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Natalia Belîi

INTENSE POSTOPERATIVE PAIN — RISK FACTORS AND PREVENTION: PROSPECTIVE, COHORT STUDY

Chair of Anesthesiology and Reanimatology "Valeriu Ghereg", Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

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Наталья Белий

ИНТЕНСИВНАЯ ПОСЛЕОПЕРАЦИОННАЯ БОЛЬ — ФАКТОРЫ РИСКА И ПРОФИЛАКТИКА: ПЕРСПЕКТИВНОЕ, КОГОРТНОЕ ИССЛЕДОВАНИЕ

Введение. Неадекватное обезболивание в раннем послеоперационном периоде является широко распространенным явлением, которое поражает пациентов как в краткосрочной, так и долгосрочной перспективе, а интенсивная острая послеоперационная боль, как известно, — доказанный фактор риска для хронификации боли. Возможность точно оценивать и прогнозиро-

вать риск развития интенсивной острой послеоперационной боли позволила бы предупредить хронификацию. Как правило, интенсивная острая послеоперационная боль ассоциируется с женским полом, возрастом < 55 лет, предоперационной болью и приемом анальгетиков, психоэмоциональным состоянием. В данной работе были исследованы ряд новых параметров на предмет их явления факторами риска (например, хирургическое вмешательство в ночное время, отсрочка операции, факторы окружающей среды, такие как искусственное или дневное освещение в послеоперационном периоде и т. д.).

Материал и методы. Прогнозное/перспективное, обсервационное, когортное исследование с согласием Научно-исследовательского Комитета по этике, а также пациента. В когорту были включены 296 совершеннолетних пациентов, I–II по шкале ASA. Проведен статистический анализ 292 полностью заполненных карт данных пациентов. Были зарегистрированы антропометрические параметры, тип операции, продолжительность анестезии, продолжительность хирургического вмешательства и ряд параметров, проверенных на предмет явления факторами риска для интенсивной послеоперационной боли (предоперационные, операционные и послеоперационные), которые непосредственно связаны с пациентом, с самим медицинским действием или назначенными лекарствами. Используемое статистическое программное обеспечение: GraphPad Prism, версия 6 (Graph Pad Software Inc., CA, США).

Результаты. Изучаемая хирургическая популяция однородна по массе тела, росту, продолжительности анестезии, хирургическому вмешательству и гендерно гетерогенна (преимущественно женщины), а также по типу операций (44,9 % — лапароскопическая холецистэктомия). Факторы риска для острой интенсивной послеоперационной боли: психоэмоциональное состояние (депрессия (RR=4,9; [95 % CI: 2,0–11,7], p=0,0093), предоперационная тревога (RR=6,6; [95 % CI: 3,3–13,2], p<0,0001), пессимизм (RR=6,4; [95 % CI: 2,9–13,8], p=0,001), страх боли (RR=3,0; [95 % CI: 1,4–6,4], p=0,0043)), катастрофизация боли (Шкала катастрофизации Боли ≥ 27) (RR=5,0; [95 % CI: 1,7–14,8], p=0,0033); наличие интенсивной предоперационной боли (RR=5,1; [95 % CI: 2,4–10,6]); предоперационное использование анальгетиков (RR=5,5; [95 % CI: 2,2–14,2], p=0,0156); острая интенсивная боль при пробуждении после анестезии (RR=4,6; [95 % CI: 2,2–9,5], p=0,0003); послеоперационная тревога (RR=5,0; [95 % CI: 2,2–11,2], p=0,0037); нейропатический компонент острой послеоперационной боли (RR=5,0; [95 % CI: (1,2–5,2), p=0,0225); послеоперационная рвота (RR=4,4; [95 % CI: 1,8–10,9], p=0,0130); кишечный парез ≥ 48 ч (RR=7,8; [95 % CI: 3,5–17,8], p=0,0050); послеоперационная сонливость (RR=2,6; [95 % CI: 1,1–5,95], p=0,0414); послеоперационная бессонница (RR=8,1; [95 % CI: 4,1–15,9], p<0,0001) и лихорадка ≥ 38 °C (RR=4,9; [95 % CI: 2,0–11,8], p=0,0092).

Выводы. Плохой психоэмоциональный статус пациента, наличие интенсивной предоперационной боли, предоперационное использование анальгетиков и острая интенсивная боль при пробуждении после анестезии являются факторами риска для интенсивной послеоперационной боли. Длительная операция чревата использованием больших доз опиоидов и, как следствие, наблюдаются особо неблагоприятные явления, включая индукцию гипералгезии и острой интенсивной послеоперационной боли.

