procedures, were given Clavien II scores.

The interventional therapeutic procedures that mandated $\geq$Clavien III scores included operative biliary or vascular reconstructions as well as radiologic procedures such as bile duct or blood vessel dilatation or stenting. Distinctions of Clavien IIIa and b were not used for analysis because patients are given sedation under anesthesiologist supervision for essentially all radioendoscopic and other invasive procedures at our center.

Table 1
Clavien classification of surgical complications.

Grades	Definitions
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications; blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic or radiological intervention a. Intervention not under general anesthesia b. Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications)[a] requiring IC/ICU management a. Single organ dysfunction (including dialysis) b. Multiorgan dysfunction
V	Death of a patient

CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.
[a] Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks.

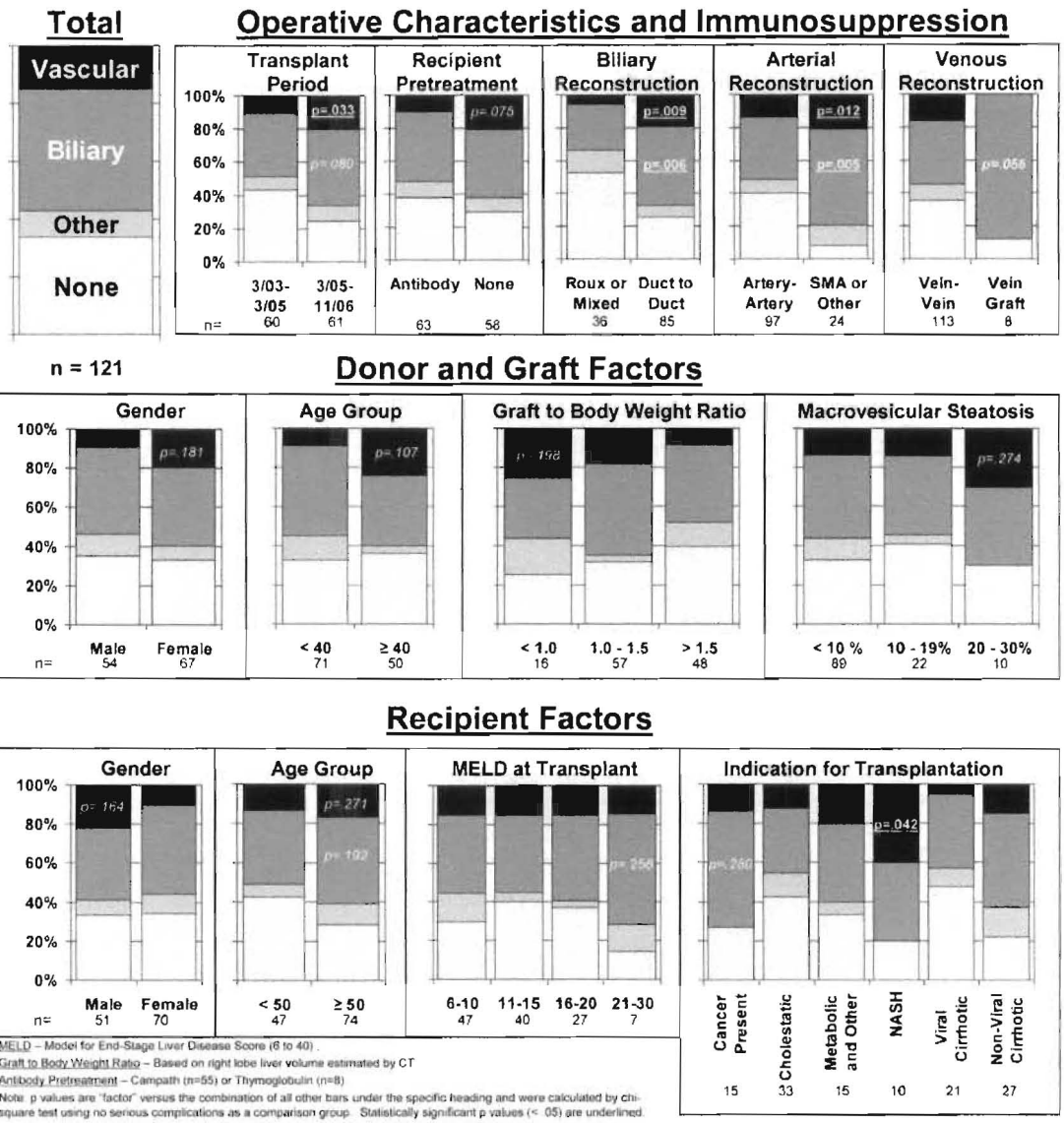

Fig. 1. Schematic depiction of a univariate analysis of factors potentially associated with ≥ Clavien III recipient complications: hepatic vascular (black), biliary (dark gray), non-graft related (light gray). The upper left bar graph is the reference, showing the overall incidence of the three different kinds of complications. Top tier – paired slender bar graphs show the association or lack thereof of complications and operative factors. The incidence of vascular complications was significantly higher in the second half of our experience than in the first half ($p = .033$) (first double bar), and was further associated with the method of revascularization ($p = .012$) (4th double bar). Middle tier – donor and intrinsic graft factors had association trends with complications: female sex, older age, low graft/body weight ratio, steatosis. However, these were not significant. Bottom tier – the only significant recipient factor was the pretransplant diagnosis of NASH ($p = .042$).

Subgrouping of Clavien IV complications also were consolidated into a single group for analysis. Retransplantations within the first year that were derivative from the seminal complication, or complications that necessitated a return to intensive care within one year, were classified as Clavien IV. The Clavien V category consisted of deaths within the first year that were attributable to a complication, no matter how much earlier the complication had first occurred.

2.3. Statistical analysis

