






The Value of Pain Sensitivity Questionnaire in Predicting Postoperative Pain in Living Kidney Donors: A Prospective Observational Study

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Purpose: This study aimed to investigate the value of the Pain Sensitivity Questionnaire (PSQ) for the prediction of postoperative pain and the relationship between pain sensitivity and postoperative pain in kidney donors undergoing living-related kidney transplantation.

Patients and Methods: A total of 148 kidney donors were selected and the preoperative pain sensitivity questionnaire was administered the day before surgery. Kidney donors were assigned to low PSQ group (PSQ < 6.5, n = 76) or high PSQ group (PSQ ≥ 6.5, n = 72). The primary endpoint was the number of patient-controlled analgesia (PCA). Other outcomes included: the incidence of acute pain, flurbiprofen axetil remediation rate, the incidence of chronic pain, neuropathic pain assessment scale (Douleur Neuropathique 4 Questions, DN4), visual analog scale (VAS) at rest after surgery as well as the correlation between PSQ and QST (Quantitative Sensory Testing).

Results: The low PSQ group had a significantly lower number of PCA than high PSQ group (P < 0.0001). The incidence of acute pain was 75% in low PSQ group and 100% in high PSQ group (P < 0.0001). Furthermore, flurbiprofen axetil remediation rate was lower in low PSQ group than that in high PSQ group (P = 0.042). The incidence of chronic pain was significantly lower in low PSQ group than in high PSQ group (6.6% vs 61.1%, P < 0.001). Moreover, DN4 was significantly lower in low PSQ group than that in high PSQ group (P < 0.001). The PSQ-mean was significantly negatively correlated with QST in kidney donors. VAS at rest for the low PSQ group were lower than those of the high PSQ group.

Conclusion: The PSQ was found to be associated with the intensity of postoperative pain and might be used to screen patients prior to living-kidney transplantation.

Keywords: pain, pain sensitivity, pain sensitivity questionnaire, kidney donor

Introduction

Pain is a subjective feeling, and it is related to situations of trauma or disease.¹ It is difficult to measure accurately because of its complex symptoms, duration, difficulty in treatment, and the possible pain pathway associated with it.² Living kidney donor surgery is generally an open surgery, with significant trauma and slow postoperative recovery, often requiring more opioid drugs.³ The pain sensitivity questionnaire (PSQ) is a self-assessment scale of pain sensitivity that was designed by Ruth Ruscheweyh et al.⁴ It aids in the assessment of the pain sensitivity of the participant, prediction of acute postoperative pain, and screening of individuals who are at a high risk of postoperative chronic pain.^{4,5} The evaluation effect of PSQ on pain sensitivity has been fully confirmed in various studies globally.⁶⁻⁹ Some studies have also found that PSQ applies to patients with chronic pain and that its correlation with pain sensitivity in healthy patients is significant.^{10,11}

Living kidney donor surgery usually requires a long operation time, which causes excessive trauma to both the kidney donors as well as the recipients.⁴ In addition, kidney donation may be associated with long-term disease and pain.^{12,13} Inadequate treatment of postoperative pain can reduce the patient's ability to participate in rehabilitation plans, leading to poor postoperative outcomes, and delaying patient recovery and discharge time, reducing quality of life and satisfaction, increasing resource consumption and medical costs. PSQ is a non-invasive method for measuring pain sensitivity. Measuring the pain sensitivity of kidney donors can help anesthesiologists enhance postoperative pain management.

It has not been reported whether PSQ can reflect the pain sensitivity of living kidney transplant donors who are healthy patients that undergo nephrectomy. Further, it has not been reported whether PSQ is consistent with the quantitative sensory testing (QST) of pain sensitivity and whether it can help predict postoperative pain levels. Therefore, this study aimed to evaluate the value of PSQ in predicting pain sensitivity and postoperative pain in living-related kidney transplant donors.

