

Chronic, acute and acute-on-chronic pain prevalence in a tertiary care hospital setting

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Abstract. – OBJECTIVE: The aim of the study was to develop appropriate pain therapy and prevention plans; pain needs to be understood in terms of prevalence and associated predictor factors in hospital and primary care. The purpose of our research was to assess the prevalence of chronic, acute, and acute-on-chronic pain, and ascertain the effects of several factors on the likelihood of pain in an Italian Tertiary Care Hospital.

PATIENTS AND METHODS: This is a prevalence study in which the primary outcome was the prevalence rate of chronic pain inpatients. Fisher's exact tests and binomial logistic regression were performed for the prevalence measures, and to ascertain the effects of Hospital Unit, sex, age, surgery and preexisting chronic pain on the likelihood of pain during the hospitalization, respectively.

RESULTS: Chronic pain was reported in one-fifth of inpatients [21.7% (95% CI: 0.1764, 0.2625)], with a high prevalence of pain-related interference on sleep and emotional status. Nearly 70% of chronic pain patients accused acute-on-chronic pain [15.3% (95% CI: 0.1178, 0.1934)]. High pain prevalence rates were assessed at the time of the interview (37.3%; 95% CI: 0.3234, 0.4239) and in the last 24 hours of hospitalization (53.3%; 95% CI: 0.4814, 0.5850). A 2.7 and 2.6 higher odds to suffer from pain during the hospitalization were associated with surgery, and preexisting chronic, respectively.

CONCLUSIONS: This study raises awareness of the necessity to refine pain assessment and management in hospital and outpatient services. The promotion and enhancement of hospital-territory integration are essential for improving pain prescribing practices and increasing patient safety.

Key Words:

Chronic pain, Acute pain, Acute-on-chronic pain, Pain measurement, Pain management, Older adults.

Introduction

Pain and pain-related diseases represent relevant issues both in developed and middle- and low-income countries, with a significant impact on individuals and National Health Systems^{1,2}. The Global Burden of Disease Study 2019³ reaffirmed low back pain and headache disorders in the top 10 causes of Disability-Adjusted Life Years (DALY) for ages 10-24 years, and the 25-49-year age group, as well as for the 50-74-year age group. In this scenario, the aging of the population is rapidly increasing. With it, people living with two or more long-term conditions, and the related reduced quality of life and higher mortality^{4,5}. Among the various pathologies that most affect older adults, in Europe, about 19% of the adult population deals with moderate to severe chronic pain, with Italy being at third place in chronic pain prevalence⁶. Besides, increased survival represents an essential feature with the potential to experience chronic persistent pain⁷. In Italy, there was a light but sustained increase in the prescription of pain medications in the last five years, with a total 2019 expenditure of about 400 million euros for the Italian National Health System⁸. Population estimates for the prevalence of pain, both acute and chronic conditions, vary widely according to age, sex, and hospital or outpatient populations, as well as in the definition

of methods⁹. Regarding the hospital population in Italy, the FADOI-DOMINO study, carried out by the Italian Scientific Society FADOI¹⁰, has revealed that pain affected 4 out of 10 patients admitted to Internal Medicine Departments during the hospitalization. Costantini et al¹¹ performed in 30 public hospitals of the Liguria region, have encountered a 43.1% of pain patients at the time of the interview, and 56.6% of patients declared pain during the previous 24 hours from the survey. Regarding the outpatient population, an observational, multicenter, cross-sectional study from Latina et al¹², conducted in the Latium Region, has shown severe pain in 54% of the 1606 patients of the study sample.

Besides, in daily clinical practice, we often witness both situations of chronic pain, and acute-on-chronic pain, as shown from some studies carried out in Emergency Departments¹³⁻¹⁵. They reported chronic pain patients visiting the emergency departments, ranging from 10 to 40%, with a recent systematic review illustrating how chronic pain is associated with frequent emergency department visits¹⁶. In this setting, multiple pain management and treatment guidelines have been produced¹⁷⁻²³. Still, they rarely offer an integrated approach considering multimorbidity and polypharmacy in real-world pain patients, which often results in the risk of hospitalization. Moreover, nowadays, we must also address coronavirus disease 2019 (COVID-19), including symptoms that persist after recoveries, such as fatigue, joint pain, headache, myalgia, and chest pain²⁴, which could also involve chronic patients and exacerbate the epidemiological aspects of pain.

To date, various studies underlined adverse consequences of surgical procedures, such as chronic post-surgical pain (CPSP), with a prevalence rate of about 10-30%^{25,26}, but acute-on-chronic pain, in general, is still little discussed, and no prevalence data are on it. The development of the best possible pain therapy plans, and prevention schemes requires a better understanding of national, regional, and local prevalence and associated predictor factors.

Therefore, the purpose of our study was to assess the prevalence of chronic, acute and acute-on-chronic pain and ascertain the effects of Hospital Unit, age, sex, and preexisting chronic pain condition on the likelihood of pain during the hospital stay in an Italian Tertiary Care Hospital. The primary objective of this study was to evaluate the prevalence of chronic pain within patients admitted to Niguarda Hospital Depart-

ments. Secondary objectives were represented by the identification of the prevalence of pain during the last hospital 24 hours, pain at the time of the interview, and acute-on-chronic pain, the identification of the prevalence of chronic and acute pain interference on sleep, enjoyment of life, and general activity, and the ascertainment of the effects of Hospital Unit, sex, age, surgery and pre-existing chronic pain condition on the likelihood of pain during the hospital stay.

