

Postoperative Bone Marrow Lesions (BMLs) are Associated with Pain Severity in Patients Undergoing Open Wedge High Tibial Osteotomy (OWHTO)

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Abstract

Background: The purpose of the study was to investigate the relationship between postoperative bone marrow lesions (BMLs) and pain severity in patients undergoing open wedge high tibial osteotomy (OWHTO).

Methods: We retrospectively reviewed the patients undergoing OWHTO between April 2018 and April 2020. The demographic and clinical data of patients were collected. Clinically, VAS and Knee Injury and Osteoarthritis Outcome Score (KOOS) were used to assess pain level and functional outcomes of patients. Histologically, The MRI Osteoarthritis Knee Score (MOAKS) was used to assess semi-quantitatively the total BMLs size in medial tibiofemoral (MTF), lateral tibiofemoral (LTF), and patellofemoral (PF) joints.

Results: 98 patients were enrolled in the study, including 57 male and 41 female patients. The VAS scores improved significantly from 6.1 ± 0.8 to 1.5 ± 0.9 ($p < 0.001$), and all subscales of KOOS improved significantly after surgery ($p < 0.001$). There were no significant difference between the pre-and postoperative total BMLs size in PF and LTF joints ($p > 0.05$). We observed significant improvements in the total BMLs size of MTF joint ($p < 0.001$). All patients had preoperative MTF joint BMLs, in contrast, 13 patients had no postoperative MTF joint BMLs. The independent sample t-test showed that the VAS scores and KOOS pain scores improved better in patients without postoperative MTF joint BMLs ($p < 0.001$). Pearson correlations showed that postoperative MTF joint BMLs were correlated with postoperative VAS ($p < 0.001$) and KOOS pain ($p < 0.001$).

Conclusion: Our study demonstrates that MTF joint BMLs improved significantly after OWHTO. We confirmed that the presence of postoperative MTF joint BMLs are strongly associated with pain severity, the greater the improvement in postoperative MTF joint BMLs, the less pain. Our findings provide valuable understandings of OWHTO in the treatment of Knee osteoarthritis (KOA), and potential future directions for KOA treatment approaches.

Background

Knee osteoarthritis (KOA) is a common chronic disease that causes pain, stiffness, and functional disability¹⁻⁴, among which, pain is the major cause leading individuals to seek medical care⁵⁻⁸. Promisingly, many studies have demonstrated that knee pain could be relieved by open wedge high tibial osteotomy (OWHTO)⁹⁻¹².

OWHTO is an effective procedure for patients with medial unicompartmental KOA¹³⁻¹⁶. In a study conducted by Astur et.al, 66 patients who underwent OWHTO were reviewed, The postoperative scores, including Knee Injury and Osteoarthritis Outcome Score (KOOS), visual analog scale (VAS), and Tegner scores were higher than those found preoperative¹⁷. In a study conducted by Altay et.al, 34 patients who underwent OWHTO were reviewed, VAS scores improved significantly from preoperative 53.71 ± 10.02 to

postoperative 14.12 ± 6.08 , Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores improved significantly from preoperative 57.34 ± 6.37 to postoperative 31.94 ± 5.12 ¹⁸. Despite the clinical efficacy of OWHTO for pain relief has been demonstrated, the underlying mechanisms and corresponding histological changes remain unclear.

Many studies have shown that bone marrow lesions (BMLs) are strongly associated with pain in KOA^{5,19-21}. In a study conducted by Felson et.al, 401 patients with KOA were investigated, and 272 of 351 (77.5%) patients with painful knees had BMLs, comparing with 15 of 50 (30%) patients without painful knees had BMLs¹⁹. Zhang et.al investigated 651 painful knees and demonstrated that improved BMLs were strongly associated with pain relief in KOA²².

So far, only a few studies have analyzed the BMLs changes and their effect on the prognosis for patients undergoing OWHTO²³⁻²⁵. Yang et.al reviewed 105 patients who underwent OWHTO, and they did not find any correlation between preoperative bone marrow edema (BME) severity and postoperative outcomes²⁶. To our knowledge, no studies have investigated the relationship between postoperative BMLs and pain severity in patients undergoing OWHTO.

This study aimed to evaluate the relationship between postoperative BMLs and pain severity in patients undergoing OWHTO.

