Published online: 2021-03-31

Original Article

Nociceptive Profile and Analgesic use of Patients Submitted to Rotator Cuff Repair Surgery: A Prospective Cohort*

Perfil Nociceptivo e Uso de Analgésicos em Pacientes Submetidos à Cirurgia de Reparo do Manguito Rotador: Coorte Prospectiva

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Abstract

Objective This study aimed to evaluate the nociceptive profile and the intake of analgesic drugs of patients submitted to rotator cuff repair surgery. Also, to evaluate the nociceptive thresholds and the integrity of the descending inhibitory system, pain catastrophism and prevalence of nociceptive or neuropathic pain.

Methods Approved by the Ethics Committee of La Salle University (1.325.433/2015). 40 patients (>18 years old) who underwent rotator cuff repair surgery (divided in small and large injuries) were recruited. The used instruments were: Sociodemographic Questionnaire, Functional Pain Scale, Visual Analogue Scale (VAS), Quantitative Sensory Test (QST) and Conditioned Pain Modulation Task (CPM).

Results Patients had a significant difference in pain thresholds QST heat (independent samples *t* test) and quality of sleep, mood and anxiety (paired *t* test) in groups preoperative. There was a significant correlation between preoperative CPM and postoperative VAS (Pearson Correlation). It was observed that, in preoperative, 38 patients used analgesics continuously. Besides that, in postoperative, use of opioid drugs was higher in patients with small injury (13 patients) than in those with large injury (9 patients).

Conclusion Therefore, patients with rotator cuff injuries did not present alterations in the descending inhibitory system, but showed alterations in pain thresholds, which may interfere in the postoperative period and still be related to the consumption of analgesics.

Keywords
- Rotator cuff injury
- Chronic pain
- Nociceptive pain

* *Work developed in the Programa de Pós-Graduação em Saúde e Desenvolvimento Humano, Universidade La Salle, Canoas, RS, Brasil.*

received
May 25, 2020
accepted
September 16, 2020

DOI https://doi.org/10.1055/s-0040-1719087.
ISSN 0102-3616.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Objetivo O objetivo deste estudo foi avaliar o perfil nociceptivo e o uso de analgésicos em pacientes submetidos à cirurgia de reparo do manguito rotador. Além disso, os limiares nociceptivos e a integridade do sistema inibidor descendente, o catastrofismo da dor e a prevalência de dor nociceptiva ou neuropática também foram analisados.

Métodos Este estudo foi aprovado pelo Comitê de Ética da Universidade La Salle (1.325.433/2015). Quarenta pacientes (maiores de 18 anos) submetidos à cirurgia de reparo do manguito rotador (divididos entre aqueles com lesões pequenas e grandes) participaram do estudo. Os instrumentos utilizados foram o Questionário Sociodemográfico, a Escala Funcional de Dor, a Escala Visual Análoga (EVA), o Teste Sensorial Quantitativo (QST) e a Tarefa de Modulação Condicionada da Dor (CPM).

Resultados Os pacientes apresentaram diferenças significativas nos limiares de dor e QST de calor (teste *t* de amostras independentes) e qualidade do sono, humor e ansiedade (teste *t* pareado) nos grupos pré-operatórios. Houve uma correlação significativa entre CPM pré-operatória e EVA pós-operatória (correlação de Pearson). Observou-se que, no período pré-operatório, 38 pacientes utilizavam analgésico de forma contínua. Além disso, no período pós-operatório, o uso de opioides foi maior nos pacientes com lesões pequenas (13 pacientes) em comparação àqueles com lesões grandes (nove pacientes).

Conclusão Os pacientes com lesão do manguito rotador não apresentaram alterações no sistema inibidor descendente, mas sim alterações nos limiares de dor, o que pode interferir no período pós-operatório e estar relacionado ao consumo de analgésicos.

