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The effect of applying anti-osteoporosis drugs on the rehabilitation of patients with rotator cuff tears after arthroscopic rotator cuff repair: a meta-analysis

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Abstract

Background This comprehensive meta-analysis aimed to elucidate the effects of anti-osteoporosis (OP) drugs in patients who experienced rotator cuff tears and underwent arthroscopic repair.

Methods The PubMed, Embase, Web of Science, and Cochrane Central databases were searched to identify studies that examined the effects of anti-OP drugs among patients with rotator cuff tears who underwent arthroscopic rotator cuff repair. Specifically, studies that evaluated the retear rate and other subjective or objective outcomes were included in the analysis. The databases were searched from inception to January 13, 2025.

Results Ultimately, 5 articles were included in this meta-analysis. Compared with the control group, the anti-OP drug group had a lower retear rate, higher American Shoulder and Elbow Surgeon scores and a greater internal rotation angle. The Simple Shoulder Test, University of California, Los Angeles shoulder score, Constant Shoulder score, and forward flexion angle were not markedly different between the two groups.

Conclusion Anti-OP drugs markedly promoted bone-to-tendon healing and improved quality of life among patients who underwent arthroscopic rotator cuff repair, especially with respect to activities that involve internal rotation of the shoulder.

Keywords Osteoporosis, Rotator cuff tears, Retear, Meta-analysis

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Introduction

Rotator cuff tears are common injuries of the glenohumeral joint and are characterized by limited shoulder motion, weakness and pain; it is estimated that rotator cuff tears account for nearly half of all shoulder injuries [1]. The occurrence of this injury increases as individuals age; it has been reported that a quarter of individuals older than 60 years suffer from rotator cuff tears, and this prevalence rate increases to more than 45% among individuals older than 70 years [2]. As symptoms progress, quality of life decreases significantly among individuals with rotator cuff tears. Rather than relying on the limited natural healing capability of the rotator cuff and despite platelet-rich plasma being a promising method for curing rotator cuff tears [3], it is common to perform arthroscopic rotator cuff repair, which has been verified to provide satisfactory improvement in shoulder function after postoperative bone-to-tendon healing occurs [4–6]. However, retears can occur after surgery, with a prevalence rate ranging from 10 to 90% as the size of previous tears increases [7, 8]. Although numerous factors are reported to influence postoperative function, one previous meta-analysis concluded that age, body mass index, symptom duration, bone mineral density (BMD), tear size, and operative duration are risk factors for retears [9–12].

Ageing, decreased joint activity, and osteoporosis (OP) of the proximal humerus are also important factors among individuals with rotator cuff tears [13]. OP is characterized by an imbalance between osteoblasts and osteoclasts that results in a fragile bone microstructure and a low BMD [14, 15]. OP reduces the overall quality of bone at the repair site and prevents bone tendon healing by reducing the pull-out strength of an anchor, which may result in anchor loosening and bone pull-out [16]. Therefore, the management of OP may improve surgical outcomes. Compared with traditional calcium/vitamin D supplementation, pharmaceutical therapy markedly increases BMD [17]. To date, many first-line drugs, such as sex hormones, teriparatide, bisphosphonates (BPs), and denosumab, have been developed to increase BMD [18–22]. Previous studies with animal models have indicated that the application of anti-OP drugs markedly decreases the retear rate after rotator cuff repair surgery [23, 24]. After observing satisfactory results in animal models, anti-OP drugs have been introduced into clinical trials, and these trials have shown that the application of anti-OP drugs markedly reduces the retear rate and improves shoulder function after surgery [16, 25]; however, one study published in 2023 showed that although the use of BPs markedly reduced the retear rate, shoulder function did not change significantly [26]. To our knowledge, few studies have summarized the results of these studies. Therefore, it is necessary to conduct a meta-analysis to examine the effects of anti-OP drugs on shoulder function after surgery and to provide evidence-based guidance for clinical decisions.

This comprehensive meta-analysis of published data from randomized controlled trials (RCTs) and other types of comparative studies aimed to elucidate the effects of anti-OP drugs in patients who experienced rotator cuff tears and underwent arthroscopic repair.

Materials and methods

Search strategy

Two independent researchers searched the PubMed, Embase, Web of Science, and Cochrane Central databases from inception to January 13, 2025. The titles and abstracts were searched via different combinations of the following keywords: “rotator cuff”, “romosozumab”, “denosumab”, “abaloparatide”, “teriparatide”, “bisphosphonate”, “alendronate”, “clodronate”, “etidronate”, “ibandronate”, “minodronate”, “neridronate”, “olpadronate”, “pamidronate”, “risedronate”, “tiludronic acid”, and “zoledronic acid”; “raloxifene”, “androgen”, “testosterone”, “estrogen”, and “growth hormone”. The registration number for this meta-analysis is INPLASY202530006 at the International Platform of Registered Systematic Review and Meta-analysis Protocols.

