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Original Scientific Paper

EFFECTS OF PREOPERATIVE ANXIETY, DEPRESSION AND PAIN ON QUALITY OF POSTOPERATIVE RECOVERY AND ACUTE POSTOPERATIVE PAIN AFTER RADICAL PROSTATECTOMY: A PROSPECTIVE OBSERVATIONAL STUDY

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SUMMARY – Patients with prostate cancer are often in psychological distress and pain preoperatively. The aim of this study was to examine the effects of preoperative anxiety, depression and pain on the quality of postoperative recovery and acute postoperative pain after radical prostatectomy. One hundred and sixty patients scheduled for open or laparoscopic radical prostatectomy were enrolled in a prospective observational study. Psychological distress was assessed with the State-Trait Anxiety Inventory (STAI-S and STAI-T) and Center for Epidemiological Studies Depression Scale (CES-D). Postoperative recovery was assessed on postoperative days 1-3 using the Quality of Recovery-40 score (QoR-40). Numeric rating scale 0-10 was used to assess the intensity of postoperative pain at rest and on movement at 1, 6 and 24 hours post-surgery. In linear regression models, STAI-S was predictor of QoR-40 on postoperative days 1-3 (ß=-17.32; p<0,001, ß=-0.345; p=0.004, and ß=-0.326; p=0.002, respectively), and preoperative pain was predictor of pain at rest (ß=0.666; p=0.008) and on movement (ß=0.691; p=0.006). In logistic regression models, preoperative pain was predictor of clinically significant pain at rest (OR, 2.86; 95% CI 1.11-7.36) and STAI-S of clinically significant pain on movement (OR, 2.21; 95% CI, 1.08-4.52). In conclusion, state anxiety had negative impact on QoR and acute pain after radical prostatectomy. Preoperative pain was associated with acute postoperative pain.

Key words: *Anxiety; Depression; Pain; Postoperative recovery; Prostatectomy*

Introduction

Radical prostatectomy is a recommended treatment for prostate cancer, the second most prevalent cancer in men worldwide[1]. Patients diagnosed with prostate cancer have numerous causes of psychological distress

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in preoperative period, e.g., coping with diagnosis of cancer, making decision about treatment modality, considering specific complications (erectile dysfunction and/or urinary incontinence), concerns related to surgery and anesthesia, postoperative pain, and recovery in general[2,3]. Psychological distress in preoperative period may induce anxiety and depression or aggravate the existing ones, which may impact postoperative outcomes. Multiple studies associated preoperative anxiety and depression with the increased incidence of postoperative morbidity[4,5], surgical wound infection and complication rates[6], and higher levels of postoperative pain[7]. The quality of postoperative recovery (QoR) has recently gained interest as an important postoperative outcome. It includes assessment, not just isolated symptoms as commonly reported in previous research, but multiple recovery dimensions relevant to patients and clinicians. There is significant heterogeneity in the results of studies examining the effects of anxiety and depression on postoperative recovery variables[8]. In patients undergoing radical prostatectomy, preoperative anxiety and depression were associated with higher complication rates and longer length of hospital stay[9] but their effect on the quality of postoperative recovery has not been examined.

Preoperative pain is a well established predictor of acute postoperative pain[7,10] and may impair postoperative recovery. However, the predictive value of preoperative pain for development of moderate to severe postsurgical pain varies considerably depending on the type of surgical procedure[11]. Studies in patients undergoing radical prostatectomy exploring the associations of preoperative pain with acute postoperative pain are sparce. Studies exploring associations of preoperative pain with QoR are lacking. The aim of this study was to examine the effects of preoperative depression, anxiety and pain on the QoR and acute postoperative pain after radical prostatectomy.

Subjects and Methods

Patients and study design

This single center prospective observational study was conducted at Zadar General Hospital, Zadar, Croatia between February 2016 and April 2019, with approval by the institutional Ethics Committee (No. 01-156-4/16). Eligible were patients with prostate cancer scheduled for open radical prostatectomy or laparoscopic radical prostatectomy. Exclusion criteria were being unwilling to participate, inability to complete questionnaires due to language barrier or mental incapacity, severe comorbid condition precluding objective assessment of postoperative recovery or pain, history of substance abuse or chronic opioid use, and known allergy to medications used in the study protocol.

