


Interactive associations of sex and hyperlipidemia with calcific tendinitis of the shoulder in Taiwanese adults

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Abstract

Calcific tendinitis (CT) of the shoulder is a painful disorder usually identified in individuals aged 40 and 60 years. The estimated global prevalence of CT is 2.7% to 36%. We examined the association of hyperlipidemia and sex with CT of the shoulder using Taiwan Biobank (TWB) and the National Health Insurance Research Database (NHIRD).

Data were available for 9903 TWB participants who were recruited between 2008 and 2015. We used multiple logistic regression analysis to estimate the odds ratios (OR) and 95% confidence intervals (CI) for CT of the shoulder.

Overall, 1564 women, and 1491 men were identified with hyperlipidemia. Women, compared to men, had higher odds of CT of the shoulder (OR, 1.53; 95% CI, 1.08–2.16). Hyperlipidemia, compared to no hyperlipidemia, was associated with an increased risk of CT (OR, 1.40; 95% CI, 1.02–1.93). The test for interaction was significant for sex and hyperlipidemia ($P = .006$). After stratification, the odds ratio for CT was 1.95 (95% CI, 1.30–2.92) in women and 0.82 (95% CI, 0.48–1.39) in men, respectively. Compared to men with no hyperlipidemia, the odds ratio was 0.86 (95% CI, 0.53–1.38) for men with hyperlipidemia and 2.00 (95% CI, 1.29–3.10) for women with hyperlipidemia.

Importantly, our findings indicated that the risk for CT of the shoulder was higher among Taiwanese women with hyperlipidemia. However, CT risk among their male counterparts with hyperlipidemia was not significant.

Abbreviations: BMI = body mass index, CI = confidence interval, CT = calcific tendonitis, EHR = electronic health records, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification code, MOST = Ministry of Science and Technology, NHIRD = National Health Insurance Research Database, OR = odds ratio.

Keywords: calcific tendinitis, hyperlipidemia, shoulder

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1. Introduction

Calcific tendinitis of the shoulder, also called calcifying tendinosis is a painful condition commonly identified in individuals aged 40 and 60 years.^[1] It regularly affects the right shoulder and the most common location includes the supraspinatus tendon.^[2] The phase processes associated with CT include the pre-calcific (characterized by cellular changes), calcific stage (characterized by calcium deposition), and the resorptive (characterized by pain) stage.^[3] Recent findings have suggested a 2-to-8-fold increase in blood vessel growth, neovascularization (a nerve growth), macrophages, and mast cells among patients with CT.^[4] The disease prevalence ranges from 2.7% to 36%.^[3,5–8] This has so far been widely reported among Caucasians, especially women between the ages of 30 and 50.^[9] The aetiopathogenesis of the disease is yet to be fully understood even though different theories have been suggested.^[9,10] Treatment of this disorder usually involves physiotherapy and anti-inflammatory medications.^[11] Nevertheless, the treatment options have not been proven to be satisfactory enough^[5] even though several cases are believed to resolve spontaneously.^[11]

Factors previously linked to CT include metabolic diseases, genetic predisposition, and abnormal activity of the thyroid gland.^[1] Hyperlipidemia is one of the extrinsic factors that have been adversely associated with tendinopathy^[12] and its treatment.^[13] Associations of hyperlipidemia with CT have been described elsewhere^[14] but not in Taiwan.

The female sex appears to be at a greater risk of developing CT of the shoulder.^[1,15] Besides, a clinical and radiographic study has indicated that sex and age distribution of the disease differs among Southeast Asians and Western populations.^[16] However, as far as we know, there are few data on gender and CT of the shoulder, especially in Asia and Taiwan in particular. In light of this, we examined the interactive association between sex, hyperlipidemia, and CT of the shoulder among Taiwan Biobank participants who were recruited between 2008 and 2015.

