

## Risk Factors for Idiopathic Frozen Shoulder

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### Abstract

**Background:** Idiopathic frozen shoulder is a self-limiting regional skeletal problem of unknown etiology. Clinically, patients first experience a phase of pain, progressing to a freezing stage when glenohumeral motion is lost, followed by a thawing phase when pain gradually subsides and most of the lost motion returns.

**Objectives:** To identify possible specific and non-specific risk factors for idiopathic frozen shoulder.

**Methods:** We compared the medical histories, drug treatment, previous hospital as well as health management organization blood tests of 126 new consecutive frozen shoulder patients from a shoulder clinic to those of an age-matched control group of 98 consecutive patients from an orthopedic foot and ankle clinic and to the regional population disease prevalence registry. Frozen shoulder was classified as idiopathic only if there was no history of trauma and no evidence of a rotator cuff tear.

**Results:** Among the frozen shoulder patients 29.4% had diabetes and 13.5% had thyroid disorders. The risk ratio for diabetes in the frozen shoulder group was 5.9 for males (95% confidence interval 4.1–8.4,  $P < 0.001$ ) and 5.0 for females (95% CI 3.3–7.5,  $P < 0.001$ ). The risk ratio for thyroid disorders among females with frozen shoulder was 7.3 (95% CI 4.8–11.1,  $P = 0.001$ ). No significant difference was found in the prevalence of thyroid disorders between frozen shoulder and the control group, but there was a significantly higher prevalence of diabetes in males and a trend for higher prevalence in females in the frozen shoulder group.

**Conclusions:** Physicians should be aware that diabetes is a specific risk factor for idiopathic frozen shoulder in both males and females and thyroid disorders are a non-specific risk factor in females only.

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Idiopathic frozen shoulder is a self-limiting regional skeletal problem whose etiology remains an enigma. It begins insidiously, with no known trigger. Clinically, patients first experience a phase of pain, which progresses to a freezing phase when glenohumeral motion is lost, followed by a thawing phase in which pain gradually subsides and most of the lost motion returns [1]. Clinical diagnosis in the early phase of idiopathic frozen shoulder can be difficult. In the pain phase symptoms are similar to rotator cuff tendonitis. In the freezing phase the patient often compensates for decreased glenohumeral motion by increased scapulothoracic motion, masking the limitations in motion.

Biopsies have shown that the pathology of idiopathic frozen shoulder is a chronic fibrosing condition of the shoulder joint capsule. The predominant cells involved are fibroblasts and myofibroblasts which lay down a dense matrix of type I and type II collagen within the capsule [2]. What initiates the onset of the process and its eventual resolution is not known.

Identifying risk factors for a disease is one of the methods used to gain understanding of its etiology. Diabetes mellitus [3,4] and thyroid disorders [5-7] were previously reported to be associated with idiopathic frozen shoulder.

The purpose of the present prospective study was to identify possible specific and non-specific risk factors for idiopathic frozen shoulder by comparing the medical histories of new cases of frozen shoulder to those of a control group of patients with other musculoskeletal disorders and to the regional disease prevalence registry.

### Patients and Methods

All new consecutive patients who presented to a university hospital shoulder clinic during a 2.5 year period and were diagnosed as having an idiopathic frozen shoulder were asked to participate in the study. The study was approved by the Institutional Review Board. Frozen shoulder was diagnosed clinically on the basis of the presence of both active and passive restrictions of the glenohumeral joint in flexion, abduction and internal rotation, with external rotation restricted to less than 50% of the normal side with the arm at the side, and a normal radiograph of the joint [8,9]. The passive range of motion examination was done with the scapula manually stabilized by the examiner. Frozen shoulder was classified as idiopathic only if there was no history of trauma and an ultrasound study showed no evidence of a rotator cuff tear. A medical history of major medical problems and drug treatment was taken. Previous hospital and health management organization blood tests were reviewed. A patient was considered to have a thyroid abnormality if he or she was receiving drug treatment for the problem or had thyroid-stimulating hormone values below 0.5 or higher than 4.5 units. Levels of TSH between 4.5 and 10 units signified subclinical hypothyroidism. A person was considered to

CI = confidence interval

TSH = thyroid-stimulating hormone

have diabetes if he or she was receiving drug treatment for the problem or whose serum glucose was higher than 200 mg/dl.

On the basis of hospital records from previous years, we estimated that there would be between 50 and 65 new cases of idiopathic frozen shoulder attending the shoulder clinic per year. An age-matched population of 100 new consecutive patients seen in an orthopedic foot and ankle clinic during the same time period was recruited to form a control group with musculoskeletal problems other than idiopathic frozen shoulder. The prevalence of major medical problems in the frozen shoulder population was compared to the foot and ankle clinic control group. Afterwards, both groups were compared to the age-matched regional prevalence based on data from national HMOs [10]. We used the Jerusalem district of the largest of the four HMOs in Israel – Clalit Health Services – to assess the prevalence of treated hypothyroidism and diabetes. In 2004, 440,000 patients were registered in the Jerusalem district of Clalit Health Services. The prevalence was based on drug dispensing data during the first half of 2004 (different tetraiodothyronine, triiodothyronine formulations for hypothyroidism; oral hypoglycemic and insulin for diabetes), obtained through the central pharmacy data warehouse.

