


Association between Frozen Shoulder and Thyroid Diseases: Strengthening the Evidences*

Associação entre ombro congelado e tireopatias: Reforçando as evidências

Carina Cohen¹  Simone Tortato¹ Otavio Bento Souza Silva¹ Mariana Ferreira Leal¹
Benno Ejnisman¹ Flavio Faloppa¹

¹ Department of Orthopedics and Traumatology, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil

Address for correspondence Carina Cohen, PhD, Departamento de Ortopedia e Traumatologia, Escola Paulista de Medicina, Universidade Federal de São Paulo, Centro de Traumatologia do Esporte, Rua Estado de Israel, 636, São Paulo, SP, Brazil (e-mail: cacohen18@hotmail.com).

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Abstract

Objective To clarify the association of thyroid disorders and primary frozen shoulder by comparing this group with controls without shoulder disease and with patients with rotator cuff tears.

Methods We evaluated 166 patients who presented frozen shoulder with treatment in progress or already treated, which were compared with 129 patients with diagnosis of rotator cuff tears and 251 control subjects. All of the participants answered the questionnaire on the following variables: age, gender, body mass index (BMI), occupation, physical activity, presence of thyroid disorders and other comorbidities, smoking and use of alcohol.

Results When comparing the frozen shoulder group with the control and rotator cuff groups, there is a specific association between the presence of thyroid disorders and frozen shoulder. By calculating relative risk, it is possible to state that an individual with thyropathy has 2.69 more chance of developing frozen shoulder. Also, there was an association with gender, since women with frozen shoulder exceeded significantly the risk.

Conclusions Thyroid disorders, especially hypothyroidism and the presence of benign thyroid nodules, are risk factors significantly associated with frozen shoulder, rising the chances to 2.69 times of developing frozen shoulder.

This is the first study that uses, in addition to the control group, a second group with rotator cuff tears, so it was shown that there is a specific association of thyroid disorders and frozen shoulder, but not with shoulder disorders in general.

Keywords

- ▶ frozen shoulder
- ▶ adhesive capsulitis
- ▶ thyroid diseases
- ▶ hypothyroidism

Resumo

Objetivo Verificar a associação entre tireopatias e ombro congelado primário, comparando com grupo controle e com grupo de pacientes com lesão no manguito rotador.

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Palavras-chave

- ▶ ombro congelado
- ▶ capsulite adesiva
- ▶ doenças da tireoide
- ▶ hipotireoidismo

Métodos Foram avaliados 166 pacientes com diagnóstico de ombro congelado primário com tratamento em andamento ou já tratados. Este grupo foi comparado com 129 pacientes com diagnóstico de lesão de manguito rotador e com um terceiro grupo controle formado por 251 indivíduos sem acometimento dos ombros. Todos os participantes responderam questionário sobre as seguintes variáveis: idade, gênero, índice de massa corpórea (IMC), profissão, atividade física, presença de tireopatia e de outras comorbidades, hábito tabagista e etilismo.

Resultados Quando comparamos o grupo de ombro congelado com os grupos controle e lesão de manguito rotador, percebemos que existe uma associação específica entre presença de doenças da tireoide (tireoidite, hipotireoidismo, hipertireoidismo, nódulos e câncer) e ombro congelado. Através do cálculo do risco relativo, é possível afirmar que um indivíduo com tireopatia tem probabilidade 2.69 maior de desenvolver ombro congelado. Também houve associação com gênero, já que as mulheres com ombro congelado elevam significativamente esse risco.

Conclusão Os distúrbios da tireoide, especialmente o hipotireoidismo e a presença de nódulos tireoidianos benignos, são fatores de risco significativamente associados ao ombro congelado, aumentando as chances em 2,69 vezes de desenvolver a doença. Este é o primeiro estudo que utiliza, além do grupo controle, um segundo grupo com lesões do manguito rotador, de modo que foi demonstrada uma associação específica de distúrbios da tireoide e ombro congelado.

