Clinical and Structural Outcomes After Rotator Cuff Repair in Patients With Diabetes

A Meta-analysis

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Background: The impact of diabetes on clinical and structural outcomes after rotator cuff repair remains controversial.

Purpose/Hypothesis: The purpose of this study was to compare clinical outcomes and retear rates after rotator cuff repair in patients with and without diabetes. Our hypotheses were that adequate control of diabetes would decrease the retear rate after rotator cuff repair and that patients with diabetes would have worse clinical outcomes.

Study Design: Systematic review; Level of evidence, 3.

Methods: The PubMed, Embase, and Cochrane Library databases were searched for studies comparing outcomes in patients with and without diabetes after full-thickness rotator cuff repair. Clinical outcome analysis included the Constant score, the American Shoulder and Elbow Surgeons (ASES) score, and the University of California–Los Angeles shoulder rating scale; we compared preoperative, postoperative, and change in functional scores from baseline to final follow-up among the included studies. The pooled relative risk was calculated using a random-effects model for retear rates. Clinical outcomes were also pooled using a random-effects model.

Results: Overall, 10 studies were included. Compared with patients without diabetes, patients with diabetes had a worse preoperative ASES score ($P = .009$) as well as worse postoperative Constant score (final follow-up range, 9-103 months; $P = .0003$). However, there was no significant difference in the absolute mean change in clinical outcomes between patients with and without diabetes. Diabetes was associated with a higher retear rate (19.3% in patients without diabetes vs 28.2% in patients with diabetes; $P < .0001$). The retear rate according to the severity of sustained hyperglycemia in the subgroup analysis was 14.6% in patients without diabetes, versus 22.7% in patients with well-controlled diabetes (<7.0% of preoperative serum HbA1c level; $P = .12$) and 40.0% in patients with uncontrolled diabetes (HbA1c level ≥7.0%; $P < .00001$).

Conclusion: This meta-analysis suggests that diabetes mellitus is associated with an increased risk of retears after rotator cuff repair, and improved blood glucose control may reduce the risk of retears in patients with diabetes mellitus. Although effective glycemic control was associated with a decreased risk of retears in patients with diabetes, we could not prove causation because of potential bias and confounding in the included studies.

Keywords: rotator cuff; diabetes mellitus; retear; outcomes; meta-analysis

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Diabetes mellitus (DM) is relatively common; worldwide, there were 451 million people aged 18 to 99 years with the condition in 2017. This figure is expected to increase to 693 million by 2045.[17] The condition is frequently associated with various musculoskeletal disorders, which affect tendon and bone structures, healing, and vascularity.[5,15,44] Several reports and some epidemiological studies have emphasized the possible connection between DM and alterations of tendons in various parts of the body.[22,25] Poorly controlled diabetes negatively affected the mechanical properties of the native tendon and healing of an injured tendon in an experimental rat model.[30] Cho et al[18] reported that sustained hyperglycemia increased the possibility of anatomic failure in repaired rotator cuffs. Furthermore, 2 large-scale, longitudinal population-based studies found that DM was an independent risk factor for rotator cuff disease development[46] and that those with DM were at a higher risk of rotator cuff tears.[35] In general, a retear is associated with poorer clinical outcomes compared with intact repair,[43,49,50] and no single preoperative factor

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is overwhelmingly predictive of it. Compared with other comorbidities including smoking, obesity, hypercholesterolemia, and age, diabetes most dramatically affects the speed of recovery, with earlier plateaus in recovery and worse overall outcomes.[10] All of this suggests that patients with diabetes have poorer functional and structural outcomes after rotator cuff surgery compared with those without diabetes.

However, several previous studies have compared the clinical scores of rotator cuff repair between patients with and without diabetes and showed that there were no significant differences between the groups at final follow-up.[18,20,51] In addition, Clement et al[20] found that the mean improvement in pre- to postoperative outcome scores was significantly greater ($P = .0002$) in patients without diabetes compared with those with diabetes. This indicates that the impact of diabetes on outcome scores is uncertain. Furthermore, other recent studies have examined the preoperative clinical factors that predict retears after arthroscopic rotator cuff repair and have suggested that DM is not a predictive factor for rotator cuff retears.[26,31,37,40,51,55]

Until now, the effect of diabetes on outcomes after rotator cuff repair and the effect of sustained hyperglycemia on retear rates have not been well-characterized. A previous meta-analysis has shown that diabetes had a moderate negative effect on outcomes after rotator cuff repair.[61] However, only 2 cohort studies were included in the analysis, and there was no grouping analysis based on blood glucose levels. This requires further research. The purpose of our study was to compare the clinical and structural outcomes between patients with and without diabetes after rotator cuff repair and to determine the effect of glycemic control on the retear rate.

METHODS

Search Strategy

This meta-analysis was conducted in accordance with the MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines[70] and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement.[52] The study protocol was registered at PROSPERO (No. CRD42020151508). We searched articles in PubMed, Embase, and the Cochrane Library from 1976 through September 2019 without language restrictions. The keywords used are shown in Table 1. Also, we conducted hand searches that extracted relevant articles from the reference lists of included studies or previous systematic reviews to identify additional studies that had not been captured with our primary search. The search results were imported into reference manager software (NoteExpress 3.2; Beijing Aegean Software Company) to avoid the duplication of records.

TABLE 1
Keywords Used in PubMed Database

	Keyword
1	Diabetes mellitus [MeSH]
2	Rotator cuff [MeSH]
3	Cuff, rotator [title/abstract]
4	Rotator cuffs [title/abstract]
5	Teres minor [title/abstract]
6	Subscapularis [title/abstract]
7	Infraspinatus [title/abstract]
8	Supraspinatus [title/abstract]
9	2 or 3 or 4 or 5 or 6 or 7 or 8
10	1 and 9 and humans [filter]

Study Selection

Inclusion criteria were studies of (1) patients who underwent surgery for full-thickness rotator cuff tears and that included (2) preoperative and postoperative clinical or structural data as well as (3) a comparison of patients with and without diabetes. Exclusion criteria were (1) studies of patients with partial repair, revision rotator cuff repair, osteoarthritis, or a history of shoulder trauma; (2) multiple studies of the same cohort; and (3) cadaveric, animal, and other laboratory

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studies. To avoid the duplication of information, we only included the most informative article or complete study.

Data Extraction and Quality Assessment

The extracted data included year of publication, sample size, study design, postoperative rehabilitation protocol, number of retears, outcome measures (eg, Constant score, American Shoulder and Elbow Surgeons [ASES] score, University of California–Los Angeles [UCLA] shoulder rating scale), and follow-up time. The supplementary files were also examined for data extraction. Where necessary, we contacted the authors of included studies for additional information.