Demographic and clinical data collected perioperatively included age, body mass index (BMI), level of education, comorbidities, preoperative prostate-specific antigen levels, duration of anesthesia and surgery, type of surgery, estimated intraoperative blood loss, postoperative complications and intra- or postoperative transfusion of red blood cells.

Patients were approached in the evening before surgery. After informing patients about the study and obtaining written informed consent, patients completed sets of questionnaires including the State-Trait Anxiety Inventory (STAI-S and STAI-T); Center for Epidemiological Studies Depression Scale (CES-D); Brief Pain Inventory (BPI); and Quality of Recovery-40 scale (QoR-40). Two principal investigators (N.S. and T.Š.) were available for additional explanations. Assistance was provided if patients were more comfortable by questions being read to them aloud.

Research instruments

Anxiety was assessed with STAI, a self-reported questionnaire composed of two subscales with 20 items each. The items of state anxiety subscale (STAI-S) capture transient feelings of apprehension, tension, nervousness, and worry accompanied with arousal of the autonomic nervous system, which increases in response to particular situation perceived as threatening or dangerous. STAI-S measures anxiety at the time of administration and corresponds to preoperative anxiety (Cronbach α=0.94). The trait anxiety subscale (STAI-T) measures relatively stable personality traits that predispose individuals to respond with anxiety in different situations (Cronbach α=0.92). The items of STAI questionnaires are scored on a 4-point Likert scale. The scores range from 20 to 80 with higher score indicating higher levels of anxiety. The cut-off score of ≥40 for both subscales was used to differentiate between anxious and non-anxious patients. STAI was validated in the Croatian population[12].

Symptoms of depression were assessed with CES-D, a 20-item self-report questionnaire that evaluates frequency of different symptoms of depression experienced during the last week on a 4-point Likert

scale. The scores range from 0 to 60 with higher scores indicating more severe symptoms of depression. The score ≥16 was used to differentiate between depressed and non-depressed individuals (Cronbach α=0.90)[13].

Patients were screened with a single question about the presence of painful conditions and whether they were in pain currently. Patients who reported having preoperative pain were assessed with BPI. The severity of pain in the last 24 hours was assessed with both a single item, worst pain (BPI-W), and with composite pain severity score (BPI-S), which is the mean of 4 pain severity items including worst pain, least pain, average pain and pain right now. The interference of pain with daily activities (BPI-I) was assessed with the mean of 3 interference items including general activity, normal work, and relations with others. Items were rated on a numeric rating scale from 0 (no pain; does not interfere) to 10 (most severe pain; completely interferes)[14].

Recovery was assessed with the Croatian version of the QoR-40, a 40-item self-report questionnaire. The QoR-40 covers five key dimensions of postoperative recovery, i.e., physical comfort (12 items), emotional state (9 items), psychological support (7 items), physical independence (5 items) and pain (7 items). The items are scored on a 5-point Likert scale. Total score ranges from 40 to 200 with higher scores indicating better recovery (Cronbach α=0.91-0.93). It has been used as an outcome measure in clinical trials and validated for use in the Croatian surgical population[15,16].

Anesthetic management was standardized. Induction of anesthesia was performed with propofol 1.5-2 mg/kg, fentanyl 1.5-2.5 mcg/kg and rocuronium 1 mg/kg. General anesthesia was maintained with ~1 MAC sevoflurane in air/oxygen mixture with additional boluses of fentanyl and rocuronium, as needed. Depth of anaesthesia was measured with bispectral index (BIS) monitor. Ketoprofen 100 mg IV was administered approximately 30 minutes before the end of surgery. For postoperative analgesia, intravenous paracetamol, ketoprofen and tramadol were used at the discretion of attending urologist. Postoperative recovery was assessed on postoperative day (POD) 1, 2 and 3 using the Croatian version of QoR-40. Numeric rating scale (NRS) 0-10 was used to assess the intensity of postoperative pain at rest (NRS-R) and on movement (NRS-M) at 1, 6 and 24 h post-surgery. Postoperative data were collected by two principal investigators (N.S. and T.Š.).