Patients and Methods

The survey and successive cross-sectional study were approved by the Research Ethics Committee of Milan Area 3. The reporting of this research conforms to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement checklist²⁷. This is a cross-sectional one-point prevalence study based on a pain survey, carried out on May 31st, 2019, in all the Units of Niguarda Hospital, except for Outpatient Care Services, Psychiatric, Pediatric, Obstetric, Emergency, and Intensive Care Units. All patients aged 18 years and older, admitted to these available beds at Niguarda Hospital for at least 24 hours, which were cognitively intact, were recruited after giving their agreement to the interview. The only exclusion criterion was the inability to express informed consent. The sample size was defined based on the estimated prevalence from previous analyses^{6,9-15}. Assuming, therefore, that 40% of the subjects in the population had the factor of interest, the predetermined sample size was 369 patients. This method assumed a maximum error of 5% between the prevalence of the sample and the true population prevalence. A significance level of 5% was employed.

Patients' data, including age, sex, Hospital Unit, surgical treatment, and pain assessment, were collected by 48 trained nursing students, who interviewed eligible patients between 9:00 and 12:00 AM. Before the interview execution, cognitive impairment condition was ascertained by a discussion with the resident doctors and nurses. The Hospital Unit was recorded as a dichotomous variable, in Medical Unit, also including Oncology Unit, and in Surgical Unit. Surgical treatment was reported as a dichotomous variable (yes/no), considering affirmative only if a surgical procedure was performed during the current hospitalization, but not nec-

essarily in the previous seven days. The assessment of pain during the hospital stay was carried out based on a form with items containing questions about their pain experience at the time of the interview, during the last 24 hours, and before the hospitalization. The interviewer asked the patient three general questions (“Do you have pain right now?”; “Did you have pain in the last 24 hours?”; “Did you have pain before your current hospitalization?”). For all the three questions, if the response was affirmative, pain intensity was assessed both for pain at rest, and pain on movement, by means of Numerical Rating Scale (NRS) ²⁸, distinguishing it in four different categories (respectively NRS 0, none; 1-3, mild; 4-6, moderate; and 7-10, severe pain) ²⁹. For the second question, “Did you have pain in the last 24 hours”, if the response was affirmative, along with pain intensity, pain interference on sleep and general activity were assessed, based on two of the seven items of pain-related functional interference of the Brief Pain Inventory tool³⁰. The rate of pain interference could range from 0 (“does not interfere”) to 10 (“interferes completely”), dividing it into four different categories, as for pain intensity (0, none; 1-3, mild; 4-6, moderate; and 7-10, severe interference). For the third question, “Did you have pain before your current hospitalization?”, we considered only patients with chronic pain, defined as pain that lasts or recurs for more than three months³¹. If the response to the third question was affirmative, along with pain intensity, pain interference on sleep, enjoyment of life, and general activity were assessed, based on three of the seven items of pain-related functional interference of the Brief Pain Inventory tool³⁰, rated as described above. In the description of these questions to the patient, we chose to use the term “enjoyment of life” for the emotional interference item, as described in the development and validation of the PEG scale³², because of the more independent expression in comorbid depressed patients. However, differently from the PEG scale, we also chose to maintain the pain-related interference item on sleep. In fact, sleep disturbances predict more significant levels of pain interference and implications in the assessment and treatment of sleep disturbance into chronic pain therapy^{33,34}. Acute-on-chronic pain patients were defined as patients with both chronic pains as described above, and pain during the last 24 hours before the interview. The pain relief from pain treatments or medi-

cations provided was assessed on a percentage scale, from 0% “no relief”, to 100% “complete relief”³⁰.

Statistical Analysis

All data needed to compute statistical analyses were regularly collected and entered the database anonymously. Descriptive statistics were used to introduce the data. Frequency and percentage were calculated for dichotomous and ordinal variables (sex, Hospital Unit, preexisting chronic pain condition). In contrast, continuous variables (age, pain intensity, pain interferences) were presented as median values along with interquartile range, as the measure of dispersion.

A Fisher’s exact test, along with its 95% confidence interval, was performed to evaluate prevalence measures included in the primary and secondary outcomes.

A binomial logistic regression was carried out to ascertain the effects of Hospital Unit, sex, age, surgery, and preexisting chronic pain condition on the likelihood of pain during the hospital stay. The statistical analyses were conducted using IBM® SPSS Statistics® for Windows® (version 20; Armonk, NY, USA). The significance level was set at $p < 0.05$.

Results

During the one-day prevalence, 449 patients were eligible within Hospital Units on which the survey was implemented. We excluded 76 people for the following reasons: refused to participate (45 patients), out of the ward for instrumental investigations (15 patients), and other reasons not justified by the patient (16 patients). Therefore, data were collected from 373 subjects, of which 149 (39.9%) were female (Table I). The median age (interquartile range) was 63 (51-77) years, with 47.4% of people aged 65 or older. Of all 373 patients, 259 (59.4%) were admitted in Medical Units, while 114 (30.6%) subjects in Surgical ones, with 144 (38.6%) surgically treated during the hospitalization, both in medical and surgical Units. The main characteristics of the study sample are shown in Table I.

Chronic Pain

The prevalence rate of chronic pain patients was 21.7% (95% CI: 0.1764, 0.2625) (Table II). Among patients with chronic pain, 76 out of 81

Table I. Characteristics of the study sample (Study sample, N = 373).

Characteristic	Value
Sex, number of patients (%)	
Female	149 (39.9)
Male	224 (60.1)
Age, median (interquartile range)	63 (51-77)
Age ≥65, number of patients (%)	177 (47.4)
Hospital Unit, number of patients (%)	
Medicine	259 (69.4)
Surgery	114 (30.6)
Submitted to a surgical treatment during hospitalization, number of patients (%)	144 (38.6)

Percentage values are rounded up to one decimal. Definitions: Hospital Unit, recorded as a dichotomous variable, in Medical Unit, including Oncology Unit, and in Surgical Unit. Outpatient care services, Psychiatric, Pediatric, Obstetric, Emergency, and Intensive Care Units were excluded from the analysis.

subjects (20.4% of the study sample) reported pain at rest, with a median NRS score (interquartile range) of 6 (5-8). Moderate and severe pain intensity were respectively recorded in 7% (26/373) and 9.6% (36/373) of patients.

