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Idiopathic Frozen Shoulder in Individuals with Diabetes: Association with Metabolic Control, Obesity, Antidiabetic Treatment and Demographic Characteristics in Adults with Type 1 or 2 Diabetes from the DPV Registry

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ABSTRACT

Aims To examine the association of frozen shoulder (FS) with demographic and diabetes-related outcomes in individuals with type 1 (T1D) or type 2 (T2D) diabetes aged ≥ 30 years.

Materials and methods Multivariable logistic regression models, adjusted for demographics were used to calculate the proportion of FS in association with age, gender, diabetes duration, body mass index (BMI), haemoglobin A1C (HbA1c) and diabetes treatment.

Results The unadjusted percentage of FS was higher in T1D compared to T2D (0.22 % vs. 0.06 %). In T1D, adjusted regression models revealed higher prevalence of FS in women than men (0.26 [0.20–0.34] % vs. 0.15 [0.11–0.21] %, $p = 0.010$). No significant relationship of age and BMI with FS was found in both diabetes types. Longer diabetes duration was associated with a higher proportion of FS in T1D ($p < 0.001$) and T2D ($p = 0.004$). In T1D, HbA1c > 7 % was related to a higher proportion of FS compared to HbA1c ≤ 7 % (0.25 [0.19–0.32] vs. 0.12 [0.08–0.20] %, $p = 0.007$), while an inverse relationship was found in T2D (HbA1c ≤ 7 %: 0.08 [0.07–0.10] vs. HbA1c > 7 %: 0.05 [0.04–0.06] %, $p = 0.001$).

Conclusions Different associations of FS with gender and HbA1c were observed for T1D and T2D; however, longer diabetes duration increases the risk for FS independent of diabetes type. Musculoskeletal diseases are still underreported in individuals with diabetes and awareness should be raised for FS as a specific diabetes complication.

Introduction

Frozen shoulder (FS) is mostly characterised by shoulder pain together with stiffness and functional restriction at the glenohumeral joint [1]. Individuals with FS normally pass through three different phases. The first is the painful phase, lasting 2 to 9 months, with shoulder pain, especially at night. Next is the frozen phase which lasts for 4–12 months, when the joints get stiff and cause consistent pain. The third phase is the thawing phase with improved pain and shoulder flexibility (5–12 months). In the general population, people in the age group of 40 to 60 years experience the highest incidence of FS and women are more often affected than men [2]. While some studies demonstrate overweight and obesity as risk factors for FS [3], a history of slight trauma can also contribute to FS [3,4].

Therefore, frozen shoulder is categorized into idiopathic or primary FS with no clearly detectable reason for shoulder stiffness and pain, and secondary FS, which often occurs as a consequence of trauma, upper limb fracture, shoulder surgery, or other shoulder injuries such as rotator cuff tear [5, 6].

A recent study suggested a markedly higher prevalence of FS among patients with diabetes compared to the general population (4.3 % vs. 0.5 %), respectively, within a 3-months observation period in Germany [7]. One possible reason for the higher risk of FS in people with diabetes could be an accumulation of advanced glycation end products (AGEs) resulting in the solidification of collagen fibres. However, the pathophysiology is not entirely understood [8, 9].

Recent studies on the difference in the prevalence of FS between patients with type 1 diabetes (T1D) and type 2 diabetes (T2D) are only a few. A meta-analysis on the prevalence of adhesive capsulitis among patients with diabetes showed an overall prevalence of 13.4 % (95 % confidence interval (CI) 10.2–17.2 %). Additionally, we could identify three studies [10–12] that compared the prevalence of FS between T1D and T2D, but found no significant difference [13].

Among patients with diabetes, a longer diabetes duration seems to be a risk factor for FS [14, 15]. The roles of body-mass-index (BMI) [16], haemoglobin A1c (HbA1c) [14–16] and diabetes treatment are not conclusive so far [13, 15].

The aim of the current study was to examine the association of FS among ≥ 30 years old individuals having T1D or T2D with demographic characteristics, glycaemic control, BMI and diabetes therapy.

Materials and Methods

Participants and data collection

This analysis is based on data from the prospective, multicentre diabetes patient follow-up registry "Diabetes-Patienten-Verlaufsdokumentation" (DPV) which is a standardized electronic health record developed at the Institute of Epidemiology and Medical Biometry, Ulm University, Germany [17]. The initiative and analysis of anonymised data were approved by the Ethics Committee of Ulm University (approval number: 202/09) as well as by local review boards at the participating centres.

