

# Understanding the Multifactorial Influences on Postsurgical Pain After Rotator Cuff Repair

## A Retrospective Cohort Study

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*Investigation performed at the Schulthess Clinic, Zürich, Switzerland*

**Background:** The experience of chronic postsurgical pain (CPSP) can vary widely among patients after rotator cuff repair (RCR).

**Purpose:** To determine the prevalence and predictive factors of CPSP at 6 months after RCR.

**Study Design:** Cohort study; Level of evidence, 3.

**Methods:** The following assessments were conducted preoperatively and 6 months postoperatively in adult patients with RCR who had undergone primary arthroscopic RCR (N = 1987): Constant score, pain assessed on the numeric rating scale (0–10), the Subjective Shoulder Value, the Oxford Shoulder Score, and quality of life as measured by the EuroQoL–5 Dimensions–5 Level (EQ-5D-5L). Patient characteristics—including age, sex, body mass index, and smoking status—and surgical factors—including the duration of surgery and the American Society of Anesthesiologists (ASA) classification—were also reported. Multivariate logistic regression analysis was performed to determine which variables were predictors for CPSP.

**Results:** The prevalence of moderate to severe preoperative pain in the patients was 30.4% for CPSP. After adjusting for age, surgery duration, ASA classification, sex, and body mass index, results revealed that unique predictors for CPSP were as follows: (1) the presence of preoperative negative affect—assessed using the anxiety/depression dimension of the EQ-5D-5L (odds ratio [OR], 1.46 ( $P < .001$ )); (2) preoperative pain (OR, 1.17;  $P < .001$ ); and (3) shoulder function (OR, 0.96;  $P < .001$ ). None of the surgical factors appeared to predict CPSP.

**Conclusion:** Patients predisposed to CPSP can be identified during the preoperative phase. Collectively, there is a call for a more in-depth assessment of biopsychosocial risk factors that could substantially influence the postoperative pain experience.

**Keywords:** arthroscopic rotator cuff repair; chronic postsurgical pain; postoperative

Rotator cuff repair (RCR) is a common surgical procedure aimed at alleviating shoulder pain and restoring function. However, the postsurgical pain experience can vary widely among patients and may be multifactorial. Understanding how these factors interact can provide valuable insights into optimizing pain management strategies and improving patient outcomes after shoulder RCR.<sup>16</sup>

Previous studies have suggested that sociodemographic factors can contribute to the chronic postsurgical pain (CPSP) experience. For example, sex-based differences in

pain perception and response have been widely documented, with emerging evidence suggesting that women may experience greater pain sensitivity and report higher levels of pain intensity compared with men. Hormonal, genetic, psychosocial, and cultural factors are thought to contribute to these differences. In the context of RCR, sex-based disparities in pain outcomes may influence postsurgical recovery trajectories and treatment outcomes.<sup>8–11,15,18</sup> In addition, age-related changes in pain processing and musculoskeletal function can affect the experience of postsurgical pain after RCR. Older adults may exhibit alterations in pain sensitivity, reduced pain modulation capabilities, and increased prevalence of comorbidities, which can influence pain perception and recovery outcomes. Personalizing pain management

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strategies to address age-related physiological and psychosocial factors may optimize pain relief and functional outcomes in older adults undergoing RCR.<sup>22</sup>

In addition, psychosocial factors play a significant role in the perception and experience of pain. Anxiety, depression, pain catastrophizing, and fear avoidance can amplify pain processing and contribute to the development of chronic pain conditions. Those with higher levels of psychological distress may exhibit heightened sensitivity to pain and may have difficulty coping with postsurgical pain after RCR.<sup>19,24</sup>