Chronic pain on movement was experienced by 79 out of 81 subjects (21.2% of the study sample), with a median NRS score (interquartile range) of 7 (5-9). Moderate and severe pain intensity were respectively recorded in 6.2% (23/373) and 12.9% (48/373) of patients.

Chronic pain interference on sleep was reported by 14.5% (95% CI: 0.1107, 0.1846) of the study sample (54/373), with a median score (interquartile range) of 7 (5-9). Moderate to severe interference resulted in 46 out of 54 subjects (12.3% of the study sample).

Chronic pain interference on the enjoyment of life was recorded in 17.4% (95% CI: 0.1371, 0.2166) of patients (65/373), with a median interference score (interquartile range) of 8 (5-9). Moderate to severe interference resulted in 57 out of 65 subjects (15.3% of the study sample).

Chronic pain interference on general activity was experienced by 18.5% (95% CI: 0.1469, 0.2282) (69/373), with a median interference score (interquartile range) of 8 (6-9). Moderate to severe interference resulted in 61 out of 69 subjects (16.3% of the study sample).

Pain in the Last 24 Hours Before the Interview

In the last 24 hours before the interview, the prevalence rate of pain patients was 53.3% (95% CI: 0.4814, 0.5850) (Table II). Among patients with pain in the last 24 hours, 49.6% (185/373 patients) reported pain at rest, with a median NRS score (interquartile range) of 6 (3-8). Moderate

and severe pain intensity were respectively recorded in 67 (18%) and 71 (19%) patients.

Pain on movement was experienced by 51.7% (193/373) of patients, with a median NRS score (interquartile range) of 6 (5-8). Moderate and severe pain intensity were respectively recorded in 66 (17.7%) and 95 (25.5%) subjects. Table II lists all 24-hour pain prevalence rates recorded during the survey.

Pain interference on sleep was reported by 31.4% (95% CI: 0.2669, 0.3634) of the study sample (117/373), with a median score (interquartile range) of 6 (3-8). Moderate to severe interference resulted in 87 out of 117 subjects (23.3% of the study sample).

Pain interference on general activity was experienced by 42.6% (95% CI: 0.3755, 0.4782) (159/373), with a median interference score (interquartile range) of 6 (4-8). Moderate to severe interference resulted in 122 out of 159 subjects (32.7% of the study sample). Table II lists all pain in the last 24 hours prevalence rates recorded during the survey.

Acute-On-Chronic Pain

The prevalence rate of acute-on-chronic pain patients was 15.3% (95% CI: 0.1178, 0.1934)], equal to 70.4% of the 81 chronic pain ones. Among patients with acute-on-chronic pain, 53 out of 57 subjects (14.2% of the study sample) reported pain at rest, with a median NRS score (interquartile range) of 6 (4-8). Moderate and severe pain intensity were respectively recorded in 6.4% (24/373) and 5.1% (19/373) of patients.

Acute-on-chronic pain on movement was experienced by 56 out of 57 subjects (15% of the study sample), with a median NRS score (interquartile range) of 6 (5-8). Moderate and severe

Table II. Prevalence rates of pain suffering patients and pain characteristics in the study sample (Study sample, N = 373).

Characteristic	Value/Pain			
	Chronic	Last 24 hours	At Interview	Acute-on-chronic
Pain, number of patients (%)	81 (21.7)	199 (53.3)	139 (37.3)	57 (15.3)
Female	39 (10.4)	90 (24.1)	66 (17.7)	26 (7)
Male	42 (11.3)	109 (29.2)	73 (19.6)	31 (8.3)
Age, median (IQR)	66 (53-78)	62 (49-75)	62 (49-75)	65 (51-77)
Hospital Unit, number of patients (%)				
Medicine	54 (14.5)	124 (33.2)	89 (23.9)	38 (10.2)
Surgery	27 (7.2)	75 (20.1)	50 (13.4)	19 (5.1)
Intensity severity at rest, median (IQR)	6 (5-8)	6 (3-8)	5 (3-7)	6 (4-8)
Intensity at rest, number of patients (%)	76 (20.4)	185 (49.6)	130 (34.8)	53 (14.2)
None	5 (1.3)	14 (3.8)	9 (2.4)	4 (1.1)
Mild	14 (3.8)	47 (12.6)	34 (9.1)	10 (2.7)
Moderate	26 (7)	67 (18)	54 (14.5)	24 (6.4)
Severe	36 (9.6)	71 (19)	42 (11.3)	19 (5.1)
Intensity severity on movement, median (IQR)	7 (5-9)	6 (5-8)	7 (5-8)	6 (5-8)
Intensity on movement, number of patients (%)	79 (21.2)	193 (51.7)	133 (35.6)	56 (15)
None	2 (0.5)	6 (1.6)	6 (1.6)	1 (0.3)
Mild	8 (2.1)	32 (8.6)	20 (5.4)	6 (1.6)
Moderate	23 (6.2)	66 (17.7)	41 (11)	23 (6.2)
Severe	48 (12.9)	95 (25.5)	72 (19.3)	27 (7.2)
Interference severity on sleep, median (IQR)	7 (5-9)	6 (3-8)		7 (5-8)
Interference on sleep, number of patients (%)	54 (14.5)	117 (31.4)		30 (8)
None	27 (7.2)	82 (22)		27 (7.2)
Mild	8 (2.1)	30 (8)		5 (1.3)
Moderate	17 (4.6)	35 (9.4)		6 (1.6)
Severe	29 (7.8)	52 (13.9)		19 (5.1)
Interference severity on enjoyment of life, median (IQR)	8 (5-9)			
Interference on enjoyment of life, number of patients (%)	65 (17.4)			
None	16 (4.3)			
Mild	8 (2.1)			
Moderate	14 (3.8)			
Severe	43 (11.5)			
Interference severity on general activity, median (IQR)	8 (6-9)	6 (4-8)		6 (5-8)
Interference on general activity, number of patients (%)	69 (18.5)	159 (42.6)		47 (12.6)
None	12 (3.3)	40 (10.7)		10 (2.7)
Mild	8 (2.1)	37 (9.9)		7 (1.9)
Moderate	15 (4)	54 (14.5)		18 (4.8)
Severe	46 (12.3)	68 (18.2)		22 (5.9)

