

The Effect of Hypercholesterolemia on Rotator Cuff Disease

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Abstract

Background The causes of rotator cuff tendon rupture are multifactorial and still unclear. Intrinsic and extrinsic factors have been implicated as predisposing risk factors for rotator cuff rupture. Previous studies have suggested a relationship between elevated serum lipid profiles and tendon ruptures, although not rotator cuff tears specifically.

Questions/purposes We therefore asked whether patients with rotator cuff tears were more likely to have higher levels of hypercholesterolemia than patients with shoulder pain but without tears.

Methods We prospectively collected serum cholesterol and lipid profiles on two age-matched populations of patients; 74 (mean age, 66.3 years) had ruptures of their rotator cuff tendons, whereas a control group of 73 patients (mean age, 67.4 years) were seen for nontendon-related shoulder complaints.

Results Total cholesterol, triglycerides, and low-density lipoprotein cholesterol concentrations of the patients with rotator cuff tendon tears were higher, and their high-density lipoprotein cholesterol showed a trend to being lower than the control group. Forty-seven of 74 patients (63%) with

rotator cuff tears had an elevated serum cholesterol (total cholesterol greater than 240 mg/dL) as compared with an overall rate of 28% in our control group.

Conclusions Patients with rotator cuff tears were more likely to have hypercholesterolemia when compared with the control group.

Clinical relevance Measurement of serum cholesterol in patients presenting with torn rotator cuff tendons should be considered in patients whose cholesterol profiles are unknown. Future consideration of drug treatment may reduce risk for future tendon degeneration, as well as improve quality of life and reduce mortality.

Level of Evidence Level II, prognostic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Rotator cuff injuries account for a substantial portion of soft tissue injuries in the upper extremity. Approximately 23% of individuals older than age 50 have a rotator cuff tear [16, 18]. Among the tendons of the shoulder's rotator cuff, the supraspinatus tendon is most commonly injured. Full-thickness tears most commonly result from avulsion of the cuff tendon from its insertion, which requires tendon-to-bone repair [6].

The causes of rotator cuff tendon ruptures are multifactorial and still unclear. Poor vascular supply and degenerative changes are believed to play important roles in tendon ruptures [6]. Intrinsic [10] and extrinsic [2] factors have been implicated as predisposing risk factors for rotator cuff rupture. Extrinsic factors include impingement and demographic factors and those intrinsic to the cuff include age-related degeneration, hypovascularity,

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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inflammation, and oxidative stress, among others. Although chronic degenerative changes appear responsible for the majority of spontaneous acute rotator cuff tears, several studies have also suggested a relationship between elevated serum lipid profiles and tendon ruptures, although not rotator cuff tears specifically [9, 11, 19].

Cholesterol occurs in two forms: low-density lipoprotein (LDL, the so-called “bad” cholesterol) and high-density lipoprotein (HDL, the so-called “good” cholesterol). Diet, exercise, smoking, alcohol, genetics, and certain illnesses can influence the levels of both types of cholesterol [1]. The National Cholesterol Education Program defines hypercholesterolemia (also known as high cholesterol) as a blood cholesterol concentration greater than or equal to 240 mg/dL with concentrations between 200 mg/dL and 239 mg/dL considered borderline high (they define optimal cholesterol levels as below 200 mg/dL) [5]. The National Center for Health Statistics in 2005 reported that the prevalence of hypercholesterolemia in the United States (from 1999–2002) was 17% for both genders [14]. Between 1999 and 2002, the populations with the highest cholesterol levels were women 65 to 74 years of age (32.3%), men 45 to 54 years of age (23.6%), and white women (19.1%).

We therefore asked whether patients with rotator cuff tears would more likely have higher levels of hypercholesterolemia than patients with shoulder pain but without tears.

Patients and Methods

We prospectively obtained serum lipid concentrations in 160 patients seen between January 2005 and January 2008 in an outpatient tertiary care clinic for shoulder pain necessitating surgery. Eighty patients presented with full-thickness rotator cuff tears (experimental group), whereas 80 patients presented with complaints referable to the shoulder with a normal rotator cuff (control group). We followed a strict inclusion and exclusion criteria. Inclusion criteria were: (1) all patients with clinically documented surgically verified primary musculoskeletal diagnoses referable to the shoulder; (2) the experimental group had a fellowship-trained shoulder surgeon (JAA) confirm a full-thickness rotator cuff tear on examination, MRI, and

surgery; and (3) the control group had one of the authors (JAA) confirm an intact rotator cuff on examination, MRI, and surgery. Exclusion criteria were: (1) previous surgery on the affected shoulder; (2) smokers (current or past); (3) history of shoulder infection; (4) inflammatory arthritis; (5) alcoholism; (6) patients younger than age 21 years; (7) chronic steroid use; (8) chronic floxacillin use; (9) calcific tendonitis; (10) frozen shoulder; or (11) patients who did not undergo surgical treatment. Ninety patients were men and 70 were women with an average age of 66.9 years (range, 21–93 years). The dominant extremity was involved in the chief complaint of 103 of 180 patients (57%). Thirteen patients (seven patients in our control group and six in our experimental group) were excluded from the study because they did not meet our inclusion/exclusion criteria. This left an experimental group of 74 subjects (44 men and 30 women) whose mean age was 66.1 years and mean body mass index was 30.3 kg/m². The control group consisted of 73 subjects (39 men and 34 women) whose mean age was 67.2 years and mean body mass index was 28.7 kg/m². We had prior Institutional Review Board approval.