Recent research has questioned the conventional belief that the size and morphology of rotator cuff tears (RCTs) directly correlate with shoulder pain and disability. Instead, studies have indicated that structural factors have a limited predictive role in determining pain and function among patients with RCTs.<sup>4</sup> For example, a study by Simon et al<sup>22</sup> found that tear severity and concomitant arthroscopic procedures have limited influence on postoperative outcomes at 6 months. Moreover, various investigations have highlighted the influence of psychosocial factors—such as mental health and psychological distress—on pain experienced by patients with rotator cuff pathology. However, the precise connection between psychosocial factors and postoperative pain after arthroscopic RCR, especially during the early postoperative phase, remains inadequately understood.<sup>5</sup>

Collectively, the interplay of psychological and sociodemographic factors appears to significantly influence postsurgical pain outcomes after RCR. Comprehensive pain management approaches that consider the multifaceted nature of pain and individual patient characteristics are essential for optimizing postsurgical recovery and enhancing patient satisfaction.

This study aimed to explore the prevalence of postoperative persistent pain in patients who underwent arthroscopic RCR and identify the risk factors for CPSP in these patients. We hypothesized that individual characteristics (eg, demographic characteristics and psychosocial assessments) rather than surgical variables would be associated with persistent postsurgical pain.

## METHODS

### Study Procedure

The protocol for this study received approval by the regional ethics committee. This study included adult

patients diagnosed with either a partial- or full-thickness RCT who underwent primary arthroscopic RCR between June 2020 and October 2021. Patients were routinely documented as part of a local clinic register at the Schulthess Clinic, Switzerland, and those who contributed preoperative data and provided a pain score at the 6-month follow-up were considered for this study.

### Study Participants

Patients >18 years old who underwent arthroscopic RCR or were revised for arthroscopic RCR; patients diagnosed with partial or complete RCT and planned for arthroscopic RCR; patients who consented to surgical repair; and patients who gave their consent for the reuse of their clinical data for research purposes were included in the study. Excluded were patients with shoulder instability, rotator cuff revisions, or previous rotator cuff surgeries; prior contralateral shoulder surgeries; total shoulder replacement (eg, shoulder arthroplasty); legal incapacity to provide consent; substance use disorder; poor general health condition; and any condition that did not allow a clinical check-up or completion of the questionnaires (ie, due to neurological, mental, or metabolic diseases).

### Outcome Measures

Patient characteristics—including age, sex, body mass index (BMI), and smoking status—and surgical factors—including duration of surgery and the American Society of Anesthesiologists (ASA) classification—were recorded. In addition, patients underwent clinical evaluations—including subjective and clinical assessments—before surgery (preoperative) and at the 6-month postoperative mark. All self-reported data—pain on the numeric rating scale (NRS), Constant score,<sup>2,23</sup> Oxford Shoulder Score<sup>3</sup> (OSS), and EuroQol-5 Dimensions-5 Level (EQ-5D-5L)—were collected using RED-Cap, which is a free, secure, web-based application designed to support data capture for research studies.<sup>12</sup> Relevant outcome measures were CPSP according to the NRS, function according to the OSS, and negative affect as measured by the EQ-5D-5L.

Our primary outcome measure was the severity of current pain at rest (ie, CPSP) at 6 months postoperatively on the NRS—with 0 indicating no pain and 10 the worst pain. The OSS<sup>3</sup> is a 12-item patient-reported questionnaire

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and is designed to evaluate shoulder pain and function. This tool has been rigorously validated against clinician assessments and general health status measures. The OSS has notably demonstrated sensitivity to clinical improvements, boasts simplicity in completion, and has exhibited consistent reliability in assessing outcomes after shoulder surgery. Item ratings range from 1 to 5, and the total score is from the summation of all 12 rated items from 12 (best) to 60 (worst). The EQ-5D-5L is a measure of self-reported health outcomes applicable to a wide range of health conditions and treatments. It consists of 2 parts: a descriptive system (part 1) and a visual analog scale (VAS) (part 2). Part 1 of the scale consists of 5 single-item dimensions—including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has a 5-point response scale designed to indicate the level of the problem. Part 2 uses a vertical graduated VAS pain to measure health status, ranging from the worst imaginable health state to the best imaginable health state. We measured negative affect using the anxiety/depression dimension of the EQ-5D-5L.

