Epidemiology and incidence of acute and chronic
Post-Surgical pain

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BACKGROUND AND AIMS: *Post Surgical Pain (PSP) treatment represents a significant aspect of management of surgical patients. Incidence of severe PSP, with significant functional deficit is estimated at 5-10%. Most studies include a limited number of patients and this is a factor which affects power of results. Aims of our prospective observational study was to evaluate the incidence and characteristics of acute and chronic PSP in patients undergoing surgery at the university hospital of second university of naples.*
MATERIALS AND METHODS: *After Ethics Committee approval and written informed consent, the PSP acute on first day (at least 6 hours after surgery) through the International Pain Outcomes questionnaire was rated. Subsequently, patients were followed-up at 6 and 12 months; data collection took place by e-mail or phone and the Brief Pain Inventory and the DN4 were administered.*
RESULTS: *We enrolled 235 patients, 219 performed the follow-up to 6months, 195 even that to 12 The incidence of CPSP at 6 months was of 45.2% for mild pain, 15.9% for moderate pain and of 2.7% for severe pain while the incidence of CPSP at 12 months was 35.9%, 11.8% and 2.5% respectively for the pain mild, moderate and severe. Neuropathic pain occurred in 40.3% of patients who CPSP moderate at 12 months compared with 31.9% of the patients interviewed at 6 months. Incidence and characteristics of PSP varied, often considerably, depending on the type of surgery, gender, age of the patient and the presence of PSP severe in the 24 hours following surgery.*
CONCLUSIONS: *The incidence of CPSP 12 months after surgery must be improved in the next future. Preoperative pain and the percentage of time with severe pain during the first 24 hours after surgery seem to be CPSP predictors.*

KEY WORDS: Chronic pain, Opioids, Postoperative pain, Postsurgical pain, Surgery

Introduction

Over the last ten years has been well recognized that the treatment of post surgical pain (PSP) plays an increasingly significant role in the management of surgical patient. It has an incidence of 30% with variations depending on the type of surgery. The incidence of severe PSP, with significant functional deficit is estimated at 5-10% and effective approaches to prevent it are basically ignored[13]. Most studies contain data collection of a specific type of surgery and include a limited number of patients, hence the validity is limited. PAIN OUT is an international research group that deals with the improvement of the management of acute and chronic PSP through the collection of data across participating centers. The network includes about 70 PAIN OUT centers [4] and the Department of Anesthesiological, Surgical and Emergency Sciences of the Second University of Naples has taken part to the trial from 2012 to 2014. The aim of this study was to assess the impact of acute and chronic PSP. In several cases, when it occurs, PSP

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is undervalued and often patients occur chronic pain refractory to therapy [5-7]. Surgery is a major cause of chronic pain and is the only case in which there is a possibility to prevent [4]. Results obtained from this study could improve knowledge on the most important relations with the different types of surgery and the possibility of implementing perioperative prevention techniques with a major impact on the incidence of PSP. Therefore Pain Out trial, could represent an important reference for an address in the prevention and treatment of PSP.

Materials and Methods

Characteristics of the Study

The study is prospective observational trial. The aim is to evaluate the incidence and characteristics of acute and chronic PSP at the Department of Anesthesiology, Surgical and Emergency Sciences of Second University of Naples. After local Ethics Committee approval number: CE81 in date 16/Feb/2012, patients who agreed to take part in our study were asked to sign the written informed consent.

Inclusion criteria:
– Patient ≥ 18 years;
– patient in ward, available for an interview;
– Data collection should take place on first day, at least;
– 6 hours after surgery.
– The patient has undergone reoperation during admission in course;
– Patients who could provide a telephone number or an e-mail for follow-up at 6 and 12 months after surgery.

Patients were admitted at University Hospital S.U.N. in the following Units:
– General surgery;
– Urology;
– Thoracic surgery;
– Plastic surgery;
– Throat-Nose-Ear Surgery;
– Maxillofacial surgery.

