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Assessing the relationship between wrist synovitis and anxiety: a study using clinical statistics and Mendelian randomization analysis

Xunhao Wang[1,2†], Linyi Zhu[1†], Jingyi Mi[1*] and Fei Xiong[1*]

Abstract

Background Wrist synovitis often leads to persistent pain, swelling, and limited mobility, causing significant functional impairment and psychological distress, including anxiety. Although arthroscopic synovectomy can alleviate physical symptoms, whether it also improves anxiety and the causal relationship between synovitis and anxiety remains unclear.

Methods A prospective study was conducted on 44 patients diagnosed with wrist synovitis who underwent arthroscopic synovectomy. Patients were assessed preoperatively and at 2 and 4 weeks postoperatively using the Visual Analog Scale (VAS), Mayo Wrist Score, and Self-Rating Anxiety Scale (SAS). MR analysis was employed to investigate the causal relationship between wrist synovitis and anxiety using genome-wide association studies (GWAS) summary data.

Results Significant reductions in SAS and VAS scores were observed at 2 and 4 weeks postoperatively, along with improvements in wrist function as measured by the Mayo Wrist Score. MR analysis did not find statistically significant evidence of a direct causal relationship between wrist synovitis and anxiety, though a positive trend suggests that wrist synovitis may be a risk factor for anxiety.

Conclusions Arthroscopic synovectomy may alleviate anxiety symptoms and may improve wrist function in patients with wrist synovitis. While a direct causal link between wrist synovitis and anxiety was not conclusively established, the observed associations highlight the need for integrated management of physical and psychological health in these patients.

Trial registration This study was retrospectively registered with the WuXi 9th People's Hospital (WuXi Orthopaedics Hospital) Medical Ethical Committee on August 6, 2023, with reference number KS2023081.

Keywords Wrist synovitis, Anxiety disorders, Arthroscopic synovectomy, Mendelian randomization, Physical and mental health interplay

Background

Wrist synovitis, characterized by inflammation of the synovial membrane in the wrist joint, leads to persistent pain, swelling, and restricted range of motion, thereby severely impairing patients' daily functioning and quality of life [1]. Although this condition primarily affects middle-aged and older adults, younger individuals can also be affected [2]. With a globally aging population, the

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prevalence of wrist synovitis is on the rise [3, 4], making it an emerging public health concern.

Chronic inflammatory diseases are often accompanied by psychological distress, including anxiety and depression [5]. Anxiety disorders, marked by excessive worry, fear, and various physiological symptoms (such as increased heart rate and muscle tension), arise from a complex interplay of genetic, biological, and environmental factors [6]. In patients with wrist synovitis, persistent pain and functional limitations further increase psychological burden, forming a vicious cycle of stress and symptom exacerbation [7, 8]. However, this mind–body interaction is not unidirectional; rather, there is a complex, bidirectional relationship between anxiety and synovitis.

On the one hand, chronic pain and inflammation caused by synovitis can activate inflammatory pathways in the central nervous system, such as microglial activation and the release of pro-inflammatory factors, increasing the risk of anxiety and emotional dysregulation. For instance, studies on temporomandibular joint synovitis have shown that abnormal functioning in the right anterior insula leads to significant network dysfunction, impairing patients' ability to regulate emotions and intensifying their perception of pain. On the other hand, anxiety can, through neurogenic pathways, influence the onset and progression of synovitis. In a state of anxiety, the hypothalamic–pituitary–adrenal axis and autonomic nervous system become overactivated, releasing systemic pro-inflammatory cytokines that exacerbate local synovial inflammation. Moreover, anxiety can reduce levels of brain-derived neurotrophic factor (BDNF), weakening neuroprotective and reparative mechanisms and making synovitis more likely to persist and worsen. This vicious cycle along the brain-synovium axis is driven by the complex interplay of inflammatory signals, autonomic regulation, and central nervous system dysfunction [9, 10].

However, the bidirectional relationship in this psychological issue in patients with wrist synovitis have not received sufficient attention. Most existing research focuses on physiological indicators of symptom improvement, pain management, and surgical efficacy, while the potential role of anxiety in maintaining or worsening inflammation has been largely overlooked. Notably, no studies have clearly examined whether arthroscopic synovectomy, while alleviating physical symptoms, can also improve patients' anxiety levels, nor have they investigated the causal relationship between synovitis and anxiety.

In this study, we combine prospective clinical follow-up with Mendelian Randomization (MR) analysis to dynamically monitor changes in anxiety levels alongside improvements in physical function, while also exploring the potential causal relationship between wrist synovitis and anxiety. This comprehensive approach aims to deepen our understanding of their complex interaction and to provide a scientific basis for integrating psychological interventions and neuromodulation therapies with conventional treatment modalities. Ultimately, such insights may enhance the clinical management and prognosis of patients suffering from these interlinked conditions.

Methods

Study population

This prospective study was conducted on patients diagnosed with wrist synovitis who underwent surgical treatment at the Sports Medicine Department Clinic of Wuxi Ninth People's Hospital from April 2023 to April 2024. Inclusion criteria comprised individuals aged 16 years and above, presenting with symptoms of synovitis such as wrist joint pain, swelling, and limited movement. Imaging findings indicated evident synovial hyperplasia near the distal radioulnar joint and wrist joint, consistent with physical examination characteristics. Exclusion criteria comprised patients with cognitive impairment preventing questionnaire completion, limited mobility in both wrist joints, multiple joint diseases (e.g. rheumatoid arthritis, significant cartilage damage, impaction lesions, avascular necrosis, ligament injuries, triangular fibrocartilage complex (TFCC) lesions, or joint instability) alongside wrist synovitis, and conditions significantly impacting physical and mental well-being like tumors, severe physical trauma, or depression.

Surgical procedure

All patients who underwent surgery had received at least one steroid injection prior to surgery, with no noticeable effect or a duration of at least 6 months. The surgical procedure involved wrist arthroscopy to remove the synovium, following a standardized protocol. The general steps included fixing the patient's affected hand with Chinese finger clamps on a suspension device, applying approximately 15 pounds of traction force, opening the joint space, and establishing two approaches, 3–4 and 6R, for observation and surgery. The joint spaces were accessed via the STT, MCR, and MCU approaches. A 2.9 mm non-serrated planer and a plasma knife were used to clear the inflamed synovium from the midcarpal, radiocarpal, and distal radioulnar joints. The wound was then sutured, and stiches were removed after 10 to 14 days. Rehabilitation training commenced immediately post-surgery, with weight-bearing activities avoided initially. Normal weight-bearing was allowed once the wound had healed [11, 12].

