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ORIGINAL RESEARCH

Very High Prevalence of Frozen Shoulder in Patients With Type 1 Diabetes of ≥45 Years' Duration: The Dialong Shoulder Study

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Abstract

Objectives: To compare the prevalence of shoulder disorders and self-reported shoulder disability in patients with long-term type 1 diabetes mellitus and diabetes-free subjects; and to explore the association between the long-term glycemic burden and shoulder disability in the diabetes group.

Design: Cross-sectional study of shoulder diagnoses with 30 years' historical data on glycemic burden in patients with diabetes.

Setting: Diabetics center and a university hospital.

Participants: Subjects attending the Norwegian Diabetics Center in 2015 with type 1 diabetes since 1970 or earlier were eligible (N = 136). One hundred and five patients were included, and 102 (50% women; mean age, 61.9y) completed the study together with 73 diabetes-free subjects (55% women; mean age, 62.5y).

Interventions: Not applicable.

Main Outcome Measure: Shoulder diagnoses decided through clinical examination according to scientific diagnostic criteria.

Results: Frozen shoulder was diagnosed in 60 (59%) patients with diabetes and 0 diabetes-free subjects, with a lifetime prevalence of 76% in the diabetes group versus 14% in the diabetes-free subjects. Patients with diabetes had higher disability and higher mean QuickDASH scores (23.0±19.9) than diabetes-free subjects (8.9±12.0), with a mean difference of −14.2 (95% confidence interval, −19.3 to −9.0) points ($P<.001$). We found an association between chronic hyperglycemia and QuickDASH scores, with a 6.16-point increase in QuickDASH scores per unit increase in glycated hemoglobin A_{1c} (HbA_{1c}) ($P=.014$).

Conclusions: The point prevalence of frozen shoulder in patients with long-lasting type 1 diabetes was 59%, and the lifetime prevalence was 76%. The diabetes group had more shoulder disability than diabetes-free subjects. The historical HbA_{1c} level was associated with increased shoulder disability.

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Type 1 diabetes mellitus has been associated with severe disability or early death because of vascular complications. With improvements in blood glucose control, many patients now have a normative life expectancy, and an increasing number of patients live with type 1 diabetes for >50 years. The prevalence of musculoskeletal problems in people with diabetes is usually reported in mixed populations, mostly focusing on frozen shoulder (adhesive capsulitis) in patients with type 2 diabetes.[1-3] A strong relation between frozen shoulder and type 1 diabetes has been shown.[4] The reason for this is unknown, but the duration of hyperglycemia is thought to be one of the major risk factors for complications in diabetes. Glucose may react with long-lived proteins (eg, collagen) in connective tissues to form advanced glycation end-products (AGEs) that have cross-linking properties.[5] This may increase the risk of vascular complications, and possibly, of nonvascular complications, including frozen shoulder.[6]

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The prevalence of frozen shoulder in diabetes is reported to vary in the range of 7% to 31%.[2,7,8] Arkkila et al[7] studied 291 patients who had had type 1 diabetes for a mean of 29 years and found a 10.3% prevalence of frozen shoulder, which was significantly associated with age and duration of diabetes. In that study, frozen shoulder was defined as the documentation in the patient record of pain for at least 1 month and restriction of active and passive shoulder joint movements in 3 planes. No shoulder examinations were performed. Larkin et al[8] studied 1217 patients who had type 1 diabetes for a mean of 31.1 years and reported a 31% prevalence of frozen shoulder. In that study, the diagnosis was based on asking patients whether they were ever told they had frozen shoulder. Shoulder flexion was measured, but the procedure was not described, and the diagnostic criteria used were not stated. Both studies had methodologic limitations because the estimation of lifetime prevalence was based on patient history. We did not find any studies reporting the prevalence of shoulder diagnoses in long-term type 1 diabetes that were based on strict clinical diagnostic criteria.

We conducted a cross-sectional, controlled, retrospective study including patients who had type 1 diabetes for ≥45 years and a diabetes-free group. The aim was to compare the diagnoses of shoulder disorders, shoulder range of motion, and self-reported shoulder disability and pain in the 2 groups. We also explored the association between long-term glycemic burden and shoulder disability in the diabetes group.

Methods

Participants

Inclusion criteria

All patients who attended the Norwegian Diabetics Center in Oslo, Norway, in 2015 and who had type 1 diabetes since 1970 or earlier were eligible.

Exclusion criteria

Patients not able to cooperate with the clinical examination because of recent trauma or severe cerebrovascular disease were excluded.

Diabetes-free subjects

Enrolled patients were asked to bring their spouses or close friends to act as controls for the study. The subjects were required to be free of diabetes as confirmed by a current glycated hemoglobin A_{1c} (HbA_{1c}) <48mmol/mol (6.5%). First-degree relatives were excluded.

Written, informed consent was obtained from all subjects willing to take part in the study.

Ethics

The study received approval from the Regional Committee for Medical and Health Research Ethics South-East, Norway (project no 2014/851).

List of abbreviations:

AGE	**advanced glycation end-product**
CI	**confidence interval**
DASH	**Disabilities of Arm, Shoulder and Hand**
HbA_{1c}	**glycated hemoglobin A_{1c}**

Data collection

Descriptive data were collected via questionnaires, interviews, and Norwegian Diabetics Center medical records. A shoulder-specific questionnaire was completed by participants, and a standardized clinical examination was conducted by 1 experienced medical doctor blinded to group affiliation. All participants underwent shoulder radiographs and blood sampling. For calculation of the glycemic index, historical HbA_{1c} data were collected from patient files at the Norwegian Diabetics Center and from patient primary care files.

