

## Short-term Recovery and Long-Term Considerations

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### ISSUE

Discuss the short-term risks, expected recovery, and long-term considerations for living liver donors.

### DATA

The short-term risks of morbidity and mortality have been reported to be higher among living liver donors, compared to living kidney donors. For liver donors, the degree of perioperative risk is thought to be associated with the volume of liver resected.(1) Donor right hepatectomy is associated with morbidity rates of 24-40% (Clavien grade 1-4) in large cohorts reported from the U.S. and Canada.(1-3) In a recent international multi-center analysis (including high volume centers in Europe and Asia), morbidity averaged 13% for right liver donors and 9% for left liver donors.(4) Minor complications (Clavien 1-2) were similar between the groups, but major complications (Clavien 3a-4) occurred with significantly greater frequency in right liver donors (Table 1).

Potential surgical-related complications include infection, bile leak/biloma, biliary stricture, intraabdominal bleeding, prolonged ileus, incisional hernia, and remnant liver dysfunction. Data from the NIH-sponsored Adult-to-Adult Living Donor Liver Transplant (A2ALL) Consortium suggest that as many as 40% of living liver donors experience  $\geq 1$  complication during the post-operative period (measured any time post-operatively) (Table 2).(5) Of these complications, approximately 40% were graded as 'minor' and included pleural effusions, bile leak/biloma, infections, and/or psychological difficulties, while half were considered mild to moderate and required medical treatment beyond that of a 'minor' complication and/or blood transfusion.(5) Most of the risk assumed by the donor is in the initial perioperative period. The long-term risk to the donor is considered minimal once the remnant liver has hypertrophied (i.e., grown) appropriately. In addition to these complications that could impact recovery, data from the A2ALL

Consortium suggest that as many as 20% of living liver donors reported “clinically significant pain” at some point during the post-donation period.(6)

Living liver donors experience physiologic changes after hepatectomy, possibly related to a temporary alteration in portal venous flow or thrombopoietin production in the remnant liver. Splenic enlargement has been reported in half of donors and may exceed 30% of original spleen volume.(9) Donors can also exhibit a decrease in platelet count (30% below baseline), with 10% experiencing thrombocytopenia.(7-9) These changes can persist for more than 6-36 months post-donation. They are typically not symptomatic and pose minimal risk to the donor. These changes become less significant as the remnant liver hypertrophies. Percentage reconstitution of the remnant liver volume is  $80\% \pm 13\%$  in the A2ALL cohort.(10)

The average post-transplant hospitalization for a living liver donor is 5-7 days. On average, living liver donors report some diminished physical function (e.g., abdominal or back pain, pain interference) in the first three months after donation.(6) By six months these physical quality-of-life measures improve and by two years after donation, approach pre-donation levels.(6) The trend in reported measures of physical activity is similar to that for physical symptoms. At three months after donation, almost 60% of living liver donors were unable to perform “some” physical activities compared to pre-donation ability. However, physical activity improved with 67% reporting no limitation by six months.(6)

The OPTN mandates a minimum 2-year follow-up for all living donors. This includes data reporting at 6 months, 1 year and 2 years post-donation. Requisite information includes patient status, hospital readmissions, liver and surgical complications (e.g., incisional hernias), specific laboratory values, employment status, health insurance status, and, if applicable, cause of death.(11)

There are limited data on the median time to employment for living liver donors, and the time to return to employment is influenced by immediate post-operative complications, donor age, and the physical nature of the job.(12) Clinical experience suggests that most donors with less physically taxing jobs (e.g., desk-based occupations) are able to return to work 4-8 weeks after donation, although it is individualized due to a lack of published data. Those with physically intensive jobs requiring heavy lifting require prolonged recuperation of 12 weeks or longer due to weight restrictions and concerns about development of an incisional hernia.(12) Some donors are unable to return to their prior positions due to ongoing physical limitations.