All patients were treated with postsurgical pain therapy according to the protocol inside of our service and Anaesthesia and Pain Therapy relating to surgical procedures to which they are subjected. Pain Out Study is a prospective observational study with collection of data during the first day of post-operative hospital stay, using a standardized questionnaire proposed by coordinating center (International Pain Outcomes Questionnaire).
Data collected, include demographic and clinical data of the patient, information on anesthesia, analgesia and outcome. A unique ID code was generated for each patient and there was no connection between code and the patient's name or medical record numbers. The outcome was evaluated by the incidence of pain for at least 6 hours of surgery and risk factors of PSP related to the patient and the type of surgery. It was subsequently performed a follow-up at 6 and 12 months after surgery.

Questionnaire on patient outcome (Ipoq).

IPOQ (International patients outcome questionnaire) can be considered as an instrument with satisfactory psychometric properties and reliable patients outcome measurement in acute pain: pain severity, interference with function, affective experience, side effects and perceptions of care (Table I).
The questionnaire consists of 13 questions with the main secondary items: 3 items relate to the intensity of pain, 4 assess the interference of pain in activities of life, 2 explore the affective sphere, 4 deal with the adverse effects of drug treatment, 5 assess the perception of care, one asks for a possible non – pharmacological treatment of pain, and the last 3 relate to chronic pain. Most of the items are rating scales NRS, some require answers "yes" or "no." At the end of the questionnaire there is a section that asks the researcher to specify the conditions under which the questionnaire is carried out, that is, if the patient has completed alone or if he was interviewed.
The first two items, P1 and P2 (NRS), are aimed at the assessment of pain intensity after surgery by expressing it as a single score of intensity, in order to obtain the range of the pain felt from 0 (no pain) to 10 (very severe pain) (NRS).

Table I - *IPOQ (International patients outcome questionnarie)*

Worst pain in 24 hours
Least Pain in 24 hours
Percentage of time in severe pain
Pain interference with: *Activities in bed*
Breathing or coughing
Sleep
Activities out of bed
Emotional impairment due to pain: *Anxious*
Helpless
Adverse effects: *Nausea*
Drowsiness
Itching
Dizziness
Percentage of relief in 24 hours
Patient's preference of pain treatment
Patient's information of pain treatment
Participation in decision making
Satisfaction with pain treatment
Patient's treatment using non-medicine methods
Persistent painful condition for 3 monts before surgery

In Italic secondary items

In P3 patients describe for how long, in percentage, has severe pain occurred.
P4 and P5 (NRS) are items that assess the dimension in which pain interferes with physical and emotional activity. In particular P4a-bc assess mobility (P4a), respiration (P4B) and sleep (P4C) while P4D is relevant only for patients who were able to ambulate at the time of the questionnaire. And respectively P5a and b assess how the pain has affected the state of anxiety and mood of the patient.
P6 a-b-c-d (NRS) asking the patient to quantify any side effects such as nausea, drowsiness, dizziness and itching that may be related to postoperative pain treatment. These items may be useful to have a broader perspective on pain management because the side effects can significantly impair the quality of life of patients and adherence to treatment.
In P7 patients are asked to assess the degree of relief, in percentage terms, who received the treatments for pain.
The items from P8 to P11 assess how patients perceive the quality of care related to the treatment of pain and, more specifically, the degree of satisfaction that they have received with it.
P12 is finalized to assess the types of non-pharmacological strategies that patients may have used to control their own pain or that may have been provided to them by health professionals (e.g., cold compressions and / or acupuncture).
P13 contains three sub-items that ask patients if they had persistent pain in the three months prior to surgery, asking him to characterize regarding intensity and affected area. The literature shows that, when pain occurs before surgery, it may have an impact on the severity of pain in the postoperative period and this can be, therefore, one of the many factors that can influence the onset of chronic Post Surgical Pain (CPSP).

Statistical analysis.
Data were reported as means, median and SD.
For comparisons between groups, nonparametric methods were used: the Student t-test, the MannWhitney U test or the $\chi 2$ test.
It was considered as the index of statitical significance set at $p < 0.05$.