Ключевые слова: острая послеоперационная боль, факторы риска.

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Natalia Belîi

INTENSE POSTOPERATIVE PAIN — RISK FACTORS AND PREVENTION: PROSPECTIVE, COHORT STUDY

Introduction. Inadequate management of postoperative pain (POP) is a widespread phenomenon, that affects the patient both in the short and long term of surgery, and the intense postoperative pain (IPOP) is known to be a risk factor for chronification of pain. The ability to accurately assess and forecast the risk of developing an IPOP, would allow us a preemptive approach of this problem. IPOP

was associated with female gender, age < 55 years, pain and use of analgesics in preoperative, psychoemotional condition. In this study, there was investigated the quality of risk factor of a number of new proposed parameters (eg., night surgery, postponing the intervention, environmental factors such as artificial or natural illumination in the postoperative period, etc.).

Material and methods. Prospective, observational, cohort study. Research Ethics Committee and eligible patient's agreement — obtained. There were enrolled adult patients, ASA I–II. Complete data of 292 cards of patients were analyzed. There recorded anthropometric parameters, type of intervention, duration of anesthesia, duration of intervention and a set of hypothetical parameters, tested as risk factors for IPOP — factors (preoperative, intraoperative and postoperative) that are directly related to the patient or the medical act itself and the administered medication. Statistical software were used: GraphPad Prism, version 6 (Graph Pad Software Inc., CA, USA).

Results. Studied surgical population — homogeneous in terms of body mass, height, duration of anesthesia and surgical intervention; gender (predominantly women) and by type of surgery (44.9% laparoscopic cholecystectomies). Risk factors for IPOP: psychoemotional condition (depression (RR=4.9; [95% CI: 2.0–11.7], p=0.0093), preoperative anxiety (RR=6.6; [95% CI: 3.3–13.2], p<0.0001), pessimism (RR=6.4; [95% CI: 2.9–13.8], p=0.001), fear of pain (RR=3.0; [95% CI: 1.4–6.4], p=0.0043), hypervigilance personality (PCS=27), (RR=5.0; [95% CI: 1.7–14.8], p=0.0033); intense preoperative pain (RR=5.1; [95% CI: 2.4–10.6]; use of analgesics in preoperative (RR=5.5; [95% CI: 2.2–14.2], p=0.0156); intense pain on waking from anesthesia (RR=4.6; [95% CI: 2.2–9.5], p=0.0003); postoperative anxiety (RR=5.0; [95 Cl: 2.2–11.2], p=0.0037); acute neuropathic pain following surgery (RR=5.0; [95% CI: (1.2–5.2); p=0.0225); postoperative vomiting (RR=4.4; [95% CI: 1.8–10.9], p=0.0130); intestinal paresis = 48 hours (RR=7.8; [95% CI: 3.5–17.8], p=0.0050); postoperative sleepiness (RR=2.6; [95% CI: 1.1–5.95], p=0.0414); postoperative insomnia (RR=8.1; [95% CI: 4.1–15.9], p<0.0001) and fever = 38°C (RR=4.9; [95% CI: 2.0–11.8], p=0.0092).

Conclusions. Patient's altered psycho-emotional status, intense pre-operative pain, preoperative analgesic use, and IPOP at awakening from anesthesia, are risk factors for IPOP. The long-term intervention, which involves a comparatively higher consumption of opioids, precipitates in specific adverse events, including the induction of hyperalgesia and IPOP.

Key words: acute postoperative pain, risk factors.

Introduction

The discovery of sedating gases such as ether, chloroform and nitrous oxide, marks the beginning of a new era — where pain associated with surgery is no longer an inevitable fact. With innovations in anesthesia and surgery, the pharmaceutical (synthesis of morphine, aspirin) and technological (syringe invention) industry proposed new tools for pain management. However, even today, a large proportion of patients still experience intense postoperative pain (IPOP).

The International Association for the Study of Pain (IASP) defines pain as an "unpleasant sensory and emotional experience, determined or related to a real or potential tissue lesion, or described in terms of such injury". Although, these terms are not found in the IASP taxonomy, chronologically, pain can be classified as acute and chronic. With regard to postoperative pain (POP), acute pain signifies the initial phase of the pathophysiological cascade, triggered by tissue damage and which, usually resolves as the postoperative wound heals. With the remark that this healing time may be variable, however, a large number of patients complains of persistent postoperative pain (PPOP), even after complete healing of the surgical lesion.

