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The effect of lipid levels on patient-reported outcomes in patients with rotator cuff tears

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Background: Lipid disorders could be associated with the prevalence and outcomes of rotator cuff diseases. This study aimed to learn how levels of various types of lipids influence the patient-reported outcomes of patients with rotator cuff tears (RCTs).

Methods: Data from a cohort study of 135 patients with RCTs were used. The outcome measures included Western Ontario Rotator Cuff (WORC) index, American Shoulder and Elbow Surgeons (ASES) standardized shoulder assessment form, Single Assessment Numeric Evaluation, visual analog scale for pain and satisfaction, and Veterans RAND 12-Item Health Survey (VR-12). Multivariable random-effects models were built to examine how total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein, and ratio of total cholesterol to HDL influence each outcome, controlling for covariates.

Results: After adjusting for age, gender, surgery, smoking, and baseline outcome values, patients with triglycerides >150 mg/dL had significantly higher pain visual analog scale ($\beta = 5.86$; $P = .017$) and lower VR-12 physical component summary ($\beta = -2.71$; $P = .002$) scores. Patients with low HDL had significantly worse WORC ($\beta = 132.26$; $P = .020$) and ASES ($\beta = -7.05$; $P = .005$) scores, more pain ($\beta = 6.69$; $P = .024$), and less satisfaction ($\beta = -6.53$; $P = .008$). The ratio of total cholesterol to HDL was associated with worse WORC ($\beta = 58.46$; $P = .006$) and ASES scores ($\beta = -2.74$; $P = .002$), more pain ($\beta = 4.49$; $P < .001$), and worse VR-12 physical component summary score ($\beta = -1.03$; $P = .017$).

Conclusions: Dyslipidemia may decrease the improvement of patient-reported outcomes in patients undergoing treatment for RCTs; high triglycerides and low HDL may have the most impact.

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Rotator cuff diseases are of great concern in the musculoskeletal area because of their high prevalence, with an overall prevalence of >50% among patients older than 80 years.^{8,22} Rotator cuff tears (RCTs) have been proved to lower patients' quality of life by causing pain, weakness, and loss of shoulder range of motion.¹⁷ Therefore, it is necessary for researchers to look into the risk factors of RCTs and to study how they influence patient-reported outcomes.

The pathogenesis of RCTs remains unknown.²⁰ Extrinsic and intrinsic theories have been developed to explain RCTs.¹¹ The major extrinsic factor is shoulder impingement. The intrinsic mechanisms, however, are more complicated. Degeneration, inflammation, oxidative stress, and hypovascularity are all thought to be intrinsically related to RCTs, and lipid disorders may play an important role in some of these conditions.²² Most of the lipids in the tendons

have been shown to be derived from the lipids in circulation.²⁴ Several studies have associated hyperlipidemia with a range of musculoskeletal manifestations, including tendon xanthomas, tendo Achillis tendinitis, transient tendo Achillis pain, migratory polyarthritides, and oligoarthritis.¹³ In a mouse model, Beason et al⁵ showed that hypercholesterolemia could reduce the tendon elastic modulus and may have a detrimental effect on overall tendon properties.

Several studies have investigated the relationship between dyslipidemia and rotator cuff diseases, finding that hyperlipidemia is an independent risk factor for the development of rotator cuff disease and that patients with dyslipidemia had a higher prevalence of RCTs.^{10,14} More specifically, total cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol were found to be positively associated with RCTs, whereas high-density lipoprotein (HDL) cholesterol was inversely related to tears.¹ With regard to patient-reported outcomes, it has been found that among patients diagnosed with supraspinatus tendinopathy, the pain decreased significantly less after nonsurgical treatment in the hyperlipidemia group than in the nonhyperlipidemia group.¹² To the authors' knowledge, no cohort study has been done to study the effects of specific lipid concentrations on the outcomes of RCTs.

This study was approved by the University of Michigan Institutional Review Board: HUM00056320.

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This study aimed to learn how levels of various types of lipids may influence the patient-reported outcomes of patients with RCTs. We hypothesized that dyslipidemia, which includes higher total cholesterol, triglycerides, and LDL or lower HDL, had a detrimental effect on the improvement of the designed outcome measures.

Methods

The project used data collected during a prospective cohort study supplemented by a chart review of included patients. The choice of intervention (surgical vs. nonsurgical) was determined by the patient and physician as a part of standard clinical practice. Given that these patients all had RCTs, surgery repair was done or the patients received physical therapy. Patients with potential RCTs were identified by attending clinicians from March 26, 2012, to March 3, 2015. Inclusion criteria were age 18 years or older, full-thickness RCT of any size or location as diagnosed by magnetic resonance imaging or diagnostic musculoskeletal ultrasound, unilateral tear, first tear of the affected shoulder, and nonoperative treatment for <4 weeks. Exclusion criteria were a RCT in which complete footprint coverage was not possible; any history of prior surgery, fracture, dislocation, or infection of the affected shoulder; inflammatory joint disease of the affected shoulder, including rheumatoid arthritis; and an open repair, including the subscapularis.