Methods

Participants

We performed a prospective observational clinical study. The study received ethical approval from the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Anhui Provincial Hospital). An informed consent was given by every patient and the study was registered on the China Clinical Trials Registry (Registration number: ChiCTR2200058704). We confirm that this study complies with the Declaration of Helsinki. Initially, 168 kidney donors who underwent elective living-related kidney transplantation between April 2022 and December 2022 in our hospital were included. We confirmed that all kidney donors signed and provided informed consent to donate their kidneys, along with confirmation that this consent was given voluntarily and under free will.

Inclusion criteria were as follows: (1) age, 40–80 years; (2) ASA class I–II; (3) no speech or communication impairment; (4) no history of chronic pain or long-term use of analgesic drugs.

Exclusion criteria: (1) postoperative delirium or other serious complications; (2) reoperation within 3 months; (3) postoperative admission to an intensive care unit (ICU); (4) loss of visit.

Outcomes

The primary endpoint was the number of patient-controlled analgesia (PCA). It is defined as the number of effective patient-controlled analgesia by kidney donors after surgery. Other outcomes included the incidence of acute pain, flurbiprofen axetil remediation rate, the incidence of chronic pain, neuropathic pain assessment scale (Douleur Neuropathique 4 Questions, DN4), VAS at rest after surgery and correlation between PSQ and QST (Quantitative Sensory Testing). Acute pain was defined as the pain after surgery that requires PCA for kidney donors. Chronic pain was defined as the presence of pain in the donor three months after surgery.

Anesthesia and Analgesia Protocol

Preoperative fasting for 8 h and water fasting for 6 h was routine and was ensured without preoperative medication. After admission, ECG, SpO₂, ABP, P_{ET}CO₂, and BIS were monitored. Further, 1–2mg/kg of intravenous propofol, 0.5ug/kg of sufentanil, and 0.2mg/kg of cis-atracurium bromide were administered to induce anesthesia. The I-gel mask was placed for mechanical ventilation to maintain P_{ET}CO₂ at 35–45 mmHg. 2.5mg/L, remifentanil TCI (Ce2.5–4ng/L), inhalation of 1–1.5% sevoflurane, BIS of 40–60. Moreover, continuous pumping of phenylephrine to maintain systolic blood pressure >140 mmHg, supplementation of crystalloids according to ABP, bleeding, and urine output was ensured. Ondansetron (8 mg) was used to prevent postoperative nausea and vomiting. After surgery, the analgesic pump was connected to perform patient-controlled analgesia (PCA). Sufentanil 2ug/kg was diluted to 100 mL with saline, and the first dose was 4 mL. The background infusion rate was 1 mL/h, the PCA dose was 4 mL, and the lock time was 20 min. If the patient complains of inadequate PCA analgesia and the VAS score is >4, accordingly, the nurse can press the PCA once (4mL) and record. In case of the pain was still not relieved, flurbiprofen axetil (50 mg) is administered intravenously for pain rescue. The anesthesiologist, surgeon, recovery room nurse or follow-up coordinator were blinded to the PSQ results.

considered that the patient's pain threshold value is 1024N. Record the QST value at five painful and non-painful times. The measurement time lasts 10 minutes. The arithmetic mean was determined as the patient's mechanical pain threshold.^{15,16}

The number of effective PCA and flurbiprofen axetil remedial analgesia rates in the kidney donors for 48 h after surgery were recorded, and VAS scores at rest on the first postoperative day (POD 1), third postoperative day (POD 3), and seventh postoperative day (POD 7) were determined. Three months after discharged, Neuropathic Pain Assessment Scale (Douleur Neuropathique 4 Questions, DN4) was recorded by telephone follow-up. The DN4 is composed of nine questions, total score 0–9, with > 4 scores as positive. The occurrence of chronic pain was recorded, and a score greater than 0 indicated the presence of chronic pain.

Statistical Analysis

SPSS 27.0 was used for analysis. Normal distribution data were expressed as mean \pm standard deviation (SD). Non-normally distributed data were expressed as the median and interquartile range (IQR). The χ^2 test was used to compare the count data. Pearson correlation analysis was used for normally distributed data, and Spearman correlation analysis was used for non-normally distributed data. $P < 0.05$ was considered statistically significant.

