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Longterm outcomes in living liver donor “Heroes” after the spotlight fades

Gerald Scott Winder¹, Robert J. Fontana²

¹ Department of Psychiatry, ² Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, MI

Address all correspondence to

Robert J. Fontana, MD
Professor of Medicine
3912 Taubman Center
Ann Arbor, MI 48109-0362
Tel: (734) 936-4780
Fax: (734) 936-7392

Email addresses:

Gerald Scott Winder gwinder@med.umich.edu

Robert Fontana rfontana@med.umich.edu

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Abbreviations

LDLT Living donor liver transplantation

LLD Living liver donation

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Sports and military heroes frequently receive extensive public praise and admiration for their exceptional performance and acts of bravery. In that vein, an individual who donates a part of their liver to a family member or close friend is a medical “hero” to the recipient as well as the broader community. Living liver donors (LLDs) voluntarily agree to incur substantial personal risk (i.e. mortality of 1 in 250 to 1 in 500) in an effort to help a fellow human being in dire need of a life-saving liver transplant. Not surprisingly, living liver and kidney donors have a higher level of resilience and perseverance to overcome adversity when compared with population controls¹. Although liver donors experience significant postoperative pain and up to 3 months of functional disability and lost wages, they are not financially incentivized nor recognized for their good deeds. However, the majority of living donors are rewarded by their sense of self-fulfillment and gratification that persists for many years after donation.²

Since the annual number of adult-to-adult living donor liver transplants (LDLT) is limited, the frequency, type, and severity of complications among donors are not well known nor are the donor or recipient features associated with adverse outcomes. Medical risks within the first year of donation include biliary complications (20%), infections (20%-30%), and need for reoperation (5%-10%)^{3,4}. In addition, there are rare reports of severe psychiatric complications in adult liver donors that may occur remote from transplants. In this issue, investigators from New York help improve our understanding of the longterm health and functional outcomes of adult LLD⁶. The data in this study arose from a statewide quality-assurance effort that was initiated in New York in 2004 and included the development of a liver-donor-specific questionnaire to assess 7 quality-of-life domains.

The 220 liver donors in the current report expand our understanding of functional outcomes previously reported by the Adult to Adult Living Donor Transplantation Cohort Study (A2ALL) and from Toronto^{2, 7} (Table 1). Notable strengths of this multicenter report include the high rate of eligible participant involvement over 6 years (70%) and the ability to extract new issues and concerns over time by a combination of multiple choice and open-ended telephone survey questions. Study limitations include the lack of baseline donor psychosocial profiles, information regarding the type of LLD performed and recipient outcomes which could significantly impact donor views and perceptions. Furthermore, the lack of a paired comparison of individual patients over time could have substantially underestimated the frequency and severity of complications. Nonetheless, the majority of LLD reported high rates of willingness to donate again (>90% through year 5 postdonation), feeling “very satisfied” after donation (81%-88% over time), and an increased positive outlook and self-worth related to LLD (82%). Interestingly, all of this positivity occurred in a cohort that also incurred substantial financial expense with 12% having spent >\$3000 for LLD-related expenses and 8% reporting that donation was a major financial hardship for them. In addition, 28% reported abdominal incisional pain negatively impacting their quality of life and 21% did not return to their predonation occupation for unspecified reasons. Overall, these data are generally reassuring to transplant teams with the low rate of severe or unexpected medical sequelae after 1 year and may help inform administrators and policy makers of the substantial nonmedical costs

associated with LLD.

Concerning new insights provided by Rudow et al. include the sizable rates of post-LLD emotional distress reported in this otherwise highly selected and resilient population of healthy donors. While 70% of the cohort reported no emotional distress during follow-up, 6% to 12% of donors consistently reported emotional problems at 2 to 6 years of follow-up. Unfortunately, the reported emotional symptoms (anxiety, intrusive thoughts, depression) were not well characterized nor confirmed by a clinician. Furthermore, it is not clear if these emotional issues were related to liver donation, recipient outcomes, or other life circumstances. Nevertheless, the finding that no donors had received *any* type of counseling or therapy is of concern and highlights the need for more careful assessment and monitoring of LLD after initial recovery from donation.