Five hundred one diabetes centres from Germany, Austria, Switzerland and Luxembourg provided anonymised data on diabetes treatment and outcome to the DPV registry until March 2020. Twice a year, participating centres report de-identified data for central analysis at Ulm University. The transferred data are checked for inconsistency or implausibility and reported back to the respective centres for correction, if necessary.

Patients recorded in the DPV initiative were selected if they had a clinical diagnosis of T1D or T2D and were more than 30 years of age.

Definition of frozen shoulder and group selection

FS was defined according to the ICD-10 code M75.0 which includes: frozen shoulder, adhesive capsulitis of the shoulder and periarthritis humeroscapularis (PHS) as well as the ICD-10 code M25.61 that characterizes shoulder stiffness.

To ensure that only idiopathic frozen shoulder was included, patients with a documented fracture at the shoulder or humerus, as well as individuals with a history of trauma or injury at the shoulder (e.g. rotator cuff tear), were excluded together with individuals with FS as a consequence of surgery. In the control group, patients with other shoulder lesions (ICD-10 codes M75.1-M75.9) were excluded from this analysis.

Individuals were categorized into T1D and T2D and further allocated to two groups each: T1D-FS group (type 1 diabetes with frozen shoulder), T1D-control group (type 1 diabetes without frozen shoulder), T2D-FS group (type 2 diabetes with frozen shoulder), and T2D-control group (type 2 diabetes without frozen shoulder).

For patients with a documented date of diagnosis for FS, data +/- 6 months from this date were analysed. If no date of diagnosis was available, data +/- 6 months from the first documentation of FS were analysed. If only FS – with unknown time-lag – was documented and in control patients without FS, the last documented year was analysed. For each subject, data were aggregated if the individual had more than one visit in the respective documentation period.

Patient data

For descriptive comparison of demographics and diabetes-related outcomes between the T1D/T2D-FS group and the T1D/T2D-control group, the parameters gender, age, age at diabetes onset, diabetes duration, height, weight, BMI, type of treatment and HbA1c (%; mmol/mol), were analysed.

BMI was calculated as weight divided by height squared (kg/m^2). For T1D patients, type of treatment was categorized as insulin injection therapy (injection) or pump therapy (pump). Treatment groups for T2D patients were insulin therapy with or without additional oral antidiabetic medication (OAD), treatment with OAD if at least one OAD but no insulin was documented, or no medication (lifestyle), if neither insulin nor OAD was documented during the observation period. HbA1c values were standardised to the Diabetes Control and Complications Trial reference range of 4.05 %–6.05 % (20.7–42.6 mmol/mol) using the multiple of the mean transformation method to account for different laboratory methods [18].

Statistical analysis

All statistical analyses were carried out using SAS (Statistical Analysis Software, SAS Institute Inc., Cary, NC, USA) Version 9.4 TS1M5. Descriptive statistics were performed for population characteristics. The results were shown as median with quartiles for continuous variables using the Kruskal-Wallis-test to compute unadjusted *p*-values and as proportions for binary variables using the χ^2-test.

For the primary analyses, we used multivariable logistic regression models to calculate the percentage of patients with frozen shoulder among different sub-groups for gender, age (30–50, >50–65 and >65 years in T1D; 30–65, >65–80 and >80 years in T2D), diabetes duration (0–10, >10–20 and >20 years in T1D; 0–2, >2–10 and >10 years in T2D), BMI (<25, ≥25 in kg/m^2 T1D; <25, ≥25–30 and ≥30 kg/m^2 in T2D), type of treatment (see above) and HbA1c (≤7 %, >7 %). All regression models were adjusted for age groups, gender and age at onset groups (≤30, >30 years in T1D; ≤60, > 60 years in T2D) and were stratified by diabetes type.

