



# Donor quality of life after living donor liver transplantation: a review of the literature

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**Abstract:** Living donor liver transplantation (LDLT) provides a source for transplant in the setting of the deceased donor organ shortage. Seeing as living donors do not derive any medical benefit from the procedure, fully understanding the impact of donation on donor health-related quality of life (HRQOL) is essential. A systematic search of the MEDLINE database was performed from 2008–2020, using relevant Medical Subject Headings. Articles were evaluated for study design, cohort size and follow-up time and excluded if they contained significant methodological flaws. A total of 43 articles were included: 20 (47%) were cross-sectional and 23 (53%) were longitudinal. The mean number of donors per study was 142 (range: 8–578) with follow-up ranging from 12–132 months. Forty-two unique HRQOL metrics were implemented across the 43 studies, the majority of which were questionnaires. Of the 31 studies that used the Medical Outcomes Study Short Form 36 questionnaire, 9.1% of donors reported physical QOL did not return to pre-LDLT levels for at least 2 years after donation. Mental QOL remained stable or improved after LDLT, with mean mental composite scores increasing from 50 to 52 at 3 months post-LDLT in one study. The predicted probability of poor sexual desire decreased at 1-year post-LDLT (male: 0.08, female: 0.26) relative to pre-LDLT (male: 0.44, female: 0.76;  $P < 0.001$ ) and three months post-LDLT (male: 0.35, female 0.69;  $P = 0.001$ ). Forty percent of donors found LDLT to be financially burdensome at 3 months and 19% at 2 years post-LDLT. Female gender and obesity were consistent predictors of worse HRQOL. Laparoscopy-assisted donor hepatectomy was associated with shorter hospitalizations than open donor hepatectomy (10.3 vs. 18.3 days,  $P = 0.02$ ). No studies used the National Institutes of Health Patient Reported Outcomes Measurement Information System (PROMIS) measures of HRQOL. Our review demonstrates that LDLT can have a long-lasting negative impact on physical QOL in 9.1% of donors and can cause both sexual dysfunction and significant financial strain. Future studies should consider using standardized and extensively validated patient reported outcomes measures, such as PROMIS, in order to directly compare outcomes across studies and gain further insight into the impact of LDLT on D-HRQOL.

**Keywords:** Living donor liver transplantation (LDLT); health-related quality of life (HRQOL); patient-reported outcome measures

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## Introduction

Liver transplantation (LT) is the only life-saving intervention for end-stage liver disease. Despite notable innovation in graft optimization (1-3) and the organ allocation process (4,5) over the past two decades, the shortage of available donor organs remains profound and represents a prominent challenge in LT (6). Living donor liver transplantation (LDLT) is one option to address this critical shortage of liver grafts in the United States (7), yet donor risks must be critically assessed and weighed against obvious recipient benefits.

Donors achieve no medical benefits from LDLT, but are subject to the risks of an extensive surgery, which includes death. In the U.S., the donor mortality rate is 0.2–0.4% (8-10), similar to the mortality rate in elective surgeries (11). Reported donor complication rates vary significantly in the literature ranging from 24–67%, with the majority of these complications classified as minor and resolving within one year of surgery (8,12,13). Reported morbidity and mortality rates, however, do not fully capture the global donor experience, which is multifaceted and better summarized by health-related quality of life (HRQOL) (14). HRQOL can be assessed using patient interviews and patient-reported outcome (PRO) measures, which largely comprise of questionnaires such as the widely used Medical Outcomes Study Short Form 36 (SF-36) and the World Health Organization Quality of Life-BREF (WHOQOL-BREF) (15).

It is imperative that the impact on donor HRQOL be assessed rigorously and critically in order to optimize donor selection, education and post-operative care. Past systematic reviews have summarized the short-term physical and mental quality of life in donors following LDLT, with overall favorable outcomes (16-19). Yet, until recently, there were few studies on donor HRQOL more than one year after surgery. With the multi-center Adult-to-Adult Living Donor Liver Transplant Cohort Study (A2ALL) and a multitude of other recent publications, we have a better understanding of the short-term and long-term impact of LDLT on donor HRQOL. We also have new insight into the psychiatric impact, sexual dysfunction and the financial burden reported after donation. In order to synthesize the new data available, we performed an updated systematic

review of the literature to supplement our review published in 2010 (16).