Materials And Methods

Patient Selection

We retrospectively reviewed the patients undergoing OWHTO between April 2018 and April 2020. The study was approved by the institutional ethics committee, and all patients signed consent forms. All procedures were performed in accordance with relevant guidelines. The inclusion criteria were (1) symptomatic medial KOA, (2) first OWHTO on the affected side, and (3) clinical data integrity. The exclusion criteria were (1) revision surgery, and (2) simultaneous bilateral OWHTO.

Perioperative Management.

All patients received standard medical care, and all procedures were performed by the same surgical team. The osteotomy was performed under fluoroscopy and the osteotomy site was fixed with the Tomofix plate system. Postoperative antibiotic prophylaxis and analgesia were administered in all patients, low molecule weight heparin was used for the prevention of venous thromboembolism. One year after hardware implantation, the hardware was removed and magnetic resonance imaging (MRI) was performed (Figure 1).

MR imaging and analysis

MR images were analyzed by two expert musculoskeletal radiologists who were blind to any clinical information. The intraclass correlation coefficient (ICC) was calculated to assess interobserver variability. The MRI Osteoarthritis Knee Score (MOAKS) was used to assess semi-quantitatively the total BMLs size in medial tibiofemoral (MTF), lateral tibiofemoral (LTF), and patellofemoral (PF) joints. The criteria of the score are as follows: 0 = no BMLs in subregion; 1 = size of BMLs / subregional volume < 33%; 2= size of BMLs / subregional volume < 66; 3= size of BMLs / subregional volume > 66%. The maximum possible BMLs size was 15 in the MTF joint, 15 in the LTF joint, and 12 in the PF joint (Figure 2).

Data collection

The demographic and clinical data of patients were collected, including gender, age, height, weight, body mass index (BMI), smoking, and size of osteotomy gap. Clinically, VAS and KOOS were used to assess pain level and functional outcomes of patients. Histologically, MOAKS was used to assess semi-quantitatively the total BMLs size in MTF, LTF, and PF joints.

Statistical Analysis

The measurement data were expressed as mean value \pm standard deviation (SD); the pre-and postoperative parameters were compared using paired t-tests and Wilcoxon test. An independent sample t-test was used to compare pain scores in patients with or without BMLs. The Pearson correlation test was used for correlation analysis. The SPSS 22.0 software was used for statistical analysis, and $P < 0.05$ was considered statistically significant.

Results

98 patients were enrolled in the study, including 57 male and 41 female patients. The mean age of the patients was 65.1 ± 5.7 years, and the mean BMI was 28.1 ± 3.4 kg/m². The characteristics of the patients are shown in Table 1.

Table 1
Patient characteristics.

Characteristics (n = 98)	
Gender (male/female)	57/41
Mean age (years)	65.1 ± 5.7
BMI (kg/m ²)	28.1 ± 3.4
Smoking (%)	26 (26.5)
Alcohol consumption (%)	31 (31.6)
Hypertension (%)	45 (45.9)
Diabetes mellitus (%)	19 (19.4)
Osteotomy gap (mm)	11.3 ± 2.8
BMI = body mass index	

As shown in Table 2, the VAS scores improved significantly from 6.1 ± 0.8 to 1.5 ± 0.9 ($p < 0.001$), and all subscales of KOOS improved significantly after surgery (Figure 3).

Table 2
Preoperative and postoperative VAS and KOOS scores

	preoperative	postoperative	<i>P</i> -value
VAS	6.1 ± 0.8	1.5 ± 0.9	< 0.001
KOOS Pain	46.5 ± 8.2	78.3 ± 9.4	< 0.001
KOOS Symptoms	51.2 ± 9.1	81.5 ± 7.8	< 0.001
KOOS ADL	52.4 ± 10.9	78.8 ± 8.2	< 0.001
KOOS SR	30.3 ± 9.1	64.2 ± 7.2	< 0.001
KOOS QoL	39.4 ± 9.2	60.9 ± 8.4	< 0.001
KOOS = Knee injury and Osteoarthritis Outcome Score, ADL = activities of daily living, SR = sport and recreation, QoL = quality of life.			

ICC for all parameters were more than 0.8 in MRI measurements. As shown in Table 3, there was no significant difference between the pre-and postoperative total BMLs size in PF and LTF joints. We observed significant improvements in the total BMLs size in MTF joint(Figure 4).

