

Mirabilite with ice pack after Total Knee Arthroplasty: A Randomized Controlled Trial Study

Ying Zhong

the First Affiliated Hospital of Zhejiang Chinese Medical University

Cheng Zheng

the first clinical medical college of Zhejiang Chinese Medical University

Wenxi Du

the first affiliated hospital of Zhejiang Chinese Medical University

Jiahua Zheng

Xianju people's hospital

Shanchun Xu

the first affiliated hospital of Zhejiang Chinese Medical University

Peijian Tong (✉ tongpeijian@163.com)

Zhejiang Hospital of Traditional Chinese Medicine <https://orcid.org/0000-0003-0948-8674>

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Abstract

Background

Total knee arthroplasty (TKA) is a well-established procedure for end-state arthritis of knee with complications such as swelling and pain. The aim of this study is to evaluate the effect of mirabilite with ice pack versus ice pack alone on relieving pain, reducing swelling, range of motion (ROM), and serum CRP level in patients after TKA.

Methods

Eighty patients undergoing primary unilateral TKA were randomly assigned to two groups (MIP group and WIP group). We used VAS to measure knee pain at 24 h, 48 h, and 72 h after the surgery respectively. Knee swelling degree was evaluated by measuring the girth of leg at the center of patella and 10 cm above and below it at the same frequency. The active ROM of the knee was measured by using a universal goniometer of plastic material at 72 h postoperatively. The serum CRP level was also measured at 72 h postoperatively.

Results

The MIP group showed statistically significant lower knee girth at 48 h ($p \leq 0.05$), 72 h ($p < 0.05$) postoperatively and VAS score at 72 h ($P = 0.018$) at postoperatively after TKA than WIP group. The ROM of MIP group were significantly wider than WIP group ($P = 0.024$). The CRP level ($P = 0.036$) and length of stay (LOS) ($P = 0.037$) of MIP group were significantly lower than WIP group.

Conclusions

Mirabilite with ice pack after TKA showed superiority in relieving pain, reducing swelling, and improving ROM than ice pack alone.

Trial registration:

Chinese Clinical Trial Registry (ChiCTR), ChiCTR-OCN-15006356. Registered 6 MAY 2015, <http://www.chictr.org.cn/showproj.aspx?proj=10927>

Background

Total knee arthroplasty (TKA) is a well-established procedure for end-state arthritis of knee that has been demonstrated to improve pain, mobility, function and quality of life^[1]. Patients treated with TKA often

experience localized swelling and pain resulting from tissue damage and inflammatory response, which usually peaks 24 to 48 hours after surgery and influence postoperative opiate use, requirement for blood transfusion and postoperative rehabilitation^[2]. This can further cause increased length of stay (LOS) and cost^[3].

Non-pharmaceutical treatment such as cryotherapy plays a role in addressing immediate postoperative complications such as pain and swelling^[2]. Basic cryotherapy includes basic gel packs and crushed ice. New generation cryotherapy such as electronic temperature control device can guarantee a sustained fixed temperature during cooling to achieve better effect, but with higher costs^[4].

Mirabilite or know as Glauber's salt, is a hydrous sodium sulfate mineral with the chemical formula $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ that has the function of reducing inflammation and swelling^[5]. In China, ice pack used with mirabilite is considered efficient in reducing swelling and pain after TKA. Mirabilite has much lower economic cost than new generation cryotherapy, an ideal choice for patients with financial difficulties if proved effective.

The aim of this study is to evaluate the effect of mirabilite with ice pack versus ice pack alone on relieving pain, reducing swelling, range of motion (ROM), and serum CRP level in patients after TKA and to assess the prime targets for improving patient outcomes. ice pack

Methods

Study design

This is a single-center, randomized controlled trial (Level of evidence: 1). All patients who underwent single-stage TKA from January 2017 to March 2018 in department of orthopedics, the First Affiliated Hospital of Zhejiang Traditional Chinese Medicine University were included.