Eligibility criteria and study identification

The inclusion criteria were as follows: (1) target population—individuals who suffered from rotator cuff tears; (2) intervention—arthroscopic rotator cuff repair, with one group using anti-OP drugs after surgery and the other group not using anti-OP drugs; (3) outcomes—the primary outcome was retear rates; other outcomes evaluating shoulder function and other subjective or objective outcomes were also acceptable; (4) type of study—although RCTs were desirable, other types of comparative studies are also accepted; and (5) language—English.

On the basis of the inclusion criteria listed above, the two researchers independently screened the titles and abstracts of the retrieved studies. The full texts of the potentially eligible articles were subsequently screened. Any disagreements were resolved by discussion with a third investigator.

Data extraction and risk of bias assessment

The two researchers extracted the following data from the included studies: first author names, publication year, the number of patients allocated to each group, the number of male patients in each group, the baseline BMD of each group, the mean age of each group, the intervention method used in each group, and follow-up durations. The quality of the RCTs was assessed via the Cochrane Risk of Bias Tool [27], whereas the quality of other types of comparative studies was assessed via the Newcastle–Ottawa Scale (NOS) [28].

Statistical analysis

RevMan 5.3 software was used to conduct the statistical analyses. The odds ratio (OR) and 95% confidence interval (CI) were computed as summary statistics for the dichotomous variables, and pooled summary statistics were calculated via a random effects model. The mean difference (MD) and 95% CI were computed as summary statistics for continuous variables, and pooled summary statistics were calculated with the use of a fixed effects model if there was no significant heterogeneity; otherwise, a random effects model was applied. $P < 0.05$ was the threshold for statistical significance. Statistical heterogeneity was quantified using the chi-square ($\chi 2$) and I2 tests, and $P < 0.05$ or I2 > 50% indicated significant heterogeneity. Sensitivity or subgroup analysis was used to reduce the degree of heterogeneity.

Results

Literature search

After duplicate articles were excluded, 403 studies were retrieved from the electronic databases via the above-mentioned search strategy. Among these studies, 374 were retrieved from PubMed, 10 were retrieved from Embase, 11 were retrieved from Web of Science, and 8 were retrieved from the Cochrane Central database. A total of 358 studies were subsequently excluded because they were not RCTs or comparative cohort trials (CCTs), because they were conducted on animals, or because they were not published in English. After screening the full texts of the remaining articles, 30 studies were found to have data that could not be included in the meta-analysis; for example, they did not provide the exact number of retear patients or retear rates, or they compared only two drugs or two diseases and did not establish a placebo group. Ultimately, 5 articles were included in this meta-analysis [25, 26, 29–31]. Figure 1 presents the study selection process.

Study characteristics

The main characteristics of the 5 included studies are summarized in Table 1. Only one study was an RCT. Three studies examined the use of zoledronic acid, whereas the other two studies examined the use of denosumab and teriparatide separately. Three studies had follow-up durations of 6 months, whereas the other two studies had follow-up durations of at least 2 years. The included studies were published between 2019 and 2024. A total of 534 patients were involved in the included