Shoulder outcomes

Primary outcome

The primary outcome was the prevalence of diagnoses of shoulder disorders. We used a diagnostic routine modified from the Southampton examination schedule[9] to identify the point prevalence (appendix 1).[10,11] Most shoulder diagnoses are based on clinical tests with reported intrarater reliabilities between .63 and .94.[12,13] To determine the presence of frozen shoulder, our measurements of range of motion were compared to the normative values from Muir et al[12]: active flexion, active external rotation and passive external rotation and from Macedo and Magee[14]: passive abduction. Passive external rotation and at least one of active flexion or passive abduction had to be reduced two standard deviations or more to give the diagnosis. A normal shoulder radiograph was also required. Frozen shoulder typically has 3 phases. In phase 1 (2−9mo), the shoulder becomes increasingly painful and stiff. This phase is very bothersome, and the diagnosis is usually linked with pain. In phase 2 (4−12mo), the pain gradually disappears, but the stiffness remains. In phase 3, the stiffness gradually resolves, and movement typically normalizes within 12 to 42 months.[15] A stiff shoulder without pain is therefore categorized as a phase 3 frozen shoulder. Most patients regain normative range of motion without pain within these time limits, but up to 6% experience severe symptoms that last >4 years.[16] There is a gradual transition between the phases, and some patients never become pain free.[16]

A stiff shoulder with pain in active abduction was regarded as phase 1 or phase 2 frozen shoulder. Otherwise, shoulder stiffness was classified as phase 3 frozen shoulder. All participants had standard radiographs taken of both shoulders, and the films were evaluated by an unbiased radiologist blinded for group affiliation. Subjects with radiologic glenohumeral osteoarthrosis and shoulder pain had the diagnosis of osteoarthrosis.

All participants were asked whether they had ever been diagnosed with frozen shoulder and, if so, in which year the disease started. For the patients with diabetes, the records at the Norwegian Diabetics Center were also reviewed, and any documented diagnosis of frozen shoulder was included. The participants who had a previous diagnosis of frozen shoulder but whose examination in 2015 was normative were included in the calculation of lifetime prevalence. The duration of frozen shoulder was calculated for those participants who still had the disorder at examination in 2015.

Secondary outcomes

The Disabilities of the Arm, Shoulder and Hand (DASH) is a region-specific, patient-reported outcome measure.[17] It covers many aspects of shoulder functioning.[18] The short form, Quick-DASH, consists of 11 questions regarding symptoms and degree

of disability of the upper limb. All items are scored on a 5-point ordinal scale from no difficulty to unable. The total score ranges from 0 (best) to 100 (worst). Both versions have been translated[19] and validated for use in the Norwegian population.[20] Normative age-specific data are available.[21]

Shoulder range of motion sitting or standing was measured with a manual goniometer as active flexion and external rotation and passive abduction and external rotation. Normative values for range of motion[12,14,22] are given in table 1. The protocol is given in appendix 2.

Shoulder muscle strength was measured using a handheld dynamometer for external rotation and abduction with the patients standing (see appendix 2).

Glycemic index

HbA_{1c} was measured in 2015 (current HbA_{1c}) at the Oslo University Hospital, Ullevaal, Norway, by high-performance liquid chromatography (Variant[a]), with a reference range of 20 to 42mmol/mol (4.0%−6.0%±2%) and an intra-assay coefficient of variation of <3%. All HbA_{1c} measurements are reported in International Federation of Clinical Chemistry units (mmol/mol) and National Glycohemoglobin Standardization Program Units (%). The 30-year HbA_{1c} was defined as the mean of all HbA_{1c} measurements for the individual during the years 1980 to 2015, whereas the estimated full-duration HbA_{1c} also incorporated the unknown mean HbA_{1c} from diagnosis to the first measurement by extrapolating from the mean of the first 3 years of measurement (appendix 3). To determine whether the patients with diabetes attending the Norwegian Diabetics Center were representative of the Norwegian population, we compared our measurements with those in the national Norwegian Diabetes Register for Adults.[23]

Demographic factors

Educational level was reported in 5 categories ranging from primary school to college/university and dichotomized into low (upper secondary school) versus high education level (college/university). Smoking was reported in 3 categories: current smokers, past smokers, and never smoked. Height and weight were measured in light clothing without shoes. Body mass index was calculated (kg/m^2), and waist circumference was measured (cm). The patients' files were checked for mention of rheumatic disease.

Statistical methods

Baseline characteristics are presented as means with SDs, medians with ranges, or proportions. Between-group differences in the measures of range of motion, isometric muscle strength, and QuickDASH scores were calculated using Student *t* test. The chi-square test or Fisher exact test for contingency tables were applied to detect associations between categorical independent

Table 1 Point prevalence of diagnosed shoulder disorders, shoulder disability, range of motion and strength

