Body Mass Index and Waist to Hip Ratio are Causally Related to Rotator Cuff Tears

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INTRODUCTION:
Degenerative Rotator Cuff Tears (DCTs) are among the most common musculoskeletal injuries, affecting 30 to 50% of individuals over 50. In a recent systematic review and meta-analysis, we showed obesity was associated with a 44% increased odds of rotator cuff disease (including DCTs). However, lack of temporality, heterogeneous outcome definition, and bias inherent to observational study design, has made causal inference difficult. Despite evidence linking obesity with tendinous changes, like muscle atrophy and fatty infiltration, the causal relationship between obesity and DCT is still understudied.
METHODS:
To improve evidence of causality for obesity and DCT, we first performed a prospective investigation on the association between obesity measures (body mass index [BMI] and waist to hip ratio [WHR]) at baseline and incident rotator cuff tear surgery with the UK Biobank (UKB) data using multivariable-adjusted cox-proportional hazard models (CPHM). We then performed Medelian randomization (MR) studies to assess for evidence of causal relationship between obesity exposures (BMI and WHR) and DCT. We performed genome-wide association studies (GWAS) for DCT using data from UKB and Vanderbilt University Medical Center biorepository (BioVU) and meta-analyzed them; this was the primary source of outcome for MR analyses. Genetic instruments for exposures were obtained from GWAS of BMI in the Mlillion Veteran Program (MVP), and previously published GWAS for WHR. We used two-sample MR with inverse variance weights (IVW) as the primary MR method. Because BMI and WHR are correlated, three additional sensitivity analyses were also conducted: 1) an additional univariate MR using summary statistics for which WHR was already adjusted for BMI, 2) an MVMR analysis adjusting for the effect of BMI on the association between WHR and DCT, and 3) an additional MVMR analysis evaluating the effects of BMI on DCT, while adjusting for WHR.
RESULTS:
Overall, in the UKBB, 498,705 individuals without any history of rotator cuff disease or prior surgery for rotator cuff tear at baseline were followed up until they received surgery for rotator cuff tear, were lost-to-follow-up, died or were administratively censored, whichever came first. During this period 3,806 incident surgery procedures were performed for rotator cuff tears. CPHM revealed each 1 Standard deviation increase in BMI and WHR was associated with 5% (HR: 1.05, 95% CI: 1.01-1.08) and 8% (HR: 1.08, 95% CI: 1.04-1.11) elevated risk of future rotator cuff surgery. Additionally, individuals categorized as overweight and obese were at 7% (HR: 1.07; 95% CI: 0.989-1.16) and 11% (HR: 1.11; 95% CI: 1.02-1.21) increased risk of future rotator cuff surgery compared to individuals of normal weight. MR of 8,785 cases and 441,483 controls, demonstrated a causal relationship between measures of obesity and DCT with each standard deviation increase in BMI and WHR being associated with a 15.7% (OR: 1.157, 95% CI: 1.107-1.209) and 33.1% (OR: 1.331, 95% CI: 1.097-1.614) higher odds of DCT, respectively. Summary statistics for WHR which was adjusted for BMI a priori, demonstrated 11.4% increased odds (IVW OR: 1.114, 95% CI: 0.981, 1.264) of DCT per one standard deviation increase in WHR. Performing a similar analysis where WHR results were adjusted for BMI using MVMR demonstrated a slightly an attenuated but still positive effect of WHR on DCT when adjusting for BMI (IVW OR: 1.207, 95% CI: 0.9821, 1.484), suggesting that the observed relationship between WHR and DCT is likely in-part due to correlation with BMI. On the other hand, MVMR analyses support the conclusion that the effect of BMI on DCT development is statistically independent of an effect of WHR, as adjusted estimates (IVW OR: 1.123, 95% CI: 1.055, 1.195) approximate univariate BMI estimates.
DISCUSSION AND CONCLUSION:
Overall obesity, and central obesity are temporally associated with DCT surgery in individuals with no previous diagnosis of rotator cuff disease. Furthermore, our MR analyses suggest central obesity and especially overall obesity may be causally linked with DCT. A greater understanding of the underlying mechanisms, including fatty infiltration, chronic inflammation related to obesity, or muscle atrophy may inform clinical or therapeutic interventions.

Obesity and RCT Images/Figures:

Table 1. Cox Proportional Hazard Model for Obesity and Rotator Cuff Tear in UKBB

	Rotator Cuff Repair			
Unadjusted Results				
	Rotator Cuff Repair (N=3,806)	**Total (N=488,705)**	**HR**	**95% CI**
WHR				
1 unit increase	3,795	496,456	2.24	1.54- 3.27
1 SD increase	3,795	496,456	1.08	1.04 - 1.11
BMI continuous				
5 kg/m2 increase	3,782	495,629	1.05	1.01-1.08
1 SD increase	3,782	495,629	1.05	1.01- 1.08
BMI Categorical				
Normal (<25 kg/m2)	870	164,178	ref	ref
Overweight (25-30 kg/m2)	1,704	210,513	1.07	0.989- 1.16
Obese (>30 kg/m2)	1,208	120,937	1.11	1.02- 1.21
Adjusted Results				
	Rotator Cuff Repair (N=3,779)	**Total (N=484,895)**	**HR**	**95% CI**
WHR*				
1 unit increase	3,792	495,716	1.76	1.08-2.88
1 SD increase	3,792	495,716	1.05	1.01-1.10
BMI continuous*				
5 kg/m2 increase	3,779	494,895	1.05	1.01-1.08
1 SD increase	3,779	494,895	1.05	1.01-1.08
BMI Categorical*				
Normal (<25 kg/m2)	869	163,928	ref	ref
Overweight (25-30 kg/m2)	1,702	209,212	1.03	0.947-1.12
Obese (>30 kg/m2)	1,208	120,746	1.08	0.993-1.18

Exposure variables were assessed at baseline
WHR= waist-to-hip ratio, BMI= Body Mass Index, HR= Hazard Ratio, 95% CI= 95% Confidence Interval
*Adjusted for Age, Sex, Race, Townsend Deprivation Index, and Type I diabetes