Association of Antihypertensive and Statin Medication Usage With Postoperative Stiffness After Arthroscopic Rotator Cuff Repair

A Retrospective Cohort Study

Andres R. Perez,* BA, Henson Destiné,* MD, Nathaniel Kern,* BS, Neel K. Patel,* MD, Anya T. Hall,* MD, Manoj Reddy,* MD, Austin Looney,* MD, Kevin B. Freedman,* MD, and Fotios P. Tjoumakaris,*† MD
Investigation performed at the Rothman Orthopaedic Institute, Philadelphia, Pennsylvania, USA

Background: Angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and statins may be able to modulate postoperative stiffness, a major cause of morbidity after arthroscopic rotator cuff repair (aRCR).

Purpose: To determine whether there is an association between ACEi, ARB, or statin usage and stiffness after aRCR.

Study Design: Cohort study; Level of evidence, 3.

Methods: Patients who underwent primary aRCR between January 2016 and December 2019 were categorized into 4 groups depending on the usage of ACEi (n = 45), ARB (n = 27), statins (n = 53), or none of these medications (controls; n = 113). Range of motion in flexion, abduction, internal rotation (IR), and external rotation (ER) was recorded preoperatively and at 6 weeks and 3, 6, and 12 months postoperatively. Functional outcomes were assessed with the American Shoulder and Elbow Surgeons (ASES) score, the Single Assessment Numeric Evaluation (SANE), and the Simple Shoulder Test (SST) preoperatively and at 1 and 2 years postoperatively. The groups were compared using *t* test or Mann-Whitney *U* test for continuous data and chi-square or Fisher exact test for categorical data.

Results: Preoperatively, compared with controls, the ACEi group had decreased flexion ($P = .038$), abduction ($P = .001$), ER ($P = .009$), and IR ($P = .015$); the ARB group had decreased abduction ($P = .012$) and IR ($P = .019$); and the statins group had decreased abduction ($P = .015$), ER ($P = .008$), and IR ($P = .011$). Postoperatively, compared with controls, the ACEi group had decreased 6-month abduction ($P = .034$) that resolved by 12 months and 3-month ER ($P = .004$) that persisted into 6 months, the ARB group had greater ER at 12 months ($P = .006$), and the statins group had increased 6-week abduction ($P = .017$) that normalized by 3 months. Patients taking ACEi had lower postoperative ASES (30 vs 58.6; $P = .001$) and SANE scores (28.4 vs 52.3; $P = .002$) at 1 year and lower SST scores at 2 years (74.7 vs 85.5; $P = .002$) versus controls.

Conclusion: Patients who used ACEi showed an increased risk of stiffness 6 months postoperatively and had worse SST scores at 2 years after aRCR, while those who used ARB demonstrated improved postoperative ER and IR, with no changes in functional outcomes at longer-term follow-ups.

Keywords: angiotensin-converting enzyme inhibitor; angiotensin receptor blocker; range of motion; rotator cuff repair; statin; stiffness

Postoperative stiffness is a major cause of morbidity after arthroscopic rotator cuff repair (aRCR), with rates in the literature reported to be as high as 23%.[5,31] Stiffness can be a source of dissatisfaction after surgery and may require secondary procedures to alleviate motion loss.[20] There is

The Orthopaedic Journal of Sports Medicine, 13(1), 23259671241305089
DOI: 10.1177/23259671241305089

a wide variety of studies in the literature attempting to determine risk factors that contribute to postoperative stiffness and identify measures that can be used to prevent postoperative stiffness.[12] Some of these risk factors include preoperative shoulder stiffness, early postoperative pain, concomitant biceps procedures, diabetes mellitus, female sex, hypothyroidism, prolonged immobilization, timing of rehabilitation, and glenohumeral synovitis.[7,9,17,35,36] Medications that have yet to be investigated in the rotator cuff literature are angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and statins.

ACEi and ARB are known to reduce the expression of transforming growth factor-β (TGF-β).[10] TGF-β is theorized to be an important regulator of the inflammatory process and tissue healing and has been the subject of significant research in the nonorthopaedic literature.[22,27] In murine models, high levels of TGF-β can lead to failures in skeletal muscle tissue regeneration.[10] In other medical specialties, such as nephrology and cardiology, investigations have revealed a connection between TGF-β and tissue fibrosis.[14,39] One mechanism of TGF-β expression in the body is via the renin-angiotensin system.[30] Blockade of this system can be achieved through ACEi and ARB. The prevalence of using these medications is high and increasing in the United States population.[21] Investigations in the orthopaedic literature thus far are limited to knee arthroplasty and have yet to reveal any association between ACEi/ARB usage and postoperative stiffness.[18,23] We are unaware of any published literature pertaining to any relationship between ACEi/ARB usage and outcomes after aRCR.