Follow up of wrist function post-operation

Preoperatively and at 2 and 4 weeks postoperatively, participants completed the Visual Analog Scale (VAS), Mayo Wrist Score, and Self-Rating Anxiety Scale (SAS) questionnaires according to a standardized protocol to evaluate pain, wrist function, and anxiety levels. The SAS questionnaire comprises four items, each scored from 0 to 25 using standard statistical methods. Grip strength was assessed bilaterally using a dynamometer at baseline and at 2 and 4 weeks postoperatively, with three trials per hand and the mean value calculated. The range of motion for the operated hand—including flexion, extension, pronation, elevation, ulnar deviation, and radial deviation—was measured with a dynamic goniometer. All assessments were performed by the same physical therapist using consistent equipment at each time point.

Statistical analysis

T-tests were conducted to compare the differences in VAS, Mayo Wrist Score, grip strength, range of motion, and SAS scores between the two groups before surgery, at 2 weeks post-surgery, and at 4 weeks post-surgery.

Outcome genome-wide association studies summary statistics

In this study, we estimated the causal effect between anxiety and the risk of wrist synovitis using the genome-wide association studies (GWAS) summary data. These data indirectly evaluated the causal impact between anxiety and the risk of wrist synovitis via MR analysis. At the end of those parts, we directly assessed the causal effect of the risk of wrist synovitis on the anxiety by utilizing GWAS summary data.

Selection of genetic instrumental variants

We employed stringent criteria to select SNPs as the genetic instrumental variables from the GWAS summary data of anxiety. Initially, SNPs with genome-wide significance ($p < 5 \times 10 - 8$, $R2 < 0.001$, $kb = 10{,}000$) of anxiety were selected. Subsequently, the clumping process ($R2 > 0.001$, window size = 10,000 kb) was executed to ensure that all the SNPs were not in linkage disequilibrium (LD) with the clump data function. Thirdly, if an SNP was not present in the outcome GWAS during the R calculation process, it would also be excluded. Fourthly, any ambiguous or palindromic SNPs that were ambiguous with nonconcordant alleles (e.g., A/G vs. A/C) or with an ambiguous strand (i.e., A/T or G/C) were excluded. Finally, using the PhenoScanner tool (http://www.phenoscanner.medschl.cam.ac.uk/) [13–15], we excluded any SNPs associated with the confounding factor of the outcome, and we used the F-statistic to indicate the strength of the genetic instrumental variants.

Two-sample MR analysis

The instrumental SNPs were utilized to carry out a two-sample MR analysis for the purpose of evaluating the causal effect between anxiety and the risk of wrist synovitis. Detailed methods of MR analysis included inverse variance weighting (IVW)-random effects, IVW-fixed meta-analysis, maximum likelihood, weighted median (WM), and MR-Egger regression, and penalized weighted median was applied to estimate the effects. Bonferroni correction (p-value = 0.05/11 outcomes) was used to adjust for multiple testing ($p = 0.0045$) in this MR. All of these analyses were conducted in R V.4.2.0 by using R packages of "Two-Sample MR" (https://mrcieu.github.io/TwoSampleMR/reference/clump_data.html) [16] and p-values < 0.05 were considered statistically significant.

Robust analysis

IVW (random effect and fixed effect) and MR Egger regression were used to assess the potential horizontal pleiotropic effects of the SNPs. Cochran Q-test statistics were used to quantify heterogeneities. Furthermore, we performed a "leave-one-out" sensitivity analysis to identify potentially influential SNPs. In this method, we excluded each SNP in turn and checked whether it was responsible for the association. We also applied the MR Steiger filtering method to verify the causality between anxiety and the risk of wrist synovitis.

Results

In this study, a total of 44 patients who satisfied the specified inclusion and exclusion criteria were enrolled. Detailed demographic and clinical characteristics of the participants are presented in Table 1. Data pertaining to the SAS, VAS, Mayo Wrist Score, and wrist range of motion were systematically collected at three time points: pre-operation(pre), 2 weeks post-operation(2w) and 4 weeks post-operation(4w). Subsequent analyses focused on evaluating preoperative to postoperative variations in these indicators and exploring their associations with anxiety levels.

Follow-up results

At 2w and 4w, significant reductions in SAS and VAS scores were observed compared to preoperative values, with additional significant decreases noted between the two intervals (Fig. 1a, b). The Mayo Wrist Score also showed significant improvements at 2w and 4w relative to pre, with further enhancements from 2 to 4w (Fig. 1c, d).

At 4w, the angles of wrist flexion, extension, pronation, and supination significantly increased compared to pre-operation, with additional improvements from two to four weeks post-operation (Fig. 1e–h). Notably,

Table 1 Baseline characteristics and surgical data of patients

Characteristic	Description	Number
Gender	Man	29
	Woman	15
Age (years)	≤ 20	1
	21–30	16
	31–40	15
	41–50	10
	51–60	2
Surgical side	Dominant hand	28
	No-dominant hand	16
Occupation	Student	13
	Light labor	7
	Heavy labor	23
	Sedentary	1
Previous surgical history	No	37
	Skin trauma	4
	Radial styloid tenosynovitis	2
	Carpal tunnel syndrome	1
Illness duration (months)	≤ 6	28
	≤ 12	9
	≤ 18	1
	≤ 24	3
	> 24	3
Cultural literacy	Junior high school and below	9
	High school	12
	Undergraduate	20
	Graduate or above	3
Duration of unable for work or exercise (months)	≤ 6	23
	≤ 12	10
	≤ 18	3
	≤ 24	4
	> 24	4

at 2 weeks postoperation, the extension angle showed a significant increase from pre-operation, whereas flexion, pronation, and supination angles did not differ significantly (Fig. 1e–h).

The difference in range of motion between the patient's affected wrist and unaffected wrist decreased steadily from before surgery to four weeks after surgery. (Fig. 2a–d). Concurrently, VAS scores exhibited a downward trend (Fig. 2e), while Mayo Wrist Scores showed an upward trend (Fig. 2f). SAS scores also decreased gradually, indicating that improvements in wrist pain and function were paralleled by reductions in anxiety symptoms.

Case report

Based on a representative case, preoperative MRI of the affected wrist revealed abnormal masses near the distal radioulnar and radiolunate joints, presenting with low T1 and high T2 signal intensities and no significant bone abnormalities (Fig. 3a1–a4). The patient exhibited significant restrictions in pronation, supination, flexion, and extension (Fig. 3c1–c4). Intraoperatively, arthroscopy revealed extensive inflammatory synovial proliferation without evidence of cartilage, bone, or ligament damage. The proliferative synovium was excised using a planer and plasma knife (Fig. 3b1–b4), followed by immediate initiation of rehabilitation.

At the two-week follow-up, significant improvements were noted in pronation and extension, with modest gains in supination and flexion compared to preoperative measurements (Fig. 3d1–d4). By the four-week follow-up, all measured angles of wrist motion, including flexion, extension, pronation, and supination, showed significant improvements (Fig. 3e1–e4). These findings indicate that arthroscopic debridement of proliferative synovial tissue can effectively enhance wrist mobility in patients with synovitis.