Results

Cohort Characteristics

A total of 148 relative living-related kidney transplant donors were included in this study and their clinical characteristics are shown in Table 1. Six cases did not meet the inclusion criteria, and two patients were re-operated within 3 months. Further, one patient was transferred to the ICU after surgery, five patients were excluded due to incomplete follow-up data, and six patients refused to be enrolled in the trial. Finally, 148 patients were enrolled, including 76 cases in PSQ < 6.5 group and 72 cases in the PSQ \geq 6.5 group (Figure 2).

Patient Features

The general data of the patients are shown in Table 1. Overall, the mean (SD) age was 58.7 \pm 9.3 years old, the mean (SD) BMI was 24.2 \pm 3.1 kg/cm², the average operation time was 128.4 \pm 25.1 minutes, the median (IQR) PSQ-mean was 6.4 (4.0–7.2) and the median (IQR) QST was 177.5 (87.5–315.2). The number of male subject was 70 (47.3%), 131 (88.5%)

Table 1 Patient Demographic and Operative Characteristics

	Overall (n=148)	Low PSQ Group (n=76)	High PSQ Group (n=72)	P value
Age(years)	58.7 \pm 9.3	59.4 \pm 8.1	57.9 \pm 10.4	0.316
Gender				0.522
Male	70(47.3%)	34(44.7%)	36(50.0%)	
Female	78(52.7%)	42(55.3%)	36(50.0%)	
BMI(kg/m ²)	24.2 \pm 3.1	24.3 \pm 3.1	24.1 \pm 3.1	0.356
ASA				0.387
I	104(70.3%)	51(67.1%)	53(73.6%)	
II	44(29.7%)	25(32.9%)	19(26.4%)	
Surgical site				0.512
Left	131(88.5%)	66(86.8%)	65(90.3%)	
Right	17(11.5%)	10(13.2%)	7(9.7%)	
Operation time(min)	128.4 \pm 25.1	125.1 \pm 13.1	132.0 \pm 16.9	0.095
PSQ-mean	6.4(4.0–7.2)	4.0(2.4–5.4)	7.2(7.0–7.9)	<0.001
QST	177.5(87.5–315.2)	301.5(196.5–477.7)	86.0(54.9–168.4)	<0.001

Notes: The variables are presented as mean \pm SD, median (IQR) or N (%). Low PSQ and High PSQ groups indicate PSQ score < 6.5 and PSQ score \geq 6.5.

Abbreviations: BMI, body mass index; PSQ, pain sensitivity questionnaire; QST, quantitative sensory test of pain sensitivity.

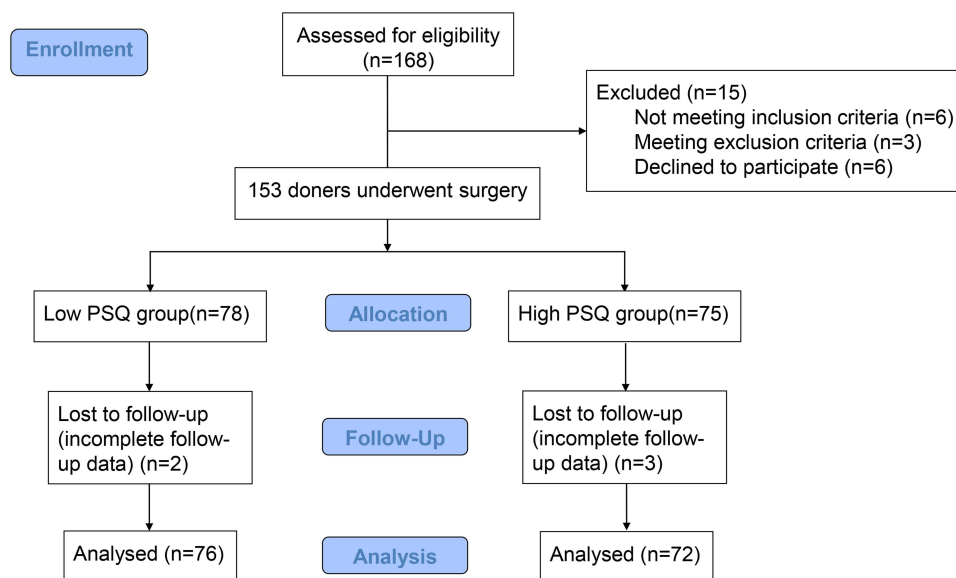


Figure 2 Flowchart of clinical procedures for the study.