Similarly, statin medications are a class of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors with widespread use in the United States.[28] Statin use has thus far been investigated in the orthopaedic literature for associations with tendinopathy and surgical revision rates. Statin therapy, through downstream cytokine actions, is thought to impact bone formation and resorption. It is associated with decreased revision rates after total knee arthroplasty (TKA).[11] In rotator cuff disease, via its effect on reduction of hyperlipidemia,[6] statin use has shown to be associated with a decreased rate of revision after RCR and may decrease the development of rotator cuff disease altogether.[40] Conversely, statin therapy may also cause tendinopathy via downstream actions on matrix metalloproteinases.[15] While there have been some publications in the orthopaedic literature on statin usage and patient outcomes,[25,26,41] there are no studies on their association with range of motion (ROM) outcomes. In animal models, statins have been shown to be effective in preventing postoperative adhesions.[8] Thus, an investigation into their impact on postoperative ROM outcomes in patients after aRCR is also merited.

This study aimed to determine whether there is an association between ACEi, ARB, or statin usage and postoperative ROM, postoperative patient-reported outcome measures (PROMs), and the need for additional procedures after primary aRCR. We hypothesized that there would be no association between the use of these medications and postoperative outcomes.

METHODS

Inclusion/Exclusion Criteria

A retrospective review was conducted examining all patients at a single institution who underwent primary arthroscopic RCR between January 1, 2016, and December 31, 2019. Patients were identified using Current Procedural Terminology code 29827 and were included in the study if they had a minimum of 2-year postoperative follow-up data and documented ROM data. The exclusion criteria were as follows: concomitant adhesive capsulitis, calcific tendinosis, glenohumeral arthritis, and concomitant labrum repair; a history of previous shoulder surgery; a history of humeral fractures; workers' compensation claims; age <18 years; an irreparable rotator cuff tear; a history of substance abuse; or dialysis. Patients were then categorized into 4 groups based on taking ACEi, ARB, statins, or none of these medications (controls). This study was considered exempt from approval by an institutional review board.

Data Collection

A chart review was performed on all eligible patients. Demographic information—such as age, sex, race, ethnicity, body mass index (BMI), surgical history, concomitant procedures, rotator cuff tear size, physical therapy protocol, preoperative ROM, medication usage as well as dosage, concurrent medical diagnoses (eg, diabetes, hypothyroidism, hyperlipidemia, and hypertension)—and follow-up procedures were collected via chart review. Physician and physical therapy notes were examined to determine

†Address correspondence to Fotios P. Tjoumakaris, MD, Rothman Orthopaedic Institute, 2500 English Creek Avenue, Building 1300, Egg Harbor Township, NJ 08234, USA (email: Fotios.Tjoumakaris@rothmanortho.com).

*Rothman Orthopaedic Institute, Philadelphia, Pennsylvania, USA.

Final revision submitted May 14, 2024; accepted June 17, 2024.

One or more of the authors has declared the following potential conflict of interest or source of funding: N.K.P. has received grant support from DJO and education payments from Smith + Nephew, Paladin Technology Solutions, Eclipse Technology Solutions, and Mid-Atlantic Surgical Systems. M.R. has received education payments from Arthrex and Medical Device Business Services and hospitality payments from Stryker. A.L. has received education payments from Arthrex and hospitality payments from Stryker. K.B.F. has received grant support from Vericel; education payments from Liberty Surgical; and consulting fees from DePuy, Vericel, and Innocoll. F.P.T. has received consulting fees from DePuy/Medical Device Business Services, royalties from Tigon Medical, and hospitality payments from MicroVention and Smith + Nephew and has stock/stock options in Trice Medical. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

Ethical approval for this study was waived by Philadelphia University and Thomas Jefferson University (ref No. 21E.1042).

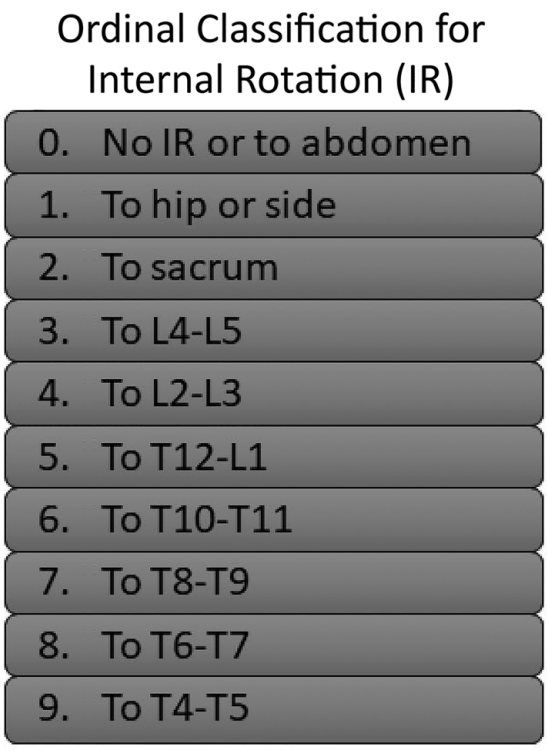

Figure 1. Ordinal classification for internal rotation.

ROM—flexion, abduction, internal rotation (IR), and external rotation (ER)— preoperatively and at 6 weeks, 3 months, 6 months, and 12 months postoperatively. IR was initially measured as the nearest vertebral level that patients could reach using their thumb with the arm behind their back and was then converted into an ordinal classification, as has been similarly performed in previous studies[33] (Figure 1). PROMs were assessed using the American Shoulder and Elbow Surgeons (ASES) score, the Single Assessment Numeric Evaluation (SANE), and the Simple Shoulder Test (SST) preoperatively and 1 and 2 years postoperatively.

