Anxiety, but not pain catastrophizing, represents a risk factor for severe acute postoperative pain: a prospective, observational, cohort study

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Abstract

Introduction: The prevalence of severe acute postoperative pain (SAPP), i.e. pain intensity $\geq 5/10$ measured with Numeric Rating Scale (NRS), is still high, 24-46% in Western European countries and 64% in Republic of Moldova.

Objective of the study: We tested the hypothesis that anxiety and pain catastrophizing perception (interpreted as hypervigilance) represent risk factors for SAPP.

Materials and methods: 176 patients scheduled for abdominal surgery under general anaesthesia were enrolled in this study, after approval by the University's Research Ethics Committee and after obtaining patient written informed consent. Preoperatively, all patients filled a Pain Catastrophizing Scale (PCS) questionnaire and self-assessed the anxiety level on a numeric rating scale that was bounded by 0 (denoting no anxiety) and 10 (denoting maximal imaginable anxiety). Duration of surgery, intraoperative administration of fentanyl and pain intensity at 24 hours postoperatively on NRS was also recorded. Statistical analysis comprised the following tests: odds ratio (OR), relative risk (RR), positive and negative predictive values (PPV and NPV, respectively), likelihood ratio, receiver operating characteristic (ROC) curves, and Pearson correlation test.

Results: "Hypervigilant" patients did not show an increased risk for SAPP based on histogram calculations (OR = 1.51 [95CI = 0.62-3.65], p = 0.39). However, based on ROC curve calculations (OR = 2.34 [1.13-4.83], p = 0.0029), these patients showed a risk for SAPP. On average, anxiety determined a fivefold increase of the SAPP risk (OR = 5.1 [95CI = 1.44-18.50], p = 0.011). Intraoperative fentanyl consumption had a weak but significant correlation with pain intensity at 24 h postoperatively (Pearson r = 0.26; p = 0.0008). Surgery duration did not correlate with pain intensity (Pearson r = -0.10; p = 0.46).

Conclusion: Anxiety, but not pain catastrophizing, represents a risk factor for SAPP. Intraoperative fentanyl consumption had a weak correlation with postoperative pain intensity.

Keywords: risk factors, severe acute postoperative pain, anxiety, hypervigilance

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Introduction

Despite progress in the management of postoperative pain, the proportion of patients with severe acute postoperative pain (SAPP) remains high, ranging between 24%-46% in Western Europe and 64% in the Republic of Moldova [1-4]. The list of complications from inadequately treated SAPP is quite long: delayed

Address for correspondence: Adrian Belîi, MD, PhD Department of Anaesthesia and Intensive Care "Valeriu Ghereg" State University of Medicine and Pharmacy "Nicolae Testemitanu" 165, Stefan cel Mare si Sfant Ave. MD-2004 Chisinau, Rep. of Moldova E-mail: adrian.belii@usmf.md functional recovery, increased incidence of the "traditional" postoperative complications, cognitive dysfunction, sleep disorders, depression, social isolation and distress, decreased work capacity, and chronic pain. All these complications are inevitably associated with significant economic losses and sustainable reduction in life quality [5-8].

Persistent postoperative pain (PPP), one of the complications of SAPP, is the second most common cause of neuropathic pain after low back pain, and is present in 20%-40% of the patients who seek treatment in Pain Clinics [9-11]. Although adherence to the current guidelines on SAPP management significantly reduces its frequency [12], the frequency of PPP is

still high: up to 30% at 6 months postoperatively, and 5%-10% of patients present severe symptoms [13-15]. Therefore, both SAPP and PPP represent an important medical and social issue that is yet unsolved [16, 17]. Research on identification and management of specific risk factors that began more than a decade ago could help to reduce the frequency of SAPP and, consequently, to reduce the PPP [18, 19].

The objective of this study was to test the hypothesis that in patients undergoing abdominal surgery under general anaesthesia, anxiety and/or pain catastrophizing (interpreted as "hypervigilance") represent risk factors for SAPP.

