Risk factors associated with the development of adhesive capsulitis in patients with type 2 Diabetes Mellitus

Fatores de risco associados ao desenvolvimento de capsulite adesiva em pacientes com Diabetes Mellitus tipo 2

Factores de riesgo asociados con el desarrollo de capsulitis adhesiva en pacientes con Diabetes Mellitus tipo 2

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ABSTRACT
Background: The association with musculoskeletal disorders is described in diabetic patients, among them adhesive capsulitis, which considerably compromises their quality of life. However, the predictive factors that would justify the development of this disease in such group

of individuals are not yet well known. Purpose: This study aimed to identify risk factors associated with the development of adhesive capsulitis in patients with type 2 diabetes mellitus. Methods: Case-control study that evaluated the presence of risk factors raised comparatively in patients with type 2 diabetes mellitus and adhesive capsulitis (cases) with type 2 diabetes mellitus patients without adhesive capsulitis (control). Patients with history of trauma, surgery and other shoulder diseases were excluded. Data analysis was performed using odds-ratio and adjusted for confounding factors using multiple logistic regression. The probability of rejecting the null hypothesis was 5%. Results: From a total of 119 patients, after selection criteria, 98 patients remained. There were 23 cases of adhesive capsulitis. For the multivariate logistic regression, the following factors were selected such as married marital status, non-white color/race, monthly income of 3-4 minimum wages, education greater than 8 years, treatment with insulin and glycated hemoglobin outside the target. Non-white race proved to be a statistically significant risk factor for the development of adhesive capsulitis with a 95% confidence interval of 1.061 to 1.556. Conclusion: Non-white race is an independent risk factor for the development of adhesive capsulitis on type 2 diabetic patients, with an adjusted odds-ratio of 1.351.

Keywords: shoulder, adhesive capsulitis, Diabetes Mellitus, case-control studies, risk factors.

RESUMO

Introdução: A associação com distúrbios musculoesqueléticos é descrita em pacientes diabéticos, entre eles a capsulite adesiva, que compromete consideravelmente sua qualidade de vida. Entretanto, os fatores preditivos que justificariam o desenvolvimento dessa doença nesse grupo de indivíduos ainda não são bem conhecidos. Objetivo: Este estudo teve como objetivo identificar os fatores de risco associados ao desenvolvimento de capsulite adesiva em pacientes com diabetes mellitus tipo 2. Métodos: Estudo caso-controle que avaliou a presença de fatores de risco levantados comparativamente em pacientes com diabetes mellitus tipo 2 e capsulite adesiva (casos) com pacientes com diabetes mellitus tipo 2 sem capsulite adesiva (controle). Os pacientes com histórico de trauma, cirurgia e outras doenças do ombro foram excluídos. A análise dos dados foi realizada usando a razão de chances e ajustada para fatores de confusão usando regressão logística múltipla. A probabilidade de rejeição da hipótese nula foi de 5%. Resultados: De um total de 119 pacientes, após os critérios de seleção, restaram 98 pacientes. Houve 23 casos de capsulite adesiva. Para a regressão logística multivariada, foram selecionados os seguintes fatores: estado civil casado, cor/raça não branca, renda mensal de 3 a 4 salários mínimos, escolaridade superior a 8 anos, tratamento com insulina e hemoglobina glicada fora da meta. A raça não branca demonstrou ser um fator de risco estatisticamente significativo para o desenvolvimento de capsulite adesiva com um intervalo de confiança de 95% de 1,061 a 1,556. Conclusão: A raça não branca é um fator de risco independente para o desenvolvimento de capsulite adesiva em pacientes diabéticos tipo 2, com um odds-ratio ajustado de 1,351.

Palavras-chave: ombro, capsulite adesiva, Diabetes Mellitus, estudos de caso-controle, fatores de risco.