A quality assessment was performed using the Newcastle-Ottawa scale (NOS).[73] This scale evaluates the quality of nonrandomized studies to be included in a systematic review and uses a "star scoring system" to judge 3 aspects of the study groups: (1) selection, (2) comparability, and (3) ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively. The lower the risk of bias, the higher the number of stars awarded to the article, with 9 being the maximum.

There were 2 investigators (L.Y., D.R.) who independently conducted the study selection, data extraction, and quality assessment; a third investigator (W.S.) was consulted to resolve any discrepancies.

Statistical Analysis

The relative risk (RR) was used as a common measure of the association between diabetes and the retear rate in cohort studies. Results were combined by using a random-effects model, and statistical heterogeneity was quantified by using the I^2 value, which describes the variation in the effect size that is attributable to heterogeneity across studies.[34] According to the *Cochrane Handbook for Systematic Reviews of Interventions*, an I^2 value of 0%-40% was considered to indicate unimportant heterogeneity, 30%-60% moderate heterogeneity, 50%-90% substantial heterogeneity, and 75%-100% considerable heterogeneity.[33] Subgroup analysis of the retear rate was conducted by stratifying patients into those with controlled diabetes (<7.0% preoperative serum HbA1c level), those with uncontrolled diabetes (≥7.0% preoperative serum HbA1c level), and those without diabetes. Sensitivity analysis was performed in which we omitted 1 study in turn to investigate the influence of a single study on the combined risk estimates and to test the stability of the main results. Publication bias was not determined because there were fewer than 10 included studies. A P value <.05 was judged as statistically significant. RevMan 5.3 (Cochrane Collaboration) was used for all analyses.

RESULTS

Literature Search

Details on study identification, screening, and selection are given in Figure 1. We initially retrieved 133 relevant reports from electronic databases and 3 studies from hand searches, of which 23 were excluded for being duplicate studies and 82 excluded after reviewing titles and abstracts, mainly because they were reviews, animal studies, or not relevant to our analysis. Thus, 31 articles were screened for the next step. Then, according to the inclusion criteria, 21 records were excluded. Ultimately, 10 studies were included in the final analysis.[**]

Baseline Characteristics and Quality Assessment

The general characteristics of all the included studies are summarized in Table 2. Overall, 9 retrospective cohort studies and 1 case-control study[37] were included. Only 1 study[16] selected open repair of full-thickness rotator cuff tears and then assessed active and passive range of motion separately. In total, there were 1989 participants, 374 patients with diabetes and 1615 patients without diabetes. The follow-up duration ranged from 9 to 103 months. The mean NOS score of the included studies was 7.6 (range, 7-8); 6 articles were awarded 8 stars, and 4 were awarded 7 stars (Table 3). This indicated that the quality of the included literature was good and ensured greater reliability in the conclusion of our meta-analysis.

Clinical Outcomes

Preoperative. There was no significant difference in the preoperative Constant score ($I^2 = 29\%$; $P = .61$) or UCLA score ($I^2 = 67\%$; $P = .09$) between patients with and without diabetes, however diabetes was significantly associated with a poorer preoperative ASES score ($I^2 = 41\%$; $P = .009$) (Figures 2–4). Subsequently, sensitivity analyses were conducted to explore any potential sources of heterogeneity and to examine the effect of various exclusion criteria on the combined risk estimates. Sensitivity analysis was also performed to exclude 1 study[10] from the group of preoperative ASES scores, which revealed different results ($I^2 = 65\%$; $P = .11$), with substantial evidence of heterogeneity.

Postoperative. Diabetes was significantly associated with poorer postoperative clinical outcomes, except for the ASES score ($I^2 = 91\%$; $P = .13$) and UCLA score ($I^2 = 88\%$; $P = .34$), with considerable heterogeneity. The Constant score analysis showed that patients without diabetes had higher postoperative scores ($I^2 = 0\%$; $P = .0003$), with no heterogeneity. Further exclusion of any single study did not materially alter the results (Figures 5-7).

Preoperative Versus Postoperative. There was no significant difference in the absolute mean change in clinical outcomes from baseline to last follow-up between patients with and without diabetes. The results were consistent across all analyses. Moderate heterogeneity was observed in the Constant score ($I^2 = 47\%$; $P = .39$) and ASES score ($I^2 = 48\%$; $P = .65$). Substantial heterogeneity was observed in the UCLA score ($I^2 = 93\%$; $P = .73$). Further exclusion

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[**] References 10, 16, 18-20, 26, 37, 41, 51, 55.