Palavras-chave

- lesões do manguito rotador
- dor crônica
- dor nociceptiva

Introduction

According to the International Association for the Study of Pain (IASP), pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[1,2] IASP also defined chronic pain as that which lasts for more than 3 months, characterized by persistent physical pain, disability, emotional disturbance, and social withdrawal symptoms, exist- ing together and influencing one another.[3] Neuropathic pain is usually caused by a lesion or a disease of the somatosensory nervous system.[4]

At hospitals, the most prevalent acute pain is postoperative pain, usually associated with tissue damage prevailing after long surgeries, such as toracic, abdominal, renal and orthopedics.[5] Incidence, intensity and locus depends on several factors, such as anxiety, fear, depression, genetic and environmental factors that influence pain sensibility.[6] After a surgical procedure, prolonged noxious stimuli usually cause suffering, body damage and postoperative complications.[7]

Postoperative pain intensity and the need for large amounts of analgesics in the first days after surgery are predictors for chronic pain.[8] A systematic review evidenced that persistent postsurgical pain (PPSP) is experienced by 10% to 50% of patients, can be serious in about 5% to 10% of individuals. Due to this condition, 20% of patients seek care in a pain clinic.[9]

Rotator cuff injuries are the most frequent cause of shoulder pain.[10] Complete rotator cuff rupture is related to young individuals due to traumatic situation, while in elderly patients it has as etiology a tendon fragility, with repetitive microtraumas related to acromial anatomy and poor tendon vascularization.[11] Such injuries are more common the supraspinatus tendon injury, which has an insertion in the greater tuber of the humerus. Supraspinatus injury can be divided into partial or complete.[12] Partial rotator cuff injuries has an incidence of 13% to 37% of world population.[13] However, rotator cuff surgical repair, either open or arthroscopic, is the best conduct in case of persistent pain and evolutive muscle weakness.[14] Peripheral nerve block may provide adequate analgesia in immediate postoperative until 20 hours.[15]

The most used therapy for analgesia are non steroidal anti inflammatory drugs (NSAIDs) and high doses of opioids, administered orally or intravenously used for a short time. Analgesics mechanism of action is based on prostaglandin synthesis inhibition, responsible for mild and moderate pain, local vasodilation and increase of vascular permeability.[16] Opioids are potent analgesics with recommendation for moderate or intense pain treatment. NSAIDs are used as single agents or associated to opioids, it does not cause respiratory depression, reduces the opioid necessary amount and consequently the incidence of adverse effects.[17]

Since there are no previous studies evidencing the difference between small and large injury pain levels in chronic pain patients that underwent to rotator cuff repair surgery, this evaluation is needed. Therefore, this study aimed to compare the nociceptive profile and analgesic use between

patients with small and large injuries with chronic pain submitted to rotator cuff repair surgery.

Material and Methods

Reports are according to STROBE guidelines. Approval of this study was made by the Ethics Committee (1.325.433/2015). Protocols are according to the Declaration of Helsinki (Resolution 466/12 of National Health Council).

Study Design

This is a prospective cohort, in which evaluated patients with rotator cuff injury who were submitted to open repair surgery. Measurement and determination of injury extension were performed by a surgeon and classified as small injury between 1 cm to 3 cm and large injury between 3 cm to 5 cm.[18]

Participants

Inclusion criteria: more than 18 years old, pain for more than 6 months, not made rotator cuff repair surgery yet, interned in the hospital to undergo rotator cuff repair surgery and sign an informed consent to participate in the study.

Exclusion criteria: indication of other surgical procedure besides rotator cuff repair, difficulty in questionnaires understanding, use of systemic corticosteroids and oncologic disease or diabetes, since it was described in the literature that these pathologies could interfere in pain thresholds.

Sample Size Calculation

Visual Analogue Scale (VAS) represents one of the main measurements of pain that would demonstrate patient improvement in postoperative. For sample size calculation it was used 2 articles that showed significant alterations in VAS in patients on rotator cuff repair preoperative and postoperative. Effect size was 3.51 and 2.78 (*d* de Cohen), using a *t* test for independent samples, with a 0.05 two-tailed alpha error, 80% of power and the same sample size for each group. Sample size calculation was made in *gpower* program. Sample size determined was 40 patients.