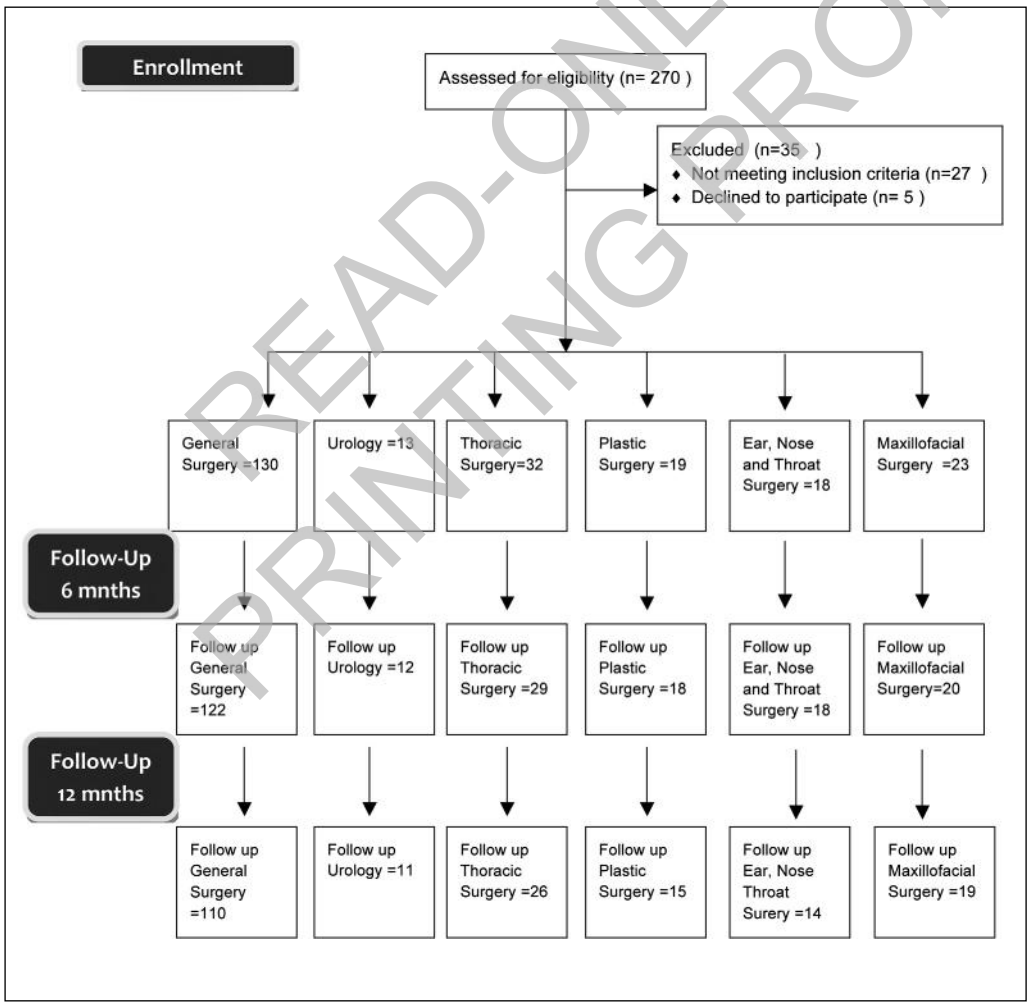

Fig. 1: Consort Flow Chart.

Results

The questionnaire was carried out to 235 patients who underwent surgery in the period between February and December 2012 (101 men and 134 women), of which 130 (51 men and 79 women) from general surgery, 32 (18 men and 14 women) from thoracic surgery, 13 (10 men and 3 women) from urology, 19 (3 men and 16 women) from plastic surgery, 18 (9 men and 9 women) from Ear, Nose, Throat Surgery and 23 (10 men and 13 women) from the maxillofacial surgery (Fig. 1). Patients were from 18 to 84 years old. The analysis was made out by comparing the results provided by various Units of our University Hospital, the results gender-related, results obtained in the different age groups (Table II).

In Figure 2 are shown the averages of measurements of pain intensity minimum and maximum scales made of NRS, obtained in different departments, for at least 6 hours after surgery. The average of 06.04 against 05.15 of general surgery of thoracic surgery and the other still below average, up to 2.9 Ear, Nose, Throat are observed. Similarly, the measurement of the incidence of severe and very severe pain (NRS values 7-8 and 9-10) showed differences that are similar to those observed for medium-sized, with a higher incidence in the group of general surgery (Fig. 2).