RESUMEN

Introducción: Está descrita la asociación de trastornos musculoesqueléticos en pacientes diabéticos, entre ellos la capsulitis adhesiva, que compromete considerablemente su calidad de vida. Sin embargo, aún no se conocen bien los factores predictivos que justificarían el desarrollo de esta enfermedad en dicho grupo de individuos. Objetivo: Este estudio tuvo como objetivo identificar los factores de riesgo asociados al desarrollo de capsulitis adhesiva en pacientes con

diabetes mellitus tipo 2. Métodos: Estudio de casos y controles que evaluó la presencia de factores de riesgo planteados comparativamente en pacientes con diabetes mellitus tipo 2 y capsulitis adhesiva (casos) con pacientes con diabetes mellitus tipo 2 sin capsulitis adhesiva (control). Se excluyeron los pacientes con antecedentes de traumatismo, cirugía y otras enfermedades del hombro. El análisis de los datos se realizó mediante odds-ratio y se ajustó por factores de confusión mediante regresión logística múltiple. La probabilidad de rechazar la hipótesis nula fue del 5%. Resultados: De un total de 119 pacientes, tras los criterios de selección, quedaron 98 pacientes. Hubo 23 casos de capsulitis adhesiva. Para la regresión logística multivariante, se seleccionaron los siguientes factores: estado civil casado, color/raza no blanco, ingresos mensuales de 3-4 salarios mínimos, educación superior a 8 años, tratamiento con insulina y hemoglobina glicosilada fuera del objetivo. La raza no blanca resultó ser un factor de riesgo estadísticamente significativo para el desarrollo de capsulitis adhesiva, con un intervalo de confianza del 95% de 1,061 a 1,556. Conclusión: La raza no blanca es un factor de riesgo independiente para el desarrollo de capsulitis adhesiva en pacientes diabéticos de tipo 2, con una odds-ratio ajustada de 1,351.

Palabras clave: hombro, capsulitis adhesiva, Diabetes Mellitus, estudios de casos y controles, factores de riesgo.

1 INTRODUCTION

Adhesive capsulitis (AC) is a shoulder disease characterized by pain and decreased range of passive and active motions. It has an estimated prevalence between 2 and 5% of the general population and has a higher incidence in middle-aged women (FERNANDES, M. R., 2024). There is a direct relationship with some comorbidities such as diabetes mellitus, thyroid disease, heart disease, dyslipidemia and breast cancer (FERNANDES et al., 2023; WANG et al., 2013).

Type 2 diabetes mellitus (T2DM) is a chronic disease in which insulin resistance occurs in peripheral organs, in addition to the progressive deficiency in insulin secretion by the pancreas, which would lead to an increase in blood glucose levels (PETERSEN; SHULMAN, 2018; PETERSMANN et al., 2019). In the majority of cases, T2DM does not cause symptoms, and laboratory evaluation can be established through fasting blood glucose, oral glucose tolerance test and glycated hemoglobin (AMERICAN DIABETES ASSOCIATION PROFESSIONAL PRACTICE, 2022; COBAS et al., 2022).

The association with musculoskeletal disorders is described in diabetic patients, among them AC, which considerably compromises their quality of life (PARK et al., 2020). However, the predictive factors that would justify the development of AC in this group of individuals are not yet well defined in literature. Thus, the objective of the study was to identify the risk factors associated with the development of AC in patients with T2DM. The hypothesis was that patients

with glycated hemoglobin outside the target range would be the main risk factor in the appearance of this disease.

2 METHODS

2.1 STUDY DESIGN AND LOCATION

This is a case-control study carried out in patients with T2DM, treated at the endocrinology outpatient clinic of Clinical Medicine Department of a University Hospital. The study was approved by the Research Ethics Committee of Goiás Federal University Hospital (number: 5.178.256). All research participants signed a Free and Informed Consent Term.

2.2 ELIGIBILITY CRITERIA

Patients who were undergoing clinical treatment for T2DM were included, and we excluded those with: T2DM after the onset of AC; type 1 diabetes mellitus; thyroid diseases; history of trauma or other orthopedic diseases, such as rotator cuff tear, calcareous tendinitis, blocked dislocation, avascular necrosis of the humeral head, glenohumeral arthrosis and malunion of the proximal humerus; previous shoulder surgery; breast cancer and stroke.