patients underwent left nephrectomy, and 104 (70.3%) patients was ASA grade I (Table 1). Age, gender, BMI, surgical location, and time of surgery were not statistically significant in both groups ($P > 0.05$). The preoperative PSQ-mean was 4.0 (2.4–5.4) in the low PSQ group and 7.2 (7.0–7.9) in the high PSQ group, and the difference was statistically significant ($P < 0.0001$). The preoperative QST was 301.5 (196.5–477.7) in the low PSQ group and 86.0 (54.9–168.4) in the high PSQ group, and the difference was statistically significant ($P < 0.0001$).

Differences Between PSQ Groups

The number of PCA was significantly lower in the low PSQ group than that in the high PSQ group, and the difference was statistically significant ($P < 0.0001$). The incidence of acute pain was 75% in the low PSQ and 100% in the high PSQ group ($P < 0.0001$). The flurbiprofen axetil remediation rate was lower in the low PSQ group (21.1%) than that in the high PSQ group (36.1%) ($P = 0.042$). The incidence of chronic pain was significantly lower in the low PSQ group (6.6%) than that in the high PSQ group (61.1%) ($P < 0.001$) (Table 2).

As well as DN4, the low PSQ group was significantly lower than the high PSQ group, with a statistically significant difference ($P < 0.001$) (Table 2). VAS scores at rest on the first, third, and seventh day after donor surgery were statistically lower in the low PSQ group than that in the high PSQ group ($P < 0.001$; $P = 0.031$ and $P = 0.027$, respectively) (Table 3).

Correlation Between PSQ and QST

The PSQ-mean in the overall group of kidney donors was significantly negatively correlated with QST ($r = -0.88$, $P < 0.0001$) (Figure 3A). Similarly, the PSQ-mean in the low PSQ group of kidney donors was significantly negatively

Table 2 Postoperative Pain and Remediation Indicators

	Overall (n=148)	Low PSQ Group(n=76)	High PSQ Group (n=72)	P value
Number of PCA	5.0(2.3–8.0)	3.0(0.2–4.0)	8.0(6.0–10.0)	< 0.001
Acute pain	129(87.2%)	57(75.0%)	72(100%)	< 0.001
Flurbiprofen axetil remediation	40(27.0%)	16(21.1%)	26(36.1%)	0.042
Chronic pain	49(33.1%)	5(6.6%)	44(61.1%)	< 0.001
DN4	0(0–1.0)	0(0–0)	1.0(0–2.0)	< 0.001

Notes: The variables are presented as median (IQR) or N (%).

Abbreviations: PCA, Patient-controlled analgesia; DN4, Douleur Neuropathique 4 Questions.

Table 3 VAS on Postoperative Days 1, 3, and 7

Timepoint	Low PSQ Group	High PSQ Group	P value
POD 1	3.0(2.0–4.0)	5.0(4.0–6.0)	< 0.001
POD 3	1.0(0–1.0)	1.0(0–1.0)	0.031
POD 7	0(0–0.8)	0(0–1.0)	0.027

Notes: The variables are presented as median (IQR).

Abbreviations: VAS, Visual analog scale (VAS) score; POD, postoperative day.

correlated with QST ($r = -0.74$, $P < 0.0001$) (Figure 3B). The PSQ-mean in the high PSQ group of kidney donors was also significantly negatively correlated with QST ($r = -0.72$, $P < 0.0001$) (Figure 3C).

Discussion

In this prospective cohort study, the high PSQ group had more times of PCA compressions as compared to the low PSQ group. Moreover, the high PSQ group had higher postoperative rest pain on POD 1, 3, and 7. Further, it was noted that PSQ had a significant negative correlation with QST in living-related kidney transplant donors, indicating that PSQ could predict postoperative pain in living-related kidney transplant donors.

