



# Effect of hyperuricemia on functional outcomes and complications in patients with elbow stiffness after open arthrolysis combined with hinged external fixation: a retrospective study

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**Background:** Hyperuricemia is considered a risk factor for increased postoperative complications and adverse functional outcomes in a variety of orthopedic surgeries. The purpose of this retrospective study was to investigate the clinical efficacy of patients with different uric acid levels after elbow arthrolysis.

**Methods:** The study included 131 patients with post-traumatic elbow stiffness who underwent arthrolysis between March 2014 and March 2016. All patients were divided into 4 groups based on the preoperative serum level of uric acid (UA). The quartile method was used for grouping patients, including 33 in Q1 (UA <293 μmol/L), 34 in Q2 (293–348 μmol/L), 32 in Q3 (348–441 μmol/L), and 32 in Q4 (441–710 μmol/L). At baseline and each time point of follow-up, functional performance, Mayo Elbow Performance Score, visual analog scale for pain, and complications were evaluated.

**Results:** Preoperative data were not significantly different among the 4 groups (Q1, Q2, Q3, and Q4). At the final follow-up, the following data showed significant differences among the 4 groups: extension ( $P = .031$ ), flexion ( $P = .008$ ), range of motion ( $P = .003$ ), Mayo Elbow Performance Score ( $P = .011$ ), and visual analog scale ( $P = .032$ ). Interestingly, patients in the Q4 group had the poorest clinical outcomes. However, no significant differences were found among the 4 groups in new onset or exacerbation of nerve symptoms ( $P = .919$ ), reduced muscle strength ( $P = .536$ ), instability ( $P = .567$ ), or infection ( $P = .374$ ) at the last follow-up.

**Conclusion:** This study confirms that in patients with post-traumatic elbow stiffness, abnormal serum uric acid metabolism was a risk factor for poor performance and postoperative pain after arthrolysis. Therefore, detecting the preoperative serum uric acid levels of the patients would be helpful for evaluating the postoperative outcomes.

**Level of evidence:** Level III; Retrospective Cohort Comparison; Treatment Study

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**Keywords:** Post-traumatic elbow stiffness; open arthrolysis; gout; hyperuricemia; serum uric acid level; VAS (visual analog scale); clinical outcomes; MEPS (Mayo Elbow Performance Score)

Institutional review board approval was not required for this retrospective study.

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Currently, hyperuricemia has become a major public health concern worldwide. In 2007-2008, the National Health and Nutrition Examination Survey indicated that the overall prevalence of hyperuricemia (HUA) in the general population of the United States was 21.4%. Compared with the results from 1988 to 1994 by National Health and Nutrition Examination Survey III, there was an increase of 3.2%.<sup>36</sup> The prevalence of hyperuricemia in adults in China was 8.4% according to the data from the Chinese Chronic Kidney Disease Epidemiology Collaborative Group. It is estimated that the number of Chinese adult patients with hyperuricemia has reached 93 million.<sup>11</sup> Hyperuricemia is characterized by a progressive increase in serum uric acid levels. Gout is a type of inflammatory arthritis that might be caused by hyperuricemia. Previous studies have shown that hyperuricemia is associated with an increased risk of hypertension, cardiovascular diseases, diabetes, chronic kidney disease, fracture, arthritis, and postoperative pain.<sup>6,13,23,26,27,37</sup> In recent decades, studies have paid increasing attention to hyperuricemia and its effects on musculoskeletal diseases.<sup>10,17,21,24,29,32</sup> Paik et al<sup>24</sup> reported that a history of gout is associated with a modestly increased risk of hip fracture in women. Similarly, Tzeng et al<sup>29</sup> showed that gout history is considered a risk factor for fractures, particularly in female patients and fracture sites located at the spine or upper/lower limbs.