The case group were patients with T2DM and AC. Those type 2 diabetic individuals from the same clinic with normal shoulder movements constituted the control group. AC was predefined as constant shoulder pain more than four weeks and decreased shoulder range of motion in all planes (anterior elevation, external rotation 0°/90° of abduction and internal rotation at 90° of abduction), after applying the exclusion criteria through shoulder subsidiary exams (x-rays and magnetic resonance imaging). So, this was the “diagnostic criteria” for adhesive capsulitis disease.

2.3 DATA COLLECTION

A sociodemographic and clinical questionnaire was applied to the patients in the study for nine months, providing data for both groups. Patients who reported shoulder pain were submitted to an evaluation of arc of motions using a digital goniometer (Kaptron, 360°), both active and passive, in anterior elevation, external rotation at 0°/90° of abduction and internal rotation at 90° of abduction.

The visual analogue scale (VAS) was used to characterize shoulder pain intensity at rest, movement and at night. Weight and height data were obtained using a digital anthropometric scale (LD 1050), while capillary blood glucose data were obtained using a digital blood glucose meter (Match II).

2.4 OUTCOME AND INDEPENDENT VARIABLES

The outcome was the presence of AC. The sociodemographic variables were: age (in years); gender (male/female); marital status (single/married/divorced/widowed); race (self-reported white/brown/ yellow/black and later categorized as white/non-white); monthly income (minimum wages); schooling (in years of formal study); Body Mass Index – BMI (kg/m²).

Clinical variables related to T2DM were: time since DM diagnosis (years); insulin use (yes/no); use of other medications to treat DM in addition to insulin (yes/no); types of drugs used (metformin/metformin + others/only others); practice of physical activity (yes/no); time of weekly practice of physical activity (minutes); nutritional monitoring (yes/no); capillary blood glucose - HGT (mg/dL); glycated hemoglobin (within target range/outside target range); glycated hemoglobin – HbA1C (%).

Glycated hemoglobin was considered within the target range, for patients aged 60 years or older who had HbA1C levels < 7.5%, as well as patients younger than 60 years who had HbA1C < 7.0%, in line with the official guideline of the Brazilian Society of Diabetes of 2022 (PITITTO et al., 2022).

As for AC, the following variables were collected: dominance (right-handed/left-handed); affected shoulder (right/left), onset time (months); pain intensity at rest, on movement and at night (VAS scale).

2.5 DATA ANALYSIS

The characterization of the sociodemographic and clinical profile of the patients was performed using absolute frequency, relative frequency for categorical variables; mean and standard deviation for continuous variables. Data parametricity was verified using the Kolmogorov-Smirnov test. The profile distribution of patients in the case and control groups was tested by applying Pearson's chi-square test and Student 's t-test.

Multiple logistic regression analysis was performed based on exploratory variables that presented $p < 0.20$ in the univariate analysis. The data were analyzed with the help of Statistical

Package for Social Science, 26.0. The probability of rejecting the null hypothesis was 5%

3 RESULTS

Of a total of 119 patients, six patients were excluded because they had type 1 diabetes mellitus; four for being at increased risk for diabetes Mellitus; three due to having thyroid diseases; five due to a history of trauma and three patients due to previous surgery on the shoulder or axillary emptying on the same affected side. Thus, 98 participants remained in the study, with 23 patients in the case group (23.5%) and 75 in the control group (76.5%).