Although the arsenal of analgesics and anesthetic techniques are increasing, still reported unreasonably high prevalence of moderate or severe POP: 70% (2003) [1], 41% (2008) [2], 29.6–55% (2010) [3], 62% (2015) [4].

Risk factors and prevention strategies are still a hot topic of debate [5]. The most important reported predictors are: female sex [6], age [7], psychosocial factors [5], pain anamnesis: linked with present surgery or other localization [5]; type of surgery. The most commonly mentioned intraoperative factors are major surgery and general anesthesia [2]. IPOP induces anxiety and helplessness, depression, sleep disturbances, delayed recovery, prolonged stay in the hospital and increases the risk of developing PPOP.

It has been estimated, that in current economic and medico-social realities, 5–10% of the population underwent surgery every year and risk to have a IPOP experience. To point out the existence of this problem, 2017, the current year, was declared by IASP as the *"Global Year Against Postoperative Pain"*.

The purpose of the paper was to test the quality of risk factors for a series of perioperative parameters (patient-related, linked with the process of medical care or medication itself) for the development of IPOP.

Material and methods

Design and parameters of the study

The prospective, observational, cohort study, was conducted in March 2011 — April 2012 in Clinic of Anesthesia and Reanimation of the Medicine Institute of Emergency from Chisinau (Republic of Molcdova) and enrolled 296 patients. The research protocol was approved by the Research Ethics Committee (REC) of the Nicolae Testemitanu State University of Medicine and Pharmacy (registered with No. 2 of 09.12.2010. President of the REC — Prof. Mihai Gavriliuc). All enrolled patients signed the informed consent to participate in the study.

Participants

There were evaluated for eligibility 608 pacients; 312 of them were excluded. On the first postoperative day, were enrolled 296 patients. During primary 24 hours follow-up — 4 patients missed. Complete data of 292 cards analyzed. The CONSORT flow chart of enrolled patients is shown in Fig. 1.

The study inclusion criteria were:

— adult patient (≥18 years) without preexisting chronic pain;

— signing the informed consent to participate in the study;

— ASA I-II;

— patients' ability to understand and answer questions in the questionnaire in their native language;

— abdominal surgery and locomotor apparatus;

— minimum presence of 6 hours in the surgical unit (after transfer from the recovery room).

Exclusion criteria in the study were:

— patient's desire to leave the study;

— failure to complete the questionnaire.

After receiving the informed consent, personal and clinical data such as comorbidities, preadmission analgesic therapy, type of surgery and details of anaesthesia were completed in the study record of the patient. On the day before surgery, patients completed the Pain Catastrophizing Scale (PCS). In the first 24 hours, patients assessed their pain with visual numeric scale (VNS) and completed internationally validated pain evaluation questionnaires, offered for completion in their native language (Romanian, Russian): PCS (Pain Catastrophizing Scale), DN4Interview (diagnosis questionnaire for neuropathic pain, fr. *Douleur Neuropathique*). A value of VNS≥5 was considered as IPOP. The chronology of recording parameters is shown in the study diagram (Fig. 2).

