

## DISCUSSION

This case is typical in terms of patient age and histopathologic findings but is notable for the size and location of the lesion. The lower abdominal location, rather than the more common head and neck distribution, represents an uncommon presentation of JXG. JXG typically presents as a solitary cutaneous lesion in infancy or early childhood, with a strong predilection for the first two years of life.

Cutaneous lesions usually regress spontaneously within 3-6 years and rarely require treatment. However, atypical presentations may raise concern for extracutaneous involvement and warrant careful evaluation.<sup>1</sup> Characteristically, JXG lesions appear as red or yellow papules or nodules measuring 0.5-2 cm.<sup>4</sup> Although most found on the head, neck, or upper trunk, lesions can occur anywhere on the body. Abdominal involvement has been reported but remains rare; to our knowledge, lower abdominal cutaneous JXG has not been previously described, highlighting the uniqueness of this case.

Extracutaneous involvement, while uncommon, has been reported in the central nervous system, lungs, liver, spleen, kidneys, bone marrow, and gastrointestinal tract.<sup>5</sup> Ocular involvement may occur, particularly in children younger than two years or in those with multiple lesions, and can lead to serious complications, including vision loss.<sup>1</sup>

JXG is thought to originate from macrophages derived from dermal dendrocytes.<sup>7</sup> The clinical differential diagnosis includes Spitz nevus, mastocytoma, dermatofibroma, molluscum contagiosum, and malignancy.<sup>8</sup> Biopsy often is necessary to confirm the diagnosis and exclude alternative conditions. Immunohistochemical staining provides additional support: lesional histiocytes are typically positive for CD68, CD163, and CD4, and negative for CD1a, CD207 (langerin), and S100, which helps distinguish JXG from Langerhans cell histiocytosis.<sup>4,9</sup>

In rare cases (<1%), JXG is associated with juvenile myelomonocytic leukemia (JMML) and neurofibromatosis type 1 (NF1).<sup>10</sup> In patients with NF1, the presence of JXG is considered a warning sign for JMML, with a 20- to 30-fold increased risk compared to those with NF1 alone.<sup>10</sup> Although systemic involvement is uncommon, it can result in significant morbidity and, rarely, mortality. Treatment generally is not required, and systemic therapy is reserved for rare cases with visceral involvement affecting vital organ function.<sup>10</sup>

## CONCLUSIONS

This case illustrates a rare histiocytic skin disorder with an unusual lower abdominal presentation and possible early multifocality, which prompted diagnostic biopsy. In infants presenting with an enlarging papule or nodule, JXG should be included in the differential diagnosis, and histologic confirmation should be pursued when the presentation is atypical, or the diagnosis is uncertain. Although most JXG lesions regress spontaneously, shave biopsy can serve both diagnostic and therapeutic purposes. In this case, there was no evidence of ocular or systemic

involvement consistent with the typically benign course of the disease. Caregivers should be counseled regarding the potential for ocular and systemic involvement, particularly in patients with multiple lesions, and the importance of close follow-up should be emphasized.

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## ARTICLE INFORMATION

Received Nov. 6, 2025; Accepted for publication March 2, 2026; Published online Apr. 16, 2026, *Kans J Med* 2026 Mar-Apr; 19:40-42. <https://doi.org/10.17161/kjm.vol19.24768>.

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**Funding Sources:** No funding was utilized in the preparation of this manuscript.

**Conflict of Interest Disclosure:** Brandon R Litzner is Board member of Rural Access Dermatology Society.

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*Keywords:* juvenile xanthogranuloma; lower abdominal lesion; cutaneous nodule; pediatric dermatology; case report

## Critical Appraisal of a Systematic Review Comparing Surgical and Conservative Therapies in Treating Meniscus Root Tears

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**Manuscript Citation:** Hayashi M, Isaji Y, Kurasawa Y, Kitagawa T. Effectiveness of Meniscus Root Tear Repair Versus Conservative Therapy and Adjunct Therapies: A Systematic Review. *Cureus*. 2024 Dec 13;16(12):e75645. PMID: 39803041.<sup>1</sup>

**Type of Investigation:** Systematic review.

**Question:** Meniscus root tears (MRT) can result in knee cartilage damage and osteoarthritis; there are currently several treatment options available in clinical practice. The published study aimed to address the question of which type of management of MRTs results in better quality of life (QOL) and activities of daily living (ADL) scores:

1. Surgical management of MRT (consisting of surgical repair or partial meniscectomy) versus conservative therapy (medications)
2. Conventional physical therapy (PT) versus multimodal therapy (traditional PT plus manual therapy) or adjunct therapies (conventional PT plus electrostimulation/electromyographic feedback)

