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Research Article

Influence of Demographic Factors on Pain Perception and Postoperative Opioid Consumption

Abad-Torrent A[1]*, de Miguel M[1], Sanaú B[2], Cortiella P[1], Suescun MC[1], Suárez-Edo E[1]

[1]Department of Anesthesiology, Vall d'Hebron University Hospital, Barcelona, Spain

[2]Department of Research and Development, Quantium Medical - Mataró, Spain

***Corresponding author:** Abad-Torrent A, Department of Anaesthesiology and Resuscitation, University Hospital Vall d'Hebron - Barcelona, Spain

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Abstract

Purpose: The purpose of this study was to analyse the influence of demographic factors on pain perception and opioid consumption in patients undergoing robotic prostatectomy and laparoscopic hysterectomy.

Methods: A total of 93 patients were included in this observational, prospective study. A telephone interview was carried out after one month of the surgery. The patients were asked about demographic information, academic training, employment situation and the perception of their pain by assessing the Visual Analogue Scale (VAS) before and after the intervention. During their hospital stay, the total consumption of morphine and VAS were collected.

Results: There were no statistically significant differences in VAS scores on the first postsurgical day and one month after the operation by sex, origin and academic training. On multivariate logistic regression analysis, qualified work and inactive status were independent protective factors for moderate-severe postoperative pain on the first day after surgery. There was higher morphine consumption in men compared with women in the first four postoperative hours (mean difference: 0.029 mg/kg; 95% CI: 0.006 to 0.05).

Conclusion: Sex, race and academic formation did not influence the perception of the intensity of postoperative pain and the opioid consumption, except for the first 4 hours of the postoperative period, in which women required fewer doses of morphine than men. Qualified work and inactive status were independent protective factors for moderate-severe postoperative pain on the first day after surgery. Before surgery, inactive patients had higher VAS scores than retired and active workers.

Keywords: Postoperative Pain; Academic Formation; Sex; Race; Employment Situation; Morphine

Abbreviations

VAS: Visual Analogue Scale; BMI: Body Mass Index; TCI: Target-Controlled Intravenous Infusion; EC: Effect-Site Concentration; TOF: Train Of Four; IV: Intravenous; PACU: Post-Anaesthesia Care Unit; PCA: Patient-Controlled Analgesia; IQR: Interquartile Range; OR: Odds Ratio; CI: Confidence Interval; SD: Standard Deviation

Introduction

Pain is a subjective, unpleasant, multidimensional experience, which comprises different emotional components, whether affective or cognitive. Even today, patients and some professionals interpret it as an acceptable and expected experience during any surgery.

The interindividual variety of each patient in the perception of nociception makes the management of postoperative pain extraordinarily tricky in any of its scenarios. There is a high chance that the amount of opiates to achieve proper analgesia varies according to the patient, despite undergoing the same surgery. Pain sensibility is measured by sociocultural (family history, gender roles and stereotypes or socioeconomic level), psychological (anxiety, depression, fear, catastrophism and both cognitive and behaviour aspects) or biological (age, genetics, sex, race) factors. Thus, we should not only focus on the development of new drugs or delivery systems but the indicators involved in individualised nociception and personalised analgesic treatment as well [1,2].

The point of this study was to analyse the subjective pain perception and opioid consumption in patients undergoing prostatectomy and hysterectomy according to their sex, race, study level, and socioeconomic status. The telephonic interview conducted a month after the surgery was the method used to examine the demographic factors.

It was intended to raise information to treat postoperative pain not only pharmacologically but considering psychosocial aspects.

Materials and Methods

A prospective observational study was conducted at a single-centre, including 106 adult patients, of both sexes, ASA physical status scores I-III, scheduled for robotic prostatectomy or non-oncological laparoscopic hysterectomy under general anaesthesia. The Ethics Committee of Vall d'Hebron Hospital (Barcelona, Spain) and the Spanish Agency of Medicines and Sanitary Products (Code EudraCT 2016-002824-98. Protocol Code: ANE_HEPUNOX) approved this study. Informed consent was obtained from all patients.