Information gathered from the operative notes was merged with factors normally present in our transplant information system to create an evaluable dataset. With IRB approval (IRB# PR007110379 and 009120185), this limited data set containing the outcomes and complications along with the demographic, anatomic, immunologic, and operative parameters was provided to researchers for retrospective analysis. These studies were carried out by two separate teams between which communication was prohibited. The results and conclusions were then validated by an external liver transplantation expert. The person who performed all of the recipient operations and directed postoperative care is no longer on the faculty, and did not contribute to preparation of the manuscript.

Enough recipient data were available to allow tabularization of complications in the first post-transplant year by body systems, recipient original disease diagnoses, and other variables. Parameters were summarized with continuous variables expressed as mean and standard deviation and discrete variables as frequencies. The 121 patients

Table 2
Population characteristics over time.

Factors	All $n = 121$ (3/2003–11/06)	By date of transplant		
		First Half $n = 60$ (3/03–3/05)	Second Half $n = 61$ (3/05–11/06)	p (1st vs. 2nd half)
Donor features				
Age (years)	36.6 ± 11.0	35.7 ± 10.9	37.4 ± 11.2	.383
Female %/Male %	55/45	53/47	57/43	.655
Related donor	94 (78%)	49 (82%)	45 (74%)	.297
Right lobe volume (by CT) (cc)	1085 ± 236	1057 ± 239	1112 ± 232	.201
% Macrovesicular steatosis	5.46 ± 7.18	4.90 ± 6.95	6.02 ± 7.42	.395
Positive crossmatch	14 (12%)	4 (7%)	10 (16%)	.094
Recipient features				
Age	51.0 ± 13.3	50.0 ± 14.3	53.0 ± 12.2	.219
Female %/Male %	58/42	58/42	57/43	.915
MELD at transplant	12.7 ± 4.7	13.7 ± 4.8	11.7 ± 4.4	***.022***
No antibody pretreatment	58 (48%)	14 (23%)	44 (72%)	***.000***
Donor cell infusion	10 (8%)	–	10 (16%)	***.001***
Graft/recipient body weight	1.49 ± 0.51	1.46 ± 0.46	1.53 ± 0.57	.426
Surgery time (minutes)	520 ± 125	538 ± 123	502 ± 126	.117
Duct to duct biliary reconstruction	85 (70%)	39 (65%)	46 (75%)	.210
More than 1 donor bile duct	42 (35%)	21 (35%)	21 (34%)	.947
Normal arterial reconstruction	97 (80%)	44 (73%)	53 (87%)	.062
Use of portal vein graft	8 (7%)	2 (3%)	6 (10%)	.150
Diagnostic categories				.947
Cancer present	15 (12%)	8 (13%)	7 (12%)	
Cholestatic	33 (27%)	15 (25%)	18 (30%)	
Metabolic and other	15 (12%	8 (13%)	7 (12%)	
NASH	10 (8%)	4 (7%)	6 (10%)	
Viral cirrhotic	21 (17%)	10 (17%)	11 (18%)	
Non-viral cirrhotic	27 (22%)	15 (25%)	12 (20%)	
Serious complications				
Biliary	51 (42%)	23 (38%)	28 (46%)	.080
Vascular	18 (15%)	6 (10%)	12 (20%)	***.033***
Other	11 (9%)	5 (8%)	6 (10%)	.281
No serious complications	41 (34%)	26 (43%)	15 (25%)	[a]
One year patient/graft survival (%)	91/84	95/88	87/80	