Table 3
Preoperative and postoperative MOAKS

	preoperative	postoperative	<i>P</i> -value
PF joint	1.3 ± 0.8	1.3 ± 0.7	0.566
LTF joint	1.8 ± 0.8	1.9 ± 0.7	0.083
MTF joint	7.9 ± 2.2	3.4 ± 2.0	< 0.001
MOAKS = MRI Osteoarthritis Knee Score, PF joint = patellofemoral joint, MTF joint = medial tibiofemoral joint, LTF joint = lateral tibiofemoral joint.			

All patients had preoperative MTF joint BMLs, in contrast, 13 patients had no postoperative MTF joint BMLs. The VAS scores were 1.7 ± 0.8 in patients with postoperative MTF joint BMLs and 0.2 ± 0.4 in patients without postoperative MTF joint BMLs. The KOOS pain scores were 76.9 ± 9.0 in patients with postoperative MTF joint BMLs and 87.8 ± 5.4 in patients without postoperative MTF joint BMLs. The independent sample t-test showed that the VAS scores and KOOS pain scores improved better in patients without postoperative MTF joint BMLs (Figure 5).

Pearson correlations showed that postoperative MTF joint BMLs are correlated with postoperative VAS ($r = 0.945, p < 0.001$) and postoperative KOOS pain ($r = -0.472, p < 0.001$).

Discussion

KOA is a degenerative joint disease, which causes pain and decreased physical function¹⁻⁴. Knee pain is the major cause leading individuals to seek medical care⁵⁻⁸. KOA - associated pain involved in abnormal structural alterations, including articular cartilage, subchondral bone, and synovial tissue²⁷⁻³⁰. The goal of KOA management is to relieve pain, improve knee function, and change the disease process. Although there are no approved drugs for changing KOA process, many interventions are available to address pain and function^{1,31,32}.

Many studies have demonstrated that knee pain could be relieved by OWHTO⁹⁻¹². A systematic review found that clinical scores improved significantly after open or closed wedge high tibial osteotomy, including VAS, the American Knee Society Score, Hospital for Special Surgery Knee Score, and Lysholm score³³. Identification of the mechanism of pain relief by OWHTO is important, an understanding of the mechanism may be helpful for targeted anti-KOA therapy and individualized therapy.

BMLs are poorly delineated lesions below the subchondral bone which occur in high mechanical load condition generally, such as knee malalignment^{5,34,35}. Some studies have shown that BMLs were more commonly observed in painful knees with OA than non-painful knees^{19,20}. Meanwhile, increased BMLs were strongly associated with new onset frequent knee pain in non-painful knees³⁶. Zhang et.al investigated 651 painful knees and demonstrated that improved BMLs were strongly associated with

pain relief in KOA²². These and other studies have implied that BMLs are a cause of pain in KOA and a potential therapeutic target for pain in KOA^{5,35,37,38}.

The primary purpose of OWHTO was to reduce the mechanical load of medial compartment of the knee. Interestingly, a recent study implied that reducing mechanical load can decrease BMLs and relieve knee pain³⁹. Moreover, a few studies have demonstrated that BMLs of the knee were significantly improved after OWHTO^{23,25}. These findings prompted us to further analyze the relevance between BMLs and pain states in patients undergoing OWHTO.

Lately, a few studies have revealed the relationship between preoperative BMLs and postoperative clinical outcomes including pain relief^{24,26}. However, to our knowledge, no studies have investigated the relationship between postoperative BMLs and pain states in patients undergoing OWHTO. This might be because postoperative MRI is relatively unnecessary, expensive, and time-consuming, which increases the time and economic burden of patients. Meanwhile, data collection and analysis would require long-term effort, not only for physicians but also for radiologists.

In summary, We semi-quantitatively analyzed the BMLs changes in patients undergoing OWHTO. We first confirmed that the presence of postoperative MTF joint BMLs is strongly associated with pain severity in patients undergoing OWHTO, furthermore, the greater the improvement in postoperative MTF joint BMLs, the less pain.

This study has several limitations: First, it is a small retrospective study. Second, The research is a single-center study, a further larger, multicenter research was needed to confirm our findings.

Conclusion

Our study demonstrates that MTF joint BMLs improved significantly after OWHTO. We confirmed that the presence of postoperative MTF joint BMLs are strongly associated with pain severity, the greater the improvement in postoperative MTF joint BMLs, the less pain. Our findings provide valuable understandings of OWHTO in the treatment of KOA, and potential future directions for KOA treatment approaches.