Variable	Diabetes-Free Group	Diabetes Group	Group Difference (95% CI)	*P*
Diagnosis				
Frozen shoulder, phases 1−3	0 (0)	60 (58.8)		<.001
Frozen shoulder, phases 1−2*	0 (0)	19 (18.6)		<.001
Frozen shoulder, phase 3†	0 (0)	41 (40.2)		<.001
Any diagnosis except frozen shoulder	15 (20.6)	17 (16.7)		ns
Subacromial pain	5 (6.9)	5 (4.9)		ns
Rotator cuff tear	2 (2.8)	1 (1.0)		ns
Glenohumeral osteoarthritis	2 (2.8)	5 (4.9)		ns
Acromioclavicular osteoarthritis	2 (2.8)	1 (1.0)		ns
Other	4 (5.6)	5 (4.9)		ns
No diagnosis	58 (79.5)	26 (25.5)		<.001
Disability				
QuickDASH‡	8.9±12.0	23.0±19.9	−14.2 (−19.3 to −9.0)	<.001
QuickDASH, women	10.9±12.9	31.0±21.0	−20.1 (−27.7 to −12.6)	<.001
QuickDASH, men	6.5±10.6	15.1±15.0	−8.6 (−14.6 to −2.6)	.005
Range of motion, normative value degrees (2SD)				
Active flexion, 160 (20)	166±10	151±16	15 (11 to 19)	<.001
Active external rotation, 55 (32)	49±13	27±14	22 (18 to 26)	<.001
Passive external rotation, 68 (32)	44±14	23±13	22 (18 to 26)	<.001
Passive abduction, 85 (38)	86±9	71±12	16 (12 to 19)	<.001
Hand behind back, cm§	20±6	30±10	10 (7 to 12)	<.001
Muscle strength				
Muscle strength external rotation, N	93 (27)	88 (24)	5.4 (2.3 to 13.1)	.166
Muscle strength abduction, N	88 (31)	86 (29)	2.6 (6.5 to 11.3)	.577

NOTE. Values are n (%), mean ± SD, or as otherwise indicated.
Abbreviation: ns, not significant difference.
* Includes persons with 1 painful and 1 stiff shoulder.
† One or 2 stiff shoulders.
‡ Sum score out of 100 (100 worst possible).
§ Centimeters ± SD from the C7 spinous process.

variables. Pearson correlation was used to explore the association between long-term HbA_{1c}, QuickDASH score, and shoulder range of motion. Univariable and multivariable linear regression analysis was performed to study the associations between measures of glycemic burden and QuickDASH scores. The crude and adjusted (for age, sex, smoking, and body mass index) results are presented as regression coefficients (β) with 95% confidence intervals (CIs) and *P* values. We used IBM SPSS version 23 software.[b]

Results

One hundred and thirty-six patients who had had type 1 diabetes for ≥45 years were registered at the Norwegian Diabetics Center in 2015. All patients were asked to participate in the study, and 105 accepted. Three did not attend the examination because of illness; therefore, 102 patients (77%; mean age, 61.9y; range, 49−77y) were examined in 2015 together with 73 diabetes-free subjects (mean age, 62.5y; range, 50−81y). The mean duration of diabetes was 50.6 years (range, 45−67y). Demographic data are presented in table 2.

Seventy-six (75.5%) patients in the diabetes group and 15 (20.6%) persons in the diabetes-free group had a diagnosis of shoulder disorder. Sixty (58.8%) patients in the diabetes group had frozen shoulder versus none in the diabetes-free group. Of these, 18 had only 1 affected shoulder, whereas 42 (70%) were bilaterally affected, including 6 with 2 painful shoulders, 11 with 1 painful and 1 nonpainful shoulder, and 25 with 2 stiff, nonpainful shoulders. Diagnoses of other shoulder disorders were rare and did not differ significantly between the groups (see table 1).

Sixty-three (61.8%) patients in the diabetes group said they had previously been given a diagnosis of frozen shoulder. Seventeen of these had no symptoms or signs of frozen shoulder at our examination. Adding these 17 to the 60 people we diagnosed gave a total of 77 patients with frozen shoulder in the diabetic group, with a lifetime prevalence of 75.5%. In the diabetes-free group, 10 persons stated they had been previously diagnosed with frozen shoulder, giving a lifetime prevalence of 13.7%. Forty of the patients with diabetes currently diagnosed with frozen shoulder remembered the year of its onset. The duration of frozen shoulder in this group was 13.6±9.3 years.

Patients with diabetes had higher QuickDASH scores (23.0±19.9) than the diabetes-free subjects (8.9±12.0), with a mean difference of −14.2 (95% CI, −19.3 to −9.0) points (*P*<.001). Women in the diabetes group had significantly higher scores (31.0±21.2) than the women in the diabetes-free group (10.9±12.9, *P*<.001), and compared with men in the diabetes group (15.1±15.0, *P*<.001).

The subgroup diagnosed with painful frozen shoulder (phases 1−2) had the highest QuickDASH score (40.3±15.5), with a mean difference of −20.7 points (95% CI, −31.3 to −10.1; *P*<.001) compared with patients without shoulder stiffness. The difference was −22.5 points (95% CI, −37.7 to −7.3; *P*=.005) for women and −18.5 points (95% CI, −32.1 to −4.9; *P*=.010) for men in this subgroup. We found no significant differences in QuickDASH scores between the groups with stiff shoulders without pain (see table 3).

There were significant differences between the diabetes and diabetes-free groups for all measurements of shoulder range of motion, and the patients with diabetes with painful frozen shoulder had the highest level of stiffness. Muscle strength measured in abduction and external rotation did not differ significantly between the groups (see tables 1 and 3).

