

# Pain expectancy, prevalence, severity, and patterns following donor nephrectomy: Findings from the KDOC Study

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## Funding information

National Institute of Diabetes and Digestive and Kidney Diseases, Grant/Award Number: R01DK085185

Postoperative pain is an outcome of importance to potential living kidney donors (LKD). We prospectively characterized the prevalence, severity, and patterns of acute or chronic postoperative pain in 193 LKDs at six transplant programs. Three pain measurements were obtained from donors on postoperative Day (POD) 1, 3, 7, 14, 21, 28, 35, 41, 49, and 56. The median pain rating total was highest on POD1 and declined from each assessment to the next until reaching a median pain-free score of 0 on POD49. In generalized linear mixed-model analysis, the mean pain score decreased at each pain assessment compared to the POD3 assessment. Pre-donation history of mood disorder (adjusted ratio of means [95% confidence interval (CI)]: 1.40 [0.99, 1.98]), reporting "severe" on any POD1 pain descriptors (adjusted ratio of means [95% CI]: 1.47 [1.12, 1.93]) and open nephrectomy (adjusted ratio of means [95% CI]: 2.61 [1.03, 6.62]) were associated with higher pain scores across time. Of the 179 LKDs who completed the final pain assessment, 74 (41%) met criteria for chronic postsurgical pain (CPSP), that is, any donation-related pain on POD56. Study findings have potential implications for LKD education, surgical consent, postdonation care, and outcome measurements.

## KEYWORDS

anesthesia/pain management, clinical research/practice, donors and donation, donors and donation: donor follow-up, donors and donation: living, health services and outcomes research, kidney transplantation/nephrology, kidney transplantation:living donor, quality of life (QOL)

## 1 | INTRODUCTION

Living donor nephrectomy is performed routinely globally with little morbidity. In the United States alone, 6857 donor

nephrectomies were performed in 2019.<sup>1</sup> Postoperative pain is an expected outcome after most elective surgeries, including donor nephrectomy, and an outcome of importance to potential living kidney donors (LKDs).<sup>2</sup> Cross-sectional and retrospective studies

**Abbreviations:** CPSP, chronic postsurgical pain; ERAS, enhanced recovery after surgery; KDOC, Kidney Donor Outcomes Cohort; LDEQ, Living Donation Expectancies Questionnaire; LKD, living kidney donor; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; POD, postoperative day; REDCap, research electronic data capture; SF-MPQ, Short-Form McGill Pain Questionnaire.

have found that few LKDs report pain in the months or years after donation.<sup>3-6</sup> However, no prospective studies have characterized the prevalence, severity, and patterns of acute or chronic postoperative pain in LKDs.

In addition to acute pain, characterizing the prevalence of chronic postsurgical pain (CPSP) and its correlates is important as it may have implications for long-term LKD recovery, return to pre-donation functional status, and satisfaction with the overall donation experience. CPSP refers to pain that develops after surgery, persists for at least 2 months, and is not caused by other conditions.<sup>7,8</sup> In addition, pain assessment data may guide discussions with prospective donors during the evaluation phase about pain, its intensity and duration, and those who may be at higher risk for CPSP.

In this study, we prospectively examined pain expectancy, prevalence, pattern, and predictors in LKDs at six transplant centers in the United States. Based on prior retrospective studies with LKDs,<sup>3-6</sup> we hypothesized that a majority of LKDs would report complete pain resolution by 2 months postdonation and that younger age, preexisting pain, high intensity early postsurgical pain, and longer hospital length of stay would be significant predictors of pain across time.

## 2 | METHODS

### 2.1 | Kidney Donor Outcomes Cohort (KDOC)

LKDs, their transplant recipients, and healthy controls at six kidney transplant programs in the United States (Arizona, Iowa, Maine, Massachusetts, New York, and Rhode Island) were enrolled in a prospective cohort study from September 2011 to November 2013. Cohort enrollment details have been described previously.<sup>9,10</sup> LKDs were told about the study after they were deemed medically suitable for donation, based on each program's eligibility criteria. LKDs completed questionnaires before surgery and at 1, 6, 12, and 24 months after donation. Transplant recipients and healthy controls completed questionnaires at similar times; however, only LKDs completed pain assessments during the first 2 months postdonation and, therefore, they are the sole focus of the current analysis. Site coordinators gathered medical and surgical data throughout the study and transmitted them via REDCap (Vanderbilt University) to the coordinating site. The institutional review boards at all sites approved the study, which was registered on ClinicalTrials.gov (NCT01427452).

