Evaluating Persistent Postoperative Pain in One Tertiary Hospital: Incidence, Quality of Life, Associated Factors, and Treatment

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Abstract

Background: Persistent postoperative pain (PPP) is defined as persistent pain after surgery of greater than three months’ duration. Objectives: Identify the incidence of PPP in our hospital and its associated factors; evaluate quality of life (QoL) and treatment of patients.

Patients and Methods: We conducted an observational prospective study in adults proposed to various types of surgery using the brief pain inventory short form preoperatively (T0), one day after surgery, and three months later (T3). If the patient had pain at T3 and other causes of pain were excluded, they were considered to have PPP, and the McGill Pain Questionnaire Short Form was applied. QoL was measured with the EuroQol 5-dimension questionnaire (EQ-5D).

Results: One hundred seventy-five patients completed the study. The incidence of PPP was 28%, and the affected patients presented lower QoL. The majority referred to a moderate to severe level of interference in their general activity. Cholecystectomies were less associated with PPP, and total knee/hip replacements were more associated with it. Preoperative pain, preoperative benzodiazepines or antidepressants, and more severe acute postoperative pain were associated with the development of PPP. Half of the patients with PPP were under treatment, and they refer a mean symptomatic relief of 69%.

Conclusions: This study, apart from attempting to better characterize the problem of PPP, emphasizes the lack of its treatment.

Keywords: Chronic Pain, Postoperative Pain, Quality of Life

1. Background

Persistent postoperative pain (PPP) is considered a silent epidemic that is in urgent need of better understanding of its pathophysiology (1). The consequences of PPP can be variable, from mild to severe loss of quality of life (QoL). The international association for the study of pain (IASP) defines it as persistent pain after surgery of greater than three months’ duration (1). Before making a diagnosis of PPP, it is critical that other common causes of pain from surgery be ruled out.

The first publication that identified surgery as a major risk factor for chronic pain appeared in 1998 (2). An important increase in interest in this subject has occurred since that publication.

The problem is not limited to major surgery, as even minor procedures such as herniotomy can have important consequences with regard to development of PPP. Some consider it the most common and serious long-term problem after repair of an inguinal hernia (3).

The consequences of PPP are significant, not only in terms of suffering and reduced QoL for the individual patient, but also with regard to the subsequent costs to the health care and social support systems of our societies (4).

The incidence of PPP varies according to definition and surgical procedure, ranging from 5% to 50% (1). Recently, in a cross-sectional survey performed in Norway, PPP was reported by 40.4% of the patients, with moderate to severe PPP reported by 18.3% (5). In a Portuguese cross-sectional epidemiological study, 6% of patients with chronic pain attributed its etiology to surgery (6).

In 2013, the Portuguese directorate-general of health published a strategic plan for prevention and control of pain (7). One of its guiding principles is the duty of pain control, and it states that all health professionals should adopt strategies for prevention and control of pain in their patients. It is also mentioned that particular attention should be given to the prevention and management of pain caused by diagnostic or therapeutic acts.

The majority of publications about PPP address issues such as definition, incidence, risk factors, preventive strategies, and the evolution of pain. However, the treatment of established PPP is less studied. Previous studies have confirmed the severe multidimensional impact...
of chronic pain, as the QoL of patients with chronic non-malignant pain is among the lowest observed for any medical condition (8, 9). Due to its importance, we decided to study this problem in our hospital.

2. Objectives

To identify the incidence of PPP in our hospital; to identify factors associated with the development of PPP; and to evaluate QoL and current treatment of patients with PPP.

3. Patients and Methods

We conducted an observational prospective study approved by our institutional ethics committee. Informed consent was obtained from each patient included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in the approval by our institutional ethics committee. We included adults proposed to surgery in June 2013. As we would not be able to study all surgeries scheduled in our hospital, we decided to include thoracotomies, hysterectomies, mastectomies, inguinal hernia repairs, thyroidectomies, laparoscopic cholecystectomies, amputations, and total knee or hip replacements (TKHR). The choice of these surgical procedures was made after a reunion of anesthesiologists to take into account the procedure’s relevance and logistics. Patients with American society of anesthesiologists (ASA) physical status 4 were excluded. We registered age, gender, ASA physical status, medical history, and current medications for all patients.