The HbA_{1c} mean values were current HbA_{1c}: 58mmol/mol (7.4%±0.79%), 30-year HbA1c: 62mmol/mol (7.9%±0.75%), and estimated full-duration HbA_{1c}: 63mmol/mol (8.0%±0.79%). Patients with diabetes and painful frozen shoulder had a current HbA_{1c} of 59mmol/mol (7.6%±0.86%), a 30-year HbA_{1c} of 66mmol/mol (8.2%±0.70%), and an estimated full-duration HbA_{1c} of 68mmol/mol (8.3%±0.79%), representing a significant difference from patients with diabetes and without frozen shoulder (table 4). The reported mean HbA_{1c} in 2015 in the Norwegian Diabetes Register of patients with diabetes duration of ≥45 years was 7.6% compared with our figure for current HbA_{1c} of 7.4% (*P*=.078).

The correlation coefficients between the results of the hand-behind-back test and current HbA1c, 30-year HbA_{1c}, and estimated full-duration HbA_{1c} were *r*=.35, *r*=.45, and *r*=.47 (*P*<.001), respectively. The correlation between active flexion and

Table 2 Demographic data and comorbidity

Demographic	Diabetes-Free Group (n=73)	Diabetes Group (n=102)	*P*
Age (y), mean ± SD, range	62.5±7.1 (50−81)	61.9±7.1 (49−77)	.554
Females	40 (54.8)	51 (50.0)	.544
Duration of diabetes (y), median, mean (range)		49, 50.6 (45−67)	
HbA_{1c}, mmol/mol	5.48±0.28	7.44±0.79	<.001
BMI, kg/m^2	25.8±4.3	26.2±4.0	.559
Waist circumference, cm	90.0±12.7	91.7±13.0	.402
Smoking			
Current smokers	6 (8.2)	4 (3.9)	.536
Past smokers	28 (38.4)	39 (38.2)	
Never smoked	39 (53.4)	58 (56.9)	
Education level (high)	54 (74.0)	63 (61.8)	.091
Comorbidity			
Rheumatoid arthritis	0 (0)	1 (1.0)	.399
Polyosteoarthritis	5 (6.8)	3 (2.9)	.214
Psoriasis arthritis	4 (5.5)	0 (0)	.038

NOTE. Values are n (%), mean ± SD, or as otherwise indicated.
Abbreviation: BMI, body mass index.

Table 3 QuickDASH scores, range of motion and maximal isometric muscle strength for the subgroups of patients with diabetes with frozen shoulder

Disability, Mobility, and Strength	Frozen Shoulder, Phases 1–3	Frozen Shoulder, Phases 1–2	Frozen Shoulder, Phase 3	No Frozen Shoulder	Mean Difference (95% CI)	*P*
Shoulder disability						
QuickDASH, all subjects with diabetes*	25.4±19.2			19.6±20.5	−5.7 (−13.6 to 2.2)	.152
		40.3±15.5		19.6±20.5	−20.7 (−31.3 to −10.1)	<.001
			18.5±16.8	19.6±20.5	1.2 (−7.0 to 9.4)	.774
QuickDASH, women	38.3±16.1			23.4±23.1	−14.9 (−26.1 to −3.8)	.010
		45.9±13.3		23.4±23.1	−22.5 (−37.7 to −7.3)	.005
			32.7±16.1	23.4±23.1	−9.4 (−23.1 to 4.4)	.175
QuickDASH, men	15.5±15.2			14.2±15.1	−1.3 (−10.4 to 7.7)	.768
		32.7±15.7		14.2±15.1	−18.5 (−32.1 to −4.9)	.010
			10.2±10.6	14.2±15.1	3.9 (−4.0 to 11.9)	.319
Shoulder mobility and strength						
Active flexion, deg.	147±15	140±17	148±15	158±16		.002†
Active external rotation, deg.	22±12	19±10	22±12	34±14		<.001†
Passive external rotation, deg.	18±10	19±10	17±10	30±13		<.001†
Passive abduction, deg.	66±11	62±11	66±11	78±9		<.001†
Hand behind back, cm‡	33±9	36±10	32±8	26±11		<.001†
Muscle strength external rotation, N§	89.0±25.8	78.6±24.5	89.6±24.9	85.4±20.5		.166†
Muscle strength abduction, N§	87.4±32.1	74.1±30.1	89.2±31.2	82.9±23.9		.577†

NOTE. Values are mean ± SD or as otherwise indicated.

* Sum score out of 100 (where 100 is worst possible).

† *P* value between all patients with frozen shoulder and those without frozen shoulder.

‡ Centimeters ± SD from the C7 spinous process.

§ One kilogram = 9.8N.

30-year HbA_{1c} and estimated full-duration HbA_{1c} were $r = .28$ and $r = .30$ ($P = .004$), respectively.

In the diabetes group, the univariable linear regression analysis showed a significant crude (unadjusted β) association between QuickDASH score and all measures of glycemic burden: current HbA_{1c} (unadjusted β = 5.10; 95% CI, 0.21–10.0; $P = .041$), 30-year HbA_{1c} (unadjusted β = 8.05; 95% CI, 3.01–13.1; $P = .002$), and estimated full-duration HbA_{1c} (unadjusted β = 8.15; 95% CI, 3.45–12.9; $P = .001$). The values after adjustment (adjusted β) for the effects of age, sex, body mass index, education, and smoking were for current HbA_{1c} (adjusted β = 3.06; 95% CI, −1.63 to 7.75; $P = .200$), 30-year HbA_{1c} (adjusted β = 5.50; 95% CI, 0.33–10.67; $P = .037$), and estimated full-duration HbA_{1c} (adjusted β = 6.16; 95% CI, 1.26–11.05; $P = .014$). For each increase of 1 unit in the estimated full-duration HbA_{1c}, the QuickDASH score increased by 6.16 points.