Data Analysis

After data were split into their respective groups based on their medication, descriptive analyses were performed by comparing each group to the control group. Continuous data were reported as means with standard deviations or medians with interquartile ranges, and categorical data were reported as counts with percentages. After assessing normality, continuous data were compared using either the t test or the Mann-Whitney U test. Categorical data were assessed by either running a chi-square test or a Fisher exact test. Then, a set of regressions were performed looking at how ROM was affected at various time points looking at the primary variable of the control group to the various medications while controlling for diabetes. All regression models underwent thorough assumption checks to ensure the validity of their results for reporting and interpretation. Significance was determined at $P < .05$. All statistical analyses were done using R Version 4.1.2 (RStudio).

RESULTS

A total of 304 patients who underwent aRCR met the inclusion criteria for this study. After applying the exclusion criteria and removing 37 patients for not having a 2-year postoperative follow-up, 125 patients were included in the case group (ACEi group: n = 45 patients; ARB group: n = 27 patients; statins group: n = 53 patients) and 113 in the control group. The breakdown of the number of patients in each group and the number of patients lost to follow-up in each group is presented in Figure 2. Patients in the ACEi and statin groups had more diagnoses of diabetes when compared with controls (P = .017 and

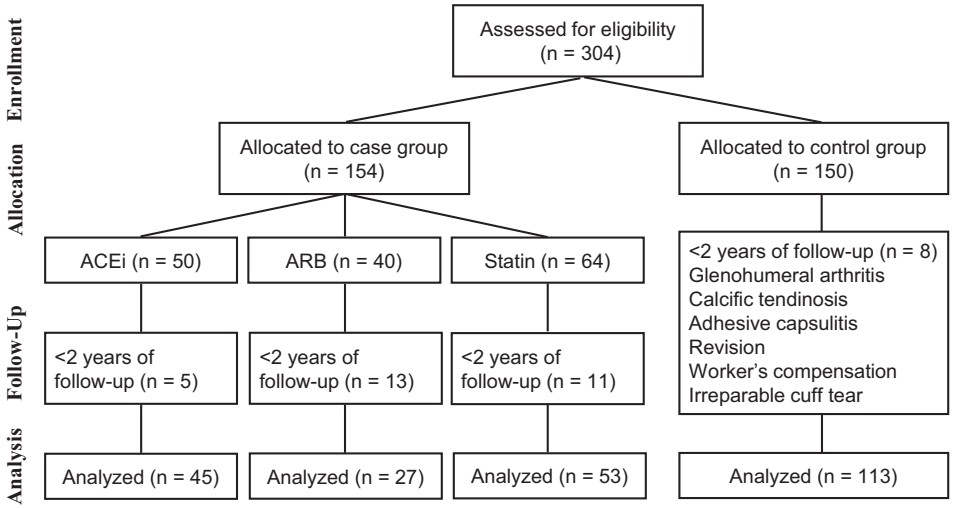

Figure 2. CONSORT diagram of patient inclusion in the study. ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CONSORT, Consolidated Standards of Reporting Trials.

TABLE 1
Patient Characteristics[a]

	Study Group				*P*		
	Control (n = 113)	ACEi (n = 45)	ARB (n = 27)	Statin (n = 53)	Control vs ACEi	Control vs ARB	Control vs Statin
Sex					.224	.913	.981
Male	75 (66.4)	35 (77.8)	17 (63)	35 (66)			
Female	38 (33.6)	10 (22.2)	10 (37)	18 (34)			
Age, y	63.8 ± 8.79	62.6 ± 7.91	64.6 ± 6.40	65 [59-69.2]	.286	.751	.403
BMI, kg/m^2	31 ± 6.97	31.4 ± 6.49	29.3 ± 4.85	30.9 (5.57)	.458	.597	.946
Hypothyroid	7 (6.19)	2 (4.44)	3 (11.1)	2 (3.77)	≥.999	.406	≥.999
Diabetes	15 (13.3)	14 (31.1)[b]	0 (0)	16 (30.2)[b]	**.017**	.076	**.001**
RC tear					≥.999	.569	.878
Partial	10 (14.3)	7 (16.3)	3 (11.1)	6 (13)			
Full	60 (85.7)	36 (83.7)	24 (88.9)	40 (87)			

[a]Data are presented as mean ± SD, median [IQR], or n (%). Bold *P* values indicate a statistically significant difference between groups ($P \leq .05$). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; IQR, interquartile range; RC, rotator cuff.
[b]Statistically significant difference compared with the control group.