Statistical analysis

Continuous variables were reported as median and interquartile range (IQR). The normality assumption of continuous variables was assessed with Shapiro-Wilk test. Categorical variables were expressed as number of occurrence with proportion expressed as percentage.

Spearman rank correlations were used to examine association between metric variables.

Mean postoperative NRS scores for pain at rest and on movement were used for correlation analysis and regression models.

Three stepwise multivariable linear regression models were constructed to explore associations between QoR-40 scores on postoperative days 1, 2 and 3 (POD 1-3) as a dependent variable with STAI-S, STAI-T, CES-D, preoperative pain, age, BMI, American Society of Anesthesiologists (ASA) grade, type of surgery, duration of surgery, volume of crystalloids, transfusion of red blood cells, and preoperative QoR-40 score.

Two stepwise multivariable linear regression models were constructed to explore associations between mean pain at rest and pain on movement as dependent variables with STAI-S, STAI-T, CES-D, preoperative pain, age, BMI, ASA physical status grade, type of surgery, duration of surgery, volume of crystalloids, and estimated intraoperative blood loss.

Two multivariable logistic regression models were constructed to explore the association of clinically relevant pain at rest and on movement defined with NRS ≥4 as dependent variables using the same predictors as linear regression models for pain.

In all regression models, STAI-S, STAI-T and CES-D were entered as continuous variables but preoperative pain was dichotomized. Statistical significance was set at $p<0.05$.

Correlation with rho range 0-0.19 was regarded as very weak, 0.2-0.39 as weak, 0.40-0.59 as moderate, 0.6-0.79 as strong, and 0.8-1 as very strong.

Statistical analysis was performed using MedCalc® Statistical Software version 20.100 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2022) and IBM SPSS 23 (IBM Corp. Released 2015; Armonk, NY, USA).

Results

Of 175 patients enrolled, 160 completed the study. Figure 1 shows a flow chart of study enrolment and

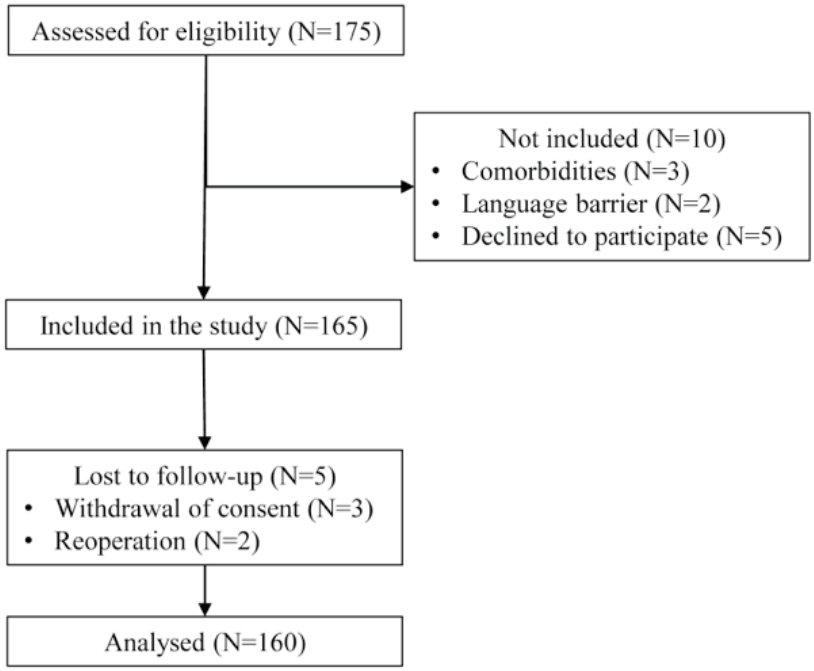

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

reasons for patient exclusions from analysis. The majority of patients were overweight (59.4%) and 19.4% were obese. Demographic and perioperative data are shown in Table 1.

Median value of state anxiety (STAI-S) was 35 (IQR 29-43), trait anxiety (STAI-T) 33 (IQR 28-40), and CES-D 8 (IQR 4-15). High levels of state anxiety (STAI-S) were present in 56 (35%) patients and high levels of trait anxiety (STAI-T) in 41 (26%) patients. High levels of depression were present in 33 (21%) patients.