### METHODS

**Design.** Systematic review of randomized controlled trials (RCT's) and cohort studies on MRT management (surgical or conservative) from various electronic bibliographic databases including PubMed, Ovid, EBSCO and the Physiotherapy Evidence Database in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).<sup>2</sup>

**Population.** The population consisted of both males and females of all ages who had experienced a MRT, from any country, in studies published up to April 22, 2023. Exclusion criteria included osteoarthritis of the knee only, knee cartilage degeneration only, surgery other than MRT repair, and meniscus injury with ligament rupture. A total of 546 patients were included across eight (8) cohort studies and three (3) RCT's, screened from a total of 3,837 articles.

**Intervention/Exposure.** MRT surgical repair.

**Comparator.** Conservative therapies (medication, rehabilitation, physical therapy, exercise, manual therapy, orthotic intervention, aerobic exercise program, injection therapy. Multimodal therapy included manual rehabilitation in addition to exercise therapy.

**Outcome.** The primary outcome was comparison of ADL and QOL scores between surgical and conservative management of MRT's. The secondary outcomes included pain, body mass index (BMI), physical functionality, Kellgren and Lawrence (KL) classifications, and Ahlback classifications. Various scoring systems

and analysis tools were used to assess ADL and QOL among studies before and after treatment. The Knee Injury and Osteoarthritis Outcome Score (KOOS)<sup>3</sup> subscales were calculated for ADL's and QOL comparing surgical intervention versus conservative/conventional therapy, and multimodal versus adjunct therapy from zero up to twenty-four months post-intervention. Both the Lysholm knee scoring scale and Tegner activity score were utilized to assess time-bound differences (zero up to twenty-four months) in QOL and ADLs between surgical versus traditional PT or multimodal therapy. The Newcastle-Ottawa Scale,<sup>4</sup> a star-based rewarding system out of 9, was used to compare the quality of the eight cohort studies.

**Statistical analysis.** The GRADEpro system developed by Cochrane<sup>5</sup> was used to assess the quality of evidence for each study, categorizing it from high to very low certainty. Outcomes compared surgical versus conservative management, as well as conventional versus multinomial therapy, using KOOS subscales for ADLs and QOL. Statistical significance was set at  $p < 0.05$ , with intervention effects reported using 95% confidence intervals. Risk of bias was evaluated using the Cochrane Collaboration's Risk of Bias 2 tool for randomized controlled trials and the Newcastle-Ottawa Scale for cohort studies.

When feasible, meta-analysis was conducted for continuous outcomes (ADL and QOL) using mean differences (MD) or standardized MD, along with 95% confidence intervals, when at least two RCTs were available. Dichotomous outcomes were analyzed using risk ratios with 95% confidence intervals. A random-effects model was applied. Heterogeneity was assessed using the  $I^2$  statistic and  $I^2$ , with  $I^2 > 50\%$  and a  $Q$  statistic  $p$ -value of 0.05 indicating significant heterogeneity. Data analysis was performed using Review Manager software (RevMan 5.4).<sup>6</sup>

**Follow-Up.** There was a vast range of follow-up timing in the studies included in this review. RCT's ranged from one week to two months, whereas cohort studies ranged from three months to four years.

### RESULTS

Both ADL and QOL scores improved with surgical and conservative management. Conservative management demonstrated greater short-term improvements, followed by a plateau over time, whereas surgical management was associated with better long-term outcomes in both KOOS domains (see Figures 3 and 4).

GRADE evaluation of ADL (KOOS subscale) showed a mean score of 84.5 points, with conservative therapy MD of 9.1 points lower than surgical management (95% CI: -22.09 to 3.89). For QOL, the mean KOOS score was 54 points, with conservative therapy showing a MD of 0.5 points lower than surgical management (95% CI: -18.74 to 17.74).

Compared with conventional therapy, multimodal therapy

demonstrated a MD ranging from 1.70 to 2.78 points higher on the KOOS ADL subscale (95% CI: -5.74 to 6.69) and from -1.00 to 1.78 points on the KOOS QOL subscale (95% CI: -13.51 to 6.66).

However, the certainty of evidence across comparisons was very low due to study limitations, including risk of bias, small sample sizes, and short follow-up durations. Therefore, the relative effectiveness of MRT repair surgery, conservative therapy, and multimodal therapy remains inconclusive based on this systematic review.