TABLE 2
Preoperative and Postoperative ROM in the ACEi and ARB Groups[a]

	Study Group			*P*		
ROM	Control (n = 113)	ACEi (n = 45)	ARB (n = 27)	Control vs ACEi	Control vs ARB	ACEi vs ARB
Flexion, deg						
Preop	139	119[b]	133	**.038**	.143	.369
6 weeks postop	103	89	104	.262	.838	.377
3 months postop	138	128	133	.156	.480	.732
6 months postop	154	151	150	.108	.430	.781
12 months postop	144	155	158	.736	.323	.462
Abduction, deg						
Preop	139	92[b]	110[b]	**.001**	**.012**	.296
6 weeks postop	69.7	60	97	.956	.414	.251
3 months postop	117	102	122	.153	.632	.270
6 months postop	146	127[b]	141	**.034**	.426	.199
12 months postop	135	154	162	.330	.268	.853
External rotation, deg						
Preop	50	43[b]	55	**.009**	.836	.075
6 weeks postop	41	37	28	.530	.146	.260
3 months postop	53	39[b,d]	53[d]	**.004**	.959	**.038**
6 months postop	56	43[b,d]	56[d]	**<.001**	.978	**.003**
12 months postop	42	52	68[b]	.178	**.006**	.076
Internal rotation[c]						
Preop	5.9	4.5[b]	4.5[b]	**.015**	**.019**	.921
6 weeks postop	4	5.8	3	.192	.419	.102
3 months postop	5.1	4.5	4.3	.446	.234	.807
6 months postop	6	5	5.5	.061	.272	.490
12 months postop	4.7	4[d]	6.6[d]	.370	.052	**.023**

[a]Bold *P* values indicate statistically significant differences between groups ($P \leq .05$). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; postop, postoperative; Preop, preoperative; ROM, range of motion.
[b]Significant difference compared with the control group.
[c]See Figure 1 for the key to ordinal classifications.
[d]Significant differences between ACEi and ARB.

P = .001, respectively). No significant differences were found between groups with regard to demographic characteristics (age, sex, BMI), hypothyroidism, and cuff tear size (full/partial thickness) (Table 1).

Patients taking ACEi had significantly decreased preoperative flexion (P = .038), abduction (P = .001), ER (P = .009), and IR (P = .015) compared with the control group. Those on ARB showed significantly decreased preoperative abduction (P = .012) and IR (P = .019) when compared with controls (Table 2). Patients on statins had significantly decreased preoperative active abduction (P = .015), ER (P = .008), and IR (P = .011) compared with the control group (Table 3).

Postoperatively, patients on ACEi had significantly decreased 6-month active abduction (P = .034) that resolved by 12 months and 3-month active ER (P = .004) that persisted into the 6 months when compared with the control group. Patients taking ARB had significantly greater ER at 12 months (P = .006) when compared with the control group (Table 2). Patients taking statin had significantly increased 6-week active abduction (P = .017) that normalized to the control group by 3 months (Table 3). All other ROM measurements were not significant at different time points. When comparing ACEi to ARB directly, ER at 3 months postoperatively (P = .038) was significantly lower in the ACEi group, and this difference persisted at 6 months (P = .003) before resolving at the 12 months. In addition, IR was significantly lower in the ACEi group compared with the ARB group at 12 months (P = .023) postoperatively (Table 2).

TABLE 3
Preoperative and Postoperative ROM in the Statin Group[a]

	Control (n = 104)	Statin (n = 57)	P
Flexion, deg			
Preop	150	145	.109
6 weeks postop	86	89	.783
3 months postop	145	140	.822
6 months postop	160	152	.891
Abduction, deg			
Preop	130	85	**.015**
6 weeks postop	58	95	**.017**
3 months postop	119	120	.414
6 months postop	150	120	.066
External rotation, deg			
Preop	50	40	**.008**
6 weeks postop	34	34	.966
3 months postop	50	50	.189
6 months postop	54	63	.174
Internal rotation[b]			
Preop	5	4	**.011**
6 weeks postop	3.2	4	.546
3 months postop	5	5.5	.350
6 months postop	6	7	.056

[a]Bold P values indicate a statistically significant difference between groups ($P \leq .05$). postop, postoperative; Preop, preoperative; ROM, range of motion.
[b]See Figure 1 for the key to ordinal classifications.

Multivariate Regression Analysis

When adjusting for diabetes between both cohorts and comparing them to controls (Table 4), patients on ACEi had significantly decreased 6-month abduction (P = .017), 3- and 6-month ER (P = .010 and $P < .001$, respectively), and 6-month IR (P = .039). Patients on ARB had significantly increased 12-month ER (P = .006) and 12-month IR (P = .05). Patients on statin medication had significantly decreased 6-month abduction (P = .034).

Patients taking ACEi were found to have significant decreases in postoperative ASES scores at 1 year (P = .001), SANE scores at 1 year (P = .002), and SST scores at 2 years (P = .002) compared with the control group. When comparing ACEi against ARB, the ACEi group was found to have significantly lower postoperative SANE scores at 1 year (P = .015). No significant differences were found in ARB or statins (Table 5). No significant differences were found when looking at postoperative complications, secondary procedures (ie, capsular release), or revision surgery between all cohorts (Table 6).

DISCUSSION

We hypothesized that there would be no association between ACEi, ARB, or statin usage and postoperative ROM, the need for additional procedures, or PROMs after aRCR. ER and abduction were found to be affected the most in the patients taking ACEi, ARB, or statins. ER was increased in patients taking ARB while decreased in those taking ACEi. Abduction was increased in those taking statins and decreased in those taking ACEi, while IR was also increased postoperatively in those taking statins. When adjusting for diabetes between all groups, ER was similarly decreased in ACEi and increased in ARB, while IR was decreased in those taking ACEi and increased in those taking ARB. Interestingly, while patients on ACEi had a similar decrease in abduction, patients on statin medication had decreased abduction. ASES and SANE scores were decreased in patients taking ACEi at the 1-year mark, while SST scores at 2 years were decreased in those taking ACEi compared with controls.

