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Original Article

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Diabetes mellitus affects the prognosis of frozen shoulder

Per Hviid Gundtoft¹, Mikkel Lindegaard Attrup^{3, 4}, Anne Krog Kristensen², Jette Wessel Vobbe², Lilli Sørensen² & Per Hölmich^{3, 4}

1) Orthopaedic Department, Kolding Hospital, 2) Orthopaedic Department, Vejle Hospital, 3) Sports Orthopaedic Research Centre-Copenhagen (SORC-C), 4) Department of Orthopaedic Surgery, Amager-Hvidovre Hospital, Denmark

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ABSTRACT

INTRODUCTION: The aim of this study was to establish whether diabetes mellitus (DM) affects the prognosis for patients with a frozen shoulder.

METHODS: In this prospective two-year follow-up study, we included 235 patients with newly diagnosed unilateral frozen shoulder. Among the 235 patients, 34 (14%) were diagnosed with DM prior to their inclusion in the study. Patients were asked to fill out a questionnaire at the time of diagnosis and at six-, 12- and 24-month follow-ups. The questionnaire included the Oxford Shoulder Score (OSS) and a visual analogue scale (VAS) for both maximum and average daily pain. DM status was recorded for all patients and glycated haemoglobin was measured for patients not diagnosed with DM.

RESULTS: Overall, patients with and without DM had a similar OSS ($p = 0.22$) and VAS score for maximum ($p = 0.46$) and average ($p = 0.46$) daily pain at the time of diagnosis compared with patients without DM. Both groups improved their OSS and VAS score, but patients with DM had a poorer OSS at the six-month ($p = 0.04$) and 24-month follow-ups ($p = 0.02$); poorer VAS scores for maximum daily pain at the six-month ($p = 0.04$), 12-month ($p = 0.03$) and 24-month follow-ups ($p = 0.03$); and poorer VAS scores for average daily pain at the six-month ($p = 0.02$) and 12-month follow-ups ($p = 0.01$).

CONCLUSIONS: This study shows that patients with frozen shoulder may expect a gradual improvement of both pain and movement during a two-year follow-up, but also that having DM is associated with a poorer prognosis.

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TRIAL REGISTRATION: NCT01978886.

Frozen shoulder), also known as adhesive capsulitis, is a condition characterised by pain and stiffness of the shoulder [1]. It most commonly affects women aged between 40 and 60 years [1]. The course of the disease has been described as comprising three phases: 1: “Freezing” with pain and progressive stiffness, 2: “Frozen”: with decreasing pain but remaining stiffness and 3: “Recovery” with an absence of pain and gradual improvement of stiffness [2]. Whether patients may expect a full recovery or if some residual pain and stiffness may remain has been the subject of some debate [3-5].

The pathogenesis of frozen shoulder is poorly understood [6], but the disease has been associated with several conditions, one of which is diabetes mellitus (DM) [7]. Patients with DM are often described as having an aggravated disease course [5, 7-10], rationalised by the theory that DM is a chronic inflammatory condition [11] with excessive glucose concentration causing an increase in collagen cross-linking and stabilisation of connective tissue [12]. However, whether patients with DM have a more severe course in the long term has not

previously been studied, and recent studies have not confirmed this association [13].

The hypothesis of this study is that patients diagnosed with frozen shoulder and DM have a more severe and painful disease course than patients without DM.

METHODS

In this multicentre cohort study, we prospectively and consecutively included patients who were newly diagnosed with frozen shoulder at one of three participating orthopaedic departments. The inclusion period began on 26 March 2014 and concluded on 25 November 2015.

All authors agreed on the following definition of frozen shoulder:

A slow progression of shoulder pain and stiffness, with no other explanation than frozen shoulder.

Restricted passive and active movement of the shoulder, especially in external rotation and abduction, and often not pain-related.

X-rays, ultrasound scans and magnetic resonance imaging were performed routinely at the three participating departments as part of diagnosing the shoulder problem, but none of these tests formed part of the inclusion criteria.

The exclusion criteria were: age under 25 or above 75 years; inability to read, speak, and/or understand Danish; non-Danish citizens; mental illness, substance abuse problems, or dementia, bilateral frozen shoulder and other shoulder diseases in the affected shoulder.

All patients who had not already been diagnosed with DM were invited to be tested with the glycated haemoglobin (HbA_{1c}) blood test. If HbA_{1c} was above 6.5%, the patient was classified as having DM, in accordance with international guidelines [14].