[a] The statistical significance of biliary, vascular, and other complications was tested with a chi-square method using the no serious complications group as a comparator. For all other factors, t-tests were used for continuous variables and chi-square tests for categorical variables. Statistically significant P values are in italics.

were divided into four complication-defined categories. One group consisted of patients who either were complication-free or had complications that did not require operative intervention and, therefore, generated only Clavien I or II scores. The patients with ⩾Clavien III complications were categorized as biliary, hepatic vascular, or non-graft related. Using chi-square and t-tests, the significance of the covariates listed in Table 2 and depicted in Fig. 1 was determined for the complications overall and by types, using as the comparator patients who did not have ⩾III complications. Recipient Kaplan–Meier survivals were evaluated by a log-rank test.

3. Results

3.1. Recipient and donor population characteristics

The 94 consanguineous (genetically related) donations (Table 2) were offspring to parent ($n = 53$[44%]), sibling to sibling ($n = 29$[24%]), parent to offspring ($n = 6$[5%]), and other ($n = 6$[5%]). Non-related donors were spouses ($n = 8$), friends ($n = 12$), in-laws ($n = 5$), or altruistic volunteers ($n = 2$). All donors were ABO identical with their recipients. There were only three examples of HLA identity, all siblings. Fourteen of the organs were transplanted to recipients with antidonor cytotoxic antibodies (positive crossmatch).

The first 60 right lobar LDLTs were performed between March 2003 and mid-March 2005 and the next 61 between mid-March 2005 and November 2006 (Table 2). With the exception of immunosuppression (see below) and lower MELD scores in the second half, there were no significant differences between the donor and recipient features in the two periods.

All recipients had baseline immunosuppression with tacrolimus, and all were exposed to prednisone at some time, either prophylactically or in response to breakthrough rejection. However, immunosuppression was not constant (Table 2). Sixty-three (52%) of the 121 recipients had antilymphoid antibody (Ab) treatment before allograft revascularization: 55 with a single

30 mg infusion of alemtuzumab (Campath^R), and 8 with an infusion of 5 mg/kg antithymocyte globulin (ATG, Thymoglobulin^R).

The use of lymphoid depletion decreased over the time of case compilation except in the 10 recipients in the second period who were lymphoid-depleted with alemtuzumab, begun on tacrolimus 22 days before LDLT, and infused with leukopheresed donor cells one day later. After 3 weeks of low dose daily tacrolimus, right lobar LDLT was performed with continued minimum daily tacrolimus. The strategy in these 10 patients is described elsewhere [16].

3.2. Recipient complications

3.2.1. Overall rate

Clavien I and II complications were considered for our purposes to be no more serious than those of other major surgical procedures and were therefore grouped with the small number of patients with no complications. This allowed attention to be focused on the ⩾Clavien III complications that occurred in 80 (66%) of the 121 recipients (Table 3). Sixty-nine (86%) of the 80 primary complications were of the biliary tract ($n = 51$) or the liver's vasculature ($n = 18$) (Table 3). The 11 non-hepatic complications that constituted the "other" subgroup included 8 pulmonary (e.g. empyema), 2 post-operative hemorrhages, and 1 intraoperative stroke. Postoperative bleeding or pulmonary complications also occurred in 10 of the recipients whose seminal complications were biliary or vascular; these were not counted separately.