Percentage values are rounded up to one decimal. Definitions and abbreviations: IQR, interquartile range. Chronic pain, defined as pain that lasts or recurs for more than 3 months³¹. Last 24 hours, defined as pain in the last 24 hours before the interview. At Interview, defined as pain at the time of the interview. Acute-on-chronic pain, defined as pain in the last 24 hours before the interview in patients with pain that lasts or recurs for more than 3 months. Pain intensity measured by means of Numerical Rating Scale (NRS)²⁸. Severity of pain intensity: none (NRS scoring 0), mild (NRS scoring from 1 to 3), moderate (NRS scoring from 4 to 6), and severe (NRS scoring from 7 to 10)²⁹. Pain-related interferences with sleep, enjoyment of life and general activity, measured by means of an 11-point response scale, ranging from 0 to 10³⁰. Severity of pain-related interferences with sleep, enjoyment of life and general activity: none (scoring 0), mild (scoring from 1 to 3), moderate (scoring from 4 to 6), and severe (scoring from 7 to 10). Hospital Unit, recorded as a dichotomous variable, in Medical Unit, including Oncology Unit, and in Surgical Unit. Outpatient care services, Psychiatric, Pediatric, Obstetric, Emergency and Intensive Care Units were excluded from the analysis.

pain intensity were respectively recorded in 6.2% (23/373) and 7.2% (27/373) of patients.

Of the 57 acute-on-chronic pain patients, 52.6% reported pain interference on sleep during the hospitalization [equal to 8% (95% CI: 0.0549,

0.1128) of the study sample (30/373 patients)], with a median score (interquartile range) of 7 (5-8). Moderate to severe interference resulted in 25 out of 57 subjects (43.8% of acute-on-chronic pain patients; 6.7% of the study sample).

Pain interference on general activity was experienced by 82.4% of acute-on-chronic pain patients [equal to 12.6% (95% CI: 0.0941, 0.1640) (47/373)], with a median score (interquartile range) of 6 (5-8). Moderate to severe interference resulted in 40 out of 57 subjects (70.2% of acute-on-chronic pain patients; 10.7% of the study sample). Moreover, 58% of chronic pain patients also experienced pain at the time of the interview [12.6% (95% CI: 0.0941, 0.1640)], and 50.6% complained about both pain during the last 24 hours before the interview, and at the time of this latter [11% (95% CI: 0.0800, 0.1462)]. Table II lists all acute-on-chronic pain prevalence rates recorded.

Pain at the Time of Interview

The prevalence rate of pain patients, at the time of the interview, was 37.3% (95% CI: 0.3234, 0.4239) (Table II). Among patients with pain at the time of the interview, 130 out of 139 subjects (34.8% of the study sample) reported pain at rest, with a median NRS score (interquartile range) of 5 (3-7). Moderate and severe pain intensity were respectively recorded in 14.5% (54/373) and 11.3% (42/373) of patients.

Pain on movement at the time of the interview was experienced by 133 out of 139 subjects (35.6% of the study sample), with a median NRS score (interquartile range) of 7 (5-8). Moderate and severe pain intensity were respectively recorded in 11% (41/373) and 19.3% (72/373) of patients. Table II lists all pain at the time of the interview prevalence rates recorded during the survey.

Reporting of Pain, Treatment Received, Pain Relief After Treatment, and Reassessment of Pain During the Hospital stay

Of 373 patients of the study sample, 68.9% (95% CI: 0.6393, 0.7357) reported having denounced pain to healthcare professionals during the hospitalization. Of the other 116 subjects, who did not point out pain during the hospitalization, 94 (25.2% of the study sample) indicated that they did not experience pain during the hospital stay. Four patients reported that they were waiting for healthcare professionals to ask, while 18 patients stated that they did not report pain to healthcare professionals because of its tolerability.

Of 257 patients of the study sample who reported pain during the hospitalization, 92.6% (95% CI: 0.8870, 0.9549) received pain treatment.

Of these 238 subjects, 89.5% (95% CI: 0.8489, 0.89309) has reported at least a 50% pain relief after treatment, while a reassessment of pain therapy by a healthcare professional was indicated by 186 out of 238 patients who were given treatment for pain [78.1% (95% CI: 0.7236, 0.8323)].

Likelihood of Pain During the Hospital Stay

A binomial logistic regression was performed to ascertain the effects of Hospital Unit, age, sex, surgical treatment, and preexisting chronic pain condition on the likelihood of pain during the last 24 hours of hospital stay. There was one standardized residual with a value of 2.614 standard deviations, which was removed from the analysis. The logistic regression model was statistically significant, $\chi^2(5) = 45.072$, $p < 0.0005$. The model explained 15.2% (Nagelkerke R^2) of the variance in pain during the last 24 hours of hospital stay, and correctly classified 66.4% of cases. Sensitivity was 67.8%, specificity was 64.7%, positive predictive value was 68.9%, and negative predictive value was 63.6%. Of the five predictor variables, only three were statistically significant: undergoing surgery during the hospitalization, preexisting chronic pain condition, and age, as shown in Table III. As a matter of fact, patients who underwent surgery during the hospitalization had 2.7 higher odds to suffer from pain during the hospital stay, as well as patients with preexisting chronic pain had 2.6 higher odds to experience pain during the hospitalization. Increasing age was instead associated with a reduction in the likelihood of reporting pain during hospitalization. However, there was no statistically significant association between Hospital Units and sex and pain during the hospitalization.