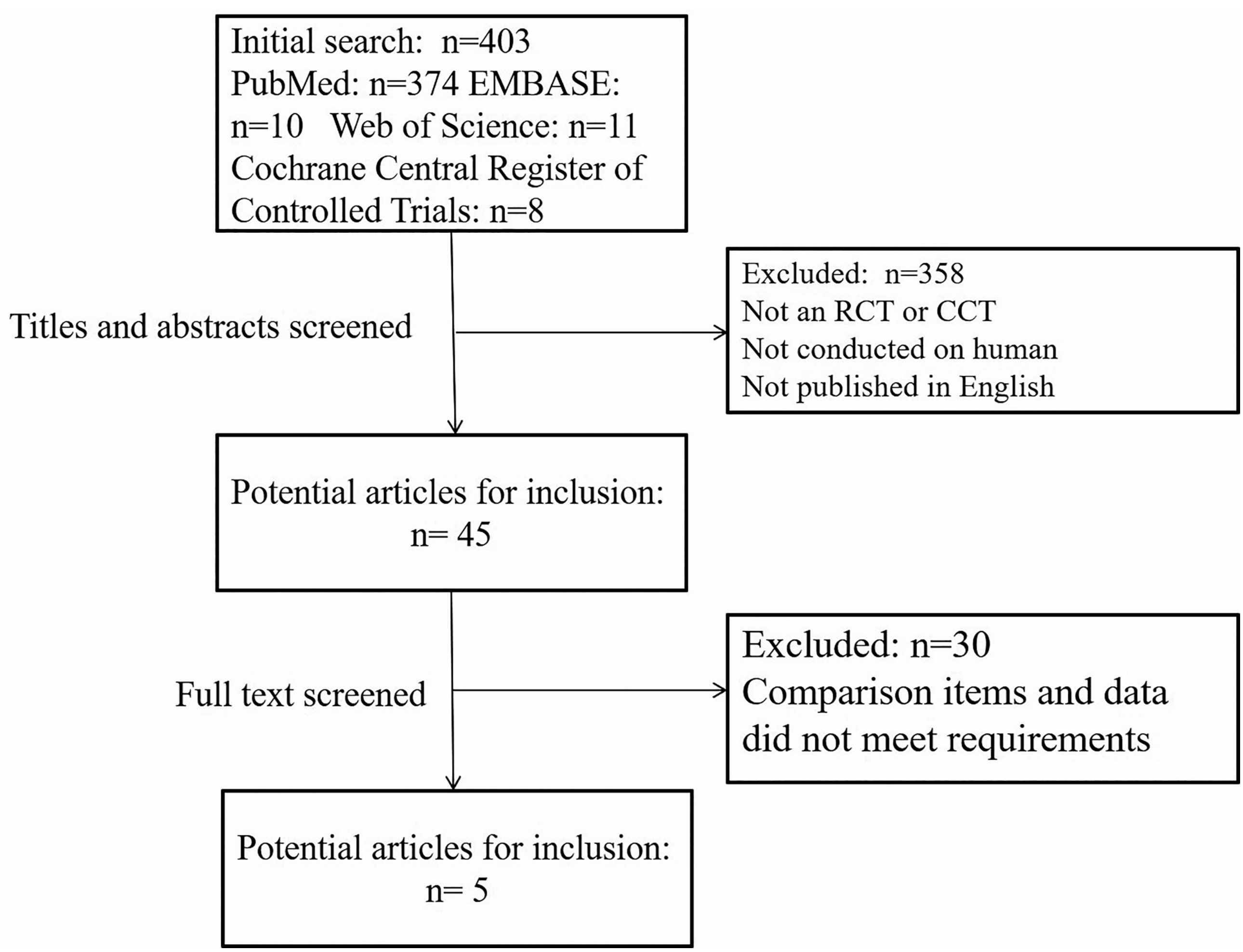

Fig. 1 Flow chart of the study selection process

Table 1 Characteristics of the included studies

First author name	Publication year	Number of included patients in the anti-OP/control groups	Age of patients in the anti-OP/control groups	Number of male patients in the anti-OP/control groups	Baseline BMD of patients in the anti-OP/control groups	Anti-OP intervention	Follow-up duration
Mingjie Lei	2023	61/63	65 ± 9/64 ± 9(mean ± SE)	0/0	-3.0 ± 0.6/-3.1 ± 0.5(T-score) (mean ± SE)	ARCR followed by intravenous 5 mg zoledronic acid infusions at postoperative day 1 and 1 year later	2 years
Ki-Tae Kim	2024	34/68	68.35 ± 7.27/65.37 ± 8.35 (mean ± SD)	0/0	-2.83 ± 0.75/-0.97 ± 1.20(T-score)(mean ± SD)	60 mg subcutaneous injection of denosumab two days after ARCR	6 months
Joo Han Oh	2019	31/124	64.3 ± 7.4/63.9 ± 8.0(mean ± SD)	11/53	-1.6 ± 1.1/-1.6 ± 1.3(T-score) (mean ± SD)	Daily subcutaneous injections of teriparatide 20 mg were administered for 3 months after surgery	26.0 months (24–30)/27.6 months (25–31) (mean, range)
Jae-Hoo Lee	2022	30/60	73.7 ± 4.9/72.0 ± 4.2(mean ± SD)	0/0	-3.6 ± 0.7/-0.4 ± 0.8(T-score) (mean ± SD)	ARCR followed by intravenous zoledronate 2 mg infusions at postoperative day 2	6 months
Yan Zhao	2024	30/33	62.8 ± 7.4/64.5 ± 5.9(mean ± SD)	9/13	-3.0 ± 0.3/-3.2 ± 0.5(T-score) (mean ± SD)	ARCR followed by intravenous zoledronic acid 5 mg infusions at postoperative day 3	6 months