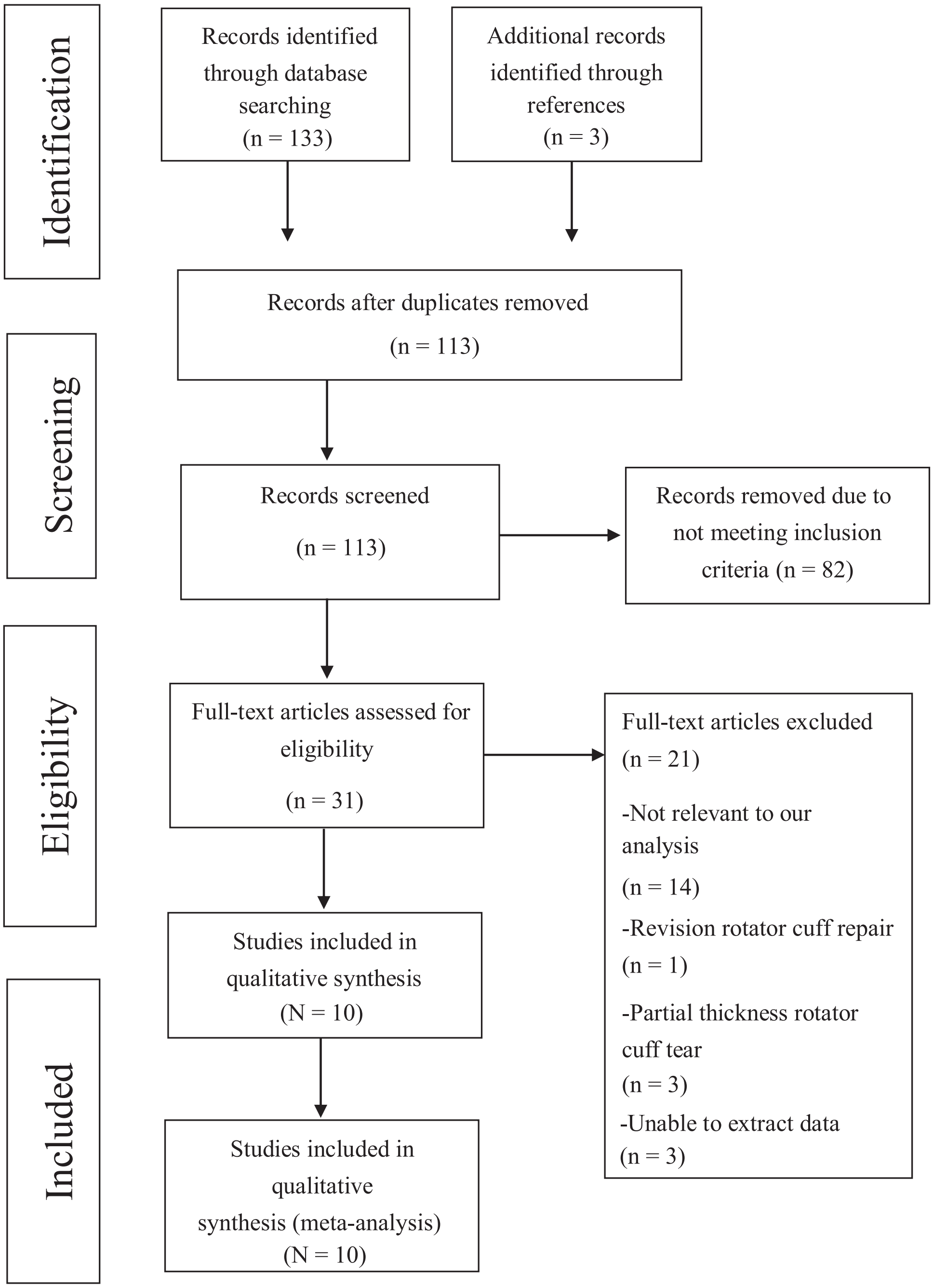


Figure 1. Search flow: trials identified and search process using the PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) guidelines.

of any single study did not materially alter the results (Figures 8-10).

Retear Rate

Overall, 7 studies[18,19,26,37,41,51,55] provided data concerning the rate of retears, and 2 of the studies[18,51] mentioned the relationship between glycemic control and retears. There was no heterogeneity across the included studies ($I^2 =$ 0%). There was a significant difference in the retear rate between the diabetic (28.15≈28.2%) and nondiabetic (19.3%) groups ($P < .0001$; RR, 1.71 [95% CI, 1.34-2.17]; $I^2 = 0\%$) (Figure 11). To test the robustness of our findings, subgroup analyses were performed, and the results were relatively consistent. There was a significant difference in retear rates between the uncontrolled diabetic and nondiabetic groups ($P < .00001$; RR, 2.77 [95% CI, 1.83-4.21]; $I^2 =$ 0%). In analyzing the retear rates according to the severity of sustained hyperglycemia, retears were found in 58 of 397 (14.6%) patients without diabetes, versus 10 of 44 (22.7%)

TABLE 2
Characteristics of Included Studies[a]

				Rehabilitation					
Author (Year)	Tear Size[b]	Intervention	Immobilization	Passive ROM	Active ROM	Strengthening	Outcomes	Follow-up, mo	Imaging Method
Berglund[10] (2018)	All sizes	Arthroscopic	Immediately (shoulder immobilizer)	On first day after surgery	6 wk	12 wk	ASES, active ROM, other	12	NS
Chen[16] (2003)	Massive tears excluded	Open	NS	On first day after surgery	6-8 wk	10-12 wk	ASES, passive ROM, active ROM	24-70	MRI
Cho[18] (2015)	Medium to large	Arthroscopic	NS	On first day after surgery	6 wk	24 wk	Retear rate, Constant, UCLA, active ROM, other	Minimum 12	MRI
Chung[19] (2011)	All sizes	Arthroscopic	Immediately (abduction brace)	On first day after surgery but restricted for 2-4 wk postoperatively in patients with large to massive tears	4-6 wk	9-12 wk	Retear rate, other	Minimum 12	CTA, US
Clement[20] (2010)	Massive tears excluded	Arthroscopic	Immediately (sling)	On first day after surgery	8-10 wk	12 wk	Constant, active ROM, other	12	MRI, US
Dhar[26] (2013)	All sizes	Arthroscopic	Immediately (shoulder immobilizer)	First 6 wk	6 wk	20 wk	Retear rate, ASES, active ROM, other	Minimum 12	MRI
Jeong[37] (2018)	Large	Arthroscopic	NS	NS	NS	NS	Retear rate, other	Minimum 9	MRI
Kim[41] (2018)	Medium to large	Arthroscopic	Immediately (abduction brace)	On first day after surgery	6 wk	12 wk	Retear rate, other	Minimum 24	MRI
Miyatake[51] (2018)	Medium or large	Arthroscopic	Immediately (abduction brace)	NS	6 wk	12 wk	Retear rate, UCLA, active ROM, other	Minimum 12	MRI
Nakamura[55] (2016)	Large or massive	Arthroscopic	Immediately (sling with abduction pillow)	On first day after surgery	4-6 wk	8-12 wk	Retear rate, other	Minimum 24	MRI

[a] ASES, American Shoulder and Elbow Surgeons; CTA, computed tomography arthrography; MRI, magnetic resonance imaging; NS, not specified; ROM, range of motion; UCLA, University of California–Los Angeles; US, ultrasound.

[b] Tear size: small/medium, 1-3 cm; large, 3-5 cm; and massive, >5 cm.