Introduction

Frozen shoulder is a clinical condition that affects the glenohumeral joint, causing pain and limitation in range of motion. Because it has an insidious course, it is difficult to define its exact incidence, because many patients do not seek medical attention. In general, it affects 2 to 5% of the population, with a slight predilection for the female gender.¹ The incidence peak occurs between 40 and 60 years old, and a positive family history is present in up to 9.5% of the cases.²

This clinical condition was described in 1896 by Duplay³ as a scapulohumeral periartthritis. Codman,⁴ in 1934, however, created the term "frozen shoulder" to name the cases of painful, long lasting onset of shoulder stiffness often related to periods of immobilization or disuse of the joint. Since then, several definitions and classifications have been proposed. The consensus of the American Shoulder and Elbow Surgeons defines it as "a condition of uncertain etiology, characterized by significant restriction of active and passive movement of the shoulder, which occurs in absence of a well-known intrinsic shoulder disorder."⁵ The most recent consensus published by the Upper Member Committee of the International Society of Arthroscopy Knee and Orthopedic Surgery (Isakos) discourages the use of the widely used term "adhesive capsulitis", and defines rigid shoulder as a global term covering any amplitude restriction of movement of the shoulder, being classified, according to the etiology, in frozen shoulder (or idiopathic primary) and secondary.⁶ In this way, the term "frozen shoulder" would be used solely to describe those cases of rigid shoulder of unknown cause. On the other hand, the term "secondary rigid shoulder" is

restricted to cases secondary to trauma, surgery or specific disease of the shoulder (rotator cuff injury, fractures and calcinate tendinitis).⁶

There are several factors, although their mechanism of action is unknown, which can predispose to rigid shoulder, such as diabetes mellitus (DM), thyropathies (thyroiditis, hypothyroidism, hyperthyroidism, nodules and cancer), neoplasms, heart, pulmonary and neurological diseases, Dupuytren contracture, emotional factors, use of certain medications and previous immobilization.⁶⁻¹⁰

As with other diseases already mentioned, thyropathies are mentioned in several studies as one of the factors associated with frozen shoulder and other musculoskeletal disorders, but still without a proper understanding.^{8,11-13}

The term thyropathy groups a series of thyroid diseases, and hypothyroidism is characterized by a deficiency of hormone production by the thyroid gland, most commonly found in the general population. Although the prevalence of hyperthyroidism has been reported in 1.5%, hypothyroidism is almost ten times more frequent. Its prevalence varies according to studies (6-20%) depending on age, gender, race, iodine sufficiency, as well as the reference level of the thyroid stimulating hormone (TSH).¹⁴⁻¹⁶

Some authors suggest an autoimmune etiology in the relationship between Hashimoto thyroiditis, which is the most common cause of hypothyroidism in the general population, and frozen shoulder.^{9,11,12,17}

Thus, the present study aimed to verify the association between thyropathies and frozen shoulder, comparing this with the control group of individuals without shoulder involvement and with a group of patients with rotator cuff

injuries, considering factors such as age of involvement, gender, bilaterality, and time of injury.

Material and methods

Casuistic

Between June 2012 and May 2016, at the shoulder and elbow Outpatient Clinic of our institution, we recruited patients with frozen shoulder diagnosis and individuals with rotator cuff injury. In group 1, 166 patients with primary frozen shoulder diagnosis, with treatment in progress or already treated, were included. The diagnosis was made by clinical examination (patients with pain during active mobilization and passive shoulder and global movement restriction compared to the contralateral side) and confirmed by magnetic resonance imaging (MRI) in all cases. Magnetic resonance imaging was used mainly to rule out differential diagnoses. Thus, patients who presented rotator cuff injuries, calcar tendinitis, shoulder dislocation, traumas, fractures or previous surgery for treating of secondary rigid shoulder cases, and not frozen shoulder.

Group 2 consisted of 129 patients with clinical diagnosis and MRI of the rotator cuff without clinical and radiological evidence of frozen shoulder, paired by gender and age with group 1.

Group 3 was the control group, consisting of 251 individuals assisted in the orthopedics service, without any complaint, trauma or diagnosis of orthopedic disease involving the shoulder joint.

