Original Article

Smokers Achieved Minimal Clinically Important Difference for Visual Analog Scale and American Shoulder and Elbow Surgeons Scores at a Lower Rate Than Nonsmokers Even When Repaired Supraspinatus Tendons Were Intact on Postoperative Magnetic Resonance Imaging

W P Yau, M.B.B.S., F.R.C.S.Ed., F.R.C.S.Ed. (Ortho.), F.H.K.C.O.S., F.H.K.A.M. (Orthopaedic Surgery)

Purpose: To investigate the impact of smoking on clinical outcomes after repair of supraspinatus tendon in patients who had an intact repair found on postoperative magnetic resonance imaging. **Methods:** Patients who received primary complete repair of supraspinatus tendon tear between 2014 and 2020 were retrospectively identified. Patients were excluded if a postoperative magnetic resonance imaging scan was not available or if the follow-up was less than 2 years. Visual analog score (VAS), American Shoulder and Elbow Surgeons (ASES) score, and active forward flexion were assessed at the 2-year follow-up. The percentage of patients acquiring minimal clinically important difference (MCID) was reported. **Results:** One hundred primary supraspinatus tendon repairs were included. The healing rate was 77% in smokers and 90% in nonsmokers. Smoking was the independent predictor of a poorer 2-year VAS ($P < .001$) and ASES ($P < .001$) scores. Significant improvement in clinical outcomes was observed between preoperation and the 2-year follow-up, regardless of the integrity of the repair or smoking status ($P < .001$). When the repaired tendon was intact, nonsmokers had a greater chance of achieving MCID in 2-year VAS and ASES scores than smokers. Ninety-nine percent of nonsmokers, compared with 82% of smokers, achieved MCID in VAS at the 2-year follow-up ($P = .023$). The corresponding figures for ASES were 98% and 71%, respectively ($P = .004$). **Conclusions:** In this study, smoking was associated with poorer clinical outcomes, including a greater 2-year VAS pain score and a lower 2-year ASES score, when compared with nonsmokers, even in cases in which there was no full-thickness retear of the repaired supraspinatus tendon. **Level of Evidence:** Level III, retrospective cohort study.

Smoking is associated with a reduction of tissue perfusion,[1] impaired tissue healing,[2] and poorer clinical outcomes after surgery.[3-5] The detrimental effect of smoking on surgical outcomes has been proposed to be secondary to its negative impact on tissue oxygen tension,[2,6] tissue glucose level,[1] and reduction in collagen synthesis.[7]

Issues related to tobacco use have been found to have a significant impact on the outcomes of orthopaedic interventions.[4,8-16] Furthermore, evidence suggests that smoking is associated with increased symptoms in orthopaedic patients.[17-20] Considering the rising popularity of vaping and nicotine use,[21] it is important to note that these behaviors may have similar detrimental effects on orthopaedic outcomes.[22]

Although multiple studies have shown that the chance of retear after rotator cuff repair is greater in smokers,[4,10-12,16] there are controversies regarding whether smoking affects clinical outcomes after rotator cuff repair.[3,5,10] Kim et al.[3] reported that smokers with rotator cuff retear had a greater odds ratio for poor

From the Department of Orthopaedics and Traumatology, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pok Fu Lam, Hong Kong.

Received August 9, 2023; accepted December 26, 2023.

Address correspondence to W P Yau, Room 509, 5/F, Professorial Block, Queen Mary Hospital, No. 102, Pokfulam Rd., Hong Kong, Hong Kong Special Administrative Region, The People's Republic of China. E-mail: peterwpy@hku.hk

2666-061X/231134

https://doi.org/10.1016/j.asmr.2023.100877

clinical outcomes when compared with nonsmokers with the same problem. Mallon et al.[5] reported that the improvement of pain and function score after rotator cuff repair was less in smokers when compared with nonsmokers. However, in a systematic review of 73,817 patients, Fan et al.[10] concluded that there was no difference between smokers and nonsmokers in clinical outcomes, in terms of postoperative pain scores and function scores (including the American Shoulder and Elbow Surgeons [ASES] score; Simple Shoulder Test; and University of California at Los Angeles Shoulder Score).

The purpose of this study was to investigate the impact of smoking on clinical outcomes after repair of supraspinatus tendon in patients who had an intact repair found on postoperative magnetic resonance imaging (MRI). It was hypothesized that smokers would experience poorer clinical outcomes when compared with nonsmokers, even if the repaired tendon was intact, at a minimum clinical follow-up of 2 years.

Methods

A retrospective cohort study with prospectively collected data was carried out at the author's institution from July 2014 to December 2020.

Inclusion and Exclusion Criteria

Patients were included in the study if they (1) were scheduled for primary arthroscopic rotator cuff surgery; (2) suffering from reparable supraspinatus tendon tear; (3) received a complete repair of the torn supraspinatus tendon back to the footprint; and (4) were operated in the author's institution between July 2014 and December 2020. Patients were excluded if (1) there was significant postoperative complication leading to deviation of rehabilitation protocol; (2) postoperative MRI was not performed; and (3) the patients had a follow-up of less than 2 years.

Preoperative Assessment

Patients were assessed at a preoperation assessment clinic 2 weeks before the surgery for (1) demographic data, including the premorbid activity level of the involved shoulder; (2) medical history (including smoking, diabetes mellitus, hyperlipidemia, obesity); (3) severity of pain in term of VAS score (on a scale of 0-10); (4) functional assessment in terms of ASES score; and (5) physical examination findings of the involved shoulder. All data were prospectively collected.

Smoking was defined as the inhalation of the fumes of burning tobacco, including smoking cigars, cigarettes, and smoking pipes. Smokers were defined as those who had the habit of active smoking, regardless of the amount of tobacco consumed and whether they stopped smoking at the time of surgery. Smokers were classified into 3 groups: chronic smokers, social smokers, and ex-smokers. Chronic smokers were patients who smoked regularly on a daily basis. Social smokers were patients who smoked on an irregular basis. Ex-smokers were individuals who had stopped smoking before surgery, regardless of the length of time they had stopped. Nonsmokers were defined as patients who never smoked at the time of surgery. Diabetes mellitus was considered positive for patients who required regular consumption of hypoglycemic drugs (including both oral hypoglycemic agent and insulin injection) or those with an elevated fasting blood glucose level of more than 7 mmol/L. Hyperlipidemia was considered present if patients required regular taking of hypolipidemic agent (eg, statin) or those with an elevated fasting blood cholesterol level of more than 6.2 mmol/L. Premorbid activity level was classified as sedentary, light, moderate, and strenuous according to the published data of Chen et al.[23] Body mass index was calculated.

