

# Association of Anxiety and Depressive Symptoms in Patients with Adhesive Capsulitis

## *Associação de sintomas ansiosos e depressivos em pacientes com capsulite adesiva*

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Rev Bras Ortop 2023;58(1):127–132.

### Abstract

**Objective** The present study aimed to assess the association between anxiety and depression symptoms in patients with adhesive capsulitis.

**Methods** This was a cross-sectional study carried out in a single center from a tertiary hospital with patients presenting with secondary adhesive capsulitis. The control group did not have shoulder disease, thyroid disease, anxiety, and/or depression. The instrument used was the Hospital Anxiety and Depression Scale (HADS). An analysis of covariance compared HADS scores between groups. The significance level was 5%.

**Results** The final sample consisted of 17 patients (case group) and 27 (control group). The Shapiro-Wilk test revealed normal distribution ( $p > 0.05$ ). A HADS score  $> 0.70$  (Cronbach alpha) was reliable and presented good internal consistency. Patients with adhesive capsulitis reported “doubtful” (average/standard deviation = 8.88/4.50) “anxious symptoms” ( $p = 0.019$ ) but no “depressive symptoms” (average/standard deviation = 6.41/3.69), despite  $p = 0.015$ .

**Conclusion** There is a “doubtful” positive association between anxiety symptoms and adhesive capsulitis but a negative association with depressive symptoms.

### Keywords

- ▶ anxiety
- ▶ adhesive capsulitis
- ▶ depression
- ▶ shoulder
- ▶ signs and symptoms

Study developed at the Universidade Federal de Goiás, Goiânia, GO, Brazil.

received

June 24, 2021

accepted after revision

November 22, 2021

article published online

February 15, 2022

DOI <https://doi.org/10.1055/s-0042-1742693>.

ISSN 0102-3616.

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

**Resumo**

**Objetivo** Avaliar a associação entre sintomas ansiosos e depressivos em pacientes com capsulite adesiva.

**Métodos** Trata-se de um estudo transversal realizado em centro único de um hospital terciário com pacientes portadores de capsulite adesiva secundária. O grupo controle não apresentava doença do ombro, tireoidopatias e nem ansiedade e/ou depressão. O instrumento utilizado foi a escala hospitalar de ansiedade e depressão. A análise da covariância foi utilizada para comparação dos escores do Hospital Anxiety and Depression Scale (HADS, na sigla em inglês) entre os grupos. O nível de significância foi de 5%.

**Resultados** A amostra final foi de 17 pacientes (caso) e 27 (controle). Os dados amostrais apresentaram distribuição normal por meio do teste de Shapiro-Wilk ( $p > 0,05$ ). A instrumento HADS com pontuação  $> 0,70$  (alfa de Cronbach) se mostrou confiável e com boa consistência interna. Os pacientes com capsulite adesiva, no quesito “sintomas ansiosos” ( $p = 0,019$ ), relataram sintomas no patamar de “duvidosos” (média/desvio padrão = 8,88/4,50). Eles não apresentaram “sintomas depressivos” (média/desvio padrão = 6,41/3,69), apesar do  $p = 0,015$ .

**Conclusão** Existe uma associação positiva “duvidosa” entre sintomas ansiosos e capsulite adesiva, mas negativa para sintomas depressivos.

**Palavras-chave**

- ▶ ansiedade
- ▶ capsulite adesiva
- ▶ depressão
- ▶ ombro
- ▶ sinais e sintomas

**Introduction**

Adhesive capsulitis (AC) is a condition that causes pain and limited active or passive movement of the shoulder joint. Pain can be severe and hinder daily living activities. Its diagnosis is eminently clinical, with radiographs showing locoregional osteopenia. Magnetic resonance imaging (MRI) demonstrates a reduced axillary recess and thickening of the coracohumeral ligament, an important restrictor of external rotation.<sup>1,2</sup>

Although primary adhesive capsulitis develops spontaneously, its etiology remains uncertain. Some associated factors were reported, including diabetes mellitus, thyroid diseases, breast cancer, hemiplegia, and trauma; shoulder surgery followed by immobilization can result in secondary adhesive capsulitis.<sup>3</sup>

In addition, these patients supposedly have a characteristic constitutional profile with psychological abnormalities such as anxiety and depression, although the causal relationship between AC and these disorders is not well defined.<sup>4,5</sup> The Hospital Anxiety and Depression Scale (HADS), a questionnaire used to detect the general status and severity of anxious and depressive symptoms, has been used to research psychological factors associated with several diseases.<sup>6-8</sup>

Several orthopedic diseases relate to anxiety and depression,<sup>9</sup> but studies on the association between these psychological factors and AC are scarce and show divergent findings.<sup>4,10,11</sup> Thus, the present study aimed to evaluate the association of anxiety and depression symptoms in patients with adhesive capsulitis. It is thought that patients with AC are positively associated with anxiety but not with depressive symptoms.

