

CLINICAL RESEARCH

# The effects of preoperative anxiety on anesthetic recovery and postoperative pain in patients undergoing donor nephrectomy



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## KEYWORDS

Anesthesia recovery period;  
Anxiety;  
Living donors;  
Postoperative pain;  
Kidney transplantation

## Abstract

**Background and objectives:** It is suggested that 38-45% of patients experience preoperative anxiety. We observe that patients undergoing living donor nephrectomy suffer from anxiety. Preoperative anxiety may complicate a patient's recovery from anesthesia and postoperative pain control. This study investigates the preoperative anxiety rate and its effect on anesthetic recovery and postoperative pain in patients undergoing donor nephrectomy.

**Methods:** Forty-eight individuals undergoing living-related renal donor nephrectomy were included in this analytic prospective observational cohort study. Their preoperative anxiety was measured with the STAI-I and STAI-II inventories. The relationships between anxiety scores with data regarding demographics, recovery from anesthesia, and postoperative pain scores were investigated.

**Results:** The findings were remarkable in that the anxiety scores of living renal donors were significantly correlated with their recovery variables, which are spontaneous respiration time, sufficient respiration time, extubation time, and PACU discharge time ( $p < 0.01$ ). Anxiety scores were significantly positively correlated with the pain scores of the 30th minute, 1st, 2nd, 4th, 8th, 12th, 24th hours, and the total amounts of analgesic administered in 24 hours ( $p < 0.05$ ). A significantly negative correlation was also determined between anxiety scores and patients' satisfaction.

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**PALAVRAS-CHAVE**

Período de recuperação da anestesia;  
Ansiedade;  
Doadores vivos;  
Dor pós-operatória;  
Transplante renal

**Conclusion:** Our study showed that patients undergoing living-related donor nephrectomy with high anxiety levels had late recovery times and high postoperative pain scores. Thus, determining those patients with high preoperative anxiety level is crucial to providing patients with satisfactory emerging from anesthesia and the control of their postoperative pain during donor nephrectomy.

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### Efeitos da ansiedade pré-operatória na recuperação anestésica e na dor pós-operatória em pacientes submetidos a nefrectomia para doação

**Resumo**

**Justificativa e objetivos:** Estima-se que 38-45% dos pacientes apresentem ansiedade pré-operatória. Observamos que doadores vivos submetidos à nefrectomia para doação apresentam ansiedade. A ansiedade pré-operatória pode complicar a recuperação anestésica e controle pós-operatório de dor do paciente. O presente estudo mediu as taxas de ansiedade no pré-operatório e seus efeitos na recuperação anestésica e dor pós-operatória em pacientes doadores submetidos a nefrectomia.

**Método:** Quarenta e oito doadores vivos submetidos à nefrectomia para doação de rim foram incluídos neste estudo de coorte prospectivo observacional. A ansiedade pré-operatória foi medida usando os inventários IDATE-I e IDATE-II. As relações entre os escores de ansiedade e dados relacionados a demografia, recuperação da anestesia e escores de dor no pós-operatório foram estudadas.

**Resultados:** Os achados foram notáveis porque os escores de ansiedade de doadores renais vivos se correlacionaram de maneira significativa com as variáveis de recuperação, a saber tempo para respiração espontânea, tempo para respiração adequada, tempo para extubação e tempo para alta da RPA ( $p < 0,01$ ). Os escores de ansiedade apresentaram correlação significativamente positiva com os escores de dor do 30º minuto e horas 1, 2, 4, 8, 12 e 24, e a quantidade total de analgésicos administrada nas 24 horas ( $p < 0,05$ ). Foi observada também correlação significativamente negativa entre os escores de ansiedade e satisfação dos pacientes.

**Conclusão:** Nosso estudo mostrou que doadores vivos submetidos à nefrectomia para doação com altos níveis de ansiedade apresentaram tempos de recuperação tardios e altos escores de dor no pós-operatório. Assim, a identificação dos pacientes com alto nível de ansiedade no pré-operatório é crucial para propiciar recuperação da anestesia e controle da dor no pós-operatório satisfatórios durante a nefrectomia para doação de órgão.

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**Introduction**

For patients with end-stage kidney failure, kidney transplant is the most effective treatment in terms of quality of life and longevity. Living donor nephrectomy is a surgical procedure to obtain a healthy kidney for transplant into a recipient with end-stage kidney disease. The procedure offers excellent graft survival rates.<sup>1</sup> Today, of all kidney transplants performed, 20% to 25% come from living donors. Before surgery, each of these donors is evaluated at a transplant council with a psychiatrist and a psychologist. Although agreeing to be kidney donors, it appears that some of these people have anxieties or other mental health issues such as concern and depression during preoperative evaluation.