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Exclusion criteria were obesity (Body Mass Index (BMI) >35 kg/m^2 for women and >42 kg/m^2 for man), anxiety-depressive disorder, chronic psychotropic or opiate treatment, pregnancy, alcohol abuse, documented allergy to the study analgesics, history of neurological disease or refusal to take part in the study. Anaesthesia was achieved in all patients with Target-Controlled Intravenous infusion (TCI) of Propofol and Remifentanil using the Orchestra® Primea system (Fresenius-Kabi). Remifentanil was diluted to a concentration of 50 µg/ml for an Effect-Site Concentration (EC) proposed by Minto and propofol 1% for an EC proposed by Schnider. Rocuronium was used as a muscle relaxant in bolus according to TOF control. The patients were premedicated with 2 mg of Midazolam IV. Intraoperatively, they were administered Paracetamol 1 g IV after the anaesthetic induction and Dexketoprofen 50 mg IV 20 minutes before the end of surgery.

On transfer to the Post-Anaesthesia Care Unit (PACU), the patient's level of analgesia was measured on a Visual Analogue Scale (VAS) from 0 to 10 (0 = no pain; 1-3 = mild pain; 4-6 = moderate pain; 7-10 = severe pain). If the first VAS score was 3, the patient was given Metamizole 2 g IV if it persisted at a level equal to or greater than 3, the nurse administered intravenous Morphine boluses until a good level of analgesia was achieved without exceeding 10 mg of the total dose.

Afterwards, an intravenous PCA pump (patient-controlled analgesia) of Morphine was initiated for the treatment of pain during the first 12 hours after surgery. The infusion system CADD-Legacy® PCA Ambulatory Infusion Pump, Model 6300 was programmed to a concentration of 1 mg/ml, just in requested bolus, of 0.5 mg of Morphine with a closing time of 10 minutes and a maximum dose of 3 mg/h. Likewise, rescue analgesia was prescribed if the staff deemed it necessary or if the patient specifically requested pain medication. During that time, the nursing staff digitally registered the pain value with the VAS, the administered analgesic medication, the haemodynamic signs and possible adverse events. Later, the information of the PCA (intended and administered bolus and total morphine dose) was written down into the record sheet.

One month after surgery, all participants were asked to answer a telephone survey. It consisted of a set of questions about demographic information, academic training, employment status and perception of pain before and after the intervention. Pain intensity was assessed according to VAS from 0 to 10 (0 without pain and 10 with maximum pain). The primary outcome was to evaluate the relationship between demographic factors with postoperative pain.

Statistical analysis

Continuous data were expressed as mean (standard deviation), or median and Interquartile Range (IQR) as appropriate, and frequencies and percentages (%) for categorical data. To study the possible relationship between qualitative variables, the Pearson X2 test or Fisher's exact test was used.

Student's t-test or Mann–Whitney U test was employed as appropriate to analyse the relationship between a quantitative variable and a dichotomous qualitative test. One way ANOVA followed by a post hoc Bonferroni t-test was used to compare more than two means between groups for normally distributed continuous data.

For Continuous data which did not follow a normal distribution, the Kruskal-Walis test was applied to compare more than two means. A Friedman statistical test for repeated measures was employed to compare pain (VAS scores) at different times of study, and two-sampled comparisons between the different times of study were evaluated using the Wilcoxon signed-rank test.