**Materials and Methods****Study Design**

This is a cross-sectional study carried out in a single center from a private tertiary hospital located in a capital city in the central region of Brazil between February 2019 and November 2020.

**Participants**

The study sample was nonprobabilistic, of the consecutive type, consisting of patients with secondary AC. Adhesive capsulitis was defined by constant shoulder pain for at least 4 weeks with anterior elevation of up to 130° and external rotation of up to 50°;<sup>12</sup> in addition, it was secondary to systemic diseases and extrinsic or intrinsic to the glenohumeral joint. Imaging showed osteopenia from local disuse on radiographs and volume reduction, as well as thickening of capsuloligamentous structures from the axillary recess on nuclear magnetic resonance imaging.

The inclusion criteria were subjects  $> 18$  years old with AC secondary to the following factors, according to Zuckerman et al.:<sup>13</sup> previous surgery, trauma to the affected shoulder, prolonged immobilization, cervical radiculopathy, rotator cuff tear, calcareous tendinitis, diabetes mellitus, neuropathies, and hypothyroidism or hyperthyroidism during treatment.

Patients with glenohumeral arthrosis, blocked shoulder dislocation, humeral head necrosis, vicious consolidation of the proximal humerus, and primary AC were excluded from the study.

**Data Collection Procedure**

Data collection was carried out prospectively by three researchers in a reserved environment and at a single

moment; for the case group, data collection occurred before the beginning of treatment with serial suprascapular nerve blocks. The control group consisted of healthy people, not from the hospital environment, aged between 40 and 70 years old, who did not have AC or thyroid diseases and were not under treatment for anxiety and/or depression. The study subjects were invited to participate and signed an Informed Consent Form.

The self-administered instrument, HADS, contains 14 multiple-choice questions divided into two subscales, one for anxiety and one for depression, with seven items each. It is a short and easy to fill instrument, and answers refer to the last week. The global score ranges from 0 to 21 for both anxiety and depression, with  $\leq 7$  for negative cases, 8 to 10 for doubtful cases, and  $\geq 11$  for positive cases.<sup>6,8</sup>

### Outcomes/Independent Variables

The primary outcomes included symptoms of anxiety and depression surveyed using HADS. The independent variables were the following: age (in years); gender (male/female); race (white/non-white); education (in formal years); monthly income (in minimum wages); pain duration (months); illness duration (months); side affected (right/left); and dominant side (right/left).

### Statistical Analysis

Data analysis used IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Sample characterization employed absolute ( $n$ ) and relative (%) frequency for categorical variables and mean and standard deviation/median and interquartile range for continuous variables. The Shapiro-Wilk test assessed data normality. The Student t-test and the Pearson chi-squared test determined the homogeneity of sociodemographic features between case and control groups. Internal consistency, measured as Cronbach alpha, established the reliability of the HADS questionnaire.

A post-hoc chi-squared test, with Bonferroni correction, assessed the distribution of anxiety and depression symptoms from the HADS instrument between the case and control groups. If there were significant differences in the sociodemographic variables between groups, an analysis of covariance (ANCOVA) was performed to control its confounding effect when comparing HADS scores. The probability of rejecting the null hypothesis was 5%.

The Research Ethics Committee of the institution approved the present study.