Overall, patients with wrist synovitis demonstrated a trend towards improvement in anxiety, pain, and wrist function following surgery, compared to their preoperative status. Notably, some range of motion parameters did not show significant changes at the two-week postoperative assessment, potentially due to pain and associated anxiety experienced during the early rehabilitation phase, which may have temporarily hindered wrist mobility. However, as pain and anxiety levels decreased, significant enhancements in wrist function were observed.

Data sources

To investigate the potential causal relationship between wrist synovitis and anxiety disorders, we employed Mendelian randomization analysis. We identified GWAS identifiers for both conditions from the FinnGen database (https://www.finngen.fi/fi). The study population for wrist synovitis included 167,843 individuals, with a corresponding 16,380,306 SNPs. For anxiety disorders, the sample size

(See figure on next page.)

Fig. 1 Evaluation of Preoperative and Postoperative Anxiety, Pain, Function, and Wrist Mobility. **a** Trends in Self-Rating Anxiety Scale (SAS) scores for patients before surgery and at two and four weeks postoperatively. **b** Visual Analogue Scale (VAS) scores assessing pain at preoperative, two weeks, and four weeks post-surgical intervals. **c**, **d** Mayo Wrist Score metrics and results assessed before surgery and at two and four weeks after the intervention. **e**, **f** Range of motion assessments including wrist flexion, extension, pronation, and supination measured preoperatively and at subsequent two-week intervals. pre: pre-operation, 2w: 2 weeks post-operation, 4w: 4 weeks post-operation

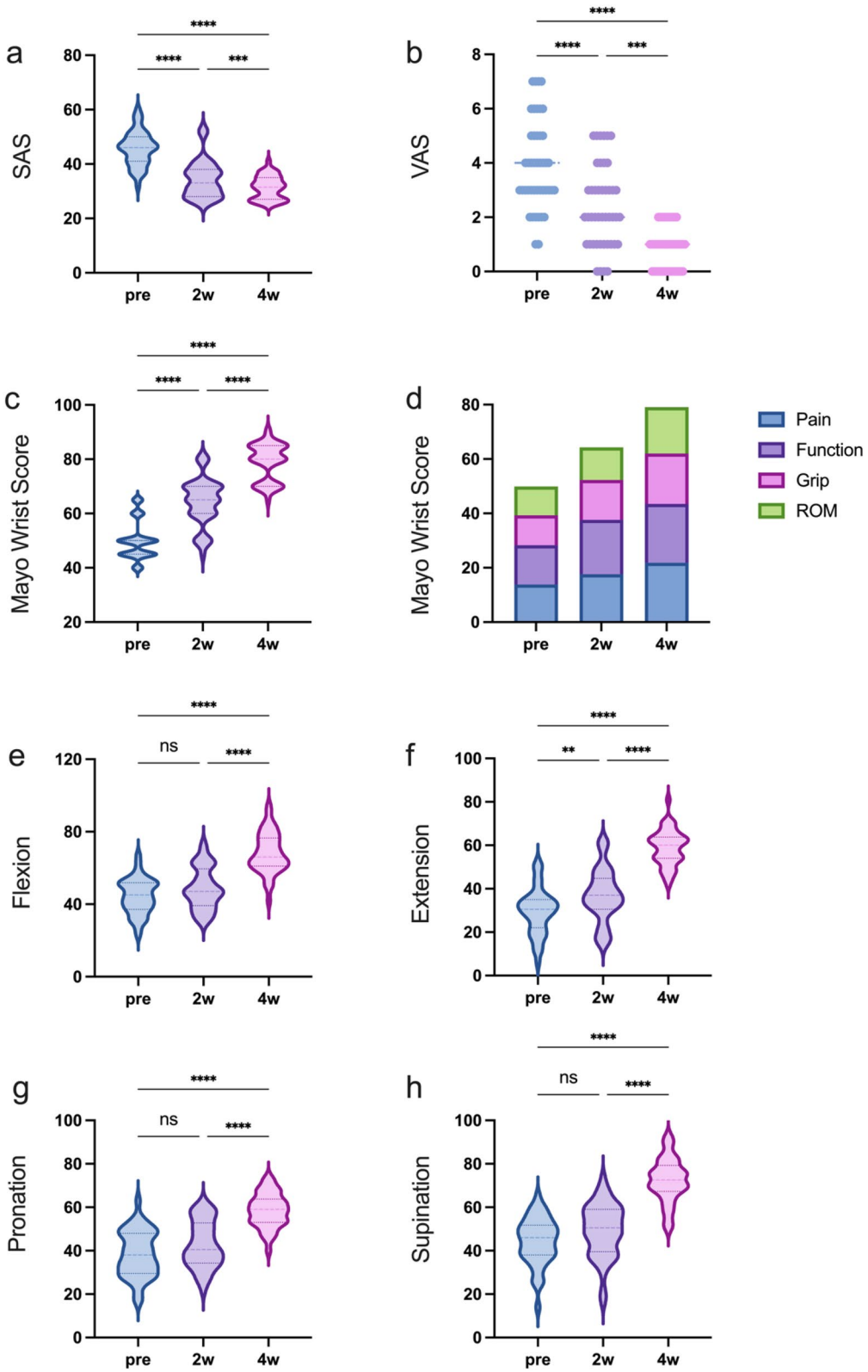

Fig. 1 (See legend on previous page.)