Inclusion criteria: unilateral primary TKA; severe osteoarthritis (in Kallgren-Lawrence grade-4); 65–85 years old. Exclusion criteria: severe varus or valgus deformity; hematological or rheumatologic osteoarthritis etiologies; history of deep vein thrombosis; active Phlebitis; venous insufficiency; a coagulation disorder; untreated diabetes; untreated hypertension; skin damage or sensibility alterations (such as hypersensitivity to cold, mirabilite).

Eighty patients were included (38 males, 42 females) and randomly assigned to two groups: the water ice pack (WIP) group (n = 40) received traditional cryotherapy (crushed ice packs) and the mirabilite with ice pack (MIP) group (n = 40) with mirabilite packs under ice bags. In this study we apply simple randomization using sealed opaque randomization envelopes containing equal numbers of “WIP” and “MIP” notes. There were no dropouts or withdrawals. In the WIP group, an impermeable PVC pack with 500 g of crushed ice packed in was put on the patella and pressurized secured by gauzes. In MIP group, 500 g granular mirabilite was spread in a 25cm*30 cm textile pack and placed around the knee joint

before applying the ice pack like the WIP group. In both two groups, cryotherapy was applied in the first 6–72 h after the operation. The surgeons replaced mirabilite packs and ice packs every 12 h and paid attention to the limb sensory, range of motion and local skin color.

The visual analog scale (VAS) pain scores and knee girth (the girths at the center of patella (S0) and 10 cm below (S1), 10 cm above (S2) the center of patella) were measured at before and 24, 48, and 72 h after the operation. The value of swelling equaled the girth of operative knee minus the girth of healthy knee. In addition, CRP as an indicator of inflammation, was measured 72 hours after operation.

The active ROM of the knee was measured by using a universal goniometer of plastic material at 72 h after the operation according to the Daniel^[6]. The goniometer was positioned on the articular line of the knee; The fixed arm was parallel to the lateral surface of the femur in the direction of the greater trochanter and the mobile arm was parallel to the lateral side of the fibula in the direction of the lateral malleolus.

Arthroplasty procedures

The arthroplasty procedures were carried out by the same group of surgeons, using a midline anterior incision with a medial parapatellar arthrotomy and with the use of posterior Cruciate-Stabilizing knee prosthesis (Stryker®, NGR) in all patients. The anesthesia and postoperative analgesia protocols used were standardized and similar in the two groups. The mean procedure duration was 70 minutes (60–100). The procedure was performed with a tourniquet in all cases. It was released before closing the wound to realize complete hemostasis. Local injection of 20 ml 5% tranexamic acid into periarticular soft tissue was performed before closing the incision. A patient-controlled analgesia (PCA) pump was applied within 48 h after surgery. Tramadol 100 mg/mL (after 48 hours) were employed for breakthrough pain. Anticoagulant therapy was initiated 6 hours after the end of surgery in all patients. In all patients, the hemorrhage drain was taken out 48 h postoperatively. The same rehabilitation program was used for all patients: partial weight bearing was allowed, using crutches, since the first day after surgery and progressively increased as tolerated. Active and passive mobilization was started from the first day after surgery. Venous ultrasonography ultrasound was performed when deep vein thrombosis (DVT) suspected.

Statistical Analysis

Median (25–75 percentile) or mean \pm standard deviation or percentage was determined for patient baseline demographics, clinical features, and laboratory parameters, when appropriate. Differences between MIP group and WIP group were evaluated by Student's t-test for parametric data, the Mann–Whitney test or Kruskal-Wallis test for nonparametric data. The chi-square test (χ^2) or Fisher's exact test for comparisons of percentages between groups, as appropriate.

Repeated measures ANOVA was performed to evaluate the girth of operative knee and VAS pain score at 3 postoperative time points (24 h, 48 h, and 72 h). Given the ordinal nature of VAS scoring, we used both ANOVA and linear mixed models to compare treatment effect at different time point. Preliminary tests

including detecting extreme outliers, Shapiro-Wilk normality test, and Mauchly's test of sphericity were performed to check if the model assumptions are met. Post-hoc tests for significant two-way interaction was decomposed into 2 models: simple main effect (one-way) model, where we evaluate treatment effect at each level of postoperative time points, and simple pairwise comparisons (paired test) to determine which groups are different. Bonferroni multiple testing correction method was used to adjust p values, and compound symmetry correlation structure was applied for linear mixed models. We checked for correlation matrix between continuous variables by using Spearman method to compute correlation coefficient. Statistical analyses were performed using R project version 3.6.0. Package "rstatix" and "nlme" were used for repeated measures ANOVA and linear mixed models. A P-value < 0.05 was considered statistically significant.