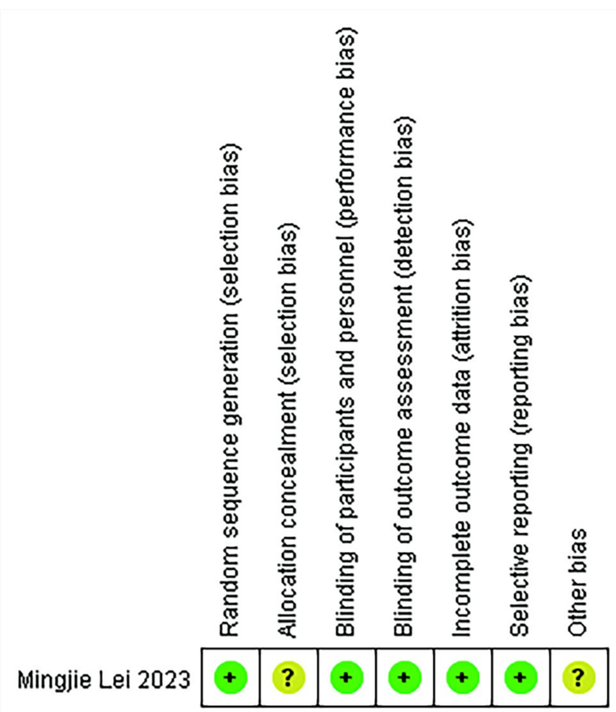

Fig. 2 Quality of the included RCT

studies, including 20 males across two of the studies. The mean age of the participants in one study was greater than 70 years. The mean T score of only one study was greater than – 2.

Study quality

The five included studies were of relatively high quality (Fig. 2). The RCT was considered to have a low risk of bias in terms of random sequence generation, performance and detection bias, completeness of the outcome data and selective reporting domains. The CCTs were of good quality, with 3 of the 4 CCTs receiving a score of 8 on the NOS and one study receiving a score of 7 (Table 2).

According to Egger et al. [32], publication bias cannot be reliably assessed when the sample size is smaller than 10 studies. Therefore, a funnel plot was not constructed to evaluate publication bias.

Retear rate

Figure 3 shows the results for the retear rate evaluated by magnetic resonance imaging computed tomography arthrography or ultrasonography in accordance with the classification of Sugaya et al. [33]. The forest plots suggest that, compared with the control group, the anti-OP group had a considerably lower retear rate.

Subjective scores

Figures 4, 5 and 6, and 7 present forest plots of the Simple Shoulder Test (SST), University of California, Los Angeles (UCLA) shoulder score, American Shoulder and Elbow Surgeon (ASES) score and Constant Shoulder Score (CSS). The results revealed that these subjective scores were not significantly different between the two groups. To reduce heterogeneity, the study conducted by Joo Han Oh et al. was excluded from the analysis of the SST score since the data provided in this study did

Table 2 Quality of the included cohort trials

		Ki-Tae Kim(2024)	Joo Han Oh(2019)	Jae-Hoo Lee(2022)	Yan Zhao(2024)
Selection					
	Representativeness of the exposed cohort	*	*	*	*
	Ascertainment of exposure	*	*	*	*
	Outcome not present at the start of the study	*	*	*	*
Comparability					
	Comorbidities	*	*	*	*
	Other factors	*	*	*	*
Outcome					
	Assessment of the outcome	*		*	*
	Follow-up long enough for the outcome to occur	*	*	*	*
	Adequacy of the follow-up	*	*	*	*
Total		8	7	8	8