All of the study participants underwent a clinical evaluation, conducted by interview from a single physician, and responded the same questionnaire about the following variables: age, gender, weight/height for calculating body mass index (BMI), profession, activity, presence of thyrothyopathy diagnosed by a physician and other comorbidities (DM, hypertension, cardiopathies, psychiatric disorders), smoking habit and alcohol consumption. For patients with frozen shoulder, it was also evaluated the side and dominance of the affected arm, as well as the duration of the disease.

All of the participants of the study signed a free-informed consent term, with a model approved by the Research Ethics Committee of our institution (opinion 51436).

Statistical Analysis

Statistical Analysis was performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to verify the distribution of continuous variables. When the variables did not follow a normal distribution, we chose to present the results in median and interquartile deviation. We performed three analyses comparing the following groups: a) frozen shoulder (Group 1) and control (Group 3); b) rotator cuff (Group 2) and control (Group 3) and c) frozen shoulder (Group 1) and rotator cuff (Group 2). For this, we performed a univariate logistic regression considering Group 1 or Group 2 as dependent variable and each clinical or demographic variable as independent variable. Subsequently, the variables significantly associated with each of the diseases were included

in a multivariate logistic regression. These analyses were corrected for three comparisons. Significant statistical differences were considered when $p < 0.05$.

Sample description

Group 1 consisted of 60% female patients with age of impairment varying from 30 to 74 years old (median \pm interquartile deviation [DI]: 51 ± 11 , **Table 1**). Bilateral involvement was observed in 20% of the patients. Among the unilateral cases, the dominant side was affected in 54%. From the total number of patients, 57% were in the active phase of the disease. For the other patients, whom were considered treated, the duration of the disease ranged from 1 to 60 months (median \pm DI: 8 ± 6). In addition, 34% of the patients reported a medical diagnosis previously confirmed by blood or imaging of some thyrothyopathy (**Table 1**). Other affections have been reported, such as psychiatric diseases (33%), dyslipidemia (26%), hypertension (22%), renal lithiasis (13%), diabetes (11%), malignant neoplasms (10%), fibromyalgia (8%) and hyperuricemia (2%). Alcoholism was reported in 5% and smoking in 37%. In relation to body mass index (BMI), 50% of the patients were overweight or obese. Additionally, 14% reported performing a manual professional activity, and 55% reported the practice of physical activity (**Table 1**).

Group 2 consisted of 59% of female patients with age of impairment varying from 28 to 59 years old (median \pm DI: 52 ± 8 , **Table 2**). In addition, 5% of the patients reported a previous medical diagnosis of some thyrothyopathy (**Table 2**). Other affections have been reported, such as hypertension (52%), dyslipidemia (21%), diabetes (7%), fibromyalgia (7%), psychiatric disorders (6%), renal lithiasis (3%), malignant neoplasia (1%) and hyperuricemia (1%). Alcoholism was reported in 16% and smoking in 36%. In relation to BMI, 62% of the patients were overweight or obese. Additionally, 43% reported performing a manual professional activity and 35% reported practicing physical activities (**Table 2**).

Group 3 consisted of 60% of female individuals aged between 30 and 75 years old (median \pm DI: 50 ± 10 , **Tables 1 and 2**). From the total of individuals, 14% reported previous medical diagnosis of some thyrothyopathy (**Tables 1 and 2**). Other affections have been reported, such as SAH (37%), DM (18%), dyslipidemia (17%), malignant neoplasia (8%), psychiatric disorders (3%), diagnosed fibromyalgia (1%) and renal lithiasis (1%). Alcoholism was reported in 18% and smoking in 39%. In relation to BMI, 60% of the individuals presented overweight or obesity. Additionally, 50% reported performing a manual professional activity and 41% reported practicing physical activity (**Tables 1 and 2**).