Surgery and Intraoperative Assessment

All surgeries were performed by the same surgeon (W.P.Y.). After diagnostic arthroscopy, debridement of the unhealthy, degenerative rotator cuff tear was performed. The size of the tear was then assessed, and the reparability of the rotator cuff tear was checked. The tear was considered to be reparable if the entire stump of the torn supraspinatus tendon could be reduced to its footprint. In case the tear was found to be irreducible or could only be reduced with significant tension, sequential surgical releases were performed. These releases included bursal-side release, articular-side release, interval slide, and medialization of footprint by 5 mm. The extent of surgical release depended on the reducibility of the tear and the tension encountered. The tear was classified according to the Cofield classification as small, medium, large, and massive.[24] In addition, regardless of the size, the tear was classified as a massive tear according to the Gerber classification when there were 2 or more than 2 full-thickness, full-width rotator cuff tendon tears.[25] Supraspinatus tendon repair was performed if the involved tendon tear was a full-thickness tear or if it was a partial-thickness tear with more than 50% thickness involvement. Partial supraspinatus tendon repair was defined as repairing only part of the torn stump of the supraspinatus tendon to its anatomical footprint at proximal humerus. A salvage procedure was defined as the inability to repair the torn supraspinatus tendon back to its humeral footprint, and the gap between the glenoid and humerus was bridged by either a patch graft or superior capsular reconstruction. Concomitant biceps tendon surgery and acromioplasty were performed as necessary.

Rehabilitation

Patients who received complete repair of the supraspinatus tendon tear were required to follow a standard rehabilitation protocol with physical therapy provided in a designated rehabilitation center. Patients were asked to wear an abduction shoulder immobilizer for a total of 6 weeks after surgery. Assisted active mobilization was started at week 7 onwards, and free active mobilization of the shoulder was started at postoperation week 13. Passive stretching of the joint and muscle-strengthening exercises were continued until 9 months to 1 year after the index surgery. Patients were followed up regularly in a designated shoulder clinic at 1 week, 6 weeks, 3 months, 6 months, 9 months, 1 year, and then annually after the operation. Patients were assessed for VAS pain score, ASES score, and physical examination findings of both shoulders at each follow-up. The patients and the assessors in the clinic were not blinded to the status of rotator cuff repair.

Postoperative MRI

Reassessment MRI of the operated shoulder was arranged in the postoperative period for all patients. The radiologist issuing the official MRI report was asked to comment on the presence of a full-thickness retear of the repaired supraspinatus tendon on the MRI.

Assessment of Outcomes

The primary outcomes assessed were the postoperative pain score (VAS), function score (ASES), and active forward flexion of the operated shoulder documented at the 2-year follow-up. The secondary outcomes were the MCID (minimal clinically important difference) of the VAS pain score, ASES score, and active forward flexion of the operated shoulder at the 2-year assessment.

MCID was documented according to the difference of the concerned scores (i.e., VAS pain score and ASES score in this study) between the preoperative status and the 2-year follow-up. Patients were considered to have achieved MCID if the improvement in the concerned scores was at least half the standard deviation of the result of the entire cohort.

Statistical Analysis

Descriptive statistics were reported for patient demographics and clinical outcomes. Changes in the VAS pain score, ASES score, and active shoulder forward flexion between preoperative and the 2-year follow-up were assessed by paired *t*-test. If the sample size was less than 10, the Wilcoxon signed ranks test was used. The potential association of the 2-year clinical outcomes with known covariates, including (1) patient demographic (age, sex, laterality of involved shoulder, dominant shoulder involvement, premorbid activity, smoking); (2) past medical disease (diabetes mellitus, hyperlipidemia, obesity); (3) compensation issue; (4) Cofield grading of tear size and Patte grading of tear retraction; and (5) presence of full-thickness retear on reassessment MRI were examined. Independent *t*-test was used in the analysis of the parametric data. For continuous data with a sample size of less than 25, repeated analysis was performed using the Mann−Whitney *U* test. Nonparametric data were assessed by the χ^2 test or Fisher exact test. If more than one covariate was found to be statistically associated with the outcome assessed, regression analysis was carried out to determine the independent predictor of the concerned outcome. Statistical significance was assumed to be present if $P < .05$.

A subgroup analysis was performed using a matching study between smokers and nonsmokers with an intact repair. The matching criteria included workers' compensation issues, the Cofield classification of tear size ("small and medium" vs "large and massive"), and the Patte classification of tendon retraction ("Patte I and Patte II" vs "Patte III").

Sample Size Calculation

A sample size analysis was performed. The average postoperative VAS pain score of nonsmokers reported in the systematic review by Fan et al.[10] was 1.01 ± 1.26. The reported mean difference in the postoperative pain score (VAS) between smokers and nonsmokers after rotator cuff repair was 1.25. The reported percentage of smokers in the subgroup for the analysis of postoperative pain score in the study by Fan et al.[10] was 33%.[10] The reported standard deviations of postoperative pain score for smokers and nonsmokers were 2.76 and 1.26, respectively. The enrollment ratio was set as 2. The alpha and power of the study were set as 0.05 and 0.8, respectively. The minimum number of shoulders required was 48 (16 for smokers and 32 for nonsmokers). The effect size was 0.6, which was considered to be medium to large.

The current study was approved by the local ethic committees (approval document number = UW 22-115).

Results

A consecutive series of 172 patients scheduled for arthroscopic rotator cuff surgeries were performed at the author's institution from July 2014 to December 2020. One hundred thirty-eight patients met the inclusion criteria. Thirty-eight cases were excluded. A total of 100 supraspinatus tendon repairs with postoperative MRI and a minimum follow-up of 2 years were enrolled (Fig 1). The mean follow-up was 45.6 months. Postoperative reassessment MRIs were performed at a mean duration of 18.5 ± 11 months from the index operation.