Patients were asked to fill out a questionnaire on the day of their diagnosis, and a more extensive questionnaire was sent to them by mail or e-mail at six, 12 and 24 months following their diagnosis.

The questionnaire used at inclusion comprised the validated Danish version of the Oxford Shoulder Score (OSS) [15] and the visual analogue scale for pain (VAS pain) for both maximum and average daily pain. For the OSS, patients answered 12 questions regarding function and pain using a five-point scale. The points from the 12 questions are added to form a total score ranging from 12 (best) to 60 (worst). At six, 12 and 24 months, patients received a questionnaire with the same 12 questions and additional questions about whether the pain and stiffness had improved since the last time they answered the questionnaire. Patients were asked if any arthroscopic surgery for the frozen shoulder had been performed and if any injections with corticosteroids had been given (and how many) since the previous questionnaire.

The study was approved by the Danish Data Protection Agency, project-id: 13/28396, and by the Regional Committee on Health Research Ethics, project-id: S-20130006. The study was reported to clinicaltrials.org, project-id: NCT01978886.

Statistical analysis

The differences in OSS between patients with and without DM at zero, six, 12 and 24 months were analysed using linear regression adjusting for age and sex. The assumption of same and normal distribution was checked by diagnostic plots of residuals and was not violated. The difference in VAS pain for both average and maximum daily pain was analysed with Student's T-test. Q-Q plot was used to test the assumption of normality, which was not violated.

Since the patients were also included in a parallel study [16] and post hoc power sample calculation is not recommended, no power sample calculation was done for this study.

The Procordo ApS software was used for data management, and STATA 14.0 statistics were used to perform all statistical analyses.

Trial registration: NCT01978886.

RESULTS

The study included 235 patients. DM was diagnosed in 34 (14%) of the patients (20 Type 2 and 14 Type 1). In the group of patients not previously diagnosed with DM, 61% agreed to be tested with the HbA_{1c} test. None of the patients tested had an elevated HbA_{1c}.

The groups of patients with DM more often had other diseases in their contralateral shoulder ($p = 0.02$), had a higher prevalence of Dupuytren's contracture ($p = 0.04$) and hypercholesterolaemia ($p = 0.04$) and had a higher BMI ($p = 0.01$) (see **Table 1**).

TABLE 1 / Patients characteristic for patients with and without diabetes mellitus.

	Total (N = 235)	Patients with DM (n = 34)	Patients without DM (n = 201)	p-value
Age, mean (95% CI), yrs	52.7 (51.5-53.9)	53.7 (50.9-56.5)	52.5 (51.1-53.8)	0.49
Female sex, %	52	54	51	0.86
Frozen shoulder in dominant arm, %	41	35	42	0.53
Frozen shoulder following surgery, %	11	11	11	1.00
Frozen shoulder following trauma, %	21	18	21	0.67
Hyperthyroidism, %	6	3	6	0.29
Other disease in contralateral shoulder, %	8	20	6	0.02
<i>Previously diagnosed with frozen shoulder, %</i>	15	14	16	1.00
In the same shoulder	15	14	16	
In the contralateral shoulder	85	86	84	
Smoker, %	23	29	21	0.47
BMI, mean (95% CI), kg/m ²	25.9 (25.3-26.5)	27.8 (26.2-29.4)	25.6 (25-26.2)	0.01
Dupuytren's contracture, %	4	12	3	0.04
Hypercholesterolaemia, %	23	53	17	< 0.001
Absent from work due to frozen shoulder, %	25	18	26	0.08

CI = confidence interval; DM = diabetes mellitus.

The OSS was similar at the time of diagnosis for patients with and without DM: difference 1.6 ($p = 0.31$), but

patients with DM reported significantly poorer scores at six months: difference 3.9 points ($p = 0.04$) and 24 months: difference 3.8 points ($p = 0.03$) (see **Figure 1**). The VAS pain for both maximum and average daily pain followed a similar pattern with worse pain in the DM group (see **Figure 2** and **Figure 3**). When asked specifically, most patients reported that they had experienced an improvement in their range of motion since the first six months (71%), between six and 12 months (72%) and between 12 and 24 months (66%).

FIGURE 1 / Oxford Shoulder Score for patients with (-) and without (-) diabetes mellitus. Mean value and 95% confidence intervals.