Discussion

This study investigates several measures of pain prevalence in patients admitted to Niguarda Hospital Departments. To the best of our knowledge, this is one of the few studies that examine different prevalence times about pain in an Italian hospital setting, including multiple hospital wards. First of all, patients admitted to our Departments are represented by a heterogeneous population, of which more than 40% aged 65 years and older. In this scenario, we found that 1 out of 5 subjects [21.7% (95% CI: 0.1764, 0.2625)] was suffering from a pain condition for more than

Table III. Logistic Regression Predicting Likelihood of Pain during the Hospital Stay, based on Hospital Unit, Sex, Age, Surgical treatment during the hospitalization, and Preexisting chronic pain condition.

	B	SE	Wald	df	p	Odds Ratio	95% CI for Odds Ratio	
							Lower	Upper
Hospital Unit	0.096	0.298	0.103	1	0.748	1.100	0.613	1.974
Sex	0.399	0.229	3.021	1	0.082	1.490	0.950	2.335
Age	-0.013	0.006	4.396	1	0.036	0.987	0.975	0.999
Surgical treatment	0.981	0.281	12.177	1	0.001	2.668	1.538	4.630
Chronic Pain	0.946	0.284	11.087	1	0.001	2.576	1.476	4.497
Constant	0.206	0.416	0.245	1	0.620	1.229		

Definitions: Pain during the hospital stay, defined as pain during the last 24 hours before our interview. Chronic Pain, defined as pain that lasts or recurs for more than 3 months³¹. Hospital Unit, recorded as a dichotomous variable, in Medical Unit, including Oncology Unit, and in Surgical Unit. Outpatient care services, Psychiatric, Pediatric, Obstetric, Emergency and Intensive Care Units were excluded from the analysis. B, coefficient for the constant in the null model. SE, standard error around the coefficient for the constant. Wald, Wald chi-square test. df, degrees of freedom for the Wald chi-square test. p, p-value. CI, confidence interval. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 20; Armonk, New York, NY, USA). The significance level is 0.05. *Note:* Hospital Unit is for surgical unit compared to medical unit; Sex is for females compared to males; Surgical treatment is for patients who underwent surgical treatment during the hospital stay compared to patients who did not undergo surgery; Chronic Pain is for patients with chronic pain compared to patients without chronic pain.

three months before the hospitalization, with a median pain intensity score of 6 and 7 out of 10, at rest and on movement, respectively. In other words, 81.6% of patients with chronic pain at rest have experienced moderate to severe pain, as well as about 90% of patients with pain on movement. Pain interference on sleep was frequent, as 14.5% of patients reported sleep disorders, with a moderate-severe intensity in more than 80% of cases. Pain interference on the enjoyment of life was even more frequent on hospitalized chronic pain patients, as 17.4% of the study sample complained of pain-related emotional disorders, with a more than mild intensity in 88% of patients, along with interference on general activity (18.5% of the study sample). Several studies^{1,12,35-37} have reported similar or higher prevalence rates of chronic pain in hospitals and general populations. A systematic review of Fayaz et al³⁵ showed that 43.5% (95% CI: 38.4, 48.6) of adult residents in the United Kingdom were affected by a chronic pain condition. Regarding the general population in the United States, the analysis of 2016 National Health Interview Survey data¹ underlined a 20.4% prevalence of chronic pain patients, and an estimated 60% of older adults reported at least some persistent pain³⁶. In Italy, recent studies have highlighted a prevalence rate of 28.4% of patients with chronic pain³⁷, with severe pain in more than 50% of the chronic pain population¹². We still have to consider that the prevalence rate of chronic pain is quite high.

As for acute pain, instead, several studies^{10,11,38-42} have pointed out that acute pain is widespread both in Western and low- and middle-income countries. In our research, identification of pain was performed using the Numerical Rating Scale²⁸, one of the most used scales for pain severity scoring. Turning to acute pain prevalence and predictors of pain during the hospitalization, the data presented in our study are consistent with the findings of previous studies^{10,11}, revealing a high pain prevalence both at the time of the interview (37.3%; 95% CI: 0.3234, 0.4239) and in the last 24 hours before the interview (53.3%; 95% CI: 0.4814, 0.5850). Patients who underwent surgery during the hospitalization had 2.7 higher odds to suffer from pain during the hospital stay, as well as patients with chronic pain had 2.6 higher odds of experiencing pain during the hospitalization. Consistent with some previous analyses^{43,44}, our data suggest a reduction in the likelihood of reporting pain during hospitalization with increasing age. However, the presence of this association may be due to the small sample size, the different population of the study, or the different study setting, as other studies reported the opposite in terms of age for predicting pain^{45,46}.