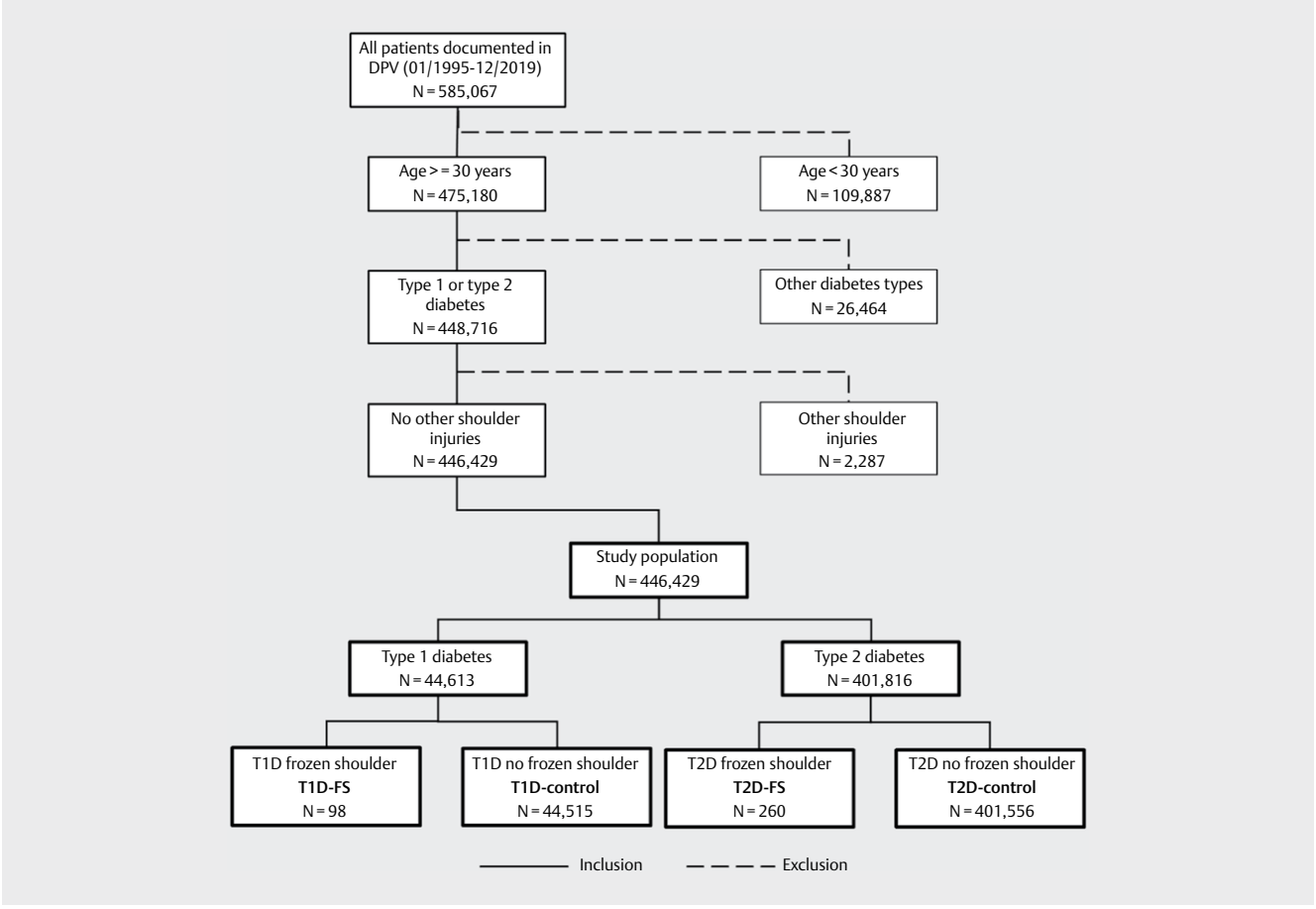
We also analysed the relation between lipid values as well as micro- and macrovascular diseases with FS to obtain better insight into the underlying mechanisms of FS in our study cohort (results are mentioned in the supplement). Therefore, we performed linear regression analyses for triglycerides [mg/dl], total cholesterol [mg/dl], high density lipoprotein (HDL [mg/dl]) and low density lipoprotein (LDL [mg/dl]) and compared individuals with FS and the control group adjusted for age, gender, age at onset, BMI and HbA1c. We also performed logistic regression analyses for the proportion of patients with micro- and macrovascular complications among the FS-group and the control group, adjusted for the same confounders. Microvascular diseases comprised diabetic retinopathy, neuropathy and nephropathy, while macrovascular diseases comprised coronary artery disease, myocardial infarction, stroke, transient ischemic attack, and peripheral artery occlusive disease. All regression models were stratified by diabetes type.

Results from logistic regression models were presented as adjusted proportions together with 95 %-CI. Linear regression models were shown as the adjusted mean together with lower and upper quartile of the respective lipid values in mg/dl. $P<0.05$ indicated a significant difference.

Results

Study population

Among all patients registered in DPV, 446,429 were aged ≥30 years, had a diagnosis of T1D or T2D and fulfilled the inclusion criteria (▶ **Fig. 1**). Ninety-eight of 44 613 adults with T1D had a documented idiopathic FS. In patients with T2D, idiopathic FS was diagnosed in 260 of 401 816 individuals. Therefore, the unadjust-



▶ **Fig. 1** Study population and group selection. T1D = type 1 diabetes; T2D = type 2 diabetes; FS = frozen shoulder.