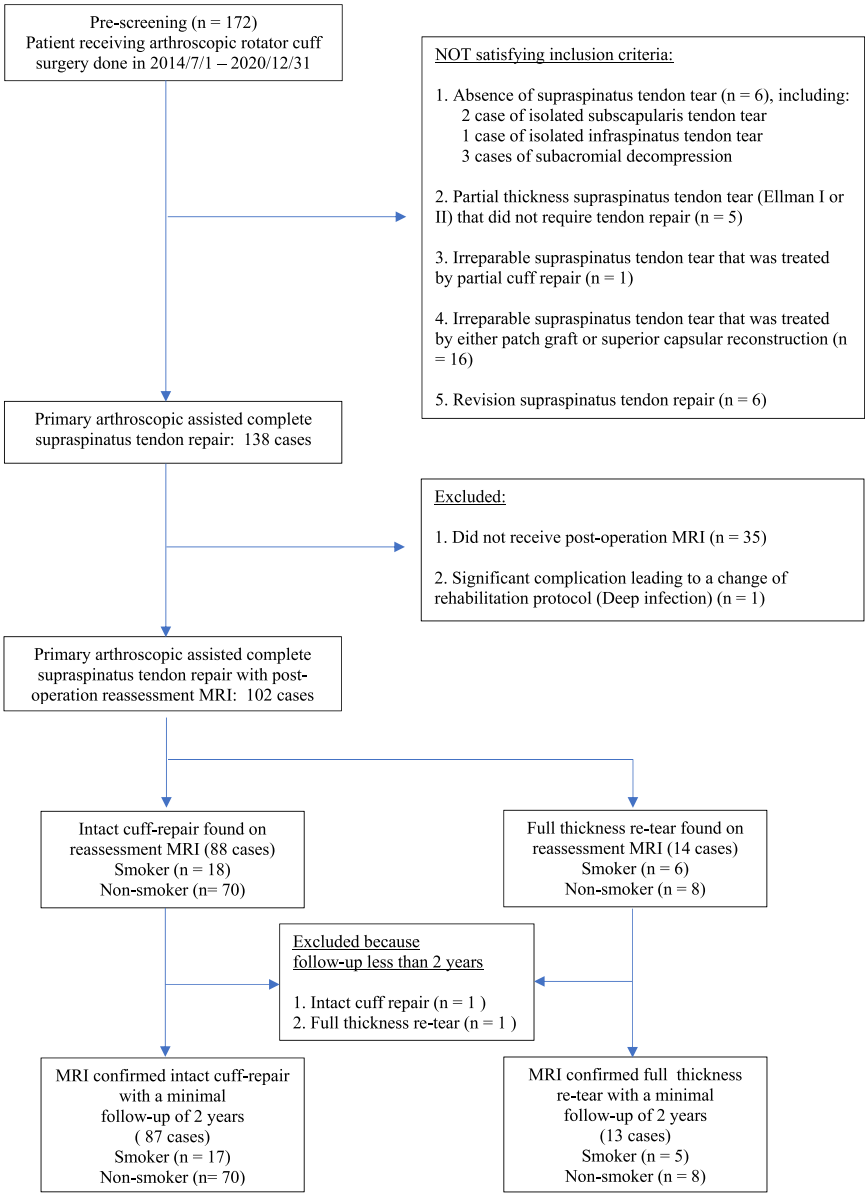

Fig 1. Enrollment of subjects. (MRI, magnetic resonance imaging; n, number.)

Whole Cohort

Thirteen full-thickness retears of the repaired supraspinatus tendon were identified in the postoperative MRI, giving a full-thickness retear rate of 13%. Five retears occurred in smokers and 8 retears occurred in nonsmokers.

Regardless of the presence of full-thickness retear in postoperative MRI, significant improvements in VAS and ASES were observed between preoperative and the 2-year assessment. However, although significant improvement in active forward flexion of the involved shoulder between preoperative and the 2-year follow-up was found in the group with intact repaired tendon, it was not found in the group with full-thickness retear (Table 1).

A univariate analysis was carried out to identify potential associations between the covariates and the 2-year clinical outcomes. The results are presented in Table 2.

The covariates that were associated with greater VAS score at 2-year follow-up were (1) age younger than 60 years old at the time of surgery ($P = .027$, independent t-test); (2) male patient ($P = .008$, independent t test); (3) hyperlipidemia ($P = .017$, independent t-test); (4) smoker ($P < .001$, Mann−Whitney U test); (5) patients having workers' compensation issues ($P = .018$, independent t-test); (6) absence of concomitant biceps surgery ($P = .043$, independent t-test); and (7) absence of concomitant acromioplasty ($P = .04$, Mann−Whitney U test). Linear regression was carried out, and it was

Table 1. Comparison of VAS, ASES, and Active Forward Flexion of the Involved Shoulder Between Preoperative and the 2-Year Follow-Up

	Preoperation	2-Year Follow-Up	*P* Value (Paired *t* Test)
VAS			
Smokers (n = 22)	5.8 ± 1.8	3.4 ± 2.5	$P < .001$*
Nonsmokers (n = 78)	5.8 ± 2.1	1.4 ± 1.4	$P < .001$*
Intact repaired tendon (n = 87)	5.8 ± 2.0	1.7 ± 1.9	$P < .001$*
Full-thickness retear (n = 13)	5.9 ± 1.9	2.3 ± 2.1	$P = .005$* (Wilcoxon signed-rank test)
ASES			
Smokers (n = 22)	39.9 ± 14.0	60.2 ± 25.4	$P < .001$*
Nonsmokers (n = 78)	40.2 ± 15.5	81.2 ± 15.5	$P < .001$*
Intact repaired tendon (n = 87)	40.5 ± 14.9	78.1 ± 19.0	$P < .001$*
Full-thickness retear (n = 13)	36.8 ± 17.5	67.8 ± 23.4	$P = .009$* (Wilcoxon signed-rank test)
Active forward flexion of the involved shoulder, °			
Smokers (n = 22)	122 ± 49	140 ± 41	$P = .028$*
Non-smokers (n = 78)	115 ± 46	158 ± 26	$P < .001$*
Intact repaired tendon (n = 87)	117 ± 47	159 ± 24	$P < .001$*
Full-thickness retear (n = 13)	112 ± 44	122 ± 49	P = ns (.383) (Wilcoxon signed-rank test)

ASES, American Shoulder and Elbow Surgeons; VAS, visual analog scale.
*Statistically significant.

found that smoking was the only significant independent predictor for poorer VAS scores assessed at the 2-year follow-up ($P < .001$) (Table 2).

Concerning 2-year ASES score, the significant covariates associated with a lower ASES score were (1) age younger than 60 years old at the time of surgery ($P = .006$, independent *t*-test); (2) male patient ($P = .01$, independent *t*-test); (3) hyperlipidemia ($P = .039$, independent *t*-test); (4) smoking ($P < .001$, Mann–Whitney *U* test); and (5) patients having work compensation problems ($P = .03$, independent *t*-test). After running a regression analysis, smoking was found to be the only significant predictor of the 2-year ASES score ($P < .001$) (Table 2).

The covariates that were associated with a smaller active forward flexion of the involved shoulder at the 2-year follow-up were (1) retear of supraspinatus tendon repair ($P = .011$, Mann–Whitney *U* test) and (2) an initial Cofield tear size of large or massive rotator cuff tear ($P = .003$, Mann–Whitney *U* test). After running a regression analysis, only cuff retear remained to be the independent predictor of 2-year active shoulder forward flexion ($P < .001$) (Table 2).

There were 22 smokers and 78 nonsmokers. Among the smokers, there were 10 chronic smokers, 1 social smoker, and 11 ex-smokers. Five retears occurred in smokers (23%), and 8 occurred in nonsmokers (10%). Of the 5 retears that occurred in smokers, 1 occurred in chronic smokers and 4 occurred in ex-smokers.

Differences between smokers and nonsmokers were observed in terms of age, sex, body mass index, and involvement in workers' compensation issues (Table 3).

Regardless of smoking status, significant improvements in VAS, ASES, and active forward flexion of the involved shoulder were observed between preoperation and the 2-year follow-up (Table 1).