Data collection

All demographic information was collected at baseline, including age, gender, weight, height, workers' compensation (yes/no), comorbidities, shoulder range of motion, tear size, location, days since injury, cause of injury, and medical history. Outcome measurements were collected at baseline and 4, 8, 16, 32, 48, and 64 weeks by e-mail. Lipid profiles were obtained from patients' electronic health records.

Exposure and covariates

The major exposure variables in this study, the lipid profiles, were continuous variables. We also dichotomized the variables on the basis of standards of the National Heart, Lung, and Blood Institute¹⁹ for the borderline high and high total cholesterol level (≥ 200 mg/dL), borderline high and high LDL cholesterol level (≥ 130 mg/dL), low HDL cholesterol level (< 40 mg/dL), and borderline high and high triglyceride level (≥ 150 mg/dL).

Other covariates in the analysis included age, gender, smoking, and surgery, which were collected at baseline.

Outcomes

A variety of tools were used to measure the outcomes of RCTs, including functional outcomes, psychological conditions, and pain. The primary outcome was the Western Ontario Rotator Cuff (WORC) index, which is a self-reported instrument to assess the quality of life of patients with rotator cuff disease.¹⁶ Secondary outcomes included the American Shoulder and Elbow Surgeons (ASES) standardized shoulder assessment form, Single Assessment Numeric Evaluation (SANE), visual analog scale (VAS) for pain, VAS for satisfaction, and Veterans RAND 12-Item Health Survey (VR-12).

WORC index

The WORC is commonly used to evaluate the patient's quality of life. This scale consists of 21 items focusing on 5 domains: physical symptoms, sports/recreation, work, lifestyle, and emotions. Each item has a score range of 0–100, with a possible total score sum of 0–2100. Higher scores correspond to lower quality of life.¹⁶

ASES standardized shoulder assessment form

The ASES assesses patients with shoulder diseases through both self-reporting and medical professionals' evaluations. The self-report consists of 2 sections: pain (1 question) and activities of daily living (10 questions). Each section weights equally, and all sections combined form a total score of 0–100.¹⁸

SANE

The SANE rating is determined by the patient's written response to only 1 question: How would you rate your shoulder today as a percentage of normal (0%–100% scale, with 100% being normal)? Patients are instructed to provide SANE ratings in whole numbers.²⁵

Pain and satisfaction VAS

A VAS is usually a 100-mm horizontal line to measure a characteristic or attitude that is believed to range across a continuum of values. The patient marks the line at the point that best represents the patient's perception of current state.⁹ This study used VAS for pain (from no pain to worst possible pain) and satisfaction (from least satisfied to most satisfied) separately, both ranging from 0 to 100 points.

VR-12

The VR-12 is a self-reported health survey used to measure health-related quality of life and disease burden. The 12 items in the survey indicate the following 8 domains: general health perceptions, physical functioning, role limitations due to physical or emotional problems, bodily pain, energy fatigue, social functioning, and mental health. Two scores are derived from the 12 items; one mainly focuses on physical health (physical component summary [PCS]), and the other mainly focuses on mental health (mental component summary [MCS]), with lower scores indicating worse conditions.²³

Statistical analysis

SAS 9.4 (SAS Institute, Cary, NC, USA) was used in all statistical analyses. Demographic, surgical, and comorbidity characteristics and baseline outcome values were compared between our target population, who had lipid profiles in their electronic health records, and those without lipid profiles. The *t*-test and Wilcoxon rank sum test (if variables are or are not normally distributed, respectively) were used to compare continuous variables (age and all the baseline outcome values) between the 2 groups of patients, and χ^2 test was used to compare categorical and binary variables (gender, having surgery or not, smoking or not; Table I).

The mean value of each specific lipid and also the percentage of high total cholesterol, high triglycerides, high LDL, and low HDL were summarized (Table II). To determine the overall trend of each outcome, we also plotted the means of the outcomes by each lipid group during the 64-week period.

To explore the potential true effects of lipids on longitudinal outcomes and the influence of covariates, we used multivariable random-effects models, setting each outcome measure as the response variable, each binary lipid variable as exposure, and adjusting for age, gender, surgery, smoking, week since baseline, and corresponding baseline outcome values. Multiple imputation (10 data sets for each model) was used to replace missing outcome data, which is a statistical technique to analyze incomplete data sets. The effects are summarized in Table III using beta estimates with 95% confidence intervals. Statistical significance was defined as *P* value < .05.