Results

None of the patients experience any skin or vessel complications due to ice pack or mirabilite pack. No infection, DVT or pulmonary embolism are found after TKA in 2 groups. The baseline characteristics of two groups are showed in Table 1. The chi-square test shows no significant difference in gender ($p = 0.258$). Also, the age, operation time, BMI, height, weight, postoperative drainage, preoperative VAS score and preoperative knee girth show no statistically significant difference ($p > 0.05$). The baseline characteristics of 2 group are regarded homogenous. As Table 1. Shows, the LOS postoperatively and CRP at 72 h postoperatively in MIP group is significantly lower than in WIP group ($p = 0.037$) while the ROM at 72 h postoperatively in MIP group is wider than in WIP group ($p = 0.024$).

Table 1
Comparison of baseline characteristics and clinical feature between 2 groups

	MIP Group	WIP Group	P Value	
Male	20 (50.00%)	14 (35.00%)	0.258	
Age (years)	72.00 (69.00–76.00)	70.50 (69.00–73.00)	0.275	
Weight (kg)	69.40 (64.67–74.48)	69.10 (63.15–75.55)	0.927	
Height (m)	1.64 (1.59–1.71)	1.65 (1.61–1.72)	0.443	
BMI (kg/m ²)	25.56 (22.90-27.67)	25.17 (23.40-27.29)	0.658	
Operation time (min)	68.00 (64.00-75.25)	70.00 (65.75–77.25)	0.383	
Postoperative drainage (mL)	41.50 (33.75-48.00)	41.00 (35.00-47.50)	0.912	
preoperative VAS score	5.00 (4.00–6.00)	5.00 (4.00–5.00)	0.806	
Preoperative girth (cm)	S0	40.00 (38.68–42.90)	41.85 (39.77–45.12)	0.077
	S1	34.50 (32.90-37.23)	36.50 (33.20–39.40)	0.179
	S2	45.40 (42.58–48.52)	45.50 (42.85–49.62)	0.577
Length of hospital stay (LOS) (days)	9.00 (8.00–10.00)	8.00 (7.00-9.25)	0.037	
ROM at 72 h postoperatively	72.00 (67.75-75.00)	74.50 (70.00–80.00)	0.024	
CRP at 72 h postoperatively (mg/dL)	20.50 (18.00–27.00)	18.00 (14.75-22.00)	0.036	
Abbreviation: BMI, Body Mass Index.				
Boldface indicates P value < 0.05				

The VAS score and girth difference at S0, S1, S2 have significant difference in pre-operation and post-operation in both 2 groups. Repeated measure ANOVA shows that the time interaction effect is statistically significant ($F = 407.9, p < 0.001$; $F = 87.3, p < 0.001$; $F = 48.6, p < 0.001$; $F = 81.5, p < 0.001$ respectively). The interaction between treatment and time effect is not statistically significant in VAS score ($p = 0.052$). There is statistically significant interaction between treatment and time effect in girth difference at S0, S1, S2 ($p < 0.05$).

The post-hoc for treatment compare in ANOVA shows that VAS scores at 72 h in MIP group are significantly lower than in WIP group (3 vs 4, $p = 0.018$). There is no statistically significant difference in VAS score at 24 h, 48 h postoperatively between 2 groups ($p > 0.05$) (**Figure. 1**).

There is no statistically significant difference in knee girth difference on S0, S1 and S2 ($p > 0.05$) at 24 h postoperatively. Girth difference on S0, S1, S2 at 48 h ($p = 0.045$; $p = 0.002$; $p = 0.022$ respectively) and

72 h ($p < 0.001$; $p = 0.014$; $p < 0.001$ respectively) postoperatively in MIP group are significantly lower than in WIP group (**Figure.2**).