Preoperative pain was present in 33 (20.6%) patients. Pain originated from lower back pain in 23 (70%), cervicobrachial syndrome in 4 (12%), arthritis in 4 (12%) patients, gonarthrosis in 1 (3%) patient, and only 1 (3%) patient had urologic pain. Pain scores were BPI-Severity 2.3 (IQR 1.5-2.9), BPI-Worst 3.0 (IQR 2-4) and BPI-Interference 1.7 (IQR 0.86-3.07).

Preoperative pain was significantly more prevalent in patients with high trait anxiety and high levels of depression. Fifteen out of 41 patients with high trait anxiety also reported preoperative pain (p=0.003) and 13 out of 33 patients with high levels of depression reported having preoperative pain (p=0.003).

On the day of surgery, 88 (55%) patients were administered tramadol at a median dose of 100 mg (IQR 75-100). On POD 1, 37 (23%) patients received tramadol at a median dose of 100 mg (IQR 75-100). On POD 2, 9 (6%) patients received tramadol at a median dose of 50 mg (IQR 50-100).

Quality of recovery

Global QoR-40 scores and scores of five recovery dimensions are presented in Table 2. Dimensions of physical independence, physical comfort and pain showed largest decrease compared to preoperative values.

The results of Spearman correlation analysis of preoperative STAI-S, STAI-T, CES-D and BPI scores with POD 1-3 QoR-40 scores are presented in Table 3. Preoperative measure of state anxiety STAI-S showed moderate negative correlations with global QoR-40 on POD 1-3 (-0.418 to -0.428), with low to moderate negative correlations with all QoR-40 dimensions (-0.237 to -0.529). Measures of trait anxiety STAI-T and depression CES-D showed weak negative correlations with global QoR on POD 1-3 (STAI-T -0.316 to -0.324, CES-D -0.372 to -0.386) and weak negative correlations with all QoR-40 dimensions (-0.19 to -0.463) except for physical independence on POD 1 and 3.

Measures of preoperative pain BPI-S, BPI-I and BPI-W showed very weak negative correlations with global QoR-40 on POD 1 and 3 (-0.165 to -0.196), with psychological support dimension on POD 1

Table 1. Demographic and clinical data

Age (years) [median (IQR)]	65 (59-68)
Body mass index (kg/m^2) [median (IQR)]	27.45 (25.22-29.32)
Education [n (%)]	
Elementary school	15 (9.4)
High school	90 (56.3)
College/university 3 yrs	19 (11.9)
College/university ≥4 yrs	36 (22.5)
Prostate-specific antigen [ng/mL] [median (IQR)]	7.7 (5.7-13.2)
ASA status [n (%)]	
ASA 2	127 (79.4)
ASA 3	33 (20.6)
Type of surgery [n (%)]	
Laparoscopic radical prostatectomy	88 (55)
Open radical prostatectomy	72 (45)
Intraoperative or postoperative red blood cell transfusion [n (%)]	9 (5.6)
Duration of anesthesia (min) [median (IQR)]	185 (160-210)
Intraoperative crystalloids (mL) [median (IQR)]	2000 (1500-2100)
Intraoperative blood loss (mL) [median (IQR)]	275 (200-400)
Duration of surgery (min) [median (IQR)]	155 (135-185)
Regional lymphadenectomy [n (%)]	
Not performed	78 (48.8)
Negative lymph nodes	64 (40.0)
Positive lymph nodes	18 (11.3)
Gleason score [n (%)]	
≤6	34 (21.4)
3+4	84 (52.8)
4+3	24 (15.1)
≥8	17 (10.7)
Postoperative complications [n (%)]	25 (15.6)
Tracheobronchitis	3 (12)
Cough with bronchospasm	3 (12)
Postoperative hemorrhage with transfusion	4 (16)
Urinary infection	1 (4)
Lymphocele	3 (12)
Fever with antibiotic therapy	1 (4)
Surgical site infection	1 (4)
Arm numbness and swelling	1 (4)
Painful shoulder – impingement syndrome	3 (12)
Allergic reaction to analgesic	1 (4)
Pneumonia	1 (4)
Sepsis	1 (4)
Deep vein thrombosis	2 (8)

