

# Comparison of Culture-Negative Adult Knee Septic Arthritis Patients with Culture-Positive Patients

Cafer Özgür Hançerli<sup>1</sup>, Necati Doğan<sup>2</sup>

<sup>1</sup>Department of Orthopedics and Traumatology, Bahçeşehir University Faculty of Medicine, Medical Park Göztepe Hospital, İstanbul, Türkiye

<sup>2</sup>Department of Orthopaedics and Traumatology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

## ABSTRACT

**Objective:** This study aimed to clinically compare patients with culture-negative (CN) adult knee septic arthritis and culture-positive (CP) adult knee septic arthritis patients.

**Materials and Methods:** 51 patients who were operated on with the diagnosis of adult knee septic arthritis between June 2016 and May 2023 were retrospectively examined. While 23 patients with CN were called Group 1, 28 patients with CP were called Group 2. Age, gender, side, C-reactive protein (Crp) value at admission, culture results, hospital stay and follow-up periods were evaluated. In clinical evaluation, knee ROM (range of motion) and visual analog score (VAS) were evaluated.

**Results:** Both groups had similar distributions in terms of age, gender, side and follow-up periods. Group 1's Crp level at admission and total hospital stay were lower than Group 2. ( $p=0.018/p=0.0001$ ) ROM and VAS scores of both groups were similar. No patient developed deep infection.

**Conclusion:** In CN adult knee septic arthritis patients, the average Crp values at the time of admission are lower and the hospital stay is shorter. Clinically, they have similar results to CP patients in terms of ROM and VAS.

**Keywords:** Adult knee septic arthritis, culture negative septic arthritis, culture positive septic arthritis

**How to cite this article:** Hançerli CÖ, Doğan N. Comparison of Culture-Negative Adult Knee Septic Arthritis Patients with Culture-Positive Patients. CM 2024;16(2):118-122

## INTRODUCTION

Septic arthritis is an acute orthopedic joint infection that can be seen in all age groups and requires joint debridement under emergency conditions. Serious joint and cartilage damage occurs in delayed treatments. Prompt diagnosis and joint debridement are necessary to prevent cartilage damage.<sup>[1,2]</sup>

Adult septic arthritis may occur secondary to hematological, immunosuppression, rheumatological diseases or iatrogenic reasons. These patients, who apply to the emergency department with sudden swelling in the joint, inability to step, and limitation of movement, should be diagnosed immediately by joint aspiration and the treatment process should begin.<sup>[3,4]</sup>

The main element of treatment is to give appropriate antibiotic therapy based on the factor to which the microorganism

grown in the culture is sensitive and to monitor its effectiveness with C-reactive protein (Crp).<sup>[5]</sup> In some patients, culture is negative (CN) and the treatment process is observed with broad-spectrum antibiotics for possible factors.

Studies comparing culture-negative and culture-positive (CP) septic arthritis in the literature have been found to be quite limited. For this reason, this study aimed to clinically compare patients with CN adult knee septic arthritis and CP adult knee septic arthritis patients.

## MATERIALS and METHODS

Fifty-one patients who were operated on with the diagnosis of adult knee septic arthritis between June 2016 and May 2023 were retrospectively examined after local ethics committee approval was obtained. Ethics committee date and topic



**Address for Correspondence:** Necati Doğan, Department of Orthopaedics and Traumatology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

**E-mail:** drnecatidogan@gmail.com **ORCID ID:** 0000-0001-9503-5676

**Received date:** 13.02.2024

**Revised date:** 14.02.2024

**Accepted date:** 26.02.2024

**Online date:** 18.04.2024



number: (Date: 12.07.2023) (KAEK/2023.07.87). The study was conducted in accordance with the Declaration of Helsinki.

Only adult patients over the age of 18 and monoarticular involvements were included in the study. Late admissions to the emergency department, neglected septic arthritis, iatrogenic cases, and septic arthritis secondary to underlying diseases (inflammatory, etc.) were not included in the study.

While 23 patients with CN were called Group 1, 28 patients with CP were called Group 2.

Joint aspiration is performed immediately for patients presenting to the emergency department after a clinical indication is established according to the Kocher criteria. The aspiration material is sent to the laboratory for cell counting, gram staining and culture. If the cell count is  $>50,000$  leukocytes and  $>75\%$  PNL, the diagnosis of septic arthritis is confirmed and they are operated on under emergency conditions. The joint is abundantly washed and debrided through a mini-open lateral incision.<sup>[5]</sup>

After the surgery, appropriate broad-spectrum antibiotic therapy is initiated by consulting an infection doctor. Once the culture result becomes clear within an average of 3 days, antibiotics sensitive to the agent are applied with the recommendation of the infection doctor. Broad-spectrum antibiotics are continued for CN patients. Crp monitoring of the patients is done daily, and when the patient's current clinical condition improves and Crp becomes negative, the patient is discharged with oral antibiotic therapy after obtaining the opinion of the infection doctor. Oral antibiotic therapy is completed in 6 weeks. Joint exercises are started immediately after discharge. Full weight bearing is also allowed immediately after the edema and pain subside.