While it is indisputable that ACEi and ARB offer beneficial antihypertensive effects for those who require blood pressure control, minimal research has been conducted regarding their effect on postoperative ROM after aRCR. A recent study conducted by Bi et al[3] found that taking ARB or ACEi did not significantly affect the rate of postoperative arthrofibrosis after shoulder arthroscopy. This study in particular defined postoperative arthrofibrosis as requiring manipulation under anesthesia or a new diagnosis of adhesive capsulitis after shoulder arthroscopy. While our study drew similar conclusions with regard to postoperative complications, our study introduced ROM monitoring at multiple time points throughout the pre- and postoperative periods that gave a more detailed view of ROM progression. For example, our results showed that the ACEi cohort had decreased ER at 3 and 6 months after surgery before normalizing at 12 months, a result that end-point variables—such as manipulation under anesthesia or adhesive capsulitis—would not be able to bring to light. In our study, we were able to gather ROM

TABLE 4
Multivariate Regression Adjusting for Diabetes Within Cohorts[a]

	Control vs ACEi	Control vs ARB	Control vs Statin
Flexion			
6 weeks postop	−19.63 (−45.68 to 6.42); P = .146	4.64 (−20.73 to 30.01); P = .722	−15.93 (−38.31 to 6.46); P = .168
3 months postop	−8.86 (−21.62 to 3.91); P = .177	−7.184 (−22.07 to 7.70); P = .346	2.53 (−7.83 to 12.88); P = .634
6 months postop	−1.55 (−10.89 to −7.79); P = .746	−6.14 (−18.00 to 5.72); P = .313	0.64 (−10.67 to 11.95); P = .912
12 months postop	10.93 (−10.92 to 32.78); P = .335	13.79 (−12.95 to 40.53); P = .321	28.09 (−27.05 to 83.23); P = .331
Abduction			
6 weeks postop	−16.21 (–76.44 to 44.02); P = .604	29.39 (−12.78 to 71.56); P = .185	35.21 (−2.44 to 72.86); P = .079
3 months postop	−14.87 (−38.59 to 8.86); P = .226	4.727 (−22.52 to 31.98); P = .735	−1.77 (−21.95 to 18.41); P = .864
6 months postop	−23.92 (−42.82 to −5.02); **P = .017**	–5.07 (−29.21 to 19.07); P = .683	−29.31 (−55.27 to −3.34); **P = .034**
12 months postop	16.61 (−22.61 to 55.84); P = .424	23.57 (−10.21 to 57.35); P = .201	—[b]
External rotation			
6 weeks postop	−4.96 (−26.27 to 16.35); P = .651	−12.78 (−31.22 to 5.66); P = .183	−7.29 (−23.79 to 9.22); P = .392
3 months postop	−13.37 (−23.31 to 3.44); **P = .010**	−0.88 (−13.10 to 11.34); P = .888	3.90 (−5.26 to 13.07); P = .407
6 months postop	−13.36 (−20.13 to −6.58); **P < .001**	−0.36 (−8.37 to 7.65); P = .930	6.43 (−3.78 to 16.64); P = .222
12 months postop	12.05 (−3.33 to 27.43); P = .141	27.25 (10.68 to 44.02); **P = .006**	4.78 (−31.36 to 40.91); P = .801
Internal rotation			
6 weeks postop	1.73 (−0.41 to 3.87); P = .133	−0.67 (−2.67 to 1.34); P = .523	0.33 (−1.75 to 2.42); P = .758
3 months postop	−0.59 (−1.89 to 0.71); P = .380	−0.67 (−2.09 to 0.76); P = .363	0.65 (−0.61 to 1.90); P = .317
6 months postop	−1.34 (−2.57 to −1.00); **P = .039**	−0.50 (−1.77 to 0.77); P = .442	0.92 (−0.65 to 2.49); P = .255
12 months postop	−0.64 (−2.46 to 1.19); P = .504	1.94 (0.09 to 3.78); **P = .050**	−0.64 (−4.47 to 3.20); P = .751

[a]Data are reported as SE (95% CI). Bold P values indicate statistical significance ($P \leq .05$). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; postop, postoperative; ROM, range of motion.
[b]No patients with diabetes reported 12-month ROM data.

data at different postoperative intervals to determine differences between cohorts in the immediate and midterm postoperative period.