IQR = interquartile range; ASA = American Society of Anesthesiologists

Table 2. Preoperative and postoperative day 1-3 QoR-40 scores

	Median (interquartile range)				p*
	Preoperative	POD 1	POD 2	POD 3	
Global QoR-40	193 (184-198)	165 (154-176)	180 (167-188)	187 (178-192)	<0.001†
Physical comfort	58 (56 – 59.8)	52 (48.3-54)	55 (52-57)	57 (54-58)	<0.001†
Emotional state	42 (38-44)	37 (34-41)	39 (35.3-42)	41 (38-43)	<0.001‡
Physical independence	25 (25-25)	13 (11-16)	20 (17-21)	22 (21-23)	<0.001†
Psychological support	35 (34.3-35)	34 (32-35)	35 (34-35)	35 (34-35)	<0.001§
Pain	34.5 (33-35)	30 (27.3-32)	32 (29-33)	33 (31-34)	<0.001†

POD = postoperative day; QoR-40 score = Quality of Recovery-40 score; *Friedman test (post hoc Conover); †with p<0.05 there is significant difference at all 4 points; ‡with p<0.05 significantly lower on POD 1 and 2 than preoperative and POD 3 values; § with p<0.05 significantly lower on POD 1 than preoperative and POD 2 and POD 3 values

Table 3. Spearman correlation of preoperative STAI-S, STAI-T, CES-D and BPI scores with postoperative day 1-3 QoR-40 scores

	Spearman correlation Rho					
	STAI-S	STAI-T	CES-D	BPI-S	BPI-I	BPI-W
QoR-40 POD 1						
Global QoR-40	-0.418**	-0.316**	-0.372**	-0.189*	-0.196*	-0.190*
Physical comfort	-0.354**	-0.279**	-0.252**	-0.146	-0.137	-0.141
Emotional state	-0.449**	-0.327**	-0.379**	-0.108	-0.109	-0.111
Physical independence	-0.274**	-0.245**	-0.291**	-0.036	-0.064	-0.045
Psychological support	-0.312**	-0.202*	-0.295**	-0.170*	-0.185*	-0.170*
Pain	-0.256**	-0.193*	-0.248**	-0.276**	-0.250**	-0.275**
QoR-40 POD 2						
Global QoR-40	-0.428**	-0.318**	-0.386**	-0.121	-0.111	-0.120
Physical comfort	-0.359**	-0.224**	-0.277**	-0.097	-0.077	-0.097
Emotional state	-0.529**	-0.407**	-0.445**	-0.062	-0.058	-0.063
Physical independence	-0.246**	-0.190*	-0.262**	-0.053	-0.058	-0.050
Psychological support	-0.334**	-0.246**	-0.297**	-0.017	-0.024	-0.017
Pain	-0.264**	-0.224**	-0.291**	-0.286**	-0.264**	-0.283**
QoR-40 POD 3						
Global QoR-40	-0.422**	-0.324**	-0.381**	-0.165*	-0.150	-0.165*
Physical comfort	-0.368**	-0.283**	-0.321**	-0.110	-0.085	-0.113
Emotional state	-0.471**	-0.385**	-0.463**	-0.133	-0.127	-0.133
Physical independence	-0.237**	-0.126	-0.146	-0.073	-0.077	-0.073
Psychological support	-0.344**	-0.289**	-0.386**	0.007	0.001	0.009
Pain	-0.247**	-0.208*	-0.250**	-0.314**	-0.291**	-0.311**
Pain						
Mean NRS-R	0.090	0.111	0.036	0.161*	0.166*	0.161*
Mean NRS-M	0.197*	0.169*	0.082	0.205*	0.206*	0.206*

POD = postoperative day; QoR-40 score = Quality of Recovery-40 score; STAI-S = state anxiety; STAI-T = trait anxiety; CES-D = depression; BPI-S = preoperative pain severity; BPI-I = preoperative pain interference; BPI-W = preoperative pain worst; NRS-R = pain at rest; NRS-M = pain on movement; **p<0.001; *p<0.05

Table 4. Results of linear regression analysis for QoR-40 on postoperative day 1-3