Intact Repair Group

Among the 87 patients with intact rotator cuff repairs, significant differences existed between smokers and non-smokers in terms of sex ($P < .001$, Fisher exact test) and body mass index ($P = .041$, Mann–Whitney *U* test). The incidence of workers' compensation issues was 47% in smokers and 26% in nonsmokers, respectively ($P = .079$) (Table 4).

When the repaired tendon was intact, significant improvements were observed in VAS pain scores and ASES scores between the preoperative and the 2-year follow-up, irrespective of smoking status (VAS: $P < .001$ in nonsmokers and $P < .001$ in smokers; ASES: $P < .001$ in nonsmokers and $P = .012$ in smokers). The active forward flexion of the involved shoulder improved from 115 ± 47° to 161 ± 22° in nonsmokers ($P < .001$, paired *t*-test). There was no difference in active forward flexion of the involved shoulder between preoperative and the 2-year follow-up in smokers ($P = .061$, Wilcoxon signed rank test).

There was a difference between smokers and nonsmokers in the 2-year VAS pain score ($P < .001$, Mann–Whitney *U* test) and 2-year ASES score ($P < .001$, Mann–Whitney *U* test). The percentage of nonsmokers achieving MCID in VAS pain score and ASES score was 99% and 98%, respectively. Nonsmokers were 14.6 times (95% confidence interval [CI] 1.1-150) and 24 times (95% CI 2.4-237) more likely than smokers to achieve MCID in terms of the 2-year VAS score and 2-year ASES score, respectively (Table 5).

A greater proportion of nonsmokers than smokers were able to achieve an active forward flexion of at

Table 2. Univariate Analysis of Association Between Covariates and the 2-Year Clinical Outcomes

	2-Year VAS (Student *t*-Test, Unless Specified)	2-Year ASES (Student *t*-Test, Unless Specified)	2-Year FF (Student *t*-Test, Unless Specified)
Full-thickness retear	2.3 ± 2.1	68 ± 23	122 ± 49
Yes vs no	1.8 ± 1.9 (P = ns) (Mann–Whitney U test)	78 ± 19 (P = ns) (Mann–Whitney U test)	159 ± 24 (P = .011*) (Mann–Whitney U test)
Age, y			
≥60	1.5 ± 1.4	79 ± 16	150 ± 34
<60	2.2 ± 2.3 (P = .027*)	74 ± 24 (P = .006*)	158 ± 26 (P = ns)
Sex			
Man	2.2 ± 2.2	75 ± 23	155 ± 32
Woman	1.6 ± 1.5 (P = .008*)	79 ± 16 (P = .01*)	153 ± 30 (P = ns)
Laterality			
Right	1.9 ± 1.9	76 ± 19	151 ± 33
Left	1.8 ± 2.0 (P = ns)	78 ± 21 (P = ns)	158 ± 27 (P = ns)
Dominant shoulder involvement			
Yes	2.0 ± 1.9	77 ± 19	152 ± 33
No	1.6 ± 2.0 (P = ns)	78 ± 21 (P = ns)	157 ± 28 (P = ns)
Premorbid activity			
"Sedentary and light"	1.9 ± 1.7	77 ± 16	152 ± 29
"Moderate and strenuous"	1.8 ± 2.1 (P = ns)	77 ± 23 (P = ns)	156 ± 33 (P = ns)
Workers' compensation issues			
Yes	2.4 ± 2.2	71 ± 25	147 ± 37
No	1.7 ± 1.7 (P = .018*)	80 ± 16 (P = .03*)	157 ± 27 (P = ns)
BMI			
>25	2.3 ± 1.8	72 ± 19	146 ± 34
≤25	1.6 ± 1.9 (P = ns)	79 ± 19 (P = ns)	157 ± 26 (P = ns)
Diabetes mellitus			
Yes	2.1 ± 2.3	75 ± 22	152 ± 32
No	1.7 ± 1.7 (P = ns)	78 ± 19 (P = ns)	154 ± 31 (P = ns)
Hyperlipidemia			
Yes	2.2 ± 1.9	73 ± 18	153 ± 32
No	1.4 ± 1.8 (P = .017*)	81 ± 21 (P = .039*)	155 ± 29 (P = ns)
Smoking status			
Smoker	3.4 ± 2.5	60 ± 25	140 ± 41
Nonsmoker	1.4 ± 1.4 (P < .001*) (Mann–Whitney U test)	81 ± 16 (P < .001*) (Mann–Whitney U test)	158 ± 26 (P = ns) (Mann–Whitney U test)
Tear size			
"Small and medium"	1.9 ± 1.9	76 ± 20	160 ± 24
"Large and massive"	1.6 ± 1.8 (P = ns)	78 ± 20 (P = ns)	141 ± 39 (P = .003*)
Tear retraction			
"Patte I and Patte II"	1.8 ± 1.9	77 ± 20	156 ± 30
"Patte III"	1.9 ± 1.9 (P = ns) (Mann–Whitney U test)	74 ± 16 (P = ns) (Mann–Whitney U test)	142 ± 30 (P = ns) (Mann–Whitney U test)
Concomitant biceps surgery			
Yes	1.4 ± 1.6	80 ± 19	150 ± 33
No	2.1 ± 2.0 (P = .043*)	75 ± 21 (P = ns)	156 ± 29 (P = ns)
Concomitant acromioplasty			
Yes	1.7 ± 1.9	78 ± 20	154 ± 30
No	2.8 ± 1.7 (P = .04*) (Mann–Whitney U test)	69 ± 18 (P = ns) (Mann–Whitney U test)	154 ± 38 (P = ns) (Mann–Whitney U test)

ASES, American Shoulder and Elbow Surgeons; FF, active forward flexion of the involved shoulder; ns, not significant; VAS, visual analog scale.
*Statistically significant.

least 150° at the 2-year follow-up (P = .037, χ^2 test). The odds ratio was 3.8 (95% CI 1.02-13.8) (Table 5). Sixty-three percent of nonsmokers compared with 41% of smokers achieved MCID at FF at 2-year follow-up (P = not significant). None of the smokers with intact cuff repair suffered from persistent pseudoparalysis. Two nonsmokers had only 80° active forward flexion at the 2-year follow-up.