Results

The cohort included 222 patients, of whom 135 patients had lipid profiles and were included in this analysis. In comparing those with

Table I
Characteristics of patients with and without lipid profiles in the cohort study

	Patients with lipid profiles (N = 135)		Patients without lipid profiles (N = 87)		P
	Mean or %	SD	Mean or %	SD	
Age (y)	61.12	9.62	59.43	9.58	.201
Male (%)	57.78		63.22		.419
Surgery (%)	51.11		67.82		.014*
Smokers (%)	9.63		17.24		.095
WORC baseline	1142.80	439.20	1230.90	431.90	.144
ASES baseline	55.22	21.83	51.53	19.04	.228
SANE baseline	28.33	23.30	28.36	24.17	.795
VAS for pain baseline	49.89	27.18	53.36	26.15	.366
VAS for satisfaction baseline	82.18	20.83	81.49	19.67	.475
VR-PCS baseline	37.75	9.99	38.41	9.77	.631
VR-MCS baseline	50.34	12.53	49.45	11.10	.337

ASES, American Shoulder and Elbow Surgeons standardized shoulder assessment form; SANE, Single Assessment Numeric Evaluation; SD, standard deviation; VAS, visual analog scale; VR-MCS and VR-PCS, Veterans RAND 12-Item Health Survey, mental component summary and physical component summary; WORC, Western Ontario Rotator Cuff index.

* Significant P value (< .05).

and without lipid profiles, only a single variable differed between the samples, with the patients not having lipid profiles being more likely to have had a surgical intervention (67.82% vs. 51.11%; $P = .014$); there were no other demographic or baseline differences between groups (Table I). For our included sample of patients with lipid profiles, we summarized details of their lipid profiles and demographic and baseline characteristics, stratified by treatment, in Table II. There was no difference in the lipid data of patients having surgical treatment or not, but patients who had surgery appeared to be slightly younger (58.97 vs. 63.36 years; $P = .008$), and a higher proportion were male (68.12% vs. 46.97%).

The overall trends in the patient-reported outcome measures are presented in Appendix S1. As shown in the scores, all overall trends, in particular those related to physical function (eg, WORC, ASES,

SANE, VAS for pain, VR-PCS), were similar in patients with and without lipid disorders, although patients with lipid disorders appeared to have more fluctuations over time. However, in the outcome measures related to psychological function (eg, VAS for patient satisfaction and VR-MCS), the overall trends were different in patients with and without lipid disorders. Of note, patients with high triglyceride levels had overall higher (poorer) WORC scores, lower (worse) ASES scores, more pain, and lower (worse) PCS scores during the 64-week follow-up period. Patients with lower HDL levels had lower ASES scores, more pain, and less satisfaction than those with normal HDL levels at all time follow-up points.

The results of the random mixed-effects regression models are summarized in Tables III and IV. After adjusting for age, gender, surgery, smoking, and baseline outcome values, patients with borderline high and high triglyceride levels (≥ 150 mg/dL) had higher ($\beta = 5.86$) pain VAS scores ($P = .017$) and lower ($\beta = -2.71$) VR-PCS scores ($P = .002$) than those with normal triglyceride levels. Patients with low HDL cholesterol level (< 40 mg/dL) had higher (poorer) WORC scores ($\beta = 132.26$; $P = .020$), lower ASES scores ($\beta = -7.05$; $P = .005$), higher pain VAS scores ($\beta = 6.69$; $P = .024$), and lower satisfaction VAS scores ($\beta = -6.53$; $P = .008$) than those with normal HDL level. Total cholesterol and LDL did not seem to affect outcomes over time. However, the ratio of total cholesterol to HDL (TC/HDL) seemed to play a significant role in most of the outcomes. A 1-unit increase in the ratio was associated with a WORC score increase of 58.46 ($P = .006$), ASES score decrease of 2.74 ($P = .002$), pain VAS score increase of 4.49 ($P < .001$), and VR-PCS score decrease of 1.03 ($P = .017$). In all regression models, worse baseline values were predictive of worse outcome ($P < .001$). The follow-up point, measured longitudinally in weeks, predicted decreased scores on the WORC index and pain VAS and higher scores on the ASES, VR-MCS, VR-PCS, and SANE. The variable treatment group (surgical vs. nonsurgical) was associated with most of the outcomes, except VR-MCS. Those taking surgical treatment were more likely to have lower WORC scores and pain VAS scores as well as higher ASES scores, SANE scores, satisfaction VAS scores, and VR-PCS scores. No other variables appeared to predict the outcomes.

