Variability Of Allostatic Load Index And Its Components In Rotator Cuff Repair Patients

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Introduction: Rotator cuff tears are a common shoulder condition, highly prevalent in patients over 60 years of age, and often affect shoulder function and quality of life. Patients with persistent symptoms typically undergo surgical rotator cuff repair (RCR) to restore function and reduce pain. Unfortunately, re-tearing after RCR occurs in 20%-30% of patients, despite decades of effort to improve both surgical techniques and physical therapy protocols [1]. While age and tear size are well-appreciated predictors of failed RCR healing [2], they do not capture most of the variability in healing that is observed. Attempts have been made to further identify biological predictors of healing such as sex, yet conflicting results persist. The literature demonstrates that chronic stress and inflammation are associated with poor wound healing [3, 4], and chronic inflammation has been linked to reduced stem cell differentiation, impaired tissue regeneration, and adverse manifestations such as accumulation of fat deposits in bone and muscle tissues [5]. These data led us to postulate that chronic biophysiological stress and chronic inflammation could negatively impact rotator cuff healing. Hence, we are currently investigating the relationship between the cumulative effects of chronic stress on physiological function –measured as a cumulative *allostatic load index (ALI)* – and rotator cuff repair healing. Here we report our preliminary data on the variability of allostatic load index (ALI) and its components [6], and correlations with the age and sex, of patients undergoing RCR.

Methods: Patients with full-thickness RC tears undergoing arthroscopic double-row repair of the supraspinatus and/or infraspinatus tendons at our institution between 2020 and 2023 were enrolled [IRB #21-811]. Patient height, weight, waist-hip ratio (WHR), body mass index (BMI), and blood pressure (BP), all components of ALI, were recorded at baseline. Penn Shoulder Score (PSS) was collected at baseline (pre-op) and 6mo post-op. Tear size was measured intraoperatively. Additional ALI parameters were measured from fasting blood and urine samples collected at 6mo (**Table 1**). ALI for each patient was computed using a 12-point scale where 1 point was assigned for any component that fell outside the healthy cut-off values adopted by our institution [6]. A Spearman test was used to test correlations of ALI variables and age, and Point-Biserial test was used to test correlations with sex ($p<0.05$, significant).

Results: To date, 34 of a planned 50 patients have reached 6mo follow-up and 28 have complete data on all 12 ALI variables (**Table 1**). The current cohort averages 59.9(7.58) years and is 71% male and 82% white. Mean baseline Penn Shoulder Score (PSS) is 43.5(16.7) points with median anteroposterior (AP) tear width of 2.0[1.5,3.0] cm and mediolateral (ML) tear width of 1.5[1.3,2.0] cm. Median PSS score at 6mo is 87.8 [78.3,94.7]. Summary statistics of the ALI variables for the whole cohort and females/males separately can be found in **Table 1**. Females had significantly higher TC (p=0.04) and HDL (p=0.002) and lower WHR (p<0.001) than males, although the healthy cut-off is also higher for HDL and lower for WHR in females (**Table 2**). Older age was negatively correlated with BMI (p=0.01). Median ALI for the full cohort was 4.0[3.0,6.25] out of 12 points, *with scores ranging from 2 to 9*. No significant correlation of the cumulative ALI with patient age (p=0.36) or sex (p=0.48) was found. More than 70% of the cohort (males and females) had SBP, BMI and WHR outside of healthy cut-off values (**Table 2**). Only CRP level was within the healthy range in all patients.

Discussion: To our knowledge, this is the first study to describe the variability of a broad range of biophysiological variables in a routine cohort of RCR patients. Our preliminary data show that ALI, derived from these variables as a surrogate for chronic stress and inflammation, varies considerably among RCR patients. ALI was not significantly correlated with age or sex, and a substantial number of patients show elevations of ALI parameters outside of healthy cut-off values; thus, continued investigation of ALI and its individual components as independent predictors of failed RCR healing is warranted.

