HRT Decreases the Odds of Developing Soft Tissue Disorders of the Shoulder in Post-Menopausal Women

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INTRODUCTION: In females, estrogen loss has been associated with musculoskeletal dysregulation. During menopause, when estrogen levels decrease, it is known that bone health is harmed and connective tissue integrity decreases. The incidence of soft tissue disorders of the shoulder in females increases significantly with age, specifically during and after the menopausal transition. The objective of this study was to determine whether postmenopausal females prescribed systemic estrogen or progesterone hormonal replacement therapy (HRT) have decreased odds of developing soft tissue disorders of the shoulder such as adhesive capsulitis (AC), bicep tendinitis (BT), calcific tendinitis (CT), atraumatic rotator cuff tendinopathy or tears (RCTD), shoulder impingement (SIS), and synovitis compared to women without an active HRT prescription.

METHODS: The TriNetX U.S. Collaborative Network, which is a large de-identified patient database of over 300 million patients, was queried. Women aged 40 to 60 years who were in menopausal state as identified by ICD code N95.1 and primary ovarian insufficiency by ICD code E28.3. Patients were grouped according to HRT prescription status by ICD code Z79.890. Patients were one-to-one propensity matched using the nearest neighbor algorithm through the TriNetX platform matching on age, race, and specific risk factors, specifically diabetes mellitus, hypothyroidism, and hyperlipidemia. The odds of developing AC, BT, CT, RCTD, SIS or synovitis identified by ICD codes M75.0, M 75.2, M 75.3, M75.1, M75.4, M65.8, respectively, was studied.

RESULTS SECTION: After propensity-score matching, there were 299,723 females in each cohort. There were no significant differences between cohorts for all variables after propensity score matching (SMD > 0.002). In the HRT cohort, 2,227 (0.75%) developed AC, 1,475 (0.50%) developed BT, 965 (0.32%) developed CT, 2,799 (0.95%) developed RCTD, 2,836 (0.96%) developed SIS, and 186 (0.06%) developed synovitis. In the non-HRT cohort, 2,817 (0.95%) developed AC, 2,090 (0.70%) developed BT, 1,173 (0.39%) developed CT, 4,176 (1.42%) developed RCTD, 3,798 (1.29%) developed SIS, and 314 (0.11%) developed synovitis. Postmenopausal women who are not using HRT had an increased odds of developing AC (OR: 1.266, 95% CI,1.198 – 1.339, $p < 0.001$), BT (OR: 1.418, 95% CI,1.327 – 1.516, $p < 0.001$), CT (OR: 1.214, 95% CI,1.115 – 1.322, $p < 0.001$), RCTD (OR: 1.497, 95% CI,1.426 – 1.570, $p < 0.001$), SIS (OR: 1.341, 95% CI,1.277 – 1.408, $p < 0.001$), and synovitis (OR: 1.689, 95% CI,1.409 – 2.024, $p < 0.001$).

DISCUSSION: Menopausal female patients prescribed HRTs containing estrogen and progesterone had a statistically significant decreased odds of developing soft tissue disorders of the shoulder. Future research needs to be conducted to understand if this large database study translates into a retrospective cohort study and potentially, a prospective study impacting the female population.

SIGNIFICANCE/CLINICAL RELEVANCE: Postmenopausal women experience a higher risk of developing soft tissue shoulder disorders, which may be partially mitigated via hormone replacement therapy. Identifying HRT as a potentially protective factor highlights the importance of hormonal status when evaluating and managing musculoskeletal conditions in older female patients.

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Table 1: Baseline patient characteristics between HRT and non-HRT cohorts before and after one-to-one propensity score matching.

	Before Matching			After Matching		
	HRT (n=338,131)	Non-HRT (n=336,018)	SMD	HRT (n=299,723)	Non-HRT (n=299,723)	SMD
Demographics						
Age, years (range)	52.6 ± 5.6	53.1 ± 4.9	0.098	52.8 ± 5.0	52.9 ± 4.9	0.004
White	248,068 (73.4%)	220,475 (65.6%)	0.169	212,520 (70.9%)	212,548 (70.9%)	<0.001
African American	34,362 (10.2%)	44,891 (13.4%)	0.099	33,704 (11.2%)	33,894 (11.3%)	0.002
Asian	12,041 (3.6%)	15,077 (4.5%)	0.047	11,758 (3.9%)	11,600 (3.9%)	0.003
Unknown Race	27,682 (8.2%)	37,308 (11.1%)	0.099	26,754 (8.9%)	26,515 (8.8%)	0.003
Hispanic or Latino	26,933 (8.0%)	28,543 (8.5%)	0.019	25,358 (8.5%)	25,318 (8.4%)	<0.001
Not Hispanic or Latino	244,736 (72.4%)	221,638 (66.0%)	0.139	209,202 (69.8%)	209,881 (70.0%)	0.005
Unknown Ethnicity	66,462 (19.7%)	85,837 (25.5%)	0.141	65,163 (21.7%)	64,524 (21.5%)	0.005
Diagnoses						
Diabetes Mellitus	27,482 (8.1%)	25,277 (7.5%)	0.023	23,287 (7.8%)	22,971 (7.7%)	0.004
Hyperlipedemia	59,371 (17.6%)	47,948 (14.3%)	0.09	46,834 (15.6%)	46,293 (15.4%)	0.005
Hypothyroidism	59,371 (17.6%)	47,948 (14.3%)	0.169	37,970 (12.7%)	37,893 (12.6%)	0.001

Table 2: Incidence and odds of soft tissue disorders of the shoulder after propensity score matching.

Outcome	HRT	Non-HRT	Odds Ratio	P- Value
Adhesive Capsulitis	2,227 (0.752%)	2,817 (0.950%)	1.266 (1.198, 1.339)	**<0.0001**
Bicepital Tendinitis	1,475 (0.496%)	2,090 (0.702%)	1.418 (1.327, 1.516)	**<0.0001**
Calcific Tendinitis	965 (0.324%)	1,173 (0.394%)	1.214 (1.115, 1.322)	**<0.0001**
Rotator Cuff Tendinopathy and Tears	2,799 (0.951%)	4,176 (1.417%)	1.497 (1.426, 1.570)	**<0.0001**
Shoulder Impingement Syndrome	2,836 (0.963%)	3,798 (1.287%)	1.341 (1.277, 1.408)	**<0.0001**
Shoulder Synovitis	186 (0.062%)	314 (0.105%)	1.689 (1.409, 2.024)	**<0.0001**