### Data Collection

Age, gender, side, C-reactive protein (Crp) value at admission, culture results, hospital stay and follow-up periods were evaluated. In clinical evaluation, knee ROM (range of motion) and visual analog score (VAS) were evaluated.

### Statistical Analysis

IBM SPSS Statistics 26 (IBM, Chicago, IL, USA) program was used for statistical analysis. Descriptive statistics (mean, standard deviation, median, frequency, ratio, range) and data distribution were evaluated using the Shapiro-Wilk test. Students' t-tests were used to compare the data distributed between the two groups. The statistical significance level was determined as  $p < 0.05$  in all analyses.

## RESULTS

While the number of Group 1 patients was 23, the number of Group 2 patients was 28. While the average age in Group 1 was 61, it was 57.9 in Group 2. While the female-male sex ratio was 1.3 in Group 1, it was 1 in Group 2. In terms of the infected knee side, the right/left ratio was 1.09 in Group 1 and 0.75 in Group 2. In terms of follow-up periods, the average follow-up period in Group 1 was 43.3 months, while in Group 2 it was 46.2 months. Both groups had similar distributions in terms of age, gender, side and follow-up periods ( $p > 0.5$ ) (Table 1).

In Group 2, 18 patients developed methicillin-sensitive staph aureus (Mssa), 6 patients developed methicillin-resistant staph aureus (Mrsa), 2 patients developed escherichia coli (E. coli) and 2 patients developed enterobacter.

When the Crp values at admission were compared, the average Crp value of Group 1 was 210.43, while it was 267.85 in Group 2. The average Crp level of Group 1 at the time of admission was significantly lower than that of Group 2 ( $p = 0.018$ ). When we compare it according to the total hospital stay, the average hospital stay in Group 1 was 10.9 days, while it was 23.5 days in Group 2. The average total hospital stay in Group 1 was significantly lower than in Group 2 ( $p = 0.0001$ ) (Table 1).

In clinical evaluation, when we evaluated in terms of knee ROM, the average knee ROM in Group 1 was 117 degrees, while it was 120 degrees in Group 2. In the VAS evaluation, Group 1 was 2.78 points, while Group 2 was 3.14 points. No significant difference was detected in terms of ROM and VAS scores of both groups ( $p > 0.5$ ) (Table 1).

No patient developed deep infection or other possible complications.

## DISCUSSION

In this study, we revealed that the Crp values at the time of admission and the total hospitalization duration of adult CN knee septic arthritis patients were lower compared to CP patients, and their clinical outcomes were similar.

Studies on CN septic arthritis are quite limited. In a pediatric hip septic arthritis study in the literature,<sup>[6]</sup> pediatric patients with CN hip septic arthritis were compared with CP pediatric patients, and it was claimed that the clinical outcomes of CN patients caused similar sequelae to CP patients. They also recommended that patients who are clinically compatible with septic arthritis should be treated in the acute phase, even if they have CN. In another study

**Table 1. Demographic data of all patients and parameters that are followed**

	<b>Culture-negative (Group 1) n=23</b>	<b>Culture-positive (Group 2) n=28</b>	<b>p</b>
Age			
Avg±SD	61.08±16.43	57.92±11.38	0.439
Min-max	21–86	29–72	
Gender			
Male	10	14	0.65
Female	13	14	
Side			
Right	12	12	0.517
Left	11	16	
CRP value at admission			
Avg±SD	210.43±93.55	267.85±96.17	0.018*
Min-max	25–361	78–393	
Culture results			
Mssa	0	18	–
Mrsa	0	6	
<i>E. coli</i>	0	2	
<i>Enterobacter</i>	0	2	
Hospital stay			
Avg±SD	10.91±8.16	23.5±14.53	0.0001*
Min-max	4–31	5–55	
Follow-up time (months)			
Avg±SD	43.3±23.65	46.28±21.09	0.64
Min-max	12–96	12–84	
Range of motion			
Avg±SD	117.82±20.87	120±20.36	0.71
Min-max	90–150	90–150	
Visual analog score			
Avg±SD	2.78±2.08	3.14±2.17	0.55
Min-max	0–6	0–7	

\*: p<0.05. Avg: Average; SD: Standard deviation; CRP: C-reactive protein

reporting the results of CN pediatric septic arthritis,<sup>[7]</sup> although the results were not bad, the need for different diagnostic tests for etiological research was emphasized. In another similar study,<sup>[8]</sup> they stated that failure to identify the causative agent in pediatric septic arthritis cannot exclude the diagnosis of septic arthritis, and therefore broad-spectrum antibiotics should be used. While the sequelae caused by septic arthritis in adult patients mostly concern the relevant joint, in pediatric patients it is more important as it paves the way for different complications such as growth defects, deformity, septicemia and contracture.