Donor candidates may feel under emotional pressure arising from social expectations or health (their own or the recipient's) in the future.<sup>2-5</sup>

Preoperative anxiety is a state of unease and restlessness related to poor expectations or lack of knowledge about the procedures one is about to experience, such as hospitalization, anesthesia, and surgery. A number of studies have examined the link between preoperative anxiety and postoperative pain.<sup>6-11</sup> People undergoing donor nephrectomy constitute a specific group because they are to undergo an operation even though they have no specific health problem. There is a paucity of trials revealing the effects of preoperative anxiety on anesthetic recovery and postoperative pain in patients undergoing donor nephrectomy. In this study

we hypothesize that increased levels of preoperative anxiety disrupts the recovery from anesthesia and the control of postoperative pain.

## Methods

Upon approval by the Ethics Committee of the Faculty of Medicine, Ege University (n° 14–5.1/5), individuals who would undergo donor nephrectomy were prospectively included in the study between January 1, 2015 and December 31, 2015. All patients had renal transplant council approval for donor nephrectomy. Patients were told about the surgical and anesthetic procedure, perioperative events that were likely to occur, the State Trait Anxiety Inventory (STAI) I and II tests, how to use the intravenous Patient-Controlled Analgesia (PCA) pump (Abbott Pain Management Provider, USA), and were briefed on the Visual Analogous Scale (VAS, 0 no pain to 10 worst pain). After the patients were thoroughly informed about the study, their informed consent was obtained.

Fifty-three consequent patients were examined for our study. Of these, 48 who agreed to participate in the study and who met the inclusion criteria were studied. Inclusion criteria were their agreement to participate in the study and being aged between 18 and 60 years. Patients with delayed surgery, chronic pain, a history of allergy to any drug that could be used in the perioperative period, with psychiatric disorders and using any antidepressant, opioids, or anxiolytic were excluded. These candidates for donor nephrectomy were considered as patients in the study. On the day before surgery, the anxiety level of each patient was measured using the STAI-I (for state anxiety) and STAI-II (for trait anxiety) scales in the organ transplantation ward. Each scale contains 20 questions and scores are ranged from 20 to 80. Two anesthesiologists were on duty: one to obtain the STAI-I and II scores, the second to perform the anesthesia procedure and collect postoperative data. This second anesthesiologist was blinded to the patient's STAI-I and II scores.

## Surgical procedure

All patients were operated on with open technique at lateral position, with a lateral incision made on the kidney side.

## Anesthetic approach

As a standard institutional approach, after 16–18G venous cannula insertion, standard ASA monitoring as Electrocardiography (ECG), peripheral oxygen saturation (SpO<sub>2</sub>), and non-invasive blood pressure were carried out, patients were given inhalational-based general anesthesia with tracheal intubation. Anesthesia was induced with the administration of propofol at 2 mg.kg<sup>-1</sup>, fentanyl at 1–2 μg.kg<sup>-1</sup> and rocuronium at 0.6 mg.kg<sup>-1</sup>, and maintained with isoflurane of 0.8–1.2% in 40% FiO<sub>2</sub> and remifentanyl infusion of 0.25–1 μg.kg<sup>-1</sup>.min<sup>-1</sup> and rocuronium boluses of 0.15 mg.kg<sup>-1</sup>, when necessary. The anesthesiologist applying the anesthesia was blinded to the STAI scores of the

patients. After the anesthesia began, invasive radial arterial pressure was used for close monitoring of the blood pressure. No patient had neuraxial anesthesia/analgesia or central venous catheterization. Postoperative pain control procedure was initiated by an administration of 0.1 mg.kg<sup>-1</sup> intramuscular morphine when estimated time to the end of operation was 30 minutes. Neuromuscular block was reversed with 0.5 mg atropine and 0.04 mg.kg<sup>-1</sup> neostigmine.