Table II
Lipid summaries for patients with lipid profiles

	Total (N = 135)		Treatment groups				P
	Mean or %	SD	Surgical (n = 69)		Nonsurgical (n = 66)		
			Mean or %	SD	Mean or %	SD	
TC (mg/dL)	185.01	37.20	182.50	33.10	184.80	41.32	.960
TG (mg/dL)	142.50	85.39	135.30	65.07	150.00	102.40	.327
LDL (mg/dL)	102.50	31.89	106.30	28.81	98.47	4.26	.152
HDL (mg/dL)	53.91	16.10	51.78	15.08	56.14	16.94	.117
High TC (%)	29.63		28.99		30.30		.867
High TG (%)	35.56		36.23		34.85		.867
High LDL (%)	18.52		18.84		18.18		.922
Low HDL (%)	19.26		24.64		13.64		.105
Age (y)	61.12	9.62	58.97	8.85	63.36	9.94	.008*
Male (%)	57.78		68.12		46.97		.013*
Smokers (%)	9.63		10.14		9.09		.836
WORC baseline	1142.83	439.16	1175.60	385.4	1109.00	489.10	.382
ASES baseline	55.22	21.84	52.93	20.05	57.59	23.48	.249
SANE baseline	28.33	23.30	27.22	22.64	29.48	24.10	.633
VAS for pain baseline	49.89	27.18	54.37	24.79	45.27	28.91	.063
VAS for satisfaction baseline	82.18	20.83	83.08	20.25	81.27	21.54	.823
VR-PCS baseline	37.75	9.99	38.37	9.64	37.11	10.37	.466
VR-MCS baseline	50.34	12.53	51.47	12.57	49.17	12.47	.274

ASES, American Shoulder and Elbow Surgeons standardized shoulder assessment form; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SANE, Single Assessment Numeric Evaluation; SD, standard deviation; TC, total cholesterol; TG, triglycerides; VAS, visual analog scale; VR-MCS and VR-PCS, Veterans RAND 12-Item Health Survey, mental component summary and physical component summary; WORC, Western Ontario Rotator Cuff index.

* Significant P value (< .05).

Table III
Random-effects regression models for each outcome

Outcome	Total cholesterol			Triglycerides			High-density lipoprotein			Low-density lipoprotein			Ratio of total cholesterol to high-density lipoprotein		
	Beta estimate	95% CI	P	Beta estimate	95% CI	P	Beta estimate	95% CI	P	Beta estimate	95% CI	P	Beta estimate	95% CI	P
WORC	-35.01	-147.05 to 77.02	.537	49.60	-47.81 to 147.02	.317	132.26	20.47-244.06	.020*	-0.61	-125.72 to 124.50	.992	58.46	16.96-99.96	.006*
ASES	2.53	-2.18 to 7.25	.289	-2.93	-7.25 to 1.39	.181	-7.05	-11.89 to -2.21	.005*	0.23	-5.73 to 6.19	.938	-2.74	-4.50 to -0.99	.002*
SANE	-0.03	-6.46 to 6.39	.991	-1.63	-7.28 to 4.02	.571	-3.55	-10.35 to 3.25	.306	-2.01	-9.59 to 5.57	.601	-1.93	-4.47 to 0.61	.136
VAS for pain	0.24	-5.38 to 5.87	.933	5.86	1.04-10.67	.017*	6.69	0.88-12.49	.024*	5.18	-1.50 to 11.86	.128	4.49	2.37-6.61	<.001*
VAS for satisfaction	2.23	-1.87 to 6.32	.286	-0.08	-3.91 to 3.75	.969	-6.53	-11.37 to -1.70	.008*	0.28	-4.82 to 5.39	.914	-1.41	-3.23 to 0.41	.129
VR-PCS	0.13	-1.78 to 2.05	.892	-2.71	-4.46 to -0.96	.002*	-0.98	-3.08 to 1.12	.359	-0.54	-2.95 to 1.87	.657	-1.03	-1.87 to -0.18	.017*
VR-MCS	0.35	-1.84 to 2.54	.754	0.66	-1.40 to 2.72	.531	-1.88	-4.30 to 0.53	.126	-0.32	-3.03 to 2.40	.819	-0.69	-1.65 to 0.26	.153

ASES, American Shoulder and Elbow Surgeons standardized shoulder assessment form; CI, confidence interval; SANE, Single Assessment Numeric Evaluation; VAS, visual analog scale; VR-MCS and VR-PCS, Veterans RAND 12-Item Health Survey, mental component summary and physical component summary; WORC, Western Ontario Rotator Cuff index.

Each beta estimate corresponds to a single independent multivariable model, adjusting for age, gender, surgery, smoking, week, and corresponding baseline outcome values. All lipids are binary variables (high vs. low), except for ratio of total cholesterol to high-density lipoprotein, which is a continuous ratio variable.