Outcomes

A sociodemographic questionnaire elaborated by the research group was applied. Primary outcome was Visual Analogue Scale (VAS), it quantifies pain from 0 to 10. Pain Catastrophizing Scale (PCS) was performed to evaluate total catastrophism, rumination, magnification and hopelessness. LANSS scale (Leeds Assessment of Neuropathic Symptoms and Signs) was to differentiate neuropathic pain from nociceptive pain. VAS (from 0 to 10) was used to evaluate sleep quality, humor and anxiety. Profile of Chronic Pain Scale (PCP:S) was made to evaluate pain frequency and intensity, its effect on activities and on emotions.

Use of Quantitative Sensory Testing (QST) was to determine the maximum tolerated temperature and heat pain threshold on volar side of the forearm of the contralateral limb to the surgical shoulder. Patient pressed a button when he felt first heat sensation, first pain sensation and when he can not tolerate heat increase.

Conditioned Pain Modulation (CPM) was the difference between two painful stimuli: a heat applied in the unoperated shoulder arm with pain that was previous measured in QST task as 6, concomitantly with a painful stimuli the patient immersed the contralateral foot in water at a temperature of 0 to 1,5°C for 30 seconds. Since the patients were in a postoperative period in the shoulder, the cold stimuli was performed in the same body side as the shoulder operated, providing equal results as if it was made in the operated shoulder. After stimuli, registered pain magnitude was through VAS.

Setting

All patients were submitted to ipsilateral brachial plexus block injury, through interscalene, guided by ultrasound. Anesthetics used were ropivacaine 0.375% and lidocaine 1%. After complete sensitive block of the area to be operated confirmation, sedation was with 0.05 mg of fentanyl and 1 to 5 mg of midazolam.

In postoperative period, patients received analgesic drugs according regular prescription: acetaminophen 750 mg associated with codeine 30 mg orally every 6 hours. A patient screening was made when patient was interned, one day before surgery.

Statistical Analysis

Verification of normality was through Shapiro-Wilk test. Continuous variables were parametric and were described as mean $\pm$ standard deviation. To evaluate possible correlations between pre and post operative, it was used Pearson Correlation. When continuous variables were compared between two measures from the same patient, paired *t* test was used. To evaluate the effect of injury size it was used an independent sample *t* test. Categorical data were by Fisher exact test or Chi-Square. For all analysis the significance level established was $P < 0.05$. Analysis were through SPSS 20.0 (Chicago, IL)

Results

There was an inclusion of a total of 40 patients in the study; description of sample sociodemographic characteristics are in ►**Table 1**.

Among participants, there was a significant difference in groups ages, with a large injury in those older patients. When analyzing laterality, 57.5% (23) were affected in the right side, while 42.5% (17) on the left side.

Regarding use of drugs, in preoperative most patients (38) used analgesics continuously. Besides that, in postoperative, use of opioid drugs was higher in patients with small injury (►**Figure 1**.), morphine being the most used.

►**Table 2** shows results regarding pain thresholds and descending inhibitory system evaluation, in which significant found alterations were in heat QST in small injury patients.

When performing *t* test to evaluate pain thresholds between small injury preoperative and large injury preoperative there was no significant difference. However, when performing

Table 1 Sample Sociodemographic Characteristics

Variable	Small injury	Large injury	P Value
Age (mean ± SD)	55.82 ± 7.84	62.00 ± 10	0.035*
Sex			0.748
Female	15	12	
Male	08	05	
Alcoholism			0.428
Yes	6	2	
No	17	15	
Smoking			0.707
Yes	6	3	
No	17	14	
Shoulder			0.848
Right	13	10	
Left	10	07	
Psychoactive Substances			0.432
Yes	3	4	
No	20	13	
Previous Diseases			0.896
Yes	4	10	
No	19	7	
Psychiatric Disorders			0.730
Yes	7	4	
No	16	13	
Pain Drugs			1.000
Yes	22	16	
No	1	1	

*Significant difference (independent samples *t* test). Fisher's exact test or Chi-Square.