Discussion

In this study, the high current and lifetime prevalence of diagnosed shoulder disorders in patients with type 1 diabetes of 50 years' duration is attributable to the high prevalence of frozen shoulder. The current prevalence of painful frozen shoulder was 18.6%, which is almost double that found by Arkkila et al[7] in patients who had had type 1 diabetes for an average of 29 years. In addition, 40% of our diabetes patients had pain-free shoulders with a severely reduced range of motion, representing phase 3 frozen shoulder,[16,22] giving a total point prevalence of 58.8%. This is the highest prevalence of frozen shoulder ever reported in patients with diabetes. We found that our participants had a prolonged course (13.6y) of frozen shoulder compared with that reported in a long-term study of a population with only a few patients with diabetes.[16] Our estimate of the lifetime prevalence of frozen shoulder using patient-reported data and data from patient files was 75.5%. Larkin et al[8] also used a self-reported diagnosis of frozen shoulder and found a lifetime prevalence of 31% in patients who had had type 1 diabetes for an average of 31 years. The high point and lifetime prevalence observed in the present study is most likely because of the very long duration of diabetes in the study population and the prolonged duration of frozen shoulder. Increased formation of AGEs could explain an irreversible frozen shoulder in the diabetes group. The patients with painful frozen shoulders had significantly higher long-term HbA_{1c} than the rest of the diabetes group, in contrast with results reported by Arkkila.[7] The reason for this is unknown, but patients with type 1 diabetes have higher levels of circulating AGEs,[24,25] and the formation of AGEs and their cross-linking of collagen have been postulated as a possible mechanism by which patients with diabetes develop stiff joints. Furthermore, the AGE methylglyoxal may evoke pain by stimulating the ion channel transient receptor potential action channel, subfamily A, member 1, which is expressed in nociceptive sensory neurons.[26] This may be the mechanism by which long-term high blood glucose is associated with pain. However, the role of AGEs in shoulder stiffness is unknown and warrants further study.

Shoulder range of motion was significantly decreased in the diabetes group compared with the diabetes-free group for all

Table 4 Glycemic burden in the diabetes group for patients diagnosed with frozen or stiff shoulder

Group		n	Current HbA_{1c}			30-y HbA_{1c}			Estimated Full-Duration HbA_{1c}		
			Mean ± SD	Mean Between-Group Difference (95% CI)	*P*	Mean ± SD	Mean Between-Group Difference (95% CI)	*P*	Mean ± SD	Mean Between-Group Difference (95% CI)	*P*
All patients in the diabetes group		102	58 (7.44±0.79)			62 (7.86±0.75)			63 (7.96±0.79)		
Frozen shoulder, phases 1−2	Yes	19	59 (7.55±0.86)	−0.13 (−0.53 to 0.27)	.518	66 (8.18±0.70)	−0.39 (−0.76 to −0.02)	.039*	68 (8.34±0.79)	−0.46 (−0.85 to −0.07)	.021*
	No	83	58 (7.42±0.78)			62 (7.79±0.74)			63 (7.88±0.77)		
Frozen shoulder, phase 3	Yes	52	58 (7.48±0.75)	−0.09 (−0.40 to 0.23)	.590	62 (7.86±0.67)	−0.02 (−0.28 to 0.31)	.922	64 (7.97±0.68)	−0.02 (−0.33 to 0.30)	.916
	No	50	57 (7.40±0.83)			62 (7.87±0.83)			63 (7.95±0.90)		
Frozen shoulder, phase 1−3	Yes	60	59 (7.54±0.75)	−0.25 (−0.56 to 0.06)	.118	63 (7.93±0.68)	−0.16 (−0.46 to 0.14)	.287	64 (8.04±0.71)	−0.18 (−0.49 to 0.14)	.266
	No	42	56 (7.30±0.83)			61 (7.77±0.84)			62 (7.86±0.90)		

NOTE. All HbA_{1c} measurements are reported in International Federation of Clinical Chemistry units (mmol/mol) and Glycohemoglobin Standardization Program Units (%). The patients are grouped by whether or not they have a diagnosis of frozen shoulder. The mean difference represents the difference between the group of patients with diabetes without frozen shoulder and the patients diagnosed with frozen shoulder phase 1 or 2, frozen shoulder phase 3, or all patients with frozen shoulder.

* Significant difference at the .05 level.

measurements. The mean differences were all >15° with narrow confidence intervals. The observed association between the hand-behind-back test, active flexion, and long-term HbA_{1c} is consistent with the findings by Larkin et al,[8] and suggests that good blood glucose control positively influences shoulder motion.

The patients with diabetes included in this study reported a high mean QuickDASH score (23.0), and the patients with a painful frozen shoulder had the highest mean QuickDASH score of 40.3. This is consistent with earlier high-quality studies in patients without diabetes that reported considerable shoulder-related disability for painful frozen shoulder.[27,28] The patients with phase 3 frozen shoulder reported less disability than patients with painful (phases 1−2) frozen shoulder, indicating that pain is an important factor in shoulder disability.

Women in the diabetes group reported significantly higher disability than men. This sex difference has been reported previously,[8,21,29] but its mechanisms are not known.