**Study Conclusion.** The authors conclude that surgical management of MRT is associated with higher ADL and QOL scores compared with conservative management, potentially due to restoration of normal joint mechanics. However, the true effectiveness of these interventions requires evaluation in studies with longer follow-up periods. Short follow-up duration was a key limitation across the three RCTs, which otherwise suggested that both multimodal and adjunct therapies improve ADL and QOL outcomes.

The overall certainty of evidence was low based on GRADE assessments, and the risk of bias, particularly due to lack of blinding of participants and outcome assessors, limits confidence in the findings. As a result, the comparative effectiveness of surgical versus conservative management and conventional physical therapy versus multimodal therapy for MRT remains unclear.

Although the included cohort studies were generally of high quality and may be applicable to broader populations, well-designed RCTs remain the preferred standard. Future studies with larger sample sizes, longer follow-up periods, and lower risk of bias are needed to better inform clinical decision-making.

**Commentary.** The purpose of the systematic review by Hayashi et al.<sup>1</sup> was to evaluate the outcomes of different interventions for MRTs, surgical versus conservative management and conventional versus multimodal physical therapy, on short- and long-term scores. Data were sparse, which limited the ability to conduct robust statistical comparisons. Hayashi et al.<sup>1</sup> presented four forest plots based on two RCTs and one cohort study, all of which yielded inconclusive results, as indicated by confidence intervals overlapping zero (Figures 10-13). Similar findings were reported in the GRADE summaries. Secondary outcomes, such as pain, physical functionality, and body mass index (BMI), were not evaluated.

Although some studies attempted to demonstrate improved outcomes over time (Figures 3-9), many lacked consistent follow-up periods. Research indicates that surgical repair of an MRT requires long-term follow-up to adequately assess outcomes such as osteoarthritis.<sup>7</sup> It is possible that the studies included in the review were not optimally selected or did not adhere strictly to a pre-determined PICOS framework. This could have led to significant heterogeneity in patient populations, interventions, comparators, and study designs (RCT vs. cohort).

Both the interventions (medial or lateral MRTs) and comparator groups (various conservative therapies) encompassed multiple scenarios, further complicating comparisons. Moreover, cohort studies are often susceptible to selection and other biases, whereas randomized trials better control for bias, making direct comparisons between these study types inappropriate.

Overall, the results from the eleven studies included in the systematic review were inconclusive, and most were rated as high risk of bias and/or low quality of evidence. It appears that the research questions and literature search were too broad to be effectively summarized through a systematic review, and additional methodological weaknesses may be revealed with a more rigorous assessment.

**Assessment Instruments.** We used two instruments for critiquing systematic reviews: the PRISMA 2020 checklist<sup>2</sup> and the Critical Appraisal Skills Programme (CASP) checklist<sup>8</sup> to evaluate the study by Hayashi et al.<sup>1</sup> The PRISMA checklist was chosen because the authors reported adherence to this guideline, and it allows verification of whether all checklist items were addressed. Based on this evaluation, we summarize the strengths and weaknesses of the Hayashi et al.<sup>1</sup> study. The completed PRISMA checklist is provided in Appendix A (available online at journals.ku.edu/kjm), along with results from an abbreviated CASP assessment.

**Weaknesses.** Completion of the PRISMA checklist revealed that, while many items were reported, several notable exceptions were identified. The Abstract did not disclose the inclusion/exclusion criteria. PRISMA Item 4 (Objectives) requires an explicit statement, and when evaluating the effects of interventions, it recommends using the Population, Intervention, Comparator, Outcome (PICO) framework or a variant. Hayashi et al.<sup>1</sup> did not apply PICO in the Abstract, nor was it followed in the Introduction section:

*Abstract: This study aimed to compare the effectiveness of MRT repair versus conservative therapy and conservative therapy versus multimodal or adjunct therapy in patients with MRTs.*

*Introduction: This study had two aims: first, to determine the effectiveness of MRT repair versus conservative therapy for patients with MRTs, and second, to assess the effectiveness of conventional versus multimodal or adjunctive therapies in these patients.*

Thus, the outcome was missing from the objectives, and it is unclear what is meant by the term effectiveness.

The Methods section had several deficiencies, including inadequate handling of missing data (Items 10b and 13b) and insufficient detail on methods used to explore possible causes of heterogeneity (Item 13e). Additionally, no information was provided regarding sensitivity analyses (Item 13f). In the Results section, there were omissions related to heterogeneity (item 20c) and risk of bias due to missing data (Item 21). For the Discussion section, limitations of the review process were not reported (Item 23c).