In the experimental group, the rotator cuff tendon ruptures were diagnosed from the history, physical examination maneuvers, and MRI. The ruptures were right-sided in 44 of 74 patients (60%) and left-sided in 30 of 74 patients (40%). None of the patients experienced a rotator cuff rupture previously. Fifteen of 74 patients (20%) ruptured their rotator cuff while playing sports, 21 of 74 patients (28%) ruptured their rotator cuff after a fall or trauma, and 38 of 74 patients (52%) could not recall a specific injury to their shoulder, but rather they reported the insidious onset of shoulder pain. All patients included in the experimental group had a full-thickness rotator cuff tear of at least one tendon; 46 of 74 patients (62%) had a single-tendon rotator cuff tear, 22 of 74 patients (30%) had a two-tendon rotator cuff tear, and six of 74 patients (8%) had a rotator cuff tear involving more than two tendons. Twenty-one of 74 patients (29%) were on medication for hypercholesterolemia. Fifty-seven of 74 patients (74%) were white, 10 of 74 patients 14% were black, and seven of 74 patients 9% were other (Table 1).

The control group’s chief complaint was referable to the right shoulder in 40 of 73 patients (55%) and the left

Table 1. Experimental group data

Cause of tear	Percent	Number of rotator cuff tendons torn	Percent	Race	Percent	Side injured	Percent
Playing sports	20%	1	62%	White	77%	Right	60%
Trauma/fall	28%	2	30%	Black	14%	Left	40%
Did not remember	52%	➤ 2	8%	Other	9%		

Table 2. Control group data

Diagnosis	Percent	Race	Percent	Injured side	Percent
Subacromial bursitis	8%	White	70%	Right	55%
Acromioclavicular arthritis	7%	Black	15%	Left	45%
Glenohumeral arthritis	23%	Other	15%		
Proximal humerus fracture	21%				
Superior labral tear	9%				
Glenohumeral instability	14%				
Clavicle fracture	8%				
Avascular necrosis	4%				
Spinoglenoid notch cysts	3%				
Miscellaneous tumors	3%				

shoulder in 33 of 74 patients (45%). The diagnoses noted in the control group were made based on history, physical examination, MRI and radiographs, and surgical findings. They consisted of subacromial bursitis (six), acromioclavicular arthritis (five), glenohumeral arthritis (17), proximal humerus fracture (15), superior labral tear (seven), glenohumeral instability (10), clavicle fracture (six), avascular necrosis (three), spinoglenoid notch cysts (two), and miscellaneous tumors (two). Fifteen of 73 patients (21%) in the control group were on medication for hypercholesterolemia. Fifty-one of 73 patients (70%) were white, 11 of 73 patients (15%) were black, and 11 of 73 patients (15%) were other (Table 2).

We recorded data on age, race, gender, height, weight, dominant extremity, affected arm, mechanism of injury, date of injury when applicable, medical history, surgical history, social history, medications used, physical examination findings, MRI findings recorded by the senior author (JAA) and the radiologist report, surgical findings, and the final diagnosis reached.

Our serum lipid evaluation measured the concentrations of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Blood samples for serum lipid evaluation were obtained from all patients within 30 days of their diagnosis.

We examined the tearing of the rotator cuff as a function of the lipid panel. Data including the age of the patient, gender, and body mass index, in the presence or absence of an intact rotator cuff, were all tested for statistical association to minimize the possibility of having a confounding variable and to verify that our experimental and control groups were equivalent. For the data, the associations among the presence of cuff tears, HDL, LDL, TG, TC,

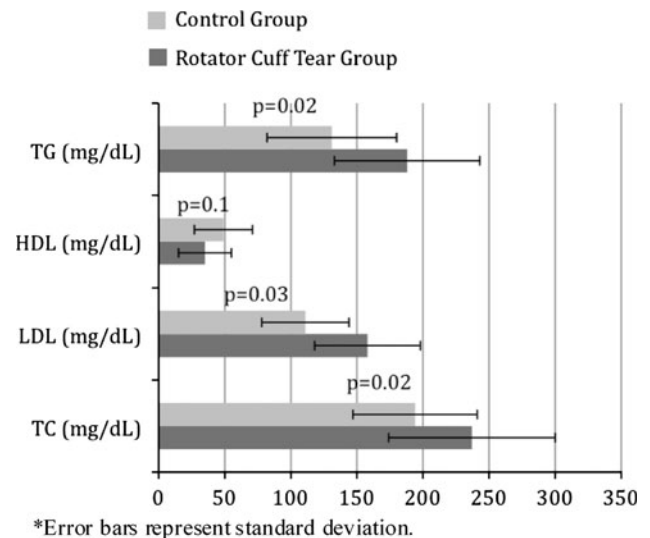


Fig. 1 Values measured in (mg/dL) for total cholesterol (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglyceride (TG) for our experimental and control groups are shown. Patients with rotator cuff tears had a higher incidence of hypercholesterolemia as compared to patients with normal rotator cuff tendons.