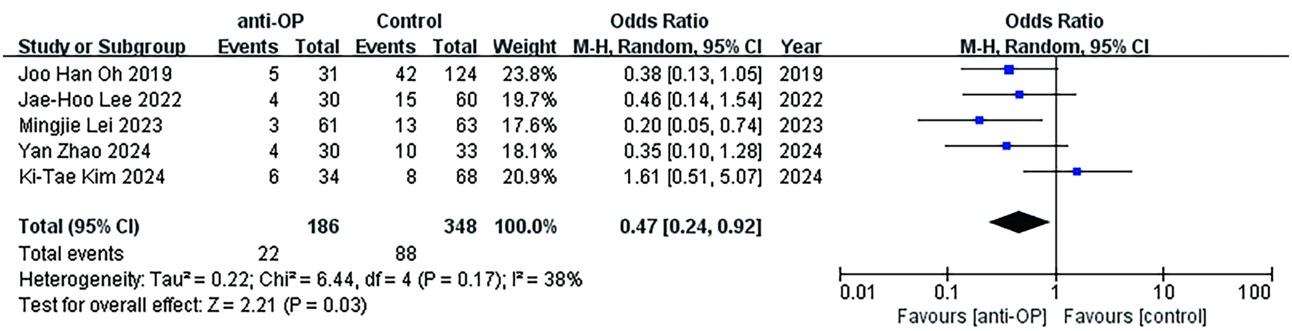

Fig. 3 Forest plots of the retear rate

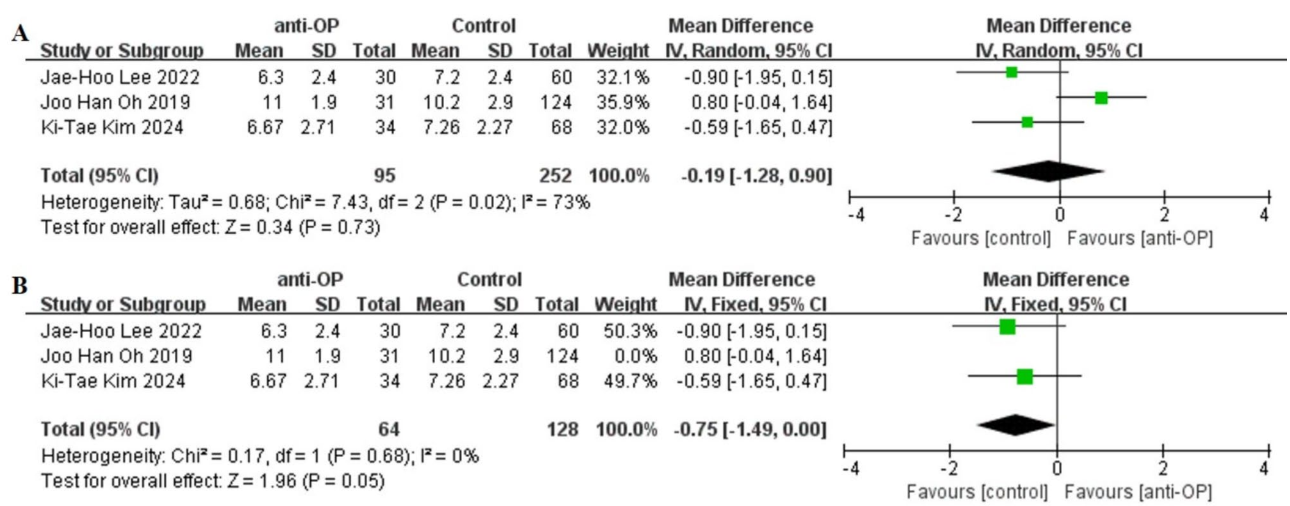

Fig. 4 Forest plot of the SST; **A**, primary meta-analysis; **B**, sensitivity analysis

not match concise follow-up time points; however, the results did not change after this exclusion. The study conducted by Jae-Hoo Lee et al. was excluded from the analysis of the ASES score since the mean age of patients in this study was more than 70 years; this led to a marked decrease in heterogeneity, and the results revealed that anti-OP drugs considerably increased the ASES score, thus indicating an improvement in shoulder function. For the other two parameters, heterogeneity could not be reduced via subgroup or sensitivity analyses.

Range of motion(ROM)

Figures 8 and 9 present the forest plots of the ROM in the forward flexion and internal rotation fields. The results suggested that there were no significant differences in these two terms. However, the anti-OP group had a greater internal rotation angle after the study