Results

Univariate logistic regression analysis showed different variables associated with shoulder development and rotator cuff injury, in relation to control subjects (**Tables 1, 2 and 3**). When these variables were inserted in the multivariate logistic regression model, there was association between the development of frozen shoulder and thyrothyopathies (thyroiditis,

Table 1 Univariate logistic regression analysis with variables associated with frozen shoulder development (Group 1) comparing to control subjects (Group 3)

Clinical and demographic variables	Group 1	Group 3	OR	95%	p-value
Age (median \pm DI)	51 \pm 11	50 \pm 10	1.01	0.99–1.04	0.26
Female gender [N (%)]	100 (60%)	151 (60%)	1.00	0.67–1.50	0.99
Overweight or obesity ^a [N (%)]	83 (50%)	152 (60%)	0.65	0.44–0.97	0.03
Manual profession [N (%)]	23 (14%)	126 (50%)	0.16	0.10–0.26	< 0.01*
Physical Activity [N (%)]	92 (55%)	103 (41%)	1.79	1.20–2.70	< 0.01*
Thyropathy [N()]	56 (34%)	35 (14%)	3.14	1.94–5.08	< 0.01*
Thyroiditis [N()]	6 (4%)	4 (2%)	2.32	0.64–8.33	0.20
Hypothyroidism [N()]	29 (17%)	21 (8%)	2.32	1.27–4.23	< 0.01*
Benign nodules [N()]	16 (10%)	6 (2%)	4.36	1.67–11.38	< 0.01*
Cancer [N (%)]	5 (3%)	4 (2%)	1.92	0.51–7.25	0.34
Diabetes [N()]	19 (11%)	46 (18%)	0.58	0.32–1.02	0.06
Dyslipidemia [N (%)]	43 (26%)	43 (17%)	1.69	1.05–2.73	0.03
Renal lithiasis [N (%)]	22 (13%)	2 (1%)	19.02	4.41–82.07	< 0.01*
Fibromyalgia [N (%)]	13 (8%)	2 (1%)	10.58	2.36–47.52	< 0.01*
Hypertension [N (%)]	37 (22%)	92 (37%)	0.50	0.32–0.78	< 0.01*
Hyperurecemia [N (%)]	3 (2%)	0 (0%)	2.49	<0.01- <0.01	0.99
Malignant neoplasia [N (%)]	16 (10%)	20 (8%)	1.23	0.62–2.45	0.55
Psychiatric diseases [N (%)]	54 (33%)	8 (3%)	14.65	6.74–31.81	< 0.01*
Continuous use medication [N (%)]	112 (66%)	179 (71%)	0.83	0.55–1.28	0.40
Alcoholism ^b [N()]	9 (5%)	45 (18%)	0.26	0.13–0.55	< 0.01*
Tobacco ^c [N()]	62 (37%)	98 (39%)	0.93	0.62–1.39	0.70

Abbreviations: DI, interquartile deviation; CI, confidence interval; N, number of patients; OR (odds ratio), the odds ratio for an event to occur.

^aIMC > 25.

^bAlcoholics and ex-alcoholics.

^cSmokers and ex-smokers.

* $p < 0.02$.

hypothyroidism, hyperthyroidism, nodules and thyroid cancer), renal lithiasis and psychiatric disease (depression, sleep and anxiety disorders, behavioral disorders diagnosed and treated by a physician) in relation to group 3. Considering individuals with rotator cuff injury, thyropathy, neoplasia, psychiatric diseases, hypertension and alcoholism were associated with the development of frozen shoulder.

Regarding thyropathy (including all categories) and comparing Group 1 with Groups 2 and 3, it is possible to conclude that there is an association between the development of some type of thyropathy and frozen shoulder (**► Tables 1 and 2**), even when correcting for different covariates. This association was not observed in patients with rotator cuff injury, comparing them with the control group (**► Table 3**). Therefore, the development of some type of thyropathy seems to be specific in cases of frozen shoulder. In this group, the types of thyroid abnormalities reported were hypothyroidism (17%), benign nodules (10%), thyroiditis (4%) and thyroid cancer (3%) (**► Table 1**). The presence of hypothyroidism and benign nodules was associated with the development of frozen shoulder in relation to control subjects (**► Table 1**) and with rotator cuff lesion (**► Table 2**).