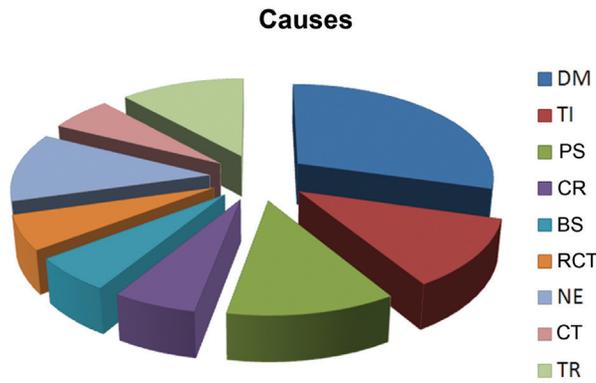
### Results

From a total of 46 patients with AC admitted to the single-center outpatient clinic where the present study was

**Table 1** Sociodemographic and clinical data from the case ( $n = 17$ ) and control ( $n = 27$ ) groups

	Groups		Total $n = 44$	<i>p</i> -value
	Case 17 (38.6%)	Control 27 (61.4%)		
<i>Mean ± standard deviation</i>				
Age <sup>a</sup>	56.12 ± 10.37	48.44 ± 7.80	51.41 ± 9.55	0.01*
Educational level <sup>a</sup>	12.13 ± 2.41	15.67 ± 5.09	14.40 ± 4.62	0.02*
Monthly income <sup>b</sup>	8.12 ± 13.60	6.48 ± 4.84	7.03 ± 8.63	0.58*
Pain duration <sup>c</sup>	5.85 ± 4.58			na
Disease duration <sup>c</sup>	5.41 ± 4.93			na
<i>n (%)</i>				
Gender				
Female	8 (47.1)	15 (55.6)	23 (52.3)	0.58**
Male	9 (52.9)	12 (44.4)	21 (47.7)	
Ethnicity				
White	8 (47.1)	21 (77.8)	29 (65.9)	0.07**
Non-white	9 (52.9)	6 (22.2)	15 (34.1)	
Affected side				
Right	7 (41.2)			na
Left	10 (58.8)			
Dominant side				
Left	0 (0.0)			na
Right	17 (100.0)			

\*Student t test; \*\*Pearson chi-squared test; <sup>a</sup>years; <sup>b</sup>minimum wage; <sup>c</sup>months.  
%, relative frequency; n, absolute frequency; na, not applicable.



**Fig. 1** Direct and indirect causes of secondary adhesive capsulitis (n = 17). Abbreviations: DM: diabetes mellitus; TI: thyroid diseases; PS: previous shoulder surgery; CR: cervical radiculopathy; BS: breast surgery; RCT: rotator cuff tear; NE: neuropathies; CT: calcareous tendinitis; TR: trauma.

performed, we excluded 9 for presenting the primary form of the disease, 10 for not accepting treatment, 8 for being unable to answer the questionnaire, and 2 because the disease was not characterized as primary or secondary. Thus, the final sample consisted of 17 patients in the case group and 27 subjects in the control group.

► **Table 1** shows the sociodemographic and clinical data from both groups.

Direct or indirect causes of secondary AC included the following: previous shoulder surgery (11.76%), shoulder mobility restriction after breast surgery (5.88%), trauma (fracture and instability; 11.76%), cervical radiculopathy (5.88%), rotator cuff tear (5.88%), calcareous tendinitis (5.88%), diabetes mellitus (29.41%), neuropathies (11.76%), and thyroid diseases (11.76%) (► **Fig. 1**).

The Shapiro-Wilk test sample revealed normal data distribution ( $p > 0.05$ ). A HADS score  $> 0.70$  was reliable and presented good internal consistency (► **Table 2**).

► **Table 3** shows the comparative distribution of anxiety and depression symptoms according to the HADS in both

**Table 3** Comparative distribution of anxiety/depression symptoms on the Hospital Anxiety and Depression Scale between the case (n = 17) and control (n = 27) groups