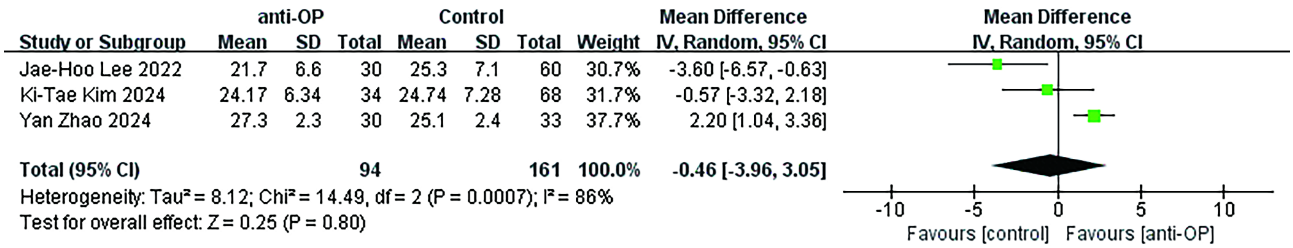

Fig. 5 Forest plot of the UCLA shoulder score

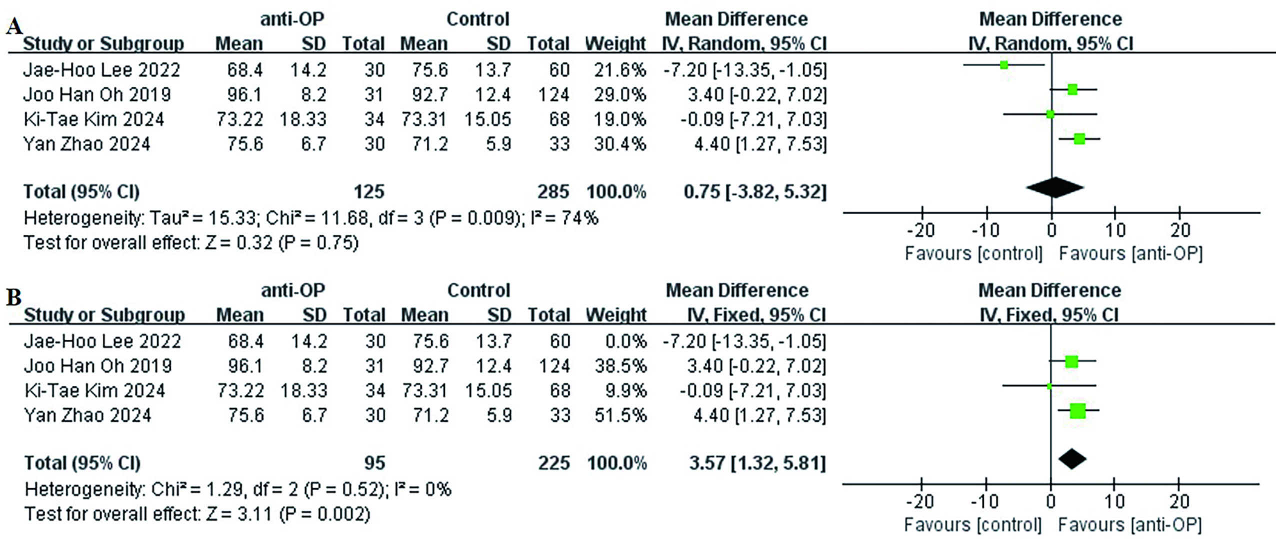

Fig. 6 Forest plot of the ASES score; **A**, primary meta-analysis; **B**, sensitivity analysis