Materials and methods

This prospective, observational, cohort study was conducted between 06.03.2011 - 06.04.2012, at the National Scientific and Practical Center of Emergency Medicine in Chisinau (Republic of Moldova) and included 176 patients. The research protocol was approved by the Research Ethics Committee of the State University of Medicine and Pharmacy "Nicolae Testemitanu". All study patients signed written informed consent before inclusion in the study cohort. Inclusion criteria were: age ≥ 18 years, absence of persistent chronic pain, ASA I-II, ability to understand and respond to the study questionnaire, patients undergoing elective abdominal surgery (appendectomy, laparoscopic cholecystectomy, and inguinal hernia repair), and a minimum duration of 6 hours elapsed after patient transfer from the recovery room to the surgery ward. Patients who did not fill the questionnaire or who requested to exit the study were excluded.

One day before surgery, patients completed the Pain Catastrophizing Scale (PCS) questionnaire translated and adapted to Romanian language, consisting of 13 items rated from 0-4 (Appendix), and resulting in a total score between 0 and 52 points. Relying on the type of statements, catastrophic perception of pain may be stratified into three components: *rumination* (tendency to focus on pain sensations), representing of the sum of items 8, 9, 10, 11; *amplification* (exaggeration of danger amplitude) – the sum of items 6, 7, 13; *helplessness* (the sensation of inability to control the pain symptoms) – the sum of items 1, 2, 3, 4, 5, 12 [20]. Additionally, patients self-rated the degree of their anxiety with numeric rating scale (NRS: bounded by 0 – no anxiety, 10 – maximal imaginable anxiety).

All patients received total intravenous anaesthesia with thiopental 4 mg/kg and fentanyl 4 μ g/kg for induction, and benzodiazepine and fentanyl for maintenance. Tracheal intubation was facilitated by the administration of intravenous (i.v.) atracurium 0.5 mg/kg.

Duration of surgery and the intraoperative fentanyl consumption were recorded.

Postoperative analgesia was provided by i.v. administration of 100 mg ketoprofen after surgical incision, and 10 mg subcutaneous morphine at the end of the surgery. Subsequently, patients received 100 mg of ketoprofen orally every 12 hours, for 5 days. Severe pain episodes (> 5 points on NRS) were treated with 100 mg of tramadol i.m. All patients self-assessed their pain intensity using the numerical rating scale at 24 hours postoperatively.

The study sample size was calculated using online "sample size calculator" (http://www.raosoft.com/ samplesize.html), assuming a 5% error and a confidence interval of 95%, a population of > 20,000 and also assuming that at least 10% of the population presents pain catastrophizing perception. Thus, the sample size required by the study was calculated as 138 patients.

According to the cut-off values "catastrophizer-noncatastrophizer", obtained from histogram or receiver operating characteristic (ROC) curves, the following were calculated: odds ratio (OR), relative risk (RR), sensitivity and specificity, the positive and negative predictive value (PPV and NPV, respectively), and the likelihood ratio. Pearson test was used to assess the degree of correlation between postoperative pain intensity and duration of surgery (in minutes), pain intensity and intraoperative fentanyl consumption (in μ g). A value of p < 0.05 was considered statistically significant. Data are presented as mean, 95% confidence intervals (95% CI) and percentages. Statistical analysis was performed using GraphPad Prism software, version 5.00 for Windows (San Diego, CA, USA, www.graphpad.com).

Results

The flow chart of the study is shown in Fig. 1. In order to estimate the role of pain catastrophizing perception in determining the SAPP and to specify whether a certain score or sub-score of the PCS acts as a risk factor for SAPP, its cut-off values "catastrophizer" vs "noncatastrophizer" were identified (Fig. 2).

The cut-off value for PCS total score was 27 points (based on the histogram) and 15 points (based on the ROC curve). For PCS sub-scores, the cut-off values were: 10 points – for rumination; 6 points – for amplification; 12 points – for helplessness (based on the histogram), and respectively, 5 points – for rumination; 4 points – for amplification; 7 points – for helplessness (based on the ROC curves). As a result, the obtained proportion of "catastrophizers", according to the PCS cut-off value \geq 27, was 23%, while according to the PCS cut-off value of \geq 15, it was 55%.