## Data Analysis

After an initial univariate analysis, each variable was individually assessed for its association with the outcome of interest using appropriate statistical tests—such as chi-square tests for categorical variables and *t* tests or Mann-Whitney *U* tests for continuous variables. In addition, a correlation analysis was conducted to evaluate the relationships between continuous variables using the Pearson or Spearman correlation coefficients, depending on the distribution of the data. Variables showing significant correlations with each other ( $r > 0.7$ ) were flagged for potential multicollinearity concerns. Variables with  $P < .20$  in the univariate analysis and those that were not highly correlated were considered for inclusion in the multivariate model. All selected variables were then entered into a reverse-selection multivariate logistic regression to identify independent predictors of the outcome (CPSP at 6 months postoperatively) while controlling for potential confounding factors. The odds ratios (ORs) and 95% CIs of each independent predictor were calculated. Combinations of the independent predictors were used to explore the predictive ability of the model for the outcome.  $P < .05$  was considered the threshold for statistical significance.

Based on the CPSP cutoff, logistic regression formulas were created to predict the likelihood of a patient experiencing moderate/severe pain at 6 months postoperatively. We addressed multicollinearity in our multivariate logistic regression analysis by ensuring that no variance inflation factor exceeded 5, indicating that the predictor variables were sufficiently independent of each other. The type 1 error rate was 0.05.

In the multiple logistic regression model, the main predictors were negative affect (assessed by the EQ-5D-5L depression/anxiety dimension), adjusted for the most clinically prominent factors of CPSP—such as age, sex, preoperative pain on the NRS, preoperative function on the

OSS, surgical procedure, tear severity, surgical duration, and ASA classification—with a grade of  $>2$  associated with an increased risk of medical and surgical complications.

In this study, the performance of the logistic regression model was evaluated using several key metrics to assess its effectiveness in classifying observations. Accuracy—defined as the proportion of correctly classified instances out of the total number of instances—was used to measure the overall correctness of the model's predictions. Precision—representing the proportion of correctly predicted positive cases out of all predicted positive cases—and recall (sensitivity)—indicating the proportion of true positive cases correctly identified by the model—were employed to assess the model's ability to minimize false positives and capture all positive cases, respectively. The area under the receiver operating characteristic curve (AUC) was used to evaluate the model's ability to distinguish between classes, plotting the true-positive rate against the false-positive rate across different threshold values. These metrics collectively offered a comprehensive assessment of the predictive ability and generalization performance of the logistic regression model.

*Missing Data.* In our study, we adopted a rigorous approach to manage missing data by employing the multivariate imputation by chained equations (MICE) technique. Our missing data were 26% and could potentially introduce bias and diminish statistical power. To mitigate these issues, we leveraged the MICE algorithm, which is implemented in the *mice* package within the R studio environment (RStudio Team). The MICE algorithm tackles missing values by iteratively modeling each variable with missing data conditional on other variables in the dataset. Through this iterative process, multiple imputed datasets are generated, each comprising plausible values for the missing data based on observed data patterns. To ensure the robustness of our analyses, we generated 5 imputed datasets. Subsequently, we conducted separate analyses on each imputed dataset using logistic regression, with pain severity at 6 months postoperatively serving as a binary outcome variable; patients with moderate or severe pain ( $\geq 3$  of 10) were classified as 1, and those with mild or no pain ( $< 3$  of 10) were classified as 0 based on previous reports<sup>13,20</sup>. For our logistic regression models, we included only predictors with imputed values. By analyzing each imputed dataset independently, we were able to capture the uncertainty associated with imputation. Finally, we combined the results obtained from these separate analyses using appropriate rules—such as Rubin rules—to derive valid estimates and standard errors. This integrated approach allowed us to effectively address missing data while upholding the integrity of our analyses and fortifying the reliability of our findings.