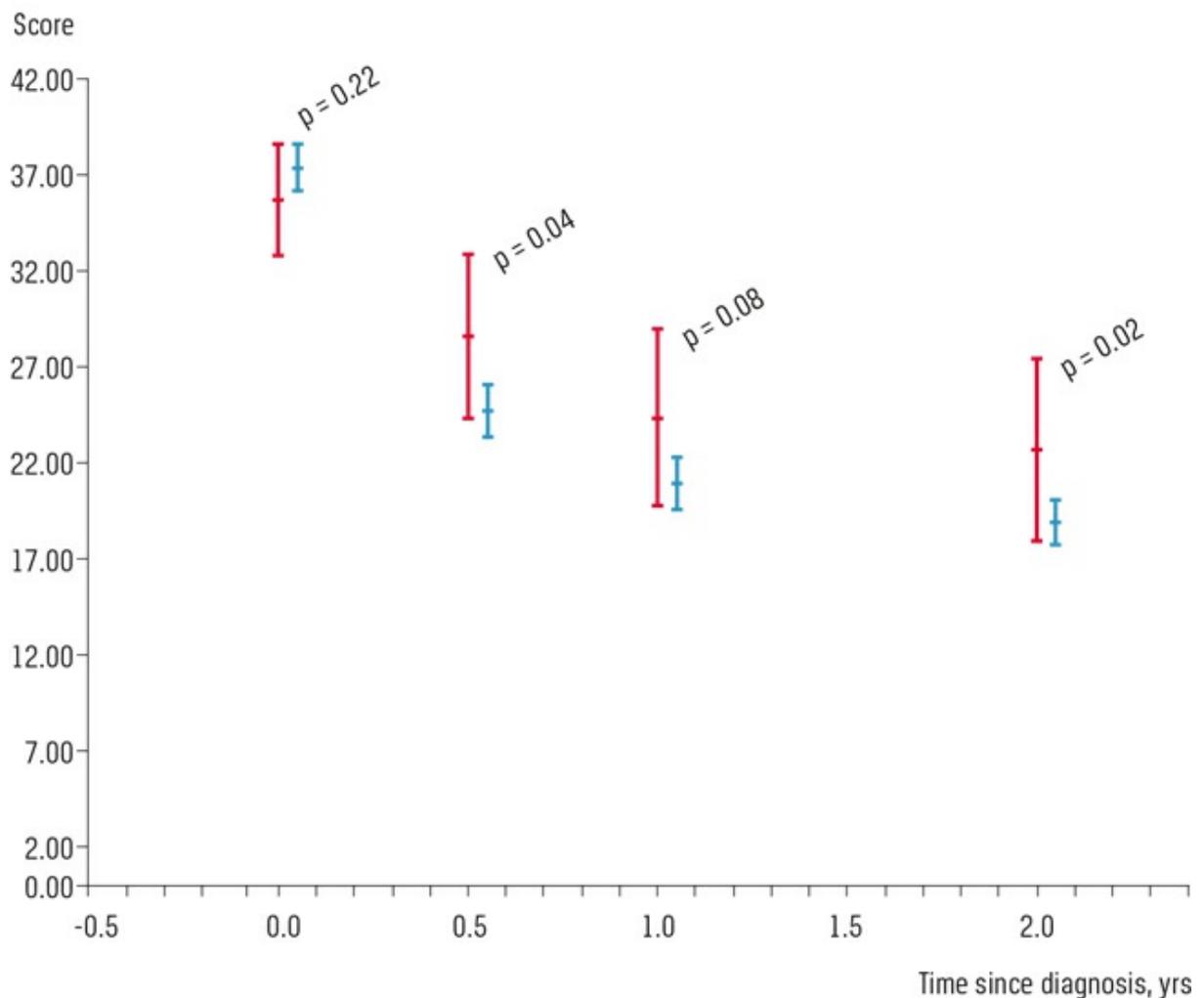


FIGURE 2 / Average visual analogue score of pain for patients with (-) and without (-) diabetes mellitus. Mean value and 95% confidence intervals.