TABLE 3
Methodological Quality Assessment (Risk of Bias) of Included Studies by Newcastle-Ottawa Scale[a]

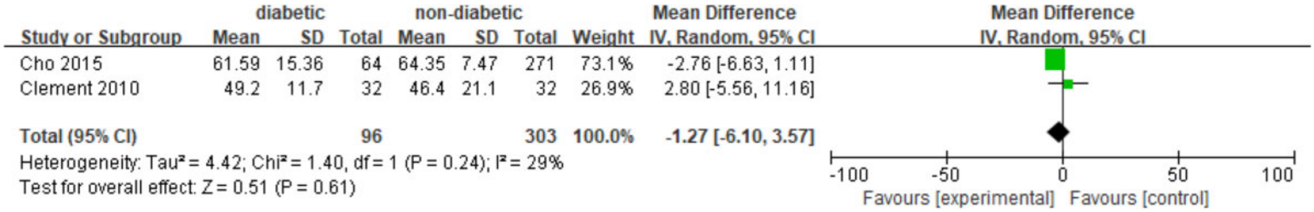
	Selection					Outcome				
Author (Year)	Exposed Cohort	Nonexposed Cohort	Ascertainment of Exposure	Outcome of Interest	Comparability	Assessment of Outcome	Length of Follow-up	Adequacy of Follow-up	Total Score	Risk of Bias[b]
Berglund[10] (2018)	*	*	*	—	*	*	*	*	7	Medium
Chen[16] (2003)	*	—	*	*	**	*	*	*	8	Low
Cho[18] (2015)	*	*	*	—	**	*	*	*	8	Low
Chung[19] (2011)	*	*	*	—	*	*	*	*	7	Medium
Clement[20] (2010)	*	*	*	—	**	*	*	*	8	Low
Dhar[26] (2013)	*	*	*	—	**	*	*	*	8	Low
Kim[41] (2018)	*	*	*	—	*	*	*	*	7	Medium
Miyatake[51] (2018)	*	*	*	—	**	*	*	*	8	Low
Nakamura[55] (2016)	*	*	*	—	**	*	*	*	8	Low

	Selection					Exposure				
Author (Year)	Adequate Definition	Representativeness	Selection of Controls	Definition of Controls	Comparability	Ascertainment of Exposure	Same Method of Ascertainment	Nonresponse Rate	Total Score	Risk of Bias[b]
Jeong[37] (2018)	*	*	*	—	**	*	*	—	7	Medium

[a] Jeong[37] (2018) is a case-control study, and the rest are retrospective cohort studies.

[b] Risk of bias: low, 0-1 inadequate items; medium, 2-3 inadequate items; high, >3 inadequate items; and very high, no description of methods.

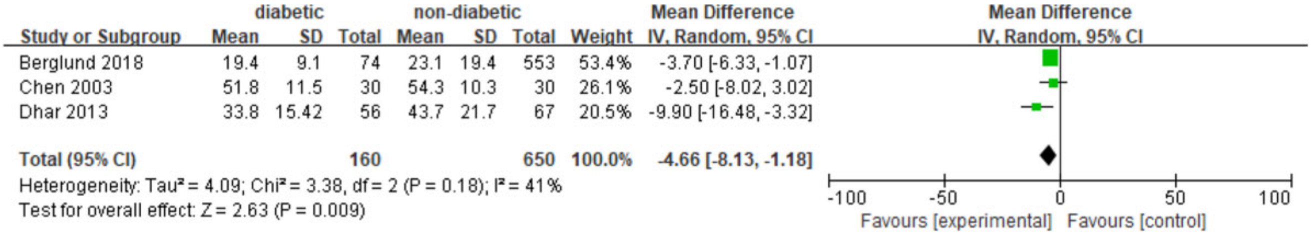
—, 0 inadequate item; *, 1 adequate item; **, 2 adequate items.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Cho 2015	61.59	15.36	64	64.35	7.47	271	73.1%	-2.76 [-6.63, 1.11]
Clement 2010	49.2	11.7	32	46.4	21.1	32	26.9%	2.80 [-5.56, 11.16]
Total (95% CI)			**96**			**303**	**100.0%**	**-1.27 [-6.10, 3.57]**

Heterogeneity: Tau² = 4.42; Chi² = 1.40, df = 1 (P = 0.24); I² = 29%
Test for overall effect: Z = 0.51 (P = 0.61)

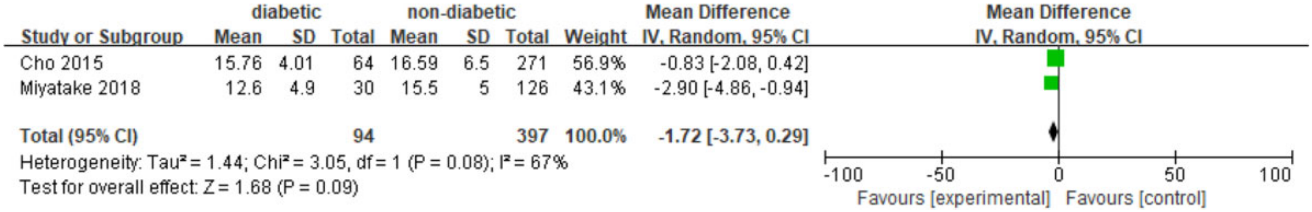
Figure 2. Forest plot showing the preoperative Constant score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Berglund 2018	19.4	9.1	74	23.1	19.4	553	53.4%	-3.70 [-6.33, -1.07]
Chen 2003	51.8	11.5	30	54.3	10.3	30	26.1%	-2.50 [-8.02, 3.02]
Dhar 2013	33.8	15.42	56	43.7	21.7	67	20.5%	-9.90 [-16.48, -3.32]
Total (95% CI)			**160**			**650**	**100.0%**	**-4.66 [-8.13, -1.18]**

Heterogeneity: Tau² = 4.09; Chi² = 3.38, df = 2 (P = 0.18); I² = 41%
Test for overall effect: Z = 2.63 (P = 0.009)

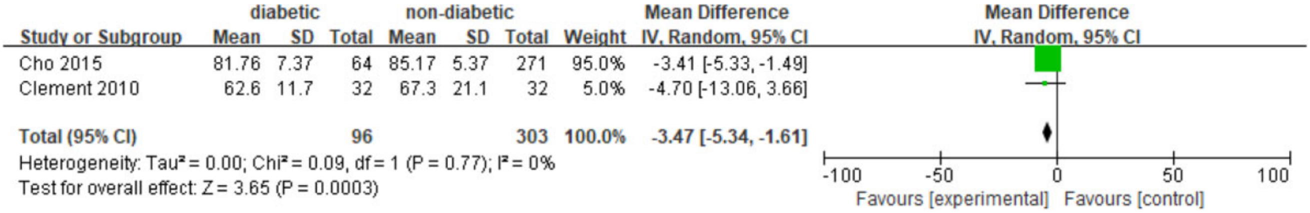
Figure 3. Forest plot showing the preoperative American Shoulder and Elbow Surgeons score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Cho 2015	15.76	4.01	64	16.59	6.5	271	56.9%	-0.83 [-2.08, 0.42]
Miyatake 2018	12.6	4.9	30	15.5	5	126	43.1%	-2.90 [-4.86, -0.94]
Total (95% CI)			**94**			**397**	**100.0%**	**-1.72 [-3.73, 0.29]**