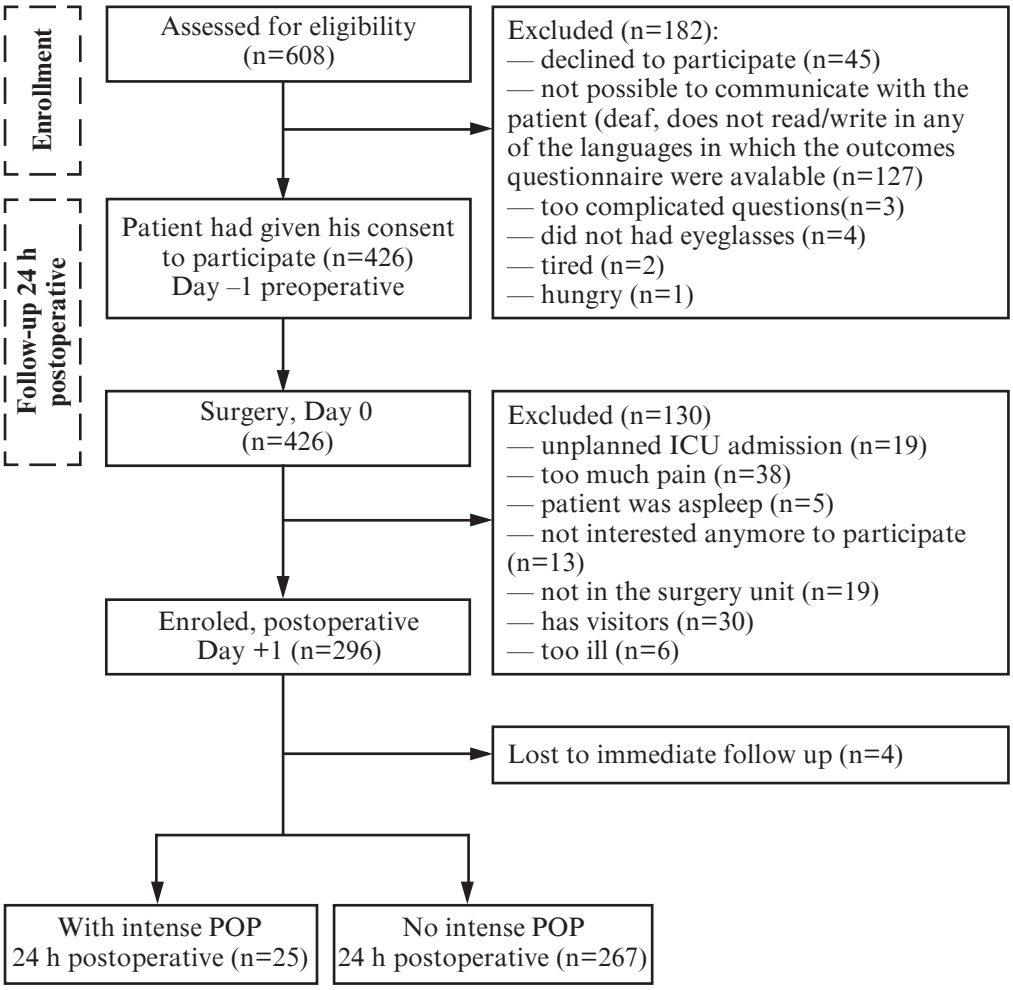

Fig. 1. CONSORT flow diagram of enrolled patients

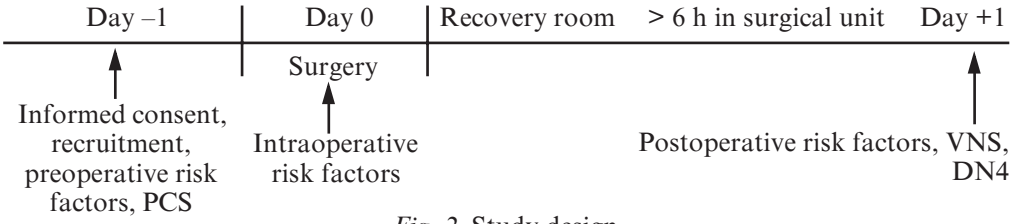

Fig. 2. Study design

The PCS questionnaire consists of 13 items, each being rated between 0 (never) and 4 (all time), the total score ranging from 0 to 52. PCS can be split into three other subscores by summarizing the items, specific to each emotional state: magnification (6, 7, 13 items), rumination (8–11 items) and helplessness (1–5, 12 items). A PCS score ≥ 27 denotes a hypervigilant personality. Magnification, rumination and helplessness were reported at ≥ 5, ≥ 11, ≥ 13.

DN4 Interview is the adapted form for self-assessment of the DN4 Neuropathic Pain Diagnosis Questionnaire and consists of 7 characteristics, marked "yes" (presence) or "no" (absence), assuming a patient's self-assessment of the sensations. A DN4≥4 score indicates a neuropathic pain.

Anesthetic assistance

Both, programmed (laparoscopic cholecystectomies) and emergency surgeries (appendectomies) received general inhalation anesthesia. Patients who have been scheduled for inguinal hernioplasty and knee arthroscopy, have received spinal anesthesia and/or epidural anesthesia. Postoperative analgesia was provided by the combination of NSAIDs and opioids (Table 1). In the hospital where this study was conducted, there is no Acute Pain Therapy Unit, so, in postoperative, analgesics have been prescribed according to the preference of each physician individually. We mention that 2 NSAIDs has not been combined.