### 2.2 | Pain management

Postoperative pain management approaches varied both within and between participating programs. Pain was not the primary a priori outcome for the larger KDOC study; thus, we did not plan to examine pain based on management strategy. Consequently, pain management was left to the discretion of individual donor surgeons in collaboration with LKDs. Most commonly, this included

patient-controlled analgesia with a narcotic agent plus acetaminophen for the first day or two, transition to oral narcotics plus acetaminophen until discharge, and then oral narcotics (7- to 10-day prescription) and acetaminophen, as needed, after discharge.

## 2.3 | Pain assessments

### 2.3.1 | Pain expectancy

One item from the Living Donation Expectancies Questionnaire (LDEQ)<sup>11</sup> was used to assess pain expectancy before donation: "As an organ donor, I expect to experience a great deal of pain and discomfort" (strongly disagree, disagree, neutral, agree, strongly agree). At 6, 12, and 24 months postdonation, LKDs responded to the same question with a change in verb tense to assess whether their pre-donation expectation was realized: "As an organ donor, I experienced a great deal of pain and discomfort". For this study, we examined responses to the pre-donation and 6-month postdonation questions.

### 2.3.2 | Donation-specific pain

Three pain measurements were obtained from LKDs at 10 time points: Postoperative day (POD) 1, 3, 7, 14, 21, 28, 35, 41, 49, and 56: (a) The Pain Rating Index consisted of 15 pain descriptors (11 sensory, 4 affective) from the Short-Form McGill Pain Questionnaire (SF-MPQ),<sup>12</sup> each rated for intensity (0 = none, 1 = mild, 2 = moderate, 3 = severe). (b) Present Pain Intensity was captured by asking LKDs to rate the intensity of pain at the moment of assessment, from 0 (no pain at all) to 10 (worst pain possible). If the participant reported a decimal value, we rounded up to the next integer value. (c) Overall Pain Intensity included one question at POD56 that asked about the intensity of the donation-related pain experience overall, not just at the present moment (0 = no pain, 1 = mild, 2 = discomforting, 3 = distressing, 4 = horrible, 5 = excruciating). For each measurement, LKDs were instructed to respond based only on their perceived pain from donation surgery. POD 1 measurement was captured during hospitalization, and all subsequent measurements were completed by phone.

## 2.4 | Predictors of postsurgical pain across time

Based on prior literature,<sup>3-6</sup> several predictors of postsurgical pain were examined. Sociodemographic variables included age, sex, race/ethnicity, marital status, employment, health insurance, and household income. Predonation characteristics included body mass index (BMI), systolic and diastolic pressures, smoking (any cigarette use in past year), opioid abuse history, affective disorder history, physical activity (moderate and vigorous), prescribed pain medications prior to surgery, pain expectancy, and pre-morbid bodily pain (predonation SF36 Health Survey Bodily Pain score<sup>13</sup>).

Peri- and postoperative variables included operative time, nephrectomy side, surgical approach, any complication related to donor nephrectomy, reoperation within 30 days of donor nephrectomy, hospitalization duration, and POD1 pain severity (not severe vs severe).

## 2.5 | Chronic postsurgical pain

Chronic postsurgical pain was operationalized as a Pain Rating Index >0 on POD56, which is consistent with the 2-month criterion used to define CPSP at time of study initiation.<sup>7,8</sup>