Subgroup Analysis: Matching Study Between Smokers With Intact Repair and Nonsmokers With Intact Repair

Seventeen matched pairs were identified. There were no differences between the matched pairs regarding tear size, tear retraction, and workers' compensation status. However, the 2 groups differed in terms of sex (P < .001) and body mass index (P = .05). The average

Table 3. Demographics and Surgical Data of Patients of the Whole Cohort

	Smokers	Nonsmokers	*P* Value (Mann–Whitney *U* Test, Unless Specified)
Total number in cohort	22	78	–
Length of follow-up, mo	40.7 ± 18.2	49.0 ± 19.5	P = ns (.057)
Time of postoperative MRI, mo	18.9 ± 10.7	18.4 ± 11.7	P = ns (0.737)
Age, y	55.2 ± 9.1	59.4 ± 9.3	P = .035*
Male/female	22 / 0	25 / 53	P < .001* (Fisher exact test)
Right/left	12 / 10	47 / 31	P = ns (.631) (χ^2 test)
Dominant shoulder involved	62%	61%	P = ns (.962) (χ^2 test)
Premorbid activity: sedentary/light/moderate/strenuous	0 / 9 / 10 / 3	3 / 40 / 30 / 5	P = ns (.466) (χ^2 test)
Workers' compensation issues	55%	26%	P = .01* (χ^2 test)
BMI	27.3 ± 2.7	25.0 ± 4.2	P = .007*
Diabetes mellitus	40%	24%	P = ns (.164) (χ^2 test)
Hyperlipidemia	73%	50%	P = ns (.058) (χ^2 test)
Tear size: small / medium / large / massive	5 / 8 / 2 / 7	28 / 27 / 4 / 19	P = ns (.63) (χ^2 test)
Tear retraction: Patte (1 vs 2 vs 3)	7 / 12 / 3	33 / 35 / 10	P = ns (.663) (χ^2 test)
Concomitant biceps surgery	27%	40%	P = ns (.285) (χ^2 test)
Concomitant acromioplasty	86%	88%	P = ns (.519) (Fisher exact test)

–, not calculated; BMI, body mass index; MRI, magnetic resonance imaging; ns, not significant.
*Statistically significant.

age of the patients at the time of operation was 54.4 years in the smoker group and 60.6 years in the nonsmoker group (P = .053). Diabetes mellitus was present in 35% of smokers and 6% of nonsmokers (P = .062) (Table 6).

It was found that the 2-year VAS score and 2-year ASES score were significantly better in the nonsmokers group compared with the smoker's group in the matched group analysis. The proportion of patients achieving MCID in the 2-year VAS and 2-year ASES was 94% and 94%, respectively, in nonsmokers with intact repair, and 82% and 71%, respectively, in smokers with intact repair (Table 7).

Cuff Retear Group

Among the 13 patients suffering from full-thickness retears, 5 were smokers and 8 were nonsmokers. The mean 2-year VAS, ASES, and active forward flexion of the ipsilateral shoulder were 3 ± 2.7, 63.3 ± 32.9, and 110 ± 63°, respectively, for smokers, and 1.9 ± 1.7, 70.6 ± 17.3, and 129 ± 41°, respectively, for nonsmokers. The proportion of patients reaching MCID in VAS, ASES, and FF was 80%, 60%, and 20%, respectively, for smokers, and 88%, 75%, and 38%, respectively, for nonsmokers. In total, 40% of smokers with full-thickness retear suffered from persistent pseudoparalysis, compared with 13% in nonsmokers (Table 8).

Discussion

One of the most important findings of this study is that smoking is associated with a greater VAS pain score and a lower ASES score at the 2-year follow-up, even if the repaired tendon was found to be intact in the postoperative MRI. Among all the covariates investigated in the current study, smoking was the only significant independent predictor of poorer 2-year VAS and ASES scores. Significant improvements in VAS and ASES scores between preoperative and the 2-year follow-up were observed in all patients receiving rotator cuff repair (regardless of whether the repaired tendon was intact or not). However, significant improvement in active shoulder forward flexion was only found in patients with an intact rotator cuff repair.

The findings of our study resemble those of Baumgarten, et al.,[26] Cuff et al.,[27] Kukkonen et al.,[28] Mallon et al.,[5] and Zabrzynski et al.[29] in terms of demonstrating a difference in clinical outcomes after rotator cuff repair between smokers and nonsmokers. However, the other studies quoted did not perform MRI follow-up that allowed for a subset analyzation of intact repairs. The current study finds that smoking has a negative impact on postoperative VAS pain scores and ASES scores, even if the repaired tendon is intact. Smoking was found to be associated with an increased prevalence of shoulder pain[30] and enhanced pain levels in patients suffering from chronic pain.[31]

Table 4. Demographics and Surgical Data of Patients With Intact Supraspinatus Tendon Repair

	Smoker	Nonsmoker	*P* Value (Mann-Whitney *U* Test, Unless Specified)
Total number in cohort	17	70	—
Length of follow-up, mo	40.5 ± 19.3	47.3 ± 21.4	*P* = ns (.191)
Time of postoperative MRI, mo	19.4 ± 11.1	18.3 ± 11.5	*P* = ns (.489)
Age, y	54.4 ± 10.2	58.4 ± 9.2	*P* = ns (.087)
Male / female	17 / 0	23 / 47	*P* < .001 * (Fisher exact test)
Right / left	8 / 9	41 / 29	*P* = ns (.391) (χ^2 test)
Dominant shoulder involved	56%	60%	*P* = ns (.801) (χ^2 test)
Premorbid activity: sedentary / light /moderate / strenuous	0 / 8 / 7 / 2	2 / 36 / 27 / 5	*P* = ns (.82) (χ^2 test)
Workers' compensation issues	47%	26%	*P* = ns (.079) (χ^2 test)
BMI	26.8 ± 2.6	25.0 ± 4.3	*P* = .041*
Diabetes mellitus	35%	20%	*P* = ns (.179) (χ^2 test)
Hyperlipidemia	63%	50%	*P* = ns (.127) (χ^2 test)
Tear size: small / medium / large / massive	5 / 6 / 2 / 4	28 / 26 / 2 / 14	*P* = ns (.414) (χ^2 test)
Tear retraction: Patte (1 vs 2 vs 3)	6 / 9 / 2	32 / 33 / 5	*P* = ns (.671) (χ^2 test)
Concomitant biceps surgery	24%	36%	*P* = ns (.201) (Fisher exact test)
Concomitant acromioplasty	88%	87%	*P* = ns (.634) (Fisher exact test)

—, not calculated; BMI, body mass index; MRI, magnetic resonance imaging; ns, not significant.
*Statistically significant.

Smoking is proinflammatory.[32] The prevalence of metabolic syndrome is greater in smokers than in nonsmokers.[33] Smoking leads to an elevated number of proinflammatory T helper cell[31] and an increased production of proinflammatory cytokines.[34] The presence of inflammatory cytokines results in peripheral neuronal sensitization and increases the severity of pain perceived.[35,36] The increase in systemic inflammation