2. Materials and methods

2.1. Data source

Participants phenotypic data were collected from the Taiwan Biobank database, while data on calcific tendinitis and hyperlipidemia diagnoses between 1998 and 2015 were collected from the National Health Insurance Research Database (NHIRD). Through the Health and Welfare Data Science Center (HWDC) repository, data from both sources were linked using personal identification numbers. The present study was approved by the Institutional Review Board of Chung Shan Medical University (Approval No. CS2-16114). All experiments were performed following the relevant guidelines and regulations. Written informed consent was obtained from each participant prior to attending the biobank assessment center.

2.2. Study participants

Study data were from 9903 participants that were recruited into TWB between 2008 and 2015 and whose data were linked to the NHIRD using personal identification numbers. Participants had provided blood samples for DNA and completed questionnaires covering a wide range of medical, social, and lifestyle information. In the Biobank cohort ($n=9903$), we excluded participants with incomplete data ($n=13$). Of the remaining cohort, 214 individuals were identified with CT of the shoulder. These individuals, together with 9676 control individuals were eligible for inclusion. Calcific tendinitis of the shoulder was diagnosed based on ICD-9-CM code 726.11 while hyperlipidemia was identified based on either two-outpatient visits or one-time hospitalization with reported ICD-9-CM code 272.

2.3. Statistical analysis

Relationships between categorical data were tested using the Chi-Squared test. We used multiple logistic regression analysis to test the association of CT of the shoulder with sex and hyperlipidemia. Adjusted variables included educational level, smoking, drinking, physical activity, body mass index, tea consumption, coffee drinking, vegetarian diet, diabetes (ICD-9-CM: 250), and hypertension (ICD-9-CM: 401–405). The ORs and 95% CI were estimated. We performed statistical analyses using the statistical analysis system (SAS) 9.4 software (SAS Institute, Cary, NC).

3. Results

Eligible participants included 5316 women and 4574 men (Table 1). In total, 1564 women and 1491 men were identified with hyperlipidemia. Women, compared to men had higher odds of CT of the shoulder (OR, 1.53; 95% CI, 1.08–2.16) as shown in Table 2. Hyperlipidemia, compared to no hyperlipidemia was associated with an increased risk of CT of the shoulder

Table 1

Demographic characteristics of study participants according to sex.

	Women		Men		P value
	N	%	N	%	
CT shoulder					.0130
No	5183	97.50	4493	98.23	
Yes	133	2.50	81	1.77	
Age (years)					.0680
30–39	1270	23.89	1131	24.73	
40–49	1456	27.39	1188	25.97	
50–59	1552	29.19	1284	28.07	
60–70	1038	19.53	971	21.23	
Educational level					<.0001
Elementary school	520	9.78	231	5.05	
Junior/senior high school	2475	46.56	1649	36.05	
University above	2321	43.66	2694	58.90	
Smoking					<.0001
No	5092	95.79	2583	56.47	
Yes	224	4.21	1991	43.53	
Alcohol intake					<.0001
No	5197	97.76	3666	80.15	
Yes	119	2.24	908	19.85	
Physical activity					.0070
No	3145	59.16	2584	56.49	
Yes	2171	40.84	1990	43.51	
BMI (kg/m ²)					<.0001
<18.5	202	3.80	52	1.14	
18.5–23.9	3047	57.32	1642	35.90	
24–26.9	1257	23.65	1699	37.14	
≥27	810	15.24	1181	25.82	
Tea consumption					<.0001
No	3715	69.88	2498	54.61	
Yes	1601	30.12	2076	45.39	
Coffee drinking					<.0001
No	3509	66.01	3211	70.20	
Yes	1807	33.99	1363	29.80	
Vegetarian diet					<.0001
No	4667	87.79	4194	91.69	
Yes	649	12.21	380	8.31	
Diabetes					.0010
No	4611	86.74	3864	84.48	
Yes	705	13.26	710	15.52	
Hypertension					<.0001
No	4228	79.53	3281	71.73	
Yes	1088	20.47	1293	28.27	
Hyperlipidemia					.0010
No	3752	70.58	3083	67.40	
Yes	1564	29.42	1491	32.60	

CT shoulder = calcifying tendinitis of the shoulder.