▶ **Table 1** Baseline characteristics of individuals with frozen shoulder vs. individuals without frozen shoulder (control), stratified by diabetes type.

Characteristic	Type 1 diabetes			Type 2 diabetes		
	Frozen shoulder	Control	*p*-value	Frozen shoulder	Control	*p*-value
N (%)	98 (0.22)	44,515		260 (0.06)	401,556	
Gender [% female]	60.2	46.4	0.051	48.2	47.0	1.000
Age [y]	51.1 [44.3; 58.9]	51.5 [40.8; 63.3]	1.000	67.8 [60.4; 77.7]	70.3 [60.4; 78.3]	0.987
Age at diabetes onset [y]	18.7 [11.1; 35.6]	31.6 [19.7; 44.2]	**<0.001**	56.4 [45.8; 66.1]	58.8 [49.1; 68.3]	0.061
Diabetes duration [y]	30.6 [18.0; 39.5]	18.4 [6.8; 30.6]	**<0.001**	10.0 [5.1; 17.2]	8.6 [3.0; 15.4]	**0.009**
Height [cm]	170 [163; 178]	172 [165; 179]	0.816	167 [160; 175]	169 [162; 176]	0.104
Weight [kg]	75.0 [66.5; 84.6]	76.0 [65.7; 88.0]	1.000	86.0 [75.8; 101.0]	85.0 [74.0; 100.0]	1.000
BMI [kg/m^2]	26.3 [23.4; 28.7]	25.5 [22.8; 29.1]	1.000	30.7 [27.0; 33.9]	29.8 [26.2; 34.3]	0.987
HbA1c MOM-DCCT [%]	7.7 [7.1; 8.6]	7.6 [6.8; 8.7]	1.000	6.8 [6.2; 7.6]	7.2 [6.3; 8.5]	**0.002**
HbA1c MOM-DCCT [mmol/mol]	61 [54; 70]	59 [50; 72]		51 [44; 59]	55 [45; 69]	
T1D: Pump therapy [%]	38.6	22.4	**0.030**			
T2D: Insulin therapy [%]				26.9	50.0	**<0.01**
T2D: OAD-only therapy [%]				35.8	26.6	
T2D: Lifestyle therapy [%]				37.3	23.3	

Data are presented as median [lower quartile; upper quartile] or as proportion (%). BMI = body mass index; HbA1c = haemoglobin A1c; OAD = oral antidiabetics; lifestyle = no antidiabetic medication.

ed proportion of FS was higher in T1D (0.22 %) than in T2D (0.06 %, ▶ **Table 1**).

Unadjusted comparisons between the FS group and the control group revealed that T1D patients with FS were significantly younger at diabetes onset, had longer diabetes duration and used pump therapy more often compared to the T1D-control group (▶ **Table 1**).

Individuals in the T2D-FS group had significantly longer diabetes duration and a lower HbA1c than T2D-controls. In individuals with T2D and FS, insulin therapy was used less often, but OAD and lifestyle therapy were significantly more frequent compared to those in the T2D-control group (▶ **Table 1**).

FS in relation to HbA1c, treatment and demographics

Adjusted regression models revealed a higher prevalence of FS in females than males in the T1D group ($p = 0.010$), while in T2D no significant gender difference could be detected (▶ **fig. 2**). In both, T1D and T2D age groups did not differ significantly (▶ **fig. 2**).

FS was related to longer diabetes duration in both T1D and T2D. In T1D, the highest percentage of FS was observed in diabetes duration >20 years compared to a diabetes duration of >10–20 years ($p < 0.001$) or <10 years ($p < 0.001$). In T2D, less FS was observed in the diabetes duration of 0 to 2 years than that in >2–10 years ($p = 0.008$) or >10 years ($p = 0.003$) (▶ **fig. 2**).

In T1D no significant association of insulin treatment regimen with FS was found. In T2D, the insulin group revealed the lowest prevalence of FS, which was significantly different compared to that in the OAD group ($p < 0.001$) and the lifestyle-only group ($p < 0.001$) (▶ **fig. 2**).