The type of anesthesia was administered according to the type of surgery. Thoracotomies and hysterectomies were performed under combined anesthesia (general anesthesia plus epidural anesthesia). Mastectomies, inguinal hernia repairs, thyroidectomies, and laparoscopic cholecystectomies were performed under general anesthesia. Amputations and TKHR were performed under spinal anesthesia, and an epidural catheter was also placed to administer postoperative analgesia. The anesthetic protocol in general anesthesia was standardized in all patients: midazolam, fentanyl, and propofol were used for induction of anesthesia, and patients were paralyzed with rocuronium or cisatracurium. Anesthesia was maintained with sevoflurane or desflurane and either fentanyl or remifentanil, as preferred by the attending anesthesiologist. Epidural analgesia with local anesthetic plus opioid and intravenous analgesia according to the world health organization’s analgesic ladder was used in the other surgeries. Our acute pain unit works 24 hours per day, every day of the week, and provides acute pain care according to recommended standards.

Sample size was calculated for an incidence of 35%, a confidence interval of 90%, and a margin of error of 5%, and the result was 175 patients.

We applied the validated Portuguese version of the brief pain inventory short form (BPI-SF) (10) preoperatively (T0), one day after surgery (T1), and three months later (T3). The BPI-SF evaluates pain severity on an 11-point numerical rating scale (from 0 or “no pain” to 10 or “worst pain imaginable”), pain interference in daily activities (general activity, mood, walking, work, interpersonal relations, sleep, and enjoyment of life), intake of pain analgesics, perception of analgesic relief, and pain location (11). BPI-SF is a valid instrument to measure pain in patients with and without cancer (11, 12).

At T3, the first question asked was “Do you still have any pain that you could relate to the surgical procedure?” This is an adaptation of the BPI-SF first question on pain prospection, and it was performed in other similar studies (13). If the patient answered “yes” and other causes of pain were excluded, he or she was considered as having PPP, and we applied the Portuguese version of the McGill pain questionnaire short form (MPQ-SF). The MPQ-SF is a useful tool in situations in which the standard questionnaire takes too long to administer, yet qualitative information is desired (14). Patients with PPP were also asked about their current pain treatment: intake of pain medications, analgesic prescribers, and perception of analgesic relief.

QoL was measured with the Portuguese version of the EuroQol 5-Dimension questionnaire (EQ-5D) at T0 and T3. EQ-5D is a standardized instrument to measure health outcome, and contains five dimension questions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (15). The Portuguese version of the EQ-5D has good accessibility, reliability, and validity in measuring health (16).

All questionnaires were administered after previous authorizations from their authors. For analysis purposes, we converted the numeric rating used in BPI-SF into categorical variables: “0” to none, “1-3” to mild, “4-6” to moderate, and “7-10” to severe. Non-parametric and parametric tests were performed for comparison between numerical variables according to their distribution, and a chi-square test for categorical variables.

4. Results

We recruited 190 patients, and 175 patients completed the study. We were unable to contact 15 patients at T3. Table 1 presents the main characteristics of our sample. The
incidence of PPP was 28% (49 patients) according to IASP definition (1) and the incidence of moderate to severe PPP was 12.6%.

Table 1. Characteristics of the Sample (N = 175)

| Variable                  | Values                  |
|---------------------------|-------------------------|
| Age, y (M, [P₂₅ - P₇₅])  | 63 [48.0 - 70.5]        |
| Gender                    |                         |
| Male                      | 35.8                    |
| Female                    | 64.2                    |
| ASA physical status       |                         |
| I                         | 13.7                    |
| II                        | 63.2                    |
| III                       | 23.1                    |
| Surgical Specialty       |                         |
| Thoracic Surgery          | 7.7                     |
| General Surgery           | 59.2                    |
| Vascular Surgery          | 10.9                    |
| Gynecology                | 5.9                     |
| Orthopedics               | 11.2                    |
| Plastic Surgery           | 5.1                     |

Abbreviations: M, Median; P₂₅, 25th percentile; P₇₅, 75th percentile.
*Values are expressed as percentage except for age.