Likewise, focusing our research on patients with acute-on-chronic pain, we can see how about 70% of chronic pain patients have experienced pain during the hospital stay, representing nearly 15% of the study population, often with

moderate or severe intensity, and sleep or general activity interference. This is very interesting because it shows that acute and chronic pain, despite Italy promulgated a law to guarantee people have access to pain therapy (Act 38, March 15th, 2010), is still frequent, and at risk of undertreatment. However, 92.6% (95% CI: 0.8870, 0.9549) of our patients received a pain treatment, with nearly 90% that reported at least a 50% pain relief after the treatment. We still have to point out that less than 80% of the treated patients received a reassessment of clinical conditions, suggesting that an improvement in acute and persistent pain management is needed. As already mentioned in the introduction section, numerous treatment guidelines have been generated^{17-23,47}, although rarely ensuring an optimal approach that takes account of multiple pain dimensions in the real-world subjects. In fact, these patients are frequently suffering from several pathological conditions, along with polypharmacy, both for non-pain and pain disorders. Consequently, they are characterized by the concomitant assumption of different therapeutic classes, such as opioids, benzodiazepines, anticonvulsants, antidepressants, and antipsychotics, with a significant increase in harmful clinical outcomes^{21,48,49}. As shown in our analysis, there is a high prevalence of pain interference on patients' sleep and emotional status. This situation may increment the use of medications like benzodiazepine and non-benzodiazepine receptor agonists, or antidepressants, such as tricyclic antidepressants, and Selective Serotonin Reuptake Inhibitors (SSRI), or Serotonin-Norepinephrine Reuptake Inhibitors (SNRI). Psycholeptics also represent an important and common type of potentially inappropriate medication class prescribed, as precisely described by various lists of criteria for appropriate drug prescription⁵⁰⁻⁵². In fact, older adult patients seem to be most disposed to develop adverse effects, such as cardiovascular events, hyponatremia, and anticholinergic effects⁵³. Furthermore, as inappropriate polypharmacy is associated with an increased risk of adverse drug events and a higher probability of hospitalization^{54,55}, chronic pain condition itself is shown to be related to greater use and overcrowding of the Emergency Departments, fueling healthcare system costs, reducing the quality of care and degree of patients' satisfaction¹⁶.

Despite all the evaluations of pain prevalence discussed above, we have to underline some limitations of our study: first, this is a single-center

study, with a relatively small study sample compared to other investigations. Second, we focus only on the presence of pain, without investigating its underlying causes and medication classes used for pain relief. Furthermore, because of the sensitive background of some departments, the implementation of this prevalence study throughout the entire hospital was not possible to realize, thus excluding some important population categories. Consequently, pain assessment was reported only in patients with the ability to express informed consent to the survey, thus excluding non-communicating patients. Another limitation of this study is that surgical treatment was registered only as a dichotomous variable, not reporting the time frame between surgery and the onset of pain. However, it must be added that a considerable number of patients were included in this experience, within the majority of Hospital Units.

Measures of pain prevalence here introduced show how necessary is to improve pain management during hospitalization. Pain reporting and detection is a crucial element of every diagnostic and therapeutic pain guidance pathway. The acquisition of pain history is essential, as outlined by the increase in the likelihood of suffering from pain during the hospital stay if a preexisting pain is present. However, this point of view is also a mirror of what happens in outpatient services, because one out of five subjects is already suffering from pain when they are admitted to the hospital setting, and nearly 70% of these patients will experience pain during the hospital stay. It is, therefore, vital the identification of methodologies for hospital-territory integration. Within this context, electronic medical records may help both hospital and primary care physicians to communicate and implement a shared diagnostic-therapeutic care pathway about persistent pain patients, aiming at increasing patient safety, and improving prescribing practices. Another measure that may lead to better integration between hospital and primary care services may be widening the pool of healthcare professionals, inserting connection figures that could create a bridge, such as family nurses, psychologists, and healthcare providers.

Conclusions

This study provides insights into the prevalence of persistent, acute, and acute-on-chronic pain during an Italian Tertiary Care Hospital stay. Chronic pain was reported in one out of five

patients during the hospitalization, with a high prevalence of moderate-severe pain-related interference on sleep and emotional status, and nearly 70% with acute-on-chronic pain. Acute pain, therefore, was even more frequent, ranging from about 37% to 53% of patients, at the time of the interview and in the last 24 hours before the interview. A 2.7 and 2.6 higher odds to suffer from pain during the hospital stay were associated with surgical treatment during the hospitalization, and preexisting chronic pain, respectively. This study is important to raise awareness of the necessity to improve pain assessment and management, in all patient populations, both in hospital and outpatient services, with special attention to acute experience in persistent pain subjects.

In this direction, our wish is the promotion and enhancement of hospital-territory integration. Widening the pool of healthcare professionals, with family nurses, psychologists, and other professional figures, as well as strengthening electronic medical records, may help the communication within the healthcare system. The implementation of a shared diagnostic-therapeutic pathway may improve pain prescribing practices and increase patient safety. This approach may answer the necessity of a guide to the best possible appropriate management for pain-suffering patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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References