Table 5. Clinical Outcome of Intact Supraspinatus Repair at the 2-Year Follow-Up

	Smoker	Nonsmoker	*P* Value (Mann−Whitney *U* Test, Unless Specified)
Preoperative VAS	5.8 ± 1.9 (Missing: 0)	5.8 ± 2.0 (Missing: 1)	*P* = ns (.974)
2-y VAS	3.5 ± 2.5 (Missing: 0)	1.3 ± 1.4 (Missing: 0)	*P* < .001*
2-y VAS reaching MCID	82% (Missing: 0)	99% (Missing: 1)	*P* = .023* (Fisher exact test) odds ratio = 14.6 (95% CI = 1.41-150.53)
Preoperative ASES	41.2 ± 14.0 (Missing: 0)	40.5 ± 15.0 (Missing: 4)	*P* = ns (.959)
2-y ASES	59.0 ± 23.5 (Missing: 3)	82.6 ± 14.9 (Missing: 6)	*P* < .001*
2-y ASES reaching MCID	71% (Missing: 3)	98% (Missing: 9)	*P* = .004* (Fisher exact test) odds ratio = 24 (95% CI = 2.43- 237.3)
Preoperative active shoulder FF, °	126 ± 46 (Missing: 0)	115 ± 47 (Missing: 0)	*P* = ns (.395)
Preoperative pseudoparalysis	24% (Missing: 0)	24% (Missing: 0)	*P* = ns (.611) (Fisher exact test)
2-y active shoulder FF, °	149 ± 29 (Missing: 0)	161 ± 22 (Missing: 0)	*P* = ns (.107)
2-y active shoulder FF ≥150, °	71% (Missing: 0)	90% (Missing: 0)	*P* = .037* (χ^2 test) odds ratio = 3.8 (95% CI = 1.02-13.8)
2-y persistent pseudoparalysis	0% (Missing: 0)	3% (Missing: 0)	*P* = ns (.646) (Fisher exact test)
2-y active shoulder FF reaching MCID	41% (Missing: 0)	63% (Missing: 0)	*P* = ns (.181) (Fisher exact test)

NOTE. Pseudoparalysis is defined as an inability to actively forward flex the involved shoulder to 90° forward flexion. Missing is defined as missing data.
ASES, American Shoulder and Elbow Surgeons; CI, confidence interval; FF, forward flexion; MCID, minimal clinically important difference; ns, not significant; VAS, visual analog scale (on a scale of 0 to 10).
*Statistically significant.

Table 6. Matched Pair Analysis: Demographics and Surgical Data of Patients With Intact Supraspinatus Tendon Repair

	Smoker	Nonsmoker	*P* Value (Mann−Whitney *U* Test, Unless Specified)
Total number in cohort	17	17	−
Age, y	54.4 ± 10.2	60.6 ± 6.1	P = ns (.053)
Male / female	17 / 0	3 / 14	$P < .001$* (Fisher exact test)
Right / left	8 / 9	14 / 3	$P = .035$* (Fisher exact test)
Dominant shoulder involved	56%	82%	P = ns (.105) (Fisher exact test)
Premorbid activity: sedentary / light /moderate / strenuous	0 / 8 / 7 / 2	0 / 7 / 8 / 2	P = ns (.936) (χ^2 test)
Workers' compensation issues	47%	47%	P = ns (1) (χ^2 test)
BMI	26.8 ± 2.6	25.1 ± 4.3	$P = .05$*
Diabetes mellitus	35%	6%	P = ns (.062) (Fisher exact test)
Hyperlipidemia	63%	59%	P = ns (.473) (χ^2 test)
Tear size: small / medium / large / massive	5 / 6 / 2 / 4	7 / 4 / 1 / 5	P = ns (.756) (χ^2 test)
Tear retraction: Patte (1 vs 2 vs 3)	6 / 9 / 2	7 / 8 / 2	P = ns (.943) (χ^2 test)
Concomitant biceps surgery	24%	42%	P = ns (.232) (Fisher exact test)
Concomitant acromioplasty	88%	88%	P = ns (.699) (Fisher exact test)

−, not calculated; BMI, body mass index; ns, not significant.
*Statistically significant.

related to smoking and the subsequent peripheral sensitization of nociceptive nerve endings are likely explanations for the poorer 2-year VAS score in smokers observed in the current study.

In addition, the degeneration of tissues from smoking may be another possible explanation of the findings of this study. It is well-known that nicotine is a potent vasoconstrictor,[1] and smoking is associated with impeded collagen synthesis.[7] Histologic examination of biopsy specimens confirmed that the tendons of smokers were more avascular compared with nonsmokers, and there were more compact and amorphous noncollagenous materials in the degenerated tendons in smokers.[37] It is possible that smokers suffering from chronic tendinopathy have poorer tendon quality compared with nonsmokers with the same problem. As a result, despite a successful repair, smokers may be more prone to suffer from "failure with continuity," which was defined by McCarron et al.[38] as "tendon retraction without a recurrent defect." McCarron et al.[38] observed elongation of the repaired tendon and medial "retraction" of the repaired stump, even in the absence of a full-thickness retear. Due to the differences in study design, it is not possible for us to investigate whether "failure with continuity" occurred in some of the smokers in the current study and whether this was the reason leading to the observed difference in 2-year VAS and 2-year ASES between smokers and nonsmokers.

In the case of patients who underwent reassessment MRI before the 24-month mark (which was when the clinical outcomes were assessed in this study), it cannot be ruled out that some previously intact repairs had developed retear before the 2-year follow-up, potentially affecting the 2-year clinical outcomes. Studies have shown that smokers have an increased risk of requiring revision surgery after rotator cuff repair.[39] Compared with nonsmokers with intact repair, it is more likely that a greater proportion of smokers will experience a retear during subsequent follow-ups. This could be another plausible explanation for the poorer 2-year VAS and 2-year ASES observed in smokers with "intact repair" compared with nonsmokers.

Retear of rotator cuff repair was the most important factor in affecting active shoulder forward flexion at the 2-year follow-up (P = .011, Mann−Whitney *U* test). Kim et al.[3] reported that there was no difference between the final forward flexion and the preoperation forward flexion in 45 patients with retear of rotator cuff repair. This was similar to our observation. Kim et al.[3] observed that despite the presence of cuff retear, there was significant improvement in VAS pain score and ASES score after the rotator cuff repair. This was different from the findings of our study. However, Kim et al.[3] did not perform a detailed analysis of the clinical outcomes with respect to the status of smokers and nonsmokers. This may be the reason for the difference in observation between these 2 studies.

Table 7. Matched Pair Analysis: Clinical Outcome of 17 Matched Pairs With Intact Supraspinatus Repair at the 2-Year Follow-Up