While it was evident that these patients had decreased ROM preoperatively, the incidence of continued decreased ROM at certain time points is interesting, as ACEi is widely known to have antifibrotic properties through its anti-TGF-β1 effects, which decrease fibrosis and promote the healing of articular cartilage[19,24,38] Despite these characteristics of ACEi, patients taking ACEi had decreased ROM postoperatively compared with the control group. On the other hand, patients taking ARB had increased postoperative ROM. Similarly, a recent study by Arraut et al[2] found increased ROM in patients undergoing TKA that were prescribed losartan, although this finding was not statistically significant, as it is in our study. While ACEi and ARB both operate through the renin-angiotensin-aldosterone system, the point at which each medication acts in the pathway differs. This perhaps affects the antifibrotic potential of each medication.[16,42]

The effect of statins on decreasing the rate of RCR revision has been studied by Cancienne et al.[6] More recently, Amit et al[1] reported no differences in PROMs, retear rate, and fatty infiltration on magnetic resonance imaging at 12 months after RCR in patients with hyperlipidemia treated with statins compared with controls. While our study found similar results in PROMs and complication rates, there was an increase in active abduction at the 6-week postoperative period followed by a decrease in abduction when adjusting for diabetes. This increase in ROM may be due to the perceived reduction in proinflammatory compounds such as isoprenoids and matrix metalloproteinase 3 and 9.[4] It is possible that when adjusting for diabetes and effectively removing a set of patients who have a condition known to

TABLE 5
Preoperative and Postoperative Patient-Reported Outcomes[a]

	Study Group				*P*			
	Control	ACEi	ARB	Statin	Control vs ACEi	Control vs ARB	Control vs Statin	ACEi vs ARB
ASES score								
Preop	50.1 ± 20.8	43.7 ± 17.7	49.5 ± 14.2	50.7 ± 17.8	.099	.871	.612	.183
1-year postop	58.6 ± 47.5	30 ± 25.1[b]	52.8 ± 37.2	48.2 [47.7-56.1]	**.001**	.711	.147	.055
2-year postop	84.1 ± 19.7	82.9 ± 18.7	80.8 ± 19.4	87.5 [70.5-96.7]	.570	.320	.679	.675
SANE								
Preop	38.8 ± 20.8	35.1 ± 23	45.7 ± 22.6	40.8 ± 20.9	.463	.265	.162	.112
1-year postop	52.3 ± 31.6	28.4 ± 25.6[b,c]	58.5 ± 37.6[c]	47.9 [29.8-56.1]	**.002**	.435	.619	**.015**
2-year postop	80.7 ± 24.8	75 ± 23.5	85.7 ± 15.8	87.7 [74.3-93.2]	.157	.811	.952	.135
SST								
Preop	41.6 ± 25.3	34.9 ± 21.7	42.1 ± 21.7	41.7 [16.7-58.3]	.269	.795	.586	.275
1-year postop	52 ± 30.4	50 ± 27.5	65.8 ± 40.7	48.1 [34.9-56]	.982	.213	.253	.213
2-year postop	85.5 ± 22.1	74.7 ± 21.2[b]	81.5 ± 20.1	91.7 [75-100]	**.002**	.126	.117	.189

[a]Data are presented as mean ± SD or median [IQR]. Bold *P* values indicate a statistically significant difference between groups ($P < .05$). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASES, American Shoulder and Elbow Surgeons; IQR, interquartile range; postop, postoperative; Preop, preoperative; SANE, Single Assessment Numeric Evaluation; SST, Simple Shoulder Test.
[b]Significant difference compared with controls.
[c]Significant difference between ACEi and ARB.

TABLE 6
Postoperative Complications[a]

	Control	ACEi	ARB	Statin
Revision surgery				
No	106 (93.80)	42 (93.30)	24 (88.90)	48 (90.60)
Yes	7 (6.20)	3 (6.70)	3 (11.10)	5 (9.40)
Postop complications				
None	106 (93.80)	43 (95.60)	25 (92.60)	48 (90.60)
Recurrent RC tear	5 (4.42)	2 (4.44)	2 (7.40)	5 (9.40)
Infection	1 (0.88)	0 (0)	0 (0)	0 (0)
Nerve injury	1 (0.88)	0 (0)	0 (0)	0 (0)
Vessel injury	0 (0)	0 (0)	0 (0)	0 (0)

[a]Data are presented as n (%). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; Postop, postoperative; RC, rotator cuff.

increase proinflammatory markers, the impact potential that statins may have had in those without diabetes was not profound enough to reach significance.[13,37]

While current evidence may recommend discontinuing ACEi and ARB before surgery because of the risks of hypotensive episodes intraoperatively[32,34] and continuing statins in the perioperative period,[29] our results report that in the postoperative period, patients taking ACEi may be at a disadvantage when trying to regain active ROM while ARB and statins may offer an advantage of achieving greater ROM more quickly. Future studies where these medications can be safely introduced in the postoperative population and be further stratified into medication subclasses may offer more insight into whether an objective advantage or disadvantage is noticed when it comes to redeveloping ROM.

Limitations

Our study is not without limitations. One limitation is the retrospective nature of this study. Randomization of the participants is not something that can be achieved with this type of analysis since the medical history of hypertension and hyperlipidemia dictates medical therapy for these conditions. Second, we did not document compliance with medication usage of either statin therapy or angiotensin blockers/inhibitors. Simply being on the medication was a determinant of inclusion, regardless of dosage. Third, there is inherent variability in the ROM measurements documented by providers. While all included patients had ROM documented in their charts from our single institution, different physicians and physical therapists may conduct measurements differently. Our study only gathered

ROM data for patients taking ACEi or ARB up to the 12-month postoperative period and statins up until the 6-month postoperative period. Having longer ROM follow-up data for these cohorts can allow us to see whether ROM stabilizes between groups or if 1 medication cohort consistently has greater or worse ROM measurements. We do believe, however, that we would capture the impact of ROM on the outcome as we did track functional outcome scores for all patients at the final follow-up.