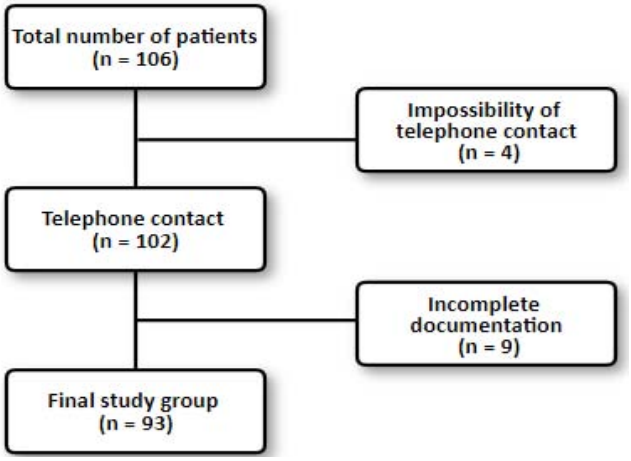

Figure 1: Study inclusion Flow chart.

It was analysed the bivariate relationship between each factor and moderate-severe postoperative pain (VAS ≥ 4 at day one after surgery, and day 30 after surgery. The Odds Ratio (OR) and the 95% Confidence Interval (CI) for all exposure factors also were calculated. Subsequently, forward stepwise multivariable logistic regression was performed to identify independent risk factors for moderate-severe postoperative pain at day one after surgery, and day 30 after surgery. Candidate variables included: gender, age, BMI, origin, academic formation, employment situation and pre-operative pain. In all cases, a p-value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 20.0 statistical package (IBM Corp., Armonk, New York, USA).

Results

A total of 106 patients were recruited. Four patients were excluded for being unable to contact by telephone and nine for presenting incomplete documentation. Finally, the population sample analysed was 93 patients (Figure 1).

Demographic data and variables of preoperative and postoperative pain

The median age was 54.7 years (95% CI:52.4 to 56.9), 52.7% of the population were women, and 77.4% were from Europe. The 39.8% studied at Elementary and Middle School, 22.6% completed the training cycle at High School.

Pre-operatively, 46.3% of participants reported pain and 22.5% could not sleep because of that discomfort. 96.7% of the patients had pain on the first postoperative day, and 76.3% of cases, it lasted for up to a month. Demographic and peri-operative pain data appear in (Table 1).

Pain intensity and socio-demographic factors

There were statistically significant differences in pain intensity measured by the VAS scale between women and men before the

Table 1: Demographic and anthropometric data and perioperative pain characteristics (n=93).

Demographic and anthropometric DATA	n (%)
Age (years) mean (95% CI)	54.7 (52.4-56.9)
Male/Female	44 (47.9) /49 (52.7)
BMI (kg/m^2) mean (95% CI)	26.1 (25.3-26.8)
Origin:	
Europe	72 (77.4)
South America	19 (20.4)
Africa	2 (2.2)
Academic formation	
Elementary and Middle School (6-14 years old)	38 (40.9)
High School (15-18 years old)	20 (21.5)
Vocational and Technical Schools (15-18 years old)	15 (16.1)
University studies	20 (21.5)
Employment situation	
Retired	28 (30.1)
Qualified work	22 (23.7)
Unqualified work	27 (29.1)
Inactive or unemployed	6 (6.5)
Sick leave	8 (8.6)
Preoperative pain	
Pain before surgery	43 (46.3)
Pain interrupts sleep	21 (22.5)
Analgesic consumption before surgery	33 (35.4)
Postoperative pain	
Pain on the first postoperative day	90 (96.7)
Pain after the first month of surgery	71 (76.3)
Pain interrupts sleep	6 (6.7)
Analgesic consumption after surgery	54 (58.5)
Impact of pain on quality of life	
A lot	5 (4.8)
A little	36 (39.3)
Nothing	52 (56)

surgical procedure (median VAS women: 4.5, IQR: 7 *vs* median VAS men: 0, IQR: 0; p <0.001). Otherwise, there was no statistical significance in the VAS records between women and men on the first postoperative day and one month after the operation. In men, the median VAS before surgery was 0 (IQR: 0), in the early 24 hours of 4.5 (IQR: 5) and one-month later of 2 (IQR: 3) (p <0.001). 33.3% of men and 28.6% of women had pain for more than one week (p=0.6). Results on VAS based on sex at different times are shown in (Figure 2).