3.2.2. Biliary complications

Fifty-one (42.1%) of the 121 recipients had biliary complications, exclusive of 6 cases in which biliary complications were secondary to vascular problems (next section). Forty-six of the 51 complications were bile leaks ($n = 28$), strictures ($n = 14$), or both ($n = 4$) (Table 3). The other 5 consisted of isolated ampullary dysfunction that required sphincterotomy. Forty-five of the 51 biliary complications were treated with open abdominal operations (e.g. 20 biliary reconstructions), endoscopic surgical procedures or external biliary drainage and retained a Clavien III grade.

Six (11.8%) of the 51 biliary complications, all bile leak-related, were responsible for Clavien IV scores. Two had successful retransplantation, while the other 4 ultimately required prolonged intensive care due mainly to pulmonary failure. No death within the first year was directly related to biliary complications that occurred in the absence of a vascular complication. However, 2 patients who had refractory biliary complications at one year had retransplantation at 18 and 25 months and died 3 weeks and 2 months later, respectively.

3.2.3. Vascular complications

Eighteen (15%) of the 121 recipients had vascular complications within the first year (Table 3). The small for size syndrome (SFSS) ($n = 5$) was included in the vascular category because it is an expression of allograft circulatory compromise [18,19]. The other 13 vascular complications directly involved the hepatic arterial supply ($n = 11$) or portal vein ($n = 2$). Eight (44.4%) of the 18 vascular complications resulted in recipient death within the proscribed one year of analysis (120 ± 104 days range 11–289). A ninth patient died on day 373. A tenth recipient with a thrombosed hepatic artery had multiple morbidities before dying at 3 years.

The primary allograft was salvaged in 2 (11%) of the 18 patients, one with balloon dilatation of an arterial

Table 3
Number of recipient ⩾ Clavien III first-year complications.[a]

Type of complication	Clavien Grade			Total	
	III	IV	V	*n*	(%)
Biliary					
Leak	23	5		28	(23)
Stricture	14			14	(12)
Leak and Stricture	3	1		4	(3)
Ampullary dysfunction	5			5	(4)
Biliary Total	**45**	**6**		**51**	**(42)**
Vascular					
Hepatic Artery Thrombosis	2	4	2	8	(7)
SFSS		2	3	5	(4)
Hepatic Artery Stenosis/Stricture	1	1		2	(2)
Portal Vein Stricture/Thrombus			2	2	(2)
Hepatic Artery Rupture			1	1	(<1)
Vascular Total	**3**	**7**	**8**	**18**	**(15)**
Other	6	3	2	11	(9)
Grand Total	**54**	**16**	**10**	**80**	**(66)**

[a] All percentages in parentheses are of 121 LDLT.

stricture, and the other by arterial reconstruction with a vascular allograft. Seven patients underwent retransplantation with a deceased donor liver after 64 ± 103 days (range 3–289). Six of the 7 survived for one year from the time of their primary transplantation, qualifying them for a Clavien IV score in the one year complication analysis, but 2 died at 372 and 684 days.

Six of the 13 patients with ⩾III vascular problems other than SFSS also had bile fistulas, bilomas, or other serious biliary complications. Because these apparently were secondary to the vascular complications, only the seminal vascular event was given a Clavien score. If these 6 derivative biliary complications were counted, the incidence of ⩾III biliary complications would be 57/121 (47.1%) rather than 51/121 (42.1%).

3.2.4. Factors associated with recipient complication

The proportions of recipients with ⩾Grade III biliary ($n = 51$), hepatic vascular ($n = 18$), and non-hepatic ($n = 11$) complications and of recipients without such complications ($n = 41$) are summarized in the top left box of Fig. 1. As shown in the top bank of panels, the complications were more frequent in the second half of our experience, in recipients who were not given a preemptive antilymphoid antibody infusion, when biliary reconstruction was with duct to duct rather than a Roux-y anastomosis, and when liver revascularization required a variant technical procedure (Fig. 1).