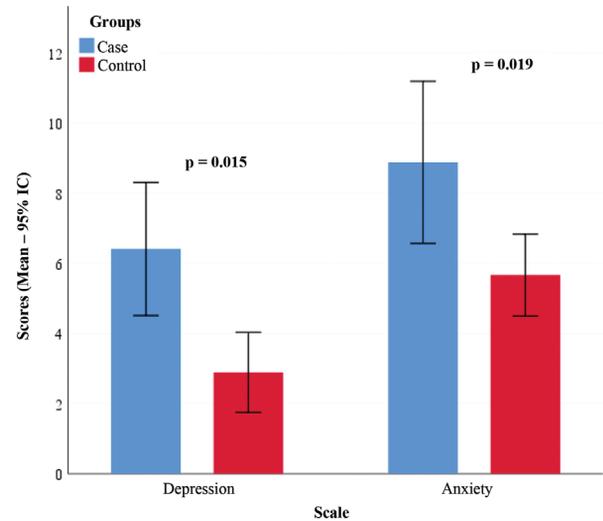
	Groups		Total	p-value*
	Case n (%)	Control n (%)		
<b>Anxiety</b>				
No symptoms	6 (35.3)	18 (66.7)	24 (54.5)	0.025
Doubtful	4 (23.5)	8 (29.6)	12 (27.3)	0.074
Anxiety symptoms	7 (41.2)	1 (3.7)	8 (18.2)	0.001
<b>Depression</b>				
No symptoms	12 (70.6)	25 (92.6)	37 (84.1)	0.037
Doubtful	2 (11.8)	2 (7.4)	4 (9.1)	0.200
Depression symptoms	3 (17.6)	0 (0.0)	3 (6.8)	0.024

\*Post-hoc chi-squared test; %, relative frequency; n, absolute frequency.

**Table 2** Reliability and internal consistency analysis of the Hospital Anxiety and Depression Scale using Cronbach alpha

	Number of items	Groups	
		Case	Control
Anxiety	7	0.76	0.71
Depression	7	0.72	0.74
Total	14	0.81	0.77

Cronbach's alpha.



**Fig. 2** Bar graph showing mean and 95% confidence interval (95%CI) values for anxiety and depression scores.

groups. Anxiety symptoms ( $> 11$  points) with no depressive symptoms ( $\leq$  to 7 points) were predominant in the case group, with  $p = 0.001$  and  $0.037$ , respectively, when compared with the control group.

► **Fig. 2** shows mean and confidence interval values for anxiety and depression symptom scores in the case and control groups.

**Table 4** Comparison of mean anxiety/depression scores between the case ( $n = 17$ ) and control ( $n = 27$ ) groups

	Groups		Total	<i>p-value*</i>
	Case M $\pm$ SD	Control M $\pm$ SD		
Anxiety	8.88 $\pm$ 4.50	5.67 $\pm$ 2.95	6.91 $\pm$ 3.91	0.019
Depression	6.41 $\pm$ 3.69	2.89 $\pm$ 2.89	4.25 $\pm$ 3.62	0.015

Abbreviations: M, mean; SD, standard deviation.

\*ANCOVA ( $r^2 = 0.14$ ); covariables: age, educational level.

The homogeneity analysis between the two groups revealed a significant difference in two variables, namely age and education ( $p < 0.05$ ). Thus, when comparing the HADS scores of the two groups, an ANCOVA was performed, and this significant difference did not change the final analysis of our findings ( $\rightarrow$  **Table 4**).

The group with AC reported “doubtful” “anxious symptoms” (score = 8.88) despite the difference compared with the control ( $p = 0.019$ ). This group presented no “depressive symptoms” (score = 6.41), despite  $p = 0.015$ .

## Discussion

There was a “doubtful” positive association between anxiety symptoms and AC, with a mean HADS score of 8.88 (range: 8 to 10), despite the difference from the control group ( $p = 0.019$ ). Regarding “depressive symptoms”, although there was a significant difference ( $p = 0.015$ ) between mean values from the case (6.41) and control (2.89) groups, an association with AC was not determined because these figures are  $< 7$ .<sup>6-8</sup> Our hypothesis was partially correct, because we expected to have confirmed, rather than doubtful anxiety symptoms.

A pioneering study by Fleming et al.<sup>14</sup> evaluated the association between AC and personality traits using the Middlesex Hospital Questionnaire. The authors found evidence of personality differences from normal inpatients with adhesive capsulitis. Furthermore, they showed an association for somatic anxiety, especially in females.

Ding et al.<sup>4</sup> carried out a similar study using the HADS scale and found a prevalence of depression and anxiety of 28.2 and 24.2%, respectively. Two mental parameters presented statistical differences compared with the control group; however, the mean values were  $< 7$ , indicating “no symptoms.” We believe there was an interpretation bias when analyzing these findings. Anyway, this corroborates our findings from the point of view of depression, but not of anxiety.