Between the European and South American patients, VAS before surgery for South American patients was 5 (IQR: 8) *vs* VAS of 0 (IQR: 4) in European (p = 0.01). There was no difference in pain on the first postsurgical day and one month after the operation. Similarly, academic training did not show statistically significant differences in pain VAS scores between groups of different education levels in the

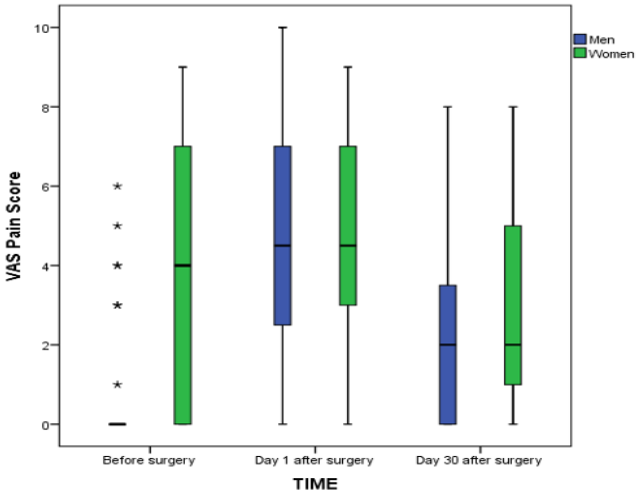

Figure 2: VAS scores at different times according to sex.
The median is represented by the horizontal line within the box. The whiskers represent the maximum (minimum) observation below (above) the upper (lower) fence, where the upper and lower fences are defined as ±1.5* IQR from the box boundaries. The symbols outside the box represent observations more extreme than the upper and lower fences. *VAS*, visual analogue scale; *IQR*, intraquartile range.

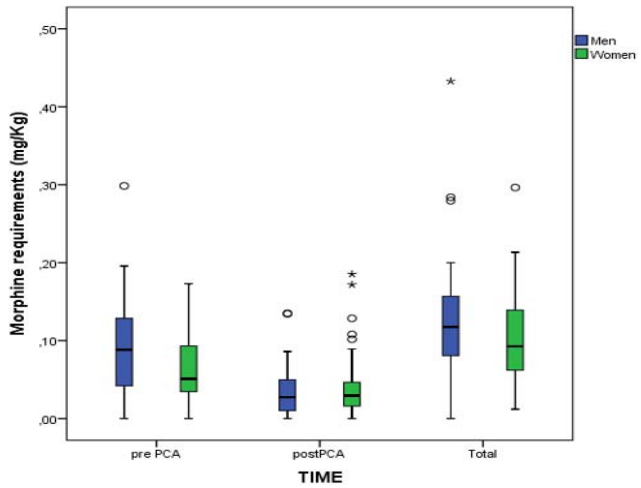

Figure 3: Morphine requirements by sex at different times studied.
The median is represented by the horizontal line within the box. The whiskers represent the maximum (minimum) observation below (above) the upper (lower) fence, where the upper and lower fences are defined as ±1.5* IQR from the box boundaries. The symbols outside the box represent observations more extreme than the upper and lower fences. *VAS*, visual analogue scale; *IQR*, intraquartile range.

three periods studied.

By comparing the intensity of pain with the employment situation of the participants, it was found that the inactive patients had higher VAS scores before surgery than the retired people (median inactive VAS: 5, IQR: 5 *vs* median VAS retired: 0, IQR: 1, respectively; p = 0.004) and the active workers (median VAS: 0, IQR: 4; p = 0.03). On the first postoperative day, median VAS was 5 (IQR:5) in retired people, 5 (IQR:4) in unqualified workers, 3 (IQR:4) in qualified workers, 3 (IQR:3) in inactive patients and 4.5 (IQR:4.5) in sick leave

Table 2: Characteristics of patients with and without moderate-severe postoperative pain at day 1 after surgery.