*Sensitivity Analysis.* We conducted a sensitivity analysis where we alternately calculated the CPSP by taking the difference between preoperative and 6-month postoperative pain intensity instead of using a postoperative cutoff score. Subsequently, we ran a multivariate linear regression analysis to evaluate the same predictors using change in pain intensity as the continuous outcome (as opposed to binary for the primary analysis) and assess this model's

TABLE 1  
Baseline Clinical and Demographic Characteristics  
of the Patients (N = 1988)<sup>ab</sup>

Characteristic	Value
Age, y	59 ± 10
Female sex	770 (39)
ASA classification <sup>c</sup>	
1	469 (24)
2	1282 (65)
3	234 (12)
4	1 (0)
Surgery duration, min	81 ± 30
BMI, kg/m <sup>2</sup>	26 ± 4
Smoking status, No. of cigarettes per day	2 ± 6
Preoperative pain, NRS, 0-10	5.5 ± 2.3
Oxford shoulder score, 12-60	28.7 ± 8.4
Negative affect, EQ-5D-5L depression/anxiety, 0-4	1.5 ± 0.8
Subjective shoulder value, 0-100	52.4 ± 21.4
Constant score	53.84 ± 7.05
ROM, deg	
Abduction, 0-200	125 ± 40
Flexion, 0-200	136 ± 36
External rotation at 0, 0-100	52 ± 17
External rotation at 90, 0-100	69 ± 22
Internal rotation at 90, 0-100	43 ± 24
Tear severity, Gerber classification	
Partial tear	425 (22)
Single full tear	664 (35)
2 or 3 tendons, only 1 fully ruptured	381 (20)
Massive tear	439 (23)
Treatment biceps	
Already ruptured/treated	203 (11)
Tenotomy	342 (18)
Tenodesis	1102 (58)
No treatment	259 (14)
Additional procedures	
Acromioplasty	1196 (68)
AC resection and acromioplasty	325 (19)
Capsulotomy and acromioplasty	89 (5)

<sup>a</sup>Data are presented as mean ± standard deviation or n (%). AC, acromioclavicular; ASA, American Society of Anesthesiologists; BMI, body mass index; EQ-5D-5L, EuroQol-5 Dimensions-5 Level; NRS, numeric rating scale; ROM, range of motion.

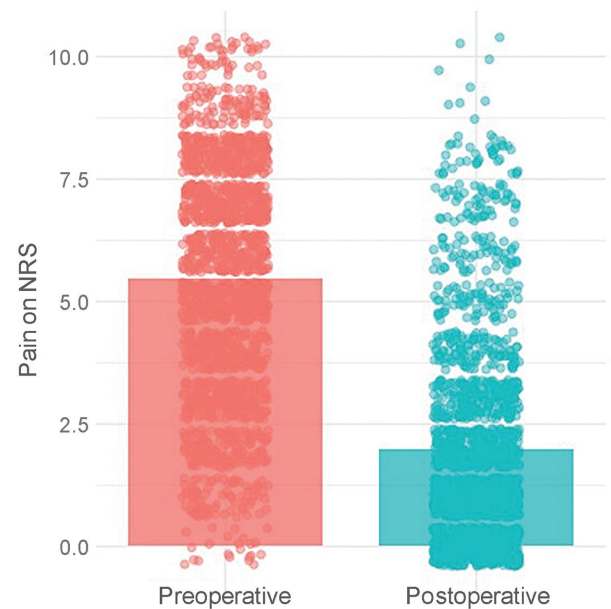
<sup>b</sup>Due to missing data in some variables all sections do not equal the total and percentages are based on the number with data for that variable.

<sup>c</sup>1 = healthy patient; 2 = mild systemic disease; 3 = severe systemic disease; 4 = severe systemic disease that poses a constant threat to life.

performance. This sensitivity analysis provided additional context for interpreting findings from our primary analysis by identifying predictors that were robust enough to be associated with different ways CPSP has been defined in the literature.