Abbreviations

BMLs: Bone marrow lesions; OWHTO: Open wedge high tibial osteotomy; KOOS: Knee injury and Osteoarthritis Outcome Score; MOAKS: MRI Osteoarthritis Knee Score; MTF joint: Medial tibiofemoral joint; LTF joint: Lateral tibiofemoral joint; PF joint: Patellofemoral joint; KOA: Knee osteoarthritis; VAS: Visual analog scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; BMI: Body mass index; SD: Standard deviation; ADL: Activities of daily living; SR: Sport and recreation; QoL: Quality of life; ICC: intraclass correlation coefficient

Declarations

Acknowledgements

Not applicable.

Authors' contributions

BZ, TF-W, DS-C, JW-Z contributed to the conception of the study. BZ, TF-W, DS-C, JW-Z performed the study, Bo Zhu and Tong-Fu Wang contributed equally to this work and should be considered as equal to co-first authors. BZ, TF-W, DS-C, JW-Z, ZL-W, JGa-C, JW-Z performed the data analyses and wrote the manuscript. De-Sheng Chen and Jia-Wang Zhu designed and approved the manuscript and should be considered as corresponding authors. The author (s) read and approved the final manuscript.

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Availability of data and materials

The dataset used during the current study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethics approval was obtained by the ethical committee of Tianjin Hospital. A written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