(OR, 1.40; 95% CI, 1.02–1.93). We also found that older age was a risk factor for CT. Compared to the 30–39-year age group, the odds ratio for CT was 1.88 (95% CI 1.08–2.16) in the 40–49-year age group, 4.03 (95% CI, 2.24–7.25) in the 50–59-year age group, and 5.59 (95% CI, 3.02–10.35) in the 60–70-year age group, respectively. We found an interaction between sex and hyperlipidemia (P for interaction = .006). After stratification, the OR for CT was 1.95 (95% CI, 1.30–2.92) in women and 0.82 (95% CI, 0.48–1.39) in men, respectively (Table 3). For the 50–59-year age group, the OR for CT was 7.57 (95% CI, 2.91–19.67) in women and 1.80 (95% CI, 0.79–4.09) in men. In the 60–70-year age group, the OR was 7.55 (95% CI, 2.79–20.49) in women and 4.52 (95% CI, 2.00–10.24) in men. Compared to

Table 2
Risk of calcific tendinitis in study participants.

	OR	95% CI	
Sex (ref: men)			
women	1.53	1.08	2.16
Hyperlipidemia (ref: No)			
Yes	1.40	1.02	1.93
Age (ref:30–39)			
40–49	1.88	1.01	3.51
50–59	4.03	2.24	7.25
60–70	5.59	3.02	10.35
Educational level (ref: Elementary school)			
Junior/Senior high school	1.38	0.85	2.25
University and above	1.74	1.05	2.88
Smoking (ref: No)			
Yes	0.87	0.56	1.35
Alcohol intake (ref: No)			
Yes	1.32	0.80	2.17
Physical activity (ref: No)			
Yes	1.11	0.83	1.49
BMI (ref:18.5–23.9)			
<18.5	0.67	0.21	2.15
24–26.9	1.27	0.93	1.75
≥27	1.17	0.80	1.74
Tea consumption (ref: No)			
Yes	0.60	0.44	0.84
Coffee drinking (ref: No)			
Yes	0.90	0.66	1.23
Vegetarian diet (ref: No)			
Yes	0.70	0.41	1.19
Diabetes (ref: No)			
Yes	1.31	0.93	1.86
Hypertension (ref: No)			
Yes	0.98	0.71	1.36

OR = odds ratio; BMI = body mass index.

men with no hyperlipidemia, the OR was 0.86 (95% CI, 0.53–1.38) in men with hyperlipidemia, 1.04 (95% CI, 0.68–1.61) in women with no hyperlipidemia, and 2.00 (95% CI, 1.29–3.10) in women with hyperlipidemia (Table 4).

4. Discussion

In the current study with 214 cases of CT of the shoulder and 9676 control individuals, we found that

1. consistent with previous findings,^[1,15,17] women, compared to men were at greater risk of developing CT.

Table 3
Risk of calcific tendinitis under stratification by sex.

	Women			Men		
	OR	95% CI		OR	95% CI	
Hyperlipidemia (ref: No)						
Yes	1.95	1.30	2.92	0.82	0.48	1.39
Age (ref:30–39)						
40–49	2.46	0.89	6.82	1.66	0.74	3.71
50–59	7.57	2.91	19.67	1.80	0.79	4.09
60–70	7.55	2.79	20.49	4.52	2.00	10.24

Adjusted for educational level, smoking, alcohol intake, physical activity, body mass index, tea consumption, coffee drinking, vegetarian diet, diabetes, and hypertension. Sex*hyperlipidemia=0.006.

Table 4
Risk of calcific tendinitis based on sex and hyperlipidemia.