Continuous variables are expressed as mean  $\pm$  SD, and categorical variables as percentages. Prevalence rates are presented as percentage and compared among different patient groups by the chi-square test. Risk ratio with 95% confidence interval was reported for point estimation. To avoid the potential confounding influence of age, the method of indirect standardization was used. The prevalence rate comparison was performed using the actual population rather than calculated projected rates. All reported *P* values are two-sided and *P* < 0.05 was considered significant. The statistical tests were performed using Statistical Package for the Social Sciences (SPSS) version 12 (version 12.0; SPSS Inc, Chicago, IL, USA).

## Results

Altogether, 126 patients were diagnosed as having idiopathic frozen shoulder. Full data were available for all. Seventy-six patients were female (age range 38–80, mean age 55.0  $\pm$  8.4 years) and 50 were male (age range 37–75, mean age 54.7  $\pm$  8.7 years). Of all the diseases affecting this population, only thyroid disorders, diabetes, hypercholesterolemia and hypertension exceeded a prevalence of 5%. Sixteen females and one male were treated with L-thyroxine. An additional seven female patients had subclinical hypothyroidism on the basis of their TSH values. Of the 100 subjects in the foot and ankle clinic control group, full data were available for 98. Sixty-four of them were female (age range 46–64, mean age 56.0  $\pm$  5.5) and 34 were male (age range 46–64, mean age 54.4  $\pm$  5.6). Seven females and one male were treated with L-thyroxine. There were no cases of subclinical hypothyroidism on the basis of TSH values.

The prevalence of treated hypothyroidism in the idiopathic frozen shoulder group and in the foot and ankle clinic control

group was compared to the regional prevalence according to gender [Table 1]. Risk ratios were referenced to the gender-matched regional prevalence. There was a significantly higher prevalence of treated hypothyroidism among female patients with idiopathic frozen shoulder (risk ratio 7.3, 95% CI 4.8–11.1) and among females from the foot and ankle clinic (risk ratio 3.8, 95% CI 1.9–7.5) than in the age-matched population.

The prevalence of diabetes in the idiopathic frozen shoulder group and in the foot and ankle clinic control group was compared to the regional prevalence according to gender [Table 2]. Risk ratios were referenced to the gender-matched regional population. There was a significantly higher prevalence of diabetes among both males and females with frozen shoulder and among females from the foot and ankle control group than in the age-matched regional population.

The frequencies of diabetes and treated hypothyroidism were

**Table 1.** Frequency of treated hypothyroidism in patients with idiopathic frozen shoulder and patients from a foot and ankle clinic as compared to the age-matched regional prevalence

	Gender	Prevalence (treated hypothyroidism)	Risk ratio (95% CI)	<i>P</i>
Regional population	Male	(0.8%)		
	Female	(7.9%)		
Idiopathic frozen shoulder (n=126)	Male	1/50 (2.0%)	2.6 (0.4–17.0)	0.32
	Female	16/76 (21.1%)	7.3 (4.8–11.1)	< 0.001
Foot and ankle clinic (n=98)	Male	1/34 (2.9%)	3.8 (0.6–23.4)	0.15
	Female	7/64 (10.9%)	3.8 (1.9–7.5)	< 0.001

CI = confidence interval

**Table 2.** Frequency of diabetes in patients with idiopathic frozen shoulder and patients from a foot and ankle clinic as compared to the age-matched regional prevalence

	Gender	Prevalence (diabetes)	Risk ratio (95% CI)	<i>P</i>
Regional population	Male	(6.5%)		
	Female	(4.7%)		
Idiopathic frozen shoulder (n=126)	Male	19/50 (38.0%)	5.9 (4.1–8.4)	< 0.001
	Female	18/76 (23.7%)	5.0 (3.3–7.5)	< 0.001
Foot and ankle clinic (n=98)	Male	3/34 (8.82%)	1.5 (0.5–4.3)	0.51
	Female	8/64 (12.5%)	2.8 (1.4–5.1)	0.003

**Table 3.** Frequency of diabetes and treated hypothyroidism in patients with idiopathic frozen shoulder as compared to patients from a foot and ankle clinic

	Gender	Idiopathic frozen shoulder No./Total no. (%)	Foot and ankle clinic No./Total no. (%)	Relative risk (95% CI)	<i>P</i>
Diabetes	Male	19/50 (38.0)	3/34 (8.8)	4.3 (1.6–11.3)	0.003
	Female	18/76 (23.7)	8/64 (12.5)	1.9 (0.9–4.0)	0.09
Treated hypothyroidism	Male	1/50 (2.0)	1/34 (2.9)	0.7 (0.1–10.1)	0.78
	Female	16/76 (21.1)	7/64 (10.9)	1.9 (0.9–4.3)	0.11

HMO = health management organization

compared between the frozen shoulder population and the control group from the foot and ankle clinic [Table 3]. There was a higher prevalence of diabetes in males and a tendency for a higher prevalence of diabetes in females in the frozen shoulder group. There was no statistically significant difference between the prevalence of treated hypothyroidism among female or male patients with frozen shoulder as compared to patients from the foot and ankle clinic. If the patients from the frozen shoulder group who had subclinical hypothyroidism are added to those with treated hypothyroidism, then the relative risk of hypothyroidism is 2.8 (95% CI 1.3–6.0,  $P = 0.001$ ) in females with frozen shoulder as compared to the women in the foot and ankle clinic.