CONCLUSION

Patients on ACEi therapy are at an increased risk of stiffness in the early postoperative (6 months) period and are at risk for worse functional outcomes (SST) at the 2-year follow-up after aRCR. Meanwhile, patients on ARB therapy demonstrated improved postoperative motion in ER and IR with no changes in functional outcomes at longer-term follow-ups. Surgeons should use this information to guide patient education and rehabilitation perioperatively after aRCR.

ORCID iD

Henson Destiné https://orcid.org/0000-0003-3098-1367

REFERENCES

1. Amit P, Kuiper JH, James S, Snow M. Does statin-treated hyperlipidemia affect rotator cuff healing or muscle fatty infiltration after rotator cuff repair? *J Shoulder Elbow Surg*. 2021;30(11):2465-2474.
2. Arraut J, Lygrisse K, Singh V, Fiedler B, Schwarzkopf R, Rozell J. The effect of losartan on range of motion and rates of manipulation in total knee arthroplasty: a retrospective matched cohort study. *Arch Orthop Trauma Surg*. 2022;143(7):4043-4048.
3. Bi AS, Li ZI, Triana J, et al. Angiotensin receptor blockers and angiotensin-converting enzyme inhibitors have no significant relationship with postoperative arthrofibrosis after shoulder arthroscopy. *Arthrosc Sports Med Rehabil*. 2023;5(4):100748.
4. Biasucci LM, Biasillo G, Stefanelli A. Inflammatory markers, cholesterol and statins: pathophysiological role and clinical importance. *Clin Chem Lab Med*. 2010;48(12):1685-1691.
5. Brislin KJ, Field LD, Savoie FH. Complications after arthroscopic rotator cuff repair. *Arthroscopy*. 2007;23(2):124-128.
6. Cancienne JM, Brockmeier SF, Rodeo SA, Werner BC. Perioperative serum lipid status and statin use affect the revision surgery rate after arthroscopic rotator cuff repair. *Am J Sports Med*. 2017;45(13):2948-2954.
7. Cho CH, Bae KC, Kim DH. Incidence and risk factors for early postoperative stiffness after arthroscopic rotator cuff repair in patients without preoperative stiffness. *Sci Rep*. 2022;12:3132.
8. Choi GJ, Park HK, Kim DS, Lee D, Kang H. Effect of statins on experimental postoperative adhesion: a systematic review and meta-analysis. *Sci Rep*. 2018;8(1):14754.
9. Chung SW, Huong CB, Kim SH, Oh JH. Shoulder stiffness after rotator cuff repair: risk factors and influence on outcome. *Arthroscopy*. 2013;29(2):290-300.
10. Cohn RD, van Erp C, Habashi JP, et al. Angiotensin II type 1 receptor blockade attenuates TGF-beta-induced failure of muscle regeneration in multiple myopathic states. *Nat Med*. 2007;13(2):204-210.
11. Cook MJ, Sorial AK, Lunt M, Board TN, O'Neill TW. Effect of timing and duration of statin exposure on risk of hip or knee revision arthroplasty: a population-based cohort study. *J Rheumatol*. 2020;47(3):441-448.
12. Denard PJ, Lädermann A, Burkhart SS. Prevention and management of stiffness after arthroscopic rotator cuff repair: systematic review and implications for rotator cuff healing. *Arthroscopy*. 2011;27(6):842-848.
13. Devaraj S, Dasu MR, Jialal I. Diabetes is a proinflammatory state: a translational perspective. *Expert Rev Endocrinol Metab*. 2010;5(1):19-28.
14. Dobaczewski M, Chen W, Frangogiannis NG. Transforming growth factor (TGF)-β signaling in cardiac remodeling. *J Mol Cell Cardiol*. 2011;51(4):600-606.
15. Eliasson P, Dietrich-Zagonel F, Lundin AC, Aspenberg P, Wolk A, Michaëlsson K. Statin treatment increases the clinical risk of tendinopathy through matrix metalloproteinase release—a cohort study design combined with an experimental study. *Sci Rep*. 2019;9(1):17958.
16. Fogari R, Zoppi A, Lazzari P, et al. ACE inhibition but not angiotensin II antagonism reduces plasma fibrinogen and insulin resistance in overweight hypertensive patients. *J Cardiovasc Pharmacol*. 1998;32(4):616-620.
17. Guity MR, Sobhani Eraghi A, Hosseini-Baharanchi FS. Early postoperative pain as a risk factor of shoulder stiffness after arthroscopic rotator cuff repair. *J Orthop Traumatol*. 2021;22(1):25.
18. Hernandez NM, Cunningham DJ, Kabirian N, et al. Angiotensin receptor blockers were not associated with decreased arthrofibrosis after total knee arthroplasty. *Orthopedics*. 2021;44(2):e274-e280.
19. Huard J, Bolia I, Briggs K, Utsunomiya H, Lowe WR, Philippon MJ. Potential usefulness of losartan as an antifibrotic agent and adjunct to platelet-rich plasma therapy to improve muscle healing and cartilage repair and prevent adhesion formation. *Orthopedics*. 2018;41(5):e591-e597.
20. Huberty DP, Schoolfield JD, Brady PC, Vadala AP, Arrigoni P, Burkhart SS. Incidence and treatment of postoperative stiffness following arthroscopic rotator cuff repair. *Arthroscopy*. 2009; 25(8):880-890.
21. Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. Trends in prescription drug use among adults in the United States from 1999-2012. *JAMA*. 2015;314(17):1818-1831.
22. Kim KK, Sheppard D, Chapman HA. TGF-β1 signaling and tissue fibrosis. *Cold Spring Harb Perspect Biol*. 2018;10(4):a022293.
23. Langston JR, Ramsey DC, Skoglund K, Schabel K. Angiotensin II blockade had no effect on range of motion after total knee arthroplasty: a retrospective review. *J Orthop Surg*. 2020;15(1):48.
24. Logan CA, Gao X, Utsunomiya H, et al. The beneficial effect of an intra-articular injection of losartan on microfracture-mediated cartilage repair is dose dependent. *Am J Sports Med*. 2021;49(9):2509-2521.
25. Lübbeke A, Garavaglia G, Rothman KJ, et al. Statins may reduce femoral osteolysis in patients with total Hip arthroplasty. *J Orthop Res*. 2013;31(5):814-820.
26. Ma B, Sun J, Diao S, Zheng B, Li H. Effects of perioperative statins on patient outcomes after noncardiac surgery: a meta-analysis. *Ann Med*. 2018;50(5):402-409.
27. Meng XM, Nikolic-Paterson DJ, Lan HY. TGF-β: the master regulator of fibrosis. *Nat Rev Nephrol*. 2016;12(6):325-338.
28. Mercado C, DeSimone AK, Odom E, Gillespie C, Ayala C, Loustalot F. Prevalence of cholesterol treatment eligibility and medication use among adults—United States, 2005-2012. *MMWR Morb Mortal Wkly Rep*. 2015;64(47):1305-1311.
29. Mohebi R, Rosenson R. Statins in the perioperative period. *F1000Res*. 2019;8:F1000 Faculty Rev-688.
30. Morales MG, Vazquez Y, Acuña MJ, et al. Angiotensin II-induced profibrotic effects require p38MAPK activity and transforming growth factor beta 1 expression in skeletal muscle cells. *Int J Biochem Cell Biol*. 2012;44(11):1993-2002.
31. Parsons BO, Gruson KI, Chen DD, Harrison AK, Gladstone J, Flatow EL. Does slower rehabilitation after arthroscopic rotator cuff repair lead to long-term stiffness? *J Shoulder Elbow Surg*. 2010;19(7):1034-1039.