	OR	95% CI	
Sex and HL (ref: Men with no HL)			
Men with HL	0.86	0.53	1.38
Women with no HL	1.04	0.68	1.61
Women with HL	2.00	1.29	3.10
Age (ref:30–39)			
40–49	1.89	1.02	3.53
50–59	4.02	2.24	7.23
60–70	5.45	2.95	10.08

HL = hyperlipidemia. Adjusted for educational level, smoking, drinking, physical activity, body mass index, tea consumption, coffee drinking, vegetarian diet, diabetes, and hypertension.

2. Hyperlipidemia, compared to no hyperlipidemia was associated with an increased risk of CT of the shoulder.
3. There was an interaction between sex and hyperlipidemia on CT risk.

Further analyses of our data provided strong evidence of an association between CT of the shoulder and hyperlipidemia among Taiwanese women.

It is not fully understood why this association is stronger in women. However, estrogen or thyroid disorders appear to play an essential role in its pathophysiology.^[18] Previous studies cited above have suggested a higher risk of CT of the shoulder among women of other ethnicities. However, they did not include hyperlipidemia in their analyses models.

Hyperlipidemia is one of the metabolic disorders previously associated with tendinopathies even though the pathophysiology is not clearly understood.^[19] According to previous findings, mechanical properties of tendons are affected by lipids that pile up within the extracellular matrix when an individual develops hyperlipidemia.^[14,20]

So far, few studies have attempted to assess correlations between hyperlipidemia and the development of CT of the shoulder. In a longitudinal follow-up study, Lin and his colleagues reported that hyperlipidemia was an independent risk factor for the occurrence of CT among Taiwanese individuals.^[21] In a separate study, hyperlipidemia was negatively associated with the treatment of tendinopathy among Korean individuals.^[13] In contrast, previous works in India and Italy have shown no association between hyperlipidemia and CT of the shoulder.^[22,23] Despite the inconsistency in these findings, our study has contributed more knowledge on the relationship between hyperlipidemia and CT of the shoulder.

Age is one of the risk factors for CT of the shoulder. As stated earlier, CT of the shoulder is more common among individuals aged 40–60 years. In this study, we found that the average age of Taiwanese individuals who were diagnosed with CT was 49 years. We also found that disease risk increased with older age. For instance, CT risk was greater among adults aged 50 to 59 (OR, 4.03; 95% CI, 2.24–7.52) and 60 to 70 (OR, 5.59; 95% CI, 3.02–10.35) years compared to those aged 30 to 39 years.

Associations have also been reported between diabetes and CT.^[24,25] Contrarily, our results failed to show an association between both conditions. Further studies will be required to broaden our knowledge in this area. According to findings from a previous study, not much is known about the pathogenesis of diabetic tendinopathy.^[26] However, tendon injury in diabetes patients has been linked to advanced glycation end products (AGEs).^[27,28]

The strength of this study is the large sample size, made possible through the use of electronic health records (EHR) data, which presumably provides the statistical power to examine sex × hyperlipidemia interaction in association with CT. According to previous findings, people who have worked 25 to 35 years may develop CT.^[29] However, information on employment or labor force status was not available in our data sources. Besides, data on common shoulder injuries were not available in the Taiwan Biobank database.

5. Conclusions

Taken together, our primary findings indicated that the risk of CT of the shoulder was higher in Taiwanese women with hyperlipidemia. The risk among their male counterparts with hyperlipidemia was not significant. Nevertheless, men aged 60 to 70 years were more likely to develop CT relative to those aged 30 to 39 years. We hope that these findings would improve knowledge about sex-specific associations between calcific tendinitis and risk factors, including hyperlipidemia.

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Author contributions

Contributions: CCL, ONN, CLS, SYH, DMT, and YPL conceived and designed the study. SYH, ONN, DMT, and YPL analyzed and interpreted data. CCL and CLS drafted the manuscript. All authors critically reviewed and approved the final version of the manuscript.

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