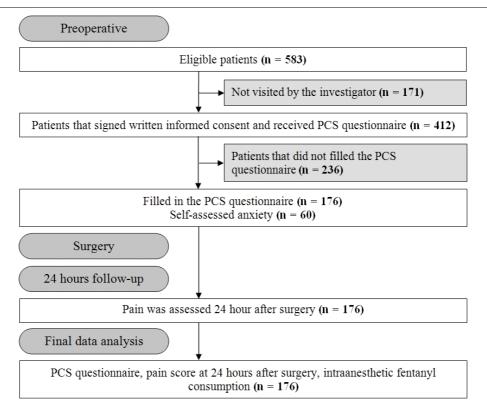


Fig. 1. Study's flow-chart. PCS - Pain Catastrophizing Scale

Pain catastrophizing perception was not identified as a risk factor for severe postoperative pain, based on the cut-off values corresponding to the 75th percentile (third quartile, Q3) on histograms (Table 1). Alternativelly, it was proven to be a risk factor for SAPP based on the cut-off values of ROC curves. In this case, "catastrophizers" had a twofold risk of developing SAPP than "noncatastrophizers" (Table 2).

The proportion of "catastrophizers" who developed SAPP was 54.2% and 63.6% for the total PCS score cut-off values of \geq 15, and \geq 27, respectively. The proportion of "noncatastrophizers" who developed SAPP was 65% and 59% for the total PCS score cut-off values of < 15, and < 27, respectively. No correlation

was found between pain catastrophizing and SAPP regardless of the cut-off values ($\geq 15 \text{ or } \geq 27$) (Fig. 3).

Of the 60 patients who self-assessed their level of anxiety, 29 considered themselves as anxious (NRS \geq 5/10). These patients had on average a 5-fold higher risk for SAPP compared with "calm" people (NRS \geq 5/10) (Fig. 4).

Intraoperative fentanyl consumption indicated a weak but statistically significant correlation with postoperative pain intensity (r = 0.26 [95CI 0.11 to 0.40], p = 0.0008, Pearson test) (Fig. 5). Implicitly, a longer intervention inevitably leads to higher intraoperative total opioid consumption. However, duration of surgery, *per se*, did not correlate with postoperative pain intensity (r = -0.10, p = 0.46, Pearson test).

Table 1. PCS score cut-off values based on histograms and their role in determining of SAPP risk

Cut-off value	OR	RR	Sensit. (%)	Specif. (%)	PPV (%)	NPV (%)	LR	р
PCS (tot) = 27	1.51 0.62-3.65	1.16 0.86-1.56	25 16-36	82 68-91	69 49-85	40 31-51	1.38	0.39
PCS (amp) = 6	2.26 0.82-6.13	1.28 0.98-1.66	28 19-40	85 70-94	78 58-91	39 29-50	1.89	0.16
PCS (rum) = 10	1.82 0.66-5.0	1.21 0.91-1.60	24 15-36	85 70-94	75 53-90	38 28-49	1.62	0.33
PCS (hel) = 12	2.25 0.82-6.13	1.28 0.98-1.66	28 18-40	85 70-94	78 58-91	39 29-50	1.89	0.16

PCS – pain catastrophizing scale, PCS (tot) – PCS total score, PCS (amp) – PCS sub-score amplification, PCS (rum) – PCS sub-score rumination, PCS (hel) – PCS sub-score helplessness, SAPP – severe acute postoperative pain, OR – Odds ratio, RR – relative risk, PPV – predictive positive value, PNV – predictive negative value, LR – likelihood ratio. Data are presented as mean and 95% confidence intervals (95% CI)