Elbow stiffness is one of the most common complications of the elbow and is characterized by a reduction in active or passive range of motion (ROM).<sup>5</sup> It is usually caused by trauma, craniocerebral trauma, and rheumatoid arthritis, with an incidence from 3% to 20%.<sup>9</sup> Because of mobility limitations, elbow function may be greatly affected. Arthrolysis is recommended when conservative therapy does not have an obvious effect.<sup>2,28</sup> Open arthrolysis is the most popular and effective treatment, with a low rate of complications.<sup>1,18,22,25</sup>

Many studies have shown that hyperuricemia is a risk factor for increased postoperative complications and adverse functional outcomes in a variety of orthopedic surgeries. However, there has been no study focusing on the effect of different uric acid levels on the outcomes of arthrolysis for post-traumatic elbow stiffness. Therefore, we hypothesized that hyperuricemia would have a similar negative effect on outcomes after elbow arthrolysis. The purpose of this retrospective study was to investigate the clinical efficacy of patients with different uric acid levels after elbow arthrolysis.

## Materials and methods

### Patients

This study was a retrospective case-control study of patients with elbow stiffness who received open arthrolysis at our institution between December 2013 and July 2016. All patients' medical

records were recorded in the electronic database through a uniform format. The inclusion criteria were (1) ROM less than 100°, (2) skeletally mature, (3) treatment with open arthrolysis, (4) standardized rehabilitation training, (5) follow-up time of at least 3 years, and (6) trauma as the factor of the disease. The exclusion criteria were (1) prior elbow release, (2) central nervous system injuries, (3) severe burn, (4) combined rheumatoid arthritis, (5) severe articular surface damage requiring total elbow arthroplasty, (6) nonunion or malunion of the elbow, (7) postmenopausal women, and (8) unwillingness to participate in the study. During the study, we identified 182 patients with elbow stiffness. Among them, 141 patients met the inclusion and exclusion criteria. After screening the patients' medical records, we excluded 7 individuals because of incomplete records. Three of 134 patients were excluded because of loss to follow-up. Finally, 131 patients were included in the study. They were divided into 4 groups based on the preoperative serum level of uric acid. The quartile method was used for grouping patients, including 33 in Q1 (UA <293 μmol/L), 34 in Q2 (293-348 μmol/L), 32 in Q3 (348-441 μmol/L), and 32 in Q4 (441-710 μmol/L). Informed consent was provided by all study participants. General demographic characteristics, including sex, age, body mass index, dominant limb, tobacco use, diabetes mellitus, and hypertension, were recorded. The following baseline clinical features were also recorded: follow-up time, disease duration, original injury types, history of treatment, and elbow function. Original injury types included simple elbow dislocation, distal humeral fracture, radial head fracture, olecranon fracture, coronoid fracture, Monteggia fracture, terrible-triad injury, and multiple fractures. Elbow function was evaluated by flexion, extension, supination, pronation, ROM (flexion-extension), and forearm rotational ROM (supination-pronation). The Mayo Elbow Performance Score (MEPS)<sup>34</sup> is a widely used elbow functional evaluation system assessing pain, ROM, stability, and activities of daily living. This questionnaire has a total score of 100. A higher score indicates better elbow function. The visual analog scale (VAS) for pain is a widely used tool for patients to measure pain intensity along a 10-cm line, ranging from no pain (left end) to worst pain (right end). At the final postoperative follow-up, complications, including new onset or exacerbation of nerve symptoms, reduced muscle strength, elbow instability, and infection, were evaluated. The Dellon classification was used to evaluate ulnar nerve symptoms. All data were recorded by 3 independent observers. If there was any discrepancy regarding the medical data, the senior physician reviewed the data and made the final decision.

### Surgical technique

All patients underwent open elbow arthrolysis combined with hinged external fixation.<sup>3</sup> They underwent surgery with a sterile tourniquet under general anesthesia or brachial plexus block. All operations were performed by the same surgeon. In general, patients underwent arthrolysis via a combination of the lateral column approach and medial approach posterior to the medial epicondyle. However, when the patient had the posterior median incision, we could select the surgical incision at the original incision. Through a lateral approach, the annular ligament and radiohumeral joint can be fully exposed. The forearm rotation function will be improved by releasing the above structure. At the same time, the use of the lateral approach could effectively