In our study, we found that PSQ could predict acute postoperative pain in living kidney donors, which corroborated with a previous clinical study.¹⁷ The difference between the two studies is that we adopted the median PSQ (6.5) for the grouping criteria while calculating their study's cutoff value of PSQ (5.0).

While considering kidney donation, candidates should be aware of personal long-term risks based on the demographics and any other risks that may be attributed to kidney donation, such as hypertension and other health outcomes as well as short-term and long-term pain.¹⁸ In this study, we aimed to find a simple, economical, and robust pain sensitivity measurement method for kidney donation operation. Notably, PSQ is not related to kidney donors' characteristics, such as age, gender, BMI, ASA, surgical site, or operation time.

In this study, we proved the effectiveness of PSQ in evaluating postoperative pain of kidney donors using various indicators of pain measurement, including the number of PCA, acute pain incidence, flurbiprofen remediation incidence, chronic pain incidence, and DN4. The values of all these indicators increased as the PSQ score increased. The number of PCA may increase as kidney donors experience pain. When PCA is not effective enough to relieve the pain, a second analgesic such as flurbiprofen could alleviate the effect of formalin-induced inflammatory pain.¹⁹ Flurbiprofen axetil enhances the analgesic effect of sufentanil, reduce inflammatory reactions, and alleviate visceral pain.²⁰ Therefore, flurbiprofen axetil was used as an analgesic remedy in this study. DN4, which measured neuropathic pain using an assessment scale with nine questions,²¹ was used to assess the degree of long-term pain 3 months after surgery. These

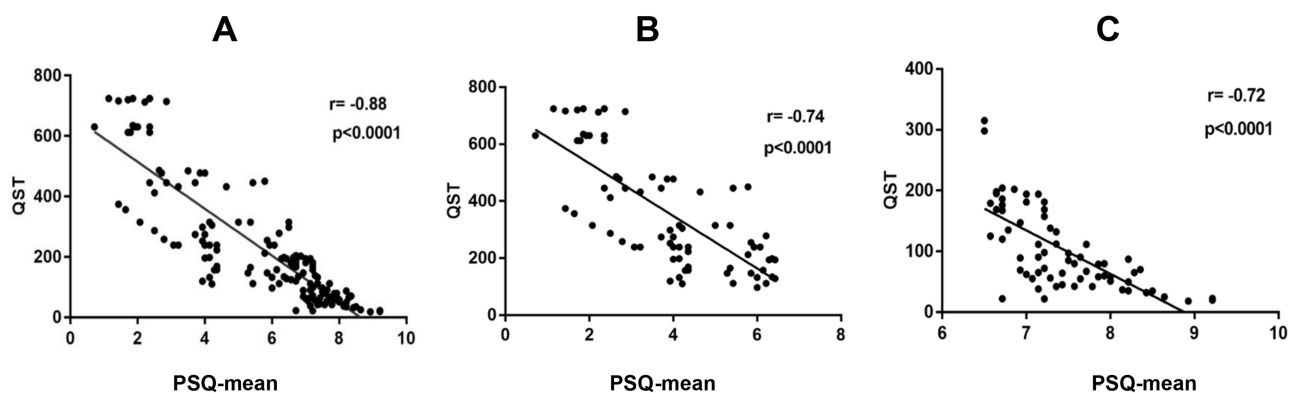


Figure 3 Illustration of the correlations between PSQ scores and QST. Linear regression lines are displayed. (A) The PSQ-mean in the overall group of kidney donors was significantly negatively correlated with QST ($r = -0.88$, $P < 0.0001$). (B) The PSQ-mean in the low PSQ group of kidney donors was significantly negatively correlated with QST ($r = -0.74$, $P < 0.0001$). (C) The PSQ-mean in the high PSQ group of kidney donors was also significantly negatively correlated with QST ($r = -0.72$, $P < 0.0001$).

results indicated that PSQ is not only applicable for the evaluation of acute pain after the kidney donor operation but also for the evaluation of chronic pain after the operation.

Visual analog scale (VAS) is widely used for pain assessment in China.²² A higher VAS score corresponds to more intense pain. The VAS score on postoperative day 1, 3 and 7 supported our findings that PSQ was a good tool for assessing the pain of living kidney donors. The difference in VAS scores between the low and high PSQ groups on postoperative days 3 and 7 was significant. This is consistent with previous study²³ that donors with high PSQ may have higher VAS after surgery.