* Significant P value (< .05).

Discussion

Our results indicated that triglycerides and HDL could influence the outcomes of RCTs. Patients with high levels of triglycerides had more pain and lower VR-PCS scores, and patients with low HDL levels had more pain, less satisfaction with their medical care, and worse physical function, as indicated in the higher WORC and lower ASES scores. Both the plots of the outcome means and the multivariable analysis demonstrated that the WORC, ASES, pain VAS, and VR-PCS are more likely to be affected by blood lipid levels; these measures all focused on functional outcomes and sense (eg, pain).

These results are consistent with some published studies. In multiple animal models (mice, rat, and monkey), Beason et al⁶ showed that hypercholesterolemic animals had increased stiffness compared with control groups on the healing response to injury. This increased stiffness in the rotator cuff could also increase overall shoulder stiffness and limit range of motion and overall joint function.⁶ As the WORC scale mainly covers the physical symptoms of rotator cuff disease and its effect on various domains of life,²¹ patients with lipid disorders are likely to have higher WORC scores because of increased physical limitation. The results of this study are also consistent with a recent study by Kim et al.¹² who used a numeric rating scale to measure pain over time in patients with supraspinatus tendinopathy after treatment. Both groups with and without hyperlipidemia had decreased pain over time, but pain decreased less for those with hyperlipidemia. By measuring the changes of passive ranges of motion, such as flexion, abduction, internal rotation, and external rotation, between baseline values and 8 weeks after treatment, they found that patients with hyperlipidemia had nonsignificantly decreased improvement. However, a study by Longo et al¹⁵ found that serum triglyceride concentration and total serum cholesterol concentration were not associated with RCTs. Therefore, a more rigorous randomized controlled trial is needed to provide evidence to testify to the association.

The results also reveal a significant factor that could be used to predict outcomes of patients with RCTs, which is the TC/HDL. In the multivariable models, higher TC/HDL is associated with higher WORC, lower ASES, higher pain, and lower VR-PCS scores. TC/HDL has been used as an important predictor in many diseases, such as subclinical atherosclerosis,³ and as a marker for cardiovascular disease⁴ because it is easy and cost-effective to measure. However, few studies in the musculoskeletal area use this ratio to predict outcomes. In this study, TC/HDL is a sensitive predictor of physical change in patients with RCTs after treatment.

VR-MCS, satisfaction VAS, and SANE outcomes were not associated with lipid levels in this study. As VR-MCS mainly focuses on mental health, and satisfaction VAS measures the attitude toward medical care, these measures are not likely to be affected by only 1 factor, and we assume that other factors may bias the results over time. The reason that SANE is not significant in all models is not clear. In a previous study, SANE was highly correlated with other shoulder rating scales, such as ASES.²⁵

The mechanism of the relationship between patient-reported outcomes and lipids (eg, triglycerides, HDL) might be explained by fatty infiltration and stiffness. Fatty infiltration, which might result from hyperlipidemia, may weaken the mechanical strength of repaired tendon and thus be inversely associated with RCT healing and functional outcomes.^{2,8} Most studies of the effects of lipid disorders on the healing outcomes of RCTs have been animal experiments. Beason et al⁷ concluded that hypercholesterolemia had a detrimental effect on tendon healing in rats because decreased healing stiffness was found in hypercholesterolemic rats compared with a control group after supraspinatus injury and repair. Further studies need to be performed to look into how dyslipidemia influences fatty infiltration and healing outcome, as these two factors may be the intrinsic reasons for the association that we found.