## Materials and methods

We performed a systematic search of the MEDLINE database from 2008–2020 to identify original studies evaluating donor HRQOL after LDLT. This time interval was chosen to ensure that this systematic review included any articles that were published between 2008 and 2010, and not captured in our previous systematic review (16). In order to include all relevant articles, we searched the MEDLINE database using the following Medical Subject Headings: “Liver donors”, “liver transplantation”, and “quality of life”. In addition to these Medical Subject Headings, we included the following keywords to ensure thorough coverage: “QOL”, “HRQOL”, “HRQL”, “liver transplant”, “liver grafting”, “liver graft(s)”, “hepatic transplantation(s)”, “hepatic transplant(s)”, “living donor hepatectomy”, “living donor hepatectomies”, “LDLT”, “live donor(s)”, “living donor hepatectomy” and “living donor hepatectomies”. Inclusion criteria limited articles to human subjects and those available in English. We excluded review articles, case reports, case series, articles that only assessed HRQOL in donors prior to LDLT and articles that exclusively assessed pediatric LT. The remaining articles were evaluated for study design, cohort size, and follow up time. Studies were excluded if they included significant methodological flaws, including small sample size ( $n < 20$ ).

The specific HRQOL instrument utilized in the study was also critically examined in order to evaluate the clinical significance of results and compare findings across studies (Table 1). Each HRQOL survey and relevant supporting literature was assessed individually to determine if the survey had been validated prior to use in the study and if so, whether or not the survey was validated in an appropriate study population. Each instrument’s psychometric properties were evaluated thoroughly to ensure that the instrument was valid and reliable. If a survey had not been validated or if it had been created by the authors specifically for the study, survey questions were assessed when available to determine if the questions were suitable and clinically relevant to live living donors’ QOL. Studies were excluded

**Table 1** Study characteristics

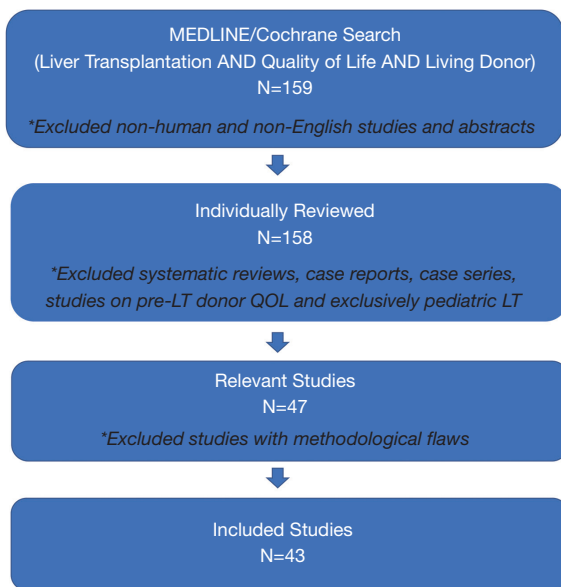
Author	Date of publication	Cohort size	Study design	Quality of life metric	Comparison population	Follow up time (months)
El-Serafy	2009	30	Cross-sectional	SF-36	Healthy adults	39.4 ( $\pm 18.7$ ) <sup>a</sup>
Schulz	2009	43	Longitudinal	SF-36, HADS, CLDQ, NDI, Caregiver burden scale, EUROTOLD questionnaire	Normative population, Potential donors	3.3 ( $\pm 0.7$ ) <sup>a</sup>
Castedal	2010	34	Cross-sectional	Study specific questionnaire	None	6 (1–12) <sup>d</sup>
Hsieh	2010	51	Longitudinal	SF-36, 6MWD	Normative population	3 <sup>a</sup>
DuBay	2010	142	Cross-sectional	SF-36, BIQ, IIRC, Confidence rating scale	Normative population	27 (3–84) <sup>d</sup>
Togashi	2011	35	Longitudinal	SF-36	Normative population	18 <sup>c</sup>
Noma	2011	40	Longitudinal	STAI, BDI, WHOQOL-BREF, PACT	None	51.4 ( $\pm 6.5$ ) <sup>a</sup>
Azoulay	2011	91	Cross-sectional	NIDDK	Normative population	77( $\pm 29$ ) <sup>a</sup>
Kousoulas	2011	55	Cross-sectional	SF-36	Normative population	94 <sup>a</sup>
Yamanouchi	2012	20	Longitudinal	SF-36	Normative population	12 <sup>c</sup>
Jin	2012	92	Longitudinal	SF-36, SCL-90-R	Normative population	12 <sup>a</sup>
Narumi	2012	33	Cross-sectional	SF-36, Hamilton anxiety and depression scale	Normative population	78 <sup>d</sup>
Toyoki	2012	27	Cross-sectional	SF-36	Normative population	72 <sup>d</sup>
Choi	2012	150	Longitudinal	NRS pain scale	None (LADH, ODH)	N/A
Takada	2012	578	Cross-sectional	SF-36	Normative population	81.6 ( $\pm 40.8$ ) <sup>a</sup>
Lei	2013	300	Longitudinal	SF-36, SCL-90-R	Normative population	5 <sup>a</sup>
Marubashi	2013	31	Longitudinal	SF-36	Normative population (ODH)	12 <sup>c</sup>
Kroencke	2014	40	Longitudinal	SF-36, HADS	Normative population, Healthy adults, Potential donors	12.6 <sup>b</sup>
Kawagishi	2014	84	Cross-sectional	SF-36	Normative population	103.6 <sup>a</sup>
Ladner	2015	374	Longitudinal	SF-36	Normative population	132 <sup>c</sup>
Suh	2015	429	Cross-sectional	Study specific questionnaire	None	32.6 (6.4–55.4) <sup>a</sup>
DiMartini	2015	208	Longitudinal	Study specific questionnaire	Potential donors	7.5 <sup>b</sup>
Bhatti	2015	60	Cross-sectional	SF-36, POMS-65	Normative population	15 ( $\pm 5.1$ ) <sup>a</sup>
Kimura	2015	142	Cross-sectional	Chart review of comorbidities	None	65.3 ( $\pm 38.2$ ) <sup>a</sup>
Humphreville	2015	107	Longitudinal	SF-36, DSS	Normative population	82.8 <sup>d</sup>
Murad	2016	68	Cross-sectional	Study specific questionnaire	None	66 (range 18–130.8) <sup>d</sup>