Table 1: Characterization of the sociodemographic and clinical profile of type 2 diabetic patients's groups

	Case	Control	Total	p
Sociodemographic data				
	(Mean ± SD)	***(Mean ± SD)***	***(Mean ± SD)***	
Age	61.6 ± 9.9	61.3 ± 10.8	61.4 ± 10.5	0.912*
	n (%)	***n (%)***	***n (%)***	
Age group				
< 60 years	8 (34.8)	28 (37.3)	36 (36.7)	0.821**
≥ 60 years	15 (65.2)	47 (62.7)	62 (63.3)	
BMI				
Normal	7 (30.4)	22 (29.3)	29 (29.6)	
Overweight	8 (34.8)	20 (26.7)	28 (28.6)	0.752**
Obesity	8 (34.8)	33 (44.0)	41 (41.8)	
Gender				
Female	17 (73.9)	52 (69.3)	69 (70.4)	0.672**
Male	6 (26.1)	23 (30.7)	29 (29.6)	
Marital status				
Married	15 (65.2)	37 (49.3)	52 (53.1)	
Divorced	2 (8.7)	8 (10.7)	10 (10.2)	0.40**
Widower	2 (8.7)	18 (24.0)	20 (20.4)	
Single	4 (17.4)	12 (16.0)	16 (16.3)	
Race				
Non-white	18 (78.3)	47 (62.7)	65 (66.3)	0.163**
White	5 (21.7)	28 (37.3)	33 (33.7)	
Monthly income				
0	0 (0.0)	6 (8.0)	6 (6.1)	
1 to 2	21 (91.3)	62 (82.7)	83 (84.7)	0.37**
3 to 4	2 (8.7)	7 (9.3)	9 (9.2)	
Education				
Illiterate	0 (0.0)	8 (10.7)	8 (8.2)	
≤ 8 years	15 (65.2)	35 (46.7)	50 (51.0)	0.14**
> 8 years	8 (34.8)	32 (42.7)	40 (40.8)	
Clinical data				

Diagnostic time				
≤ 10 years	8 (34.8)	30 (40.0)	38 (38.8)	0.65**
> 10 years	15 (65.2)	45 (60.0)	60 (61.2)	
Insulin				
Yes	14 (60.9)	33 (44.0)	47 (48.0)	0.151**
No	9 (39.1)	42 (56.0)	51 (52.0)	
Other medications				
Yes	18 (78.3)	65 (86.7)	83 (84.7)	0.326**
No	5 (21.7)	10 (13.3)	15 (15.3)	
Types of medication				
Metformin	14 (77.8)	35 (53.8)	49 (59.0)	
Metformin + others	3 (16.7)	22 (33.8)	25 (30.1)	0.223**
Others	1 (5.6)	8 (12.3)	9 (10.8)	
Physical activity				
Yes	11 (47.8)	36 (48.0)	47 (48.0)	0.98**
No	12 (52.2)	39 (52.0)	51 (52.0)	
Duration of weekly physical activity				
< 150 minutes	3 (27.3)	16 (44.4)	19 (40.4)	0.31**
≥ 150 minutes	8 (72.7)	20 (55.6)	28 (59.6)	
Nutritional monitoring				
Yes	2 (8.7)	13 (17.3)	15 (15.3)	0.326**
No	21 (91.3)	62 (82.7)	83 (84.7)	
Glucose - HGT (mg/dL)				
< 180	11 (47.8)	46 (61.3)	57 (58.2)	0.25**
≥ 180	12 (52.2)	29 (38.7)	41 (41.8)	
Glycated hemoglobin				
Off target	16 (69.6)	40 (53.3)	56 (57.1)	0.17**
Within target	7 (30.4)	35 (46.7)	42 (42.9)	

*: Student 's t test; **: Pearson chi -square test; SD: standard deviation; BMI: body mass index; HGT: hemoglucotest
Source: Prepared by the authors

The sociodemographic and clinical data of the participants in the present study are demonstrated in table 1. There were 15 browns (83.3%); two blacks (11.1%) and one yellow (5.6%) categorized as non-white race on case group and 34 browns (72.3%); 11 blacks (23.4%) and two yellows (4.3%) on control group. There were more married than the others. There was a significant difference between the means of HbA1C between the case and control groups, with the mean of the case group (8.7 ± 2.0 %) higher than the mean of the control group (7.7 ± 1.6 %) (OR = 1.35; CI = 1.02-1.79; p = 0.038).