	Moderate-severe postoperative pain (n=59)	No Moderate-severe postoperative pain (n=34)	Odds ratio	95% CI	P value
Demographics					
Women	31 (52.5%)	18 (52.9)	1.05	0.41-2.22	0.9
Age, years (SD)	55.3 (10.8)	53.8 (11.2)			0.9
BMI, kg/m^2 (SD)	26.1 (3.8)	26.2 (3.7)			0.8
Origin					0.5
Europe	44 (74.6%)	28 (82.4%)	0.63	0.18 - 1.98	
South American	14 (23.7%)	5 (14.7%)	1.79	0.53-7.06	
Africa	1 (1.7%)	1 (2.9%)	0.57	0.01 -46.1	
Academic formation					0.7
Elementary and Middle	26 (44%)	12 (35.3%)	1.43	0.57 - 3.82	
High School	14 (23.7%)	7 (20.6%)	1.12	0.39-3.97	
Vocational and Technical	8 (13.5%)	7 (20.6%)	0.6	0.17-2.21	
Schools University studies	11 (18.7%)	8 (23.5%)	0.74	0.23-2.43	
Employment situation					0.04
Retired	21 (35.6%)	7 (20.6%)	2.11	0.73-6.75	
Qualified work	9 (15.2%)	13 (38.2%)	0.29	0.09 - 0.87	
Unqualified work	22 (37.3)	7 (20.6%)	2.27	0.8 -7.24	
Inactive or unemployed	2 (3.4%)	4 (11.8%)	0.7	0.06-4.23	
Sick leave	5 (8.5%)	3 (8.8%)	1.25	0.18-6.96	
Pain before surgery	28 (47.4%)	15 (44.1%)	1.34	0.42-2.54	0.9

Table 3: Characteristics of patients with and without moderate-severe postoperative pain at day 30 after surgery**.**

	Moderate-severe postoperative pain (n=30)	No Moderate-severe postoperative pain (n=63)	Odds ratio	95% CI	P value
Demographics					
Women	19 (63.3%)	33 (52.4)	1.97	0.80-4.8	0.1
Age, years (SD)	55.1 (10.6)	54.1(11.3)			0.6
BMI, kg/m^2 (SD)	25.8 (3.7)	26.1 (3.8)			0.7
Origin					0.7
Europe	22 (73%)	50 (79.4%)	1.44	0.5- 4.57	
South American	7 (23.4%)	12 (19%)	1.28	0.38-4.12	
Africa	1 (3.3%)	1 (1.6%)	2.11	0.02-170.2	
Academic formation					0.7
Elementary and Middle	12 (40%)	26 (41.2%)	0.95	0.35- 2.5	
High School	7 (23.3%)	14 (13.9%)	1.15	0.34-3.55	
Vocational and Technical	7 (23.3%)	8 (12.7%)	1.7	0.43-6.33	
Schools University studies	4 (13.4%)	15 (23.8%)	0.51	0.12-1.72	
Employment situation					0.5
Retired	9 (30%)	19 (30.2%)	0.99	0.33-2.79	
Qualified work	4 (13.3%)	18 (28.6%)	0.39	0.09 -1.36	
Unqualified work	13 (43.3%)	16 (25.4%)	2.22	0.81 -6.18	
Inactive or unemployed	1 (3.3%)	5 (7.9%)	0.4	0.01-3.84	
Sick leave	3 (10%)	5 (7.9%)	1.25	0.18-6.96	
Pain before surgery	17 (56.6%)	26 (41.2%)	1.84	0.7-4.94	0.2

Table 4: Independent risk factors for moderate-severe postoperative pain at day 1 after surgery on multivariate analysis.

	OR	95% CI	*p*
Employment situation			0.03
Retired	(Reference)		
Qualified work	0.22	0.06-0.8	0.03
Unqualified work	1.09	0.2-3.6	0.9
Inactive or unemployed	0.12	0.02-0.9	0.03
Sick leave	0.21	0.03-1.6	0.1

patients (p= 0.06).