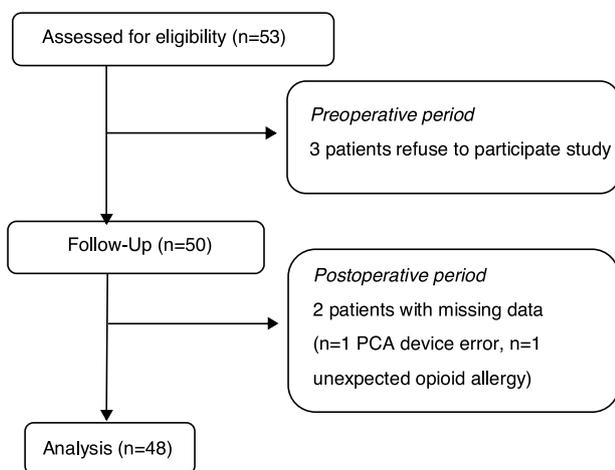
Variables of demographics, education status, smoking, previous surgery, chronic pain, kinship with the recipient, anxiety scores (STAI-I and II), duration of the surgery, anesthesia and recovery were recorded. After discontinuation of the isoflurane and remifentanyl infusion, time to first spontaneous breath was accepted as spontaneous respiration time, time to maintain respiration rate  $\geq$  8 min or E<sub>T</sub>CO<sub>2</sub> at lower than 50 mmHg as sufficient respiration time, time to extubation as extubation time, and time to the Modified Aldrete Score (MAS)  $\geq$  9 as Post Anesthesia Care Unit (PACU) discharge time.

Postoperative pain control was maintained by using i.v. PCA regimen with a morphine bolus of 0.02 mg.kg<sup>-1</sup> and a lockout time of 15 minutes. An additional 2 mg i.v. morphine was administered to the patients if their Visual Analog Scale (VAS)  $\geq$  4. If no effective analgesia was obtained within 15 minutes, 1 g i.v. paracetamol was added as a rescue analgesic.

The VAS values, total demand and delivery counts for boluses via PCA, the total amount of morphine administered, and additional analgesic requirements were recorded at the postoperative 30<sup>th</sup> minute and the 1<sup>st</sup>, 2<sup>nd</sup>, 4<sup>th</sup>, 8<sup>th</sup>, 12<sup>th</sup>, and 24<sup>th</sup> hours. On the second postoperative day (48<sup>th</sup> hour), the level of satisfaction was evaluated with a 5 point patient satisfaction scale (very dissatisfied 1, very satisfied 5).

## Statistical analysis

Since there is no other study similar to ours in the literature, the sample size was evaluated according to the correlations between the STAI-I and anesthesia recovery variables and postoperative pain (VAS) parameters in an interim analysis, and was based on the correlation between STAI-I and spontaneous respiration time with lower correlation coefficient. A sample size of 42 (studied patients during this time) achieved a power of 81% to detect a correlation of 0.42 between the parameters selected using a two-sided hypothesis test with a significance level of 0.05. Forty-eight patients at the end of the study were included for statistical evaluation. The descriptive statistics of the data were defined as the mean  $\pm$  standard deviation, minimum and maximum, median, and ratio (%) where appropriate. The distribution of variables was tested with the Kolmogorov-Smirnov Test. The relationship between STAI scores (I–II) and numerical variables were evaluated with Pearson's and Spearman's correlation coefficient tests. The significant difference between groups for normally distributed data was tested with Student's *t*-test or ANOVA test. Statistical analysis was performed by the SPSS program (Statistical Package for Social Sciences, version 21.0, IBM Corp, Armonk, NY).



**Figure 1** Flow chart.

Statistical significance was interpreted when p-values were smaller than 0.05.

## Results

Forty-eight patients aged between 18 and 60 years were included in our study, while 5 of them were excluded. The reasons for exclusion are shown in Fig. 1.

### Demographic characteristics and preoperative anxiety

During the preoperative period, mean STAI-I and STAI-II scores were calculated to be  $39.8 \pm 1.1$  and  $45.2 \pm 0.9$ , respectively. There were no statistically significant correlations between STAI (I–II) scores and preoperative features (age, weight, height, gender, ASA status, smoking, previous surgery, chronic pain, degree of kinship with the recipient, and educational status) (Table 1).

### Anesthetic recovery

Statistically significant correlations were found between STAI-I scores with spontaneous respiration times ( $r=0.47$ ,  $p<0.01$ ), adequate respiration times ( $r=0.56$ ,  $p<0.01$ ), extubation times ( $r=0.67$ ,  $p<0.01$ ), and PACU discharge times ( $r=0.67$ ,  $p<0.01$ ), while STAI-II scores were significantly correlated only with extubation times ( $r=0.32$ ,  $p<0.05$ ) (Table 2).