## RESULTS

In total, 1988 RCR patients were included in the study, excluding 63 patients who had undergone revision



**Figure 1.** Jittered preoperative and postoperative pain levels. The bars represent mean pain scores for the entire cohort, and the circles represent individual scores. NRS, numeric rating scale.

procedures. The mean patient age was  $59.05 \pm 9.55$  years, with 770 (38%) female and 1218 (61%) male patients. In total, 35% of the patients had a single full tear, approximately 40% had either a partial tear or a rupture of 2 or 3 tendons with only 1 tendon fully ruptured (Table 1).

### Postoperative Pain Severity

The mean preoperative NRS pain score was  $5.50 \pm 2.35$ , compared with  $2 \pm 2$  postoperatively (Figure 1), with high variability among patients. Preoperatively, sex-based comparisons showed that female patients reported higher scores for pain ( $5.9 \pm 2.2$  for women vs  $5.01 \pm 2.3$  for men;  $P < .0001$ ) and worse overall shoulder function according to the OSS ( $26.9 \pm 8.27$  for women vs  $29.85 \pm 8.33$  for men;  $P < .0001$ ). In total, 30.4% (596) of patients reported moderate/severe postoperative pain. Patient characteristics were less strongly correlated with postoperative pain severity at 6 months postoperatively. The mean age of those experiencing no pain was  $59.64 \pm 9.42$  years, whereas the mean age of those experiencing moderate to severe pain was  $57.68 \pm 9.69$  years ( $p < .001$ ). Of patients experiencing no pain, a larger proportion were men compared with women (13% vs 17%); of patients experiencing moderate to severe pain, a larger proportion were women compared with men (45% vs 25%) ( $p < .01$ ).

Of all the variables tested, preoperative pain and negative affect were most strongly correlated with postoperative pain (Table 2). This correlation was positive, whereby greater levels of preoperative pain were associated with greater levels of postoperative pain ( $r = 0.32$ ;  $P < .001$ ). Negative affect ( $r = 0.26$ ;  $P < .001$ ) was also

**TABLE 2**  
Correlation of Postoperative Pain With Preoperative Pain, Negative Affect, and Function<sup>a</sup>

	Postop Pain	Preop Pain	Negative Affect	Shoulder Function
Postop pain	—	—	—	—
Preop pain	0.32 <sup>b</sup>	—	—	—
Negative affect	0.26 <sup>b</sup>	0.21	—	—
Shoulder function	-0.31 <sup>b</sup>	-0.62 <sup>b</sup>	-0.28 <sup>b</sup>	—
Age	-0.11	0.006	-0.10	-0.03

<sup>a</sup>Pre- and postoperative pain were assessed using the NRS (0-10) at rest; postoperative pain was measured at the 6-month follow-up. Shoulder function was assessed using the Oxford shoulder scale. Negative affect was assessed using the EQ-5D-5L depression/anxiety dimension. EQ-5D-5L, EuroQol-5 Dimensions-5 Level; NRS, numeric rating scale; Postop, Postoperative; Preop, preoperative.

<sup>b</sup>*P* < .001.

positively correlated with postoperative pain. Preoperative shoulder function was negatively correlated with the postoperative pain (*r* = -0.31; *P* < .001). That is, less functional shoulders were more painful postoperatively. In addition, a positive, but not significant, correlation was observed between age and postoperative pain (Table 2).

### Risk Factors Associated With Postoperative Pain

Results of logistic regression analysis revealed that preoperative pain, negative affect, and shoulder function were significantly associated with postoperative pain after adjusting for demographic characteristics, BMI, smoking, operation duration, tear severity, and ASA classification. Specifically, for every 1-point increase in the preoperative pain score, the odds of experiencing postoperative pain increased by 17% (OR, 1.17 [95% CI, 1.10-1.25]; *P* < .001), holding all other variables constant. Similarly, a 1-point increase in the preoperative negative affect score (EQ-5D-5L anxiety/depression dimension) was associated with a significant increase in the odds of experiencing postoperative pain (OR, 1.46 [95% CI, 1.48-1.89]; *P* < .001). Preoperative shoulder function (OSS) was also significantly associated with postoperative pain outcomes (OR, 0.96 [95% CI, 0.94-0.98]; *P* < .001), with better preoperative shoulder function associated with lower odds of experiencing postoperative pain, after adjusting for covariates (Table 3).