## 2.6 | Statistical analysis

Mean and standard deviation are reported for continuous data. Medians (and 1st and 3rd quartile values) are reported for skewed pain data. Counts and percentages are reported for categorical data. To accomplish our primary objective, to characterize and examine predictors between pre-, peri-, and postoperative variables and LKDs present pain intensity over time, we performed a generalized linear mixed model with a Poisson distribution to conduct a repeated-measure analysis so that all follow-up time points were utilized when available. These methods maximize power and efficiency in addition to producing estimates that incorporate all informative outcome data. To account for within-subject correlation, we used a temporal variance-covariance structure. This variance-covariance structure includes a time covariate, which enables the model to recognize that the time intervals differ within subject observations. Results are presented as adjusted ratio of means and 95% confidence intervals (Cis). For the secondary analysis, we examined the univariable associations between CPSP and the pre-, peri-, and postoperative variables noted previously, using logistic regression models. Results are presented as unadjusted odds ratios and 95% confidence intervals. Pain outcomes did not differ significantly by transplant program; thus, all analyses were conducted for the entire KDOC cohort. Cases with missing covariates were excluded from analysis. REDCap was used for data collection and management and R v 3.6.1 (R Development Core Team, 2019) was used for statistical analyses.

## 3 | RESULTS

### 3.1 | KDOC cohort characteristics

Sociodemographic and clinical characteristics of the KDOC sample (N = 193) have been described previously.<sup>9,10</sup> The majority of LKDs were female, white, employed, biologically related to the recipient, and had health insurance at surgery. Mean BMI was 27.0 ( $\pm 3.8$ ), 16% had a smoking history in the year preceding donation, and 23% had a mood disorder history. Eight (4%) LKDs were taking

prescribed pain medications prior to surgery. The majority underwent laparoscopic nephrectomy (97%) and had the left kidney removed (91%). Mean operative time was 183.0 ( $\pm 58.9$ ) minutes and mean hospital duration was 73.9 ( $\pm 23.4$ ) hours. The rate of surgical perioperative complications (17.1%) was comparable to published national data<sup>14</sup> and few LKDs underwent reoperation (2%) or re-hospitalization (4%).

### 3.2 | Pain expectancy

One hundred eighty-eight LKDs completed the LDEQ prior to surgery. In response to the item: "As an organ donor, I expect to experience a great deal of pain and discomfort," 22 (12%) strongly agreed, 68 (36%) agreed, 39 (21%) disagreed, 11 (6%) strongly disagreed, and 48 (25%) were neutral in their pain expectation. One hundred fifty-four LKDs completed both the predonation and 6-month LDEQ question. At 6 months after donation, 74 (48%) LKDs reported experiencing less postdonation pain/discomfort than they expected, 15 (10%) reported experiencing more pain/discomfort than they expected, and 65 (42%) reported that their predonation pain expectations were met following donation. LKDs who expected less pain/discomfort before donation were more likely to have those expectations met than those who expected a great deal of pain/discomfort before to donation (78% vs 32%,  $P < .001$ ).

### 3.3 | Donation-specific pain

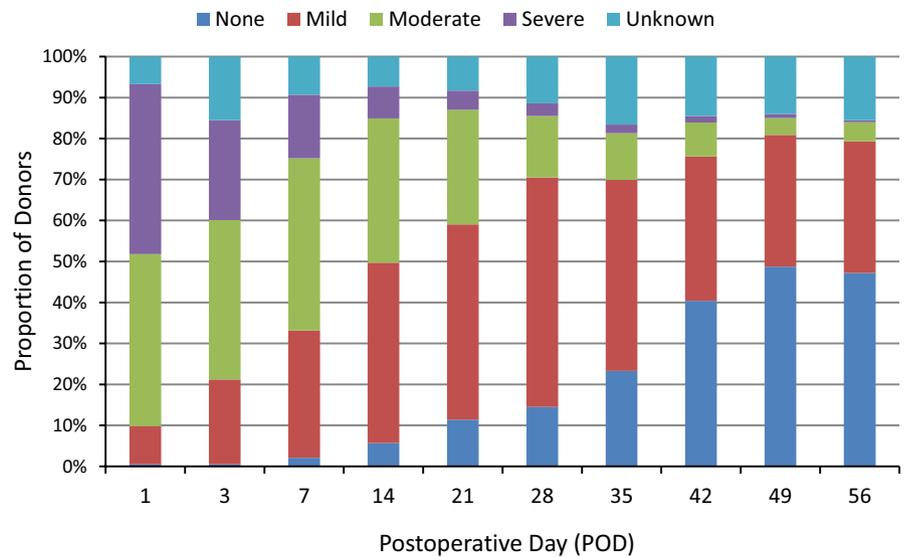
A total of 1702 postoperative pain assessments were completed, representing 88% of 1930 total assessments possible for this LKD cohort. Nearly half (n = 92, 48%) completed all 10 pain assessments; 167 (87%) completed  $\geq 80\%$  of assessments.