The middle bank of panels (Fig. 1) displays risk trends that were not statistically significant: female donors, older donor age, graft to body weight ratio <1.0, and donor macrosteatosis ⩾20%. The bottom bank depicts potential recipient risk factors, none of which was significant except non-alcoholic steatohepatitis (NASH). In the NASH group of 15 patients, there was a 40% incidence of vascular complications of which half were SFSS.

Although it did not reach statistical significance, there was a disproportionate frequency of female donors and male recipients in the 18 cases with vascular complications. In all 4 recipients in which vascular complications occurred with a graft to body weight ratio <1.0, the donors were female.

An analysis of differences in the first and second half populations (see Table 2) revealed that no risk factor contained in the dataset could account for the increase of vascular and other complications over time.

3.2.5. Follow-up survival in recipients

The effect of complications during the first year on long-term survival is shown in Fig. 2. With a mean follow-up of more than 44 months (range 24–68), the 90%/

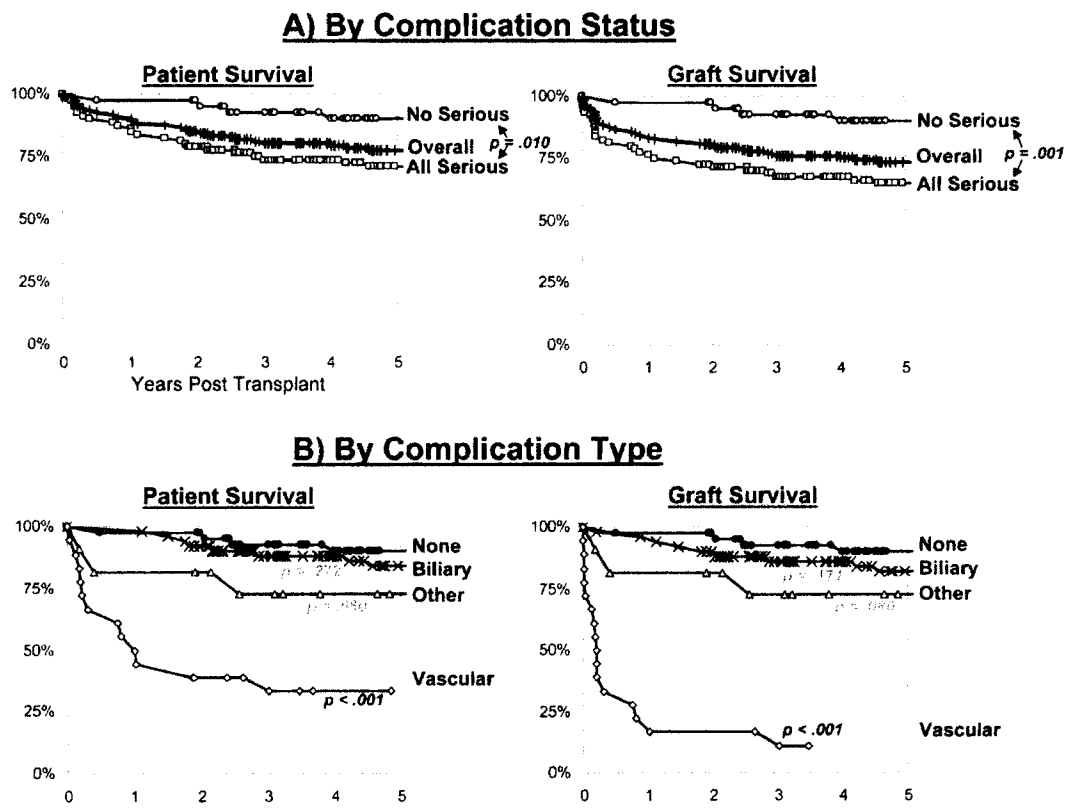

Fig. 2. Effect of Clavien grade III or greater complications during the first year on ultimate patient and graft survival. (A) Patient and graft survival was significantly better out to 5 years when there were no serious complications during the first year. (B) Vascular complications and non-graft related "other" complications jeopardized both short- and long-term patient and graft survival more than biliary complications.