**Table 1** (continued)

Table 1 (continued)

Author	Date of publication	Cohort size	Study design	Quality of life metric	Comparison population	Follow up time (months)
Dew	2016	517	Cross-sectional	SF-36, PTGI-SF, Study specific questionnaire	Normative population	72 <sup>a</sup>
Shen	2016	114	Cross-sectional	SF-36, HADS	Normative population	48 <sup>c</sup>
Wang	2016	204	Cross-sectional	GIQLI	None	24 <sup>a</sup>
DiMartini	2017	271	Longitudinal	PHQ-9, Study specific questionnaire	None	9.6 <sup>b</sup>
Cherian	2017	64	Cross-sectional	SF-36	Normative population	48 <sup>a</sup>
Kitajima	2017	153	Longitudinal	Interview	None (ODH)	36.6 (1.4–66.0) <sup>a</sup>
Chandran	2017	200	Cross-sectional	SF-36	Normative population	12(±0) <sup>a</sup>
Wang	2017	60	Cross-sectional	CES-D, WHOQOL-BREF, CHQ	Normative population	3 <sup>a</sup>
Butt	2018	297	Longitudinal	SF-36, PRIME-MD, PTGI-SF, Simmons Better Person Scale, Interview	Normative population	9.6 <sup>b</sup>
Benzing	2018	104	Longitudinal	SF-36	Normative population	41 (7–161) <sup>a</sup>
Berglund	2018	176	Longitudinal	SF-36, DSS	Normative population	99.6 <sup>a</sup>
Butt	2018	271	Longitudinal	SF-36, FACIT-Fatigue, BPI	Normative population	9.6 <sup>b</sup>
Hesimov	2018	55	Longitudinal	SF-36	Normative population	12 <sup>a</sup>
Dew	2018	517	Longitudinal	SF-36, FACIT-Fatigue, BPI, NRS pain scale, Study specific questionnaire	Normative population	N/A
Weng	2019	68	Longitudinal	SF-36	Normative population	12 <sup>a</sup>
Morooka	2019	374	Cross-sectional	SF-36, LLD-QOL	Normative population	N/A
Raza	2020	68	Longitudinal	SF-36, Study specific questionnaire	Normative population	138 (±61.2) <sup>a</sup>