Recorded parameters and statistical analyis

The recorded general parameters were: age, gender, height, body mass, type of intervention, duration of anesthesia, duration of intervention. Tested parameters as risk factors were: preoperative, intraoperative and postoperative, directly related to the patient or medical act and the administered medication — their nominal detalization is presented in Table 3. The parameter values were numbered in the Excel table and then imported in the statistical analysis software *GraphPad Prism, version 6, (Graph Pad Software Inc.,* CA, US). Data are presented as absolute and relative values, or average and 95% confidence interval of the mean. There have been calculated the relative risk (RR), sensitivity (Se), specificity (SP), positive prediction value (PPV), negative predictive value (NPV), and the veridicity report (VR). A value of $p<0.05$ was considered statistically significant.

Results

The overall characterization of patients enrolled in the study, is presented in Table 2. The studied population was homogeneous after body mass and height and heterogenous by gender distribution. The mean duration of anesthesia (minutes) 114.2 (extreme: 30–300), [95% CI: 109.1–119.2] and mean duration of surgery (minutes) was 48.6 (extreme: 10–160), [95% CI: 45.8–51.5].

The studied surgical populations were: abdominal surgery — laparoscopic cholecystectomy (133/296 [44.9%]), appendectomy (105/296 [35,5%]), inguinal hernioplasty (30/296 [10.1% hysterectomy (6/296 [2.0%]); surgery of the locomotor — knee arthroplasty (4/296 [1.4%], amputation fingers of the upper/lower member (6/296 [2.0%]), knee arthroscopy (12/296 [4.1%]).

The main outcome parameters of the study were a number of supposed risk factors that were investigated in the hypothesis of understanding whether their perioperative presence would be associated with IPOP in the immediate postoperative period (see Table 3). From the preoperative parameters, directly related to the patient, were confirmed as a risk factor for IPOP: psychoemotional factors (depression, anxiety, pessimism, fear of pain) and personality of the patient (hypervigilant personality, emotional states of PCS subscore: magnification, rumination, helplessness), intense preoperative pain and use of analgesics before sugery, intense pain when waking up from anesthesia. From postoperative risk factors for IPOP, were confirmed postoperative anxiety, intense pain when awakening from anesthesia, acute neuropathic pain following surgery and postoperative pathophysiological factors of postsurgical period (vomiting, intestinal paresis ≥48 hours, fever ≥38°C, sleepiness and postoperative insomnia).

Table 1

Local anesthetic doses, NSAIDs and opioid analgesic, used for postoperative analgesia

Drug	Single dose	Administ-ration way	24 hours sockets	Comments
NSAIDs				
Ketorolak	30 mg	i.m.	1–3 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Ketoprophene	100 mg	i.m.	1–2 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Dexketoprophene	50 mg	i.m.	1–3 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Dexalgin	50 mg	i.m.	1–2 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Metamizole	1000 mg	i.m.	1–3 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Plenalgin*	5 ml	i.m.	1–3 time/ 24 hours	Intra-anesthetic, wound closure, then — in the surgical unit
Opioid analgesics				
Promedolum	20 mg	i.m.	1 time/ 24 hours	In the postoperative surveillance unit
Morphine	2 mg	i.v.	at VNS≥5	In the postoperative surveillance unit, with pain reassessment at 5-10 min and repeating boluses until VNS=4
Tramadol	100 mg	i.m.	1–3 time/ 24 hours	In the postoperative surveillance unit as well as in the surgical unit
Omnoponi*	2% 1 ml	i.m.	1 time/ 24 hours	In the postoperative surveillance unit
Local anesthetics				
Bupivacaine	5 ml/h 0,25%	Epidural space		In the postoperative surveillance unit
Lidocaine	5 ml/h 0,5%	Epidural space		In the postoperative surveillance unit

Note. Combinations between NSAIDs and opioids in the studied series were random, * — complex drug.

Table 2

Personal data of patients enrolled in the study

Parameter	Values
Age, years	38,0 (18–80), [95% CI: 36,4–39,6]
18–24	67/296 (22.6%)
25–44	123/296 (41.6%)
45–64	103/296 (34.8%)
> 65	3/296 (1.0%)
Distribution by gender m/f	96/296 (32.4%)/200/296 (67.6%), raportul: 1/2,1
Body mass, kg	74,5 (26–126), [95% CI: 72.7–76.3]
BMI<30	214/258 (83%)
BMI>30 (obesity)	43/258 (17%)
Height, cm	169.0 (150–193.0), [95CI: 168.0–169.8]

Note. The data are presented as absolute and relative or average values and confidence interval — 95% CI.