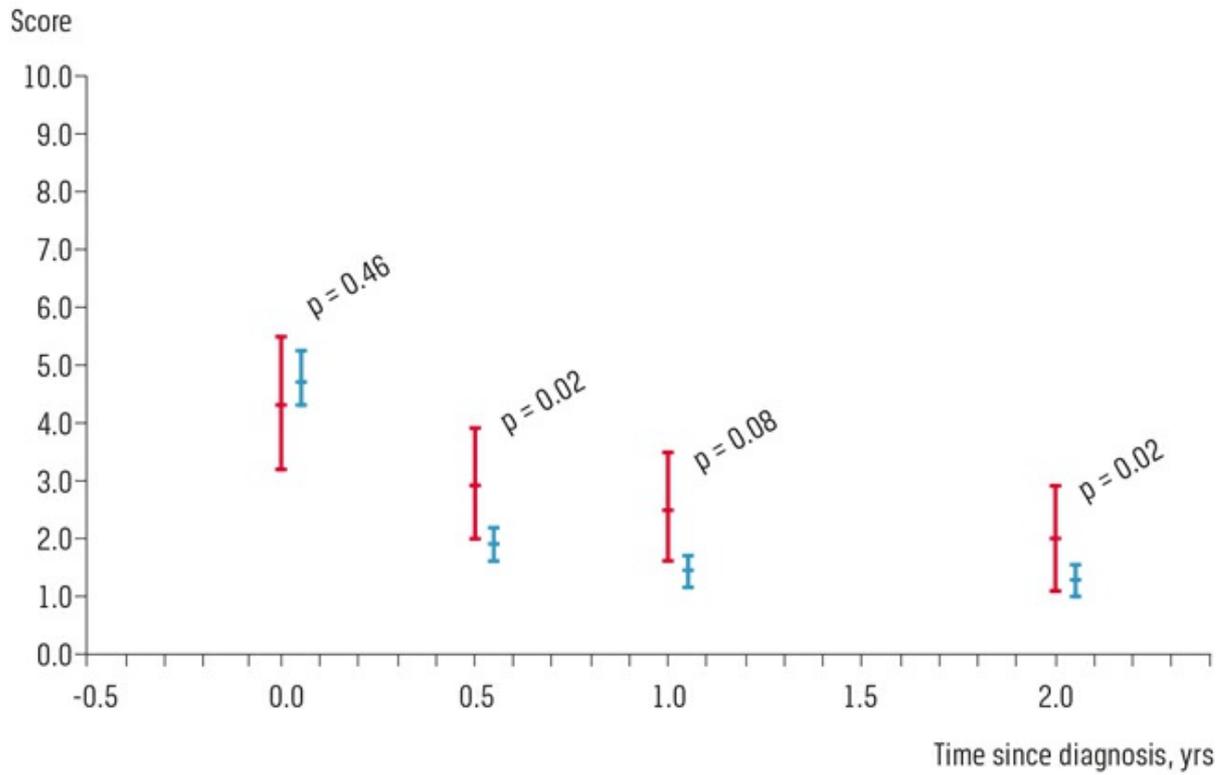
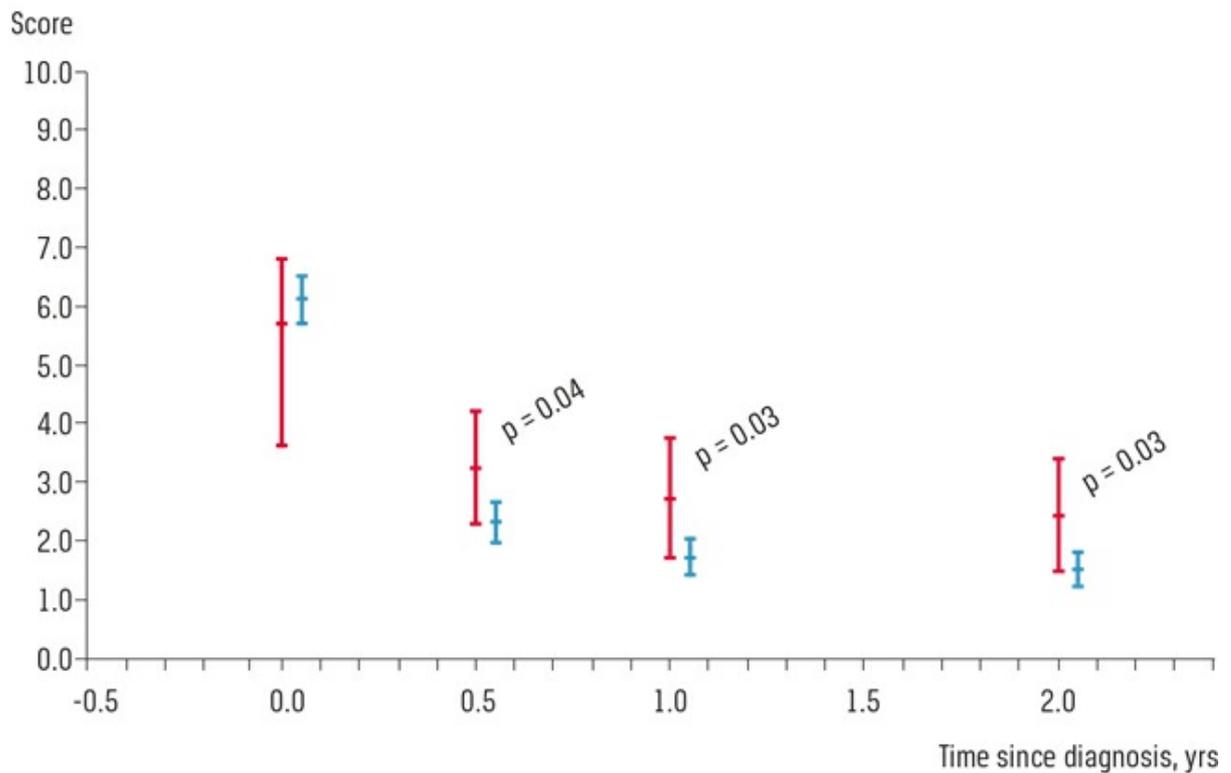