Figure 1 shows the percentage of LKDs with no pain and mild, moderate, and severe pain at each of the assessment time points based on the Pain Rating Index. The percentage of LKDs reporting no pain was as follows: POD7 (2.1%), POD14 (5.7%), POD21 (11.4%), POD28 (14.5%), POD35 (23.3%), POD42 (40.4%), POD49 (48.7%), and POD56 (47.2%). Seventy-two (37%) LKDs did not achieve total pain resolution by POD56.

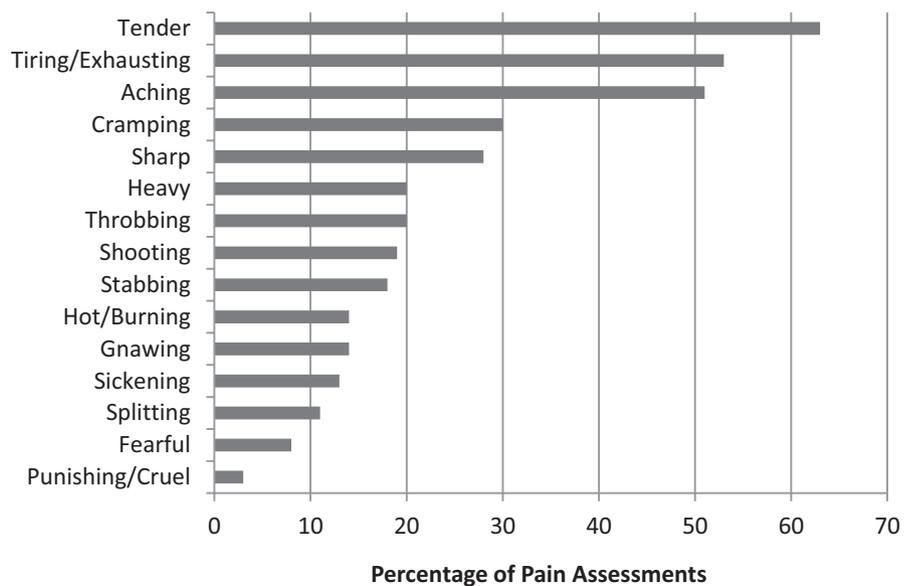
The two most common sensory descriptors at all time points were *Tender* and *Aching*, which were reported by a majority of LKDs through POD28 and which persisted for at least one-fifth of LKDs through POD56. Similarly, the most common affective pain descriptor was *Tiring or Exhausting*, reported by most LKDs through POD21. *Tender* (63%), *Tiring or Exhausting* (53%), and *Aching* (51%) were the only pain descriptors endorsed in at least half of all 1702 pain assessments completed during the study (Figure 2).

One hundred sixty-five LKDs described their Overall Pain Intensity, considering the entire donation experience, as: No Pain (n = 3, 2%), Mild (n = 37, 22%), Discomforting (n = 84, 51%), Distressing (n = 28, 17%), Horrible (n = 9, 6%), and Excruciating (n = 4, 2%). Nine and five of the 13 LKDs who reported their overall pain

**FIGURE 1** Percentage of living kidney donors with no pain and mild, moderate, and severe pain on the McGill Pain Questionnaire at each postoperative day (POD) pain assessment



**FIGURE 2** McGill Pain Questionnaire descriptors and the percentage of pain assessments (N = 1655) in which each descriptor was endorsed by living kidney donors



experience to be Horrible or Excruciating had CPSP and regretted their decision to donate, respectively.