TABLE II - *Demographic Data.*

	6 months N = 219	12 months N = 195
Age (years)	52.8 (14.2)	52.6 (14)
Gender (%) (male / female)	42.9 / 57.1	43 / 57
Weight (kg)	77.6 (14.1)	77.1 (13.8)
Height (cm)	168 (6.6)	168 (6.6)
Ethnicity (%)		
Caucasians	94	93
Afro American	3	4
Eastern	3	3
Comorbidities (%)		
(Yes/No/no information)	68/30.6/1.4	66.9/31.6/1.4

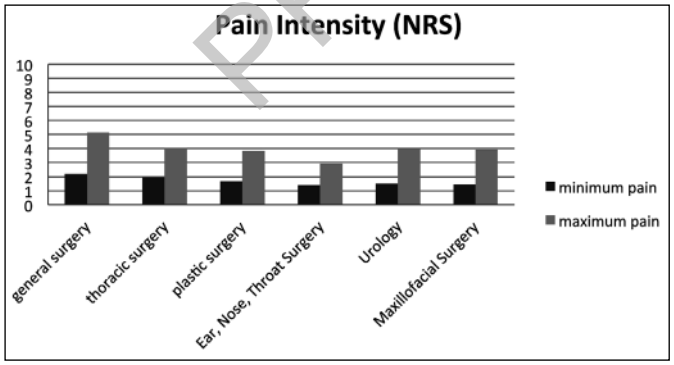

Fig. 2: Pain Intensity: NRS (0-10) mean values.

We evaluated the time of severe pain; also here in average subjects from the general surgery have expressed a longer time, slightly higher than the 40%, in which they warned severe pain compared to those from every branch where results were obtained at around 30%. The analysis of data collected referred to the quality of sleep went from pain showed that, in the whole study population, 75% of the subjects gave a value less than or equal to 4 on the NRS scale, with average similar in the different groups.

It seems clear, then, most of the subjects, in the first day after the surgical procedure, has referred trouble in sleeping (Fig. 3) or otherwise have been perceived as mild. We assessed how the pain in these patients affected hospitalization at bed; moreover were considered also the activities carried out by the bed in patients able to walk. The level of interference of the PSP on the activities of the subject, A first analysis allows us to observe that there is a greater interference in samples of general surgery, thoracic and urology, in particular on the activities in bed; the situation changes going to evaluate the interference of pain on the activity only in ambulatory patients, where it becomes evident only for the group of urology. With regard to the emotional aspects related to postoperative acute pain, our analysis shows, in general, a poor perception by the population of negative feelings such as anxiety or sense of discouragement due to pain. In all types of surgery studied, most of the subjects gave responses to the NRS is not higher than 4, with average of between 1:16 and 2.5 for anxiety and between 0.79 and 2.25 the sense of discouragement.

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In Table III are defined, as mean and SD, the values of the perception on the part of patients analyzed, the major side effects of analgesics; data always refer to the first day after surgery. In this period, the issues discussed were perceived as absent or very mild in almost all the samples; major variations were observed only with respect to

TABLE III - *Side Effects in Postoperative Time*

	Nausea	Drowsiness	Itching	Dizziness
General Surgery	1.32	2.05	0.22	0.78
Ear,Nose,Throat Surgery	1.22	2.56	0.06	1.17
Plastic Surgery	1.16	1.21	0.84	1.63
Thoracic Surgery	1.06	3.16	0.38	1.03
Urology	1.50	3.83	0.67	2.25
Maxillofacial Surgery	1.09	2.64	0.08	1.22

the parameter of sleep quality in populations of thoracic surgery and urology, where patients referred 25% of responses, respectively, greater than 5 and 6 (Table III). The comparison of the averages of the minimum and maximum levels of pain experienced throughout the sample results suggest that the perception of the PSP for at least 6 hours after surgery has a slight prevalence towards males, on average, they reported higher scores on both for minimal pain experienced both the worst.