	QoR-40 POD 1			QoR-40 POD 2			QoR-40 POD 3		
Predictor									
	ß	95% CI	p	ß	95% CI	p	ß	95% CI	p
STAI-S	-17.32	-26.04-8.61	<0.001	-0.345	-0.58-0.11	0.004	-0.326	-0.53-0.12	0.002
ORP	-0.339	-0.59-0.09	0.008	-5.810	-9.69-1.93	0.004	-6.430	-9.78-3.08	<0.001
Transfusion	-6.710	-10.8-2.63	0.001	0.384	0.18-0.59	<0.001	-8.180	-15.32-1.04	0.03
Preop QoR-40	0.426	0.20-0.65	<0.001	-12.50	-21.3-3.73	0.006	0.190	0.007-0.37	0.04
Model summary									
R^2	R^2=0.377			R^2=0.339			R^2=0.299		
F	$F_{(4, 155)}$=23.4			$F_{(4, 155)}$=19.9			$F_{(4, 155)}$=16.5		
P	p<0.001			p<0.001			p<0.001		

POD = postoperative day; QoR-40 score = Quality of Recovery-40 score; CI = confidence interval; STAI-S = state anxiety; ORP = open radical prostatectomy

Table 5. Linear and logistic regression models for pain at rest and pain on movement

	Linear regression				Logistic regression			
	NRS-R		NRS-M		NRS-R ≥4		NRS-M ≥4	
	β (95% CI)	p	β (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Preoperative pain	0.666 (0.177-1.155)	0.008	0.691 (0.200-1.181)	0.006	2.86 (1.109-7.357)	0.03		
Surgical approach (ORP)	0.547 (0.089-1.005)	0.02	0.552 (0.096-1.008)	0.02			2.81 (1.43-5.51)	0.003
Intraoperative blood loss	0.001 (0.001-0.002)	<0.001	0.001 (0-0.002)	0.01	1.003 (1.002-1.005)	<0.001		
STAI-S							2.21 (1.08-4.52)	0.03
Age	-0.035 (-0.067-0.004)	0.03			0.93 (0.869-0.999)	0.04		
Model summary	R^2=0.211		R^2=0.164		χ^2=26.6		χ^2=15.8	
	$F_{(4, 155)}$=10.34		$F_{(3, 156)}$=10.2					
	p<0.001		p<0.001		p<0.001		p<0.001	

NRS-R = numeric rating scale-at rest; NRS-M = numeric rating scale-on movement; CI = confidence interval; OR = odds ratio; ORP = open radical prostatectomy; STAI-S = state anxiety

(-0.17 to - 0.185), and weak negative correlations with pain dimension of QoR-40 on POD 1-3 (-0.250 to -0.314) (Table 3).

Results from the three linear regression models for QoR-40 on POD 1-3 are shown in Table 4. State anxiety (ß coefficients -17.32, -0.345 and -0.326), transfusion, surgical approach and preoperative QoR-40 scores were significant predictors in all three regression models (Table 4).

Acute postoperative pain

Median NRS scores for pain at rest at 1, 6 and 24 hours postoperatively were 2 (IQR 1-4), 3 (IQR 2-4) and 2 (IQR 1-4), respectively. Mean NRS for pain at rest was 2.33 (IQR 1.67-3.67). Pain at rest 24 hours postoperatively was significantly lower than pain at rest at 1 and 6 hours postoperatively (Friedman test with post hoc Conover, $p<0.001$). Median NRS scores for pain on movement at 1, 6 and 24 hours postoperatively were 4 (IQR 3-5), 4 (IQR 3-5) and 4 (IQR 3-5), respectively. Mean NRS for pain on movement was 4.17 (IQR 3.08-5-0).

Mean NRS score for pain at rest did not correlate with STAI-S, STAI-T and CES-D, but showed weak positive correlations with BPI scores (Table 3). Mean NRS score for pain on movement showed very weak positive correlations with STAI-S and STAI-T and weak correlations with BPI scores (Table 3).

Linear and logistic regression models for pain at rest and on movement are presented in Table 5. In linear regression model for pain at rest, significant predictors were preoperative pain (ß=0.666), surgical approach (open radical prostatectomy) (ß=0.547), intraoperative blood loss (ß=0.001) and age (ß=-0.035). In linear regression model for pain on movement, significant predictors were preoperative pain (ß=0.691), surgical approach (open radical prostatectomy) (ß=0.552) and intraoperative blood loss (ß=0.001).