### Postoperative period

STAI-I and STAI-II scores were found to be significantly correlated with VAS scores at the 30<sup>th</sup> minute to 24<sup>th</sup> hour ( $p<0.05$ ) (Table 3). The number of analgesic Demand (DEM) and Delivery (DEL) dosings via IV PCA is presented in Table 4. STAI-I and STAI-II scores were found to be significantly correlated with DEM and DEL counts at all time points ( $p<0.05$ , data not shown). The average morphine consumption in 24 hours was  $42 \pm 13$  mg. Morphine consumptions were significantly correlated with STAI-I and II scores as well with

$r=0.45$ ,  $p=0.001$  for STAI-I and  $r=0.53$ ,  $p<0.001$  for STAI-II, respectively.

All patients required rescue analgesics from the 30<sup>th</sup> minute, decreasing over time. STAI-I were significantly correlated with the number of patients requiring additional analgesic at the 1<sup>st</sup> to 8<sup>th</sup> hours, while STAI-II were significantly correlated at the 2<sup>nd</sup> and 4<sup>th</sup> hours postoperatively (Table 5,  $p<0.05$ ). A significant negative correlation was found between STAI-I and STAI-II scores with patient satisfaction levels ( $r=-0.366$ ,  $p=0.01$  for STAI-I and  $r=-0.29$ ,  $p=0.04$  for STAI-II, respectively).

## Discussion

In this study, patients undergoing living-related donor nephrectomy with high anxiety levels had late recovery times and high postoperative pain scores. Given the organ scarcity, live organ donation is increasingly considered a viable alternative for kidney and liver transplantation. Because these healthy individuals face a number of medical, psychosocial, or unknown risks, they might have anxiety before or after the surgery.<sup>12</sup> The authors have presented that depression scores decreased significantly after donation, but anxiety scores remained stable. This study showed that living renal donors have moderate anxiety with a mean STAI-I score of 39.8 and high anxiety with a mean STAI-II score of 45.2. STAI scores ranging between 20 and 80 may also be classified as “no or low anxiety” (20–37), “moderate anxiety” (38–44) and “high anxiety” (45–80).

Today, anxiety can be measured using different methods. STAI is widely used to examine preoperative anxiety and is regarded as the gold standard in anesthesia during various surgeries. The effect of personal traits on anxiety is not certain; conflicting results exist from studies that have evaluated patient characteristics and anxiety. The variable relationships between a patient’s anxiety level and the type of surgery, anesthesia, age, gender, ASA scores and education level have been determined in different studies.<sup>12–17</sup> Domar et al. found a mean STAI score of 45 in 523 patients, of which most (57%) consisted of gynecological patients.<sup>13</sup> Ali et al. found the preoperative anxiety rate to be 38% in laparoscopic cholecystectomy patients, and emphasized that not only the type of surgery but also the anesthesia is a major reason for anxiety.<sup>14</sup> Female gender and age may have an effect on preoperative anxiety.<sup>15</sup> Preoperative anxiety has been found to be higher in women than in men.<sup>16</sup> Elderly patients had lower preoperative anxiety levels, though age had no effect on the level of anxiety in other studies.<sup>14,16,18</sup> Female gender, older age, and low ASA score was correlated with a higher preoperative anxiety before spinal anesthesia.<sup>19</sup> ASA score was a determining factor for preoperative anxiety.<sup>18,20</sup> An ASA score over III and the complexity of the operation were shown to have significant effects on preoperative anxiety.<sup>21</sup> The ASA scale evaluates the physical status of the patient, while STAI evaluate the patient’s instantaneous and persistent anxiety levels. It might be expected that a severe patient with a higher ASA score with comorbidities should have a higher anxiety level. There are also various data regarding the relationship between education level and anxiety. While some studies suggest that a higher level of education is accompanied by a