Results of the bivariate analysis for the demographic variables in patients with and without moderate-severe postoperative pain on the first day and the thirtieth after surgery are shown in (Table 2) and (Table 3), respectively.

On multivariate logistic regression analysis, qualified work and inactive status were independent protective factors for moderate-severe postoperative pain at day one after surgery (Table 4). One month after surgical procedure, no variable was found with moderate-severe postoperative pain.

The average Morphine requirements were 0.11 mg/kg (SD: 0.07). No statistically significant differences were found in the total Morphine dose between men and women (mean difference: 0.022 mg/kg; 95% CI: -0.007 to 0.05). However, there were statistically significant differences in the first four postoperative hours, with higher consumption by men (mean difference: 0.029 mg/kg; 95% CI: 0.006 to 0.05) (Figure 3).

Discussion

Postoperative pain is a problem considered of vital importance in clinical practice, and research in recent decades suggests that it does not occur in the same way in all patients. We understand the pain in a multifactorial way with a substantial impact on the quality of life of people and their socio-labour environment.

There are two ways to define the intensity of pain. The first is mainly related to the patient's perception, while the second one depends on the number of pain relievers needed to obtain pain relief.

Despite the numerous studies that focus their research on differences in the perception of pain according to sex or gender, we still do not know the real significance that their influence may have on patients [3]. Robinson et al. [4] describe in their article "The theory of gender role" in which men and women are socialized differently to perceive pain and, therefore, to behave or respond accordingly. The willingness to express their suffering can play a crucial role in seeking medical attention or in use made of it. These differences diminish when it comes to chronic pain. In general, both sexes expect the "typical man" to have a higher resistance to pain and less willingness to report on this aspect. The "typical woman", on the other hand, has less strength and more willingness to report her aches, meaning she accepts pain as a normal part of life and therefore is laxer in expressing it [5].

In our study, gender or sex were not consistent predictors of the perception of postoperative pain nor the consumption of analgesics as traditionally believed. It assumed that the intensity of pain due to the type of surgery and surgical technique (laparoscopic hysterectomy *vs* prostatectomy with robotic assistance) were comparable. Despite not finding a significant relationship between pain intensity and sex, the female population showed higher VAS values during the pre-surgery phase, while men only showed minor ache (median VAS women: 4.5, IQR: 7 *vs* median VAS men: 0, IQR: 0; p <0.001). Even so, the presence of pain during the pre-operative period was not identified as a risk factor for suffering from significant complications in the immediate postoperative period or one month after surgery. However, as Hartmann and Bradshaw [6,7] suggest, it is necessary to remain especially attentive to those patients who have preoperative pain associated with anxiety or depression, since it could hinder the management of postoperative pain, or affect the quality of long-term life. In this regard, no statistically significant differences found in the total Morphine dose between men and women. However, men consumed higher doses of Morphine in the first four hours after surgery (mean difference: 0.029 mg kg/h, 95% CI: 0.006 to 0.05). Chia et al. [8] analysed Morphine IV administered by PCA in a total of 2,298 patients of both sexes after general anaesthesia. The gender difference was the main predictive factor of Morphine consumption since men required between 23 and 43% more Morphine during the three days after surgery. The reasons for this sex-related difference remain unclear, and several mechanisms may be involved. The amount of Morphine used to relieve pain in men or women depends not only on the pharmacodynamics [9] but also, on pharmacogenetics and pharmacokinetics. Additional studies are required that include the behaviour of endogenous opioids, neurotransmitters, the influence of the hormonal system and how the formation of active metabolites of different opiates acts according to sex [10,11,12].

Another line of research that is becoming increasingly interesting is the connection of pain with the immune system [13,14,15]. The preclinical data described in the studies by Sorge [16] and Mogil [17] conducted with rodents have shown that males use microglia to mediate pain, while females ignore this step and select T cells. Both systems are extrapolated and present in men and women. The hormonal levels of testosterone and estrogens seem to direct the immune system towards one type or another of the cell to encode the transmission of such pain.