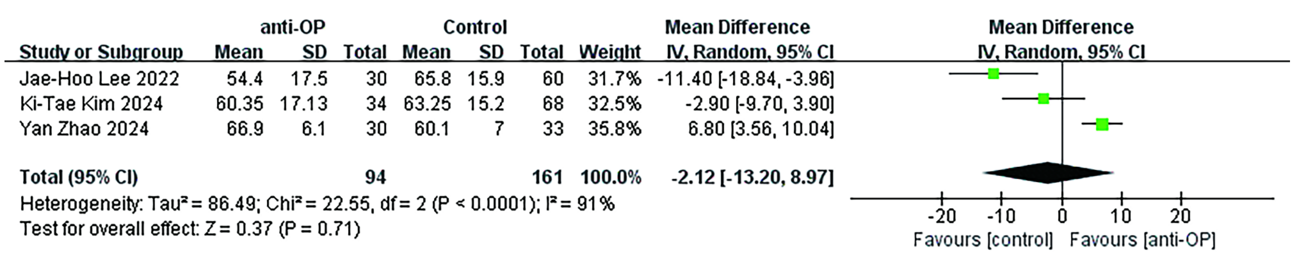

Fig. 7 Forest plot of CSS

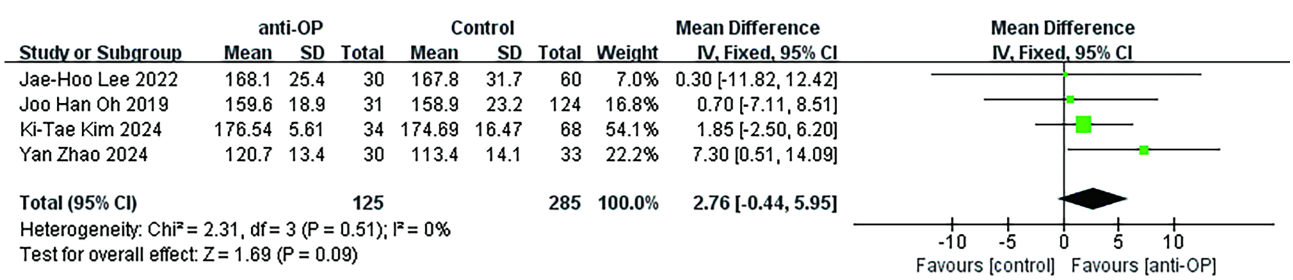

Fig. 8 Forest plot of forward flexion

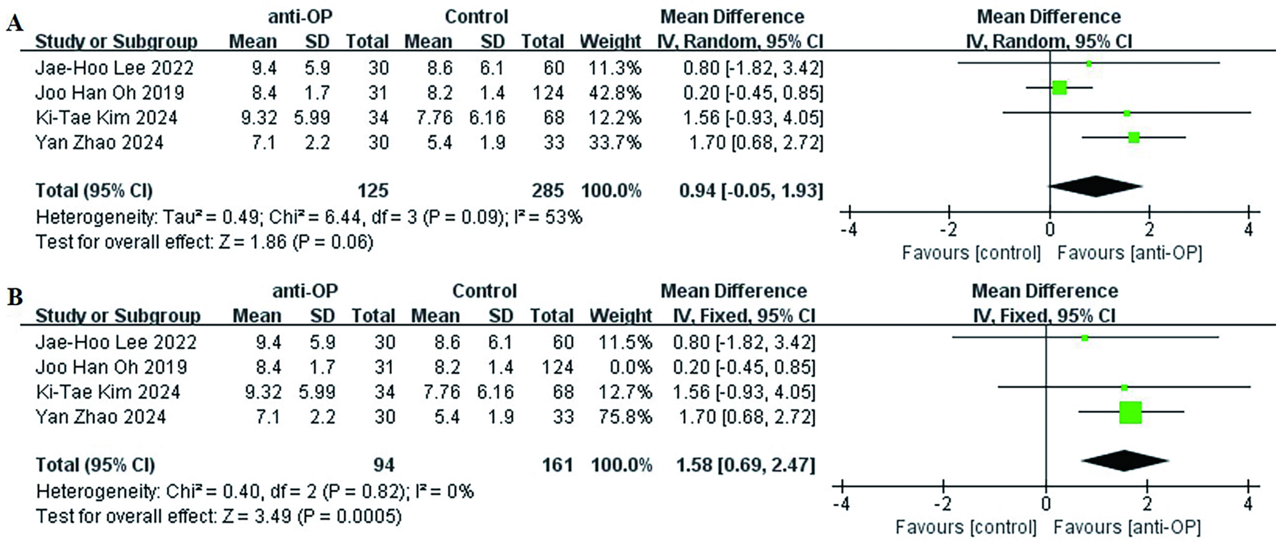

Fig. 9 Forest plot of internal rotation; **A**, primary meta-analysis; **B**, sensitivity analysis

conducted by Joo Han Oh et al. was excluded to reduce heterogeneity.

Discussion

This meta-analysis included 5 studies that used three kinds of anti-OP drugs, and the effects of these drugs can be classified as follows: teriparatide is a parathyroid hormone analogue that activates bone formation by stimulating osteoblasts and promoting calcium absorption [34], whereas BPs and denosumab act against bone resorption by inducing osteoclast apoptosis or preventing the generation of osteoclasts [35, 36]. Therefore, this meta-analysis can be considered an overall summary of the effects of first-line anti-OP drugs on retear rates after arthroscopic rotator cuff repair. The results are associated with three major parameters: retear rates, subjective scores and ROM. Overall, the results of the forest plots presented above suggest that, compared with the control treatments, anti-OP drugs led to a lower retear rate, a higher ASES score and a greater internal rotation angle. The SST, UCLA shoulder score, CSS, and forward flexion angle were not markedly different between the two groups.

One previous review reported the promotion of bone-to-tendon healing in those receiving anti-OP intervention [37]; however, the intervention methods included in that review were in vitro, animal and human methods. Furthermore, the review did not examine the first-line drugs included in the current study. In addition to the three drugs included in this meta-analysis, other drugs applied after arthroscopic rotator cuff repair, such as raloxifene and recombinant human growth hormone [38–40], were also investigated in other studies; however, these studies were either conducted on animals or did not report retear rates. One study reported the application of testosterone in humans and reported retear rates [41] and concluded that androgen use is associated with an increase in retear rates; however, this study was not a CCT. Further studies are needed to explore the effects of other drugs to increase the variety of anti-OP drugs used for patient rehabilitation.