Heterogeneity: Tau² = 1.44; Chi² = 3.05, df = 1 (P = 0.08); I² = 67%
Test for overall effect: Z = 1.68 (P = 0.09)

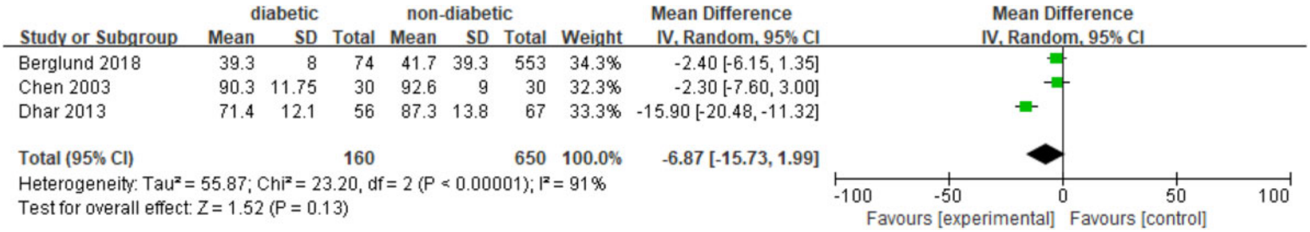
Figure 4. Forest plot showing the preoperative University of California–Los Angeles score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Cho 2015	81.76	7.37	64	85.17	5.37	271	95.0%	-3.41 [-5.33, -1.49]
Clement 2010	62.6	11.7	32	67.3	21.1	32	5.0%	-4.70 [-13.06, 3.66]
Total (95% CI)			**96**			**303**	**100.0%**	**-3.47 [-5.34, -1.61]**

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.65 (P = 0.0003)

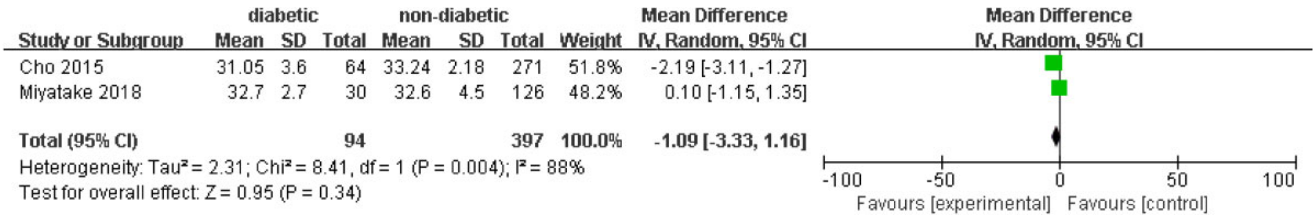
Figure 5. Forest plot showing the postoperative Constant score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Berglund 2018	39.3	8	74	41.7	39.3	553	34.3%	-2.40 [-6.15, 1.35]
Chen 2003	90.3	11.75	30	92.6	9	30	32.3%	-2.30 [-7.60, 3.00]
Dhar 2013	71.4	12.1	56	87.3	13.8	67	33.3%	-15.90 [-20.48, -11.32]
Total (95% CI)			**160**			**650**	**100.0%**	**-6.87 [-15.73, 1.99]**

Heterogeneity: Tau² = 55.87; Chi² = 23.20, df = 2 (P < 0.00001); I² = 91%
Test for overall effect: Z = 1.52 (P = 0.13)

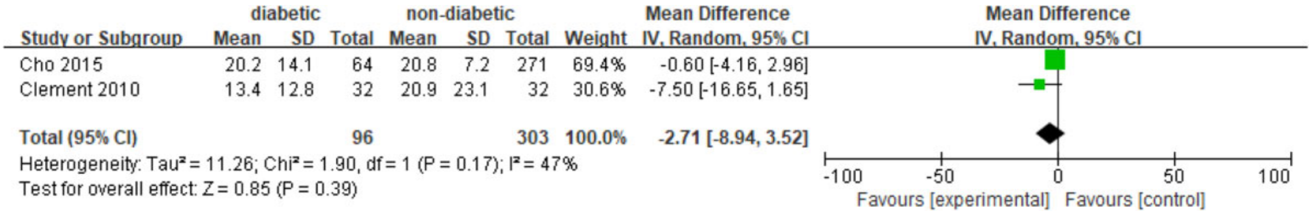
Figure 6. Forest plot showing the postoperative American Shoulder and Elbow Surgeons score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cho 2015	31.05	3.6	64	33.24	2.18	271	51.8%	-2.19 [-3.11, -1.27]
Miyatake 2018	32.7	2.7	30	32.6	4.5	126	48.2%	0.10 [-1.15, 1.35]
Total (95% CI)			**94**			**397**	**100.0%**	**-1.09 [-3.33, 1.16]**

Heterogeneity: Tau² = 2.31; Chi² = 8.41, df = 1 (P = 0.004); I² = 88%
Test for overall effect: Z = 0.95 (P = 0.34)

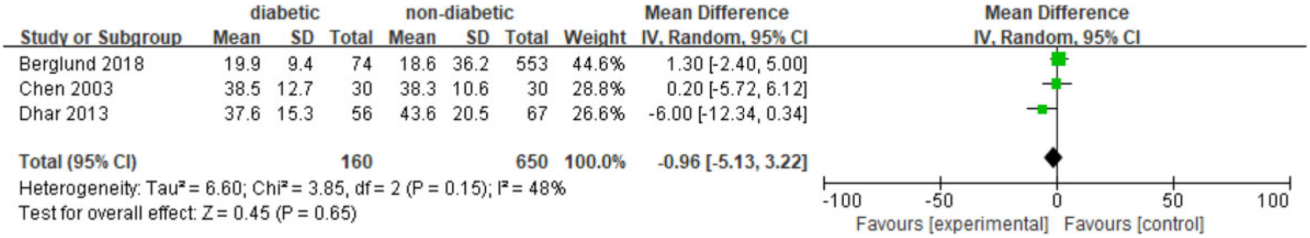
Figure 7. Forest plot showing the postoperative University of California–Los Angeles score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cho 2015	20.2	14.1	64	20.8	7.2	271	69.4%	-0.60 [-4.16, 2.96]
Clement 2010	13.4	12.8	32	20.9	23.1	32	30.6%	-7.50 [-16.65, 1.65]
Total (95% CI)			**96**			**303**	**100.0%**	**-2.71 [-8.94, 3.52]**