<sup>a</sup>, mean follow up time (months); <sup>b</sup>, mean follow up time was not provided; a weighted mean follow up time was calculated based on number of patients lost to follow up (months); <sup>c</sup>, data not available to calculate weighted mean follow up time; maximum follow up reported (months); <sup>d</sup>, median follow up time reported (months); N/A, did not report follow up time. SF-36, Medical Outcomes Study Short Form 36; HADS, Hospital Anxiety and Depression Scale; CLDQ, Chronic Liver Disease Questionnaire; NDI, Nepean Dyspepsia Index; EUROTOLD Questionnaire, Modified European Multicenter Study of Transplantation of Organs from Living Donors Questionnaire; 6MWD, six minute walk distance; BIQ, Body Image Questionnaire; IIRS, Intimacy Subscale of the Illness Intrusiveness Rating Scale; STAI, The State-Trait Anxiety; BDI, The Beck Depression Inventory; WHOQOL-BREF, World Health Organization Quality of Life Questionnaire; PACT, The Psychosocial Assessment of Candidates for Transplantation; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases Quality of Life Survey; SCL-90-R, Symptom Checklist 90 Revised; NRS pain scale, Numeric Rating Pain Scale; POMS-65, Profile of Moods; DSS, Donor Specific Survey; PTGI-SF, Posttraumatic Growth Inventory Short Form; GIQLI, Gastrointestinal Quality of Life Index; PHQ-9, Patient Health Questionnaire-9; CES-D, Center for Epidemiologic Studies Depression Scale; CHQ, Chinese Health Questionnaire; PRIME-MD, Primary Care Evaluation of Mental Health Disorders; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy Fatigue Scale; BPI, Brief Pain Inventory; LLD-QOL, Live Liver Donor Quality of Life Questionnaire.



**Figure 1** Systematic review methodology.

if they included non-validated surveys without outlining specific survey questions or if the survey questions were not deemed to be clinically relevant to living donors' QOL. Studies using surveys validated in the general population were included as living donors were thought to most closely resemble this population.

## Results

Our original MEDLINE search, restricted to the English language and human subjects, identified 159 unique articles. After evaluating each article, 43 articles met inclusion criteria and were included in the review (*Figure 1*).

Twenty studies (47%) had a cross-sectional design and 23 (53%) studies had a longitudinal design (*Table 1*). Forty-two unique HRQOL metrics were implemented across the 43 studies, the majority of which were questionnaires. The most frequently used instrument was the Medical Outcomes Study Short Form 36 (SF-36), which was used in 31 (72%) studies.

In total, 19 generic instruments, which were not designed for a specific population or disease process, were used to assess HRQOL, with the WHOQOL-BREF questionnaire, the Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale, the Hospital Anxiety and Depression Scale, the Profile of Mood States (POMS-65) and the Symptom Checklist 90-Revised (SCL-90-R) used most frequently. Fifteen of the 19 (79%)

generic instruments were validated in general populations, demonstrating acceptable construct validity and internal consistency reliability, but none of them were validated in live liver donors specifically. Thirteen surveys specific to chronic liver disease were used in 12 different studies. Of these thirteen surveys, only two were extensively validated in those with chronic liver disease (the Chronic Liver Disease Questionnaire and the National Institute of Diabetes and Digestive and Kidney Disease Liver Transplant Database Quality of Life questionnaire). The Living Liver Donor-QOL Survey (LLD-QOL) and the Donor Specific Survey (DSS), which were used in two different studies, were designed specifically for liver donors and validated in this specific population. Nine of the 13 (69%) liver disease specific surveys were designed for the individual study and were not validated. Moreover, two studies included unique questionnaires specific to abdominal surgeries, with a focus on cosmetic appearance and body image after surgery, neither of which were validated. A minority of studies employed alternate means of assessing HRQOL, with five (12%) studies using qualitative interviews rather than quantitative questionnaires and one study (2%) relying on chart review to assess the development of psychiatric comorbidities following donation (20).

The mean number of donors enrolled in the 47 studies was 142 (range: 8–578). Studies provided follow-up times as either mean, medians or total length of follow-up (*Table 1*). For the 33 studies that provided mean follow up times, the average follow-up was 31.3 months. For all included articles, follow up ranged from 3 to 132 months. Two studies did not provide follow up times or the data necessary to calculate follow up time.