remove the anterior joint capsule and clean the coronoid fossa. Through a medial approach, we can effectively preposition the ulnar nerve to prevent compression of the nerve at the elbow. In addition, the posterior band of the medial collateral ligament was released, and the posterior capsule, heterotopic ossification, or scar tissue was removed. During the operation, the anterior part of the medial collateral ligament and ulnar bundle of the lateral collateral ligament were preserved for elbow stability. The same surgical procedure was equally applicable to patients with posterior median incisions. Repair of the collateral ligament with anchor to maintain the stability of the elbow was performed.<sup>31</sup> Negative pressure drainage tubes were placed in the joint cavity. Subsequently, the skin was sutured to complete the surgery. Finally, hinged external fixation was used to promote postoperative rehabilitation and maintain elbow stability.

## Postoperative treatment

Rehabilitation began on the first day after surgery. Patients were orally administered celecoxib twice daily within 6 weeks after surgery to prevent the occurrence of heterotopic ossification. In addition, they were asked to perform 30 cycles of flexion and extension exercises on the first day. A flexion and an extension were defined as a circle. Daily functional exercise was required to be completed 3 times or more, which is active-assisted passive elbow motion. Each day after the first day, 30 cycles per day were added until 300 cycles per day were reached. Starting 1 week after surgery, the patients were instructed to perform rotation exercises for 30 minutes twice a day under protection. Hinged external fixation was removed at 6 weeks postoperatively as an outpatient procedure. This stage of exercise lasted until 3 months after surgery. After this, the patients were encouraged to start step-by-step strength training under supervision. The initial strength was recommended to be set to 2 kg. The patient's rehabilitation was followed up regularly at 6 weeks, 3 months, 6 months, and 1 year after surgery. After this, there was annual follow-up.

## Statistical analysis

Continuous variables that were normally distributed were expressed as the mean  $\pm$  standard deviation; otherwise, the median and interquartile range were used. One-way analysis of variance was used to compare continuous data, whereas the Pearson  $\chi^2$  test or Fisher exact test was used to compare qualitative data. The difference was considered statistically significant when the *P* value was less than .05. Statistical analysis was performed with IBM SPSS software (version 23.0; IBM, Armonk, NY, USA).

## Results

Preoperative data were not significantly different among the 4 groups (Q1, Q2, Q3, and Q4) (Tables I-III). At the final follow-up, the following data showed significant differences among the 4 groups: extension (*P* = .031), flexion (*P* = .008), ROM (*P* = .003), MEPS (*P* = .011), and VAS (*P* = .032). Interestingly, we also found that extension in Q4 ( $17 \pm 16$ ) was higher than that in Q1 ( $9 \pm 18$ ,

*P* = .014), Q2 ( $9 \pm 9$ , *P* = .009), and Q3 ( $10 \pm 9$ , *P* = .028). Similarly, the flexion in Q1 ( $128 \pm 11$ , *P* < .001) and Q2 ( $127 \pm 11$ , *P* = .008) was higher than that in Q4 ( $120 \pm 7$ ). However, no difference (*P* = .059) was found between Q3 and Q4. Therefore, the ROM (flexion-extension) in Q4 ( $103 \pm 20$ ) was lower than those in Q1 ( $119 \pm 23$ , *P* = .001), Q2 ( $118 \pm 18$ , *P* = .002), and Q3 ( $103 \pm 20$ , *P* = .014). In addition, the MEPS was significantly lower in Q4 ( $86 \pm 10$ ) than in Q1 ( $94 \pm 10$ , *P* < .001), Q2 ( $91 \pm 10$ , *P* = .02), and Q3 ( $91 \pm 10$ , *P* = .028). Moreover, the VAS pain score in the Q4 group was significantly higher than that in the other 3 groups (*P* = .032) (Table IV).

Furthermore, nerve symptoms, reduced muscle strength, instability, and infection were found at the last follow-up (Table V). None of the patients required reoperation at the last follow-up. No significant differences were found among the 4 groups in new onset or exacerbation of nerve symptoms (*P* = .919), reduced muscle strength (*P* = .536), instability (*P* = .567), or infection (*P* = .374) at the last follow-up.