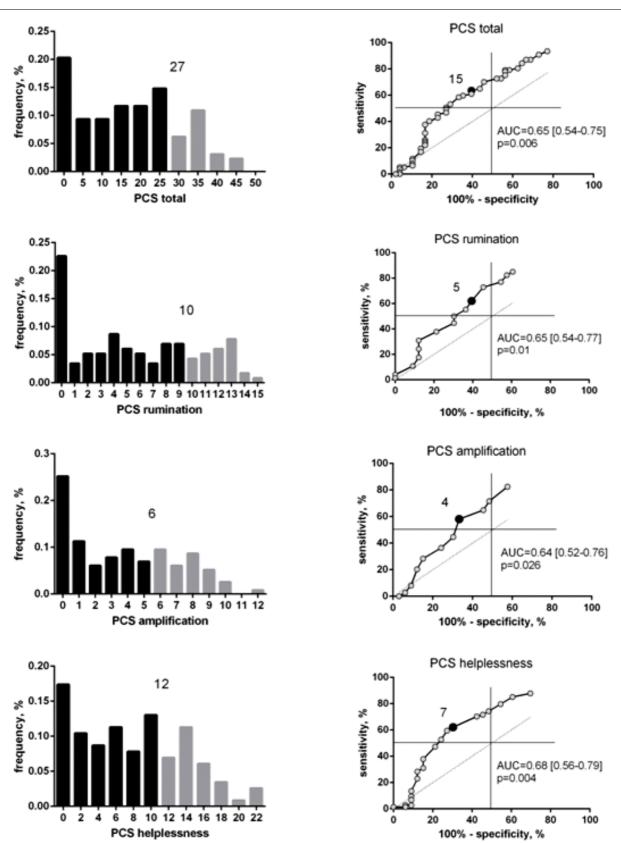


Fig. 2. Appreciation of cut-off values "catastrophizers" vs. "noncatastrophizers" based on histograms (left) and ROC curves (right) for PCS total score and its components (rumination, amplification and helplessness) in patients experiencing severe acute postoperative pain. The cut-off values indicated on the histogram corresponds to the percentile 75 (Q3) of the data series, and on the ROC curves – to values of closest point of the upper left corner of the quadrant. PCS – Pain Catastrophizing Scale, AUC – area under

Table 2. PCS score cut off-values based on ROC curves and their role in determining of SAPP	heir role in determining of SAPP risk	curves and t	on ROC	based	off-values	Fable 2. PCS score cut	Tab
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Cut-off value	OR	RR	Sensit. (%)	Specif. (%)	PPV (%)	NPV (%)	LR	р
PCS (tot) = 15	2.34 1.13-4.83	1.38 1.04-1.84	62 50-72	59 44-73	71 59-82	48 35-62	1.51	0.029
PCS (amp) = 4	2.66 1.15-6.15	1.44 1.06-1.97	53 40-66	70 53-83	73 58-85	49 36-63	1.77	0.026
PCS (rum) = 5	2.31 1.04-5.11	1.33 1.01-1.75	55 43-67	65 48-79	75 61-85	44 31-58	1.58	0.0496
PCS (hel) = 7	3.34 1.47-7.60	1.51 1.14-2.0	59 47-70	70 53-83	78 65-88	48 35-62	1.96	0.0055

PCS – pain catastrophizing scale, PCS (tot) – PCS total score, PCS (amp) – PCS sub-score amplification, PCS (rum) – PCS sub-score rumination, PCS (hel) – PCS sub-score helplessness, ROC – receiver operating characteristic, SAPP – severe acute postoperative pain, OR – Odds ratio, RR – relative risk, PPV – predictive positive value, PNV – predictive negative value, LR – likelihood ratio. Data are presented as mean and 95% confidence intervals (95% CI)

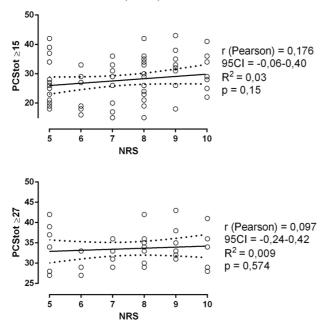


Fig. 3. Lack of correlation between pain catastrophizing scale cut-off values of \geq 15 (top) and \geq 27 (bottom) and severe acute postoperative pain. 95CI – 95% confidence interval, NRS – numeric rating scale, PCStot – pain catastrophizing scale total score

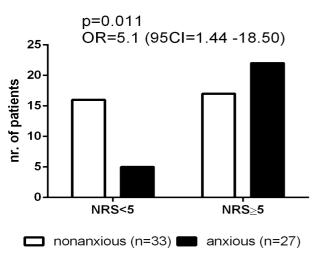


Fig. 4. Anxiety – an important risk factor for acute severe postoperative pain. OR – Odds ratio, 95CI – 95% confidence interval, NRS – numeric rating scale