### Overall Physical and Mental HRQOL

In studies that implemented the SF-36, donor HRQOL including both physical (PCS) and mental composite scores (MCS) were typically higher than the general population prior to donation (21–25). Ladner *et al.* (23) evaluated the A2ALL cohort and found mean PCS and MCS scores to be close to one standard deviation higher than the normative means before donation. Prior to donation, potential candidate donors and eventual donors were found to have higher PCS scores (57.6 and 58.0 respectively) than the general population and the healthy reference sample (25). Eventual donors also had higher MCS scores than potential candidate donors (51.8 vs. 46.8), but these scores were not significantly different from the general population or the

healthy reference sample.

Donors generally experience positive long-term outcomes in both physical and mental HRQOL after LDLT. Physical HRQOL tends to decrease and reach a nadir between 1 to 6 months directly after surgery, with PCS scores decreasing to 42.9–50.9 at 3 months (21,23,25–28). Numerous studies report rapid improvement of physical HRQOL within 3–6 months of LDLT (21,23,25–27,29). For example, in one prospective study (29), the mean PCS score decreased significantly at 1 month after surgery but fully recovered by 6 months. Togashi *et al.* (27) demonstrated similar findings, with PCS scores dropping significantly at 3 months post-surgery, but then returning to baseline 3 months later. Ladner *et al.* (23) confirmed worsening PCS scores at 3 months post-surgery and showed subsequent improvement to baseline 1 year after surgery.

In recent years, however, multiple studies that included lengthier follow up periods demonstrate that donors may take significantly longer to return to baseline physical function, ranging from 2 to 4 years post-donation. In Butt *et al.*'s (28) prospective study containing 271 patients, donors reported significant decrease in PCS scores and higher levels of fatigue, abdominal pain and back pain at 3 months post-donation. These physical HRQOL domains started improving 6 months after donation and continued to do so for 2 years, but failed to reach pre-donation levels at the end of the study, with significantly worse scores in the pain domain. Shen *et al.* (30) found a similarly prolonged recovery period, with physical domains of HRQOL taking 3 to 4 years to return to pre-operative baseline levels or levels comparable to the general population. Humphreville *et al.* (24) found that 11.2% patients reported their health as worse than prior to donation 7 years later, suggesting an even more prolonged recovery period than the majority of studies in this review. Among the studies included in this review, Raza *et al.*'s (31) study had the longest mean follow up period of 11.5 years and found PCS scores to be similar to the general U.S. population more than a decade later. Regardless of new data suggesting a longer time to recovery, our evaluation of the literature does support overall positive long-term physical quality of life amongst donors, as the majority of studies demonstrate that HRQOL returns to pre-operative levels or levels comparable to the general population after 4 years (22,32).

### *Physical symptoms*

After surgery, the most commonly reported donor

symptoms were abdominal pain, irritation or numbness of the surgical scar, and gastrointestinal complaints including irregular bowel habits, nausea and heartburn (24,25,27,33–38). In one large cross-sectional study (38), the most common post-operative symptoms were numbness and itching around the surgical site and decreased stomach tone. Approximately 6 years after surgery, 15% of donors were still endorsing donation-related medical problems, with the most common problems being hernias, nausea, diarrhea and problems relating to scar tissue and adhesions from the surgery. Berglund *et al.* (37) had a mean follow up period of 4.8 years after donation and found the most common physical complaints to be incisional discomfort (25% of respondents) and intolerance to fatty meals (20%). Kroencke *et al.* confirmed a high prevalence of gastrointestinal complaints after donation, finding that digestive symptoms were the most frequent complaint amongst donors 2 years after surgery.

A large portion of patients reported that post-operative pain was more significant than they had expected and that time to recovery was longer than they had anticipated (28,39,40). For example, in one cross-sectional study (39) containing 68 donors, 41% noted post-operative pain that was “much greater than or somewhat greater than expected.” In another study (34), 24% of patients were still having wound-related pain 10 months after surgery. Furthermore, multiple studies revealed long-lasting fatigue and limitations in physical activity following donation (28,31,35). Azoulay *et al.* (35) found that 22% of donors felt limited in their ability to perform vigorous activity such as running, lifting heavy weights or playing sports up to 6 years after donation. In another study (31), 48.5% of donors endorsed restricting the type of physical activity they performed when evaluated more than a decade after surgery.