### 3.4 | Predictors of donation-specific pain

Of the 193 LKDs in this cohort, 165 (85% of the cohort) had complete baseline data included in the generalized linear mixed model. In multivariable generalized linear mixed model analysis including pre-, peri-, and post-operative factors, the mean Present Pain Intensity score decreased at each pain assessment compared to the POD3 assessment. Of note, age and preoperative SF-36 Bodily Pain scores had nearly no effect on pain score across time (adjusted ratio of means [95% CI]: 1.00 [0.98, 1.02], 0.99 [0.97, 1.02], respectively), whereas those with a preoperative history of mood disorder had higher pain scores (adjusted ratio of means [95% CI]: 1.40 [0.99, 1.98]). Moreover, endorsement of “severe” pain on POD1 was associated with higher pain scores across time (adjusted ratio of means

[95% CI]: 1.47 [1.12, 1.93]). The mean pain score for LKDs who had an open nephrectomy was estimated to be 161% higher compared to those who underwent laparoscopic nephrectomy (adjusted ratio of means [95% CI]: 2.61 [1.03, 6.62]). The adjusted ratios and confidence intervals are reported in Table 1.

### 3.5 | CPSP incidence and correlates

Of the 179 LKDs who completed the POD56 pain assessment, 74 (74/179 = 41%; 72/193 = 37%) met our criteria for CPSP. Eleven LKDs reported moderate or severe pain at POD56, which represents 15% of those LKDs with any pain at POD56 and only 6% of the entire cohort. Those with CPSP (regardless of intensity level) reported more interference in work and other daily activities at the 1-month ( $P = .03$ ) and 6-month ( $P = .01$ ) assessments, missed more work days on average (33.1 vs 25.1,  $P = .04$ ), and were more likely to agree with the following statement: “I have returned to my previous job, but am

**TABLE 1** Multivariate predictors of Present Pain Intensity following live donor nephrectomy

| Variables   | Adjusted ratio of means (95% CI) |
|---|----------------------------------|
| Postoperative day (POD)   |                                  |
| 3 (reference)   | —                                |
| 7   | 0.70 (0.61, 0.82)                |
| 14  | 0.47 (0.39, 0.55)                |
| 21  | 0.40 (0.33, 0.48)                |
| 28  | 0.28 (0.23, 0.35)                |
| 35  | 0.18 (0.14, 0.23)                |
| 42  | 0.12 (0.09, 0.16)                |
| 49  | 0.08 (0.05, 0.11)                |
| 56  | 0.08 (0.05, 0.11)                |
| Age, y  | 1.01 (1.00, 1.02)                |
| Sex, female (vs male)   | 1.11 (0.84, 1.47)                |
| Race, White Non-Hispanic (vs non-white)   | 0.85 (0.61, 1.18)                |
| Marital Status, married/partnered (vs not married/partnered)  | 1.02 (0.78, 1.34)                |
| Work status, employed (vs unemployed)   | 1.26 (0.90, 1.76)                |
| Health insurance, yes (vs no)   | 1.55 (0.91, 2.65)                |
| Household income, ≥\$50 000 (vs <\$50 000)  | 0.83 (0.61, 1.11)                |
| Body mass index, 10 kg/m <sup>2</sup> increase  | 1.01 (0.71, 1.45)                |
| Systolic blood pressure, 10 mm Hg increase  | 0.89 (0.76, 1.05)                |
| Diastolic blood pressure, 10 mm Hg increase   | 1.16 (0.93, 1.44)                |
| Smoking history in past year, yes (vs no)   | 1.18 (0.79, 1.77)                |
| History of mood disorder, yes (vs no)   | 1.40 (0.99, 1.98)                |
| History of substance abuse, yes (vs no)   | 0.78 (0.41, 1.47)                |
| SF-36 Bodily Pain score   | 0.99 (0.97, 1.02)                |
| LDEQ expect great deal of pain and discomfort, agree/strongly agree (vs neutral/disagree/strongly disagree) | 1.24 (0.96, 1.61)                |
| Physical activity, h/wk   | 1.00 (0.97, 1.03)                |
| Muscle/strength training activity, days per week, 0 (vs ≥ 1)  | 0.85 (0.63, 1.14)                |
| Operative time, 10 min increase   | 1.02 (1.00, 1.05)                |
| Kidney removed, left (vs right)   | 0.85 (0.50, 1.45)                |
| Open nephrectomy (vs laparoscopic)  | 2.61 (1.03, 6.62)                |
| Complications related to donor nephrectomy, yes (vs no)   | 1.04 (0.76, 1.43)                |
| Reoperation, yes (vs no)  | 1.23 (0.42, 3.58)                |
| Hospital duration, h  | 1.00 (0.99, 1.01)                |
| POD1 Pain Rating Index, severe (vs not severe)  | 1.47 (1.12, 1.93)                |