**Table 1** Preoperative and intraoperative variables.

		STAI-I score	STAI-II score	
Age (years)		48 ± 11		
Weight (kg)		75 ± 15		
Height (cm)		165 ± 9		
Duration of anesthesia (min)		186 ± 26		
Duration of surgery (min)		165 ± 24		
Gender	F	24	38 ± 7	44 ± 7
	M	24	42 ± 8	47 ± 7
ASA status	I	30	39 ± 6	44 ± 7
	II	18	40 ± 10	47 ± 6
Smoking	No	27	41 ± 6	46 ± 6
	Ex	3	31 ± 18	47 ± 9
	Yes	18	40 ± 6	44 ± 8
Previous surgery	No	25	39 ± 8	45 ± 8
	Yes	23	41 ± 6	46 ± 5
Chronic pain	No	35	39 ± 8	45 ± 7
	Yes	13	42 ± 6	45 ± 6
Kinship degree	First	43	40 ± 8	45 ± 7
	Second	5	41 ± 3	44 ± 8
Educational status	Primary school	32	40 ± 8	45 ± 6
	Secondary school	4	37 ± 1	39 ± 8
	High school	6	38 ± 4	47 ± 6
	University	6	42 ± 7	46 ± 9
Overall		48	40 ± 1	45 ± 1

The data shown are the number of patients or mean ± SD.

STAI, State-Trait Anxiety Inventory; F, Female; M, Male; ASA, American Society of Anesthesiologists.

**Table 2** The correlation between recovery variables and STAI scores.

	Mean ± SD	STAI-I		STAI-II	
		r	p	r	p
Spontaneous respiration time (min)	4.0 ± 0.8	0.474	0.001	0.251	0.085
Adequate respiration time (min)	6.2 ± 1.2	0.561	<0.001	0.230	0.116
Extubation time (min)	8.3 ± 1.5	0.677	<0.001	0.320	0.026
PACU discharge time (min)	24.8 ± 5.6	0.673	<0.001	0.166	0.259

STAI, State-Trait Anxiety Inventory; PACU, Post-Anesthesia Care Unit.

**Table 3** The relationships between VAS scores and STAI scores.

Time points	VAS	STAI-I		STAI-II	
		r	p	r	p
30 <sup>th</sup> min	7.3 ± 1.1	0.501	<0.001	0.297	0.041
1 <sup>st</sup> hour	5.9 ± 0.6	0.511	<0.001	0.422	0.003
2 <sup>nd</sup> hour	4.6 ± 1.4	0.649	<0.001	0.460	0.001
4 <sup>th</sup> hour	3.3 ± 1	0.620	<0.001	0.374	0.009
8 <sup>th</sup> hour	2.5 ± 0.7	0.560	<0.001	0.381	0.008
12 <sup>th</sup> hour	1.8 ± 0.6	0.397	0.005	0.356	0.013
24 <sup>th</sup> hour	1.3 ± 0.6	0.504	<0.001	0.564	<0.001

VAS presented as mean ± SD.

VAS, Visual Analog Scale; STAI, State-Trait Anxiety Inventory.

higher level of anxiety, others indicate the level of education does not represent a risk factor for anxiety.<sup>15,20</sup> Preoperative anxiety can influence the intensity of postoperative pain and

anesthesia and analgesia requirements. In certain types of surgery, anxiety may even increase postoperative morbidity and mortality.<sup>22</sup> Studies investigating renal transplant

**Table 4** Average DEM and DEL counts at time points (mean  $\pm$  SD).

	30 <sup>th</sup> min	1 <sup>st</sup> hour	2 <sup>nd</sup> hour	4 <sup>th</sup> hour	8 <sup>th</sup> hour	12 <sup>th</sup> hour	24 <sup>th</sup> hour
DEL	1.3 $\pm$ 0.4	2.8 $\pm$ 0.7	5.1 $\pm$ 1.4	8.6 $\pm$ 2.6	14.4 $\pm$ 4.6	19 $\pm$ 5.8	24.3 $\pm$ 6.4
DEM	3.9 $\pm$ 1.8	8 $\pm$ 4.1	13.5 $\pm$ 7.4	19.8 $\pm$ 9.8	28.1 $\pm$ 12.5	35 $\pm$ 15.4	42.5 $\pm$ 17.7

DEM, number of analgesic demand dosings via IV PCA; DEL, number of analgesic deliver dosings via IV PCA.

**Table 5** Additional analgesic requirements at time points.

	30 <sup>th</sup> min	1 <sup>st</sup> hour	2 <sup>nd</sup> hour	4 <sup>th</sup> hour	8 <sup>th</sup> hour	12 <sup>th</sup> hour	24 <sup>th</sup> hour
Number of patients (%)	48 (100)	44 (91.6)	32 (66.6)	16 (33.3)	2 (4.1)	0	0

donors' anxiety levels and their effect on postoperative recovery and pain are scarce. In our study, demographics, ASA score, smoking, previous surgery, chronic pain, kinship and education status of the patients do not have an effect on preoperative anxiety. Although the live kidney transplantation program allows the selection of better donors – at least in demographics, ASA, and comorbidities – and the donors willingly undergo the surgery, they still have moderate to high anxiety levels. Perhaps donor nephrectomy surgery leads to the same levels of preoperative anxiety, regardless of the factors noted above.