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Figures

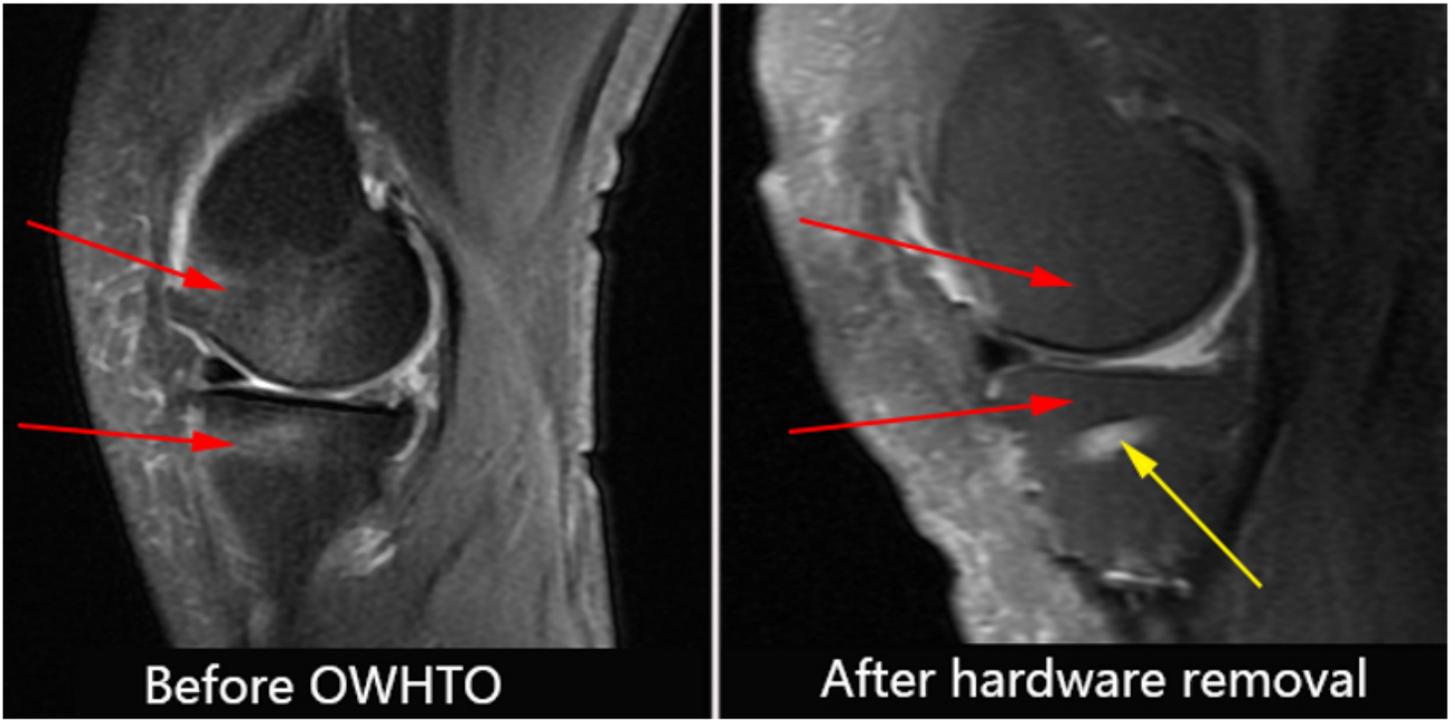


Figure 1

The BMLs in medial tibiofemoral joint improved significantly after surgery. The red arrow indicates the pre-and postoperative zone of BMLs, the yellow arrow indicates the zone after hardware removal. BMLs = bone marrow lesions