Clinically significant pain at rest was present in 31 (19.4%) patients. Logistic regression showed that predictors of clinically significant pain at rest were preoperative pain (odds ratio (OR), 2.86; 95% CI 1.109-7.357), age (OR, 0.93; 95% CI 0.869-0.999) and intraoperative blood loss (OR, 1.003; 95% CI 1.002-1.005). Clinically significant pain on movement was present in 93 (58.1%) patients. In logistic regression model, predictors of clinically significant pain on movement were STAI-S (OR, 2.21; 95% CI, 1.08-4.52) and surgical approach (open radical prostatectomy) (OR, 2.81; 95% CI, 1.43-5.51).

Discussion

The results of our study showed that preoperative state anxiety was an independent predictor of the quality of postoperative recovery after radical prostatectomy with negative impact on all recovery dimensions and it was associated with clinically significant movement pain. Although preoperative pain was associated with the severity of postoperative pain, it did not affect QoR. Trait anxiety and depression showed significant negative correlations with QoR but were not independent predictors in regression models.

Kleif *et al.* showed that anxiety was a significant predictor of QoR after laparoscopic surgery for appendicitis[17]. We had similar result in our study, but important findings of our study were that state anxiety affected all dimensions of postoperative recovery on the first three postoperative days. Recovery dimensions predominantly affected were emotional state, physical comfort and psychological support. Furthermore, our study supports the results of the study conducted by Nilsson *et al.* exploring associations of mental health with postoperative recovery in patients undergoing day surgery[18]. Low mental component of Short Form 36 Health Survey negatively affected multiple dimensions of postoperative recovery as indicated by responses to 21 out of 24 items included in the Swedish web version of the QoR score[18].

Depression and trait anxiety in our study showed significant negative correlation with global QoR and recovery dimensions. However, preoperative anxiety (STAI-S) was the only independent predictor of QoR, emphasizing the potentially detrimental effects of psychological stressors in preoperative period. Psychological stressors influence mood and emotional reactivity, inducing primarily increased anxiety and negative affect. Stressful experiences are initially processed in higher brain regions with subsequent modification of physiological responses[19]. Stress response initiated before surgery with sympatho-adreno-medullary and hypothalamic-pituitary-adrenocortical axis activation could mediate response to surgical stress potentially leading to worse surgical outcomes[20].

Preoperative pain in our study was mild on average with low interference of pain with daily activities and unrelated to the site of surgery in all but one patient. It was not an independent predictor of QoR in regression models. A possible explanation is that postoperative pain therapy provided sufficient analgesia to prevent significant interference of preoperative pain with QoR. However, preoperative pain was significantly more prevalent in patients with high trait anxiety and high levels of depression.

State anxiety has been reported as an independent predictor of clinically significant movement pain. A cut-off point for clinically significant pain (moderate to severe pain requiring analgesic intervention) determined by three different methods was ≥4 on NRS[21]. It

was leading to relevant pain-related interference with movement, sleep and mood[21]. In our study using the same cut-off, STAI-S was an independent predictor of clinically significant pain on movement confirming the importance of state anxiety in perioperative period. Our results support the findings by Katz *et al*. that greater preoperative anxiety, as assessed with STAI-S, was the only variable that contributed independently to predicting clinically significant pain 2 days after surgery[22]. Furthermore, two recent systematic reviews and a meta-analysis have shown that anxiety is a significant predictor of postoperative pain[7,23].

Preoperative depression in our study was not associated with postoperative pain. In contrary, Gebershagen *et al*. and Ene *et al*. found that in radical prostatectomy patients, both anxiety and depression (assessed by the Hospital Anxiety and Depression Scale) had significant, albeit weak correlations with moderate and severe postoperative pain after mobilization[24,25]. Depression as a predictor of postoperative pain remains controversial. Most of the published studies failed to demonstrate significant effects of depression on postoperative pain[26].

Preoperative pain in our study was a significant predictor of postoperative pain in three out of four regression models. Preoperative pain is the most consistent predictor of postoperative pain in different surgical populations[7]. After radical prostatectomy, patients with moderate-to-severe chronic pain were significantly more likely to develop moderate-to-severe postoperative pain[27]. Interestingly, 13.1% of patients had preoperative urologic pain[27] but in our study, only one patient had pain on the operative site.