Heterogeneity: Tau² = 11.26; Chi² = 1.90, df = 1 (P = 0.17); I² = 47%
Test for overall effect: Z = 0.85 (P = 0.39)

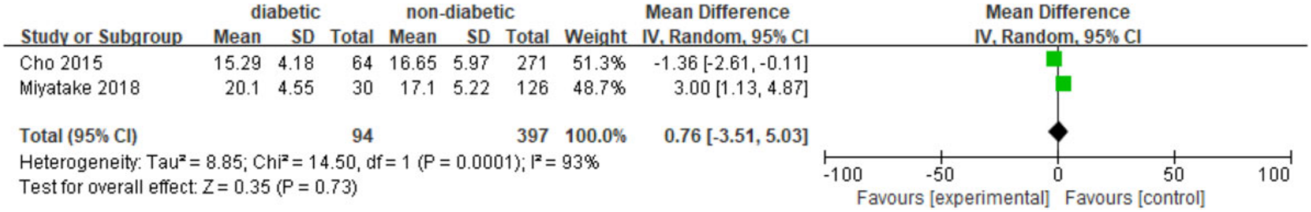
Figure 8. Forest plot showing the change in the Constant score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Berglund 2018	19.9	9.4	74	18.6	36.2	553	44.6%	1.30 [-2.40, 5.00]
Chen 2003	38.5	12.7	30	38.3	10.6	30	28.8%	0.20 [-5.72, 6.12]
Dhar 2013	37.6	15.3	56	43.6	20.5	67	26.6%	-6.00 [-12.34, 0.34]
Total (95% CI)			**160**			**650**	**100.0%**	**-0.96 [-5.13, 3.22]**

Heterogeneity: Tau² = 6.60; Chi² = 3.85, df = 2 (P = 0.15); I² = 48%
Test for overall effect: Z = 0.45 (P = 0.65)

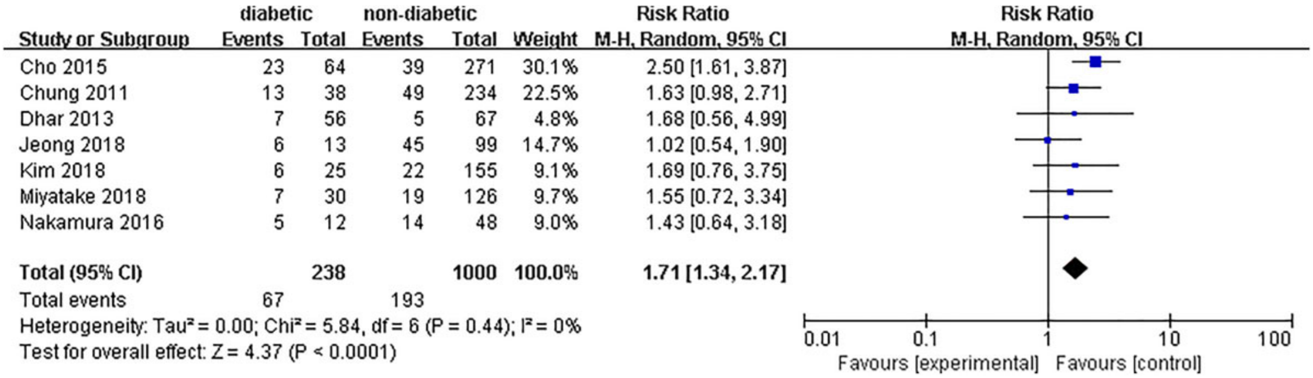
Figure 9. Forest plot showing the change in the American Shoulder and Elbow Surgeons score. IV, inverse variance.



	diabetic			non-diabetic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cho 2015	15.29	4.18	64	16.65	5.97	271	51.3%	-1.36 [-2.61, -0.11]
Miyatake 2018	20.1	4.55	30	17.1	5.22	126	48.7%	3.00 [1.13, 4.87]
Total (95% CI)			**94**			**397**	**100.0%**	**0.76 [-3.51, 5.03]**

Heterogeneity: Tau² = 8.85; Chi² = 14.50, df = 1 (P = 0.0001); I² = 93%
Test for overall effect: Z = 0.35 (P = 0.73)

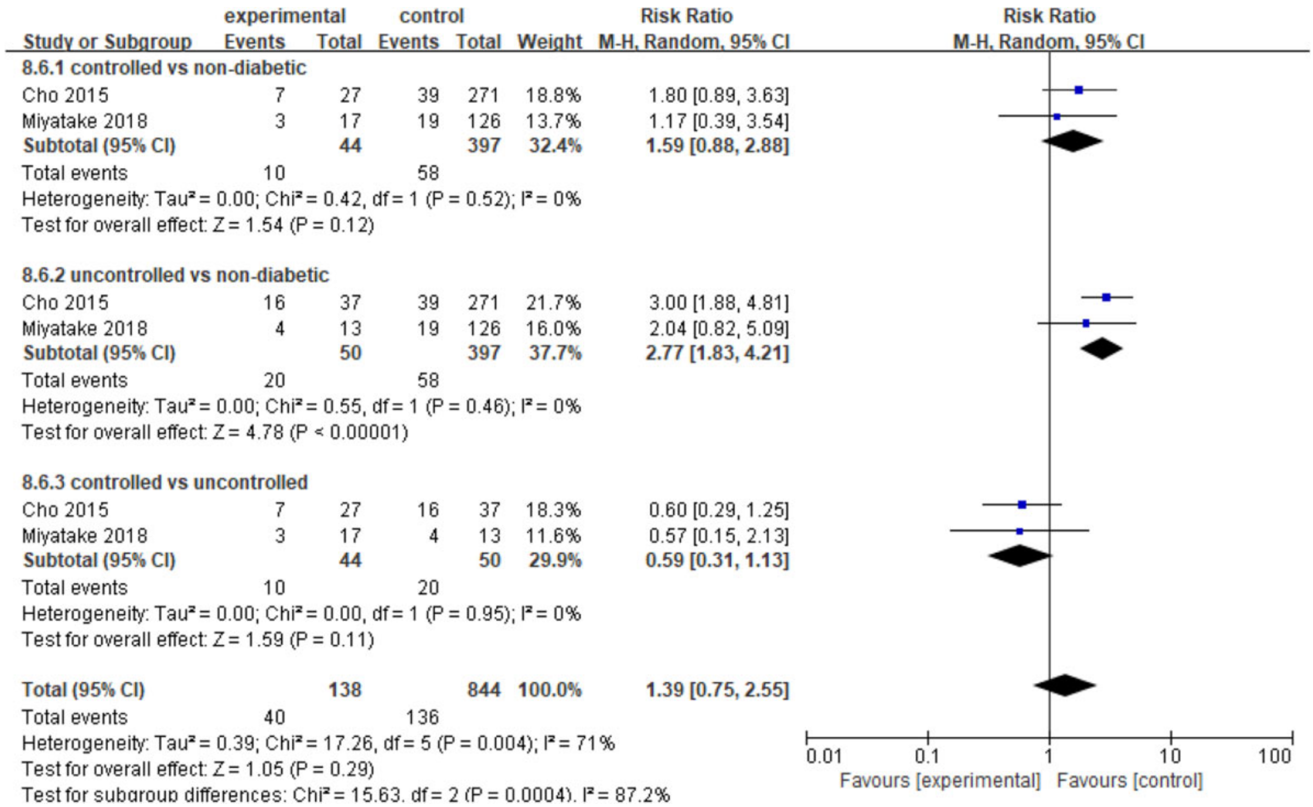
Figure 10. Forest plot showing the change in the University of California–Los Angeles score. IV, inverse variance.