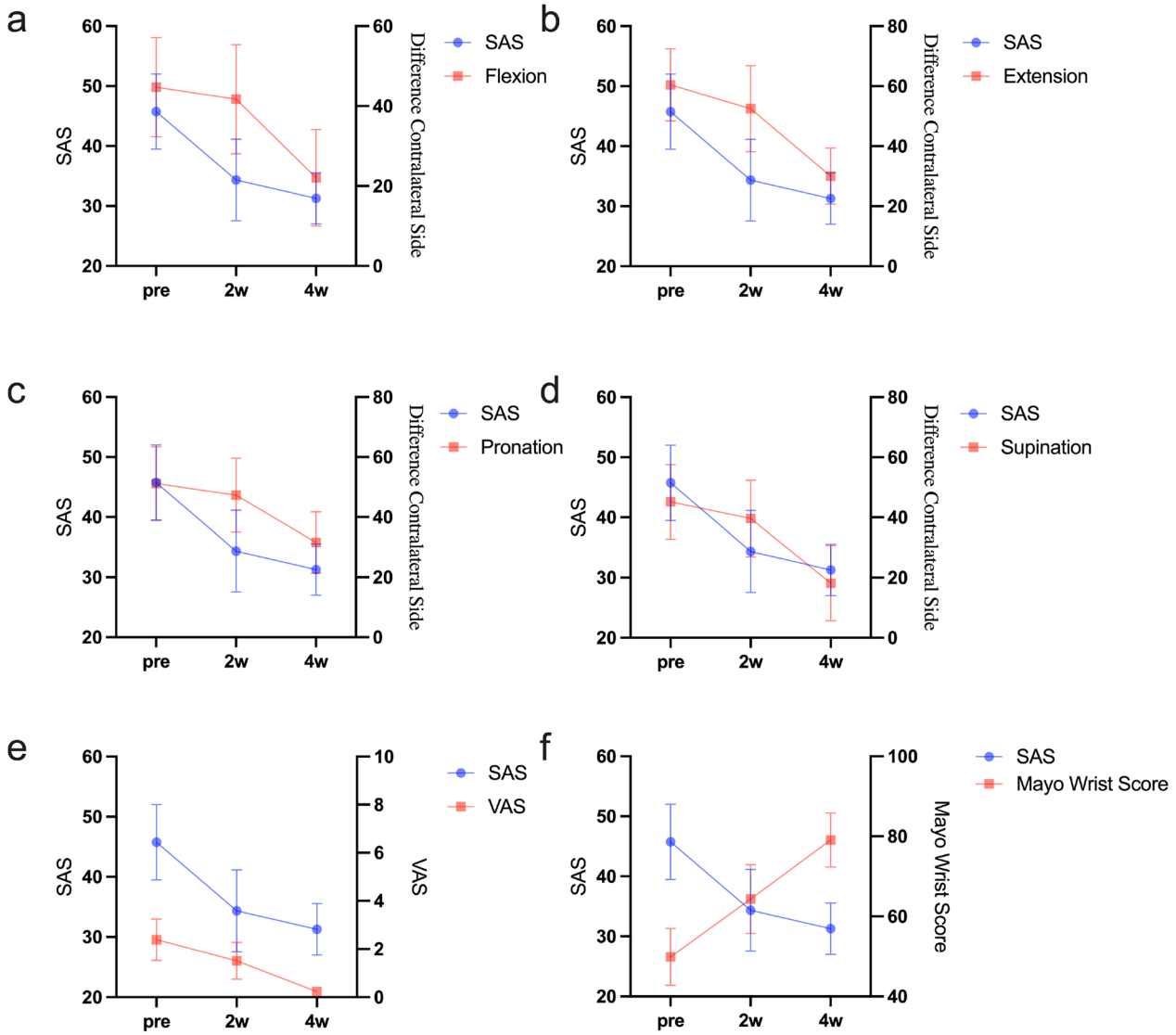

Fig. 2 Correlation between Preoperative and Postoperative Anxiety Scores, Wrist Mobility, and Functional Evaluation Trends. **a** Trends in Self-Rating Anxiety Scale (SAS) scores and changes in flexion of the wrist at preoperative, two weeks postoperative, and four weeks postoperative intervals. **b** Trends in SAS scores and changes in extension at preoperative, two weeks postoperative, and four weeks postoperative intervals. **c** Trends in SAS scores and changes in wrist pronation at preoperative, two weeks postoperative, and four weeks postoperative intervals. **d** Trends in SAS scores and changes in wrist supination at preoperative, two weeks postoperative, and four weeks postoperative intervals. **e** Trends in SAS and Visual Analogue Scale (VAS) scores at preoperative, two weeks postoperative, and four weeks postoperative intervals. **f** Trends in SAS scores and wrist function evaluation results at preoperative, two weeks postoperative, and four weeks postoperative intervals. pre: pre-operation, 2w: 2 weeks post-operation, 4w: 4 weeks post-operation

comprised 187,576 individuals, with 16,380,352 SNPs analyzed (Table 2).

Causal effect of wrist synovitis on anxiety and sensitivity analysis

Wrist synovitis was utilized as the exposure and anxiety disorders as the outcome in our Mendelian randomization analysis. The R package TwoSampleMR, specifically the extract_instruments function, was employed to read exposure factors and screen instrumental variables. The screening criteria included a significance threshold of $p < 1*10^{-5}$ to identify tool variables significantly correlated with the exposure factors; clumping was set to TRUE to remove LD tool variables; with r2 = 0.001 and kb = 10,000. After screening, 123 SNPs related to wrist synovitis were identified, of which 9 SNPs were not significantly associated with anxiety disorders. These 9 SNPs were then used as input data for