Table IV
Random-effects regression models results for each covariate

Outcome	Lipid	Follow-up week [†]		Gender [‡]		Age [§]		Surgery		Smoking [¶]		Baseline score [#]	
		Beta estimate	P	Beta estimate	P	Beta estimate	P	Beta estimate	P	Beta estimate	P	Beta estimate	P
WORC	HDL	-9.405	<.001*	-27.427	.601	-0.674	.798	-181.203	<.001*	-67.534	.424	0.583	<.001*
	LDL	-9.400	<.001*	-19.574	.718	-1.150	.668	-175.273	<.001*	-49.169	.568	0.565	<.001*
	TC	-9.424	<.001*	-25.056	.646	-1.190	.659	-172.559	<.001*	-53.711	.529	0.567	<.001*
	TG	-9.370	<.001*	-17.853	.737	-0.905	.735	-174.149	<.001*	-54.605	.519	0.564	<.001*
	TC/HDL	-9.361	<.001*	-33.588	.518	0.525	.845	-175.509	<.001*	-43.160	.605	0.565	<.001*
ASES	HDL	0.435	<.001*	0.753	.737	-0.028	.787	9.152	<.001*	-0.517	.876	0.444	<.001*
	LDL	0.435	<.001*	0.463	.844	-0.003	.977	8.769	<.001*	-1.429	.677	0.432	<.001*
	TC	0.437	<.001*	0.760	.738	-0.002	.985	8.599	<.001*	-1.226	.717	0.437	<.001*
	TG	0.434	<.001*	0.368	.871	-0.012	.913	8.726	<.001*	-1.027	.760	0.424	<.001*
SANE	TC/HDL	0.435	<.001*	1.202	.591	-0.083	.439	8.700	<.001*	-1.743	.599	0.421	<.001*
	HDL	0.515	<.001*	0.732	.805	0.062	.721	9.177	.002*	3.066	.541	0.321	<.001*
	LDL	0.514	<.001*	0.210	.944	0.074	.669	9.076	.002*	2.378	.636	0.311	<.001*
	TC	0.515	<.001*	0.430	.887	0.070	.688	8.911	.002*	2.578	.610	0.310	<.001*
	TG	0.514	<.001*	0.405	.891	0.056	.752	9.008	.002*	2.704	.591	0.319	<.001*
VAS for pain	TC/HDL	0.514	<.001*	0.857	.771	0.015	.932	9.095	.002*	2.496	.616	0.318	<.001*
	HDL	-0.323	<.001*	-2.879	.254	0.031	.837	-13.114	<.001*	-5.114	.243	0.358	<.001*
	LDL	-0.321	<.001*	-1.671	.518	0.003	.984	-13.128	<.001*	-3.849	.380	0.357	<.001*
	TC	-0.324	<.001*	-2.300	.384	0.010	.950	-12.715	<.001*	-4.172	.350	0.347	<.001*
	TG	-0.320	<.001*	-2.271	.366	0.036	.815	-12.515	<.001*	-4.943	.258	0.342	<.001*
VAS for satisfaction	TC/HDL	-0.320	<.001*	-3.272	.177	0.147	.329	-13.022	<.001*	-4.209	.316	0.367	<.001*
	HDL	0.006	.831	-2.454	.238	-0.116	.258	6.713	.001*	0.771	.827	0.339	<.001*
	LDL	0.006	.839	-2.819	.189	-0.101	.334	6.524	.002*	-0.083	.981	0.333	<.001*
	TC	0.008	.787	-2.462	.249	-0.091	.382	6.360	.002*	0.271	.939	0.336	<.001*
	TG	0.006	.828	-2.929	.163	-0.098	.354	6.527	.002*	-0.023	.995	0.333	<.001*
VR-PCS	TC/HDL	0.005	.862	-2.580	.220	-0.137	.201	6.519	.002*	-0.184	.959	0.325	<.001*
	HDL	0.133	<.001*	1.321	.142	0.051	.296	4.302	<.001*	1.905	.229	0.587	<.001*
	LDL	0.133	<.001*	1.145	.208	0.055	.262	4.282	<.001*	1.720	.279	0.588	<.001*
	TC	0.134	<.001*	1.224	.185	0.054	.269	4.229	<.001*	1.810	.253	0.589	<.001*
	TG	0.132	<.001*	1.172	.179	0.042	.383	4.165	<.001*	2.136	.166	0.581	<.001*
VR-MCS	TC/HDL	0.133	<.001*	1.504	.089	0.024	.633	0.909	<.001*	1.628	.295	0.581	<.001*
	HDL	0.036	.010*	2.006	.052	-0.033	.560	1.594	.126	-1.999	.268	0.620	<.001*
	LDL	0.035	.011*	1.793	.089	-0.027	.633	1.535	.145	-2.266	.213	0.617	<.001*
	TC	0.036	.010*	1.877	.080	-0.028	.629	1.484	.158	-2.192	.226	0.617	<.001*
	TG	0.036	.009*	1.871	.072	-0.026	.656	1.528	.146	-2.306	.204	0.617	<.001*
TC/HDL	0.035	.011*	2.020	.051	-0.049	.404	1.530	.144	-2.287	.203	0.617	<.001*	

ASES, American Shoulder and Elbow Surgeons standardized shoulder assessment form; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SANE, Single Assessment Numeric Evaluation; TC, total cholesterol; TC/HDL, ratio of total cholesterol to high-density lipoprotein; TG, triglycerides; VAS, visual analog scale; VR-MCS and VR-PCS, Veterans RAND 12-Item Health Survey, mental component summary and physical component summary; WORC, Western Ontario Rotator Cuff index.

Each outcome variable corresponds to a single independent multivariable model. All lipids are binary variables (high vs. low), except for ratio of total cholesterol to high-density lipoprotein, which is a continuous ratio variable.

* $P < .05$.