	diabetic		non-diabetic			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Cho 2015	23	64	39	271	30.1%	2.50 [1.61, 3.87]
Chung 2011	13	38	49	234	22.5%	1.63 [0.98, 2.71]
Dhar 2013	7	56	5	67	4.8%	1.68 [0.56, 4.99]
Jeong 2018	6	13	45	99	14.7%	1.02 [0.54, 1.90]
Kim 2018	6	25	22	155	9.1%	1.69 [0.76, 3.75]
Miyatake 2018	7	30	19	126	9.7%	1.55 [0.72, 3.34]
Nakamura 2016	5	12	14	48	9.0%	1.43 [0.64, 3.18]
Total (95% CI)		**238**		**1000**	**100.0%**	**1.71 [1.34, 2.17]**
Total events	67		193			

Heterogeneity: Tau² = 0.00; Chi² = 5.84, df = 6 (P = 0.44); I² = 0%
Test for overall effect: Z = 4.37 (P < 0.0001)

Figure 11. Forest plot showing the retear rate. M-H, Mantel-Haenszel.



Study or Subgroup	experimental Events	experimental Total	control Events	control Total	Weight	Risk Ratio M-H, Random, 95% CI
8.6.1 controlled vs non-diabetic						
Cho 2015	7	27	39	271	18.8%	1.80 [0.89, 3.63]
Miyatake 2018	3	17	19	126	13.7%	1.17 [0.39, 3.54]
Subtotal (95% CI)		**44**		**397**	**32.4%**	**1.59 [0.88, 2.88]**
Total events	10		58			
Heterogeneity: Tau² = 0.00; Chi² = 0.42, df = 1 (P = 0.52); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
8.6.2 uncontrolled vs non-diabetic						
Cho 2015	16	37	39	271	21.7%	3.00 [1.88, 4.81]
Miyatake 2018	4	13	19	126	16.0%	2.04 [0.82, 5.09]
Subtotal (95% CI)		**50**		**397**	**37.7%**	**2.77 [1.83, 4.21]**
Total events	20		58			
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%						
Test for overall effect: Z = 4.78 (P < 0.00001)						
8.6.3 controlled vs uncontrolled						
Cho 2015	7	27	16	37	18.3%	0.60 [0.29, 1.25]
Miyatake 2018	3	17	4	13	11.6%	0.57 [0.15, 2.13]
Subtotal (95% CI)		**44**		**50**	**29.9%**	**0.59 [0.31, 1.13]**
Total events	10		20			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%						
Test for overall effect: Z = 1.59 (P = 0.11)						
Total (95% CI)		**138**		**844**	**100.0%**	**1.39 [0.75, 2.55]**
Total events	40		136			
Heterogeneity: Tau² = 0.39; Chi² = 17.26, df = 5 (P = 0.004); I² = 71%						
Test for overall effect: Z = 1.05 (P = 0.29)						
Test for subgroup differences: Chi² = 15.63, df = 2 (P = 0.0004), I² = 87.2%						

Figure 12. Forest plot showing subgroup analyses for the retear rate. M-H, Mantel-Haenszel.

patients with well-controlled diabetes (P = .12; RR, 1.59 [95% CI, 0.88-2.88]; $I^2 = 0\%$) and 20 of 50 (40.0%) patients with uncontrolled diabetes ($P < .00001$). However, there was no significant difference between the well-controlled and uncontrolled groups (P = .11; RR, 0.59 [95% CI, 0.31-1.13]; $I^2 = 0\%$) (Figure 12).

DISCUSSION

This meta-analysis showed that diabetes was significantly associated with an increased risk of retears in patients after rotator cuff repair, with no heterogeneity found across the included studies. Subgroup analysis of 2 studies[18,51] found that the retear rate was negatively correlated with blood glucose control. In most groups, the diabetic group had worse clinical outcomes after rotator cuff repair. Further, sensitivity analysis did not materially alter the results. However, because the preoperative clinical outcomes in the diabetic group were also worse, there was no significant difference in improvement from baseline to last follow-up. Rotator cuff repair resulted in equal improvements in outcome scores in both the diabetic and nondiabetic groups.

Possible Mechanisms

DM is a complex disorder characterized by persistent hyperglycemia, and it is also a major factor contributing to the relatively poor prognosis in patients concerning a number of musculoskeletal disorders. Over 70% of people with diabetes report difficulty with routine physical activities, and diabetes alone was associated with 2 to 3 times increased odds of suffering from disabilities.[38] As nearly 10% of the United States population is diabetic, with an additional 33% being prediabetic, this is a particularly problematic health care challenge.[57]

Several studies have suggested that diabetes can affect tendon repair outcomes. Using a diabetic tendinopathy model in animals, it has been recognized that alterations in inflammatory, angiogenic, and proliferative processes may be responsible.[9,15,24] These findings are in agreement with other studies in which researchers found that the same changes occur in humans[23,28,63] and that the tendons tended to degenerate, reduce mechanical strength, and predispose patients to ruptures. Lancaster et al[42] showed that diabetic tendon preparations are approximately 13% shorter than controls in a canine model. Tendon contracture causes excessive strain on the suture-tendon interface and reduces tendon mobility, affecting tendon repair. The metabolic condition of poorly controlled diabetes negatively affects the mechanical properties of the tendon, thereby reducing the ultimate load to failure and increasing the risk of structural failure.[1,2,4] Furthermore, the tendon-suture interface is a weak link in rotator cuff repair in biomechanical and clinical studies,[21,48] making it reasonable to suspect that tendon quality may be a key factor in retears. Collagen is one of the major connective tissue components, and DM can cause decreased collagen content and defects in cross-linking[68,69,74,76,79] as well as increased deposition of advanced glycation end-products at the tendon-bone interface, affecting tendon quality, tissue healing, and functional recovery.