To reduce the heterogeneity in some forest plots, sensitivity analysis was conducted by removing two studies. The results suggested that the outcomes associated with the use of anti-OP drugs after arthroscopic rotator cuff repair are influenced by the age of the patients (or the BMD) and the follow-up duration. Further studies should conduct correlation analyses in this field. Only one included study mentioned safety [26]; this study reported mild adverse effects in the zoledronic acid group, and they concluded that BPs can be regarded as safe for postoperative application. Nevertheless, safety is an important outcome for drug use. Considering that all three included drugs have definite side effects [42–45], such as atypical femoral fracture, medication-related osteonecrosis of the jaw, and cardiac events, further studies are needed to identify this parameter and measure the necessity for the application of anti-OP drugs after arthroscopic rotator cuff repair.

In addition to outcomes assessed by forest plots, other outcomes were also reported by the included studies. However, the small number of included studies prevented us from conducting a meta-analysis. These outcomes included the external rotation angle for both groups; the serum levels of osteocalcin (OC) and C-telopeptide of type I collagen (CTX) for the anti-OP group [29]; and the abduction angle, visual analogue scale (VAS), and serum levels of N-terminal type I procollagen peptide, bone-specific alkaline phosphatase, β-cross laps, and 25-OH-vitamin D (25-OHD) for both groups [31]. The VAS results indicated that, compared with the preoperative condition and the control condition, the anti-OP drug markedly reduced pain. There was no significant difference in external rotation or abduction between the two groups. According to the results of our meta-analysis, anti-OP drugs may be more likely to help patients perform activities that involve internal rotation. Bone turnover markers are important biomarkers used to monitor therapeutic efficacy in osteoporotic patients [46, 47]. The results for 25-OHD indicated no significant difference between the two groups. Interestingly, nearly all the bone turnover marker levels in patients who received zoledronic acid decreased in the anti-OP group after surgery, and compared with those in the control group, the bone turnover marker levels were also lower in the anti-OP group, which indicated the inhibition of both osteoclasts and osteoblasts. As reported by previous studies, this inhibition has a short-term effect [48], and the included studies provided data for only 3 or 6 months after surgery; further investigations are needed in this field. For patients who received teriparatide, the OC and CTX markedly increased compared with the preoperative values; considering the mechanism of teriparatide, the results showed satisfactory results for this effect.

To our knowledge, this meta-analysis may be the first to summarize data concerning first-line anti-OP drugs in humans provided by previous studies; therefore, limitations are unavoidable. First, the major limitation of this work is the small number of included studies, despite the inclusion of CCTs to increase the number of included trials, which may decrease the reliability of the forest plots. Additionally, meta-regression analysis and funnel plots could not be used to identify the source of heterogeneity and bias due to the small number of studies. Second, the follow-up period was different among the included studies. Third, the results for direct BMD parameters were not used to compare the efficacy of the anti-OP drugs. Fourth, nearly 90% of the included patients were female, which may have caused bias and influenced the application of the results to many patients. Fifth, the mechanism of the included drugs varied; therefore, heterogeneity in several comparisons was relatively high, which may conceal the exact efficacy of one specific drug. Finally, selection bias may have affected the results since only English language articles were included.

Conclusions

This meta-analysis revealed that anti-OP drugs markedly promoted bone-to-tendon healing and improved the quality of life of patients who underwent arthroscopic rotator cuff repair, especially with respect to activities involving the internal rotation of the shoulder. However, the number of studies included in this meta-analysis was small. Further studies involving larger sample sizes and longer follow-up durations should be conducted to confirm the results and provide stronger evidence in this field.

Abbreviations

25-OHD	25-OH-vitamin D
ASES	American Shoulder and Elbow Surgeon
BMD	Bone mineral density
BPs	Bisphosphonates
CCT	Comparative cohort trial
CI	Confidence interval
CSS	Constant Shoulder Score
CTX	C-telopeptide of type I collagen
MD	Mean difference
NOS	Newcastle–Ottawa Scale
OC	Osteocalcin
OP	Osteoporosis
OR	Odds ratio
RCT	Randomized controlled trials
SST	Simple Shoulder Test
UCLA	University of California, Los Angeles
VAS	Visual analogue scale

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Author contributions
YH: conception and design, final approval of the articleJQJ: critical revision of the article for important intellectual contentJJW: administrative, analysis and interpretation of the data, drafting of the article, DSH: conception and design, final approval of the articleAll authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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