Table 3

Perioperative risk factor quality testing for IDPO (VNS≥5)

Parameters	RR	Se	Sp	PPV	NPV	VR	p
Depression	4.9 (2.0–11.7)	0.16 (0.05–0.36)	0.97 (0.95–0.99)	0.36 (0.11–0.69)	0.93 (0.89–0.95)	6.1	0.0093
Perioperative pain > 5 VNS	5.1 (2.4–10.6)	0.56 (0.35–0.76)	0.83 (0.78–0.88)	0.24 (0.14–0.37)	0.95 (0.92–0.98)	3.4	< 0.0001
Anxiety	6.6 (3.3–13.2)	0.36 (0.18–0.58)	0.95 (0.91–0.97)	0.39 (0.20–0.62)	0.94 (0.91–0.97)	6.8	< 0.0001
Insomnia	3.5 (1.2–9.8)	0.12 (0.03–0.31)	0.97 (0.94–0.99)	0.27 (0.06–0.61)	0.92 (0.88–0.95)	4.0	0.0589
Pessimistic pacient	6.4 (2.9–13.8)	0.20 (0.07–0.41)	0.98 (0.95–0.99)	0.46 (0.17–0.77)	0.93 (0.89–0.96)	8.9	0.001
Fear of pain	3.0 (1.4–6.4)	0.62 (0.41–0.80)	0.68 (0.62–0.74)	0.16 (0.09–0.25)	0.95 (0.91–0.98)	1.9	0.0043
Intense pain at awakening from anesth	4.6 (2.2–9.5)	0.40 (0.21–0.61)	0.90 (0.86–0.93)	0.27 (0.14–0.44)	0.94 (0.91–0.97)	4.0	0.0003
Absence of psychosocial support	3.2 (1.1–9.1)	0.12 (0.03–0.31)	0.97 (0.94–0.98)	0.25 (0.06–0.57)	0.92 (0.88–0.95)	3.6	0.0734

Continuation of the table 3

Parameters	RR	Se	Sp	PPV	NPV	VR	p
Delayed intervention	2.7 (0.8–9.8)	0.08 (0.01–0.26)	0.97 (0.95–0.99)	0.22 (0.03–0.60)	0.92 (0.88–0.95)	3.0	0.1757
Perioperative analgesics	5.5 (2.2–14.2)	0.12 (0.03–0.31)	0.99 (0.96–1.00)	0.43 (0.10–0.82)	0.92 (0.89–0.95)	8.0	0.0156
Age < 55 years	1.9 (0.6–6.2)	0.88 (0.69–0.97)	0.21 (0.2–0.27)	0.10 (0.06–0.14)	0.95 (0.86–0.99)	1.1	0.4362
NSAIDs at the end of intervention	3.5 (1.0–12.1)	0.08 (0.01–0.26)	0.98 (0.96–0.99)	0.29 (0.04–0.71)	0.92 (0.88–0.95)	4.2	0.1147
Increased risk of thrombotic complications	2.2 (0.6–8.2)	0.08 (0.01–0.26)	0.96 (0.94–0.98)	0.18 (0.02–0.52)	0.92 (0.88–0.95)	2.4	0.2417
Total intravenous anesthesia	1.3 (0.2–9.1)	0.06 (0.001–0.27)	0.96 (0.92–0.98)	0.10 (0.003–0.45)	0.93 (0.88–0.96)	1.4	0.5517
Emergengy intervention	0.6 (0.3–1.4)	0.76 (0.55–0.90)	0.15 (0.11–0.20)	0.08 (0.05–0.12)	0.87 (0.74–0.95)	0.9	0.2508
Locoregional anesthesia	1.1 (0.5–2.4)	0.38 (0.19–0.59)	0.64 (0.58–0.70)	0.09 (0.04–0.16)	0.92 (0.87–0.95)	1.04	1.0000
Neuraxial anesthesia	4.1 (1.2–13.6)	0.08 (0.01–0.26)	0.99 (0.96–0.99)	0.33 (0.04–0.78)	0.92 (0.88–0.95)	5.3	0.0864
Duration of the intervention ≥ 60 min	1.3 (0.5–3.5)	0.16 (0.05–0.36)	0.87 (0.83–0.91)	0.11 (0.03–0.25)	0.92 (0.88–0.95)	1.3	0.5478
Duration of the intervention ≥ 120 min	1.0 (0.4–2.3)	0.28 (0.12–0.49)	0.72 (0.66–0.78)	0.09 (0.04–0.17)	0.91 (0.87–0.95)	1.0	1.0000
Intraoperative use of thiopental	0.0 (infinity)	0.0 (0.0–0.14)	0.97 (0.94–0.99)	0.0 (0.0–0.37)	0.91 (0.87–0.94)	0.0	1.0000
Intraoperative use of ketamine	1.1 (0.4–2.8)	0.8 (0.59–0.93)	0.21 (0.17–0.27)	0.09 (0.05–0.13)	0.92 (0.82–0.97)	1.0	1.0000
Fentanyl ≥ 1000 μg intraoperative	0.0 (infinity)	0.0 (0.0–0.14)	0.98 (0.96–0.99)	0.0 (0.0–0.52)	0.91 (0.87–0.94)	0.0	1.0000