	Smoker	Nonsmoker	*P* Value Mann–Whitney *U* Test, Unless Specified
Preoperative VAS	5.8 ± 1.9 (Missing: 0)	5.9 ± 1.8 (Missing: 0)	*P* = ns (.946)
2-y VAS	3.5 ± 2.5 (Missing: 0)	1.7 ± 1.5 (Missing: 0)	*P* = .035*
2-y VAS reaching MCID	82% (Missing: 0)	94% (Missing: 0)	*P* = ns (.301) (Fisher exact test)
Preoperative ASES	41.2 ± 14.0 (Missing: 0)	39.1 ± 10 (Missing: 1)	*P* = ns (.763)
2-y ASES	59.0 ± 23.5 (Missing: 3)	77.2 ± 15.8 (Missing: 0)	*P* = .017*
2-y ASES reaching MCID	71% (Missing: 3)	94% (Missing: 1)	*P* = ns (.126) (Fisher exact test)
Preoperative active shoulder FF, °	126 ± 46 (Missing: 0)	109 ± 49 (Missing: 0)	*P* = ns (.155)
Preoperative pseudoparalysis	24% (Missing: 0)	24% (Missing: 0)	*P* = ns (.656) (Fisher exact test)
2-y active shoulder FF, °	149 ± 29 (Missing: 0)	157 ± 30 (Missing: 0)	*P* = ns (.357)
2-y active shoulder FF ≥150°	71% (Missing: 0)	88% (Missing: 0)	*P* = ns (.199) (χ^2 test)
2-y persistent pseudoparalysis	0% (Missing: 0)	6% (Missing: 0)	*P* = ns (.5) (Fisher exact test)
2-y active shoulder FF reaching MCID	41% (Missing: 0)	65% (Missing: 0)	*P* = ns (.29) (Fisher exact test)

NOTE. Pseudoparalysis is defined as an inability to actively forward flex the involved shoulder to 90° forward flexion. Missing is defined as missing data.

ASES, American Shoulder and Elbow Surgeons; FF, forward flexion; MCID, minimal clinically important difference; ns, not significant; VAS, visual analog scale (on a scale of 0 to 10).

*Statistically significant.

In a propensity score study reported by Park et al.,[12] the results of rotator cuff repairs in 34 current heavy smokers were compared with 34 nonsmokers. Park et al.[12] did not find any difference between smokers and nonsmokers in terms of postoperative VAS pain score and ASES score. However, the analysis was done without stratifying the patient groups into "cuff retear" and "intact repair." In a systematic review of 73,817 patients, Fan et al.[10] concluded that there was no difference between smokers and nonsmokers in clinical outcomes. Similarly, the studies included in the paper by Fan et al.[10] did not use postoperative imaging (e.g., MRI, ultrasound) to differentiate "cuff retear" from "intact repair" during comparison of postoperative clinical outcomes between smokers and nonsmokers. Bias may exist because "cuff retear" and "intact repair" are 2 distinct clinical groups with different profiles of clinical outcomes. As shown in the current study, the impact of smoking on clinical outcomes was best shown when the analysis was stratified according to the presence of an intact repaired tendon because cuff retear itself was an important covariate affecting the outcomes. Failure to differentiate patients having cuff retear from those with an intact repair in the analysis might be the reason why Fan et al.[10] and Park et al.[12] did not find any difference in clinical outcomes between smokers and nonsmokers.

Table 8. Clinical Outcome of Full-Thickness Cuff Retear at the 2-Year Follow-Up

	Smoker	Nonsmoker
Preoperative VAS	5.8 ± 1.6	5.9 ± 2.1
2-y VAS	3.0 ± 2.7	1.9 ± 1.7
2-y VAS reaching MCID	80%	88%
Preoperative ASES	35.6 ± 14.6	37.5 ± 20.1
2-y ASES	63.3 ± 32.9	70.6 ± 17.3
2-y ASES reaching MCID	60%	75%
Preoperative active shoulder FF, °	110 ± 64	113 ± 31
Preoperative pseudoparalysis	40%	25%
2-y active shoulder FF, °	110 ± 63	129 ± 41
2-y active shoulder FF ≥150°	40%	50%
2-y persistent pseudoparalysis	40%	13%
2-y active shoulder FF reaching MCID	20%	38%

NOTE. Pseudoparalysis is defined as an inability to actively forward flex the involved shoulder to 90° forward flexion.

ASES, American Shoulder and Elbow Surgeons; FF, forward flexion; MCID, minimal clinically important difference; ns, not significant; VAS, visual analog scale (on a scale of 0-10).

In a national all-payer database study of 114,989 patients,[39] Livesey et al.[39] reported that there was no difference in the risk of revision surgery between nonsmokers and ex-smokers who had quit smoking for more than 6 months before rotator cuff repair. However, the risk of revision surgery was greater in current smokers and ex-smokers who had quit smoking within 6 months, compared with nonsmokers. In the current study, the proportion of individuals with full-thickness retear in postoperative MRI was 1 of 10 chronic smokers, 0 of 1 social smokers, 4 of 11 ex-smokers, and 8 of 78 nonsmokers. The small sample size in the current study, the difference in the definition of failure (i.e., full-thickness retear in postoperative MRI in the current study vs revision surgery in the publication of

Livesey et al.[39]), and the lack of information regarding the duration of smoking cessation among ex-smokers in the current study are possible reasons for the differences observed between the 2 studies.

Limitations

This study has several limitations that should be taken into consideration when interpreting our results. First, the study was retrospective and not all the data were available for every subject in this study. Second, the studied groups (i.e., smokers and nonsmokers) were not comparable in terms of age, sex, body mass index, or workers' compensation status. The number of subjects who were male and who were on workers' compensation were disproportionately large. Third, the timeline for postoperative MRI was not standardized, resulting in substantial variation in the MRI follow-up periods. Although the sample size of the "intact repair" group reached the required number calculated in the power analysis, the "cuff retear" subgroup was underpowered. This study is also underpowered to detect the risk in those who have stopped smoking.

In addition, although the status of smoking was documented at the time of surgery, there was no longitudinal documentation of the smoking status in each of the subsequent follow ups. It was not known whether any nonsmokers started smoking after surgery and whether the smoker quit smoking in the postoperative period. The number and the type of tobacco consumed by the smokers also was not recorded. Furthermore, the duration of cessation of smoking among ex-smokers was not documented. Finally, during the repair of the torn supraspinatus tendon, surgical release was carried out to ensure a "tension-free repair." However, the judgment was subjective, and there was no objective measurement of tension within the repair. The possibility that some repairs were "repaired-under-tension" could not be ruled out.

Conclusions

In this study, smoking was associated with poorer clinical outcomes, including a greater 2-year VAS pain score and a lower 2-year ASES score, when compared with nonsmokers, even in cases in which there was no full-thickness retear of the repaired supraspinatus tendon.