LDLT was also found to impact donor's body image. In Dubay *et al.*'s cross-sectional study (41), donors reported significantly lower perception of their body image and lower satisfaction with their surgical scar compared to those who underwent open-donor nephrectomy. Younger age, greater pre-donation concern regarding their own health and greater post-donation perception that the recipient engaged in behaviors that risked the new liver were independently associated with negative body image.

### *Mental HRQOL and psychiatric comorbidities*

The existing literature demonstrates that mental HRQOL

remains relatively stable after donation and comparable to the general population (27,42,43), with a few studies finding an increase in overall mental HRQOL (26,40,44). While overall MCS scores remain stable, certain domains of mental HRQOL can worsen. Hesimov *et al.* (21) found that MCS scores did not change post-donation, but the social functioning component of the SF-36 assessment did drop significantly 3 months after donation and gradually returned to pre-operative levels by 12 months post-donation.

The development of psychiatric comorbidities after donation was low in the majority of studies (20,28). For example, in a cross-sectional study containing 142 donors (20), only 4.2% of patients developed psychiatric complications such as depression or anxiety. Humphreville *et al.*'s (24) study was an outlier, finding that 22.4% of donors reported depression after surgery—a percentage far higher than the remainder of the literature, which shows the prevalence of depression in donors to be similar to the general population (22). While rates of depression were not elevated, anxiety was more prevalent post-donation, ranging from 2.6–4.9% (22) compared to 0.9–1.9% in the general population (45). Alcohol use disorder was found in 2–6% of donors after LDLT and more common in men (22,28), similar to the general population (45).

### ***Sexual function after donation***

Our review showed that LDLT and even evaluation for potential donation negatively impacts sexual function (33,35,41). In a cross-sectional study containing 91 donors (41), 9% of donors had a decrease in sexual activity following surgery. Donors with low body image scores were significantly more likely to report interference with both sexual activity and intimate relationships. While donors typically report high physical and emotional functioning at evaluation, DiMartini *et al.* (33) found that donors and potential candidate donors had worse sexual function at evaluation and at 3 months post-LDLT when compared to 1-year post-LDLT, suggesting that poorer sexual function at evaluation and directly after LDLT could be due to the stresses inherent to the evaluation process and the decision to donate.

### ***Financial impact of donation***

Studies revealed that a significant portion of donors felt that donation-related expenditures were burdensome and that LDLT impacted their employment and health

insurance. In one illustrative example (33), 40% of donors reported that donation-related costs were burdensome at 3 months post-donation and 19% reported feeling similarly at 2 years post-donation. Cumulatively, 24% of donors found donation-related costs to be more than expected in this study. Furthermore, 34% of donors changed jobs or modified their work because of donation at 3 months post-donation, though only 1% reported changes in employment 2 years later. In this study, those with lower household incomes were at higher risk of poorer financial outcomes. Dew *et al.* (38) assessed financial burden approximately 6 years after donation and found that 15% of donors reported that donation expenses were burdensome; a portion of these donors changed jobs and experienced permanent income reductions. In this study, 11% of donors also experienced health or life insurance problems due to donation.

### ***Overall donor perception of LDLT***

Despite our review demonstrating that LDLT can impact short-term HRQOL and can be perceived as financially burdensome to some patients, all studies in this review found that almost all donors did not regret their decision to donate and 85–100% of participants would donate again if need be (28,35–40,46,47). The minority of patients who would not donate again were those who experienced significant post-operative complications (47) or the recipient died (28).

### ***Predictors of post-donation quality of life***

A wide variety of predictors of HRQOL were evaluated across the studies in this review, producing conflicting results. Potential predictors of HRQOL included donor gender, race, body mass index (BMI), education status, financial status, surgical approach including graft type (right versus left lobe) and incision type, post-operative complications, length of hospital admission, indication for transplant and urgency of LDLT, relationship with recipient and recipient mortality. Among the various studies, female gender (22,28,48), transplant recipient death (22,23,46) and obesity (22,46) were found to be predictors of worse post-donation physical HRQOL. Toyoki *et al.* (49) found that donors who underwent emergency hepatectomy had worse PCS scores. Female gender (22,28,43), longer post-donation hospitalization (22), higher financial burden (22), transplant recipient death (23) and emergency surgery (46) were

found to predict worse post-donation MCS and depression in multiple studies. Narumi *et al.* (50) similarly found that donors who believed that they did not have sufficient time to make a decision on donation before surgery had significantly worse social functioning and higher depression and anxiety scores. There were conflicting findings on whether post-operative complications impacted HRQOL. While some studies found that more post-operative complications led to worse HRQOL (28,32,43,51), others studies (21,46,52,53) showed that complications had no impact on HRQOL. Ladner *et al.* (23) found that the Hispanic ethnicity and an education less than a bachelor's degree to be predictors of poor PCS scores, yet ethnicity and education have not been studied extensively in the literature. Thus, these findings have not been replicated.