Table 4
Number of donor Clavien II-IV first-year complications.[a]

Type of complication	Clavien Grade			Total	
	II	III	IV	*n*	(%)
Biliary					
Surgical or endoscopic procedure		3		3	(3)
Extended drainage with antibiotics	4			4	(3)
Biliary Total	**4**	**3**		**7**	**(6)**
Vascular					
Deep vein thrombosis	1		1	2	(2)
Transfusion	1			1	(<1)
Vascular Total	**2**		**1**	**3**	**(2)**
Other					
Subacute liver failure, resolved			1	1	(<1)
Non-biliary infections	3	1	2	6	(5)
Hernia		3		3	(3)
Other singular complications[b]	2	2		4	(3)
Other Total	**5**	**6**	**3**	**14**	**(12)**
Grand Total	**11**	**9**	**4**	**24**	**(20)**

[a] All percentages in parentheses are of 121 LDLT.
[b] These included pneumothorax, post-operative bleeding, hypoglycemia, and atrial fibrillation.

90% patient and graft actuarial survival in the group experiencing no one-year serious complications ($n = 41$) is significantly better ($p < 0.01$) than the 71% recipient and 65% graft survival when there were ⩾ Grade III complications in the first 365 days ($n = 80$) (Fig. 2).

3.3. Donor complications

Eleven complications were scored Clavien II because of antibiotic administration during prolonged biliary drainage ($n = 4$) or for treatment of documented non-hepatic infections ($n = 3$) (Table 4). The nine Clavien III complications that required invasive treatment consisted of 3 incisional hernias, 3 bile leaks, 2 pulmonary events, and a hemorrhage (Table 4).

Four donors with Clavien IVa complications returned to the ICU because of subacute liver failure, a right subphrenic infection after 3 weeks, a deep vein thrombosis with bilateral pulmonary emboli, and a pleural effusion that ultimately required decortication. All 4 of these donors were obese (body mass index ⩾30) with $12.5 \pm 2.9\%$ hepatic macrovesicular steatosis compared to $5.2 \pm 7.2\%$ in the other 117 donors ($p = 0.046$). There were no obvious differences in any of the other risk factors that were available for review.

4. Discussion

The Ethics Committee of the Transplantation Society recently recommended that transplantation of non-renal organs from living donors should be done only when "...the aggregate benefits to the donor–recipient pair (survival, quality of life, psychological, and social well being) outweigh the risks to the donor–recipient pair (death, medical, psychological, and social morbidities)" [20].

Although the psychosocial components of the aggregate equation were not readily measurable in our right lobar recipients, their physical morbidity could be quantified precisely with the 5-category system [11] modified by Clavien from his earlier 4-tier model [10]. The principal modification was division of the original category 2 complications into those that could be treated medically (the new Grade II) and those requiring an invasive corrective procedure (the new Grade III) (Table 1). Because post-transplant operative and radioendoscopic procedures generate obligatory reports, examination of these records along with conventional chart reviews all but eliminated the possibility of underestimation of ⩾Grade III complications.

Patient and graft survival of 91% and 84% at one year and 85% and 81% at 2 years in our 121 low MELD right lobe recipients was within the range reported in equivalent disease severity cases of other large volume centers [21–33] and the case compilation of the NIH-supported 9-center adult to adult living donor (A2ALL) United States consortium [34]. The types of recipient complications also were similar to those elsewhere: i.e. biliary, vascular, and other in rank order. However, our 66% incidence of potentially or actually life threatening complications (i.e. ⩾Clavien III grade) was generally higher than reported from other centers, and increased instead of decreasing with time: i.e. the opposite of a learning curve. Because key members of the surgical team had an extensive prior learning experience, this observation could be viewed as a warning against relaxed vigilance once the operation becomes "routine".

The differences between centers in recipient complication rates could reflect, in part, diverse views about how these adverse events should be classified [12]. A formulaic grading system has been used only in the large single center experience in Toronto [35] and the A2ALL collection [36]. Because both series were analyzed with the less discriminating 4-tier Clavien system, detailed comparisons with our data are not possible. Nevertheless, these studies as well as studies done with non-formulaic analyses in most single centers have yielded a lower incidence of biliary and other graft-specific complications than reported here.