32. Rajgopal R, Rajan S, Sapru K, Paul J. Effect of pre-operative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists on intra-operative arterial pressures after induction of general anesthesia. *Anesth Essays Res*. 2014;8(1):32-35.
33. Rojas J, Joseph J, Srikumaran U, McFarland EG. How internal rotation is measured in reverse total shoulder arthroplasty: a systematic review of the literature. *JSES Int*. 2020;4(1):182-188.
34. Salim F, Khan F, Nasir M, Ali R, Iqbal A, Raza A. Frequency of intraoperative hypotension after the induction of anesthesia in hypertensive patients with preoperative angiotensin-converting enzyme inhibitors. *Cureus*. 2020;12(1):e6614.
35. Schneider WR, Trasolini RG, Riker JJ, Gerber N, Ruotolo CJ. Stiffness after arthroscopic rotator cuff repair: a rehabilitation problem or a surgical indication? *JSES Int*. 2020;5(1):88-92.
36. Tan Z, Hendy BA, Zmistowski B, et al. Glenohumeral synovitis score predicts early shoulder stiffness following arthroscopic rotator cuff repair. *J Orthop*. 2020;22:17-21.
37. Tsalamandris S, Antonopoulos AS, Oikonomou E, et al. The role of inflammation in diabetes: current concepts and future perspectives. *Eur Cardiol Rev*. 2019;14(1):50-59.
38. Utsunomiya H, Sekiya I, Uchida S. Editorial commentary: are we ready to apply stem cell therapy in rotator cuff tear surgery? *Arthroscopy*. 2020;36(1):86-87.
39. Wang B, Jha JC, Hagiwara S, et al. Transforming growth factor-β1-mediated renal fibrosis is dependent on the regulation of transforming growth factor receptor 1 expression by let-7b. *Kidney Int*. 2014;85(2):352-361.
40. Yang Y, Qu J. The effects of hyperlipidemia on rotator cuff diseases: a systematic review. *J Orthop Surg*. 2018;13:204.
41. Zeng GJS, Lee MJH, Chen JY, Ang BFH, Hao Y, Lie DTT. Dyslipidemia with perioperative statin usage is not associated with poorer 24-month functional outcomes after arthroscopic rotator cuff surgery. *Am J Sports Med*. 2020;48(10):2518-2524.
42. Zusman RM. Are there differences among angiotensin receptor blockers? *Am J Hypertens*. 1999;12(12)(pt 3):S231-s235.