Abbreviation: LDEQ, Living Donor Expectancies Questionnaire.

working at less than 100% capacity due to my donation surgery<sup>n</sup> (11.8% vs 1.0%,  $P = .01$ ). There was no significant association between CPSP and satisfaction with donation ( $P = .37$ ) or decision regret ( $P = .49$ ). In

**TABLE 2** Univariable associations of CPSP following live donor nephrectomy

| Variables   | Unadjusted odds ratio (95% CI) |
|---|--------------------------------|
| Age, y  | 1.01 (0.99, 1.04)              |
| Sex, female (vs male)   | 0.95 (0.52, 1.76)              |
| Race, White Non-Hispanic (vs minority)  | 1.20 (0.58, 2.58)              |
| Marital status, married/partnered (vs not married/partnered)  | 1.09 (0.60, 1.99)              |
| Work status, employed (vs unemployed)   | 0.84 (0.41, 1.74)              |
| Health insurance, yes (vs no)   | 1.45 (0.49, 4.84)              |
| Household income, ≥\$50,000 (vs <\$50,000)  | 0.95 (0.50, 1.79)              |
| Body mass index, 10 kg/m <sup>2</sup> increase  | 0.70 (0.31, 1.53)              |
| Systolic blood pressure, 10 mm Hg increase  | 0.88 (0.69, 1.12)              |
| Diastolic blood pressure, 10 mm Hg increase   | 0.95 (0.68, 1.33)              |
| Smoking history in past year, yes (vs no)   | 1.62 (0.71, 3.74)              |
| History of mood disorder, yes (vs no)   | 1.04 (0.51, 2.10)              |
| History of substance abuse, yes (vs no)   | 0.50 (0.11, 1.81)              |
| SF-36 bodily pain score   | 0.98 (0.93, 1.02)              |
| LDEQ expect great deal of pain and discomfort, agree/strongly agree (vs neutral/disagree/strongly disagree) | 1.73 (0.95, 3.19)              |
| Physical activity, hour per week  | 1.07 (1.01, 1.14)              |
| Muscle/strength training activity, days per week, 0 (vs ≥1)   | 0.52 (0.27, 0.98)              |
| Pre-operative pain medication, yes (vs no)  | 0.85 (0.17, 3.56)              |
| Operative time, 10 min increase   | 1.03 (0.98, 1.08)              |
| Kidney removed, left (vs right)   | 0.79 (0.27, 2.35)              |
| Open nephrectomy (vs laparoscopic)  | 4.39 (0.55, 89.81)             |
| Complications related to donor nephrectomy, yes (vs no)   | 1.27 (0.64, 2.49)              |
| Re-operation, yes (vs no)   | 4.39 (0.55, 89.81)             |
| Hospital duration, h  | 1.02 (1.01, 1.04)              |
| Pain rating index, severe (vs not severe)   | 1.50 (0.81, 2.81)              |
| POD1 present pain index   | 1.06 (0.92, 1.24)              |

Abbreviation: LDEQ, Living Donation Expectancies Questionnaire.

the univariable analysis (Table 2), the presence of CPSP was associated with more hours of moderate- to high-intensity physical activity per week predonation (odds ratio [95% CI]: 1.07 [1.01,1.14]), no muscle/strength training activity predonation (odds ratio [95% CI]: 0.52 [0.27,0.98]), and longer hospital admission (odds ratio [95% CI]: 1.02 [1.01,1.04]).

## 4 | DISCUSSION

In the first prospective, multicenter study to assess pain during the first 8 weeks following living kidney donation, the authors found

that predonation history of mood disorder early severe postoperative pain, and open nephrectomy were associated with higher pain scores across time and that 41% of donors still experienced some donation-related pain 8 weeks after surgery. Organ Procurement and Transplantation Network Policy 14.3 requires transplant centers to inform potential LKDs about the “temporary or permanent” risk of pain postdonation.<sup>15</sup> Indeed, LKDs want to know the intensity and duration of the pain they will experience following donation.<sup>2</sup> In addition, concern about the level of pain and discomfort following donation is a prominent reason some transplant candidates may not talk to others about living donation.<sup>16</sup> Perhaps reassuringly, we found that donation-related pain, while moderately to severely intense for many donors in the first week postdonation, lessens in intensity by POD14 for most LKDs. Nearly half of LKDs were pain-free 8 weeks after donation, which is certainly a favorable outcome of interest to potential LKDs.<sup>2</sup>