- 1) Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of chronic pain and high-impact chronic pain among adults – United States, 2016. *MMWR Morb Mortal Wkly Rep* 2018; 67: 1001-1006.
- 2) World Health Organization. Multimorbidity: technical series on safer primary care. Geneva, 2016. Licence: CC BY-NC-SA 3.0 IGO. <https://apps.who.int/iris/bitstream/handle/10665/252275/9789241511650-eng.pdf?sequence=1>. Accessed January 18, 2021.
- 3) GBD 2019 Diseases and injuries collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396: 1204-1222.
- 4) Kernick D, Chew-Graham CA, O'Flynn N. Clinical assessment and management of multimorbidity: NICE guideline. *Br J Gen Pract* 2017; 67: 235-236.
- 5) Nunes BP, Flores TR, Mielke GI, Thumé E, Facchini LA. Multimorbidity and mortality in older adults: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2016; 67: 130-138.
- 6) The Italian society of pharmacology. *Trattamento del dolore cronico in Italia: appropriatezza terapeutica con oppiacei e timore di addiction: situazione italiana vs USA*. Available at: https://sif-website.s3.amazonaws.com/uploads/document/attachment/42/sif_position_paper_dolore_oppiacei_apr18.pdf. Accessed January 18, 2021.
- 7) Glare PA, Davies PS, Finlay E, Gulati A, Lemanne D, Moryl N, Oeffinger KC, Paice JA, Stubblefield MD, Syrjala K. Pain in cancer survivors. *J Clin Oncol* 2014; 32: 1739-1747.
- 8) Italian Medicines Agency (AIFA). The medicines utilisation monitoring centre. National Report on Medicines use in Italy. Year 2019. Rome, 2020. Available at: <https://www.aifa.gov.it/documents/20142/1205984/rapporto-osmed-2019.pdf/f41e53a4-710a-7f75-4257-404647d0fe1e>. Accessed on January 18, 2021.
- 9) Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth* 2019; 123: 273-283.
- 10) Civardi G, Zucco F, Valerio A, Fontanella A, Alesandri M, Ciannamea CD, Perale L, Gussoni G, Bonizzoni E, Vescovo E, Agnelli G, Campanini M, Mazzone A, Nozzoli C. Pain management in internal medicine and effects of a standardised educational intervention: the FADOI-DOMINO Study. *Int J Clin Pract* 2015; 69: 33-40.
- 11) Costantini M, Viterbori P, Flego G. Prevalence of pain in Italian Hospitals: results of a regional cross-sectional survey. *J Pain Symptom Manage* 2002; 23: 221-230.
- 12) Latina R, De Marinis MG, Giordano F, Osborn JF, Giannarelli D, Di Biagio E, Varrassi G, Sansoni J, Bertini L, Baglio G, D'Angelo D, Colini Baldeschi G, Piredda M, Carassiti M, Camilloni A, Paladini A, Casale G, Mastroianni C, Notaro P, Pain Researchers Group into Latium Region, Diamanti P, Coaccioli S, Tarsitani G, Cattaruzza MS. Epidemiology of chronic pain in the Latium Region, Italy: a cross-sectional study on the clinical characteristics of patients attending pain clinics. *Pain Manag Nurs* 2019; 20: 373-381.
- 13) Chen E, Tsoy D, Upadhve S, Chan TM. The acute care of chronic pain study: perceptions

- of acute care providers on chronic pain, a social media-based investigation. *Cureus* 2018; 10: e2399.
- 14) Todd KH, Cowan P, Kelly N, Homel P. Chronic or recurrent pain in the emergency department: national telephone survey of patient experience. *West J Emerg Med* 2010; 11: 408-415.
 - 15) Paulin PA, Nelli J, Tremblay S, Small R, Caluyong MB, Freeman J, Romanow H, Stokes Y, Carpino T, Carson A, Shergill Y, Stiell IG, Taljaard M, Nathan H, Smyth CE. Chronic pain in the emergency department: a pilot mixed-methods cross-sectional study examining patient characteristics and reasons for presentations. *Pain Res Manag* 2016; 2016: 3092391.
 - 16) Dépelteau A, Racine-Hemmings F, Lagueux E, Hudon C. Chronic pain and frequent use of emergency department: a systematic review. *Am J Emerg Med* 2020; 38: 358-363.
 - 17) Ferrel B, Argoff CE, Epplin J, Fine P, Gloth FM, Herr K, Katz JD, Mehr DR, Reid C, Reisner L. Pharmacological management of persistent pain in older persons. *J Am Geriatr Soc* 2009; 57: 1331-1346.
 - 18) National Institute for Health and Care Excellence (NICE). Neuropathic pain in adults: pharmacological management in non-specialist settings. 2013. <https://www.nice.org.uk/guidance/cg173>. Accessed on January 18, 2021.
 - 19) National Institute for Health and Care Excellence (NICE). Multimorbidity: clinical assessment and management. 2016. <https://www.nice.org.uk/guidance/ng56>. Accessed on January 18, 2021.
 - 20) Dowell D, Haegerich TM, Chou R. CDC Guideline for prescribing opioids for chronic pain – United States, 2016. *MMWR Recomm Rep* 2016; 65: 1-49.
 - 21) National Pain Centre. The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain. https://nationalpaincentre.mcmaster.ca/documents/Opioid%20GL%20for%20CMAJ_01may2017.pdf. Accessed February 7, 2021.
 - 22) Scottish Intercollegiate Guidelines Network (SIGN). Management of chronic pain. Edinburgh: SIGN; 2013. (SIGN publication no. 136). <http://www.sign.ac.uk>. Accessed February 7, 2021.
 - 23) National Institute for Health and Care Excellence (NICE). Chronic pain: assessment and management. 2020. <https://www.nice.org.uk/guidance/in-development/gid-ng10069>. Accessed on February 7, 2021.
 - 24) Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020; 324: 603-605.
 - 25) Bruce J, Quinlan J. Chronic post surgical pain. *Rev Pain* 2011; 5: 23-29.
 - 26) Katz J, Weinrib A, Flashler SR, Katznelson R, Shah BR, Ladak SS, Jiang J, Li Q, McMillan K, Mina DS, Wentlandt K, McRae K, Tamir D, Lyn S, de Perrot M, Rao V, Grant D, Roche-Nagle G, Cleary SP, Hofer SO, Gilbert R, Wijeyesundera D, Ritvo P, Janmohamed T, O'Leary G, Clarke H. The Toronto General Hospital Transitional Pain Service: development and implementation of a multidisciplinary program to prevent chronic post-surgical pain. *J Pain Res* 2015; 8: 695-702.
 - 27) von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008; 12: 1495-1499.
 - 28) Karcioglu O, Topacoglu H, Dikme O, Dikme O. A systematic review of the pain scales in adults: which to use? *Am J Emerg Med* 2018; 36: 707-714.
 - 29) Moore RA, Straube S, Aldington D. Pain measures and cut-offs – 'no worse than mild pain' as a simple, universal outcome. *Anaesthesia* 2013; 68: 400-412.
 - 30) Bonezzi C, Nava A, Barbieri M, Bettaglio R, Demartini L, Miotti D, Paulin L. [Validazione della versione italiana del Brief Pain Inventory nei pazienti con dolore cronico]. *Minerva Anestesiol* 2002; 68: 607-611.
 - 31) Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Kosek E, Lavand'homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JWS, Wang SJ. A classification of chronic pain for ICD-11. *Pain* 2015; 156: 1003-1007.
 - 32) Krebs EE, Lorenz KA, Bair MJ, Damush TM, Wu J, Sutherland JM, Asch SM, Kroenke K. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med* 2009; 24: 733-738.
 - 33) Ravyts SG, Dzierzewski JM, Raldiris T, Perez E. Sleep and pain interference in individuals with chronic pain in mild- to late-life: the influence of negative and positive effect. *J Sleep Res* 2019; 28: e12807.
 - 34) Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, Haythornthwaite JA, Jensen MP, Kerns RD, Ader DN, Brandenburg N, Burke LB, Cella D, Chandler J, Cowan P, Dimitrova R, Dionne R, Hertz S, Jadad AR, Katz NP, Kehlet H, Kramer LD, Manning DC, McCormick C, McDermott MP, McQuay HJ, Patel S, Porter L, Quessy S, Rappaport BA, Rauschkolb C, Revicki DA, Rothman M, Schmader KE, Stacey BR, Stauffer JW, von Stein T, White RE, Witter J, Zavisic S. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008; 9: 105-121.
 - 35) Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 2016; 6: e010364.
 - 36) Molton IR, Terrill AL. Overview of persistent pain in older adults. *Am Psychol* 2014; 69: 197-207.