Table 2 presents the PPP severity and interference assessed with BPI-SF. We did not detect any differences in pain severity and interference among the specific surgeries. According to the MPQ-SF, patients with PPP presented a 6.5 median sensory pain rating index, a 0.0 median affective pain rating index, and a 6.5 median total pain rating index. We did not find differences in pain rating indexes between surgical groups.

Regarding acute postoperative pain, the worst pain considered severe in the first 24 hours was associated with higher incidence of PPP (38.8% vs 19.8%, P = 0.01). The average pain considered moderate to severe in the first 24 hours was also associated with development of PPP (40.8% vs. 23.0%, P = 0.019).

Relative to surgical groups (Table 3), cholecystectomies were less associated with the development of PPP (8.3% vs. 31.1%, P = 0.021), and TKHR were more associated with it (50.0% vs. 25.5%, P = 0.028).

We were unable to detect differences for gender, age, body mass index, diabetes, and statin medication prior to surgery (Table 4). The percentage of patients with PPP was higher in those with any preoperative pain in the related area (51.4% vs. 21.5%, P < 0.001), even when we exclude patients with presence of acute postoperative pain (55.5% vs. 10.1, P = 0.002). Patients with a history of prior surgery in the related area had a higher incidence of PPP (50.0% vs. 24.5%, P = 0.01). However, when we exclude patients with preoperative pain, there is no difference in the incidence of PPP (24.0% vs. 14.3%, P = 0.228). Patients with prior surgery in the related area had more preoperative pain when compared to those without it (26.3% vs. 7.1%, P = 0.008).

Average postoperative pain considered severe in the first 24 hours was associated with higher incidence of PPP, when compared to those with lower scores (71.4% vs. 26.2%, P = 0.009). Conversely, average postoperative pain considered mild in the first 24 hours was associated with lower incidence of PPP, when compared to higher scores (24.3% vs. 52.2%, P = 0.006). Incidence of PPP was higher in patients with the presence of any acute postoperative pain (37.0% vs. 18.5%, P = 0.021), even when we exclude patients with preoperative pain (32.2% vs. 11.1%, P = 0.001).

Regarding QoL using EQ-5D, none of the EQ-5D dimensions presented a normal distribution (the Kolmogorov-Smirnov test was performed). Initially, EQ-5D dimension distributions were not different for patients with or without PPP, except for pain dimension (M: P = 0.24; SC: P = 0.197; UA: P = 0.149; pain: P < 0.001; AD: P = 0.341; Mann-Whitney test performed). However, three months later, patients with PPP presented lower results in all EQ-5D dimension distributions (mobility: P = 0.01; self-care: P < 0.001; usual activities: P < 0.001; pain: p < 0.001; anxiety/depression: P < 0.001; Mann-Whitney test performed).

Anxiety and depression problems, measured initially with EQ-5D as previously noted, were not associated with the development of PPP (29.6% vs. 24.1%, P = 0.341). However, PPP was positively associated with preoperative current treatment with benzodiazepines (42.9% vs. 23.5%, P = 0.015) or antidepressants (61.3% vs. 21.3%, P < 0.001). The associations are maintained after excluding patients with preoperative pain (benzodiazepines: 37.5% vs. 16.7%, P = 0.013; antidepressants: 50.0% vs. 16.2%, P < 0.001). Later on, PPP patients presented more problems related to anxiety and depression at T3 (54.1% vs. 20.6%, P < 0.001). Even when we exclude the patients who previously were taking antidepressants or benzodiazepines, this association is maintained (35.0% vs. 14.1%, P = 0.027). Anxiety and depression problems were associated with higher scores for BPI-SF and pain rating indexes in patients with PPP (Table 5).