In the assessment of the duration of pain and sleep disturbance induced by pain, once again, we had men in scores that confirm a greater impact on outcome by the component in the immediate postoperative pain: in the male sample, the average response were respectively: 47% and 36% at 3.33 and 2.03 of the female sample.

We compared the medians of the responses regarding the level of interference caused by pain in the activities in bed and out of bed (in case the patient is ambulatory). The result confirmed the previous analysis, that is, the more pain interferes in the activity of bedridden patient; furthermore, it was observed that, even in this case, it takes on a more significant role in the male. Regarding the affective sphere, it was observed that anxiety and sense of discouragement were warned as mild by the majority of subjects, in congruence with previous findings; In fact, the average scores stood for anxiety about 2.59 in males and 1.82 in females, for the sense of discouragement about 2.26 in males and 1.74 in females. As shown in the table (Table IV), the reliefs on the side effects of analgesic therapy are almost similar in both sexes, and also, they don't seem to cover an important role in the first 24 hours after surgery.

Finally, the level of perception of treatment by different subjects was assessed, by analyzing a series of parameters:

– The relief obtained thanks to analgesic therapy;
– Involvement in treatment decisions;
– Satisfaction with the results of therapy;
– The use of non-conventional methods for the treatment of pain.

With regard to the first parameter, on average, we had obtained in the whole population a degree of relief between 60% and 70%.

Regarding the feeling involved in the choice of treatment, in all samples, at least 50% of the subjects gave a response equivalent to the absolute lack of involvement, i.e. a score of 0 in the NRS. In particular, in plastic surgery we had the lowest average, with over 75% of the subjects who responded with a score equal to 0 and the maximum score achieved was 5.

Interesting results were obtained from analysis of the degree of satisfaction with analgesic therapy, expressed by the study population: more than 75% of the subjects in all the samples gave a response greater than 6 on the NRS scale, averaging nearly superimposable, including between 7.5 and 7.7. In order to endorse these last results, about 80% of the population had no need to resort to unconventional strategies for the treatment of pain, although it must still consider that there remains a 20% of subjects who have used it. Of our initial sample of 235 patients, 195 have carried out both follow-up (at 6 and 12 months).

The incidence of CPSP at 6 months was of 45.2% for mild pain, 15.9% for moderate pain and of 2.7% for severe pain. The incidence of CPSP was lower at 12 months: 35.9%, 11.8% and 2.5% respectively for the pain mild, moderate and severe. 3% of patients had no pain at 6 months and at 12 months occurred CPSP. The incidence of moderate pain varied considerably according to the type of surgery (Fig. 2).

Discussions and Conclusions

The results of this study, in general, confirm the validity of the therapeutic approach adopted at our site. The measurements carried out during the first day of hospital stay in the ward have allowed us to observe that, in most cases, the pain was absent or mild, with a very low frequency of severe pain, in addition to the absence of significant adverse effects in almost all cases; appears clear that there is no link between the acute postoperative pain and the affective sphere, which becomes more important in the case of chronic pain. Another result of this study was to detect the levels of pain interference on the most simple tasks of life are reduced in ambulatory patients as early as 24 hours after the government put than enticed.

A comparison made, was put in evidence an increased susceptibility to the development of severe pain, which interferes negatively on patient outcome, in those who have undergone operations in general surgery; the risk is reduced in the other cases, but still remains in all types of intervention a proportion of subjects between

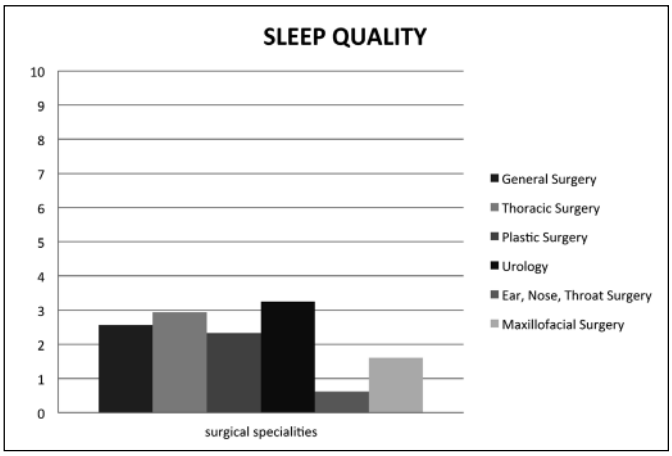

Fig. 3: Sleep Quality in patients after surgery in different surgical specialities. It has been measured using a point scale from 0 (best quality) to 10 (worst sleep quality).