The annual number of adult-to-adult LDLT will likely increase over the next decade given recent changes to deceased organ donor allocation policy and concomitant advances regarding the overall safety profile of partial hepatectomy. In particular, the potential use of laparoscopic surgical techniques could reduce both short- and longterm donor morbidity including incisional hernias as has been seen with living kidney donation. In the interim, there are several ways in which our understanding of the safety and efficacy of LLD can be improved. First, the Organ Procurement and Transplantation Network and other international regulators now mandate reporting of various medical and psychosocial complications among liver donors at the time of hospital discharge and at 6 months, 1 year, and 2 years after donations^{8,9}. However, the content and duration of follow-up in these national data reports may not be detailed enough to detect and respond to crucial nuances in donors' health and functional status. Expanded prospective medical and radiological assessments are therefore needed to detect occult portal hypertension and vascular/ biliary complications as well as changes in donor nutrition and fertility during longterm follow-up. In addition, baseline and follow-up assessments using validated psychometrics are needed to provide higher resolution data on emotional health and adjustment over time. Finally, studies of functional outcomes in LLD lack appropriate comparator groups and would benefit from the inclusion of controls such as LLD candidates evaluated at the same center but excluded on *anatomical* grounds.

Liver transplant programs are continuously challenged to maintain equipoise between living donor safety and the mortality risk to wait-listed patients. The work of Rudow et al. provides important new information to help educate potential donors of the longterm risks and benefits of LLD⁶. As we screen potential donors and communicate detailed risk and benefit information to them, we must now also carefully counsel and guide them regarding their future longterm health risks and potential financial challenges if they are unable to return to their predonation occupation. In addition, this study highlights the need for additional resources and studies to monitor, assess, and treat individual liver donors who develop clinically significant emotional distress after the spotlight of their selfless act of donor heroism fades from our memories.

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Table 1 - Studies of long-term outcomes in adult LDLT donors

	Rudow et al (6)	Dew et al (2)	Adcock et al (7)
Study Characteristics			
Description	qualitative methods, LLD-specific questionnaire Multicenter, prospective	Multicenter, cross-sectional, telephone survey	chart review; detailed medical Single center, retrospective and psychosocial data
Population	6 centers in New York	9 North American centers	Toronto
(Years of data)	(2004-2013)	(2002-2009)	(2000-2008)
# Participants (% eligible)	220 (72%)	517 (66%)	202 (82%)
Median age at donation	41	Not reported	37 (18 to 60)
(years)	(30-60)	(18-61)	
% Female	56 %	53 %	47%
% Married	Not reported	71%	57 %
% Employed	81%	87%	92%
Duration of follow-up (yrs)	Annually for 6 years	Mean = 6 yrs	Mean = 2.8 yrs
Key Findings			
Medical concerns	<ul style="list-style-type: none"> •66% > 1 LLD-related medical problem •22% abdominal pain at yr 3 •28% pain negatively affect 	<ul style="list-style-type: none"> •69% wound numbness •50% decreased abdominal wall tone •36% low back pain 	<ul style="list-style-type: none"> •41% overall complication rate •7% readmission between 1 and 12 mon
Psychological/ social benefits	<ul style="list-style-type: none"> •95% resumed normal activities at 1 yr •90-95% would donate again •81-88% "very satisfied" •82% reported increased positive outlook/self-worth •79% of respondents "very 	<ul style="list-style-type: none"> •>90% would donate again •All HRQOL measures above US population norms •Low levels of guilt, responsibility in 91 donors whose recipient died •HRQOL similar/better on 	<ul style="list-style-type: none"> •100% employed donors returned to work post-LLD (mean= 10 weeks) •62% in stable relationships •7 donors married; 3 divorced; 3 widowed
Psychiatric/ functional concerns	<ul style="list-style-type: none"> •21% had different job •16% emotional issues at 1 year •6-12% emotional issues at 2-6 years 	<ul style="list-style-type: none"> •58% LLD-related expenses; 15% burdensome •22% unable to complete prior physical tasks •11% life insurance problems 	<ul style="list-style-type: none"> •4% female donors new or recurrent Depression/ anxiety
HRQOL – health-related quality of life, LDLT – living donation liver transplantation, LLD – living liver donation, MCS – mental component summary,			

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