Unsupervised Machine Learning to Identify Clinically Meaningful Subgroups in Patients Undergoing Arthroscopic Rotator Cuff Repair

Yining Lu[1], Elyse Jordan Berlinberg[2], Harsh Hiren Patel, Morgan Westcott Rice, Vahram Ara Gamsarian, Mario Hevesi, Adam Blair Yanke[3], Brian J Cole[4], Nikhil N Verma, Brian Forsythe[5]
[1]Mayo Clinic, [2]Midwest Orthopedics At Rush, [3]Rush University Med Ctr, [4]Rush University Medical Center, [5]Midwest Orthopaedics At Rush

INTRODUCTION: Rotator cuff tears are estimated to affect 20.7% of the population, with the prevalence increasing with age. Surgery is indicated after non-response to nonoperative treatment, with arthroscopic rotator cuff repair (ARCR) as the current standard for full thickness tears. Clinically significant outcomes (CSOs) of ARCR can be measured in part with patient-reported outcomes. Notably, Single Assessment Numerical Evaluation (SANE) scores and American Shoulder and Elbow Surgeon (ASES) scores are used to assess postoperative shoulder function. This study aims to determine predictors of achieving CSO thresholds following elective ARCR by utilizing machine learning (UML).

METHODS: A retrospective case-cohort analysis of a prospectively collected database was performed to identify patients who underwent elective ARCR from 2017-2018. Tear dimensions were measured on MRI utilizing a validated technique. CSO achievements on the American Shoulder and Elbow Surgeon (ASES), the Single Assessment Numerical Evaluation (SANE), and the Constant Murley Subjective Score (CMS) at 2-years follow up were calculated. An unsupervised random forest algorithm was utilized to partition patients into optimal and suboptimal CSO achievement subgroups and subsequently internally validate partitioning based on stability, connectivity, Dunn's partition coefficient, and silhouette coefficients. This data, along with a total of 30 demographic, clinical, and preoperative PROs were assessed for prognostic value through a stepwise multivariable logistic regression.

RESULTS:

A total of 346 patients (male: 192, 55.5%; Age: 57.2±9.1, BMI: 30.1±5.4) were eligible for inclusion and followed for an average of 3.8 (range: 2.0 – 6.2 years). The random forest algorithm arrived at an optimal partition of 2 subgroups (Stability: 0.16; connectivity: 180.8; Dunn: 0.16; Silhouette: 0.05), with 176 patients in the optimal achievement subgroup and 157 patients in the suboptimal achievement subgroup. The two subgroups differed significantly (P≤0.004) in the likelihood of achievement of all CSOs. Stepwise multivariable logistic regression identified an increase of 1 mm in tear size in the sagittal dimension to predict a 10% increase in the probability of suboptimal achievement. Additional, additive risk factors for suboptimal CSO achievement included increased preoperative Constant-Murley shoulder score (OR: 1.11, 95% CI: 1.04-1.18, P<0.001), increasing number of tendons involved (OR: 14.07, 95% CI: 4.5-44.02, P<0.001), and subscapularis involvement (OR: 8.67, 95% CI: 2.45-30.71, P=0.01). Protective factors included performance of a subpectoral biceps tenodesis compared to biceps tenotomy (OR: 0.26, 95% CI: 0.05-0.92, P=0.03).

DISCUSSION AND CONCLUSION:

Clinically meaningful subgroups were uncovered using a machine learning clustering approach in patients undergoing ARCR. Tear size, number of tendons involved, and subscapularis involvement were highly significant and additive predictors of suboptimal CSO achievement at 2-year minimum follow up. Treatment of concurrent biceps pathology with tenodesis confers 74% increased likelihood of CSO achievement vs. tenotomy.

Table 1: Internal Validation of Ideal Cluster Number

Cluster Number	2	3	4	5	6
Stability	0.16	0.23	0.24	0.25	0.25
Connectivity	180.83	250.06	323.45	325.84	325.98
Dunn	0.16	0.15	0.14	0.14	0.14
Silhouette	0.05	0.03	0.03	0.03	0.02

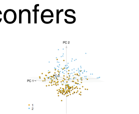

Figure 1: Visualization of the two random forest partitioned patient subgroups in 3-D feature space; the axis is generated following principal component analysis to reduce the dimensionality of the dataset for ease of visualization; 1: optimal cluster, 2: suboptimal cluster

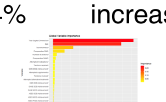

Figure 2: Global variable importance of feature contributions to the performance of the random forest clustering algorithm

Table 2: Comparison of Patient Demographics Stratified by Cluster Membership

	Optimal	Suboptimal	p
Total Number of Patients	176	157	
Male (%)	103 (58.5)	81 (51.6)	0.246
Age (mean (SD))	55.87 (10.14)	59.02 (7.61)	0.002
BMI (mean (SD))	35.99 (58.90)	375.30 (4001.49)	0.261
Arthritis (%)	23 (13.1)	34 (21.7)	0.053
Cancer (%)	12 (6.8)	13 (8.3)	0.766
Depression (%)	13 (7.4)	16 (10.2)	0.477
Diabetes (%)	13 (7.4)	12 (7.6)	1
Fibromyalgia (%)	5 (2.8)	3 (1.9)	0.846
Hypertension (%)	36 (20.5)	62 (39.5)	<0.001
Osteoporosis (%)	7 (4.0)	5 (3.2)	0.926
Thyroid Pathology (%)	15 (8.5)	19 (12.1)	0.371
Valvulopathy (%)	0 (0.0)	3 (1.9)	0.207
Alcohol Abuse (%)	4 (2.3)	8 (5.1)	0.278
Hepatitis (%)	2 (1.1)	5 (3.2)	0.359
Smoking History (%)	5 (2.8)	6 (3.8)	0.847
Medications			
ACE inhibitor	2 (1.1)	7 (4.5)	0.127
ARB	1 (0.6)	2 (1.3)	0.921
Antidepressant	3 (1.7)	5 (3.2)	0.602
Beta-blocker	3 (1.7)	3 (1.9)	1
Benzodiazepines	2 (1.1)	1 (0.6)	1
NSAIDs	5 (2.8)	5 (3.2)	1
Opioid Medications	3 (1.7)	4 (2.5)	0.879