In individuals with T1D HbA1c levels >7 % were significantly associated with FS compared to individuals with a targeted glycaemic control of HbA1c ≤7 % (0.25 [0.19–0.32] vs. 0.12 [0.08–0.20] %, $p = 0.007$), while inverse results were observed in T2D: FS frequency in HbA1c >7 % was 0.05 % [0.04–0.06] vs. 0.08 [0.07–0.10] % in HbA1c ≤7 %, $p = 0.001$) (▶ **fig. 2**). However, with additional adjustment for diabetes therapy in T2D, this difference was eliminated (HbA1c >7 %: 0.05 [0.04–0.06] % vs. HbA1c ≤7 %: 0.06 [0.05–0.07] %, $p = 0.191$).

The proportion of FS increased slightly with higher BMI in both diabetes types, but the differences were not significant (T1D: $p = 0.315$; T2D: $p = 0.174$) (▶ **fig. 2**).

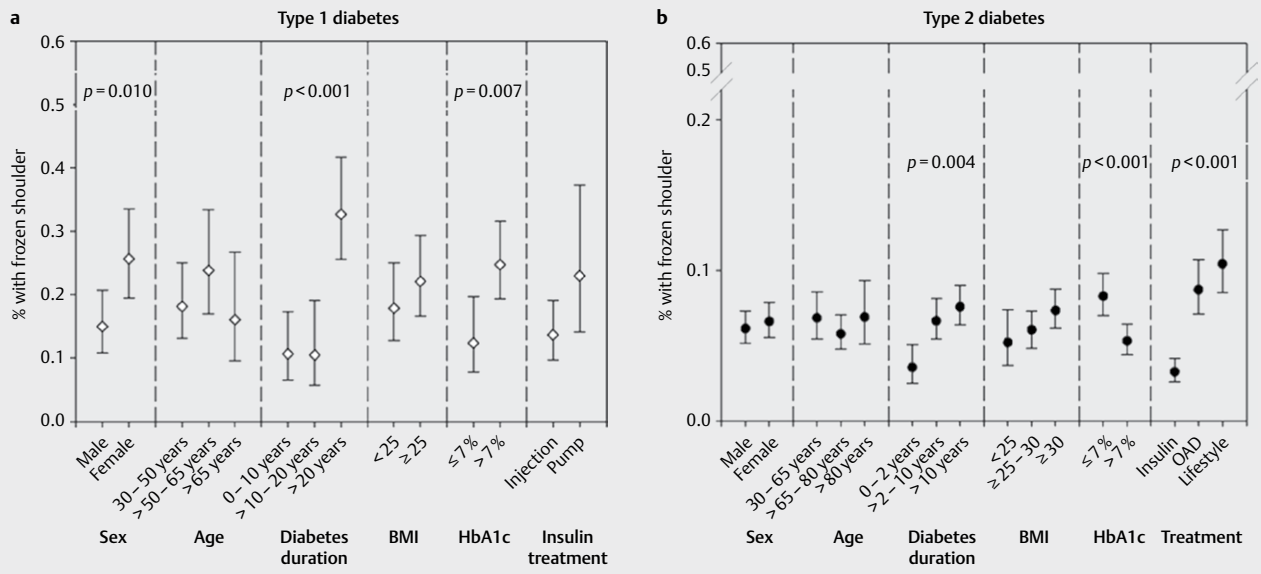
Additional results on lipid values as well as micro- and macrovascular diseases are provided in **supplemental Table 1**.

Discussion

In this large observational study on individuals with T1D or T2D aged ≥30 years, we detected different results for T1D and T2D, especially in terms of glycaemic control and gender differences.

AGEs are suspected to be responsible for increased risk of FS in individuals with diabetes, especially in those with insufficient glycaemic control over a longer period of time, as AGEs accumulate in the cells and solidify collagen [8, 9]. However, there is no clear evidence, whether individuals with T1D or T2D are often affected. A meta-analysis found no difference in the prevalence of shoulder lesion among diabetes types [13], while a study in 1996 reported a higher proportion of adhesive capsulitis in T2D than in T1D (22.4 % vs.10.3 %) [10]. In the present study, the number of total cases was too low to provide a reliable statement.

In the general population, the age between 40–60 years is associated with the highest risk of FS and women are more often affected than men [19]. Furthermore, women often suffer from higher pain intensity of FS than men [20]. This distribution of age and gender is similar to that observed in our study on T1D patients, although the difference in age groups was not significant. Patients with T2D did not exhibit any association with FS in terms of age or gender in the present study.