## Discussion

Hyperuricemia is one of the most important metabolic diseases related to the imbalance of purine metabolism, presented as the elevation of serum uric acid levels. Reduced uric acid excretion and/or increased production are the main causes of primary hyperuricemia. According to Liu et al,<sup>19</sup> the prevalence of hyperuricemia was 8.4%, which means that there were approximately 92.9 million adults with hyperuricemia in China in 2009 and 2010. Hyperuricemia was reported to be an independent risk factor for death, cerebrovascular disease (CVD), and diabetes.<sup>12,14,33</sup> In recent years, multiple studies have focused on the relationship between serum uric acid levels and musculoskeletal diseases.<sup>27</sup> Restoring elbow function and resolving neurological symptoms are the main goals of elbow arthrolysis. Recent studies have indicated that elbow arthrolysis has shown satisfactory results in the treatment of post-traumatic elbow stiffness.<sup>1,18,25</sup> To the best of our knowledge, this is the first report to discuss abnormal uric acid metabolism as a detriment to the clinical outcome of open arthritis in patients with post-traumatic elbow stiffness. This study shows an intrinsic connection between altered serum uric acid metabolism and clinical outcomes after open arthrolysis in patients with post-traumatic elbow stiffness. Considering that hyperuricemia is a metabolic disease, we excluded the effect of comorbidities on the study results by analyzing the distribution of patients with some common comorbidities in each group. Clinical efficacy was evaluated by ROM, MEPS, VAS pain score, and complications.

Before the operation, each group of patients did not show significant differences in baseline indicators such as ROM, forearm rotational ROM, MEPS, and VAS pain scores. We found that initially, with an upregulation in serum uric acid levels, there was not much difference in the elbow ROM of patients in each group (Q1-Q3). However,

**Table I** Demographic and clinical characteristics of patients

Characteristic/SUA (min-max)	Q1 (0-293)	Q2 (293.5-348)	Q3 (348.5-441)	Q4 (441.5-710)	P value
No. of patients	33	34	32	32	
Male	23 (70)	28 (82)	26 (81)	29 (91)	.196
Age (yr)	38 ± 11	36 ± 10	31 ± 11	35 ± 12	.084
BMI (kg/m <sup>2</sup> )	22 ± 3	24 ± 3	24 ± 3	24 ± 3	.179
Dominant limb	18 (55)	21 (62)	18 (56)	24 (75)	.319
Disease duration (mo)	16 ± 9	15 ± 10	20 ± 13	17 ± 9	.301
Previous elbow ORIF	27 (82)	28 (82)	30 (94)	28 (88)	.468
Tobacco use	5 (15)	11 (32)	9 (28)	10 (31)	.366
Follow-up time (mo)	46 ± 7	48 ± 7	47 ± 8	46 ± 9	.621
Immobilization time (mo)	3 ± 3	3 ± 2	2 ± 3	3 ± 3	.4
Diabetes	2 (6)	3 (9)	2 (6)	1 (3)	.817
Hypertension	1 (3)	0 (0)	1 (3)	1 (3)	.783

SUA, serum uric acid; BMI, body mass index; ORIF, open reduction and internal fixation.

Categorical variables are presented as numbers (percentages). Continuous variables are presented as the mean ± standard deviation.

**Table II** Comparison of original injury types

Characteristic	Q1 (0-293)	Q2 (293.5-348)	Q3 (348.5-441)	Q4 (441.5-710)
No. of patients	33	34	32	32
Simple elbow dislocation	7	3	2	4
Distal humeral fracture	9	16	6	13
Radial head fracture	6	1	4	5
Olecranon fracture	5	8	7	5
Coronoid fracture	0	1	0	2
Monteggia fracture	2	2	2	0
Terrible-triad injury	3	3	4	2
Multiple fracture	1	0	7	1

Data are presented as the number of cases.