- 37) Del Giorno R, Frumento P, Varrassi G, Paladini A, Coaccioli S. Assessment of chronic pain and access to pain therapy: a cross-sectional population-based study. *J Pain Res* 2017; 10: 2577-2584.
- 38) Gregory J, McGowan L. An examination of the prevalence of acute pain for hospitalised adult patients: a systematic review. *J Clin Nurs* 2016; 25: 583-598.
- 39) Mura P, Serra E, Marinangeli F, Patti S, Musu M, Piras I, Massidda MV, Pia G, Evangelista M, Finco G. Prospective study on prevalence, intensity, type, and therapy of acute pain in a second-level urban emergency department. *J Pain Res* 2017; 10: 2781-2788.
- 40) Damico V, Murano L, Cazzaniga F, Dal Molin A. Pain prevalence, severity, and assessment in hospitalized adult patients: a result of a multi-center cross sectional study. *Ann Ist Super Sanità* 2018; 54: 194-200.
- 41) Morriss WW, Roques CJ. Pain management in low- and middle-income countries. *BJA Education* 2018; 18: 265-270.
- 42) Sá KN, Moreira L, Baptista AF, Yeng LT, Teixeira MJ, Galhardoni R, de Andrade DC. Prevalence of chronic pain in developing countries: systematic review and meta-analysis. *Pain Rep* 2019; 4: 779-786.
- 43) Melotti RM, Samolsky-Dekel BG, Ricchi E, Chiari P, Di Giacinto I, Carosi F, Di Nino G. Pain prevalence and predictors among inpatients in a major Italian teaching hospital. A baseline survey towards a pain free hospital. *Eur J Pain* 2005; 9: 485-495.
- 44) Yang MMH, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S, Riva-Cambrin J. Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. *BMJ Open* 2019; 9: e025091.
- 45) Liu XK, Xiao SY, Zhou L, Hu M, Liu HM. Different predictors of pain severity across age and gender of a Chinese rural population: a cross-sectional survey. *BMJ Open* 2018; 8: e020938.
- 46) Majedi H, Amini MH, Yousefshahi F, Khazaeipour Z, Majedi M, Rahimi M, Orandi A. Predicting factors of pain duration in patients with chronic pain: a large population-based study. *Anesth Pain Med* 2020; 10: e95776.
- 47) Schug SA, Palmer GM, Scott DA, Halliwell R, Trinca J. *Acute pain management: scientific evidence*, fourth edition, 2015. *Med J Aust* 2016; 204: 315-317.
- 48) U.S. Food & Drug Administration (FDA). *Opioid Medications. FDA's 2018 Strategic Policy Roadmap*. 2018. <https://www.fda.gov/media/110587/download>. Accessed February 7, 2020.
- 49) The Government of Canada. *Federal Actions on Opioids to date*. Available at: https://www.canada.ca/content/dam/hc-sc/documents/services/substance-use/problematic-prescription-drug-use/opioids/responding-canada-opioid-crisis/federal-actions/june_2020_pager-FINAL_.pdf. Accessed February 7, 2020.
- 50) The 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. *American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults*. *J Am Geriatr Soc* 2019; 67: 674-694.
- 51) O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015; 44: 213-218.
- 52) Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIMlist: a list of potentially inappropriate medications for older people consented by experts from seven European countries. *Eur J Clin Pharmacol* 2015; 71: 861-875.
- 53) Sultana J, Spina E, Trifirò G. Antidepressant use in the elderly: the role of pharmacodynamics and pharmacokinetics in drug safety. *Expert Opin Drug Metab Toxicol* 2015; 11: 883-892.
- 54) Ruggiero C, Dell'Aquila G, Gasperini B, Onder G, Lattanzio F, Volpato S, Corsonello A, Maraldi C, Bernabei R, Cherubini A, ULISSE Study Group. Potentially inappropriate drug prescriptions and risk of hospitalization among older Italian nursing home residents: the ULISSE project. *Drugs Aging* 2010; 27: 747-758.
- 55) Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate prescription is a leading cause. *Drugs Aging* 2005; 22: 767-777.