The results of Spearman test are shown in **Figure.3**. There was no statistically significant correlation between CRP and ROM, VAS, girth difference at 72 h postoperatively.

Discussion

Total knee arthroplasty is one of the most cost-effective and consistently successful surgeries performed in orthopedics. Despite the progress in surgical techniques and postoperative care, complications such as swelling and pain become the key of optimizing patients' satisfaction^[1].

In our study, the mean girths of the knee joint strikingly increased after surgery in both groups, as was described in previous studies^[7]. In conformity with a previous study, pain score increased to the highest level within 24 h after TKA^[8]. This is probably due to the variable intra-operative soft tissue trauma with consecutive secretion, bleeding, and swelling as well as to individual post-operative reaction^[4]. Bleeding and damaged tissue caused by surgery will release inflammatory mediator like TNF- α , IL-1 β , IL-6, IL-8, increasing vascular permeability, causing inflammatory exudation and thus leading to swelling and pain which is acute phase response (APR). APR is a systemic reaction to tissue injury and does not vary significantly difference in surgical techniques^[9].

Cryotherapy is a Non-pharmaceutical treatment to relief of postoperatively pain and swelling, which involves the application of cold to the skin surrounding the injured soft tissues and in joint surgery is supposed to reduce the temperature in knee-joint^[7]. Low temperature will reduce local blood flow through vasoconstriction, which relieves the local inflammatory reaction, swelling and heat experience, and also will slow the conduction of nerve signals that potentially reducing pain transmission^[10-12]. In addition, previous study has shown that a pleasant sensation evoked by knee icing also will reduce the pain intensity after TKA^[13]. Kullenberg et al.'s^[14] study showed water ice packs were more effective than epidural analgesia in reducing pain degree after TKA. Kuo et al.^[15] also confirmed the effect of ice pack on anti-swelling and analgesic. Analysis from Thacoor A et al.^[16] showed that cryotherapy had certain efficacy in reducing swelling and pain degrees after TKA. Cryotherapy is applied to reduce the degree of swelling and pain whether in theory or clinical practice after trauma^[17].

Several cryotherapy options are available including first-generation cold therapy like crushed ice in a plastic pack, new-generation advanced computer-assisted devices with continuous controlled cold therapy^[2]. The advantage of these latter devices is controlled-temperature modulation with cooling at a specific and continuous temperature for a prolonged time, introducing better effect of resolving pain and swelling than crushed ice pack^[18]. Morad Chughtai et al.^[19] reviewed 16 studies where various types of cryotherapy were assessed and compared, concluding continuous temperature devices are the most

effective. However, using the new-generation means the much higher cost than traditional cryotherapy, which is unaffordable for most patients.

Mirabilite is a cheap hydrous sodium sulfate mineral which has the special physical properties of salt and always applied externally to relieve pain and swelling after trauma in traditional Chinese medicine. In traditional Chinese medical theory, mirabilite has a feature of clearing fire-evil which in modern medical theory we call inflammation and absorbing swelling. Some Chinese scholars show that by inhibiting reticuloendothelial system, mirabilite has a positive effect on anti-inflammation. Lu's^[20] study in rabbits shows that mirabilite can significantly decrease the expression of IL-1, IL-6, TNF- α and the severity of inflammatory responses. In our study, the MIP group shows statistically significant lower knee girth at 48 h, 72 h postoperatively and VAS sore at 72 h postoperatively than WIP group, which suggests mirabilite and ice pack can synergetic control swelling and pain. In addition, the improvement of ROM at 72 h after surgery and the reduction of LOS in MIP group indicate that compare with ice pack alone, mirabilite with ice pack can accelerate the recovery process and discharge, therefore reducing unit treatment cost. Inspired by previous studies, we recorded and analyzed the postoperative degree of serum CRP. Although, there is no statistically significant correlation between CRP and ROM, VAS, girth difference at 72 h postoperatively, our study shows that serum CRP at 72 h after surgery of MIP group is significantly lower than WIP group. These results support the viewpoints described above. The anti-inflammatory function of mirabilite may be the reason for the better postoperative performance in MIP group. However, the mechanism of mirabilite anti-inflammatory and reducing pain and swelling still needs to be further confirmed and studied.