**Table III** Clinical evaluation of patients: preoperative data

Characteristic	Q1 (0-293)	Q2 (293.5-348)	Q3 (348.5-441)	Q4 (441.5-710)	P value
Extension (°)	41 ± 21	40 ± 22	39 ± 15	38 ± 15	.92
Flexion (°)	79 ± 22	73 ± 26	75 ± 18	85 ± 20	.119
ROM (°)	38 ± 32	32 ± 26	35 ± 21	47 ± 24	.12
Pronation (°)	49 ± 32	44 ± 35	45 ± 30	45 ± 28	.927
Supination (°)	65 ± 33	70 ± 35	63 ± 32	57 ± 32	.5
FRR (°)	114 ± 61	114 ± 55	108 ± 58	102 ± 57	.828
MEPS (points)	70 ± 16	67 ± 12	71 ± 11	68 ± 11	.726
VAS (points)	1 (0, 3)	0 (0, 3)	0 (0, 3)	2 (0, 3)	.577

ROM, range of motion; FRR, forearm rotational range of motion; MEPS, Mayo Elbow Performance Score; VAS, visual analog scale; P<sub>25</sub>, 25th percentile; P<sub>75</sub>, 75th percentile.

Data are presented as the mean ± standard deviation or the median (P<sub>25</sub>, P<sub>75</sub>).

when serum uric acid levels reached a certain level (Q4), the patient's elbow ROM showed a significant decrease at the last follow-up after elbow arthrolysis. Despite this, all 4 groups of patients had significant progress in elbow ROM after surgery.

The total trend of our study suggests that elbow arthrolysis significantly improved elbow function among all

4 groups. Elevated serum uric acid levels cause sodium urate to deposit from supersaturated extracellular fluids in joints. This series of changes will cause acute arthritis. The European League Against Rheumatism notes that gout can cause joint swelling, pain, and activity dysfunction.<sup>8,30</sup> The American College of Rheumatology also mentioned the adverse effect of gout on joint function.<sup>15,16</sup> Similarly, the



**Table IV** Clinical evaluation of patients: postoperative data

Characteristic	Results				P value	Between group comparison (P value)				
	Results					Between group comparison (P value)				
	Q1 (0-293)	Q2 (293.5-348)	Q3 (348.5-441)	Q4 (441.5-710)		Q1 vs. Q2	Q1 vs. Q3	Q1 vs. Q4	Q2 vs. Q3	Q2 vs. Q4
Extension (°)	9 ± 18	9 ± 9	10 ± 9	17 ± 16	.031	.804	.014	.71	.009	.028
Flexion (°)	128 ± 11	127 ± 11	125 ± 11	120 ± 7	.008	.165	<.001	.447	.008	.059
ROM (°)	119 ± 23	118 ± 18	115 ± 17	103 ± 20	.003	.386	<.001	.524	.002	.014
Pronation (°)	68 ± 17	62 ± 27	63 ± 21	63 ± 24	.698	-	-	-	-	-
Supination (°)	79 ± 22	81 ± 18	76 ± 24	70 ± 30	.243	-	-	-	-	-
FRR (°)	147 ± 39	143 ± 40	139 ± 44	133 ± 52	.609	-	-	-	-	-
MEPS (points)	94 ± 10	91 ± 10	91 ± 10	86 ± 10	.011	.3	<.001	.928	.02	.028
VAS (points)	0 (0, 1)	0 (0, 2)	0 (0, 2)	2 (0, 3)	.032	-	-	-	-	-

ROM, range of motion; FRR, forearm rotational range of motion; MEPS, Mayo Elbow Performance Score; VAS, visual analog scale; P<sub>25</sub>, 25th percentile; P<sub>75</sub>, 75th percentile. Data are presented as the mean ± standard deviation or the median (P<sub>25</sub>, P<sub>75</sub>).

Q4 group had the lowest MEPS among the 4 groups. However, there were no significant differences among the other 3 groups. In addition, the results showed that the Q1 group (15%) had a notably higher percentage of patients with excellent scores than the Q2 group (3%), Q3 group (6%), and Q4 group (3%). Therefore, the patient's expectation of postoperative improvement of elbow function should be moderately reduced when communicating with the patient who has higher serum uric acid levels before surgery. This type of patient requires more comprehensive preoperative preparation and preoperative examination to achieve a relatively better postoperative outcome. Severe pain is a typical manifestation of hyperuricemia and gout.<sup>8,15,16,30</sup> Therefore, we focused on the VAS score after surgery. A more meaningful discovery is that we found that patients in the Q4 group had significantly higher VAS scores than the other 3 groups after elbow arthrolysis. However, there was no significant difference between the other 3 groups. This finding means that patients in the Q4 group had the most obvious postoperative pain compared with the other 3 groups. It also indicated that as the serum uric acid level gradually increases and reaches a certain critical value (Q4 level), patients begin to show significant postoperative pain. This will seriously affect the function and activity of the elbow in patients after surgery.