[†] Follow-up week refers to the timing of the outcome measurement, longitudinally.

[‡] Gender was coded as 1 = male, 0 = female.

[§] Age was treated as a continuous measures in 1-year increments.

^{||} Surgery was coded 0 = nonsurgical intervention, 1 = surgical intervention.

[¶] Smoking was coded 0 = nonsmoker, 1 = smoker.

[#] Baseline score represents the baseline score on that outcome measure.

This study has several strengths and limitations. First, this was a cohort study, and outcomes were collected during a 64-week period. Multiple imputations were used to tackle the number of missing values in the data set, which ranged from 20% to 30%. It was unlikely that these data were missing at random, and simply neglecting the data might significantly bias the results. It also helped to retain the sample size to draw a more powerful conclusion. However, this imputation was based on the assumption that the missing values do not depend on unobserved information, and we could not fully exclude this possibility. The substantial missing data are also a limitation in this study.

We also studied multiple outcomes and their association with levels of numerous lipids. Each model included only 1 outcome and 1 lipid. As lipid levels may correlate with each other, controlling for other lipids may cancel out the potential effect of a specific lipid. Triglycerides and HDL, in particular, were shown to be significantly associated with patient-reported outcomes of RCTs, and future investigations of their role in healing may be warranted.

In this study, not all the patients included in the original cohort have lipid profiles in their medical records, which might introduce selection bias. However, after comparing those with and without lipid profiles, there were no significant differences in the patients' characteristics except for the treatment they had. In comparing those with or without surgery, they were not significantly different in the outcome values that we studied. Therefore, treatment was not a confounding factor here and was unlikely to influence the conclusion we drew.

Conclusion

Overall, our study suggests that dyslipidemia may impair improvement of patient-reported outcomes of RCTs, especially physical function and pain. The lipids that appear to play significant roles in this process are triglycerides and HDLs. The TC/HDL was also found to be a possibly sensitive predictor of treatment outcomes. Therefore, in treating patients with RCTs, it is recommended that physicians obtain lipid profiles and deal with the existing dyslipidemia at the same time, especially the higher triglycerides and lower HDLs.