In a similar study conducted in adults,<sup>[9]</sup> it is claimed that the results of patients with CN septic arthritis are better than those with CP and the severity of the disease is less. In another study conducted in adults,<sup>[10]</sup> adult patients with septic arthritis were evaluated and they found that 50 percent of the patients did not reproduce. At the same time, the results of all patients diagnosed with septic arthritis were evaluated and they claimed that good results could be achieved even with more standard treatments instead of broad spectrum. In our study, it was revealed that the clinical results were similar to these studies and

that the CN group had a lower course in terms of admission Crp and hospital stay.

Some studies also claim that the effect of bacterial isolation on the outcome of septic arthritis is low.<sup>[11]</sup> Even if CN is present, the treatment process can be provided without any problems with empirical antibiotics.

We see that CN-CP results are widely discussed in adult patients, especially in prosthetic infections. There are hesitations in deciding whether to treat these implant-related infections with one-stage or two-stage treatment. In a study that claimed that the outcomes of CN patients were similar to CP patients in two-stage treatments, differences in terms of complications were suggested.<sup>[12]</sup> Another study suggests the success of single-stage treatment in CN patients. Although a new prosthesis should not be placed until the eradication of the infection is proven, they claim that this option can be successfully applied in patients who do not have the opportunity for more than one surgery.<sup>[13]</sup> In another study, one-stage and two-stage revisions of chronic CN patients were compared and it was revealed that they had similar results.<sup>[14]</sup> The eradication of CN periprosthetic infections seems to be more manageable compared to CPs, as single-stage revisions are satisfactory. Similarly, in our study, it was determined that the results of adult septic arthritis were similar and good, although those with CN were managed like CP. Based on these results, we can put forward two different hypotheses. The first of these is to carry out further examinations to clarify the diagnosis and reveal the infectious agent before starting treatment in case of over-indication surgery in CN patients. The second is that the results may be good if CN patients are managed as if they do not have any infectious agents. We believe that these hypotheses should also be tested in future studies.

Different methods have been suggested to diagnose CN patients or to reveal the causative agent. Techniques such as sequence analysis,<sup>[15,16]</sup> synovial fluid analysis and serum neutrophil-lymphocyte ratios<sup>[17]</sup> or biopsy<sup>[18]</sup> have been suggested. While some of these studies will be concluded late, some have a rapid implementation area. However, since the diagnosis of septic arthritis is made clinically and the treatment is urgent debridement, the contribution of late examinations will be low. However, identifying the etiological factor will enable empiric antibiotic therapy to be replaced with agent-specific antibiotics. This antibiotic therapy change may especially reduce the use of unnecessary broad-spectrum antibiotics.

### Limitations of the Study

Since the study was retrospective, many meaningful clinical and laboratory parameters could not be evaluated. There

is an obvious need for prospective, randomized and multi-center studies on this subject, which has very limited evaluations. We recommend that future researchers addressing this issue determine their study level in this way.

## CONCLUSION

In CN adult knee septic arthritis patients, the average Crp values at the time of admission are lower and the hospital stay is shorter. Clinically, they have similar results to CP patients in terms of ROM and VAS.

### Disclosures

**Ethics Committee Approval:** The study was approved by the Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (No: 2023.07.87, Date:12/07/2023).

**Authorship Contributions:** Concept: C.Ö.H, N.D.; Design: C.Ö.H, N.D.; Supervision: C.Ö.H, N.D.; Funding: C.Ö.H, N.D.; Materials: C.Ö.H, N.D.; Data Collection or Processing: C.Ö.H, N.D.; Analysis or Interpretation: C.Ö.H, N.D.; Literature Search: C.Ö.H, N.D.; Writing: C.Ö.H, N.D.; Critical review: C.Ö.H, N.D.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Informed Consent:** Written informed consent was obtained from all patients.