Still in group 1, the vast majority of patients with thyroid diseases were women (84%), being that the logistic regression analysis showed significant association between the involvement of the thyroid and gender, so that women with frozen shoulders are at greater risk of presenting the disease (**► Table 4**). The age of thyroid patients in this group ranged from 30 to 71 years old (median \pm DI: 51 \pm 11) and didn't differ from the age of the individuals without thyropathy (**► Table 4**). Frozen shoulder was bilateral in 20% of the thyropathies and did not differ from the patients without thyropathy (**► Table 4**). The time of injury of thyropathic patients ranged from 1 to 36 months (median \pm DI: 7 \pm 7) and did not differ from those patients without thyropathy (**► Table 4**).

Discussion

Analyzing the 3 groups, we noticed an increased prevalence of thyroid diseases in group 1 (34%), when compared to the other groups and even to the literature on thyroid diseases. According to Huang et al.¹³ who studied the prevalence and risk of developing frozen shoulder in patients with hyperthyroidism, individuals with hyperthyroidism have 1.22 times the risk of

Table 2 Univariate logistic regression analysis including variables associated with frozen shoulder development (Group 1) comparing to individuals with rotator cuff injury (Group 2)

Clinical and demographic variables	Group 1	Group 2	OR	95%CI	P-Value
Age (median \pm DI)	51 \pm 11	52 \pm 8	1.00	0.97–1.03	0.99
Female gender [N (%)]	100 (60%)	76 (59%)	1.06	0.66–1.69	0.82
Overweight or obesity ^a [N (%)]	83 (50%)	80 (62%)	0.61	0.38–0.98	0.04
Manual profession [N (%)]	23 (14%)	56 (43%)	0.21	0.12–0.37	< 0.01*
Physical Activity [N (%)]	92 (55%)	45 (35%)	2.32	1.45–3.73	< 0.01*
Thyropathy [N (%)]	56 (34%)	7 (5%)	8.87	3.88–20.29	< 0.01*
Thyroidites [N (%)]	6 (4%)	0 (0%)	13.02	< 0.01–< 0.01	0.99
Hypothyroidism [N (%)]	29 (17%)	5 (4%)	5.25	1.97–13.98	< 0.01*
Benign nodules [N (%)]	16 (10%)	2 (2%)	6.77	1.53–30.02	0.01*
Cancer [N (%)]	5 (3%)	0 (0%)	12.94	< 0.01–< 0.01	0.99
Diabetes [N (%)]	19 (11%)	9 (7%)	1.72	0.75–3.95	0.20
Dyslipidemia [N (%)]	43 (26%)	27 (21%)	1.32	0.76–2.29	0.32
Renal lithiasis [N (%)]	22 (13%)	4 (3%)	4.77	1.60–14.23	< 0.01*
Fibromyalgia [N (%)]	13 (8%)	9 (7%)	1.13	0.47–2.74	0.78
Hypertension [N (%)]	37 (22%)	67 (52%)	0.27	0.16–0.44	< 0.01*
Hyperurecemia [N (%)]	3 (2%)	1 (1%)	2.36	0.24–22.92	0,46
Malignant neoplasms [N (%)]	16 (10%)	1 (1%)	13,65	1,79–104,38	0.01*
Psychiatric diseases [N (%)]	54 (33%)	8 (6%)	7.29	3.32–16.00	<0.01*
Medication use continues [N (%)]	112 (66%)	81 (63%)	1.23	0.76–1.99	0.40
Alcoholism ^b [N(%)]	9 (5%)	21 (16%)	0.30	0.13–0.67	<0.01*
Tobacco ^c [N(%)]	62 (37%)	47 (36%)	0.99	0.61–1.60	0.97

Abbreviations: DI, interquartile deviation; CI, confidence interval; N, number of patients; OR (odds ratio), the odds ratio for an event to occur. ^aIMC > 25.

^bAlcoholics and ex-alcoholics.

^cSmokers and ex-smokers.

* $p < 0.02$.

developing the disease in comparison with the general population. In our study, we found only 2 patients with a diagnosis of hyperthyroidism, both in group 2. However, considering the groups paired by gender and age (groups 1 and 3), it is possible to say that there is a higher frequency of thyroid diseases in patients with frozen shoulder when compared with the control group. By calculating the relative risk, it is possible to affirm that an individual with thyropathy has 2.69 more chance to develop frozen shoulder. No association was observed between thyropathies and group 2, suggesting a direct association with frozen shoulder, but not with rotator cuff injuries.