Continuation of the table 3

Parameters	RR	Se	Sp	PPV	NPV	VR	p
Waking from anesthesia ≥ 60 min	0.7 (0.20–2.11)	0.13 (0.03–0.32)	0.82 (0.76–0.86)	0.06 (0.01–0.16)	0.91 (0.87–0.94)	0.7	0.5580
Incision ≥ 10 cm	2.4 (0.99–6.0)	0.2 (0.07–0.41)	0.92 (0.88–0.95)	0.19 (0.06–0.38)	0.92 (0.89–0.95)	2.4	0.0672
Postoperative anxiety	5.0 (2.2–11.2)	0.2 (0.07–0.04)	0.97 (0.94–0.98)	0.36 (0.13–0.65)	0.93 (0.89–0.96)	5.9	0.0037
Postoperative vomiting	4.4 (1.8–10.9)	0.16 (0.05–0.40)	0.97 (0.94–0.99)	0.33 (0.10–0.65)	0.93 (0.89–0.95)	5.3	0.0130
Postoperative nausea	2.1 (0.96–4.46)	0.36 (0.18–0.58)	0.8 (0.75–0.85)	0.15 (0.07–0.26)	0.93 (0.89–0.96)	1.8	0.0745
Intestinal paresis ≥ 48 hours	7.8 (3.5–17.8)	0.12 (0.03–0.31)	0.99 (0.97–0.99)	0.60 (0.15–0.95)	0.92 (0.88–0.95)	16.0	0.0050
Natural light	2.1 (0.9–4.7)	0.68 (0.47–0.85)	0.52 (0.45–0.58)	0.12 (0.07–0.18)	0.95 (0.89–0.98)	1.4	0.0926
Night light	1.1 (0.5–2.3)	0.44 (0.24–0.65)	0.58 (0.51–0.64)	0.09 (0.05–0.15)	0.92 (0.86–0.95)	1.0	1.0000
Postoperative drowsiness	2.6 (1.1–5.95)	0.24 (0.09–0.45)	0.90 (0.86–0.94)	0.19 (0.07–0.36)	0.93 (0.89–0.96)	2.5	0.0414
Postoperative insomnia	8.1 (4.1–15.9)	0.32 (0.15–0.54)	0.97 (0.94–0.99)	0.50 (0.25–0.75)	0.94 (0.90–0.96)	10.7	<0.0001
Fever ≥38°C postoperative	4.9 (2.0–11.8)	0.16 (0.05–0.36)	0.97 (0.95–0.99)	0.36 (0.11–0.69)	0.93 (0.89–0.95)	6.1	0.0092
Hypervigilant personality (PCS)	5.0 (1.7–14.8)	0.62 (0.32–0.86)	0.78 (0.72–0.84)	0.15 (0.07–0.28)	0.97 (0.93–0.99)	2.8	0.0033
DN4 postoperative	2.5 (1.2–5.2)	0.4 (0.21–0.61)	0.81 (0.8–0.9)	0.16 (0.08–0.28)	0.95 (0.89–0.96)	2.1	0.0225
Rumination	5.0 (1.6–15.6)	0.55 (0.23–0.83)	0.83 (0.77–0.88)	0.15 (0.06–0.30)	0.97 (0.93–0.99)	3.1	0.008

The end of the table 3

Parameters	RR	Se	Sp	PPV	NPV	VR	p
Magnification	3.3 (0.99–10.8)	0.64 (0.31–0.89)	0.67 (0.60–0.73)	0.10 (0.04–0.19)	0.97 (0.93–0.99)	1.9	0.0518
Helplessness	4.3 (1.4–13.5)	0.55 (0.23–0.83)	0.80 (0.74–0.85)	0.13 (0.05–0.27)	0.97 (0.93–0.99)	2.7	0.0149

Discussion

The present study aimed to test the risk factors for IPOP for a series of perioperative parameters.