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Disclaimer

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Supplementary data

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References

- Abboud JA, Kim JS. The effect of hypercholesterolemia on rotator cuff disease. *Clin Orthop Relat Res* 2010;468:1493-7. <http://dx.doi.org/10.1007/s11999-009-1151-9>
- Abtahi AM, Granger EK, Tashjian RZ. Factors affecting healing after arthroscopic rotator cuff repair. *World J Orthop* 2015;6:211-20. <http://dx.doi.org/10.5312/wjo.v6.i2.211>
- Acevedo M, Kramer V, Tagle R, Corbalan R, Arnaiz P, Berrios X, et al. Total/HDL cholesterol ratio and non HDL cholesterol as predictors for increased intima media thickness. *Rev Med Chil* 2012;140:969-76. [in Spanish]. <http://dx.doi.org/10.4067/S0034-98872012000800001>
- Aryal M, Gyawali P, Raut B, Pokheral BR. Evaluation of non-HDL-cholesterol and risk ratio as cumulative marker of cardiovascular risk in diabetes mellitus. *Clin Biochem* 2011;44(Suppl 13):S158. <http://dx.doi.org/10.1016/j.clinbiochem.2011.08.394>
- Beason DP, Abboud JA, Kuntz AF, Bassora R, Soslosky LJ. Cumulative effects of hypercholesterolemia on tendon biomechanics in a mouse model. *J Orthop Res* 2011;29:380-3. <http://dx.doi.org/10.1002/jor.21255>
- Beason DP, Hsu JE, Marshall SM, McDaniel AL, Temel RE, Abboud JA, et al. Hypercholesterolemia increases supraspinatus tendon stiffness and elastic modulus across multiple species. *J Shoulder Elbow Surg* 2013;22:681-6. <http://dx.doi.org/10.1016/j.jse.2012.07.008>
- Beason DP, Tucker JJ, Lee CS, Edelstein L, Abboud JA, Soslosky LJ. Rat rotator cuff tendon-to-bone healing properties are adversely affected by hypercholesterolemia. *J Shoulder Elbow Surg* 2014;23:867-72. <http://dx.doi.org/10.1016/j.jse.2013.08.018>
- Chung SW, Park H, Kwon J, Choe GY, Kim SH, Oh JH. Effect of hypercholesterolemia on fatty infiltration and quality of tendon-to-bone healing in a rabbit model of a chronic rotator cuff tear: electrophysiological, biomechanical, and histological analyses. *Am J Sports Med* 2016;44:1153-64. <http://dx.doi.org/10.1177/0363546515627816>
- Ciprandi G, Tosca MA, Signori A, Cirillo I. Visual analogue scale assessment of nasal obstruction might define patients candidates to spirometry. *Rhinology* 2011;49:292-6. <http://dx.doi.org/10.4193/Rhino10.303>
- Djerbi I, Chammass M, Mirous MP, Lazerges C, Coulet B, French Society For Shoulder and Elbow (SOFEC). Impact of cardiovascular risk factor on the prevalence and severity of symptomatic full-thickness rotator cuff tears. *Orthop Traumatol Surg Res* 2015;101(Suppl):S269-73. <http://dx.doi.org/10.1016/j.otsr.2015.06.011>
- Gumina S, Arceri V, Carbone S, Albino P, Passaretti D, Campagna V, et al. The association between arterial hypertension and rotator cuff tear: the influence on rotator cuff tear sizes. *J Shoulder Elbow Surg* 2013;22:229-32. <http://dx.doi.org/10.1016/j.jse.2012.05.023>
- Kim JM, Kim MW, Do HJ. Influence of hyperlipidemia on the treatment of supraspinatus tendinopathy with or without tear. *Ann Rehabil Med* 2016;40:463-9. <http://dx.doi.org/10.5535/arm.2016.40.3.463>
- Klemp F, Halland AM, Majoos FL, Steyn K. Musculoskeletal manifestations in hyperlipidaemia: a controlled study. *Ann Rheum Dis* 1993;52:44-8.
- Lin TT, Lin CH, Chang CL, Chi CH, Chang ST, Sheu WH. The effect of diabetes, hyperlipidemia, and statins on the development of rotator cuff disease: a nationwide, 11-year, longitudinal, population-based follow-up study. *Am J Sports Med* 2015;43:2126-32. <http://dx.doi.org/10.1177/0363546515588173>
- Longo UG, Franceschi F, Spiezia F, Forriol F, Maffulli N, Denaro V. Triglycerides and total serum cholesterol in rotator cuff tears: do they matter? *Br J Sports Med* 2010;44:948-51. <http://dx.doi.org/10.1136/bjsm.2008.056440>
- Longo UG, Saris D, Poolman RW, Bertoni A, Denaro V. Instruments to assess patients with rotator cuff pathology: a systematic review of measurement properties. *Knee Surg Sports Traumatol Arthrosc* 2012;20:1961-70. <http://dx.doi.org/10.1007/s00167-011-1827-z>
- McMahon PJ, Prasad A, Francis KA. What is the prevalence of senior-athlete rotator cuff injuries and are they associated with pain and dysfunction? *Clin Orthop Relat Res* 2014;472:2427-32. <http://dx.doi.org/10.1007/s11999-014-3560-7>
- Michener LA, McClure PW, Sennett BJ. American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form, patient self-report section: reliability, validity, and responsiveness. *J Shoulder Elbow Surg* 2002;11:587-94. <http://dx.doi.org/10.1067/mse.2002.127096>
- National Heart, Lung, and Blood Institute. What is cholesterol? www.nhlbi.nih.gov/health/health-topics/topics/hbc; 2017 [accessed March 7, 2017].
- Oliva F, Osti L, Padulo J, Maffulli N. Epidemiology of the rotator cuff tears: a new incidence related to thyroid disease. *Muscles Ligaments Tendons J* 2014;4:309-14.
- Raman J, Macdermid JC. Western Ontario rotator cuff index. *J Physiother* 2012;58:201. [http://dx.doi.org/10.1016/S1836-9553\(12\)70115-7](http://dx.doi.org/10.1016/S1836-9553(12)70115-7)
- Sambandam SN, Khanna V, Gul A, Mounasamy V. Rotator cuff tears: an evidence based approach. *World J Orthop* 2015;6:902-18. <http://dx.doi.org/10.5312/wjo.v6.i1.902>
- Selim AJ, Rogers W, Fleishman JA, Qian SX, Fincke BG, Rothendler JA, et al. Updated U.S. population standard for the Veterans RAND 12-item Health Survey (VR-12). *Qual Life Res* 2009;18:43-52. <http://dx.doi.org/10.1007/s11136-008-9418-2>
- von Bahr S, Movin T, Papadogiannakis N, Pikuleva I, Ronnow P, Diczfalusy U, et al. Mechanism of accumulation of cholesterol and cholestanol in tendons and the role of sterol 27-hydroxylase (CYP27A1). *Arterioscler Thromb Vasc Biol* 2002;22:1129-35.
- Williams GN, Gangel TJ, Arciero RA, Uhorchak JM, Taylor DC. Comparison of the Single Assessment Numeric Evaluation method and two shoulder rating scales. Outcomes measures after shoulder surgery. *Am J Sports Med* 1999;27:214-21.