Analyzing only patients with hypothyroidism, we observed a significantly increased prevalence (17%) in the frozen shoulder group. In group 2, the prevalence was 4%, and in group 3, 2%. Similar data were found by Schiefer et al.¹⁷ in a case-control study with 93 patients with frozen shoulder and 151 control cases, in which it a prevalence of hypothyroidism in 27.2% and 10.7%, respectively, was observed. In addition, it reported a tendency of independent association between high serum TSH levels, bilaterality and severity of the frozen shoulder.

In another study, a control case conducted in China with 182 cases of frozen shoulder, there were 25% of thyropathies and 24% of diabetics identified, compared to 16% and 9% respectively in the control group.¹⁸

According to a study by Milgrom et al. which analyzed data from 126 frozen shoulders of 98 patients in the city of Jerusalem, thyropathies represent not only a risk factor for musculoskeletal disorders in general, but also a specific risk factor for frozen shoulder in women.¹⁹

Cakir et al. evaluated patients from an endocrinological clinic and found that among patients with thyropathy, frozen shoulder was present in 10.9% of the cases, Dupuytren contracture in 8.8%, syndrome of carpal tunnel in 9.5%, limitation of articular range of motion in 4.4% and finger in trigger in 2.9% of cases.¹¹

When we analyzed the time of injury, bilaterality and age of involvement, there was no significant difference between the groups with and without thyropathy, that is, the fact of having thyropathy does not seem to influence these factors. Although Reeves²⁰ suggested that the disease presented spontaneous resolution after 30 months, Schiefer et al.¹⁷ found residual pain in 50% of the patients and some movement deficit in 60%.

Table 3 Univariate logistic regression analysis including variables associated with rotator Cuff injury (Group 2) comparing to control subjects (Group 3)

Clinical and demographic variables	Group 2	Group 3	OR	95%CI	p-value
Age (median \pm DI)	52 \pm 8	50 \pm 10	1.02	0.99–1.04	0.29
Female gender [N (%)]	76 (59%)	151 (60%)	0.95	0.62–1.46	0.82
Overweight or obesity ^a [N (%)]	80 (62%)	152 (60%)	1.06	0.69–1.65	0.78
Manual profession [N (%)]	56 (43%)	126 (50%)	0.76	0.50–1.17	0.21
Physical Activity [N (%)]	45 (35%)	103 (41%)	0.77	0.50–1.20	0.25
Thyropathy [N (%)]	7 (5%)	35 (14%)	0.35	0.15–0.82	0.03
Thyroidites [N (%)]	0 (0%)	4 (2%)	< 0.01	< 0.01–< 0.01	0.99
Hypothyroidism [N(%)]	5 (4%)	21 (8%)	0.44	0.16–1.20	0.11
Benign nodules [N(%)]	2 (2%)	6 (2%)	0.64	0.13–3.23	0.59
Cancer [N (%)]	0 (0%)	4 (2%)	< 0.01	< 0.01–< 0.01	0.99
Diabetes [N(%)]	9 (7%)	46 (18%)	0.33	0.16–0.71	< 0.01*
Dyslipidemia [N (%)]	27 (21%)	43 (17%)	1.28	0.75–2.19	0.37
Renal lithiasis [N (%)]	4 (3%)	2 (1%)	3.98	0.72–22.05	0.11
Fibromyalgia [N (%)]	9 (7%)	2 (1%)	9.34	1.99–43.89	< 0.01*
Hypertension [N (%)]	67 (52%)	92 (37%)	1.87	1.21–2.87	< 0.01*
Hyperurecemia [N (%)]	1 (1%)	0 (0%)	3.17	<0.01–<0.01	1.00
Malignant neoplasms [N (%)]	1 (1%)	20 (8%)	0.09	0.01–0.68	0.03
Psychiatric diseases [N (%)]	8 (6%)	8 (3%)	2.01	0.74–5.48	0.17
Medication use continues [N (%)]	81 (63%)	179 (71%)	0.68	0.43–1.06	0.09
Alcoholism ^b [N (%)]	21 (16%)	45 (18%)	0.89	0.50–1.57	0.69
Tobacco ^c [N (%)]	47 (36%)	98 (39%)	0.94	0.60–1.45	0.76

Abbreviations: DI, interquartile deviation; CI, confidence interval; N, number of patients; OR (odds ratio), the odds ratio for an event to occur.