Bagheri et al.<sup>10</sup> also evaluated patients with AC but used the Hamilton questionnaire for depression and anxiety. These authors detected only mild depressive symptoms, with no anxiety. Ebrahimzadeh et al.,<sup>5</sup> coauthors of the Bagheri study, used the same questionnaire and concluded that depressive symptoms (77%) were more present than anxious symptoms (27%). Both studies are inconsistent with our findings, probably because of the score of the instru-

ment, in which values  $> 8$  indicate “depression” and those  $> 14$  mean “anxiety.” Thus, he was more likely to have depressive symptoms with the use of the Hamilton questionnaire.

Beleckas et al.<sup>9</sup> evaluated patients with upper limb disease using a Patient-Reported Outcomes Measurement Information System (PROMIS), including anxiety and depression. They concluded that some shoulder conditions, including AC, were associated with high anxiety scores, with a greater prevalence than depression in this population, maybe because this shoulder dysfunction is extremely painful. The illnesses that progressed with no pain had the lowest scores for anxiety and depression.

Debeer et al.<sup>15</sup> conducted a study to determine personality differences between patients with AC using the NEO Five-Factor Inventory scale. They concluded that patients with AC did not have personality differences compared with the control group. However, this scale did not assess anxiety and depression but other personality traits.

Toprak et al.<sup>11</sup> analyzed the relationship between AC and anxiety/depression using the Beck Anxiety Inventory and Beck Depression Inventory in addition to other outcomes. They showed a high prevalence and a close relationship between anxiety and AC, but not depression, which is in line with our findings.

Although the term “psychological distress” is used in studies of musculoskeletal conditions when referring to mental health,<sup>16-18</sup> we prefer to refer separately to “anxiety” and “depression”, as several of the previously mentioned authors.<sup>4,5,11</sup> This allows for a direct and individual comparison of each term with science that would not be possible otherwise.

The cross-sectional design of the present study limits our ability to determine any cause-effect relationship between AC and anxiety/depression, since some diseases may also have such outcomes. A nonprobabilistic, consecutive sampling may have imposed a selection bias, not allowing all patients to participate in the research. Moreover, not classifying the severity of AC as mild, moderate, and severe did not allow us to verify whether more rigid patients had more anxiety and/or depressive symptoms.<sup>13</sup>

Another issue would refer to anxiety, which showed clinical and statistical differences favoring the case group; however, the mean score was 8.88, characterized as “doubtful symptoms” according to the HADS. This was probably due to the sample size, and a higher sample number could result in a higher mean score. We must remember that we are not facing a type I error with falsely rejecting the null hypothesis because there was a difference, and the issue is in interpreting the analysis performed.

On the other hand, we used a reliable HADS (Cronbach alpha  $> 0.70$ ), validated for the language of the studied sample and which assessed mental symptoms in situations of physical, nonpsychiatric alterations.<sup>19</sup> The presence of a control group with healthy subjects allowed data comparison to expand the scientific knowledge on the “psychological status” of patients with AC, as it is a disabling disease with significant functional impairment.

It is essential to emphasize that our study was not aimed at diagnosing anxiety and depression as diseases but to seek an association with these symptoms. In any case, we strengthen the idea that we must recognize these potential associative changes to better direct patients with AC to specialized treatment along with orthopedic follow-up.<sup>20–23</sup>

## Conclusion

There is a “doubtful” positive association between anxiety symptoms and AC, despite the difference from the control group ( $p = 0.019$ ). Regarding depression, although there is a higher prevalence in the case group, it is not possible to infer an association, since the mean score was below the HADS reference.

### Financial Support

There was no financial support from public, commercial, or not-for-profit sources.

### Conflict of Interests

The authors have no conflict of interests to declare.