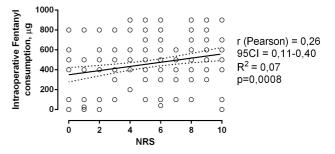


Fig. 5. A weak but statistically significant correlation between intraoperative fentanyl consumption and postoperative pain intensity. NRS – numeric rating scale

Discussion

Pain catastrophizing perception is an exaggerated negative mental state, induced by current or anticipated painful experience. It permits identification of the person's catastrophic thinking associated with pain. It consists of 13 items rated from 0-4 [20].

According to Sullivan et al., the cut-off value for PCS score for "catastrophizers" vs "noncatastrophizers" is 30 points, which corresponds to the 75th percentile (third quartile, Q3) in the series of data used for validation [20]. It should be mentioned that this cut-off value was set based on patients with chronic pain, so that may render the score less usefull in patients with acute pain. To the best of our knowledge, the cut-off values for patients with acute pain have not yet been determined and validated. For this reason, we tried to determine the cut-off values for both PCS total score and PCS sub-scores on our own data series, using two methods: the construction of ROC curves and identification of the value of the 75th percentile (Q3) on the histogram.

The intensity of postoperative pain is mainly determined by the type of surgery and the degree of adherence to an analgesic protocol. However, nonmedical factors (TV watching, visits of the relatives, mobilization) may have a significant influence on pain perception. Therefore, the follow-up time was chosen arbitrarily at 24 hours postoperatively, because we considered this period to be sufficient for the patient to get an opinion about the pain experience. A similar approach (without specifying the optimal timing for recording postoperative pain intensity) was used in the multicenter study "Pain Out" of the European Society of Anaesthesiology (http://www.pain-out.eu).

The most significant finding in our study was the identification of cut-off values for PCS score and of PCS sub-scores in acute pain settings. Based on this threshold values, we tried to determine whether pain catastrophizing and anxiety could be considered risk factors for severe postoperative pain. However, the obtained SAPP proportion, based on total PCS score cut-off value ≥ 15 seems to be discordant with the results shown in Table 2, which indicated a two-fold risk for these patients. We presume that the explanation lies in the low sensitivity and specificity of the PCS score in discriminating those patients with SAPP. Regardless, the conclusion is that we have been unable to demonstrate a relationship between pain catastrophizing and postoperative intense pain in patients undergoing abdominal surgery.

Anxiety, depression, pain catastrophizing, anger, and pessimism amplify postoperative pain intensity and increase the incidence of PPP [21, 22]. In their metaanalysis, Munafo and Stevenson showed that 9 of 11 analyzed studies proved a strong relationship between preoperative anxiety and chronic postoperative pain, regardless of the type of surgery [23]. Recently, Forsythe et al. demonstrated the important role of pain catastrophizing in the persistence of postoperative pain beyond 2 years after surgery [24]. Sullivan et al. explain this phenomenon by person's "cognitive awareness" [25].

Our study has several limitations. It is noteworthy that of the 412 patients who signed informed consent and received the PCS questionnaire, almost 60% (n = 236 patients) did not answer the survey. This is emblematic of both our continued failure of efficient institutional communication with our patients, and of the public distrust in the medical system. It is difficult to assess whether the prevalence of anxiety and pain catastrophizing in the group of nonresponders was similar with that among the patients who completed the study.

It is difficult to explain the discrepancy between the cut-off values of PCS total score and PCS subscores, identified by histograms and ROC curves. However, the area under the ROC curves is too small and cannot be used to support a higher accuracy of the cut-off values provided by ROC curves vs those provided by the 75th percentile on histograms.