In our sample, 53.1% of the patients with PPP were under treatment (96.2% with medication and 3.8% with physiotherapy). The rest of the patients (46.9%) had no treatment. Regarding their classification of average pain, treatment was performed in 37.0% of the patients with mild pain, 68.4% of the patients with moderate pain, and in all (100.0%) patients with severe pain. According to their classification of worst pain, treatment was performed in...
Table 2. Persistent Postoperative Pain Severity and Interference Assessed With Brief Pain Inventory Short Form (n = 49)

| Parameters                  | Level of Pain/Interference |
|-----------------------------|----------------------------|
|                             | No Pain/No Interference    |
|                             | Mild                       |
|                             | Moderate                   |
|                             | Severe                     |
| Pain Severity               |                            |
| Average Pain                | -                          |
|                             | 27 (55.1)                  |
|                             | 19 (38.8)                  |
|                             | 3 (6.1)                    |
| Worst Pain                  | -                          |
|                             | 10 (20.4)                  |
|                             | 17 (34.7)                  |
|                             | 22 (44.9)                  |
| Least Pain                  | 30 (61.2)                  |
|                             | 36 (72.7)                  |
|                             | 2 (4.1)                    |
|                             | 1 (2.0)                    |
| Pain at interview           | 14 (28.6)                  |
|                             | 24 (49.0)                  |
|                             | 7 (14.3)                   |
|                             | 4 (8.1)                    |
| Interference                |                            |
| General Activity            | 10 (20.4)                  |
|                             | 12 (24.5)                  |
|                             | 11 (22.4)                  |
|                             | 16 (32.7)                  |
| Mood                        | 16 (32.7)                  |
|                             | 13 (26.5)                  |
|                             | 6 (12.2)                   |
|                             | 14 (28.6)                  |
| Work                        | 12 (24.5)                  |
|                             | 11 (22.4)                  |
|                             | 10 (20.4)                  |
|                             | 16 (32.7)                  |
| Relations with others       | 24 (49.0)                  |
|                             | 14 (28.6)                  |
|                             | 5 (10.2)                   |
|                             | 6 (12.2)                   |
| Sleep                       | 20 (40.8)                  |
|                             | 14 (28.6)                  |
|                             | 7 (14.3)                   |
|                             | 8 (16.3)                   |
| Enjoyment of life           | 22 (44.9)                  |
|                             | 11 (22.4)                  |
|                             | 10 (20.4)                  |
|                             | 6 (12.3)                   |

Table 3. Persistent Postoperative Pain Among the Surgical Groups (n = 49)

| Surgical Procedures       | N in the 1st Group | PPP in the 1st Group | PPP in Others | P Valueb |
|---------------------------|--------------------|-----------------------|---------------|----------|
| Amputation                | 14                 | 30.8                  | 27.8          | 0.817    |
| Laparoscopic cholecystectomy vs. Others | 24                  | 8.3                   | 31.1          | 0.021    |
| Thoracotomy               | 14                 | 15.4                  | 29.0          | 0.292    |
| Inguinal hernia repair vs. Others | 29                  | 27.6                  | 28.1          | 0.957    |
| Hysterectomy              | 13                 | 25.0                  | 28.2          | 0.81     |
| TKHR vs. Others           | 19                 | 50.0                  | 25.5          | 0.028    |
| Mastectomy                | 38                 | 25.5                  | 36.8          | 0.17     |
| Thyroidectomy vs. Others  | 24                 | 29.1                  | 20.8          | 0.4      |

Abbreviations: N, number of patients; PPP, persistent postoperative pain; TKHR, Total knee or hip replacement.

Values are expressed as percentage.

Chi-square test.