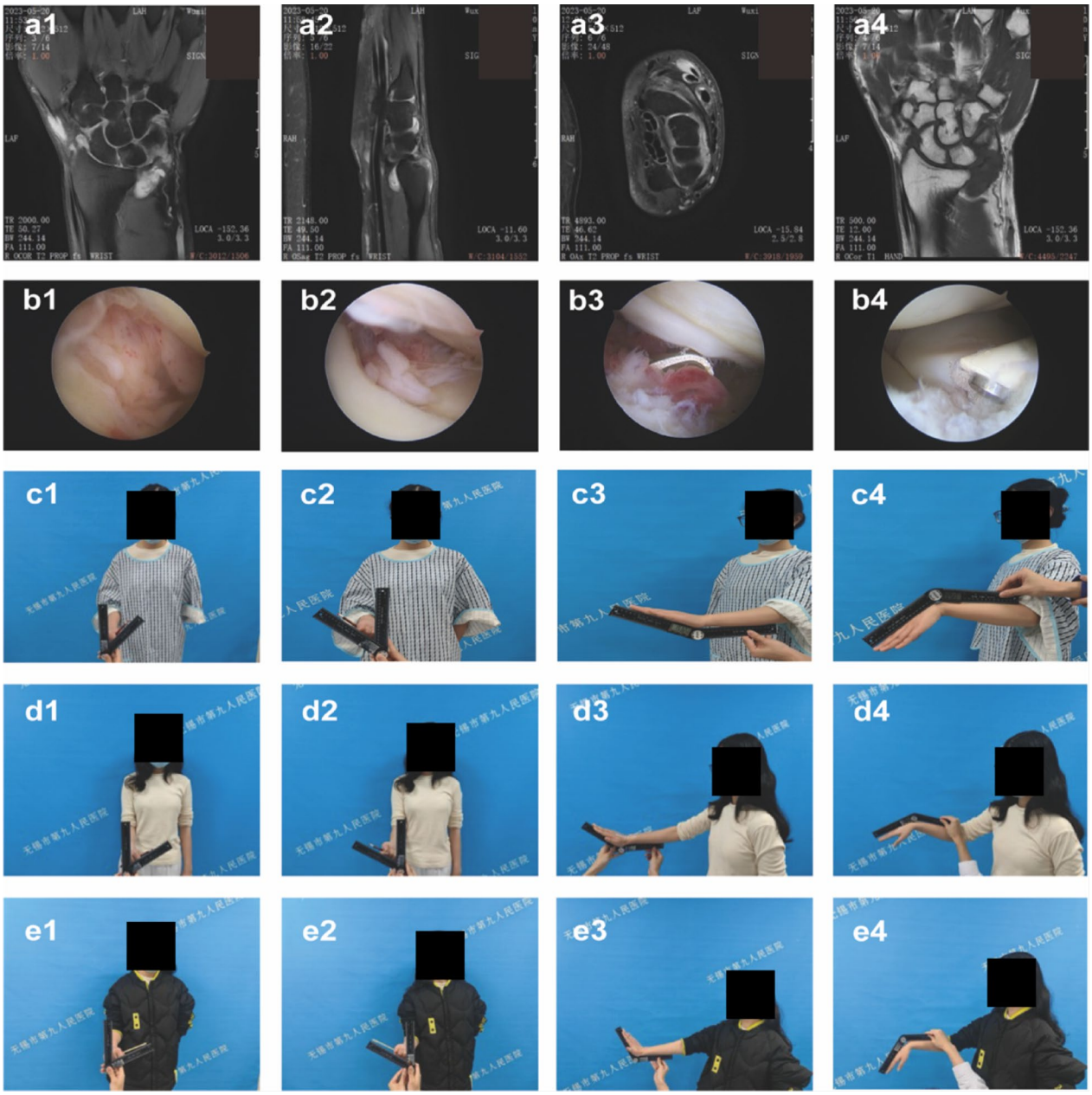

Fig. 3 Preoperative MRI, arthroscopic findings, and follow-up assessments of wrist range of motion in a representative case of wrist synovitis. **a1–4**, Preoperative MRI images of the affected wrist, demonstrating abnormal masses near the distal radioulnar and radiolunate joints. **b1–4**, Arthroscopic images showing inflammatory synovial proliferation and the debridement procedure. **c1–4**, Preoperative range of motion measurements of the affected wrist. **d1–4**, Range of motion measurements at two weeks postoperatively. **e1–4**, Range of motion measurements at four weeks postoperatively

the MR Univariate analysis of wrist synovitis and anxiety disorders.

The harmonise_data function of the TwoSampleMR package was used to standardize effect alleles and effect sizes. We employed five algorithms to conduct the MR analysis: MR Egger, weighted median, IVW, simple mode, and weighted mode. The primary results were derived from the IVW method, as shown in Table 3. The p-values for wrist synovitis were all greater than 0.05, indicating that the effect of wrist synovitis on anxiety was not statistically significant. However, the positive b value of the IVW method suggests that wrist synovitis may act as a risk factor for anxiety disorders.

Table 2 Details of exposures and outcomes

Exposure/outcome	GWAS_id	sample size	number of SNPs
Wrist synovitis	finngen_R10_M13_CHRONSYNOVITISHANDWRIST	167,843	16,380,306
Anxiety disorder	finngen_R10_KRA_PSY_ANXIETY_EXMORE	187,576	16,380,352

Table 3 Sample sensitivity analysis results

Outcome	Exposure	Q	Q_pval	se	pval
Anxiety	Wrist synovitis	4.88	0.77	0.02	0.45

We then employed SNP scatter plots to evaluate the association between the exposure (wrist synovitis) and the outcome (anxiety disorder). The IVW method was primarily utilized. The SNP effect plot demonstrated that wrist synovitis serves as a risk factor for anxiety disorders (Fig. 4A). The forest plot illustrated the predictive validity of each SNP, with those on the left indicating protective factors and those on the right indicating risk factors. Consistent with the IVW method, wrist synovitis emerged as a risk factor for anxiety disorders (Fig. 4B).

The funnel plot displayed a symmetrical distribution of SNPs, suggesting that the results of the Mendelian randomization analysis comply with Mendel's second law of randomization (Fig. 4C). Sensitivity analyses reinforced these findings. The heterogeneity test yielded a Q_pval of

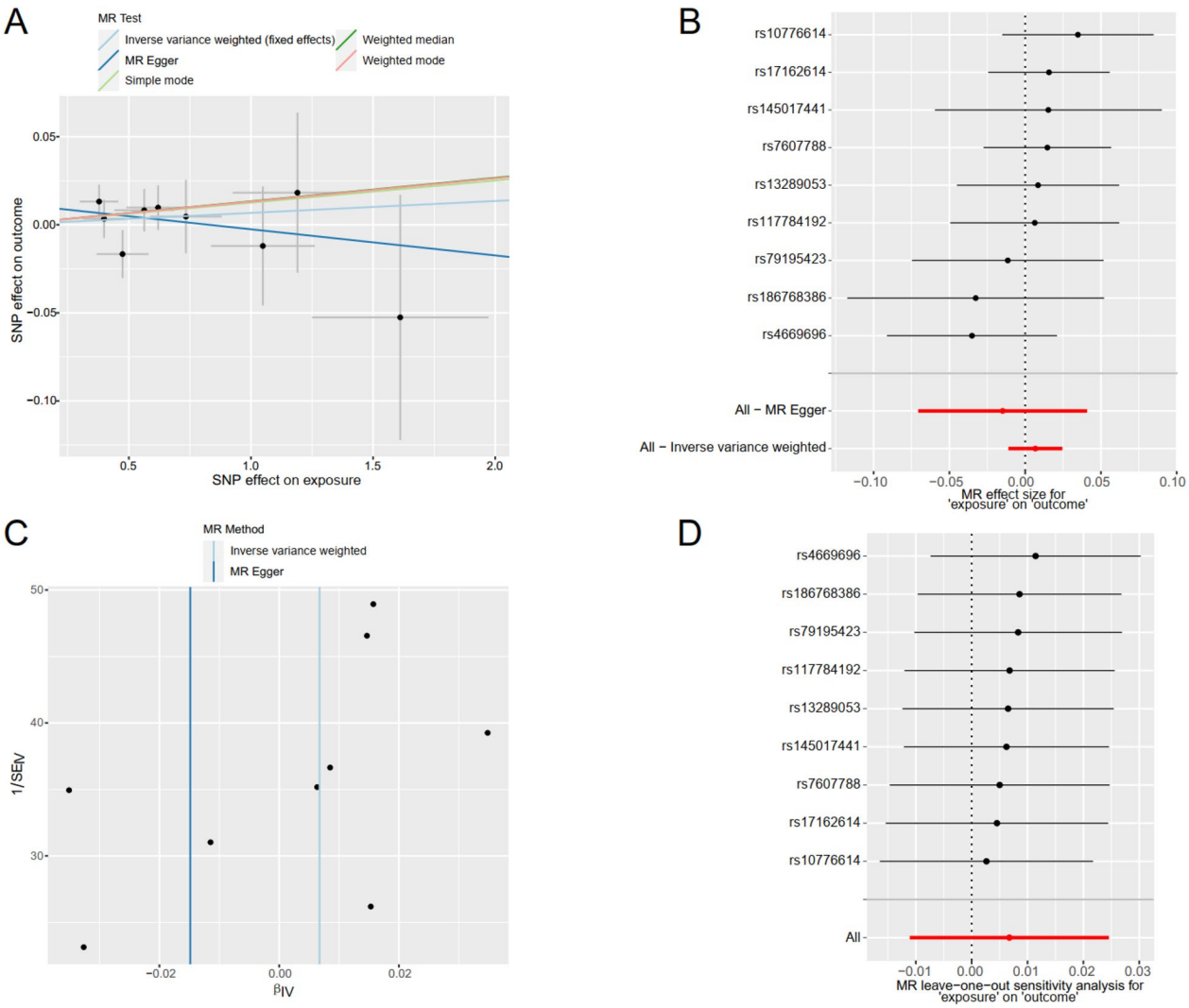

Fig. 4 Mendelian randomization analysis with wrist synovitis as exposure and anxiety as outcome. **A** Scatter diagram of SNPs effect in wrist synovitis, and the colored lines represent the fitting results of different MR algorithms; **B** SNPs forest diagram of wrist synovitis; **C** SNPs funnel diagram of wrist synovitis; **D** Leave-one-out analysis