Importantly, reports from Japan [23], China [21], and Korea [37] also indicate that the recipient morbidity of right lobar LDLT in Asia is significantly less than that of Western centers, despite the routine use of the operation for severely ill (high MELD) patients [22]. This could be explained by demographic factors: e.g. small and non-obese recipients, better donor–recipient compatibility in the more homogeneous populations, or a different spectrum of liver diseases. A simpler possible explanation could be the experience and skill acquired by hepatobiliary surgeons in treating the liver diseases that are a dominant health concern in that part of the world. The skill factor is consistent with the impressive patient survival curves in Asian centers without the rescue option of retransplantation with deceased donor livers that exists in most Western centers.

The reported donor morbidity also has been variable. The experience with our 121 right lobe donors could be directly compared to 6 published studies in which the analyses were done with the 5-tier Clavien model [24,38–43]. Our 10.7% incidence of $\geqslant$III Clavien scores was midway in the spectrum of 2–32%. It is noteworthy that the large Asian centers with the lowest recipient morbidity and best survival [21,23,24,40] also had the smallest incidence of donor $\geqslant$III Clavien complications (4.9–9%) [37–40]. Although donor studies by the Toronto group [44] and by the A2ALL consortium [45] were done with the 4-tier system, enough detail was provided to estimate an approximately 20–25% rate of $\geqslant$III Clavien complications.

The most sobering information in the A2ALL report was that 4 of the 393 donors had died, one of infection and multiple organ failure during primary hospitalization and the other 3 more than a year later from a drug overdose, a suicide, and a pedestrian-train accident [45]. The psychiatric risks of right lobar donation [46] has been exemplified at our center by a suicide attempt subsequent to the series reported here. It has been estimated that early and delayed death from transplant-related causes can be expected of approximately one in every 200–500 right lobe donors [7,8], with permanent disability of a significant number of others.

Although information about right lobar LDLT is still being gathered, enough is known to permit counseling of donor–recipient pairs and prepare meaningful informed consent documents. Joint decisions to go forward undoubtedly will vary geographically, and will be influenced by the extent to which the option of deceased donor transplantation is available. If a given donor–recipient pair selects the living donor pathway, the choice should not be subject to veto by a legislative body, agency, or committee. But neither should such decisions be promoted by family groups that identify "expendable" donors, healthcare teams, or persons with a vested economic interest.

No matter how carefully right lobar LDLT is applied, the historical verdict on the ethics of this procedure may be harsh. There is no precedent of a surgical procedure that exposes healthy persons to such a high risk on behalf of others. Aside from the aggregate risk/benefit considerations of specific pairs, the procedure has been justified by anticipated "group benefits": e.g. relief of the organ shortage and prevention of slippage of liver candidates from elective into the urgent need category. In a reversal of fortune, 9 (7.4%) of the 121 recipients reported here were converted from elective to desperate status by right lobar LDLT and underwent retransplantation with deceased donor livers within 12 months, or in 2 cases after one year; 5 of the 11 currently survive. A similar incidence of retransplantation has been reported by the A2ALL consortium (9%) [36].

A second ethical issue is the use of right lobar LDLT at our and most other American centers only for patients with low MELD scores. This policy has been justified by arguments that it helps avoid the donor despair caused by a bad recipient outcome and is a safeguard against potential omissions and errors in hastily working up donors [47]. The preferential transplantation of low risk recipients bypasses the target population of candidates in which "death while waiting" is most likely. The contrasting "sickest first" policy is, in fact, the philosophic basis for the UNOS system of deceased donor liver allocation that UPMC [48,49] and most other American centers vigorously support.

In conclusion, the role of right lobar LDLT in liver transplantation [50] requires more thorough studies. It is possible that the adverse events in both donors and recipients can be reduced with technical refinements, innovative management strategies, or new liver-protective pharmacologic agents [19,51]. Evaluation of such modifications inevitably will begin by comparisons with historical controls. This report shows how artifacts of retrospective controls can be largely eliminated with the use of the Clavien scoring system.

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