Very few studies have attempted to explore the effect of the anxiety level on the recovery from anesthesia. The extubation time and PACU discharge time in patients with high anxiety levels were found to be significantly longer than in patients with low anxiety levels, concluding that a high level of anxiety has a negative effect on the recovery from anesthesia.<sup>14</sup> Preoperative anxiety delayed recovery from anesthesia in elective arthroplasty.<sup>23</sup> It was clearly demonstrated in our study that spontaneous respiration time, adequate respiration time, extubation time, and PACU discharge time all had a positive correlation with the state anxiety score. Only the extubation time was affected by the trait anxiety score. A subtle difference exists between STAI-I and STAI-II to evaluate the effects of preoperative anxiety on recovery variables. In our opinion, delayed recovery variables determined by STAI-I might be from the release of the neuroendocrine mediators and their effects on the central nervous system, because STAI-I measures state anxiety level against the subjective fear felt by the patient, associated with the autonomic nervous system. STAI-II generally determines how the individual tends to experience anxiety, regardless of the individual's condition and circumstances. The trait anxiety measure in the donor nephrectomy patients was only correlated with extubation time.

Open nephrectomy is also associated with a significant degree of acute pain and will require opioid analgesia if regional analgesia is omitted or unsuccessful.<sup>24</sup> Patients may experience a relatively strong acute postoperative pain following open donor nephrectomy due to both a wide surgical incision and an extreme position. No doubt an epidural analgesia is important and provides the most effective analgesia; however, keeping the catheter in place is difficult due to its proximity to the surgical field when using the open nephrec-

tomy technique. Therefore, we did not insert an epidural catheter. In the conditions of epidural analgesia use, different results may be obtainable.

Some studies showed that patients with high preoperative anxiety levels have high levels of postoperative pain.<sup>8–10</sup> In other studies, however, no significant correlation was found between anxiety and pain.<sup>11</sup> It appears that anxiety level is the determinant factor of postoperative pain in gastrointestinal, obstetric and gynecological surgery and in increased analgesic requirement.<sup>6,14,25</sup> There were significant positive correlations between postoperative VAS scores both with state and trait anxiety scores in our study. All the patients also required rescue analgesics from the 30<sup>th</sup> minute, which decreased over time. STAI-I significantly correlated with the number of patients requiring an additional analgesic at all postoperative time points, while STAI-II were significantly correlated at the 2<sup>nd</sup> and 4<sup>th</sup> hours. There was a distinction between state and trait anxiety scores when determining additional analgesic requirements. Additional analgesic demand appears to be mostly related with the state anxiety level, however, both STAI-I and STAI-II scores correlated significantly negatively with patient satisfaction levels.

Although it is not within the scope of the present work (and which is covered in the second study), it is possible to say that the neuroendocrine stress response from anxiety may affect the renal donor graft function after transplantation in the recipient. The control of preoperative anxiety may also be important in this respect.

This study has a few limitations. First, the study reflects an experience only at one center. It may be possible to obtain different results under different institutional conditions where different anesthesia, surgical, and patient care protocols are applied. Second, the lack of standard neuromuscular monitoring for all patients and the use of rocuronium and neostigmine to antagonize it with clinical criteria. None of the patients were concerned about the residual neuromuscular blockade with the dose of neostigmine used in the study. In addition, we did not examine the anesthetic consumption. Patients with high anxiety levels are likely to require more anesthesia, and therefore have a delay in recovery from anesthesia. Third, although the study was powered to detect a difference in the spontaneous respiration time, it may not have had sufficient power to detect differences in other outcomes.

## Conclusion

This study indicates that increased preoperative anxiety levels disrupt the recovery from anesthesia, the control of postoperative pain and patient satisfaction. Given the effects of the high levels of anxiety in patients undergoing donor nephrectomy, an anesthesia and postoperative analgesia plan should be designed for lowering the patient's preoperative anxiety. Decreased state and trait anxiety levels in renal donor candidates may contribute to the satisfactory emerging from anesthesia and to control their postoperative pain and satisfaction. Further and larger studies are needed to test these findings.

## Conflicts of interest

The authors declare no conflicts of interest.

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