Table 4 Details of exposures and outcomes

Method	nsnp	b	pval
MR egger	9	−0.014846956	0.617859122
Weighted median	9	0.01333708	0.260608342
Inverse variance weighted (fixed effects)	9	0.00674564	0.458313286
Simple mode	9	0.012553619	0.488338835
Weighted mode	9	0.013182657	0.427120791

Table 5 Details of exposures and outcomes

Method	nsnp	b	pval
MR egger	109	0.609700156	0.310220451
Weighted median	109	0.116745893	0.65648206
Inverse variance weighted (fixed effects)	109	0.051905177	0.772212203
Simple mode	109	0.525700495	0.473376749
Weighted mode	109	0.335793903	0.594306068

0.77 for wrist synovitis, indicating no significant heterogeneity as the value exceeded 0.05 (Table 4). Horizontal pleiotropy testing resulted in a p-value of 0.45 for wrist synovitis, indicating the absence of horizontal pleiotropy (Table 4). In the leave-one-out analysis, all SNPs for wrist synovitis were positioned on the right side of the plot, indicating that the overall error margin remained largely unchanged after the exclusion of individual SNPs, thereby confirming the reliability of the results (Fig. 4D).

Causal effect of anxiety on wrist synovitis and sensitivity analysis

In this analysis, anxiety disorders were considered the exposure, and wrist synovitis was the outcome. The extract instruments function from the R package TwoSampleMR was utilized to identify exposure factors and screen instrumental variables. After screening, 4066 SNPs associated with anxiety disorders were identified, of which 109 SNPs were not significantly associated with wrist synovitis. These 109 SNPs were used as input data for the univariate MR analysis of anxiety disorders and wrist synovitis.

The harmonise data function from TwoSample MR was employed to standardize effect alleles and effect sizes. We used five algorithms to conduct the MR analysis: MR Egger, weighted median, IVW, simple mode, and weighted mode. The primary results were derived from the IVW method, as shown in Table 5. The p-values for wrist synovitis were all greater than 0.05, indicating that the effect of anxiety on wrist synovitis was not statistically significant. However, the positive b value from the IVW analysis suggests that anxiety disorders may act as a risk factor for wrist synovitis.

We further utilized SNP scatter plots to investigate the association between anxiety disorders (exposure) and wrist synovitis (outcome). The IVW method was primarily utilized. The SNP effect plot indicated that anxiety disorders are a risk factor for wrist synovitis (Fig. 5A). The forest plot demonstrated the predictive efficacy of each SNP in linking anxiety disorders to wrist synovitis, with the IVW method affirming that anxiety disorders pose a risk for wrist synovitis (Fig. 5B).

The funnel plot displayed a symmetrical distribution of SNPs, indicating that the results of the MR analysis conform to Mendel's second law of randomization (Fig. 5C). Sensitivity analyses supported these findings, with the heterogeneity test yielding a Q_pval of 0.08 for anxiety disorders, suggesting no significant heterogeneity (Table 6). Additionally, the horizontal pleiotropy test showed a p-value of 0.33, indicating no horizontal pleiotropy (Table 6). The leave-one-out analysis positioned all anxiety-related SNPs on the right side of the plot, showing that the overall error margin remained consistent after the exclusion of individual SNPs, thereby confirming the robustness of our results (Fig. 5D).

Discussion

During clinical diagnosis and treatment, we have frequently observed that patients with wrist joint pain exhibit significant anxiety. Radiographic examinations often reveal abnormal synovial hyperplasia, which is typically the primary cause of wrist swelling and functional limitation. This condition not only triggers persistent chronic pain but also severely impacts the patient's daily life, potentially exacerbating their anxiety. Following wrist arthroscopic synovectomy in our study, patients generally experience significant improvements in wrist pain, swelling, and range of motion, accompanied by substantial alleviation of anxiety symptoms. However, our Mendelian randomization analysis did not identify a significant causal relationship between wrist synovitis and anxiety.

The wrist joint is a critical component of daily functioning, especially in modern contexts where repetitive movements involving devices such as smartphones, keyboards, and mice are prevalent [17, 18]. This high demand for wrist mobility, particularly among individuals engaged in sports or repetitive tasks, predisposes the joint to strain and potential pathological changes such as synovitis. In patients diagnosed with wrist synovitis [19], the resultant pain and functional limitations profoundly disrupt their daily activities, contributing to significant psychological distress, including anxiety. Our study, which involved 44 patients undergoing wrist arthroscopic synovectomy, demonstrated