We reiterate that measurements based on the cutoff values obtained from the histogram did not reach the statistical significance. Study sample size was calculated based on the assumption that only 10% of the population without chronic pain would manifest hypervigilance towards pain. In fact, the proportion of "pain catastrophizers" in the study cohort was 23% (based on PCS total score with a cut-off value of 27 points, corresponding to the 75th percentile on histogram). Using this 23% proportion, at least 269 patients would have needed to be enrolled in order to assure sufficient statistical power. Nevertheless, our data allow us to conclude the following:

- 1. Anxiety was a significant risk factor for severe acute postoperative pain.
- 2. Intraoperative fentanyl consumption correlated with the intensity of postoperative pain, although duration of surgery did not.
- 3. The studied cohort did not allow establishing a relationship between pain catastrophizing and postoperative intense pain in patients undergoing abdominal surgery. Further studies are needed on larger samples of patients.

Conflict of interest

Nothing to declare

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Anxietatea, dar nu și percepția catastrofică a durerii, reprezintă un factor de risc pentru durerea postoperatorie intensă: un studiu prospectiv, observațional, de cohortă

Rezumat

Introducere: În prezent, prevalența durerii postoperatorii acute intense (DPOI), scor de durere postoperator $\geq 5/10$ pe scala numerică a durerii (NRS), rămâne înaltă, de 24%-46% în Europa de Vest, și de 64% în Republica Moldova.

Scopul lucrării: A fost verificarea ipotezei conform căreia anxietatea și percepția catastrofică a durerii (interpretată ca hipervigilență) reprezintă factori de risc pentru DPOI.

Material și metode: Cu avizul Comitetului de Etică și cu acordul informat scris, 176 de pacienți, supuși chirurgiei abdominale în anestezie generală, au completat preoperator chestionarul cu Scorul de Percepție Catastrofică a durerii (PCS) (*Pain Catastrophizing Scale*) și și-au estimat nivelul anxietății pe scala numerică (NRS), între 0 (lipsa anxietății) și 10 (anxietate maxim imaginabilă). Au fost înregistrate: durata intervenției chirurgicale, consumul intraanestezic de fentanyl și intensitatea durerii la 24 de ore postoperator (NRS). Analiza statistică a cuprins: odds ratio (OR), riscul relativ (RR), valorile predictive pozitive (VPP) și cele negative (VPN), verosimilitatea, curbele ROC, testul de corelatie Pearson.

Rezultate: Pacienții "hipervigilenți" nu au prezentat un risc sporit pentru DPOI în cazul calculelor efectuate în baza histogramelor (OR = 1,51 [95CI = 0,62-3,65], p = 0,39), dar riscul a fost crescut în baza analizei curbelor ROC (OR = 2,34 [1,13-4,83], p = 0,0029). Anxietatea a crescut, în medie, de 5 ori riscul DPOI (OR = 5,1 [95CI = 1,44-18,50], p = 0,011). Consumul intraoperator de fentanyl s-a corelat cu intensitatea durerii (Pearson r = 0,26; p = 0,0008), dar nu și durata intervenției (Pearson r = -0,10; p = 0,46).

Concluzii: Anxietatea, spre deosebire de hipervigilență, a reprezentat un factor de risc semnificativ pentru DPOI. Consumul intraoperator de fentanyl s-a corelat cu intensitatea durerii postoperatorii.

Cuvinte-cheie: factori de risc, durere severă postoperatorie, anxietate, hipervigilență

Appendix

PAIN CATASTROPHIZING SCALE

(According to Sullivan M, 2009 [26])

Patient's code: [][][][][][][][] [] Male [] Female Age: Date:

Everyone experiences painful situations at some point in their lives. Such experiences may include head a ches, to oth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

Points	0	1	2	3	4
Signification	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time

When	ľm	in	pain
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Item		Points:
1	I worry all the time about whether the pain will end.	
2	I feel I can't go on.	
3	It's terrible and I think it's never going to get any better.	
4	It's awful and I feel that it overwhelms me.	
5	I feel I can't stand it anymore.	
6	I become afraid that the pain will get worse.	
7	I keep thinking of other painful events.	
8	I anxiously want the pain to go away.	
9	I can't seem to keep it out of my mind.	
10	I keep thinking about how much it hurts.	
11	I keep thinking about how badly I want the pain to stop.	
12	There's nothing I can do to reduce the intensity of the pain.	
13	I wonder whether something serious may happen.	
	Total:	