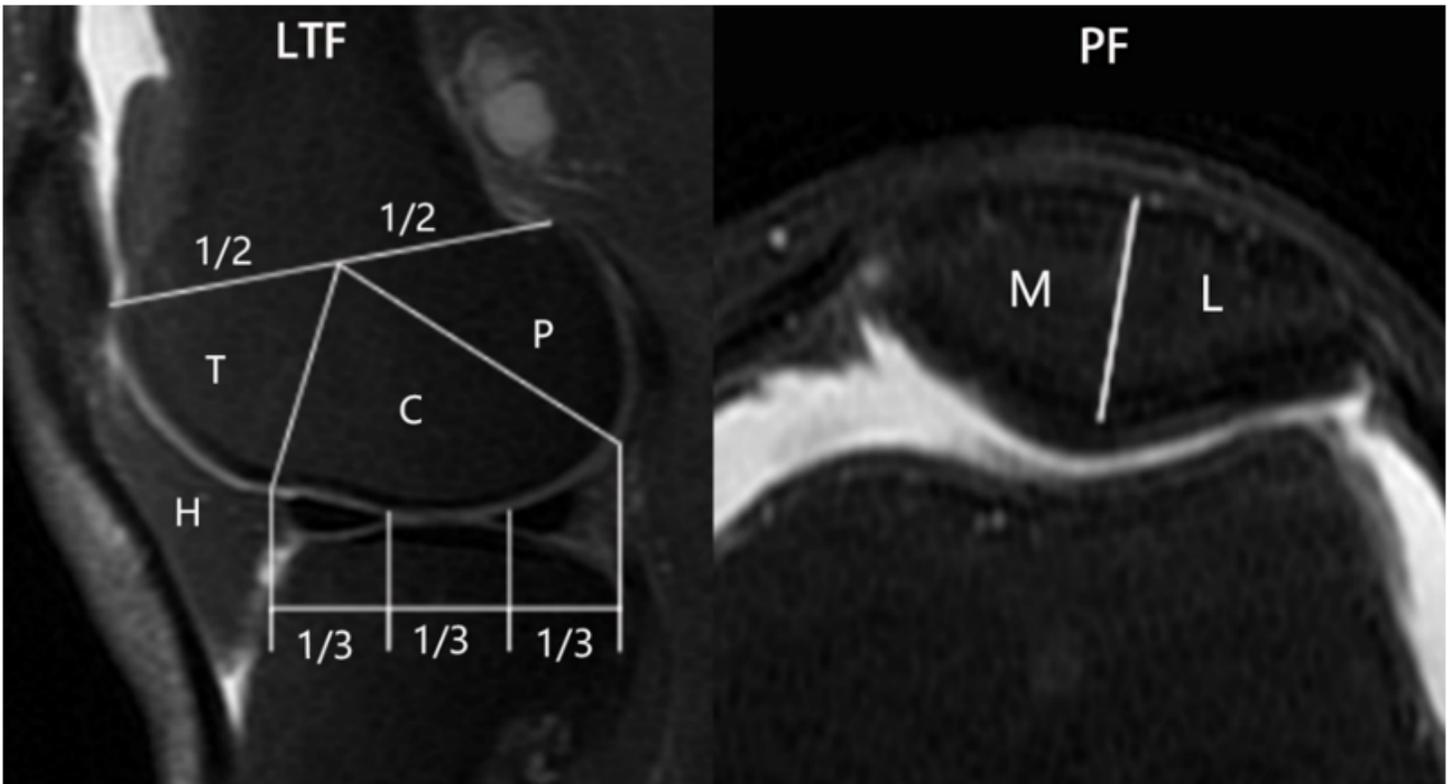


Figure 2

The LTF joint included five subregions: central (C) lateral femoral condyle, posterior (P) lateral femoral condyle, anterior subregion of tibia, central subregion of tibia, and posterior subregion of tibia. The maximum possible score in LTF joint was 15, and similarly for the MTF joint. The PF joint included four subregions: medial (M) portion of the patella, lateral (L) portion of the patella, medial trochlea (T) portion of femur, and lateral trochlea (T) portion of femur. The maximum possible BMLs size in PF joint was 12. LTF joint = lateral tibiofemoral joint, MTF joint = medial tibiofemoral joint, PF joint = patellofemoral joint.

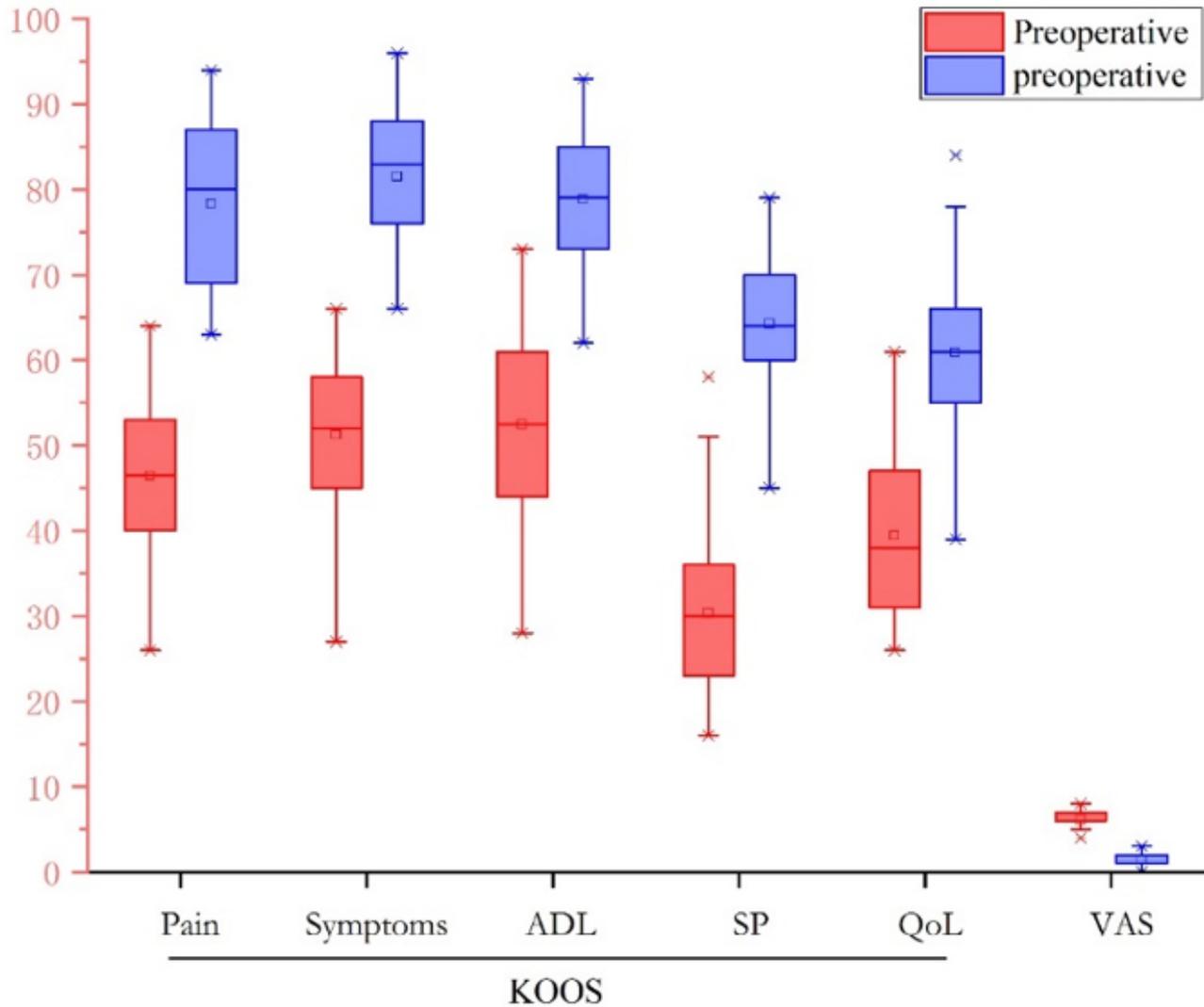


Figure 3

VAS scores and all subscales of KOOS improved significantly after surgery. KOOS = Knee injury and Osteoarthritis Outcome Score, ADL = activities of daily living, SR = sport and recreation, QoL = quality of life.