Left lobe hepatectomy was associated with fewer complications than right lobe hepatectomy, but did not impact MCS or PCS scores (32,37,53,54). When comparing a traditional open versus laparoscopic approach, the laparoscopic approach had favorable outcomes. For example, Marubashi *et al.* (29) found that recovery from bodily pain and physical disturbance after surgery was quicker in laparoscopy-assisted living donor hepatectomy (LADH) group than in open living donor hepatectomy (ODH). This study also found that donors who underwent LADH had shorter hospitalizations than those who underwent ODH. Kitajima *et al.* (55) did not find the complication rate different between LADH and ODH but reported significantly lower scar discomfort in the LAHD group than in the ODH group. Choi *et al.* (56)'s prospective study containing 150 donors was the only study to compare single-port laparoscopy-assisted donor right hepatectomy (SPLADRH) to LADH and ODH. This study found SPLADRH to have favorable outcomes, with similar complication rates, shorter operative time, and less blood loss than LADH and ODH. Moreover, patients described less post-operative pain in the SPLADRH group. Suh *et al.*'s (57) study was the only study to describe how donor satisfaction varied by incision type. In this study, upper midline incision and the transverse incision for laparoscopy resulted in higher patient satisfaction with cosmetic appearance than the inverted L incision. The upper midline incision also resulted in decreased operative time and shorter hospitalizations.

## Discussion

This review of the literature demonstrates that donor

physical and mental HRQOL are typically higher than the general population prior to donation. This is not surprising given the rigorous physical and psychosocial evaluation required to be considered a donor. Donor physical HRQOL decreases post-donation, reaching a nadir between 3-6 months after surgery, while mental HRQOL remains stable or equivalent to normative populations. Almost half of patients find post-operative pain to be far greater than expected and physical HRQOL can take many years to return to baseline, with a significant portion of donors experiencing long-lasting physical limitations. There is also a higher than expected prevalence of general anxiety disorder and alcohol use disorder (22,45) and significant financial strain experienced by donors after surgery, with almost one in four donors reporting donation related costs to be more than expected 3 months after donation.

It is noteworthy that 41% of donors found post-operative pain to be "much greater than or somewhat greater than expected" in one cross-sectional study containing 68 donors (39). This result suggests that donors may not be educated adequately on the spectrum of post-operative pain and the range of post-surgical recovery time. Moreover, an unexpected degree of post-operative pain likely contributes to overall worsening of donor physical HRQOL. We also found that physical recovery from LDLT can take longer than previously described. Prior studies found that donor physical HRQOL returns to baseline by 1 year after donation (58,59). Recent studies with lengthier follow up, however, reveal that PCS scores can take up to 3-4 years to return to baseline. Furthermore, 22-48.5% of donors report long-lasting fatigue and some degree of limitation in their physical activity for 5-10 years (31,35), underscoring the lingering physical impact of donation. While donors endorse long-lasting physical limitations, however, their overall physical HRQOL improves to pre-donation levels within 4 years and 96-100% of donors were able to return to their pre-donation occupation (35,60). These findings suggest that the physical limitations reported by donors might not alter daily activities to the extent that it has a profound effect on donor perceived QOL. Thus, the downstream effects of these physical limitations and persistent fatigue on donor health remain unclear and must be investigated further.

Interestingly, we found that alcohol use disorder was identified in 2-6% of donors, which is similar to the prevalence reported in the general population (45). Given the careful donor selection process aimed at identifying at risk drinkers, the prevalence of alcohol use disorder in



donors is surprising and therefore more rigorous screening might need to be considered. Additionally, further research is necessary to determine the potential consequences of alcohol use on donor health following LDLT.