body mass index, gender, and age were tested for significance with the nonpaired sample t-test, regression analysis, and multivariate analysis of variance. SPSS (Version 15.0.1; Chicago, IL) was used for all statistical analyses.

Results

Patients with rotator cuff tears had a higher incidence ($p = 0.02$) of hypercholesterolemia with a TC of 237 mg/dL (range, 117–340 mg/dL) as compared with patients with normal rotator cuff tendons with a TC of 194 mg/dL (range, 113–311 mg/dL) (Fig. 1). Triglyceride and LDL-C concentrations of the patients with rotator cuff tendon tears were higher ($p = 0.02$ and $p = 0.03$, respectively), with HDL-C levels trending ($p = 0.1$) lower. Forty-seven of 74 patients (63%) with rotator cuff tears had elevated serum cholesterol (TC greater than 240 mg/dL) as compared with an overall rate of 28% in our control group. We found that 17 of 22 patients (77%) with two-tendon rotator cuff tears had elevated serum cholesterol levels. We found no association with age, gender, or body mass index and rotator cuff integrity/tears in either of our two groups.

Discussion

The causes of rotator cuff tendon ruptures are multifactorial and still unclear. Intrinsic and extrinsic factors have

been implicated as predisposing risk factors for rotator cuff rupture. Several studies have suggested a relationship between elevated serum lipid profiles and tendon ruptures, although not rotator cuff tears specifically. We asked whether patients with rotator cuff tears were more likely to have higher levels of hypercholesterolemia than patients with shoulder pain but without tears.

This study has several limitations. First, we obtained no histologic/pathologic correlations for cholesterol deposition in patients who underwent surgery for their respective diagnosis. Based on ongoing animal studies, future Institutional Review Board approval may be facilitated by our preliminary findings to allow for such an evaluation. Second, one can argue the study population had a selection bias because the patients were seen at a tertiary referral center in an urban setting and may not be representative of the general US population (ie, ethnicity, race, and gender bias). We presume a future multicenter study would help minimize this bias. Third, we made no attempt to try to assess the role of regular exercise or activity level as a variable in hypercholesterolemia and/or tendon disease. This would be difficult to quantify except in a prospective followup study.

We found that patients with rotator cuff tears would more likely have higher levels of cholesterol than patients with shoulder pain but without tears. This finding is not surprising given high serum TC concentrations can contribute to the development of Achilles tendon ruptures [11]. Mathiak et al. reported that 83% of patients with Achilles tendon ruptures had elevated serum cholesterol levels; interestingly, only 19% were aware of their disease [8]. Klemp et al. reported 38% of patients with juvenile familial hypercholesterolemia had musculoskeletal system manifestations [7]. In 24 of 39 (62%) patients, the musculoskeletal manifestation antedated the diagnosis of hyperlipidemia [7]. In addition, one study suggests the soft tissue manifestations of hypercholesterolemia improved or resolved completely in 19 of 30 (63%) patients after receiving lipid-lowering treatment [7].

The mechanism by which hypercholesterolemia is believed to contribute to increased tendon injury is likely multifactorial. Previous studies demonstrate site-to-site variations in cholesterol tissue deposition with age [4, 15, 17]; small variations of cholesterol deposition occur in muscle with age, whereas these variations were larger in adipose tissue and skin and even larger in the dense connective tissues (ie, tendons such as biceps and psoas tendon) of elderly individuals. Therefore, normal connective tissue is particularly susceptible to focal deposition of cholesterol in the elderly [4]. This contributes further to the intrinsic mechanism of tendon failure previously alluded to. The deposition of cholesterol byproducts has been implicated in the formation of tendon xanthomata

(cholesterol deposits), which may change mechanical properties and evidently increase rates of Achilles tendon rupture [17]. Hypercholesterolemia may also alter the tendon's extracellular matrix (and in turn, biomechanical properties) in such a way that lends to increased injury or impaired healing [12]. Lastly, hypercholesterolemia may impair macro- and microcirculation; in tendons, this decreased vascularity may increase injury rates or retard healing [3, 13]. The inadequacy of the preventive mechanisms for the tissue may play a role in the formation of rotator cuff tears.

In conclusion, measurement of serum cholesterol in patients presenting with torn rotator cuff tendons should be considered in patients with unknown lipid profiles. Further research is needed for the acceptance of TC as a definite risk factor in rotator cuff tears and for the establishment of risk levels.

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