Larkin[8] reported a mean DASH score of 16.4 in patients with ≥2 cheiroarthropathies (defined as diagnostic entities of pain or stiffness in the shoulder or hand). They did not report explicit scores for patients with frozen shoulder or for those with shoulder pain. It seems that a long duration of type 1 diabetes can worsen a shoulder disability, and pain is an important determinant of self-perceived shoulder function. The QuickDASH score was significantly associated with long-term HbA_{1c} values (adjusted β=5.50−6.16, *P*=.037−.014), suggesting that good long-term control of blood glucose levels is important for preventing and improving shoulder pain and disability.

Study limitations

This study has several limitations. Its cross-sectional design and the relatively small number of participants limit the confidence in the reported diagnostic prevalence. Only 77% of the invited target population was examined, and we do not have diagnostic information about the remaining individuals. The estimate of lifetime prevalence may also be compromised by the participants' recall bias.

Conclusions

In this study of patients with type 1 diabetes for ≥45 years we found a very high point prevalence (59%) of frozen shoulder. The lifetime prevalence was 76% when historical data were taken into consideration. The diabetes group also reported higher shoulder-related disability and had reduced shoulder range of motion than the diabetes-free group, particularly the subgroup of patients with diabetes with painful frozen shoulder. In the subgroup of patients with diabetes who had painful frozen shoulder, poor long-term glycemic control was associated with higher QuickDASH scores and a reduced shoulder range of motion.

Patients with long-term type 1 diabetes commonly suffer from frozen shoulder with severe restrictions in shoulder movement and disability affecting daily life. We therefore recommend that a focus on shoulder assessment and treatment should be part of any treatment plan for patients with type 1 diabetes.

The association of frozen shoulder with glycemic burden suggests that good glycemic control over many years is an

important factor in reducing shoulder pain and disability. This should be investigated in future studies.

Generalizability

Although many patients with type 1 diabetes are treated in specialized diabetes outpatient clinics, health care providers in primary care deal with these patients. Attention to shoulder problems is necessary because we know that a large number of these patients will develop frozen shoulder with long-standing shoulder stiffness and high levels of shoulder disability. The high QuickDASH scores and shoulder stiffness suggest the need for shoulder rehabilitation for many patients with diabetes. The relation between shoulder disability and long-term blood glucose should encourage good glycemic control. Increased attention from the health providers may therefore reduce disability and increase quality of life for the patients with diabetes.

Suppliers

a. Bio-Rad.
b. SPSS version 23; IBM.
c. Microfet 2; Hoggan Health Industries.
d. DCA2000 analyzer; Bayer Diagnostics.

Keywords

Diabetes mellitus, type 1; Hemoglobin A, glycosylated; Pain; Rehabilitation; Shoulder

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Appendix 1 Most common shoulder diagnoses with diagnostic criteria

ICD-10 Diagnosis With Description	Symptoms	Diagnostic Criteria	Radiologic Investigations That Might Increase Diagnostic Accuracy	Study
M75.4: subacromial pain syndrome	Pain in the shoulder and proximal lateral upper arm exacerbated by activity	Typical pain and positive impingement test and pain with isometric abduction or external rotation	None	Palmer et al[9]
M79.11: myalgia in shoulder muscles	Diffuse pain outside the GH joint localized over muscles	Negative specific tests, pain when palpating muscles	None	Palmer et al[9]
M75.0: frozen shoulder (adhesive capsulitis)	Pain in the shoulder exacerbated by activity; feeling of stiffness	Reduced passive range of GH motion $>20^{\circ}$ in 2 planes	None	Palmer et al[9]
M75.1: full-thickness rotator cuff tear	Pain in the shoulder; occasional feeling of weakness	Positive impingement test and weakness with isometric abduction or external rotation	MRI and US	Palmer et al[9]
M19.8: AC joint osteoarthritis	Pain on top of shoulder, over the AC joint	Pain with joint palpation; osteoarthritis on radiograph, US, or MRI	Radiograph	Palmer et al[9]
M19.0: GH joint osteoarthritis	Pain in the shoulder; occasional feeling of stiffness	Osteoarthritis on radiograph or MRI	Radiograph	Palmer et al[9]

Abbreviations: AC, acromioclavicular; GH, glenohumeral; ICD-10, *International Classification of Diseases—10th Revision*; MRI, magnetic resonance imaging; US, ultrasound.

Appendix 2 Measurements of Range of Motion and Isometric Muscle Strength

Range of motion

The intraobserver reliability is found to be comparable for visual estimation and manual and digital goniometers.[11,12,22] An intrarater standard error of measurement of 3° to 5° is found for all used measurements of shoulder motion.[12]

Normative data were mainly collected from Muir et al[12] and supplemented with hand-behind-back numbers from Ginn et al.[30] The numbers were not age adjusted both because of missing age relevant data and the small effect of age showed by Macedo and Magee.[14]

Active range of motion (AROM) in flexion was measured with the patient sitting on a chair with a firm back, with the side to the wall. The glenohumeral rotational center of forward flexion was aligned with the center of a wall-hung measuring device with 5° increments. The patient was asked to lift his/her straight arm with the thumb up as high as possible without bending backward. The investigator read the AROM by aiming from the side using the patient's humerus as an indicator.

AROM in external rotation was measured with the patient standing with his/her back to the wall, with the arm along the side, the elbow flexed 90°, and the forearm pointing forward 90° to the ventral plane. A 2-armed manual inclinometer with 5° increments was fixed to the wall with the origo just behind and below the patients elbow and the movable arm parallel to his/her forearm. The patient was asked to rotate the hand outward, keeping the elbow in position and the back against the wall without rotating the body. Then we moved the free goniometer arm parallel to the patients forearm to measure the external rotation.