We also found that LDLT results in significant financial strain on donors, which is a predictor of worse mental HRQOL. Twenty-four percent of donors reported costs to be more than expected and 40% found donation-related costs to be burdensome. This financial burden was long-lasting, with 15% of donors endorsing financial concerns and changes in life insurance policies 6 years after donation (38). As one might expect, donors with lower household income at time of donation were more likely to worry about financial expenditures after donation (33), highlighting the socioeconomic disparity in the burden related to LDLT and the need for more financial aid towards living liver donors. The American Transplant Surgeons' (ASTS) National Living Donor Assistance Center (NLDAC) was created to provide reimbursement for donation-related expenses and thus reduce the financial disincentives to living organ donation. However, it is unclear whether the donors who were financially impacted by LDLT in the included studies were directed to the NLDAC for financial support. Based on these studies, it is paramount to clearly outline the potential short- and long-term financial burden to potential donors to allow for fully informed decisions and prevent significant financial stress that could worsen mental HRQOL post-donation.

Across the studies in this review, there were conflicting results on positive and negative predictors of HRQOL. Although female gender and obesity were found to consistently predict worse HRQOL, the positive outcomes in left lobe hepatectomy and laparoscopy-assisted donor hepatectomy were especially noteworthy. Recent studies consistently show that left lobe hepatectomy has fewer surgical complications than right lobe donor hepatectomy. Moreover, laparoscopy-assisted donor hepatectomy resulted in less post-operative pain and quicker recovery.

Finally, this systematic review highlights the fact that there is no validated and standardized patient-reported outcome measure to assess HRQOL in living liver donors. The majority of studies implemented the SF-36, but a large portion of the studies used generic instruments, none of which have been validated in the liver transplantation setting and specifically with living liver donors. Although the majority of these instruments were validated in the general population, living liver donors are often healthier than the general population, with higher reported baseline

HRQOL. Only two HRQOL surveys (DDS and LLD-QOL scale) were tested in living liver donors and were found to have construct validity and internal consistency reliability, but even these were only validated in small studies. The large spectrum of patient reported outcome measures used, the majority of which were not validated in living liver donors, is a weakness in the current literature on HRQOL in LDLT, which offers opportunity for further study. Moreover, the heterogeneity of outcome measures presents a significant limitation in a systematic review, as quality of life cannot be easily compared across studies.

One notable omission from the current studies on LDLT is the National Institute of Health (NIH) Patient Reported Outcomes Measurement Information System (PROMIS) measures of HRQOL (61). PROMIS, which was developed between 2004 and 2014, is innovative in multiple ways. It was sponsored by the NIH "roadmap" for 21st century medical research to develop a new system of brief, psychometrically sound, and flexible measures covering physical, mental, and social HRQOL, along with multiple other symptoms. Through its use of item response theory (IRT) and computer adaptive testing (CAT), PROMIS measures can draw from large banks of items to generate efficient, reliable, and parsimonious measures of patients' HRQOL. All PROMIS measures are scored on a user-friendly T-score metric that sets the mean value to 50 and standard deviation to 10, normed to the United States general population, so that any individual's score on PROMIS measures can be compared to this standard. Due to its normative reference to the general population, PROMIS measures may be particularly useful for living liver donor HRQOL assessment and tracking. Moreover, because PROMIS was developed to be applicable to a wide variety of patient populations, ranging from patients who are severely impaired to those who are high functioning, it can be applied to any study population. Hence, future studies of HRQOL in LDLT should consider using PROMIS measures.

## Conclusion

LDLT is an emerging treatment for end-stage liver disease in the United States and offers one strategy to alleviate the shortage of liver grafts. Donors achieve no medical benefits from LDLT, but are exposed to the risks of an extensive surgery. Thus, the impact of LDLT on donor health-related quality of life must be assessed critically and comprehensively in order to optimize donor selection

and to better educate donors on the risks involved in the procedure. Our review confirms that donors tolerate LDLT well and eventually return to baseline function. However, longer follow up in recent studies has revealed that some patients experience prolonged physical limitations, develop alcohol dependence and are burdened by healthcare expenditures after the surgery. Recently published studies also show that potential donors may need more comprehensive education on the spectrum of post-operative pain and the range of post-surgical recovery time. Further studies are needed to better elucidate predictors of poor HRQOL in order to improve clinical outcomes and educate potential donors accurately prior to LDLT. Moreover, the use of a standardized and extensively validated patient reported outcomes measure, such as PROMIS, could allow for direct comparison of outcomes across studies and provide further insight into the impact of LDLT on donor HRQOL.

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