▶ **Fig. 2** The adjusted proportion of frozen shoulder related to gender, age, diabetes duration, HbA1c, BMI and diabetes therapy in adults with type 1 diabetes (A, white diamonds) or type 2 diabetes (B, black circles). Data from multivariable logistic regression models, adjusted for age, gender and age at onset are shown as percentage of patients with frozen shoulder together with the 95 % CI. HbA1c = haemoglobin A1c; BMI = body-mass index; OAD = oral antidiabetics; lifestyle = no antidiabetic medication; CI = confidence interval.

Our finding that longer diabetes duration is strongly related to FS is in line with previous studies [14,15]. This leads to the assumption that AGEs may have been present in the cells over several years to induce problems such as FS.

There are no previous studies on diabetes therapy in T1D to compare the association of FS to insulin injection therapy versus insulin pump therapy among adults with T1D; we too did not find any significant difference. Until now, no relationship between the type of insulin treatment in T1D and FS has been assumed.

Only a few documented studies have compared insulin dependency among patients with T2D in terms of the proportion of FS. One study found a higher prevalence of FS in T2D with insulin therapy [15], while another study did not find any difference between treatment types [13]. In the current study, T2D patients on insulin had an even lower proportion of FS, but further studies are needed to prove this. Several studies have revealed that insulin dependency among patients with T2D does not affect the healing process of FS or the outcomes after surgical treatment of FS [21, 22], but evidently, insulin-dependence enhances the risk of recurrent FS [23] and the requirement of arthroscopic intervention [24].

Studies on the relationship between glycaemic control and frozen shoulder are rare and their findings are inconsistent. Furthermore, some studies did not discriminate between T1D and T2D making it even more difficult to interpret these data. High HbA1c was found to enhance the risk for FS in T2D [25] and in diabetes patients generally [26]. However, two other studies found no significant difference in the proportion of FS in relation to HbA1c in T2D [15] and in diabetes patients without stratification of diabetes type [27]. Another study reported that cumulative HbA1c (defined as the magnitude of HbA1c values > 7 % over time) generally increases the risk for FS in diabetes patients generally [16]. We could not find any report on the relationship between glycaemic control and FS exclusively in T1D, but our findings suggest that glycaemic control might play a more important role in the development of FS in T1D than in T2D. Studies on more individuals with FS and a clear stratification by diabetes type are needed to confirm our results.

The fact that long diabetes duration was associated with FS in our study could explain why we observed an association of HbA1c (> 7 %) with FS only in T1D, but not in T2D, as diabetes duration is generally longer and HbA1c-values are often higher in adults with T1D than T2D. Diabetes duration in T2D could be too short to affect the progression of FS noticeably. Another reason for the inverse association of HbA1c with FS in T2D could be an interaction between glycaemic control and treatment. Individuals on insulin and patients with high HbA1c revealed the lowest proportion of FS and patients with high HbA1c require insulin therapy more often to achieve their target glycaemic control [28]. With further adjustment for diabetes therapy, no association between HbA1c and FS in T2D was observed.

Obesity has been mentioned as a possible risk factor for FS in the general population [3] possibly due to dyslipidaemia in overweight and obese individuals. This is in accordance with other findings on elevated triglyceride values in people suffering from FS [26]. In addition, increased LDL values are suspected to contribute to shoulder pain and stiffness [29, 30].

Analyses of lipid values in the present study revealed no association to FS in T1D patients. In contrast, in T2D, FS was related to higher levels of total cholesterol, LDL and HDL (supplemental **Table 1**). Microvascular diseases were found to be associated with FS in both diabetes types, while results for macrovascular diseases were only significant in T2D (supplemental **Table 1**). The missing association between lipid values and FS in T1D together with the

results on HbA1c and microvascular diseases might indicate that BMI is strongly associated with FS in the general population than in T1D patients, in which other mechanisms such as the accumulation of AGEs might be more important. This is in line with another report of a normal distribution of BMI among diabetes patients with FS [31]. In T2D, higher LDL and total cholesterol levels in patients with FS along with the lack of association with HbA1c might suggest mechanisms that are more comparable to those in the general population. However, it remains unclear why HDL levels were elevated in the FS group.

The strength of the present study was the large number of adult patients aged ≥ 30 years with distinct clinical diagnoses of either T1D or T2D. Further, these real-life data were obtained from everyday clinical practice. However, the absolute number of documented patients with FS in the DPV registry was very low. By comparing the proportion of FS among diabetes patients to that in other studies reporting a prevalence of 4–22 % [7, 32], we assume that FS is underreported in diabetes-specific databases such as DPV. In the present study, no conclusive statement on the prevalence of FS can be made, therefore, we focussed on the association of FS to diabetes-related parameters. It must be mentioned that FS was diagnosed in 17 % of individuals with T1D and in 29 % of individuals with T2D according to the ICD-10 code M25.61 (stiffness of shoulder) or based on the terms periarthritis or adhesive capsulitis of the shoulder, because these terms are also mentioned besides FS, in the ICD-10 code M75.0. Another difficulty was that conditions like fracture or rotator cuff tear are likely to be insufficiently reported.