AROM in internal rotation was measured as a combined movement (hand behind back). The standing patient was asked to reach as high as possible along the spine with the thumb without bending forward. The distance from the spinose of C7 to the tip of the thumb along the vertebral column was measured in centimeters. If the person was unable to reach the spine, a horizontal line was drawn from the position of the thumb to a downward extension of the spine, and the distance to C7 was measured from here.

Passive glenohumeral range of motion (PROM) was measured with the patient seated.

PROM in external rotation was recorded with the elbow fixed along the patient's side in 90° of flexion and the hand pointing forward 90° from the ventral plane. The investigator rotated the patients forearm externally until an elastic stop was felt and read the degrees of external rotation from above with the precision of 5°.

For PROM in abduction, the investigator fixed the patient's scapula with one hand and held the patients arm under the patient's flexed elbow with the other. Starting position was along the body. The arm was abducted in slight flexion (in the scapula plane, approximately 20° of flexion) until an elastic stop was felt and the degree of abduction was read from behind with the precision of 5°.

Isometric muscle strength

Shoulder muscle strength was measured in Newtons (1kg=9.80665N) with a handheld dynamometer.[c] The device showed the result on a digital display, freezing the highest measured value. The participants were given standardized information about the examination, and the test routine was executed once before the measurement was done.

For abduction, the straight arm was internally rotated and put in 45° abduction and 20° flexion (scapula plane). The dynamometer was placed at the wrist just proximal to the ulnar styloid. The persons were instructed to elevate their straight arm with as much muscle strength as possible against the fixed dynamometer, and the maximum produced muscle strength was read on the display.

For external rotational muscle strength, the arm was positioned along the body with the elbow flexed 90° pointing straight forward and with the forearm in neutral rotation. We placed the dynamometer at the wrist between the radial and ulnar styloids and instructed the persons to rotate their hand externally with maximal muscle strength against the fixed dynamometer keeping their elbow at their side. The maximum force was read.

Abbreviations: AROM, active range of motion; PROM, passive glenohumeral range of motion.

Appendix 3 Measurements of Time-Weighted HbA_{1c}

Longitudinal HbA_1 and HbA_{1c} values were available from 1980 to 2015. The mean number of measurements taken per subject at different time intervals was 73. One laboratory method was used for HbA_1 (agarose gel electrophoresis at Oslo University Hospital, Aker, Oslo, Norway) from 1981 to 1986, and 2 different methods were used for HbA_{1c} (Diamat[a]) from 1987 to 1993 and (DCA2000 analyzer[d]) from 1993 onward. To transform old HbA_1 for the earliest time series into HbA_{1c}, we identified duplicate HbA_1/HbA_{1c} values (taken on the same date) from 50 different subjects and found a regression formula to convert HbA_1 to HbA_{1c} ($HbA_{1c}=0.526+0.776HbA_1$). We found excellent an intraclass correlation coefficient of .94 (95% CI, .89−.97) between the HbA_1 and HbA_{1c} values, which is in accordance with previous findings.

We calculated 30-year HbA_{1c} as a measure of glycemic burden, similar to the large Diabetes Control and Complications Trial and Follow-up study. Because we do not have HbA_{1c} values from time of diagnosis up until the 1980s, we calculated a new measure: estimated full duration HbA_{1c}. This method might reflect the actual glycemic burden better because we incorporated all years living with the disease. The equations are as follows:

$$30-\text{y HbA}_{1c}=\frac{1}{n}\sum_{i=1}^{n}\left(\frac{1}{m}\sum_{i=1}^{m}X_{\text{HbA1c }i}\right)$$

and

$$\text{Estimated full}-\text{duration HbA}_{1c}=\frac{\left\{\left[\frac{1}{3}\sum_{i=1}^{3}\left(\frac{1}{m}\sum_{i=1}^{m}X_{\text{HbA1c }i}\right)\right]\times(\text{Year of first HbA}_{1c}-\text{Year of diagnosis})\right\}+(30-\text{y HbA}_{1c}\times n)}{\text{Duration of type 1 diabetes in years}}$$

where n is the number of years between the first and last HbA_{1c} tests, with the last test having been carried out in 2015; m is the total number of HbA_{1c} tests per year; and $X_{HbA1c\ i}$ is the observed value for test i.

To calculate 30-year HbA_{1c}, we first calculated the mean HbA_{1c} for each year, and then the mean of these values.

To calculate the estimated full-duration HbA_{1c} we calculated the average HbA_{1c} from the first 3 years it was measured in the individual, and multiplied this by the number of years which have elapsed between diagnosis and the first measurement of HbA_{1c} (estimated HbA_{1c}). We then multiplied the 30-year HbA_{1c} by the number of years of HbA_{1c} readings, added that value to the estimated HbA_{1c}, and then divided the total value by the number of years with diabetes.