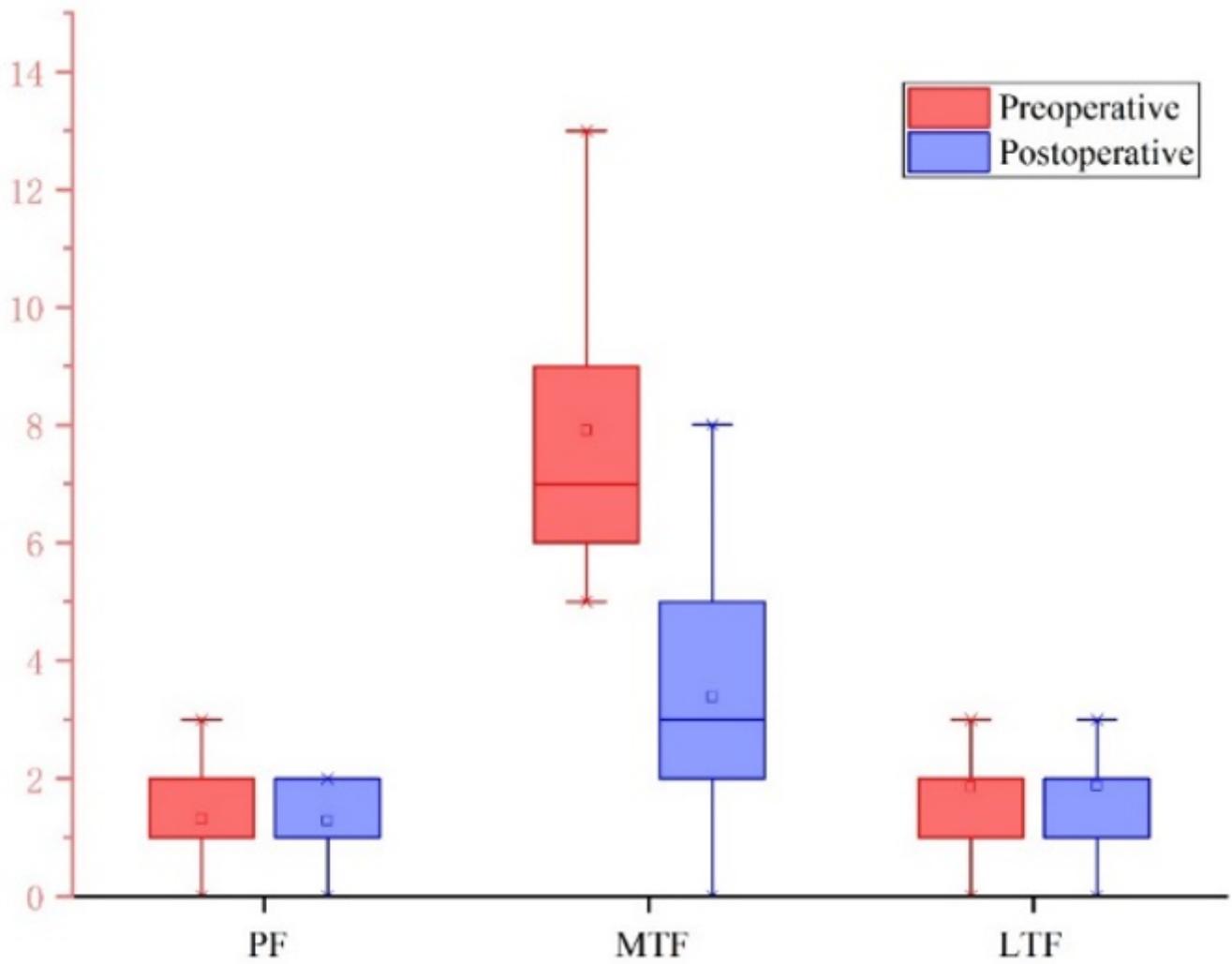


Figure 4

the total BMLs size in MTF joint improved significantly after surgery. BMLs = bone marrow lesions, PF joint = patellofemoral joint, MTF joint = medial tibiofemoral joint, LTF joint = lateral tibiofemoral joint.