40.0% of the patients with mild pain, 47.1% of the patients with moderate pain, and in 63.3% of the patients with severe pain. General practitioners are responsible for treatment in 61.5% of the patients, and surgeons for 34.6%. Only one patient was being treated in a Chronic Pain Unit. Acetaminophen was the only analgesic prescribed for 65.4% of the patients under treatment. Patients under treatment refer a mean symptomatic relief of 69%.

5. Discussion

The incidence of PPP in our study is in accordance with the literature (1, 17). However, this comparison has some limitations, as many studies have different methodologies. An important percentage of our patients have PPP, which deserves special attention and intervention from health authorities and professionals, as PPP represents a major humanitarian and socioeconomic burden (18).

The incidence of PPP was different among the selected surgical groups, which is also in accordance with the current literature. Previous studies revealed that chronic abdominal pain after cholecystectomy is common, ranging between 3% to 56%, whether open or laparoscopic (19). In a procedure-specific study, 18% of the patients submitted to laparoscopic cholecystectomy presented PPP one year later (20). Laparoscopic cholecystectomy has lower incidence of PPP when compared to open technique (19, 21). In our study, laparoscopic cholecystectomy presented the
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Table 4. Persistent Postoperative Pain and Associated Factors (n = 49)^

| Factor                                      | PPP     | Without PPP | P Value |
|---------------------------------------------|---------|-------------|---------|
| Preoperative Pain                           | 38.3    | 13.8        | < 0.001 |
| Preoperative Pain excluding patients with pain at 24 hours | 50.0    | 9.1         | 0.002   |
| Postoperative Pain at 24 hours              | 75.0    | 51.7        | 0.020   |
| Postoperative Pain at 24 hours excluding patients with preoperative pain | 79.2    | 50.0        | 0.036   |
| Gender                                      |         |             |         |
| Female                                      | 28.5    | 38.9        |         |
| Male                                        | 73.5    | 61.1        |         |
| Body Mass Index, (Median, P25, P75) kg/m^2 | 26 (24 - 28) | 26 (21 - 30) | 0.495   |
| Age, Median, P25 - P75 years                | 61 (53 - 71) | 61 (46 - 69) | 0.077   |
| Diabetes                                    | 14.3    | 21.4        | 0.284   |
| UM with Benzodiazepines                     | 36.7    | 19.2        | 0.053   |
| UM with Statins                             | 24.5    | 32.3        | 0.470   |
| UM with Antidepressives                     | 38.8    | 9.8         | < 0.001 |
| Prior surgery in the related area           | 24.5    | 9.5         | 0.016   |

Abbreviations: PPP, persistent postoperative pain; UM, usual medication.

Values are expressed as percentage except for body mass index and age.

^Chi-square Test.

With respect to preoperative risk factors, our study is in accordance with the evidence that preoperative pain is a predictor for PPP, which might reflect an independent risk factor, but could also be a manifestation of predisposing factors (26, 27, 29). Our study results suggest that higher pain severity is associated with higher incidence of PPP.

The history of prior surgery in the related area could be indirectly responsible for the development of PPP, because previous surgery in the related area was associated with the existence of preoperative pain.

Regarding postoperative risk factors, acute postoperative pain was associated with the development of PPP, which was already described in other studies. Poorly relieved acute pain is commonly mentioned as a striking risk factor in PPP development (31). Our findings are in agreement with the existence of a link between the presence of acute postoperative pain or its severity and the development of PPP. Several prospective studies have also underscored the link between the severity of acute pain and PPP (26, 31, 32).

With respect to QoL, our results are in accordance with previous findings that patients who develop PPP have lower QoL after open inguinal hernia repair (33) and mastectomy (34). Pain with significant interference, as PPP was described by our sample, not surprisingly reflects lower QoL.