Significance/Clinical Relevance: This work will investigate whether the cumulative burden of chronic stress, known as allostatic load, is a risk factor for poor RCR healing, and possibly identify modifiable components that could be addressed to improve healing and outcomes.

References: [1] F. A. M. III and C. A. R. Jr., Rockwood and Matsen's The Shoulder, 6 ed. Elsevier Health Sciences, 2021. [2] M. Livesey, et al., Orthopedics, 41, 2018. [3] J. Guidi, et al., Psychother Psychosom, 90, 2020. [4] M. Wynn and S. Holloway, Wounds UK, 15, 2019. [5] G. Lepperdinger, Curr Opin Immunol, 23, 2011. [6] S. Scheuer et al., Psychoneuroendocrino, 2018.

Table 1: ALI characteristics of the RCR cohort; Mean (SD), Median [quartiles].

Variable	All	Females	Males	N (All:F:M)
1. Fasting Glucose (FG, mg/dL)	96.1 (9.87)	92.8 (8.35)	97.7 (10.3)	29:9:20
2. HbA1c (%)	5.45 [5.30,5.70]	5.45 [5.32,5.57]	5.50 [5.27,5.73]	34:10:24
3. Total cholesterol (TC, mg/dL)	185 (37.8)	205 (44.1)	177 (32.3)	34:10:24
4. Triglycerides (TG, mg/dL)	90.5 [73.5,130]	86.0 [63.8,135]	96.0 [77.2,128]	34:10:24
5. High Density Lipoprotein (HDL, mg/dL)	49.5 [42.5,58.5]	59.0 [53.5,72.5]	46.0 [40.8,51.2]	34:10:24
6. TC/HDL (mg/dL)	3.73 (1.04)	3.50 (1.16)	3.83 (1.00)	34:10:24
7. C-Reactive Protein (CRP, mg/dL)	0.15 [0.15,0.40]	0.15 [0.15,0.30]	0.15 [0.15,0.40]	29:9:20
8. Cortisol (µg/dL)	10.2 (3.97)	10.8 (5.21)	9.85 (3.39)	29:9:20
9. Systolic blood pressure (SBP, mmHg)	130 (14.0)	128 (10.7)	131 (15.3)	33:9:24
10. Diastolic blood pressure (DBP, mmHg)	78.2 (8.78)	76.9 (8.85)	78.8 (8.88)	33:9:24
11. Body Mass Index (BMI)	28.7 [26.4,30.6]	27.0 [24.6,28.4]	29.5 [27.0,31.5]	34:10:24
12. Waist:Hip Ratio (WHR)	0.95 (0.07)	0.89 (0.04)	0.98 (0.06)	29:9:20
Allostatic Load Index (ALI)	**4.0 [3.0,6.25]**	**4.0 [3.0,6.0]**	**5.0 [3.0,7.0]**	**28:9:19**

Table 2: Number of patients outside of healthy cut-off values for the twelve ALI variables; count (%).

Variable	ALI Cut-Off	All (N=28)	Females (N=9)	Males (N=19)
1. FG	≥100	12 (43%)	1 (11%)	11 (58%)
2. HbA1c	≥5.7	8 (29%)	2 (22%)	6 (32%)
3. TC	≥200	10 (36%)	5 (56%)	5 (26%)
4. TG	≥150	7 (25%)	2 (22%)	5 (26%)
5. HDL	F: <50; M: <40	4 (14%)	2 (22%)	2 (11%)
6. TC/HDL	≥5.2	3 (11%)	0	3 (16%)
7. CRP	≥0.9	0	0	0
8. Cortisol	≤ 4.7; ≥19.5	3 (11%)	1 (11%)	2 (11%)
9. SBP	≥120	22 (79%)	8 (89%)	14 (74%)
10. DBP	≥80	16 (57%)	4 (44%)	12 (63%)
11. BMI	≥25	28 (82%)	7 (70%)	21 (88%)
12. WHR	F: ≥0.85; M: ≥0.9	25 (89%)	7 (78%)	19 (95%)