5% and 20% which will develop severe or very severe pain.
The analysis of demographic factors revealed in males at a higher risk of developing severe pain; in particular, it was noted that this would prejudice the outcome of more males than females, being warned at a higher intensity for a longer time and interfering more on sleep and activity of the subject.

Table IV - *Gender-related side effects in Postoperative time*

	Nausea	Drowsiness	Itching	Dizziness
Male	1.30	2,31	0.23	0.61
Female	1.34	1,87	0.22	0.88

Table V - *Incidence of Neuropathic pain after 6 and 12 months from surgery*

DN4 questionnaire (>4)	6 months	12 months
Any pain (NRS≥1)	23,5% (18.2-27.4)	25.3% (19.2-30.7)
Significant pain (NRS≥3)	31.9% (24.3-37.5)	40,3% (27.4-51.6)
Severe pain (NRS≥6)	31.3% (11.8-49.7)	59.3% (31.2-82.4)

Incidence of CPSP

In our patients we observed that the incidence of CPSP mild and moderate at 12 months after surgery was respectively 35.9% and 11.8%, whereas the incidence of severe CPSP 12 months was lower: 2.5%. These results confirm that although the incidence of CPSP may reach 30% among the different types of surgery, its clinical relevance is much less frequent. Our results indicate that the incidence of CPSP, whatever its severity, declines between 6 and 12 months. In few cases (i.e. 3%) patients developed CPSP between 6 and 12 months after surgery.

Characteristics and Table

The results of our study show that a quarter to half of patients with CPSP had some signs of neuropathy in M12. The neuropathic component seems to be associated with a greater intensity of CPSP. This is in line with previous studies on patients suffering from chronic pain and in particular in patients with CPSP[8]. The incidence of this neuropathic component seems to increase with time, suggesting that neuropathic pain is less suitable to spontaneous resolution than nociceptive pain. The characteristics of neuropathic varied considerably in frequency depending on the type of surgery but we must also say that small sample of patients prevents a 'reliable' interpretation (Table V).

Type of Surgery and the Risk of CPSP

Within the surgical specialties are adopted unique therapeutic protocols because the expected post surgical pain varies according to surgical procedure. As we have described previously, the incidence of moderate CPSP to 12 months varied depending on the type of surgery. With samples of various sizes for different surgical procedures, we chose to group the different types of surgeries in four different models to analyze the impact of surgery on the incidence of CPSP. We observed that the open surgery patients exposed to higher incidence of any type of CPSP compared to laparoscopic surgery. The advantage of laparoscopic surgery in the prevention of CPSP varies with the type of surgery. Our results confirm previous findings that describe a CPSP more important in cholecystectomies "open" with respect to cholecystectomies [9]. On the other hand, in line with previous studies, for hysterectomy were not observed large differences between surgery "open" and the vaginal or laparoscopic [10-11]. Finally, a relevant finding that has emerged from the study is the 'high level of satisfaction achieved in patients' group with the analgesic therapy, given that perfectly agrees with the finding of a low frequency of severe or very severe pain. The results from our study are encouraging, particularly with regard to assessing the impact of severe pain and adverse effects of analgesics, confirming the effectiveness of our therapeutic standards. More studies have suggested that in this regard, throughout the world, PSP control continues to be at levels not yet really satisfying [12-14]. Over the years there has been a gradual reduction of the phenomenon as documented by a study published in 2003 showed that in 'PSP 80% of patients and acute of these, 86% experienced a moderate to grave [15] pain; Moreover, in a previous study, conducted on 1,400 surgical patients, an incidence of moderate to severe pain ranging from 75% to 100% patients emerged [16].
Our analysis shows that a proportion of subjects between 40% and 50% of the population has experienced a moderate to severe pain; must consider, however, that the questionnaire does not allow to differentiate the pain at rest and one in motion, therefore, our results are consistent with those observed in the German study. Despite the last decade, therefore, it was observed a reduction in the incidence, the problem continues to persist at the international level with important implications both for the patient's clinical condition, the worsening quality of life, both as regards the rising costs of care. It was also demonstrated that a severe acute postoperative pain is an important risk factor for the development of chronic pain, especially when there is positive medical history for affective disorders during perioperatoria [17]. The possibility of organizing a proper follow – up by a web