Academic training was another aspect analysed from the information obtained in the telephone interview. In general terms, our study showed no difference in the intensities of postoperative pain concerning the level of academic education in both men and women. The results obtained would be more in agreement with the research lines of Yang et al. [18] o Caumo et al. [19] in which academic training would not be a predictive preoperative factor for the control and assessment of acute postoperative pain.

There were no statistically significant differences in Morphine consumption according to the academic level of the patients.

Conversely, Radinovic et al. [20] observed an association between patients with an academic education of primary studies and a high risk of severe pain in the immediate postoperative period of hip fracture.

The biocultural model proposes that different cultural or ethnic factors can influence the evaluation of pain and how it is responded to,

both emotionally and behaviourally. Therefore, social group pressure, values and attitudes learned, or memories of previous experiences may affect pain tolerance levels [21,22,23]. In the study by Liao et al. [24], participants of African American and Latin American origin expressed their pain openly. Possibly, because in these cultures, it does not represent a social stigma as it happens in Asia, as they expect to receive support from society and the family. To deal with pain, they use rather passive strategies such as spirituality and prayer [25]. They tend to be supporters of home and homoeopathic remedies. On the contrary, Asians and Caucasians found it more uncomfortable to manifest pain, and if they did, they experienced some regret or shame. Caucasians tend to be more prone to self-treatment behaviours and, like Asians, to a more active coping attitude.

In our study, ethnic or racial origin, regardless of the sex, did not represent a predictive factor in the perception of pain expressed in the telephone interview, according to VAS scores before surgery, in the immediate postoperative period or one month after the surgical procedure. In general terms, there were no statistical differences in morphine requirements depending on the continent.

As Dorner and Teasell [26,27] suggest, the employment situation could correlate with the perception of postoperative pain and the type of employment or working conditions. In our case, before surgery, the inactive patients had higher VAS scores than the retired (median inactive VAS: 5, IQR: 5 *vs* median VAS retired: 0, IQR: 1, respectively; $p = 0.004$) and active workers (median: 0, IQR: 4; $p = 0.03$). However, on multivariate logistic regression analysis, qualified work and inactive status were independent protective factors for moderate-severe postoperative pain on the first and 30th day after surgery.

Conclusion

The female population manifested higher VAS score during the pre-surgery phase, while men only had discomfort. Even so, this circumstance did not suppose a higher incidence of postoperative pain. Otherwise, there was no statistical significance in the VAS records between both sexes on the first postoperative day and one month after the operation.

The employment situation correlated with the perception of postoperative pain. In our study, before surgery, inactive patients had higher VAS scores than retired and active workers. However, in the postoperative period, qualified work and inactive status were independent protective factors for moderate-severe postoperative pain on the first and 30th day after surgery.

Similarly, sex, race, academic formation or employment situation did not influence opioid consumption after the operation, except for the first 4 hours of the postoperative period, in which women required fewer doses of Morphine than men.

Studies Limitations

Our study presents limitations. This analysis is based on the evaluation of two specific types of surgery with homogeneous groups and comparable pain intensity in both sexes. However, more studies with a larger population sample and including several types of surgical procedures are needed to confirm the same results. Similarly, depression or anxiety was an exclusion criterion in the main clinical trial that could play a role in the perception of pain, either independently or associated with other risk predictors.

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Authors' Contributions

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

Abad-Torrent A: Study design, patient recruitment, data collection, writing up the first draft of the manuscript and subsequent revision, revision and approval of the final manuscript.

de Miguel M: Analysis and interpretation of data. Revision of the drafts of the manuscript, revision and approval of the final manuscript.

Sanaú B: Analysis and interpretation of data. Revision of the drafts of the manuscript, revision and approval of the final manuscript.

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Suárez Edo E: Data collection, revision of the drafts of the manuscript, revision and approval of the final manuscript.

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