Conclusion

In adult patients with diabetes, the risk of frozen shoulder is increased with longer diabetes duration, compatible with glycation contributing to the pathogenesis. In patients with T1D, females and high HbA1c are related to FS. However, better documentation of musculoskeletal disorders is needed in individuals with diabetes for an improved understanding of the mechanisms involved in the elevated risk of idiopathic FS in diabetes patients. In this nationwide registry of individuals with diabetes, the number of documented patients with FS was low, indicating that musculoskeletal disorders are still not perceived as specific complications of diabetes. This is crucial because, in 2002, shoulder lesions represented about 3.5 % of direct illness costs resulting from musculoskeletal disorders in Germany and were among the 10 single diagnoses responsible for the highest proportion of work incapacity [33]. Furthermore, studies with a clear differentiation between diabetes types are needed as there are noticeable differences between T1D and T2D, especially in terms of the association of HbA1c with FS. Therefore, different strategies for FS prevention and treatment might be advised in individuals with T1D and T2D.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Supplementary Material

Supplemental Table 1. Comparison of micro- and macrovascular diseases and lipid values between individuals with FS vs. individuals without FS (control), stratified by diabetes type.

	Individuals with FS	Control (Individuals without FS)	*p*-value
T1D			
Microvascular disease %	85.8 (77.0; 91.6)	61.7 (61.2; 62.2)	**<0.001**
Macrovascular disease %	24.0 (15.9; 34.6)	17.1 (16.6; 17.5)	0.100
Triglycerides [mg/dl]	107.2 (84.1; 130.3)	133.7 (132.5; 134.9)	**0.025**
Total cholesterol [mg/dl]	196.8 (184.4; 209.3)	196.7 (196.0; 197.3)	0.978
HDL [mg/dl]	63.4 (58.6; 68.3)	60.0 (59.8; 60.2)	0.167
LDL [mg/dl]	115.1 (105.7; 124.5)	112.3 (111.8; 112.8)	0.557
T2D			
Microvascular disease %	85.1 (79.9; 89.2)	71.4 (71.2; 71.5)	**<0.001**
Macrovascular disease %	50.1 (43.4; 56.9)	32.9 (32.7; 33.0)	**<0.001**
Triglycerides [mg/dl]	185.5 (168.7; 202.3)	188.5 (188.0; 188.9)	0.727
Total cholesterol [mg/dl]	200.7 (192.4; 209.0)	190.5 (190.2; 190.7)	**0.016**
HDL [mg/dl]	51.2 (48.7; 53.7)	45.9 (45.8; 46.0)	**<0.001**
LDL [mg/dl]	122.2 (116.1; 128.3)	110.3 (110.1; 110.5)	**<0.001**

Micro- and macrovascular diseases are shown as estimated percentage together with 95% CI calculated with multivariable logistic regression models adjusted for age, gender, age at onset, BMI and HbA1c. Data for lipid values are presented as estimated mean with lower and upper quartile calculated with multivariable linear regression models adjusted for age, gender, age at onset, BMI and HbA1c. FS = frozen shoulder; T1D = type 1 diabetes; T2D = type 2 diabetes; microvascular disease = at least one complication out of retinopathy, neuropathy or nephropathy; macrovascular disease = at least on complication out of coronary artery disease, stroke, myocardial infarction, peripheral artery occlusive disease or transient ischemic attack; BMI = body-mass index; HbA1c = haemoglobin A1c; HDL = high density lipoprotein; LDL = low density lipoprotein; CI = confidence interval.