Pearson Correlation there were some interesting correlations. In large injuries, preoperative heat QST is correlated with postoperative heat QST ($r = 0.765$, $P < 0.001$) and preoperative tolerance QST ($r = 0.542$, $P = 0.025$). In small injuries, preoperative heat QST is correlated with postoperative heat QST ($r = 0.605$, $P = 0.002$). Preoperative pain QST is correlated with preoperative tolerance QST ($r = 0.589$, $P = 0.003$). Preoperative tolerance QST is correlated with postoperative tolerance QST ($r = 0.588$, $P = 0.003$). There was a correlation between preoperative CPM and postoperative CPM ($r = 0.468$, $P = 0.024$), between preoperative CPM and postoperative VAS ($r = 0.475$, $P = 0.022$) and between postoperative CPM and postoperative VAS ($r = 0.409$, $P = 0.053$).

Regarding small injury patients, they have a higher catastrophism when compared to large injury. ►**Table 3** presents catastrophism data

►**Table 4** demonstrates variations in sleep pattern, anxiety level and humor in patients with small and large injury in preoperative and postoperative.

Small injury patients presented significant difference in humor domain, meaning that patients with small injury present largest changes in humor when comparing preoperative to postoperative. Large injury patients presented a higher level of anxiety in first preoperative 24 hours when compared to postoperative. Data were also compared between groups (small and large injury), evaluating only preoperative or postoperative, there was no significant difference (*t* test for independent samples; $P > 0.05$)

►**Table 5** shows results of Profile of Chronic Pain Scale (PCP:S), regarding pain frequency and intensity, pain effect on activities and pain effect on emotions. Groups showed no statistical difference in preoperative and postoperative (*t* test for independent samples; $P > 0.05$).

►**Table 6** represents prevalence of nociceptive and neuropathic pain in preoperative patients with rotator cuff injury.

Discussion

Analyzing location of injuries, most patients presented right shoulder small injury, corroborating with previous studies, in which rotator cuff injuries are most common in women and the most affected side is the right one.[19]

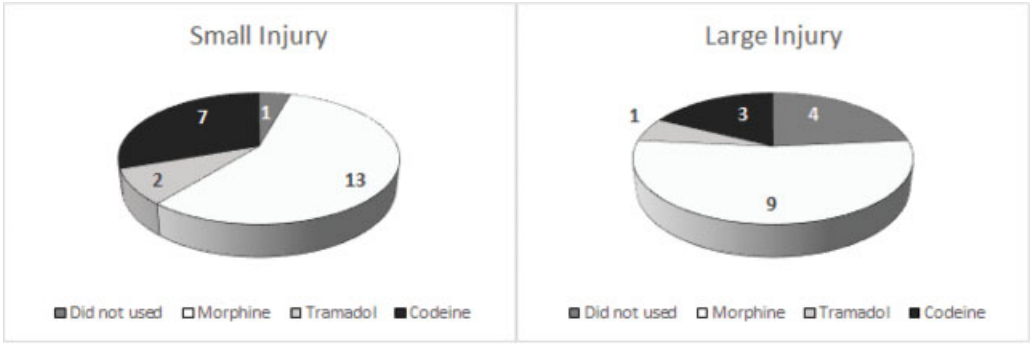

Fig. 1 Use of opioids in rotator cuff repair surgery postoperative.