Although some previous studies reported on frostbite, deep vein thrombosis and further adverse effects after cryotherapy^[14], there was no occurrence of any adverse event reported in 2 groups throughout our study. Our study shows that use of cryotherapy and mirabilite after TKA is safe.

Conclusions

Our study shows that mirabilite with ice pack in patients undergoing TKA is significantly more effective than ice pack alone with regard to reducing swelling, pain, CRP level, LOS, and improving ROM, which maybe due to anti-inflammatory property of the mirabilite. Applying mirabilite with ice pack externally after TKA appears to be a cheap, safe, and efficient procedure in clinical practice.

Abbreviations

TKA, Total knee arthroplasty

ROM, range of motion

CRP, C-reactive protein

VAS, visual analogue scale

BMI, body mass index.

LOS, length of stay

WIP, water ice pack

MIP, mirabilite with ice pack

PVC, polyvinyl chloride

PCA, patient-controlled analgesia

DVT, deep vein thrombosis

ANOVA, analysis of variance

APR, acute phase response

TNF, tumor necrosis factor

IL, interleukin

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang Chinese Medical University. The study purpose, methods, and procedures were well explained to all participants at the beginning of this study. All participants signed informed consent and were free to withdraw during the study period.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YZ and PJT made a study design. YZ, CZ, JHZ and SCX collected and analysed the data. YZ and CZ drafted and edited the manuscript. WXD revised the manuscript. All authors proofread and approved the final manuscript. YZ and CZ contributed equally to this work and should be considered co-first authors.