### Sensitivity Analysis

As expected, preoperative pain was highly and negatively correlated with change in pre- to postoperative pain intensity ( $\beta$  = -0.81; *P* < .001). In this multivariate model, physical function was not associated with a change in pain intensity (*P* > .05). In addition, surgery duration ( $\beta$  = 0.008; *P* < .05) and preoperative negative affect ( $\beta$  = 0.35; *P* < .05) were positively moderately correlated with change in pain intensity. The final model also accounted for BMI, smoking status, operation duration, tear severity,

**TABLE 3**  
Risk Factors for Postoperative Pain in RCR<sup>a</sup>

Predictor	OR (95% CI)	<i>P</i>
ASA classification	1.21 (0.99-1.48)	NS
Preoperative pain	1.17 (1.09-1.23)	<.001
Tear severity	0.98 (0.90-1.07)	NS
Sex	0.86 (0.68-1.08)	NS
Smoking	1.009 (1.02-1.04)	<.001
Surgery duration	1.004 (0.99-1.02)	<.05
Shoulder function	0.96 (0.94-0.98)	<.001
Age	0.98 (0.96-0.99)	<.001
Negative affect	1.46 (1.28-1.67)	<.001
BMI, kg/m <sup>2</sup>	1.006 (0.98-1.03)	NS

<sup>a</sup>Pre- and postoperative pain was assessed using the NRS (0-10) at rest; postoperative pain was measured at the 6-month follow-up. Shoulder function was assessed using the Oxford shoulder scale. Negative affect was assessed using the EQ-5D-5L depression/anxiety dimension. ASA, American Society of Anesthesiologists; BMI, body mass index; EQ-5D-5L, EuroQol-5 Dimensions-5 Level; NRS, numeric rating scale; NS, not significant; OR, odds ratio; RCR, rotator cuff repair.

and ASA classification and explained 42% of the variance in change in pain intensity.

### Model Performance

The logistic regression model was evaluated using several performance metrics to assess its effectiveness in classifying observations. The model demonstrated an accuracy of 73.64%, indicating that approximately three-quarters of the observations were correctly classified. Precision, measuring the proportion of correctly predicted positive cases out of all predicted positive cases, was found to be 64.01%. The logistic regression model achieved an AUC value of 0.72, indicating moderate discrimination ability in distinguishing between positive and negative cases.

As part of the sensitivity analysis, the multivariate linear regression model we developed had an *R*<sup>2</sup> value of 0.42, indicating that approximately 42% of the variance in pain intensity changes (postoperative vs preoperative) could be explained by the predictor variables included in the model. While this suggests a moderate level of predictive power, it also indicates that there is room for improvement. Additionally, the root mean square error was approximately 1.82, meaning that on average, the predictions of the multivariate regression model deviated from the actual values by around 1.82 points on the NRS pain scale.

### DISCUSSION

The main objective of this study was to determine the prevalence and predictive factors of CPSP 6 months after RCR. Independent predictors of 6-month postoperative pain were preoperative pain level, negative affect, and shoulder function. These findings suggest that patients who experience higher levels of pain and negative affect before

surgery are more likely to continue experiencing pain postoperatively. In addition, patients with more dysfunctional shoulders at baseline were more likely to report moderate to severe pain postoperatively. Other covariates—such as smoking status and age—also showed significant associations with postoperative pain, highlighting their potential contributions to the overall pain experience.

Our results are broadly in agreement with previous reports demonstrating the importance of the implementation of a comprehensive biopsychological clinical assessment for persons who develop persistent postsurgical pain after arthroscopic RCR.<sup>7,17,19</sup> For example, a recent study by Sabo et al<sup>21</sup> indicated that patient-reported outcomes after rotator cuff surgery show correlations with self-reported levels of negative affect and pain catastrophizing. Additional work has highlighted the multidimensional nature of rotator cuff-related shoulder pain. In a recent study, Lemaster et al<sup>17</sup> demonstrated that shoulder pain and disability associated with rotator cuff issues are linked to sleep disturbance, perceived symptom persistence, and sex.