Table 2 Pain Threshold and Descending Inhibitory System of Pain

	Small injury		P Value	Large injury		P Value
	Pre	Post		Pre	Post	
Heat QST	37.15 ± 2.08	36.17 ± 1.89	0.015*	36.33 ± 2.29	36.34 ± 2.29	0.975
Pain QST	43.05 ± 2.88	42.58 ± 2.62	0.345	43.36 ± 2.30	42 ± 2.21	0.610
Tolerance QST	48.61 ± 2.70	48.11 ± 3.22	0.389	48.64 ± 2.42	46.90 ± 2.54	0.320
CPM	0.33 ± 1.76	0.16 ± 2.02	0.698	-0.25 ± 1.87	0.54 ± 1.69	0.730
VAS	4.86 ± 2.83	4.82 ± 3.17	0.955	3.47 ± 2.87	4.82 ± 3.22	0.197

Data expressed as mean ± SD. *Significant difference between preoperative and postoperative evaluation. Paired *t* test. QST: Quantitative Sensory Testing; CPM: Conditioned Pain Modulation; VAS: Visual Analogue Scale.

Table 3 Pain Catastrophism in patients with rotator cuff injury

	Small Injury		P Value	Large Injury		P Value
	Pre	Post		Pre	Post	
Hopelessness	12.73 ± 6.18	13.00 ± 6.59	0.807	9.0 ± 5.12*	10.88 ± 5.76	0.213
Magnification	6.43 ± 3.89	5.86 ± 3.88	0.508	5.0 ± 3.29	4.52 ± 3.16	0.500
Rumination	9.39 ± 4.37	9.47 ± 4.25	0.900	6.70 ± 2.95*	7.82 ± 3.35	0.174
Total	28.56 ± 13.40	28.30 ± 13.67	0.500	20.70 ± 10.19*	23.23 ± 11.30	0.221

Data expressed as mean ± SD. *Significant difference between small preoperative and large preoperative. Independent samples *t* test.

Table 4 Sleep quality, anxiety and humor.

	Small Injury		P Value	Large Injury		P Value
	Pre	Post		Pre	Post	
Sleep	10.02 ± 3.52	10.71 ± 3.46	0.432	9.94 ± 3.91	11.02 ± 2.96	0.393
Anxiety	5.41 ± 3.82	3.84 ± 3.13	0.048	6.0 ± 3.48	3.52 ± 2.76	0.019*
Humor	5.32 ± 2.97	3.71 ± 2.38	0.003*	5.32 ± 2.67	3.58 ± 2.57	0.069

Data expressed as mean ± SD. *Significant difference when comparing preoperative with postoperative. Paired *t* test.

Table 5 Profile of Chronic Pain in patients with rotator cuff injury

	Small injury		P Value	Large injury		P Value
	Preop.	Postop.		Preop.	Postop.	
Frequency and Intensity	26.17 ± 3.64	24.52 ± 5.59	0.081	23.94 ± 4.81	23.20 ± 6.19	0.648
Effect on Activities	27.34 ± 7.33	29.21 ± 7.27	0.250	25.05 ± 10.70	25.11 ± 10.63	0.983
Effect on Emotions	11.95 ± 5.61	11.47 ± 6.72	0.606	10.58 ± 5.90	10.41 ± 6.76	0.900
Total Score	64.60 ± 13.83	65.21 ± 15.41	0.797	59.00 ± 17.53	58.08 ± 21.71	0.856

Data expressed as Mean ± SD. Paired *t* test.

Patients with large rotator cuff injury presented higher age when compared to small injury group. This fact was earlier cited by Miyazaki and collaborators (2015), showing that elderly patients has a potential difficulty in repairing lesions, since it is a group that presents a higher number of large injuries, inferior bone quality and presents higher comorbidities that may reduce scar response and compromise surgical management.[20]

Significant results were found in pain thresholds correlations. CPM preoperative and postoperative correlation was significant in both groups and a correlation of preoperative and postoperative CPM with postoperative VAS, showing that descending inhibitory system changes influence in postoperative outcomes. This task evaluates pain modulation and perception in descending paths, where activity starts in pain control centers, found in the brainstem.[21] A painful