In the current study, a total of 20 patients (15.3%) developed new onset or exacerbation of nerve symptoms after surgery. However, no significant differences were found between the 4 groups of patients with neurological complications. Similar to previous studies, the occurrence of neurological symptoms is mostly ulnar nerve symptoms.<sup>2</sup> In general, serum uric acid levels have no significant effect on postoperative new onset or exacerbation of nerve symptoms. We considered that the occurrence of ulnar nerve symptoms may be related to the operative procedure because we routinely exposed the ulnar nerve.

In a cross-sectional survey of individuals aged 50-74 years in China, patients' grip strength increased across increasing serum UA tertiles.<sup>35</sup> In addition, a study that followed patients for more than 3 years from InCHIANTI showed that muscle strength gradually increases in patients with a mean baseline age of 76 years as the serum uric acid level rises.<sup>20</sup> More recently, the results from the Seniors-ENRICA study have shown a negative association between baseline UA levels and the risk of muscle weakness.<sup>7</sup> García-Esquinas and Rodríguez-Artalejo<sup>4</sup> reported that the association between UA and muscle strength differed depending on age: although a negative link was observed in adults aged 20-40 years, this relationship decreased later in life and was reversed at the age of 60. In our study, 10 patients had complications of decreased muscle strength at the end of the follow-up period. However, there were no obvious differences among all 4 groups. It has been reported that the incidence of elbow instability and infection after elbow arthrolysis is relatively low, according to Cai et al.<sup>2</sup>

**Table V** Distribution of postoperative complications

Variables	Q1 (0-293)	Q2 (293.5-348)	Q3 (348.5-441)	Q4 (441.5-710)	P value
No. of patients	33	34	32	32	
New onset or exacerbation of nerve symptoms, n (%)	5 (15)	5 (15)	4 (13)	6 (19)	.919
Reduced muscle strength, n (%)	2 (6)	3 (9)	1 (3)	4 (13)	.536
Instability, n (%)	2 (6)	4 (12)	2 (6)	1 (3)	.567
Infection, n (%)	0 (0)	0 (0)	0 (0)	1 (3)	.374

Data are presented as numbers (percentages).

Similarly, in our study, the incidence of elbow infection and instability among the 4 groups was also low, and there were no significant differences between these groups. We found only 1 patient with elbow infection. We believe that the presence of this patient's infection may be related to aseptic or improper postoperative care and is not associated with uric acid levels.

There are still some limitations in our research that need to be declared. First, this is a retrospective study, so it is difficult to avoid recall bias. Second, the sample size of the study was relatively small, and the number of patients with postoperative complications was limited for meaningful statistical analysis. Third, the serum level of uric acid was not tested during the postoperative follow-up in this study. This is a limitation, as serum uric acid levels may fluctuate and perhaps have an impact on the patient's postoperative outcome. Finally, we did not use specific patient-related outcome measures, such as the American Shoulder and Elbow Surgeons Score or Liverpool Elbow Score.

## Conclusion

Arthrolysis could effectively restore motion and function in patients with elbow stiffness. However, we also found that as the level of uric acid increased beyond a certain point, the improvement in elbow function after surgery was affected. In addition, patients with higher preoperative uric acid levels would have more severe postoperative pain. This study confirms that in patients with post-traumatic elbow stiffness, abnormal serum uric acid metabolism was a risk factor for poor performance and postoperative pain after arthrolysis. Therefore, detecting the preoperative serum uric acid levels of the patients would be helpful for evaluating the postoperative outcome.

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## Disclaimer

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