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Not applicable

Authors' information

Peijian Tong, Phone: +86 517-86613684, Email: tongpeijian@163.com

Ying Zhong, Email: zhongying729@163.com

Cheng Zheng, Email: 2312183458@qq.com

Wenxi Du, Email: purpleraineer@163.com

Jiahui Zheng, Email: mushisdoctor@gmail.com

Shanchun Xu, Email: xu6452xu@126.com

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Figures

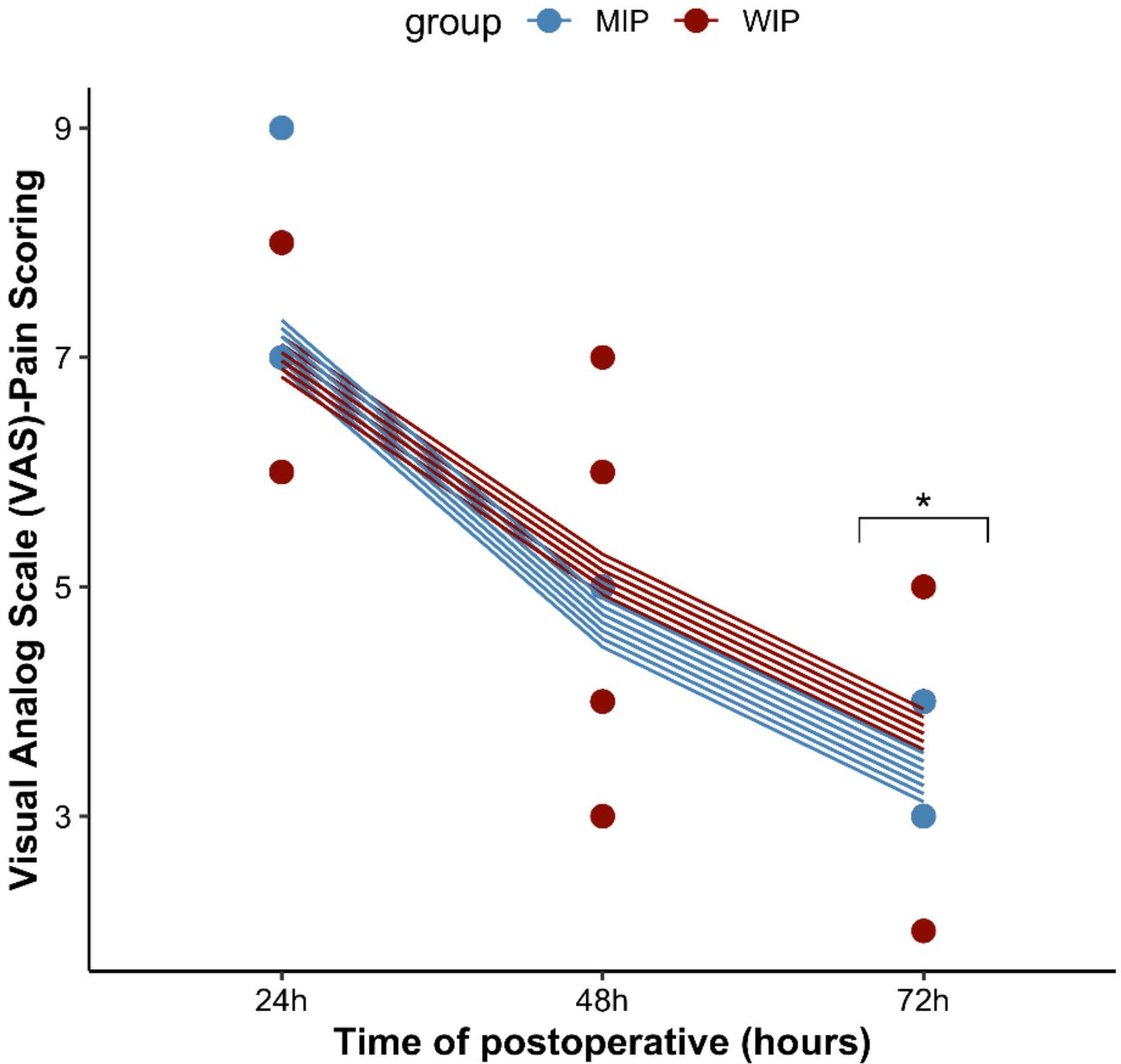


Figure 1

Deviation of VAS score postoperatively of 2 groups. Predicted VAS score at individual level for different post-operative hours. Significant difference is found at 72h after surgery in pairwise comparison.

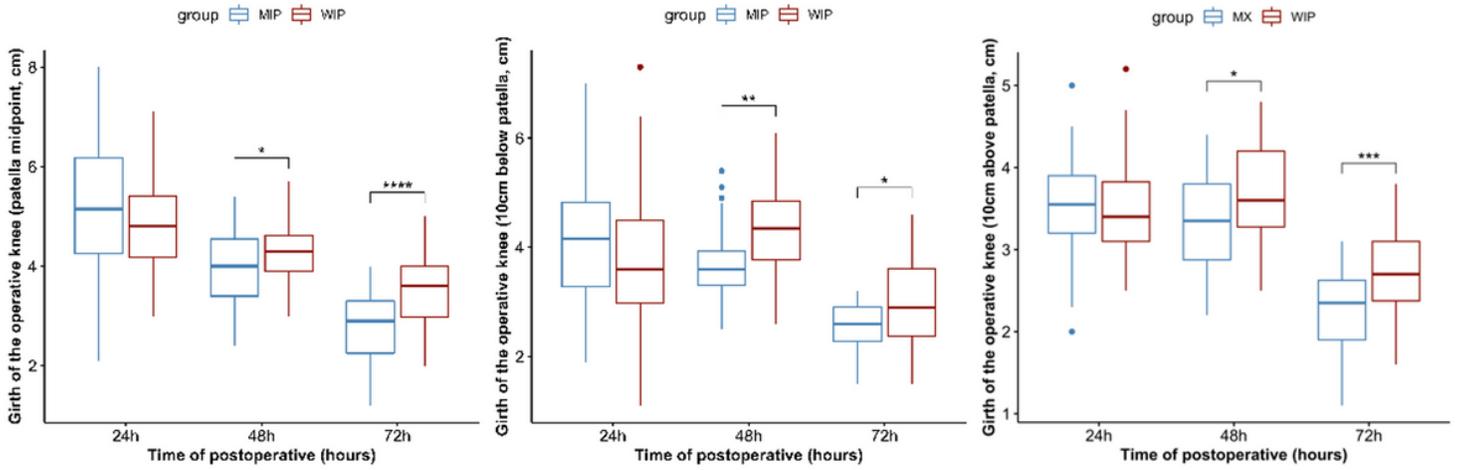


Figure 2

Comparison of Knee girth difference between two groups.