**Use of AI for Writing Assistance:** Not declared.

**Financial Disclosure:** The authors declared that this study received no financial support.

**Peer-review:** Externally peer reviewed.

## REFERENCES

- Sadowski CM, Gabay C. Septic arthritis. *Rev Med Suisse* [Article in French] 2006;2:702–8. [\[CrossRef\]](#)
- Shulman G, Waugh TR. Acute bacterial arthritis in the adult. *Orthop Rev* 1988;17:955–60.
- Esterhai JL Jr, Gelb I. Adult septic arthritis. *Orthop Clin North Am* 1991;22:503–14. [\[CrossRef\]](#)
- Ross JJ. Septic arthritis of native joints. *Infect Dis Clin North Am* 2017;31:203–18. [\[CrossRef\]](#)
- Horowitz DL, Katzap E, Horowitz S, Barilla-LaBarca ML. Approach to septic arthritis. *Am Fam Physician* 2011;84:653–60.
- Feng W, Yao Z, Liu H, Zhu D, Song B, Wang Q. Clinical characteristics of and risk factors for poor outcomes in children with bacterial culture-negative septic arthritis of the hip. *J Orthop Sci* 2023 Aug 17. doi: 10.1016/j.jos.2023.08.009. [\[Epub ahead of print\]](#). [\[CrossRef\]](#)
- Spyridakis E, Gerber JS, Schriver E, Grundmeier RW, Porsch EA, St Geme JW, et al. Clinical features and outcomes of children with culture-negative septic arthritis. *J Pediatric Infect Dis Soc* 2019;8:228–34. [\[CrossRef\]](#)
- Özcan Ç, Çamur S, Shatat KMI, Kemah B, Söylemez MS, Sağlam

- N. Comparison of clinical features and serum parameters of culture-positive children with culture-negative children in septic arthritis and acute osteomyelitis. *Acta Chir Orthop Traumatol Cech* 2021;88:131–6. [\[CrossRef\]](#)
9. Paz Z, Fowler ML, Zhu C, Lieber SB, Moore A, Shmerling RH. Patients with surgically treated culture-negative native joint septic arthritis have less severe disease and better outcomes. *Infect Dis (Lond)* 2020;52:713–20. [\[CrossRef\]](#)
  10. Cipriano A, Santos FV, Dias R, Carvalho A, Reis E, Pereira C, et al. Adult native joint septic arthritis: a nine-year retrospective analysis in a Portuguese university hospital. *Acta Med Port* 2021;34:826–32. [\[CrossRef\]](#)
  11. Malipeddi R, Nema SK, Gopisankar B, Prabu M, Pasupathy P, Suresh Gandhi B. Clinical outcomes and global health after joint debridement in adult-onset septic arthritis: a prospective observational study. *Indian J Orthop* 2021;55:912–7. [\[CrossRef\]](#)
  12. Xu Z, Huang C, Lin Y, Chen Y, Fang X, Huang Z, et al. Clinical outcomes of culture-negative and culture-positive periprosthetic joint infection: similar success rate, different incidence of complications. *Orthop Surg* 2022;14:1420–7. [\[CrossRef\]](#)
  13. Zanna L, Sangaletti R, Lausmann C, Gehrke T, Citak M. Successful eradication rate following one-stage septic knee and hip exchange in selected pre-operative culture-negative periprosthetic joint infections. *Int Orthop* 2023;47:659–66. [\[CrossRef\]](#)
  14. van den Kieboom J, Tirumala V, Box H, Oganessian R, Klemt C, Kwon YM. One-stage revision is as effective as two-stage revision for chronic culture-negative periprosthetic joint infection after total hip and knee arthroplasty. *Bone Joint J* 2021;103:515–21. [\[CrossRef\]](#)
  15. Kullar R, Chisari E, Snyder J, Cooper C, Parvizi J, Sniffen J. Next-generation sequencing supports targeted antibiotic treatment for culture negative orthopedic infections. *Clin Infect Dis* 2023;76:359–64. [\[CrossRef\]](#)
  16. Goswami K, Clarkson S, Phillips CD, Dennis DA, Klatt BA, O'Malley MJ, et al; Orthopedic Genomics Workgroup. An enhanced understanding of culture-negative periprosthetic joint infection with next-generation sequencing: a multicenter study. *J Bone Joint Surg Am* 2022;104:1523–9.
  17. Varady NH, Schwab PE, Kheir MM, Dilley JE, Bedair H, Chen AF. Synovial fluid and serum neutrophil-to-lymphocyte ratio: novel biomarkers for the diagnosis and prognosis of native septic arthritis in adults. *J Bone Joint Surg Am* 2022;104:1516–22. [\[CrossRef\]](#)
  18. Soroosh SG, Ghatfan A, Farbod A, Meftah E. Synovial biopsy for establishing a definite diagnosis in undifferentiated chronic knee monoarthritis. *BMC Musculoskelet Disord* 2023;24:23. [\[CrossRef\]](#)