The subject of depression and anxiety in pain has been extensively described over several decades of pain research and treatment (35). Depression prevalence rates in patients with persistent pain seem to be higher than in the general population and also seem to be more common.
than among other chronic illness populations, including patients with cardiac disease, cancer, diabetes, and neurologic disorders (36). It was believed that persistent pain is more likely to lead to depression, and patients with more severe, frequent, and enduring pain are at risk for more severe depression (37). However, persistent pain conditions and depression are heterogeneous. In certain pain conditions (e.g., osteoarthritis and rheumatoid arthritis), persistent pain is believed to be more strongly linked to peripheral factors (e.g., cartilage damage, inflammation) and psychosocial factors are considered to be less important. On the other hand, in other pain conditions (e.g., fibromyalgia, irritable bowel syndrome), persistent pain is believed to be more strongly linked to changes in the central nervous system (altered central processing) and psychosocial factors are considered to play a major role (35).

Anxiety and depression disorders are usually correlated with PPP. In 2009, a systematic review of the psychosocial factors related to PPP identified depression, psychological vulnerability, stress, and late return to likely be correlated with PPP (38). In our study, we failed to detect the association between anxiety or depression, measured initially with EQ-5D, and the development of PPP. However, patients under preoperative treatment with benzodiazepines or antidepressants had higher incidence of PPP. For obvious reasons, patients undergoing these treatments have problems related to anxiety and depression. Therefore, our results may suggest that the presence of anxiety and depression problems is a risk factor for developing PPP. At the same time, our results indicate that anxiety and depression can also be seen as consequences of PPP development, because patients without anxiety and depression problems prior to surgery who develop PPP had higher incidence of anxiety and depression problems.

The treatment of pain is an important issue for every health professional and organization. There are some studies that evaluate the treatment of chronic pain in Portugal (39-42), but to our knowledge, this is the first study that evaluates the specific follow-up and treatment of PPP in Portugal. There is urgent need for more research about the treatment of PPP, because very few studies have addressed it (43). In our sample, almost half of the patients with PPP (including one-third of patients with moderate to severe PPP) did not receive any treatment for their condition, a finding that should be emphasized. The worst pain considered to be moderate and severe was untreated in a very high percentage of patients, which should also be considered. Many of these patients are not treated because they are lost after discharge from hospital.

Some authors suggest that Acute Pain Services should provide an opportunity for consultation regarding continuing pain and have an important role in assessing PPP as an outcome of surgery (43). Recently, it has been reported that telephone consultation partially based on a cognitive-behavioral approach significantly reduced the intensity of pain and improved the QoL in patients with chronic pain in Japan (44). Many PPP patients will seek help from general practitioners, and therefore this group is in need of awareness and training about PPP.

Although there is limited evidence for treatment of PPP, the therapeutic scale according to the world health organization should be followed. Other professionals involved in the care of surgical patients should also be aware of this entity and refer these patients to Pain Units whenever they cannot deal with their treatment. It should be noted that it is an ethical duty to treat these patients, and that patients under treatment refer a significant improvement in symptoms.

Our sample comes from a single hospital, which could cause some bias with respect to the usual acute pain care. Our Acute Pain Unit works 24 hours per day, every day of the week, and provides acute pain care according to recommended standards. Recently, there has been an appeal to conduct procedure-specific studies that evaluate the development of PPP. However, we selected some groups of procedure-
specific surgeries in order to gain a global view of PPP in our hospital, and with that we obtained small procedure-specific groups.

To conclude, this study characterizes the problem of PPP after several types of surgery and enounces some of its associated factors and consequences. Our results emphasize the lack of identification and treatment of PPP, which should constitute a warning to health professionals and authorities involved in the treatment of postoperative pain.

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Footnote

Author Contribution: Luis Guimaraes-Pereira and Fernando Abelha developed the protocol. Luíz Guimaraes-Pereira, Ines Valdoleiros and Pedro Reis performed the data collection and clinical evaluations. Pedro Reis and Fernando Abelha performed the data analysis. Luíz Guimaraes-Pereira wrote the first draft of the paper. Fernando Abelha revised the manuscript. All authors discussed the results and commented on the manuscript. All authors have read and approved this paper.

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