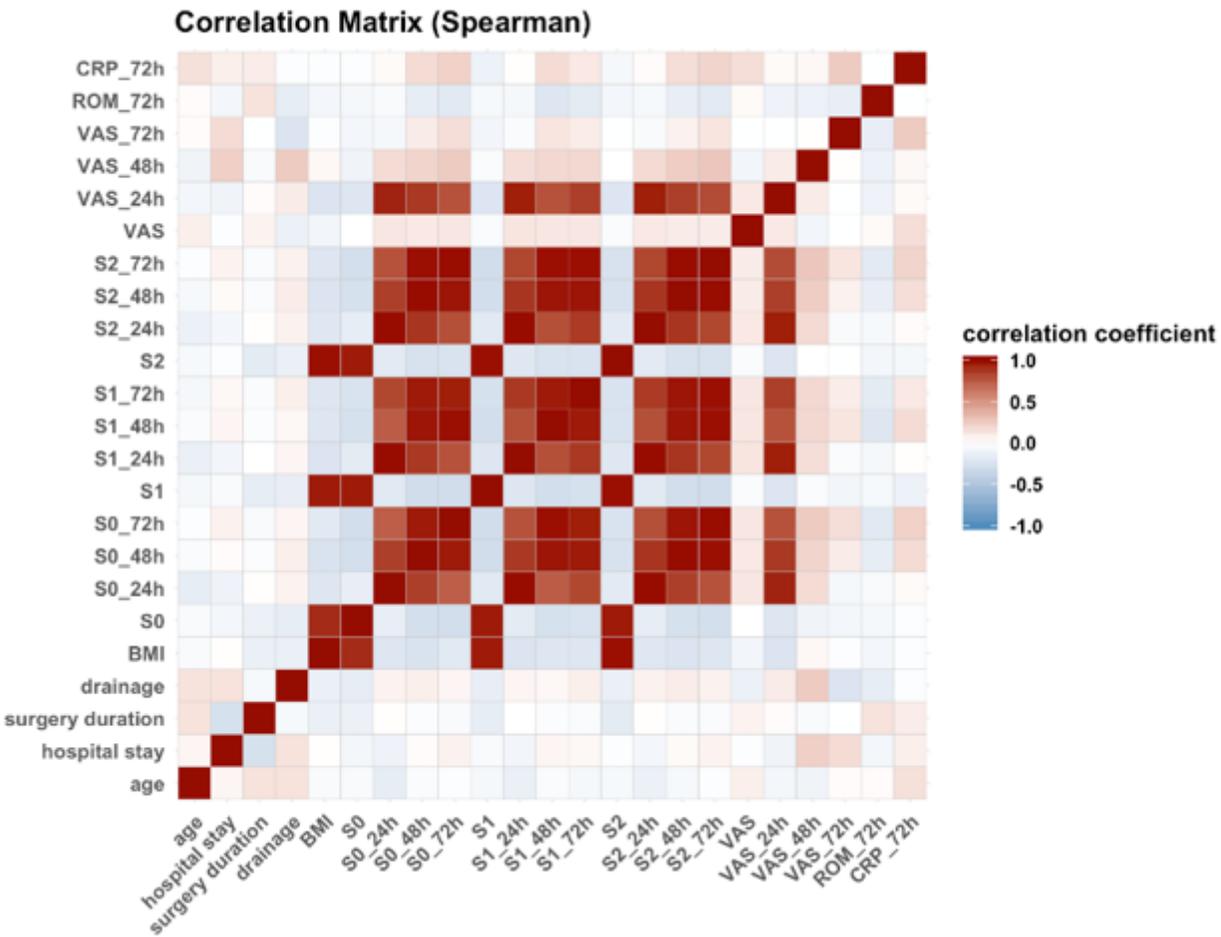


Figure 3

Result of Spearman test