^aIMC > 25.

^bAlcoholics and ex-alcoholics.

^cSmokers and ex-smokers.

* $p < 0.02$.

Table 4 Association between thyroid diseases and clinical variables of patients with frozen shoulder

Clinical and demographic variables	Thyropaths	Non-thyropaths	OR	95%CI	p-value
Age of impairment (median \pm DI)	51 \pm 11	51 \pm 10	1.02	0.97–1.06	0.47
Female gender [N (%)]	47 (84%)	53 (48%)	5.62	2.51–12.56	< 0.01*
Bilaterality [N (%)]	11 (20%)	23 (21%)	0.93	0.41–2.07	0.85
Time of injury in months (median \pm DI)	7 \pm 7	8 \pm 7	0.99	0.93–1.05	0.77

Abbreviations: DI, interquartile deviation; CI, confidence interval; N, number of patients; OR (odds ratio), the odds ratio for an event to occur.

* $p < 0.05$.

Although many studies show the relationship between frozen shoulder with DM,^{21–26} in our study this association could not be confirmed. Zreik et al.,²⁶ in a meta-analysis of prevalence, identified that diabetic patients have five times more chance of developing frozen shoulder than nondiabetic patients. In diabetic patients, frozen shoulder showed to be more severe and more resistant to treatment, as found in the present study, when a slower course was observed for the disease, with longer treatment time when compared to the group without DM.

In the past, DM was the main disease associated with frozen shoulder, but recent studies corroborate the association of frozen shoulder with thyroid diseases.²⁷ Possibly, because the diagnosis of thyroid diseases was not valued, and currently the screening of thyroid hormones is part of the routine, the diagnosis is made with higher frequency and the disease is better understood.

Our study presents some limitations. The first is regarding the different stages of the disease in patients with frozen shoulder. Although the questionnaire is appropriate for the

study, there are patients with a recent diagnosis, patients undergoing treatment and treated patients. As the objective was to analyze the clinical association with the presence of thyropathies, this heterogeneity does not interfere with the findings; however, it weakens our analysis of the course of the disease in these individuals. Another limitation is the lack of information regarding thyroid hormone levels, since the patients reported a medical diagnosis of thyropathy prior to the disease, but no laboratory diagnostic or image reconfirmation was performed in the present study. In this way, cases of subclinical hypothyroidism were not included.

Despite the limitations, our study is the first that uses, in addition to the control group, a second group with shoulder involvement due to rotator cuff injury. Since some previous studies have shown an association of thyroid disorders with musculoskeletal disorders, this choice was made to determine the existence of a specific association between thyropathies and frozen shoulder.

Conclusion

As the conclusions of the present study, we can confirm that thyropathies, in particular hypothyroidism and the presence of benign thyroid nodules, are factors associated with frozen shoulder. This association was not observed in cases of rotator cuff injury. Other factors, such as age of involvement, gender, bilaterality and time of injury were not influenced by the presence of thyropathies in patients with frozen shoulder.

Conflict of Interests

The authors declare that have no conflict of interests.