Long-term, prior living liver donors experienced “high psychological growth” post-donation, and 90% feel positively about donation.(13) Although some donors endorse donation related physical health problems or concerns, and/or socioeconomic concerns related to donation, these were often minor and did not diminish the patients’ quality of life. There was a subset of patients who experienced “low” psychological benefit with some (or low) physical and socioeconomic concerns, but the overwhelming majority of

living liver donors experience psychological benefit with only some physical and/or socioeconomic concerns.(13) It should be noted that recipient complications and outcomes can influence donor attitude and mental health quality of life.(14-16) Psychosocial outcomes of living donation are discussed in further detail in the section entitled, “Psychosocial Risks of Living Liver Donation” section. Although there are no published manuscripts on post-donation fertility, data presented at the 2018 American Transplant Congress suggest no differences in post-donation fertility or ability to carry a child,(17) which would be expected given that donation surgery does not involve the lower abdomen or pelvis.

Although large studies from Asia have not reported operative mortalities among living liver donors,(18) US data have reported the risk of early acute liver failure and/or death to range from 1 in 500 to 1 in 1,000.(19,20) There have been at least 34 published liver donor deaths internationally and more recent reports show mortality risk is 0.2% or less.(1, 21, 22) The largest long-term study of living donor outcomes in the US was published in 2012, and showed that long-term mortality of live liver donors was comparable to matched comparators. It must be noted that the mean follow-up in this study was only 7.6 years.(19) Given that the first adult-to-adult living donor liver transplantation occurred in 1998, there are no long-term survival data in whole lobe donors beyond 20 years. According to OPTN/UNOS data as of September 15, 2020, out of 5,330 living liver donors in the US, only 3 (0.06%) developed “liver failure/liver failure requiring a transplant.”

## RECOMMENDATIONS

1. The risk of short-term morbidity and mortality after living donor liver transplantation is higher than in kidney donors, but still very uncommon.
2. The long-term physical complication of living liver donation are uncommon, but a small subset do have continued physical and/or psychosocial concerns.
3. OPTN Policy 18.5 mandates 2 year follow-up of living liver donors, with data reporting requirements at 6 months, 1 year, and 2 years post-donation.

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Table 1: Comparison of morbidity between right and left donor hepatectomy (adapted from **Rosler F, et al.(4)**)

	at discharge			after 3 months			after 6 months		
	Total	RH	LH	Total	RH	LH	Total	RH	LH
<b>Any complication</b>	9.4%	9.9%	7.1%	11.9%	12.6%	9%	12.1%	12.7%	9.2%
		p<0.001			p=0.01			p=0.01	
<b>Major complications (≥IIIa)</b>	2.7%	3%	1.4%	3.6%	4%	2%	3.8%	4.1%	2.2%
		p=0.001			p=0.008			p=0.01	
<b>Minor complications (≤II)</b>	6.7%	7%	5.7%	8.3%	8.6%	7%	8.3%	8.6%	7%
		p=0.07			p=0.06			p=0.1	

Table 2: Complications associated with living donor hepatectomy in the A2ALL cohorts (adapted from Abecassis 2012)

Complication	A2ALL (Abecassis 2012)
Intraoperative Injury/Complication	2.0%
Bile leak/biloma	8.1%
Biliary Stricture	0.7%
Bleeding	1.2%
Intraabdominal abscess	1.2%
Ileus	3.4%
Bowel obstruction	1.6%
Incisional hernia	6.6%
Wound dehiscence	0.8%
Unplanned re-exploration	2.7%
Pneumothorax	0.8%
Pleural effusion	10.9%
Pulmonary edema	2.0%
Pulmonary embolism	0.9%
Ascites	2.8%
Liver failure	0
Hepatic artery thrombosis	0
Portal vein thrombosis	0.5%
IVC thrombosis	0.4%
DVT	0.8%
Neuropraxia	3.2%
Infections	13.2%
Psychological difficulties	5.7%