LKDs with a mood disorder history, those who underwent open nephrectomy, and those who experienced more pain in the immediate postoperative period had higher pain scores across time. Preexisting depression and anxiety are known risk factors for more pain following many different types of surgeries, including nephrectomy.<sup>17-20</sup> Indeed, some have found psychological factors to be more predictive of postoperative pain experience than the analgesic strategy used, particularly during the early recovery period.<sup>20</sup> Although studies have found higher pain intensity in those undergoing radical open vs laparoscopic nephrectomy,<sup>21,22</sup> others have shown no differences in pain scores and equal risk for developing chronic pain.<sup>23</sup> Considerable variations in pain measurement protocols (eg, how and when it was assessed) and differences in pain management strategies may account for these disparate findings. Nevertheless, it is clear that laparoscopic nephrectomy yields more tangible postoperative benefits for LKDs (eg, less pain, shorter length of stay, quicker return to functional status) and is now the preferred operative technique of most surgeons.<sup>24</sup> Considering these findings, programs should ensure effective management of anxiety and depression symptoms prior to donation and minimize early postoperative pain to reduce pain intensity over time.

Although persistent pain was mild for all but 11 LKDs in our study, we were surprised to find that 41% of LKDs were still experiencing some donation-related pain and met criteria for CPSP. Perhaps most noteworthy was the finding that those with CPSP, compared to those who had pain resolution by POD56, experienced more interference in work and other activities, missed more work after donation, and were more likely to be working at less than 100% capacity after donation. These associations between CPSP and functional outcomes warrant further investigation, as complete resolution of donation-related pain earlier in the postdonation period may facilitate a quicker return to work and thereby reduce the adverse financial impact of donation. The prevalence of CPSP in this prospective KDOC cohort is higher than that reported in retrospective studies of LKDs undergoing open donor nephrectomy (20.7%<sup>3</sup> and 33%<sup>5</sup>) or hand-assisted laparoscopic donor nephrectomy (24.6%).<sup>4</sup> In addition, Bruintjes et al<sup>6</sup> recently reported that only 5.7% of LKDs reported chronic pain. However,

these lower CPSP prevalence rates, relative to the KDOC cohort, may be due to retrospective study designs (most LKDs were surveyed several years after donation) and different pain assessments, some perhaps more sensitive than others. Differences in definition, duration, and assessment methodology also likely account for substantial variability in CPSP rates following general surgery.<sup>25,26</sup> Nevertheless, educational content relevant to pain experiences should include the possibility of mild pain for 2 months and potentially longer.

The paucity of data has made it challenging for providers to properly educate potential LKDs about donation-related pain and for donors to titrate their own pain expectations. Our LKDs—who were enrolled after donation evaluation and education—had variable expectations about pain—perhaps due to provider differences in describing anticipated pain during recovery, variable pain management protocols, prior surgical or trauma experiences of potential LKDs, online educational materials, testimonials from former donors, or other factors not assessed as part of our study. Nevertheless, study findings can be used to guide discussions about donation-related pain prevalence, severity, and timing following surgery.

The prevention, assessment, and management of high intensity and longer-term pain in the donor population warrant further investigation. All KDOC study centers used narcotic-based pain management protocols. More recently, however, enhanced recovery after surgery (ERAS) protocols have emerged and have been shown to reduce narcotic use, length of stay, and pain following donor nephrectomy,<sup>27,28</sup> as well as many other postoperative complications following intra-abdominal surgery.<sup>29</sup> Counterintuitively, however, we found that more intense exercise predonation was associated with higher likelihood of CPSP. Those with high levels of physical activity may be more hypersensitive to small changes in pain or discomfort than those who are more sedentary. The potential for ERAS, and predonation exercise specifically, to reduce CPSP rates postdonation is presently unknown.