FIGURE 3 / Maximum visual analogue score of pain for patients with (-) and without (-) diabetes mellitus. Mean value and 95% confidence intervals.



More patients with DM had an arthroscopic release of their frozen shoulder during the first six months: four patients with DM and six patients without DM ($p = 0.03$); and for the entire follow-up period: five patients with DM and 11 patients without DM ($p < 0.05$).

Most patients were treated with at least one intra-articular corticosteroid injection (80%). The number of injections varied from none to 11 during the two-year period with no difference between the groups ($p = 0.97$).

DISCUSSION

Of the 235 patients in this two-year follow-up study, 34 patients (14%) were diagnosed with DM. Patients with DM reported significantly less improvement in OSS and VAS scores during the follow-up period, and they were more frequently treated by arthroscopic release.

Patients in this study were also included in a previously published study on the prevalence of undiagnosed DM in patients with frozen shoulder [17].

The OSS was similar for both groups at the time of diagnosis, but it was poorer for patients with DM during the two-year period: This correlates well with improvements of VAS pain for both average and maximum daily pain during the follow-up period (see Figure 1, Figure 2 & Figure 3). In both categories, the largest improvement occurred during the first six months following the diagnosis of frozen shoulder.

The more limited improvement in OSS and VAS for patients with DM might explain why more of these patients were treated by arthroscopic release. Barbosa et al showed similar results in their study of 210 patients, where

patients with DM more often failed the initial treatment (injection therapy and physiotherapy) and underwent arthroscopic release [17]. Unfortunately, we do not have data on the indication for arthroscopic release for the patients, and it is therefore impossible to establish whether it was performed due to stiffness or pain.

Although patients with DM are often described as having a poorer prognosis [5, 7-10] than non-DM patients, this has not been shown in any previous studies. The largest study to date is by Hand et al [13], who – contrary to our study – found no statistically significant difference between patients with and without DM. However, the mean follow-up time of 4.4 years in the study by Hand et al might explain this, as most patients recover within one to three years [1, 18]. Therefore, any difference during the first six to 12 months might have receded at the 4.4-year follow-up. In the longer term, i.e., at the two-year follow-up in our study, we found results comparable to those of Hand et al [13], i.e. that most patients will have an OSS equivalent to a comparable population without shoulder problems [19].

One limitation of our study is that only 61% of the patients who had not previously been diagnosed with DM agreed to be tested with HbA_{1c}. The prevalence of undiagnosed DM in shoulder patients is generally low [20], but several patients in the non-DM group might have been misclassified. The consequence of this misclassification could be underestimation of the difference between the groups. The prognosis for patients with DM might therefore be even poorer than indicated by our study. A second limitation is that we did not collect information about how these patients' frozen shoulder was treated initially. It seems rather unlikely that patients with DM would receive a different treatment for their frozen shoulder, but as we have no data about their treatment, we cannot rule out this possibility. A third limitation is the different proportions of arthroscopic release between the two groups. As arthroscopic release often improves patients' symptoms, we probably underestimated the difference between the two groups. Excluding patients with arthroscopic release from the study would cause selection bias, so we abstained from doing so. Finally, although we intended to collect information about the patients who were excluded from the study, we failed to do so. Therefore, we cannot account for the patients not included in the study, who might differ in a number of ways from the patients who were included.

CONCLUSIONS

This study shows that patients with frozen shoulder can expect gradual improvement of both pain and movement during a two-year follow-up, but having DM is associated with a poorer prognosis.

CORRESPONDENCE: *Per Hviid Gundtoft*. E-mail: per.hviid.gundtoft@rsyd.dk

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CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at Ugeskriftet.dk/dmj

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