Disclosure

The author (W.P.Y.) declares that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

References

1. Sorensen LT, Jorgensen S, Petersen LJ, et al. Acute effects of nicotine and smoking on blood flow, tissue oxygen, and aerobe metabolism of the skin and subcutis. *J Surg Res* 2009;152:224-230.
2. Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: A randomized controlled trial. *Ann Surg* 2003;238:1-5.
3. Kim DM, Jeon IH, Yang HS, et al. Poor prognostic factors in patients with rotator cuff retear. *Orthop J Sports Med* 2021;9:2325967121992154.
4. Lobo-Escolar L, Ramazzini-Castro R, Codina-Grano D, Lobo E, Minguell-Monyart J, Ardevol J. Risk factors for symptomatic retears after arthroscopic repair of full-thickness rotator cuff tears. *J Shoulder Elbow Surg* 2021;30:27-33.
5. Mallon WJ, Misamore G, Snead DS, Denton P. The impact of preoperative smoking habits on the results of rotator cuff repair. *J Shoulder Elbow Surg* 2004;13:129-132.
6. Hopf HW, Thung TK, West JM, et al. Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. *Arch Surg* 1997;132:997-1004.
7. Jorgensen LN, Kallehave F, Christensen E, Siana JE, Gottrup F. Less collagen production in smokers. *Surgery* 1998;123:450-455.
8. Nasell H, Ottosson C, Tornqvist H, Linde J, Ponzer S. The impact of smoking on complications after operatively treated ankle fractures—a follow-up study of 906 patients. *J Orthop Trauma* 2011;25:748-755.
9. Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM, LEAP Study Group. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fracture. *J Orthop Trauma* 2005;19:151-157.
10. Fan N, Yuan S, Du P, et al. The effects of smoking on clinical and structural outcomes after rotator cuff repair: A systematic review and meta-analysis. *J Shoulder Elbow Surg* 2022;31:656-667.
11. Neyton L, Godeneche A, Nove-Josserand L, Carrillon Y, Clechet J, Hardy MB. Arthroscopic suture-bridge repair for small to medium sized supraspinatus tear: healing rate and retear pattern. *Arthroscopy* 2013;29:10-17.
12. Park JH, Oh KS, Kim TM, et al. Effect of smoking on healing failure after rotator cuff repair. *Am J Sports Med* 2018;46:2960-2968.
13. Chan YC, Yau WP. Association of smoking with graft rupture after anterior cruciate ligament reconstruction. *Orthop J Sports Med* 2022;10:23259671221127244.
14. Cancienne JM, Brockmeier SF, Werner BC. Tobacco use is associated with increased rates of infection and revision surgery after primary superior labrum anterior and posterior repair. *J Shoulder Elbow Surg* 2016;25:1764-1768.
15. Cancienne JM, Gwathmey FW, Miller MD, Werner BC. Tobacco use is associated with increased complications after anterior cruciate ligament reconstruction. *Am J Sports Med* 2016;44:99-104.
16. O'Donnell EA, Fu MC, White AE, et al. The effect of patient characteristics and comorbidities on the rate of revision rotator cuff repair. *Arthroscopy* 2020;36:2380-2388.
17. Dunn WR, Lincoln AE, Hinton RY, Smith GS, Amoroso PJ. Occupational disability after hospitalization

for the treatment of an injury of the anterior cruciate ligament. *J Bone Joint Surg Am* 2003;85:1656-1666.
18. Dunn WR, Spindler KP, MOON Consortium. Predictors of activity level 2 years after anterior cruciate ligament reconstruction (ACLR): A Multicenter Orthopaedic Outcomes Network (MOON) ACLR cohort study. *Am J Sports Med* 2010;38:2040-2050.
19. Karim A, Pandit H, Murray J, Wandless F, Thomas NP. Smoking and reconstruction of the anterior cruciate ligament. *J Bone Joint Surg Br* 2006;88:1027-1031.
20. Kowalchuk DA, Harner CD, Fu FH, Irrgang JJ. Prediction of patient- reported outcome after single-bundle anterior cruciate ligament reconstruction. *Arthroscopy* 2009;25:457-463.
21. Tehrani H, Rajabi A, Ghelichi-Ghojogh M, Nejatian M, Jafari A. The prevalence of electronic cigarettes vaping globally: A systematic review and meta-analysis. *Arch Public Health* 2022;80:240.
22. Armstrong ML, Smith N, Tracey R, Jackman H. The orthopaedic effects of electronic cigarettes: A systematic review and pediatric case series. *Children (Basel)* 2022;9:62.
23. Chen Y, Jiang F, Li H, et al. Retears and concomitant functional impairments after rotator cuff repair. Shoulder activity as a risk factor. *Am J Sports Med* 2020;48:931-938.
24. Cofield RH, Parvizi J, Hoffmeyer PJ, Lanzer WL, Ilstrup DM, Rowland CM. Surgical repair of chronic rotator cuff tears. A prospective long-term study. *J Bone J Surg Am* 2001;83:71-77.
25. Gerber C, Fuchs B, Hodler J. The results of repair of massive tears of the rotator cuff. *J Bone J Surg Am* 2000;82:505-515.
26. Baumgarten KM, Schweinle WE, Chang PS. Do patients who smoke tobacco have success with primary arthroscopic rotator cuff repair? A comparison with nonsmokers. *J Shoulder Elbow Surg* 2020;29:1650-1655.
27. Cuff DJ, O'Brien KC, Pupello DR, Santoni BG. Evaluation of factors affecting acute postoperative pain levels after arthroscopic rotator cuff repair. *Arthroscopy* 2016;32:1231-1236.
28. Kukkonen J, Kauko T, Virolainen P, Aarimaa V. Smoking and operative treatment of rotator cuff tear. *Scand J Med Sci Sports* 2014;24:400-403.
29. Zabrzynski J, Huri G, Gagat M, et al. The impact of smoking on clinical results following the rotator cuff and biceps tendon complex arthroscopic surgery. *J Clin Med* 2021;10:599.
30. Rechardt M, Shiri R, Karppinen J, Jula A, Heliovaara M, Viikari-Juntura E. Lifestyle and metabolic factors in relation to shoulder pain and rotator cuff tendinitis: A population-based study. *BMC Musculoskelet Disord* 2010;11:165.
31. Heyn J, Luchting B, Azad SC. Smoking associated with T-cell imbalance in patients with chronic pain. *Nicotine Tob Res* 2020;22:111-117.
32. Arnson Y, Shoenfeld Y, Amital H. Effects of tobacco smoke on immunity, inflammation and autoimmunity. *J Autoimmun* 2010;34:J258-J265.
33. Slagter SN, Vliet-Ostaptchouk JV, Vonk JM, et al. Associations between smoking, components of metabolic syndrome and lipoprotein particle size. *BMC Med* 2013;11:195.
34. Glossop JR, Dawes PT, Mattey DL. Association between cigarette smoking and release of tumour necrosis factor alpha and its soluble receptors by peripheral mononuclear cells in patients with rheumatoid arthritis. *Rheumatology (Oxford)* 2006;45:1223-1229.
35. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet* 2021;397:2082-2097.
36. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. *Lancet* 2005;365:965-973.
37. Zabrzynski J, Gagat M, Pacqesny L, Grzanka D, Huri G. Correlation between smoking and neovascularization in biceps tendinopathy: A functional preoperative and immunohistochemical study. *Ther Adv Chronic Dis* 2020;7:11:2040622320956418.
38. McCarron JA, Derwin KA, Bey MJ, et al. Failure with continuity in rotator cuff repair "healing." *Am J Sports Med* 41:134-141.
39. Livesey MG, Bains SS, Weir TB, et al. Does time matter? The effect of preoperative smoking cessation on the risk of infection or revision following rotator cuff repair. *J Shoulder Elbow Surg* 2023;32:1937-1944.