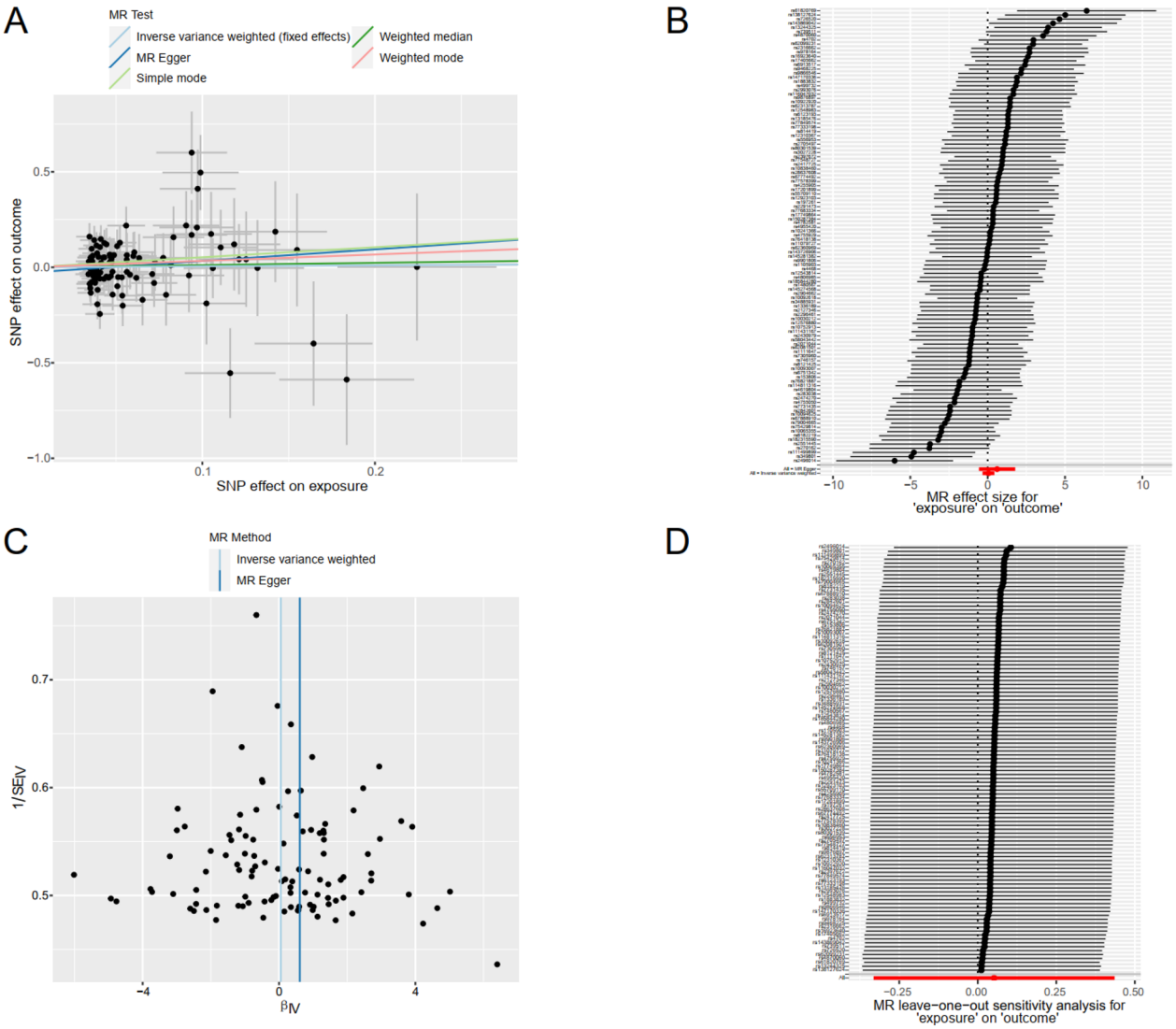

Fig. 5 Mendelian randomization analysis with anxiety as exposure and wrist synovitis as outcome. **A** Scatter diagram of SNPs effect in anxiety, and the colored lines represent the fitting results of different MR algorithms; **B** SNPs forest diagram of anxiety; **C** SNPs funnel diagram of anxiety; **D** Leave-one-out analysis

a notable prevalence of anxiety, as evidenced by elevated SAS scores. Preoperative assessments revealed that these patients commonly exhibited restricted wrist motion, increased VAS and decreased Mayo Wrist Scores, with 12 patients meeting criteria for mild anxiety, characterized by symptoms such as fear and irritability. This observed association between wrist pain and anxiety is consistent with existing literature by Andrew et al. [20] that highlights the intricate link between chronic pain and negative emotional states, including anxiety and depression. Such a relationship suggests a bidirectional interplay where the physical limitations imposed by synovitis exacerbate anxiety symptoms, and anxiety, in turn, may intensify the perception of pain and functional impairment. However, the degree of this correlation can vary depending on the self-assessment tools used and the individual patient's perception of pain. These findings underscore the complex interplay between physical and psychological health in patients with wrist synovitis, highlighting the need for comprehensive management strategies.

Table 6 Sample sensitivity analysis results

Outcome	Exposure	Q	Q_pval	se	pval
Wrist synovitis	Anxiety	128.70	0.08	0.03	0.33

At the two-week follow-up after wrist arthroscopic synovectomy, it was observed that while two patients continued to experience mild anxiety, the majority demonstrated a significant reduction in anxiety levels, as reflected by notable decreases in SAS. Extension activity and VAS showed marked improvement compared to preoperative levels, and although there were slight gains in flexion and rotation, these changes were not statistically significant at this early stage. By the four-week follow-up, anxiety symptoms had largely resolved, with significant reductions observed in both VAS and SAS from their preoperative and two-week postoperative levels. During this period, wrist function steadily improved, with all range of motion metrics and the Mayo Wrist Score showing significant gains compared to preoperative and two-week postoperative assessments. These findings align with Nixon et al.'s [21] observation that preoperative anxiety levels can be predictive of postoperative recovery outcomes, and with Meade et al.'s [22] summary that pain, functional limitations, and physical disability are closely associated with anxiety. In our study, the continuous decrease in SAS scores as wrist function and pain improved suggests a parallel relationship between the physical recovery of wrist function and the alleviation of anxiety symptoms. Research by Abramkin et al. [23] has demonstrated that anxiety and depression can significantly exacerbate the activity limitations experienced by patients with rheumatoid arthritis. Furthermore, effective psychotropic drug treatment has been shown to enhance the functional capabilities of these patients, thereby underscoring the interrelationship between inflammatory diseases and mental health disorders. This finding indicates that improvements in physical symptoms, such as reduced pain and increased mobility, can directly contribute to the reduction of anxiety, and vice versa. The bidirectional interplay between physical and psychological health in patients with wrist synovitis underscores the importance of a holistic approach to treatment, where addressing physical symptoms may simultaneously facilitate psychological recovery, and managing anxiety could potentially enhance physical rehabilitation outcomes.

Arthroscopic synovectomy alleviates pain and anxiety in rheumatoid arthritis and likely other inflammatory arthropathies through interconnected biological mechanisms. By removing proliferative synovial tissue, it interrupts the release of proinflammatory mediators (e.g., TNF-α, IL-1β, prostaglandins) fueling both local and systemic inflammation, thereby reducing nociceptor stimulation and chronic pain. Lower peripheral inflammation may attenuate neuroinflammation, microglial activation, and disturbances in key brain regions regulating pain and emotion, easing anxiety. Restoring inflammatory balance also helps normalize hypothalamic–pituitary–adrenal axis activity, decreasing cortisol levels and mitigating their adverse effects on mood. As a minimally invasive technique, arthroscopic synovectomy preserves joint function, accelerates recovery, and lessens psychological stress arising from mobility limitations. In sum, this procedure simultaneously targets inflammation, neuroinflammation, and psychological burden, enhancing both physical comfort and mental well-being [9, 10, 24].