Table 3: Comparison of Injury and Operative Characteristics Stratified by Cluster Membership

	Optimal	Suboptimal	p
Total Number of Patients	176	157	
Tendons Involved (%)			<0.001
Infraspinatus	1 (0.6)	0 (0.0)	
Subscapularis	2 (1.1)	0 (0.0)	
Supraspinatus	153 (86.9)	42 (26.8)	
Supraspinatus, Infraspinatus	6 (3.4)	73 (46.5)	
Supraspinatus, Infraspinatus, Subscapularis	3 (1.7)	15 (9.6)	
Supraspinatus, Infraspinatus, Subscapularis, Teres Minor	1 (0.6)	0 (0.0)	
Supraspinatus, Infraspinatus, Teres minor	0 (0.0)	4 (2.5)	
Supraspinatus, Subscapularis	10 (5.7)	23 (14.6)	
Anterior-Posterior Dimension (mean (SD))	19.13 (9.18)	39.77 (16.28)	<0.001
Medial-Lateral Dimension (mean (SD))	24.92 (10.21)	38.91 (14.69)	<0.001
Chronic (%)	149 (84.7)	126 (80.3)	0.361
Workman's Compensation (%)	34 (19.3)	27 (17.2)	0.721
Balloon (%)	0 (0.0)	5 (3.2)	0.053
Anchor Configuration (%)			<0.001
Double Row	80 (45.5)	34 (21.7)	
Single Row	23 (13.1)	13 (8.3)	
Suture Bridge	73 (41.5)	110 (70.1)	
Number of Anchors (mean (SD))	2.73 (1.12)	3.57 (1.29)	<0.001
Anchor Material (%)			0.034
Biocomposite	13 (7.4)	24 (15.3)	
Metal	21 (11.9)	24 (15.3)	
PEEK	142 (80.7)	109 (69.4)	
Medial Repair (%)	2 (1.1)	0 (0.0)	0.529
Marginal Convergence (%)	8 (4.5)	18 (11.5)	0.032
Patch Used (%)	2 (1.1)	8 (5.1)	0.073
Acromioplasty (%)	156 (88.6)	141 (89.8)	0.867
Biceps (%)			0.011
None	103 (58.5)	79 (50.3)	
Subpectoral	53 (30.1)	55 (35.0)	
Suprapectoral	16 (9.1)	8 (5.1)	
Tenotomy	4 (2.3)	15 (9.6)	
Number of Tendons Involved (mean (SD))	1.14 (0.44)	1.85 (0.61)	<0.001
Subscapular Involvement (%)	16 (9.1)	38 (24.2)	<0.001

Table 4: Comparison of CSOs Stratified by Cluster Membership

	Optimal	Suboptimal	p
Number of Patients	176	157	
ASES			
MCID at 2 years (%)	155 (88.1)	92 (58.6)	**<0.001**
SCB at 2 years (%)	143 (81.2)	79 (50.3)	**<0.001**
PASS at 2 years (%)	126 (71.6)	69 (43.9)	**<0.001**
CMS			
MCID at 2 years (%)	144 (81.8)	72 (45.9)	**<0.001**
SCB at 2 years (%)	140 (79.5)	66 (42.0)	**<0.001**
PASS at 2 years (%)	122 (69.3)	79 (50.3)	**0.001**
SANE			
MCID at 2 years (%)	126 (71.6)	82 (52.2)	**<0.001**
SCB at 2 years (%)	103 (58.5)	66 (42.0)	**0.004**
PASS at 2 years (%)	120 (68.2)	72 (45.9)	**<0.001**

Table 5: Predictors of Suboptimal Cluster Membership on Multivariable Stepwise Regression Model

Variables	Odds Ratio	95% CI	P-value
Thyroid disease	2.07	0.77-5.56	0.15
Preoperative CMS	1.11	1.04-1.18	**0.001**
Preoperative SANE	0.98	0.96-1	0.13
Tear size in sagittal dimension	1.10	1.05-1.15	**<0.001**
Tear size in coronal dimension	1.03	1-1.07	0.06
Number of tendons involved	14.07	4.5-44.02	**<0.001**
Subscapularis involvement	8.67	2.45-30.71	**0.01**
Subpectoral bicep tenodesis	0.61	0.27-1.4	0.2
Suprapectoral bicep tenodesis	0.22	0.05-0.92	**0.03**
Bicep tenotomy	9.52	2.16-41.96	**0.002**
Subscapularis tendon involvement*	0.01	0.01-0.28	**<0.001**

*Interaction term between number of tendons involved and subscapularis involvement demonstrated that the effects of subscapularis involvement decreased with the number of total tendons involved and vice versa.