**Strengths.** Although the Objectives lacked explicit PICO elements (Item 4), Hayashi et al.<sup>1</sup> provided detailed eligibility crite-

ria (Item 5). However, the interventions (surgical procedures) and comparators (conservative therapies) spanned a wide range, and the principal outcomes, ADL and QOL, encompassed multiple types of measures. The inclusion of multiple study designs further complicated the analysis. Individually, these elements suggest that a systematic review may not have been ideal due to their breadth; collectively, they cast doubt on whether the research objectives could be adequately addressed with only 11 studies.

Other notable strengths per PRISMA guidelines include items 6-9, where the authors provided sufficient detail to replicate the literature search, included Grey literature and ClinicalTrials.gov, and explained how studies were selected. Risk of bias was appropriately assessed using RoB 2 for RCTs and the Newcastle-Ottawa Scale for cohort studies (Item 11), and certainty of evidence was evaluated using GRADEpro software (Item 12). The GRADE system, a subjective tool by Cochrane, allows stepwise upgrading or downgrading of study quality, with RCTs starting at high quality and non-RCTs at low quality. The PRISMA flow diagram (Item 16a) also was provided, clearly showing study selection for the analysis.

**CASP Assessment.** To further evaluate the evidence presented, we conducted a CASP appraisal of the systematic review. Table 1 presents an abbreviated version of this appraisal (the full version is available in Appendix B at journals.ku.edu/kjm). The CASP assessment highlighted significant weaknesses in the Hayashi et al.<sup>1</sup> article. Of the 10 items evaluated, only two (items 4 and 5) received a "Yes" rating, largely because the included studies were well-summarized in a table that detailed PICO elements, risk of bias, and GRADEpro assessments. All other areas were rated as "No" (5 of 10) or "Can't tell" (3 of 10), underscoring the limitations in the review.

**Limitations.** The studies included in the review were not comparable due to differing PICO elements and inconsistent long-term follow-up, which limited the reliability of the evidence and rendered the results inconclusive. The authors did not directly compare surgical management versus adjunct therapies, despite this being implied by the review's title. Additionally, no

definition of effectiveness was provided for the outcomes, such as cut-off values on the KOOS subscales for QOL and ADLs. Although missing data were evident (see Table 2: Characteristics of included studies), Hayashi et al.<sup>1</sup> did not address this issue.

## CONCLUSIONS

This systematic review included studies with varying sample sizes, follow-up periods, and interventions. While KOOS subscales for ADLs and QOL, along with the GRADE evaluation, suggest potential improvements with surgical management over conservative management and with multimodal therapy over conventional therapy, the results remain inconclusive. Well-designed future studies with explicit objectives, larger sample sizes, standardized and extended follow-up, strict control of confounding variables, and robust statistical analyses are needed to determine the most effective treatment for meniscus root tears.

## COMPLIANCE WITH ETHICAL STANDARDS

All authors declared no financial support or relationships within the last 3 years of completing this work. All authors declared no other relationships or activities that could appear to have influenced this work.

**Table 1. CASP General SR Checklist: Collation of critical appraisal responses.**

Checklist Question	Yes	No	Can't Tell
<b>Is the basic study design valid for a systematic review?</b>			
Did the systematic review address a clearly formulated research question?		x	
Did the researchers search for appropriate study designs to answer the research question?		x	
<b>Is the systematic review methodologically sound?</b>			
Were all relevant primary research studies likely to have been included in the systematic review?			x
Did the researchers assess the validity or methodological rigour of the primary research studies included in the systematic review?	x		
Did the researchers extract, and present information on the individual primary research studies appropriately and transparently?	x		
<b>Are the results of the systematic review trustworthy?</b>			
Did the researchers analyze the pooled results of the individual primary research studies appropriately?		x	
Did the researchers report any limitations of the systematic review and, if so, do the limitations discussed cover all the issues in your critical appraisal?		x	
Would the benefits of intervention outweigh any potential disadvantages, harms and/or additional demand for resources associated with acting on the results?			x
<b>Are the results of the systematic review relevant locally?</b>			
Can the results of the systematic review be applied to your local population/in your local setting or context?			x
If actioned, would the findings from the systematic review represent greater or additional value for the individuals or populations for whom you are responsible?			x

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**ARTICLE INFORMATION**

Received Oct. 30, 2025; Accepted for publication March 10, 2026;  
Published online Apr. 16, 2026, Kans J Med 2026 Mar-Apr; 19:43-46. <https://doi.org/10.17161/kjm.vol19.24720>.

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**Conflict of Interest Disclosure:** None

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**Keywords:** *orthopaedic surgery; meniscus; physical therapy*