Surgical approach with open radical prostatectomy was a significant predictor in linear regression models lower quality of postoperative recovery, postoperative pain and in logistic regression model clinically significant pain on movement in our study. Moreover, the number of blood transfusions was associated with surgical approach. Seven out of 9 patients who received blood transfusion had open radical prostatectomy. This may have contributed to lower QoR.

Patients discharged on POD 1 or even on the same day after radical prostatectomy are increasing. QoR is of crucial importance in these patients. Achievement of optimal recovery with safe discharge necessitates careful patient preoperative assessment, selection and optimization. Targeted interventions or implementation of multimodal prehabilitation programs for patients scheduled for radical prostatectomy who have significant preoperative anxiety could improve postoperative QoR and postoperative pain. Anxiety followed by pain was the worst aspect of perioperative experience in a large cross-sectional study[28]. Improving preoperative anxiety could also improve overall patient experience and satisfaction.

Limitations

Our study was performed in a single center and included only radical prostatectomy patients, which precludes generalization of our results. However, such a design excludes huge variability in QoR and postoperative pain associated with different types of surgery, thus allowing for more reliable assessment of the effects of psychological factors and preoperative pain. Further, postoperative analgesia was not standardized, which may have induced bias in assessment of pain scores and QoR.

In conclusion, we showed that preoperative state anxiety had negative impact on the quality of postoperative recovery after radical prostatectomy and was associated with clinically significant pain on movement. Measures to reduce preoperative anxiety could improve the quality of postoperative recovery in this patient population. Although the mean preoperative pain scores were low, preoperative pain was a significant predictor of acute postoperative pain at rest and on movement, which should be considered in postoperative analgesia planning.

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Sažetak

UTJECAJ PRIJEOPERACIJSKE ANKSIOZNOSTI, DEPRESIVNOSTI I BOLI NA KVALITETU POSLIJEOPERACIJSKOG OPORAVKA I AKUTNU POSLIJEOPERACIJSKU BOL NAKON RADIKALNE PROSTATEKTOMIJE

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Bolesnici s karcinomom prostate u prijeoperacijskom razdoblju su često u psihološkom distresu i imaju bolove. Cilj ove studije bio je ispitati utjecaj prijeoperacijske anksioznosti, depresivnosti i boli na kvalitetu poslijeoperacijskog oporavka i akutnu poslijeoperacijsku bol nakon radikalne prostatektomije. U prospektivnu opservacijsku studiju uključeno je 160 bolesnika podvrgnutih otvorenoj ili laparoskopskoj prostatektomiji. Psihološki distress mjeren je Upitnikom anksioznosti kao stanja i osobine ličnosti (STAI-S i STAI-O) i Ljestvicom za depresiju Centra za epidemiološka istraživanja (CES-D). Poslijeoperacijski oporavak mjeren je Upitnikom o kvaliteti poslijeoperacijskog oporavka (QoR-40) prva tri poslijeoperacijska dana (POD 1-3). Jačina poslijeoperacijske boli ocijenjena je brojčanom ljestvicom 0-10 u mirovanju i pokretu 1, 6 i 24 sata nakon operacije. U lineranim regresijskim modelima STAI-S bio je prediktor za QoR-40 prva tri poslijeoperacijska dana (ß=-17,32; p<0,001, ß=-0,345; p=0,004 i ß=-0,326; p=0,002), a prijeoperacijska bol bila je prediktor za bol u mirovanju (ß=0,666; p=0,008) i u pokretu (ß=0,691; p=0.006). U logističkim regresijskim modelima prijeoperacijska bol bila je prediktor klinički značajne boli u mirovanju (OR, 2,86; 95% CI 1,11-7,36), a STAI-S klinički značajne boli u pokretu (OR, 2,21; 95% CI, 1,08-4,52). Anksioznost kao stanje (STAI-S) negativno utječe na QoR i akutnu bol nakon radikalne prostatektomije. Prijeoperacijska bol utječe na akutnu poslijeoperacijsku bol.

Ključne riječi: *Anksioznost; Depresija; Bol; Poslijeoperacijski oporavak; Prostatektomija*