– based questionnaire has been shown to be a promising option for future studies.
This study revealed an incidence of 11.8% of significant CPSP, 12 months after surgery. In multivariate analysis, preoperative pain and the percentage of time with severe pain during the first 24 hours after surgery seem to be predictors of CPSP.
Progress can still be accomplished, even with the support of our data, in order to improve the care provided to patients and further reduce levels of perceived pain in the early postoperative period [18,19]. The main objective of the international network PAIN OUT is, in fact, to improve patients' outcome suffering with CPSP, through the collection of longitudinal clinical data with the aid of standard procedures, such as the questionnaire used by us, creating a international archive of easy access at any time. This approach will allow you to access your data, as was done in our research, laying the foundation to provide any improvement in the quality of pain care and implementing the protocols used with the strategies and the most effective procedures provided by most current guidelines put available from the network. After comparing our results with those ones showed in other centers of PAIN OUT network, we hope to improve the quality of care of patients undergoing surgery. This path opens the way for a more thorough evaluation of risk factors and a better definition of the areas of intervention.

Riassunto

INTRODUZIONE ED OBIETTIVI: Il trattamento del dolore postoperatorio (PSP) riveste un ruolo sempre più significativo nella gestione del paziente chirurgico. Esso ha un'incidenza media stimata del 30% con variazioni a seconda del tipo di intervento chirurgico. L'incidenza di PSP severo, con significativo deficit funzionale, è stimato al 5-10%. La maggior parte degli studi comprende un numero limitato di pazienti e ciò costituisce un fattore che ne pregiudica la validità. L'obiettivo principale del nostro studio osservazionale prospettico è stato quello di valutare l'incidenza e le caratteristiche del dolore postoperatorio (PSP) acuto e cronico in pazienti sottoposti ad interventi chirurgici presso l'Azienda Ospedaliera Universitaria della Seconda Università degli Studi di Napoli.
MATERIALI E METODI: Dopo approvazione del Comitato Etico e consenso informato scritto, è stato valutato il PSP acuto in prima giornata (ad almeno 6 ore dalla fine dell'intervento) tramite l'International Pain Outcomes questionnaire. Successivamente ci si è avvalsi del Brief Pain Inventory e del DN4 per il follow-up a 6 e 12 mesi avvenuto tramite e-mail o telefono.
RISULTATI: Sono stati arruolati 235 pazienti, 219 hanno eseguito il follow-up a 6 mesi, 195 anche quello a 12. L'incidenza di CPSP a 6 mesi è stata del 45,2 % per quanto riguarda il dolore lieve, del 15,9 % per il dolore moderato e dello 2,7 % per il dolore severo mentre l'incidenza di CPSP a 12 mesi è stata del 35,9% , 11,8% e 2,5% rispettivamente per il dolore lieve, moderato e severo. Evidenza di dolore neuropatico si è registrata nel 40,3% dei pazienti con CPSP moderato a 12 mesi contro il 31,9% dei pazienti intervistati a 6 mesi. L'incidenza e le caratteristiche del PSP variavano, spesso notevolmente, in base al tipo di chirurgia, al sesso, all'età del paziente e alla presenza di PSP severo nelle 24 ore successive all'intervento.
CONCLUSIONI: Questo studio ha rivelato un' incidenza rilevante di CPSP significativo 12 mesi dopo l'intervento chirurgico e tale risultato deve essere migliorato nel prossimo futuro. Il dolore preoperatorio e la percentuale di tempo con dolore severo durante le prime 24 ore dopo l'intervento sembrano essere fattori predittivi di CPSP.

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