References

1. Agrawal RP, Gothwal S, Tantia P, et al. Prevalence of rheumatological manifestations in diabetic population from North-West India. J Assoc Physicians India 2014;62:788-92.
2. Banon S, Isenberg DA. Rheumatological manifestations occurring in patients with diabetes mellitus. Scand J Rheumatol 2013;42:1-10.
3. Bhat TA, Dhar SA, Dar TA, et al. The musculoskeletal manifestations of type 2 diabetes mellitus in a Kashmiri population. Int J Health Sci 2016;10:57-68.
4. Huang YP, Fann CY, Chiu YH, et al. Association of diabetes mellitus with the risk of developing adhesive capsulitis of the shoulder: a longitudinal population-based followup study. Arthritis Care Res 2013;65:1197-202.
5. Zhao J, Randive R, Stewart JA. Molecular mechanisms of AGE/RAGE-mediated fibrosis in the diabetic heart. World J Diabetes 2014;5:860-7.
6. Brownlee M. Glycation products and the pathogenesis of diabetic complications. Diabetes Care 1992;15:1835-43.
7. Arkkila PE, Kantola IM, Viikari JS, Ronnemaa T. Shoulder capsulitis in type I and II diabetic patients: association with diabetic complications and related diseases. Ann Rheum Dis 1996;55:907-14.
8. Larkin ME, Barnie A, Braffett BH, et al. Musculoskeletal complications in type 1 diabetes. Diabetes Care 2014;37:1863-9.
9. Palmer K, Walker-Bone K, Linaker C, et al. The Southampton examination schedule for the diagnosis of musculoskeletal disorders of the upper limb. Ann Rheum Dis 2000;59:5-11.
10. Walker-Bone KE, Palmer KT, Reading I, Cooper C. Soft-tissue rheumatic disorders of the neck and upper limb: prevalence and risk factors. Semin Arthritis Rheum 2003;33:185-203.
11. Juel NG, Natvig B. Shoulder diagnoses in secondary care, a one year cohort. BMC Musculoskelet Disord 2014;15:89.
12. Muir SW, Corea CL, Beaupre L. Evaluating change in clinical status: reliability and measures of agreement for the assessment of glenohumeral range of motion. N Am J Sports Phys Ther 2010;5:98-110.
13. Tveita EK, Ekeberg OM, Juel NG, Bautz-Holter E. Range of shoulder motion in patients with adhesive capsulitis; intra-tester reproducibility is acceptable for group comparisons. BMC Musculoskelet Disord 2008;9:49.
14. Macedo LG, Magee DJ. Effects of age on passive range of motion of selected peripheral joints in healthy adult females. Physiother Theory Pract 2009;25:145-64.
15. Maund E, Craig D, Suekarran S, et al. Management of frozen shoulder: a systematic review and cost-effectiveness analysis. Health Technol Assess 2012;16:1-264.
16. Hand C, Clipsham K, Rees JL, Carr AJ. Long-term outcome of frozen shoulder. J Shoulder Elbow Surg 2008;17:231-6.
17. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). Am J Ind Med 1996;29:602-8.
18. Roe Y, Soberg HL, Bautz-Holter E, Ostensjo S. A systematic review of measures of shoulder pain and functioning using the International classification of functioning, disability and health (ICF). BMC Musculoskelet Disord 2013;14:73.
19. Finsen V. [Norwegian version of the DASH questionnaire for examination of the arm shoulders and hand] [Norwegian]. Tidsskr Nor Laegeforen 2008;128:1070.
20. Haldorsen B, Svege I, Roe Y, Bergland A. Reliability and validity of the Norwegian version of the Disabilities of the Arm, Shoulder and Hand questionnaire in patients with shoulder impingement syndrome. BMC Musculoskelet Disord 2014;15:78.
21. Aasheim T, Finsen V. The DASH and the QuickDASH instruments. Normative values in the general population in Norway. J Hand Surg Eur Vol 2014;39:140-4.
22. May S, Chance-Larsen K, Littlewood C, Lomas D, Saad M. Reliability of physical examination tests used in the assessment of patients with shoulder problems: a systematic review. Physiotherapy 2010;96:179-90.
23. Norwegian Diabetes Register. Cooper J, Sandberg S, Løvaas KF, Thue G. [Report 2015] [Norwegian]. 2015. Available at: http://www.noklus.no/Portals/2/Diabetesregisteret/Tilbakemeldingsrapport%20sykehus%202015.pdf. Accessed November 1, 2016.
24. Berg TJ, Clausen JT, Torjesen PA, Dahl-Jorgensen K, Bangstad HJ, Hanssen KF. The advanced glycation end product Nepsilon-(carboxymethyl)lysine is increased in serum from children and adolescents with type 1 diabetes. Diabetes Care 1998;21:1997-2002.
25. Kilhovd BK, Giardino I, Torjesen PA, et al. Increased serum levels of the specific AGE-compound methylglyoxal-derived hydroimidazolone in patients with type 2 diabetes. Metabolism 2003;52:163-7.
26. Andersson DA, Gentry C, Light E, et al. Methylglyoxal evokes pain by stimulating TRPA1. PLoS One 2013;8:e77986.
27. Buchbinder R, Hoving JL, Green S, Hall S, Forbes A, Nash P. Short course prednisolone for adhesive capsulitis (frozen shoulder or stiff painful shoulder): a randomised, double blind, placebo controlled trial. Ann Rheum Dis 2004;63:1460-9.
28. Page MJ, Green S, Kramer S, et al. Manual therapy and exercise for adhesive capsulitis (frozen shoulder). Cochrane Database Syst Rev 2014;8:CD011275.
29. Engebretsen K, Grotle M, Bautz-Holter E, Ekeberg OM, Brox JI. Determinants of the shoulder pain and disability index in patients with subacromial shoulder pain. J Rehabil Med 2010;42:499-505.
30. Ginn KA, Cohen ML, Herbert RD. Does hand-behind-back range of motion accurately reflect shoulder internal rotation? J Shoulder Elbow Surg 2006;15:311-4.