Supplemental list 1

Aachen - Innere RWTH, Ahlen St. Franziskus Kinderklinik, Aidlingen Praxisgemeinschaft, Altötting-Burghausen Innere Medizin, Asbach Kamillus-Klinik Innere, Augsburg IV. Med. Uni-Klinik, Bad Aibling Internist. Praxis, Bad Aibling Internist. Praxis-2, Bad Driburg / Bad Hermannsborn Innere, Bad Hersfeld Innere, Bad Kreuznach-St.Marienwörth-Innere, Bad Krozingen Klinik Lazariterhof Park-Klinikum, Bad Kösen Median Kinderklinik, Bad Mergentheim - Kinderdiabetologische Praxis, Bad Reichenhall Kreisklinik Innere Med., Bad Säckingen Hochrheinklinik Innere, Bayreuth Innere Medizin, Bensheim Heilig Geist Innere, Berchtesgaden MVZ Innere Med, Bergen Gemeinschaftspraxis, Berlin DRK-Kliniken Mitte Innere, Berlin Endokrinologikum, Berlin Evang. Krankenhaus Königin Elisabeth, Berlin Klinik St. Hedwig Innere, Berlin Oskar Zieten Krankenhaus Innere, Berlin Parkklinik Weissensee, Berlin Schlosspark-Klinik Innere, Berlin St. Josephskrankenhaus Innere, Berlin Virchow-Kinderklinik, Berlin Vivantes Hellersdorf Innere, Bern Universitätsklinik für Diabetologie und Endokrinologie, Bochum Universitäts St. Josef, Bonn Schwerpunktpraxis, Bonn Uni-Kinderklinik, Bottrop Knappschaftskrankenhaus Innere, Braunfels-Wetzlar Innere, Braunschweig Kinderarztpraxis, Bremen - Mitte Innere, Castrop-Rauxel Evangelisches Krankenhaus, Castrop-Rauxel Rochus-Hospital, Chemnitz Kinderklinik, Chemnitz-Hartmannsdorf Innere Medizin - DIAKOMED-1, Coburg Innere Medizin, Coesfeld Kinderklinik, Coesfeld/Dülmen Innere Med., Darmstadt Innere Medizin, Deggendorf Gemeinschaftspraxis, Deggendorf Medizinische Klinik II, Dornbirn Innere Medizin, Dornbirn Kinderklinik, Dortmund Knappschaftskrankenhaus Innere, Dortmund Medizinische Kliniken Nord, Dortmund-Hombruch Marienhospital, Dortmund-St. Josefshospital Innere, Dortmund-West Innere, Duisburg Evang. und Johanniter Krhs Innere, Duisburg Malteser Rhein-Ruhr St. Anna Innere, Duisburg Malteser St. Johannes, Duisburg-Huckingen, Duisburg-Huckingen Malteser Rhein-Ruhr ST. Johannes, Duisburg-St.Johannes Helios, Düsseldorf Uni-Kinderklinik, Eberswalde Klinikum Barnim Werner Forßmann - Innere, Eckernförde Gem.-Prax, Eisleben Lutherstadt Helios-Klinik, Erfurt Kinderklinik, Erlangen Uni Innere Medizin, Erlangen Uni-Kinderklinik, Essen Diabetes-SPP, Essen Diabetes-Schwerpunktpraxis, Eutin St.-Elisabeth Innere, Forchheim Diabeteszentrum SPP, Frankfurt Diabeteszentrum Rhein-Main-Erwachsenendiabetologie (Bürgerhospital), Frankfurt Uni-Kinderklinik, Frankfurt Uni-Klinik Innere, Frankfurt Uni-Klinik Innere2, Frankfurt-Sachsenhausen Innere, Frankfurt-Sachsenhausen Innere MVZ, Freiburg Kinder-MVZ, Freiburg Uni Innere, Friedberg Innere Klinik, Fulda Innere Medizin, Garmisch-Partenkirchen Kinderklinik, Geislingen Klinik Helfenstein Innere, Gelnhausen Innere, Gelsenkirchen Kinderklinik Marienhospital, Gießen Ev. Krankenhaus Mittelhessen, Gießen Uni-Kinderklinik, Graz Uni Innere, Göppingen Innere Medizin, Göttingen Uni Gastroenterologie, Güstrow Innere, Hagen Kinderklinik, Halberstadt Innere Med. AMEOS Klinik, Halberstadt Kinderklinik AMEOS, Halle-Dölau Städtische Kinderklinik, Hamburg Altonaer Kinderklinik, Hamburg Endokrinologikum, Hamburg Kinderklinik Wilhelmstift, Hanau St. Vincenz - Innere, Hanau diabetol. Schwerpunktpraxis, Hannover DM-SPP, Hannover Henriettenstift - Innere, Hannover Kinderklinik auf der Bult, Heide Kinderklinik, Heidelberg St. Josefskrankenhaus, Heidelberg Uniklinik Innere, Heidenheim Arztpraxis Allgemeinmed, Heilbronn Innere Klinik, Herdecke Kinderklinik, Herford Innere Med I, Herford Kinderarztpraxis, Heringsdorf Inselklinik, Herne Evan. 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