## References

- Wu PY, Hsu PC, Chen TN, Huang JR, Chou CL, Wang JC. Evaluating Correlations of Coracohumeral Ligament Thickness with Restricted Shoulder Range of Motion and Clinical Duration of Adhesive Capsulitis with Ultrasound Measurements. *PM R* 2021;13(05):461–469
- Do JG, Hwang JT, Yoon KJ, Lee YT. Correlation of Ultrasound Findings With Clinical Stages and Impairment in Adhesive Capsulitis of the Shoulder. *Orthop J Sports Med* 2021;9(05):23259671211003675
- Wang JY, Liaw CK, Huang CC, Liou TH, Lin HW, Huang SW. Hyperlipidemia Is a Risk Factor of Adhesive Capsulitis: Real-World Evidence Using the Taiwanese National Health Insurance Research Database. *Orthop J Sports Med* 2021;9(04):2325967120986808
- Ding H, Tang Y, Xue Y, et al. A report on the prevalence of depression and anxiety in patients with frozen shoulder and their relations to disease status. *Psychol Health Med* 2014;19(06):730–737
- Ebrahimzadeh MH, Moradi A, Bidgoli HF, Zarei B. The Relationship between Depression or Anxiety Symptoms and Objective and Subjective Symptoms of Patients with Frozen Shoulder. *Int J Prev Med* 2019;10:38
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(06):361–370
- Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(02):69–77
- Botega NJ, Bio MR, Zomignani MA, Garcia C Junior, Pereira WA. Mood disorders among medical in-patients: a validation study of the hospital anxiety and depression scale (HAD). *Rev Saude Publica* 1995;29(05):355–363
- Beleckas CM, Wright M, Prather H, Chamberlain A, Guattery J, Calfee RP. Relative prevalence of anxiety and depression in patients with upper-extremity conditions. *J Hand Surg Am* 2018;43(06):571.e1–571.e8
- Bagheri F, Ebrahimzadeh MH, Moradi A, Bidgoli HF. Factors Associated with Pain, Disability and Quality of Life in Patients Suffering from Frozen Shoulder. *Arch Bone Jt Surg* 2016;4(03):243–247
- Toprak M, Erden M. Sleep quality, pain, anxiety, depression and quality of life in patients with frozen shoulder. *J Back Musculoskeletal Rehabil* 2019;32(02):287–291
- Checchia SL, Santos PD, Palomino EM, Garcia CMS, Leal HP. Tratamento da capsulite adesiva do ombro pelo bloqueio do nervo supra-escapular, associado ao uso de corticoide. *Rev Bras Ortop* 1994;29(09):627–634
- Zuckerman JD, Cuomo F, Rokito S. Definition and classification of frozen shoulder a consensus approach. *J Shoulder Elbow Surg* 1994;3(01):S72
- Fleming A, Dodman S, Beer TC, Crown S. Personality in frozen shoulder. *Ann Rheum Dis* 1975;35(05):456–457
- Debeer P, Franssens F, Roosen I, Dankaerts W, Claes L. Frozen shoulder and the Big Five personality traits. *J Shoulder Elbow Surg* 2014;23(02):221–226
- Menendez ME, Baker DK, Oladeji LO, Fryberger CT, McGwin G, Ponce BA. Psychological Distress Is Associated with Greater Perceived Disability and Pain in Patients Presenting to a Shoulder Clinic. *J Bone Joint Surg Am* 2015;97(24):1999–2003
- Martinez-Calderon J, Meeus M, Struyf F, et al. Psychological factors are associated with local and generalized pressure pain hypersensitivity, pain intensity, and function in people with chronic shoulder pain: A cross-sectional study. *Musculoskelet Sci Pract* 2019;44:102064
- Martinez-Calderon J, Meeus M, Struyf F, Miguel Morales-Asencio J, Gijon-Nogueron G, Luque-Suarez A. The role of psychological factors in the perpetuation of pain intensity and disability in people with chronic shoulder pain: a systematic review. *BMJ Open* 2018;8(04):e020703
- Cho CH, Jung SW, Park JY, Song KS, Yu KI. Is shoulder pain for three months or longer correlated with depression, anxiety, and sleep disturbance? *J Shoulder Elbow Surg* 2013;22(02):222–228
- Fernandes MR, Barbosa MA, Faria RM. Quality of life and functional capacity of patients with adhesive capsulitis: identifying risk factors associated to better outcomes after treatment with nerve blocking. *Brazilian Journal of Rheumatology* 2017;57(05):445–451
- Fernandes MR. Arthroscopic treatment of adhesive capsulitis of the shoulder with minimum follow up of six years. *Acta Ortop Bras* 2015;23(02):85–89
- Fernandes MR, Barbosa MA, Sousa ALL, Ramos GC. Suprascapular nerve block: important procedure in clinical practice. *Rev Bras Anestesiol* 2012;62(01):96–104
- Fernandes MR, Barbosa MA, Sousa ALL, Ramos GC. Suprascapular nerve block: important procedure in clinical practice. Part II. *Rev Bras Reumatol* 2012;52(04):616–622