DM is a risk factor for rotator cuff disease.[45,72] A meta-analysis[61] showed that diabetes had a significant negative effect on retears, with an odds ratio of 2.13 with homogeneity, in 2 cohorts. Thus, the results of this study confirmed what has been previously documented: DM is associated with a significantly increased risk of retears after rotator cuff repair, and improved glycemic control may reduce the risk of retears. Surprisingly however, mechanical and clinical research by Thomas et al[71] and Djerbi et al,[27] respectively, has shown that diabetes does not have any worsening effect on tendon tears. Le et al[43] showed that the diabetic status of the patient was not a significant contributor to retears ($P = .83$), but they did not assess the level or duration of glycemic control. These results appear to contrast with our findings. There is no conclusive evidence on the relationship between the presence of diabetes and the rate of rotator cuff retears. Further investigations are warranted to determine the primary factors related to the retear rate in patients with diabetes after rotator cuff repair.

A number of studies have indicated that diabetes is associated with joint stiffness.[8,11,36,39,65] Compared with those without diabetes, patients with diabetes are 5 times more likely to develop adhesive capsulitis.[78] Bunker and Anthony[12] reported a higher incidence of shoulder stiffness in patients with diabetes (36%) versus the general population (3%). High-circulating blood glucose levels may lead to fibrosis,[58,66,77] and diabetes can cause neurological decline.[3,9] A recent review[53] showed structural and metabolic impairments in the muscle of patients with type 1 diabetes, at the tissue and cellular levels, across all age groups. Furthermore, type 2 diabetes was associated with decreased muscle strength and increased muscle fatigability in the upper extremities.[59] This will affect the muscle strength and functional scores of patients with diabetes to a certain extent. That explains why patients with diabetes had worse clinical outcomes before rotator cuff surgery in our findings.

However, some researchers hold different opinions on postoperative clinical outcomes. The prevalence of frozen shoulder has no correlation with glycemic control.[75] Namdari and Green[56] showed that there was no statistically significant correlation with range of motion after 1 year of observation in patients with diabetes after rotator cuff repair. Similarly, Razmjou et al[62] found that the presence of diabetes had no negative impact on postoperative range of motion. In addition, analyses of preoperative clinical outcomes indicated inconsistent results, with several studies[16,26] showing no significant difference between patients with and without diabetes. The possible mechanism that may explain the result is that the earliest changes in diabetic neuropathy occur in sensory nerve fibers, and these changes cause hypoalgesia and numbness,[29,32] which are likely irreversible,[3] affecting the accuracy of preoperative clinical outcomes. Another plausible mechanism[53] is that glycemia and the duration of diabetes are not the major determinants of these deficiencies.

The quality of previous studies examining the association of DM and rotator cuff repair varied. The current evidence in studies remains controversial. Therefore, the effect of diabetes on clinical and structural outcomes after rotator cuff surgery is still unclear.

Recently, fructosamine has been proposed as a replacement for HbA1c in preoperative blood glucose assessments. Because testing fructosamine is simpler and cheaper than testing HbA1c, it is more predictive of early postoperative complications.[67] Fructosamine measures the level of glycated serum proteins, reflecting the average blood sugar concentration over the past 2 to 3 weeks,[7] and fructosamine levels quickly reflect blood glucose fluctuations in patients with known diabetes and those with unrecognized diabetes or hyperglycemia.[47,54,64] This can make up for the fact that HbA1c may not be able to detect early asymptomatic diabetes. However, there are currently no studies monitoring glucose levels with fructosamine in rotator cuff repair. More research is needed to see if fructosamine may be a better biomarker of glycemic control than HbA1c in rotator cuff repair.

Implications of This Research

Our meta-analysis found that repair of the diabetic rotator cuff improved function, although postoperative clinical results were worse than in nondiabetic patients. This is consistent with the results mentioned in the latest guidelines.[6] The results of the subgroup analysis indicated that compared with the nondiabetic group there was an increased risk of retears in the diabetic group with poor glycemic control ($P < .00001$), while well-controlled diabetes was associated with a decreased risk of retears ($P = .12$). Currently, we cannot accurately predict which patient will have a retear, as no study has been found to predict this precisely so far. However, we were able to roughly predict who was more likely to worsen to a retear according to the risk factors after rotator cuff repair.

Diabetes is a common condition that is relatively easy to diagnose and manage. The potentially negative effect of diabetes on rotator cuff surgery needs to be given more attention. The importance of early treatment in the prediabetic and early diabetic stages to prevent nerve fiber decline has been validated because of the irreversibility of the injury. For clinicians, these findings may contribute to the sorting and management of patients undergoing rotator cuff repair, with diabetes as a risk factor for retears. As a primary prevention strategy, maintaining blood glucose levels within the reference range may improve patient-reported outcomes and enhance rotator cuff healing after surgery, and further prospective research needs to be conducted in this area.

Limitations

Regarding study limitations, we only compared patients with and without diabetes after rotator cuff repair. There was heterogeneity in surgical techniques and rehabilitation protocols that could have affected outcomes. Most of the studies did not specify chronicity of the tear or grade of atrophy. The few studies that did provide these data used different grading systems. Our study had a large follow-up range (9-103 months), which may have affected the accuracy of the clinical outcomes. Despite the imprecise measurements, we believe that these associations deserve attention and further study. Although type 1 DM and type 2 DM have similar clinical presentations, they have different mechanisms.[14] As these data were not available in the literature, we could not classify the type of diabetes. In addition, some studies[13,60] showed no significant difference in the impact of diabetes type on rotator cuff disease. The type of diabetes is an interesting factor, and this topic may be useful for future research. Although our review had many internal and external limitations, we do not believe that they substantially detract from the conclusions of this study.

CONCLUSION

This meta-analysis found that DM was associated with a significantly increased risk of retears after rotator cuff repair, and improved glycemic control may reduce the risk of retears. Preoperative and postoperative outcome scores were significantly worse in patients with diabetes; however, the magnitude of improvement after surgery was similar to patients without diabetes. Therefore, effective glycemic control is recommended, especially during the perioperative period, in patients with diabetes undergoing rotator cuff repair. This may improve postoperative outcomes and decrease retear rates in patients with DM.

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