In the case group, 19 participants (82.6%) were right-handed and the right shoulder was affected in 14 (60.9%) of them. The average intensity of pain in the affected shoulder at rest, movement and at night by VAS was 2.96; 7.87 and 7.17, respectively. The averages of range of motion are 106.7° of anterior elevation, 50.9° of external rotation with 0°/abduction, 52.6° of external rotation with 90°/abduction and 41.8° of internal rotation.

Table 2: Final model of the univariate logistic regression analysis of the development of adhesive capsulitis in type 2 diabetic patients.

	Groups		OR	CI 95%	p
	Case	Control			
Sociodemographic data					
	n (%)	**n (%)**			
Age group					
< 60 years	8 (34.8)	28 (37.3)	1.00		
≥ 60 years	15 (65.2)	47 (62.7)	0.89	0.34 - 2.38	0.824
BMI					
Normal	7 (30.4)	22 (29.3)	1.00		
overweight	8 (34.8)	20 (26.7)	1.25	0.39 - 4.09	0.704
Obesity	8 (34.8)	33 (44.0)	0.60	0.20 - 1.85	0.384
Gender					
Female	17 (73.9)	52 (69.3)	1.25	0.44 - 3.58	0.679
Male	6 (26.1)	23 (30.7)	1.00		
Marital status					
Married	15 (65.2)	37 (49.3)	3.64	0.75 - 7.70	**0.108***
Divorced	2 (8.7)	8 (10.7)	2.25	0.27 - 8.92	0.267
Widower	2 (8.7)	18 (24.0)	3.00	0.47 - 9.03	0.444
Single	4 (17.4)	12 (16.0)	1.00		
Race					
Non-white	18 (78.3)	47 (62.7)	1.41	0.90 - 1.89	**0.172***
White	5 (21.7)	28 (37.3)	1.00		
Monthly income					
0	0 (0.0)	6 (8.0)	1.00		
1 to 2	21 (91.3)	62 (82.7)	0.77	0.52 - 1.24	0.212
3 to 4	2 (8.7)	7 (9.3)	1.63	0.89 - 2.97	**0.132***
Education					
Illiterate	0 (0.0)	8 (10.7)	1.00		
≤ 8 years	15 (65.2)	35 (46.7)	1.24	0.86 - 1.82	0.287
> 8 years	8 (34.8)	32 (42.7)	0.72	0.39 - 1.34	**0.170***
Clinical data					
Diagnostic time					
≤ 10 years	8 (34.8)	30 (40.0)	1.00		0.650
> 10 years	15 (65.2)	45 (60.0)	0.80	0.30 - 2.12	
Insulin					
Yes	14 (60.9)	33 (44.0)	1.98	0.76 - 5.13	**0.160***
No	9 (39.1)	42 (56.0)	1.00		
Other medications					
Yes	18 (78.3)	65 (86.7)	0.55	0.17 - 1.82	0.322
No	5 (21.7)	10 (13.3)	1.00		
Types of medication					
Metformin	14 (77.8)	35 (53.8)	1.15	0.94 - 1.39	0.220
Metformin + others	3 (16.7)	22 (33.8)	1.34	0.98 - 1.81	0.214
Others	1 (5.6)	8 (12.3)	1.00		
Physical activity					
Yes	11 (47.8)	36 (48.0)	1.00		
No	12 (52.2)	39 (52.0)	0.99	0.39 - 2.53	0.981

Time of weekly physical activity					
< 150 minutes	3 (27.3)	16 (44.4)	0.47	0.11 - 2.06	0.312
≥ 150 minutes	8 (72.7)	20 (55.6)	1.00		
Nutritional monitoring					
Yes	2 (8.7)	13 (17.3)	1.00		
No	21 (91.3)	62 (82.7)	2.20	0.45 - 10.57	0.324
Glucose - HGT (mg/ dL)					
< 180	11 (47.8)	46 (61.3)	1.00		
≥ 180	12 (52.2)	29 (38.7)	1.73	0.67 - 4.43	0.252
Glycated hemoglobin					
Off target	16 (69.6)	40 (53.3)	2.00	0.73 - 5.42	**0.173***
Within target	7 (30.4)	35 (46.7)	1.00		

OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index; HGT: hemoglucotest
*: p<0.05
Source: Prepared by the authors

In the univariate analysis, the variables married marital status (OR = 3.64; p = 0.108); non-white race (OR = 1.41; p = 0.172); insulin use (OR = 1.98; p=0.160); glycated hemoglobin outside the target range (OR = 2.00; p = 0.170) and monthly income of 3 to 4 minimum wages (OR = 1.63; p = 0.132) had p<0.20. The education variable with more than eight years of formal study also presented p<0.20, but as protection factor (OR = 0.72; p = 0.170). Physical activity and nutritional monitoring didn't present p<0.20 (table 2).

Table 3: Final multivariate logistic regression model of the development of adhesive capsulitis in type 2 diabetic patients

	Wald	**OR**	**CI 95%**		**p**
			Lower	**Upper**	
Marital status					
Married	1.94	3.345	0.706	15.468	0.325
Race					
Non-white	2.97	1.351	1.061	1.556	**0.042***
Monthly income					
3 to 4 minimum wages	0.47	0.710	0.250	2.010	0.343
Education					
> 8 years	0.02	0.701	0.232	1,233	0.231
Insulin					
Yes	1.20	1.123	0.911	1.612	0.512
Glycated hemoglobin					
Off target	0.13	1.231	0.546	2.11	0.151

r2: 0.24; OR: odds ratio; 95% CI: 95% confidence interval
*: p<0.05
Source: Prepared by the authors

In the logistic regression model highlighted in table 3, non-white race was the only risk factor for the development of AC in patients with T2DM (OR= 1.351; 95% CI = 1.061-1.556; p = 0.042).

4 DISCUSSION

Non-white race was the only risk factor for the development of AC in patients with type 2 diabetes mellitus (OR= 1.351; 95% CI = 1.061-1.556; p = 0.042). The hypothesis that patients with glycated hemoglobin outside the target range would be a risk factor in the onset of AC in T2DM was not confirmed, even with a difference in baseline data of the means of glycated hemoglobin between the case (8.7 ± 2.0 %) and control (7.7 ± 1.6%) (OR = 1.35; CI = 1.02-1.79; p = 0.038), probably due to a type II error.

It is very difficult to define race, but this predictive variable, in the present study, was collected in a self-reported way, in accordance with the classification based on color, used by the Brazilian Institute of Geography and Statistics, being later categorized as white and non-white (brown, yellow and black) (BAQUI et al., 2020; PERES et al., 2021). Brazilian browns have a diversity of ethnic origins and together with yellow (East Asia) and black represent about 57% of the Brazilian population. It is interesting, therefore, that our study on AC/diabetic patients and its subsequent conclusion was carried out in a country with a complex social and ethnic composition (BAQUI et al., 2020).

Identifying risk factors for a disease is important to increase knowledge of its cause.3 There is an understanding that the diabetic population is five times more likely to develop AC, but the influence of race as a predictive factor for such emergence is still little studied (ZREIK NASRI, 2016). Kingston et al. (201)8 corroborated our findings, as they pointed out that black/african-american race and Latino ethnicity were significantly associated with a higher prevalence of AC when compared to controls.

On the other hand, Rizk and Pinals (1984) described a higher frequency of AC in the caucasian population, although 24% of their patients were from the black race. Wang et al.3 identified a possible racial predilection for the development of AC, although the mechanism of this association remains open to speculation. Malavolta et al. (2018) sought to associate specific ethnicities in the development of AC, and demonstrated that the Asian was an independent risk factor for the onset of the condition, with an odds-ratio adjusted for gender and diabetes mellitus of 3.6.