Table 6 Neuropathic and nociceptive pain

	Small injury	Large injury
	Preoperative	Postoperative
Neuropathic Pain	15	06
Nociceptive Pain	08	11

stimuli is used, denominated as conditioned stimuli, which can inhibit perceived pain from a next stimulus.[22] Patients with chronic pain can present pain facilitation and inhibition mechanisms, which can also be measured by CPM. However, it is necessary to investigate if pain existence and pain from possible modulations influence in endogenous pain inhibition.[23]

QST is a method used to quantify sensorial functional, to evaluate small fiber path of nociceptive system and it is important for neuropathies diagnosis, due to conventional studies incapacity to evaluate small fiber function. Heat stimuli perception thresholds are used a parameter that reflects unmyelinated C fibers function, while heat stimuli pain and cold perception threshold indicates A-delta fibers function, and to a lesser extent C9 and C10 fibers function. However, in clinical routine, because cold threshold are more variable, heat pain threshold are preferably measured.[24] Central sensitization happens because nociceptive pain is generated from nociceptors stimuli, and can also be peripheral or central, while neuropathic pain is generated from a nervous system dysfunction, cause by a primary lesion and emerging as a consequence in the somatosensory system.[25]

Preoperative neuropathic pain when poorly controlled can complicate postoperative process and can also cause chronic pain.[26] When LANSS scale was applied to evaluate prevalence of nociceptive and neuropathic pain, 21 patients presented neuropathic pain in preoperative, which can probably be related to the long waiting period that patients from the study faced to have a specialized appointment. Patients from the study arrived at the hospital for a specialized appointment after a referral from Municipal Secretary of Health, the waiting time for a specialized appointmentation is usually up to 1 year. Neuropathic pain is a multifactorial event that involves various components from central and peripheral nervous system. Despite its complex perception, this kind of pain is frequently related to a peripheral origin, being dependent on electrical activity present in sensory neurons responsible for tissue and viscera innervation.[27]

Chronic pain can cause changes in patients' lifestyle, drug addiction, social isolation, compromises of identity and self-esteem. Besides that, stand out as a consequence of chronic pain, changes in sleep, emotional changes and difficulties in performing daily activities.[28] When quality of sleep, humor and anxiety, patients with small injury presented significant difference in preoperative humor when compared to postoperative humor, this fact is due to the higher levels of pain this group presents. Large injury patients presented significant difference in preoperative anxiety when compared to postoperative anxiety, which can be related to the preoperative, a period considered the most vulnerable one regarding necessities, such as physiological and psychological

Small injury group presented a higher catastrophism when compared to large injury group. Besides that, patients with small lesion presented, in preoperative, higher levels of rumination and hopelessness when compared to large lesion group, due to the fact that small injury group presented higher levels of pain. Small rotator cuff injuries are potentially more painful when compared to other injuries, possibly because of non physiological tension creates in remaining tendon fibers. Most symptoms occurs at night and during activities with upper limb lifting effort. This fact is reinforced by the higher number of patients with small injury that used analgesic drug in postoperative, demonstrated in this study. It was also verified that the most used drug in patients that underwent to rotator cuff repair surgery is morphine, a drug that acts as an opioid agonist, interacting with stereospecific receptor sites and saturated links in the brain, spinal cord and other tissues to change processes that affect pain perception. Morphine modulation is made by endogenous opioids (physiological), such as endorphins and enkephalins, and it is the first choice for postoperative chronic pain treatment.[29]

Given that pain interferes in various aspects of the individual health, knowing pain thresholds and possible factors that may compromise patient rehabilitation is of paramount importance, because with that it is possible to perform different interventions to get a positive outcome in postoperative.

Conclusion

After this study it is possible to conclude that patients with small rotator cuff injury has higher catastrophism and humor alterations when compared to patients with large rotator cuff injury, due to the evidence that small injuries are more painful and, consequently, emotional alterations caused by pain.

Conflict of Interests

The authors have no conflict of interests to declare.

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