We recommend that donation-related pain be assessed routinely by programs in the days, weeks, and months after donation. The SF36 is the most commonly used patient-reported outcome measure in LKD studies; however, data from the Bodily Pain scale are typically aggregated across all donors, perhaps obfuscating donation-related pain, particularly at mild levels, for some donors. In addition, although useful in assessing general pain intensity and interference in the past month, the Bodily Pain scale is not associated with or predictive of donation-specific pain. We recommend using more comprehensive pain measurement tools to query donation-related pain intensity, location, and interference in real time. The detection of CPSP, particularly if it is adversely impacting functional status, should trigger further assessment for possible underlying cause and development of a comprehensive management strategy in consultation with pain specialists.<sup>8</sup> Notably, integration of CPSP into the International Classification of Diseases, Eleventh Revision (ICD-11), to be implemented in January 2022, elevates its recognition as an important clinical construct, thus allowing for more refined analysis of its prevalence and evaluation of interventions to mitigate its functional impact postsurgery.<sup>30</sup>

Study strengths include its prospective design, the moderately large sample size from several transplant centers, use of standardized pain measurements, and the high rate of completed pain assessments. However, these strengths should be balanced with several important limitations. Any prior surgical history and the specific post-donation pain management approach for each LKD enrolled in the study, which may reasonably impact pain intensity and perception, were not captured. Similarly, we did not ask LKDs about their postdischarge narcotic use or other self-initiated pain management strategies, including over-the-counter analgesics and holistic approaches. Although we measured pain intensity and frequency, we did not assess the location of pain following donation or how it may have impacted their lives. We also did not conduct a clinical examination to confirm that the pain was directly attributable to donation. We did not measure other factors that may influence the postoperative pain experiences, such as early mobilization and nutrition. Pain assessments to describe pain overall across the donation experience (POD56) may be prone to recall bias, intensity of the most recent pain, and disproportionately influenced by peak intensity.<sup>31</sup> It is notable that we used a conservative definition of pain to meet CPSP criteria (ie, any donation-related pain at POD56), which may overestimate its prevalence. A new CPSP definition was proposed during the KDOC study, shifting the pain duration criterion from 2 to 3 months postsurgery.<sup>32</sup> Because our donation-specific pain protocol was developed to meet the original definition of 2 months duration, we were not able to determine how many LKDs met the new CPSP definition. Although it is likely that we would find a lower CPSP prevalence rate using this revised criterion, further study is needed to characterize CPSP following living donation in the context of this revised definition. How long donation-related pain persisted and whether there was any new-onset donation-related pain beyond POD56 also could not be determined in our study. Regardless, considering the great benefit accrued to transplant recipients and to society from the selfless act of living donation, any donation-related pain—regardless of its intensity—8 weeks postnephrectomy warrants our attention clinically and scientifically.

The foregoing limitations notwithstanding, study findings have potential implications for LKD education, surgical consent, postdonation care, and outcomes measurement. Pain is an outcome that should be discussed with potential LKDs and repeatedly assessed postdonation to ensure a complete resolution of donation-related pain in the weeks and months following surgery. We provide data that can be included in these predonation discussions, integrated into the surgical consent process, and considered in developing postdonation care protocols. Further research is needed to assess the effectiveness of strategies to mitigate pain intensity and duration following donation.

#### ACKNOWLEDGMENTS

This study was supported by Award No. R01DK085185 from the National Institute of Diabetes and Digestive and Kidney Diseases. The content is solely the responsibility of the authors and does not

necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health. The authors gratefully acknowledge the hard work and dedication of the study coordinators and others at the six KDOC transplant centers who assisted in the completion of this project: Aws Aljanabi, Jonathan Berkman, Tracy Brann, Rochelle Byrne, Lauren Finnigan, Krista Garrison, Ariel Hodara, Tun Jie, Scott Johnson, Nicole McGlynn, Maeve Moore, Matthew Paek, Henry Simpson, Carol Stuehm, Denny Tsai, and Carol Weintroub.

#### DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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**How to cite this article:** Fleishman A, Khwaja K, Schold JD, et al; the KDOC Study Group. Pain expectancy, prevalence, severity, and patterns following donor nephrectomy: Findings from the KDOC Study. *Am J Transplant*. 2020;20:2522-2529. <https://doi.org/10.1111/ajt.15861>