There is strong evidence that skin color (race) affects outcomes for individuals with diabetes mellitus. Campbell et al. (2012), in a systematic review of the literature, demonstrated that African-Americans, Hispanics and Asian-Americans had higher levels of glycosylated hemoglobin compared to non-Hispanic whites. Kirk et al. (2008), in a meta-analysis, also found similar results, indicating a higher HbA1c for African-Americans.

Egede et al. (2010) demonstrated longitudinal differences in veterans with T2DM, and the black race had a higher HbA1c level and worse glycemic control compared to the white race. Lynch et al. (2014) also found that the mean HbA1c was higher in the black race, in non-Hispanic adults. All of these studies have demonstrated differences in glycemic control by race and may indicate evidence of disparate care across population groups (CAMPBELL et al., 2012; EGEDE et al., 2010; KIRK et al., 2008; LYNCH et al., 2014). Also, some reviews have discussed imbalance in the prevalence of diabetes and diabetes-related complications by racial and ethnic groups in the USA (ELHUSSEIN et al., 2022; EZZATVAR et al., 2021; HASSAN et al., 2023; WANG, Li et al., 2021).

Thus, the process of glycosylation, a common biochemical abnormality in Diabetes Mellitus (DIABETES CONTROL AND COMPLICATIONS TRIAL RESEARCH GROUP, 1993), may result in the accumulation of cross-links between protein molecules causing joint stiffness. AC may be the result of this bad glycemic control (higher in non-white races) or long-term high glycaemia (GREEN et al., 2024), similar to nephropathy, neuropathy and diabetic retinopathy (WU et al., 2014), but previous studies, as well as the present research, showed no correlation between the onset of the disease and the HbA1c rate, which is the main marker of glycemic control, as a static mean over the course of three months. Chan et al. (2017), on the other hand, when using HbA1c cumulatively, demonstrated that there was association with an increase in the prevalence of AC, but used a variable not validated in the literature.

The present study, although it contributes to the understanding of possible factors associated with the development of AC in patients with T2DM, has its limitations. This is a case-control study, with patients enrolled consecutively, and thus susceptible to memory and selection bias, not being able to point out any relation of cause and effect. Again, we have to point out the possibility of a false negative result, because our hypothesis about glycated hemoglobin outside the target range as a main risk factor in the onset of AC in T2DM was not confirmed, probably by type 2 error.

It's important to mention that we had a small sample size on case group, because our exclusion criteria were very broad in order to not create bias and to investigate only type 2 diabetic patients without other comorbities which are also associated with AC. We looked for

answers about risk factors in this specific cenario and a lot of individuals with the AC disease couldn't be captured. So, homogeneous Type 2 diabetic groups were formed, except for the presence or not of AC, to respond the guiding question of the study.

On the other hand, the study has its strengths. We can highlight that the study design (case-control study) used is an excellent option to assess possible risk factors in the development of a disease, as it's employed in rare diseases with small numbers of individuals. In addition, the sample respected a minimum of three controls from the same clinic, for each eligible case, and multivariate analysis was used to eliminate possible confounding factors, allowing us to highlight race as an isolated predictive factor, even in this first moment, like few studies. There was also a careful attention to the selection of patients so that other shoulder diseases or other forms of AC were appropriately excluded.

It is noteworthy that our result was a surprise for the authors, but the study is one of the few in science that highlight race as a risk factor in the development of AC and this should be taken into account in a possible investigation of patients with stiff shoulder. Future prospective cohort designs will be essential in diabetic patients, grouping them by race, with the onset of AC as the primary outcome. Furthermore, the same study design in a multicentric way will be important to corroborate our current result.

5 CONCLUSION

This case-control study demonstrates that after the inclusion of various sociodemographic and clinical variables with univariate and multivariate models, the "non-white race" is a risk factor for the development of adhesive capsulitis on type 2 diabetic patients, with an adjusted odds-ratio of 1.351 (95% CI=1.061 - 1.556; p = 0.042).

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