According to our results, apart from negative affect, surgery duration, and preoperative pain, preoperative shoulder function also appeared to be a predictor of postsurgical pain; however, evidence of this relationship has been scattered in the literature.<sup>14,22</sup> Our sensitivity analysis, using the change score for pain intensity, demonstrated that while surgical duration, negative affect, and preoperative pain were predictors of changes in postsurgical pain, physical function was not. However, both models demonstrated moderate model performance. Relevant to these findings, ensuring accuracy in CPSP prediction is paramount in future research endeavors, particularly after testing in an independent cohort for external validation.

## Strengths and Limitations

This study's unique strengths lie in its use of registry data collected prospectively for all patients undergoing RCR, providing a robust and comprehensive dataset that allows for systematic evaluation of the relationships between predictor variables and postsurgical pain. Another strength of this study is presenting an analysis of 2 different definitions of CPSP. The definition and assessment of CPSP varies across studies and clinical settings, leading to a lack of consensus within the scientific and clinical communities. While some investigations focus solely on evaluating pain experienced postoperatively, others examine changes in pain levels from pre- to postoperative periods. This diversity in approaches underscores the complexity of defining and measuring postsurgical pain. Despite efforts to establish uniform criteria, we were unable to determine robust predictors in the absence of a universally accepted definition of CPSP; nonetheless, we attempted to mitigate this challenge in this analysis by presenting competing definitions of CPSP.

Several limitations need to be considered when interpreting results. First, the study's retrospective nature inherently introduces the potential for selection bias and confounding variables, as data collection relied on historical records rather than controlled experimental conditions.

Another limitation we acknowledge is the use of a single item from the EQ-5D-5L to assess negative affect, which may not fully capture the complexity of the issue; however, it still provides valuable insights. In addition, the high loss to follow-up presents a challenge in ensuring the consistency and reliability of our findings. Moreover, the heterogeneity of the data, resulting from the pooling of outcomes for both partial and complete rotator cuff ruptures, adds another layer of complexity to our analysis. We were not able to assess the impact of various surgical procedures—such as biceps tenodesis, acromioplasty, and distal clavicle excisions—and their relevance to our main outcomes in the multivariate analysis. This could be a limitation, particularly given that an important proportion of the cases were partial ruptures, which may not be related to the biceps-associated procedures.

In addition, we only assessed postoperative pain at the 6-month follow-up. A longitudinal analysis examining acute, subacute, and persistent pain would have been more appropriate. Typically, acute pain is assessed immediately after surgery, subacute pain is evaluated at 4 to 8 weeks postoperatively, and chronic pain is considered at 6 months postoperatively. Additionally, assessing pain both at rest and during activities as well as medication pain management would have provided a more comprehensive understanding of the pain experience. Also, we did not have access to data on every possible biopsychosocial predictor of interest; for example, factors such as sleep, medical comorbidities, pain or inflammatory modulating genes, pain sensitivity, anxiety, kinesiophobia, and pain-related catastrophizing have demonstrated predictive relevance in previous studies. For example, our study of a separate RCR cohort identified evidence for 3 different interactions between pain modulatory genes and psychological factors for predicting pre- and postoperative courses and 12-month outcomes. Finally, another limitation is that our observational cohort design precludes establishing causal linkages between variables, limiting the ability to make definitive conclusions about the relationships observed.

## CONCLUSION

The complexity of CPSP extends beyond the factors examined in this study; therefore, it is essential to conduct further research to understand the intricate relationships among these factors and their implications for developing effective postoperative pain management strategies and therapeutic interventions. In addition, the multifaceted nature of CPSP calls for a comprehensive research approach, encompassing translational investigations into biomarkers and genetics,<sup>1,6</sup> which could potentially enhance model accuracy beyond what is reported from this cohort.

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