There were no statistical differences in the frequency of hypercholesterolemia and hypertension between the frozen shoulder group, the orthopedic foot and ankle control group and the regional prevalence.

## Discussion

The premise of this study was that identifying risk factors could help elucidate the underlying mechanism of idiopathic frozen shoulder. Such an approach has been valuable for the study of cardiovascular disease [11]. In order to differentiate between diseases related to a higher incidence of musculoskeletal problems and those that are specifically related to a higher incidence of idiopathic frozen shoulder, a control group from a foot and ankle clinic was used in the study. The prevalence of diseases in the frozen shoulder and the control group were also compared to age-adjusted regional prevalence. To the best of our knowledge, this epidemiological approach to identify specific risk factors for idiopathic frozen shoulder has not been used before.

The present study did not identify any new risk factors for idiopathic frozen shoulder. The only diseases in the idiopathic frozen shoulder population with prevalence greater than 5% were diabetes, thyroid dysfunction, hypercholesterolemia and hypertension. Two of these diseases – diabetes [3,4] and thyroid dysfunction [5-7] – were previously identified to be associated with frozen shoulder. No statistical differences in the frequency of hypercholesterolemia and hypertension were found among the frozen shoulder group, the foot and ankle control group and the regional prevalence. Associations with other diseases with a lower prevalence could not be established because of the relatively small sample size.

When compared to both the regional and orthopedic foot and ankle clinic populations, diabetes was found to be a specific risk factor for idiopathic frozen shoulder in this study. The risk ratio for diabetes in the frozen shoulder population was nearly six times the regional prevalence for males and five times the regional prevalence for females.

Thyroid disorders are primarily a female problem [12], and as such, a priori have little likelihood of being related to frozen shoulder in males. In the current study, the prevalence of treated hypothyroidism was higher among female patients from the frozen shoulder group as compared to the regional population. It was also higher than that of the women from the foot and ankle clinic control group but the difference was not statistically signifi-

cant. When the female patients with subclinical hypothyroidism were included in the calculations, the difference between the female patients from the frozen shoulder and the control group reached statistical significance.

Cakir et al. [5] found in a study of patients in an endocrinology clinic that 10.9% of patients with thyroid disorders had frozen shoulder, 8.8% had Dupuytren's contracture, 9.5% carpal tunnel syndrome, 4.4% limited joint mobility and 2.9% trigger finger. They concluded that musculoskeletal disorders often accompany thyroid disorders. Our data indicate that thyroid diseases may be not only a risk factor for musculoskeletal disorders in general but a specific risk factor for frozen shoulder in females.

Little progress has been made towards understanding the actual trigger for the development of idiopathic frozen shoulder and the path to recovery since the 1940s–1950s. In the 1940s, Neviaser [12] undertook a study with the hope that through surgical exploration of the shoulder joint the pathology of frozen shoulder could be revealed. In the 10 frozen shoulder cases, operated on from 1940 to 1943, changes were demonstrated in either the capsule or the bursa or both. The microscopic sections showed a nearly consistent pathological picture of reparative inflammatory changes, such as degeneration, vascular repair, cuffing of the blood vessels, and mononuclear cells to a lower or greater degree. According to Neviaser [12], microscopic sections confirmed the presence of reparative inflammatory changes in the capsule.

Lundberg [13] compared biopsies from 14 frozen shoulders with biopsies from 13 shoulders that were operated on because of recurrent shoulder dislocations. In sections from joint capsules of frozen shoulders, the fibrous tissue appeared more compact or dense, there were more cells (mostly fibroblasts) and increased vascularity in some of the cases. However, the synovial lining was largely unchanged except for the fact that in the frozen shoulders capillaries were observed more often.

Our understanding of idiopathic frozen shoulder is further complicated by the observation that diabetics with frozen shoulder behave clinically differently than non-diabetics [14]. The time course of frozen shoulder in diabetics is much longer and they are more resistant to treatment. This observation supports the concept that there may not be a common pathway for all idiopathic frozen shoulders.

Clinicians should be aware of the association of diabetes and thyroid disorders with idiopathic frozen shoulder. A history of diabetes or thyroid disorders is a red flag in patients with atraumatic shoulder pain. Such patients must be carefully examined to determine if they are not in one of the three phases of idiopathic frozen shoulder.

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