In an absolutely natural way the studied surgical population included, predominantly, female subjects, and this could be explained by the predominance of laparoscopic cholecystectomies (44.9%) from all of interventions included in the study, biliary lithiasis being described more frequently in women.

In our study, the young age (< 55 years) did not confirm the quality of risk factors for IPOP. In the specialty literature, young age is reported as a risk factor, more dependent on the type of surgery (digestive, thoracic). On the contrary, for orthopedic interventions, age > 55 years has been found to be an aggravating factor for IPOP [8].

Although Sommer M. and colleagues (2008) [2] considered it as a factor in intensifying POP, in our study general anesthesia, was not as a risk factor for IPOP. Previous studies confirmed that the anesthetic technique does not appear to be a determinant of the IPOP.

Psychoemotional factors (fear of pain, expectation of pain, catastrophization) and preexisting preoperative pain were also confirmed by Sommer M. and colleagues (2010) [10] as important predictors for the IPOP. Hence, the importance of pre-anesthetic visit and patient education in terms of pain, self assessment of pain and it's management.

Urgent surgical interventions have not been associated more frequently with IPOP, although Adriaan Albertus Murray and his colleague (2016) [4] report the urgency of intervention as a risk factor for IPOP.

It appears that insomnia, which is detected in the pre-operative patient, tends to be a risk factor (p=0.0589) for IPOP and possibly could be confirmed in a larger sample of patients.

The strengths of the study are that it is a prospective, cohort study and based on internationally validated questionnaires.

Weak point of the study is the high rate of exclusion of patients from enrollment. A large proportion of the excluded patients in preoperative (Day -1) (127/182 [69.8%]) were due to the impossibility to communicate with the patient (hearing loss or because the patient can not understand/read/write in the languages in which the questionnaires were proposed). Another factor of bias is not clear what happened with that patients, who after their recruitment, were excluded on the first postoperative day (Day +1,) because they complained of IPOP (n=38) or they felt very sick (n=6), so they left the study.

One of the potential bias factors of this study is the question of whether different molecules and combinations of analgesics can have different efficacy. However, the differences in analgesic power between NSAIDs appear to be minor, and large samples of patients would be needed to identify them.

Another factor of bias, that we have to mention, is the fact that ladies were more receptive to the agreement to participate in the study. Caumo W. and colleagues (2002) and Adriaan Albertus Murray (2016) [4], reported female gender as an aggravating risk

factor for IPOP, but this has not been confirmed in our study. Moreover, Bisgaard T. and the team (2005) [9], analyzing the same risk factor on the laparoscopic cholecystectomy model, doubted this fact.

The intensity of acute POP is a demonstrated risk factor for PPOP. Taking into consideration that in a significant proportion of patients with PPOP it has neuropathic signs and simptoms, it seems logical to ask whether a higher intensity of pain experienced by some patients in the immediate postoperative period, does not indicate the development of acute neuropathic pain which, consequently, will remain chronic. And Martinez V. and colleagues [12] argue that an early neuropathic component of postsurgical pain is predictive for IPOP. In our study, patients, who were screened using the DN4 Interview questionnaire and were found as having acute neuropathic component of immediate POP also report higher POP intensities.

Vomiting, intestinal paresis ≥ 48 hours, and postoperative sleepiness, as postoperative risk factors for IPOP, should probably be interpreted more from the point of view of opioid consumption and their adverse effects, including that of the hyperalgesia induced by them. Postoperative insomnia, as a confirmed risk factor for IPOP, could be explained by the inadequate management of POP; and fever ≥38°C, as a risk factor for IPOP, could be just an indication of a complex surgical condition.

Montes A. (2012) [11] denies the impact of genetics on pain perception. Lately, the attention of research laboratories is geared towards epigenetic factors.

The ability to accurately assess and forecast the risk of developing of IPOP would allow us to be more effective in managing it.

Like many other predictive risk clinical tools, the risk factors for IPOP found in this study, are not specific. For the definitive elucidation of the subject of IPOP prognosis and prevention, are required further studies, that will propose new risk factors for further research and confirmation.

Conclusions

The patient's altered psychoemotional status (depression, preoperative anxiety, fear of pain, pessimism, hypervigilant personality), the existence of intense pre-operative pain, the use of analgesics in pre-operative — are risk factors for IPOP. The long-term interventions, associated with high opioid consumption represent a risk factor for IPOP, due to induced by opioids hyperalgesia.

Declaration of conflict of interests

The author declares lack of any conflict of interest (financial or nonfinancial) associated with this study.

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