Wrist synovitis, a chronic inflammatory condition often associated with autoimmune diseases such as rheumatoid arthritis, presents with symptoms including swelling, restricted movement, and persistent pain. Chronic inflammation, as increasingly recognized in existing research, plays a significant role in the pathophysiology of psychiatric disorders, including anxiety. For instance, Dang et al. [25] demonstrated that anti-inflammatory treatment with Edaravone alleviated anxiety and depression in animal models, highlighting the role of ferroptosis mediated by GPX4 in this process. Similarly, Cen et al. [26] reported that metabolic syndrome, through the elevation of chronic inflammation, increases the risk of anxiety, while Luca et al. [27] identified anxiety as a crucial factor in the gut-brain axis, particularly in Crohn's disease, where it is closely linked to disease progression. These evidence showing that systemic inflammation can exacerbate neuropsychiatric symptoms. Furthermore, excessive inflammatory responses are believed to disrupt synaptic and non-synaptic transmission in the basolateral amygdala [28], a mechanism implicated in the development of anxiety. Recent studies suggest that inflammatory synovitis, as a systemic immune-mediated condition, is associated with a range of neuropsychiatric comorbidities, including depression, schizophrenia, and anxiety, and may increase the risk of neurodegenerative diseases [29]. The interaction between immune-inflammatory processes and the central nervous system likely underpins the bidirectional relationship between synovitis and psychiatric disorders. Immune cells and their secreted factors can modulate both the peripheral and central nervous systems, potentially driving the interaction between immune-inflammatory synovitis and neuropsychiatric comorbidities. This complex interplay suggests that interventions targeting immune-inflammatory pathways may offer a novel approach to breaking the vicious cycle of chronic inflammation and psychological distress, highlighting the need for a holistic treatment strategy that addresses both the physical and psychological aspects of these conditions.

To further explore the relationship between wrist synovitis and anxiety, this study employed a two-sample MR approach, marking the first instance of such an analysis in this context. MR analysis offers a robust method to infer causal relationships by using genetic variants as

instrumental variables, thereby reducing confounding and reverse causation inherent in observational studies. Our analysis revealed that wrist synovitis may act as a risk factor for anxiety disorders, and conversely, anxiety disorders may increase the risk of developing wrist synovitis. However, despite these associations, we did not find statistically significant evidence of a direct causal relationship between anxiety disorder and wrist synovitis, a finding that diverges from earlier observational studies suggesting a more direct link. The absence of a significant causal relationship in our MR analysis raises important considerations for interpreting negative results in the context of clinical research. Previous studies across various medical fields have encountered similar challenges when employing MR to investigate complex traits and disease relationships. These discrepancies often stem from limitations such as small sample sizes, the genetic architecture of the traits involved, or the presence of unaccounted confounding factors. In our study, the relatively small sample size may have limited the power to detect subtle genetic effects, and residual confounding by lifestyle factors such as smoking and alcohol consumption, which are known to influence both inflammation and mental health, cannot be entirely ruled out. Moreover, MR analyses are inherently dependent on the quality and availability of GWAS data for both the exposure and outcome of interest. In cases where the genetic instruments used are weak or not sufficiently specific to the trait, the resulting estimates may be biased or lack precision. Additionally, pleiotropy, where genetic variants influence multiple traits, can introduce further complexity in interpreting MR results. In the context of our study, while we employed rigorous criteria to select instrumental variables and conducted sensitivity analyses to mitigate these issues, the potential for pleiotropic effects influencing our findings cannot be completely excluded.

Limitation

This study's relatively small sample size represents a substantial limitation, potentially diminishing the statistical robustness and external validity of the conclusions and restricting their applicability to broader populations or diverse clinical settings. Certainly, this limitation introduces another issue, namely the inability to perform subgroup analyses, such as those based on different occupations, given that various professional groups evidently experience distinct levels of social pressure. To address these shortcomings, future investigations should strive to enroll larger and more heterogeneous cohorts. Additionally, pooling data from multiple centers or conducting meta-analyses of similar studies may yield a more comprehensive evidence base, mitigating the limitations inherent in smaller samples.

This study, notably, was not designed as a randomized controlled trial (RCT), and the absence of a control group limits our ability to establish a definitive causal relationship between the surgical intervention and the observed reduction in anxiety. Consequently, our findings should be regarded as speculative rather than conclusive. Reverse RCTs warrant further investigation, given the potential for anxiety to influence synovitis progression through immune and inflammatory pathways. Additionally, the well-documented placebo effect associated with surgical procedures, reported to range from 40 to 70%, could plausibly account for the entirety of the observed improvements. This raises the possibility that symptom relief may not be solely attributable to the surgical technique itself [30–32].

Another limitation pertains to the short-term follow-up period, restricted to assessments at two and four weeks postoperatively. While early improvements in symptoms and anxiety were noted, the psychological impact of the intervention may extend well beyond this brief interval. Without longer-term follow-up data, it remains uncertain whether the observed benefits persist for months or years, whether anxiety recurs, or whether new psychological issues emerge over time. Extending the follow-up period to at least six months or a year would allow for a more thorough evaluation of the sustained effects on overall health and quality of life, thereby informing more effective long-term management strategies.

Our investigation also did not compare arthroscopic synovectomy with conventional open surgery, preventing us from ascertaining the relative merits of each approach. While arthroscopy may offer advantages related to minimal invasiveness and faster recovery, open surgery could be beneficial for more complex or severe cases. Moreover, long-term psychological outcomes associated with each technique remain unclear. Future studies should undertake direct comparisons in terms of symptom relief, anxiety reduction, postoperative complications, and long-term prognosis to provide clinicians with a more comprehensive basis for tailored therapeutic decision-making.

Finally, although we referenced basic scientific findings to suggest possible biological mechanisms linking inflammation and anxiety, we did not perform direct experimental validation of these pathways in patients with wrist synovitis. Without such confirmation, our understanding of these mechanisms' clinical applicability remains limited. Future research should incorporate more in-depth experimental evaluations—such as biomarker profiling or gene expression studies—to clarify the clinical significance of these putative mechanisms and to lay a more rigorous theoretical foundation for targeted therapeutic interventions.

Conclusion

Arthroscopic synovectomy for wrist synovitis may alleviate anxiety symptoms and may improve wrist function and pain relief. Although an association between wrist synovitis and anxiety is evident, the causal link remains inconclusive. These findings highlight the necessity of a comprehensive treatment approach that addresses both physical and psychological aspects to optimize patient outcomes. Further research with larger cohorts and extended follow-up periods is essential to substantiate these observations.

Abbreviations

MR	Mendelian randomization
VAS	Visual analog scale
SAS	Self-rating anxiety scale
GWAS	Genome-wide association studies
LD	Linkage disequilibrium
IVW	Inverse variance weighting
WM	Weighted median

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Author contributions

Xunhao Wang: Writing—original draft, Validation, Supervision, Project administration, Formal analysis, Data curation, Conceptualization. Linyi Zhu: Writing—original draft, Formal analysis, Data curation. Jingyi Mi: Writing—review & editing, Validation, Formal analysis, Data curation, Funding acquisition. Fei Xiong: Writing—review & editing, Validation, Supervision, Methodology, Conceptualization, Funding acquisition.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study is approved by the WuXi 9th people's hospital (WuXi orthopaedics hospital) Medical Ethical Committee on August sixth, 2023. The reference number is: KS2023081.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare no competing interests.

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