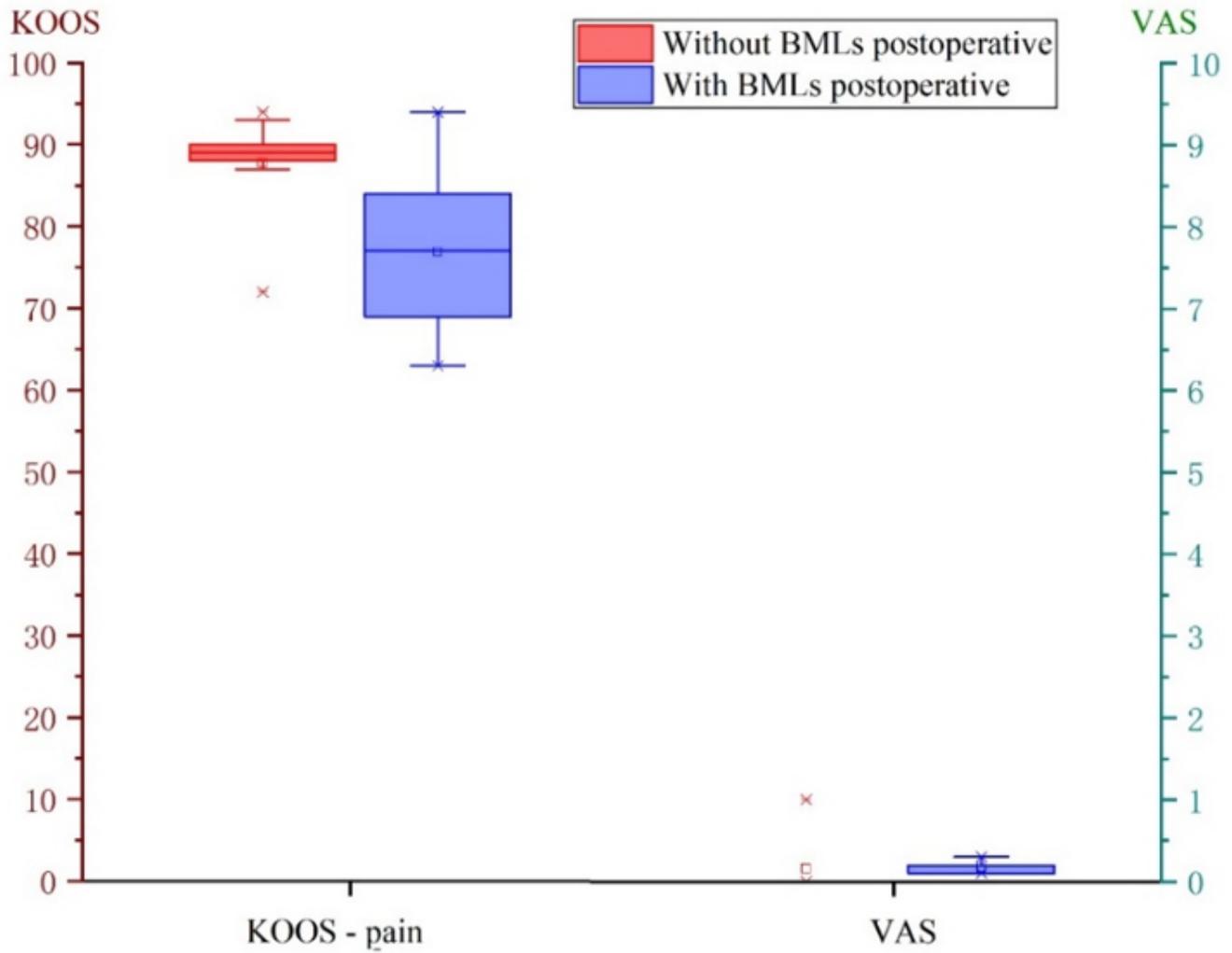


Figure 5

The VAS scores and KOOS pain scores improved better in patients without postoperative MTF joint BMLs. KOOS = Knee injury and Osteoarthritis Outcome Score, BMLs = bone marrow lesions.