References

- Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA. Current review of adhesive capsulitis. *J Shoulder Elbow Surg* 2011;20(03):502–514
- Cohen C, Ejnisman B. Epidemiology of frozen shoulder. In: Itoi E, Arce G, Bain GI, Diercks RL, Guttman D, et al. *Shoulder stiffness*. Berlin, Heidelberg: Springer; 2015:21–30
- Duplay S. De la periarthrite scapulo-humerale. *Rev Frat Trav Med*. 1896;53:226
- Codman EA. *The shoulder: rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa*. Boston: Thomas Todd Co; 1934
- Zuckerman JD, Rokito A. Frozen shoulder: a consensus definition. *J Shoulder Elbow Surg* 2011;20(02):322–325
- Itoi E, Arce G, Bain GI, et al. *Shoulder Stiffness: Current Concepts and Concerns*. *Arthroscopy* 2016;32(07):1402–1414
- Akeson WH, Amiel D, Woo SL. Immobility effects on synovial joints the pathomechanics of joint contracture. *Biorheology* 1980;17(1-2):95–110
- Summers GD, Gorman WP. Bilateral adhesive capsulitis and Hashimoto's thyroiditis. *Br J Rheumatol* 1989;28(05):451
- Wang K, Ho V, Hunter-Smith DJ, Beh PS, Smith KM, Weber AB. Risk factors in idiopathic adhesive capsulitis: a case control study. *J Shoulder Elbow Surg* 2013;22(07):e24–e29
- 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
- Cakir M, Samanci N, Balci N, Balci MK. Musculoskeletal manifestations in patients with thyroid disease. *Clin Endocrinol (Oxf)* 2003;59(02):162–167
- Reuters VS, Teixeira PdeF, Vigário PS, et al. Functional capacity and muscular abnormalities in subclinical hypothyroidism. *Am J Med Sci* 2009;338(04):259–263
- Huang SW, Lin JW, Wang WT, Wu CW, Liou TH, Lin HW. Hypothyroidism is a risk factor for developing adhesive capsulitis of the shoulder: a nationwide longitudinal population-based study. *Sci Rep* 2014;4:4183
- Vanderpump MP. The epidemiology of thyroid disease. *Br Med Bull* 2011;99:39–51
- Brenta G, Vaisman M, Sgarbi JA, et al. Task Force on Hypothyroidism of the Latin American Thyroid Society (LATS). Clinical practice guidelines for the management of hypothyroidism. *Arq Bras Endocrinol Metabol* 2013;57(04):265–291
- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med* 2000;160(04):526–534
- Schiefer M, Teixeira PFS, Fontenelle C, et al. Prevalence of hypothyroidism in patients with frozen shoulder. *J Shoulder Elbow Surg* 2017;26(01):49–55
- Li W, Lu N, Xu H, Wang H, Huang J. Case control study of risk factors for frozen shoulder in China. *Int J Rheum Dis* 2015;18(05):508–513
- Milgrom C, Novack V, Weil Y, Jaber S, Radeva-Petrova DR, Finestone A. Risk factors for idiopathic frozen shoulder. *Isr Med Assoc J* 2008;10(05):361–364
- Reeves B. The natural history of the frozen shoulder syndrome. *Scand J Rheumatol* 1975;4(04):193–196
- Arkkila PE, Kantola IM, Viikari JS, Rönnemaa T. Shoulder capsulitis in type I and II diabetic patients: association with diabetic complications and related diseases. *Ann Rheum Dis* 1996;55(12):907–914
- Balci N, Balci MK, Tüzüner S. Shoulder adhesive capsulitis and shoulder range of motion in type II diabetes mellitus: association with diabetic complications. *J Diabetes Complications* 1999;13(03):135–140
- Tighe CB, Oakley WS Jr. The prevalence of a diabetic condition and adhesive capsulitis of the shoulder. *South Med J* 2008;101(06):591–595
- Ramchurn N, Mashamba C, Leitch E, et al. Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. *Eur J Intern Med* 2009;20(07):718–721
- Yian EH, Contreras R, Sodl JF. Effects of glycemic control on prevalence of diabetic frozen shoulder. *J Bone Joint Surg Am* 2012;94(10):919–923
- Zreik NH, Malik RA, Charalambous CP. Adhesive capsulitis of the shoulder and diabetes: a meta-analysis of prevalence. *Muscles Ligaments Tendons J* 2016;6(01):26–34
- Zorzano A, Palacín M, Gumà A. Mechanisms regulating GLUT4 glucose transporter expression and glucose transport in skeletal muscle. *Acta Physiol Scand* 2005;183(01):43–58