Compared with the aforementioned pain sensitivity accessing tools, QST is a relatively objective indicator of the pain sensitivity accessing method. QST is not the routinely used in the management of living kidney donors. However, QST provides an objective numerical value. The results of this study show that PSQ and QST scores are highly correlated, both in the low and high PSQ groups. Similar findings have been observed in women with persistent pelvic pain.⁴ We further confirmed this relationship in kidney donors.

Notably, psychosomatic factors have a complex effect on pain. They may alter pain responses at the molecular and behavioral levels,²⁴ with anxiety and depression having the most significant impact on pain sensitivity. Some studies have shown that living kidney donors are more prone to anxiety and depression.^{25,26} Hermesdorf et al²⁷ compared the differences in sensitivity to stress pain and PSQ between depressed patients and healthy volunteers. They found that the pain thresholds for stress pain in depressed patients were reduced and were associated with related subjective factors. Anxiety is defined as the apprehensive anticipation of a potential threat. It is characterized by negative emotions, which result in increased attention to the environment and somatic concerns and divert attention from pain processing. Thus the pain threshold is lowered, leading to increased pain sensitivity.²⁸ Elevated pain sensitivity is a risk factor for the development of chronic pain,²⁹ leading to a high prevalence of pain in depressed patients. Furthermore, pain leads to depression³⁰ with pain and depression exacerbating each other. In this study, kidney donors with high PSQ are more likely to have higher pain sensitivity, indicating that kidney donors may be more prone to anxiety and depression. Based on the results of this study, PSQ questionnaire might be used in the future identify patients who were sensitive to postoperative pain in an early stage, so as to give timely intervention, including psychological counseling and preparation of analgesic drugs, to reduce the occurrence of anxiety and depression.

Kidney donors experienced postoperative acute pain from surgery that hindered recovery and created anxiety and fear in some.^{31,32} Furthermore, the incidence of chronic pain after donor nephrectomy was underestimated.³³ Given the voluntary and benefits of living-kidney transplantation, and complications caused by postoperative pain, anesthesiologists should be more aware of perioperative pain management strategies. Those involved with the preparation and post-operative management could use PSQ in predicting postoperative pain and guiding pain management strategies for living kidney donors in the future.

The advantage of this study is that it was designed as a prospective controlled study. There was no significant difference in the demographic and surgical site in kidney donors between the low and high PSQ groups. Another advantage is that the follow-up was completed by independent observers. Finally, the study used multiple pain assessment indicators to evaluate the effect of PSQ scores on accessing the pain sensitivity of kidney donors after surgery.

There are several limitations to our study. Firstly, the enrolled patients were categorized according to a total PSQ score of 6.5 which was determined based on the median total PSQ score, since there are no reference criteria for total PSQ scores for the low and high PSQ groups. Therefore, this value does not represent a cutoff for favorable outcomes after surgery for nephrectomy. Secondly, considering that too many questionnaires may affect the survey results of kidney donors, we did not collect anxiety and depression related data from kidney donors. Anxiety and depression may affect the pain sensitivity of kidney donors. Thirdly, this observational study cannot establish a causal relationship between PSQ and postoperative pain. Fourthly, the results of PSQ may be influenced by some potential confounding factors, such as educational level, this study did not perform such corrections although no significant relationship was found between PSQ and kidney donors' characteristics in this study. Finally, PSQ is a self-assessment questionnaire with strong subjectivity. The effect of PSQ in evaluating long-term postoperative pain in kidney donors or any surgical patients suffering from severe trauma requires further prospective cohort studies in large samples. Furthermore, future

directions require evaluating the long-term impact of PSQ on pain management outcomes and exploring its utility in different surgical populations.

Conclusions

The PSQ was found to be associated with the intensity of postoperative pain and might be used to screen patients prior to living-kidney transplantation.

Data Sharing Statement

The data presented in this study are available on reasonable request from the corresponding author.

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Disclosure

The authors report no conflicts of interest in this work.

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