

EBJIS guideline Workgroup 7: SANJO after ACL reconstruction

ESSKA & EBJIS recommendations for the management of infections after anterior cruciate ligament reconstruction (ACL-R)

Nora Renz (MD)^{1,2}, Tomislav Madjaravic (MD)³, Matteo Ferrari (MD, PhD)⁴, and Daniel Pérez-Prieto (MD, PhD)^{5,6}

- 1. Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Center for Musculoskeletal Surgery (CMSC), Berlin, Germany*
- 2. Department of Infectious Diseases, Bern University Hospital, University of Bern, Bern, Switzerland*
- 3. Department of Orthopaedic Surgery Lovran, University of Rijeka, Rijeka, Croatia*
- 4. Department of Internal Medicine, IRCCS Ospedale Galeazzi Sant'Ambrogio, Milano, Italy*
- 5. Department of Traumatology and Orthopaedic Surgery. Hospital del Mar – Universitat Autònoma de Barcelona (UAB).*
- 6. Catalan Institute for Traumatology and Sports Medicine (ICATME), Hospital Universitari Dexeus. – Universitat Autònoma de Barcelona (UAB).*

DIAGNOSIS

- **What are the clinical signs and symptoms that should raise suspicion of infection after ACL-R?**

The signs and symptoms suggestive of infection are often subtle and may be difficult to distinguish from the normal healing process after ACL-R. Increasing or persistent knee pain, tenderness upon slight percussion of the joint, recurrent or persistent knee effusion and systemic symptoms such as fever ($> 38.3^{\circ}\text{C}$), chills and malaise should call for further investigation¹⁻³. However, they are not specific and may also occur in noninfected patients with a large hematoma. Delayed range of motion (ROM) recovery, increased difficulties with physical therapy, increased warmth or swelling, drainage from the incision site/portals (most commonly affected is the tibial tunnel) or any untoward event are suggestive but not specific for infection^{1,4,5}.

The challenge of late and delayed infection is the indolent presentation of microbial biofilms involving pathogens of low virulence and hence low-grade inflammation¹. In chronic infection, arthrofibrosis after ACL-R is highly suggestive for infection⁶.

Purulent secretion, a sinus tract or intraoperative detection of intraarticular pus are confirmative signs of infection⁷.

Suggestive signs and symptoms are delayed ROM recovery, increased warmth or swelling, wound drainage and arthrofibrosis as well as unusual pain and systemic symptoms such as fever and malaise. Confirmative signs are purulent discharge/aspirate, sinus tract communication with the joint and intraoperative intraarticular pus.

SURGICAL TREATMENT

- **Is surgical treatment necessary for an infection after ACL-R? Which type of surgery is called for?**

The key aims in the management of infection after ACL-R are successful infection clearing and the complete functional recovery of the knee joint⁸⁻¹⁰. There are no prospective randomized controlled trials that compare surgical and conservative treatment for infection after ACL-R. Indeed, there are studies on native septic arthritis that showed no differences between needle aspiration and surgical debridement¹¹. However, the primary endpoint of these studies was infection cure without any assessment of functional outcomes or cartilage damage^{11,12}.

Despite the lack of evidence, the present group recommends arthroscopic debridement for the following reasons:

- Surgical treatment is necessary to wash out proteolytic enzymes and toxins which cause chondrocyte degeneration^{13,14}.
- Prompt evacuation of the joint by means of arthroscopic revision reduces the bacterial load and intraarticular pressure³.
- Arthroscopy allows for cartilage evaluation in accordance with the Gächter classification and the evaluation of graft stability and viability^{15,16}.
- Compared to open surgery, arthroscopy has proven to be less invasive and facilitates a faster recovery, without compromising the cure rate¹⁷.

However, open debridement is indicated in cases when there is subchondral bone involvement (Gächter IV)^{15,16}.

<i>Clinical staging (Gächter classification)</i>	<i>Intraoperative (arthroscopic) spread of inflammatory process</i>
<i>Stage 1</i>	<i>Turbid effusion, hyperemic synovia</i>
<i>Stage 2</i>	<i>Purulent effusion, fibrinous appositions, hypertrophic synovia</i>
<i>Stage 3</i>	<i>Synovial adhesion, necrotic areas of synovia and cartilage</i>
<i>Stage 4</i>	<i>Cartilage necrosis, bone erosion, osteolysis</i>

Although there are reports of successful treatment with percutaneous drainage or bedside arthrocentesis, this surgical alternative is reserved for selected cases which are not suited to surgery. These less invasive methods are considered inferior as removal of infection residue and mediators is insufficient.

We recommend performing arthroscopic debridement in combination with antibiotic therapy as the primary therapeutic option in every patient. In the rare case of inoperability, repeated needle aspiration might be an alternative.

- **How many arthroscopic procedures should be performed?**

Wang et al. reported that 60% of the patients were successfully treated with a single arthroscopic debridement. Repeated debridement was carried out because of persistent clinical symptoms, fever or increased C-reactive protein (CRP) levels¹⁸. According to several studies, another arthroscopic debridement should be performed in case of persistent septic arthritis with no positive evolution of clinical (i.e. local inflammatory changes, persistent wound drainage, fever) and laboratory (i.e. persistent or secondarily increased CRP) signs^{17,19}. Binnet et al. showed that an average of 2.66 procedures was required to eradicate infection²⁰. In previous reports, the graft along with its original fixation material remained in place when the graft was considered functional and did not block knee

motion²¹. Indeed, several reports have shown that about 4 out of ACL grafts can be successfully salvaged with multiple debridement procedures²². However, Vertullo et al. suggest that a failure to see improvement after 2 arthroscopic irrigations implies that the bacteria have formed a biofilm and the graft is non-viable or that osteomyelitis has also involved the femoral tunnel²³. Calvo et al. repeated joint lavage several times¹⁹. After the third lavage, the graft and implants were removed because of a persistent clinical infection, macroscopic graft damage and elevated inflammation parameters. However, those patients had presented more than one week after infection started. In cases with persistent infection, magnetic resonance imaging should be considered to evaluate the possible involvement of the tunnels and to detect cavities or abscess formation²⁴.

McAllister et al. were able to retain the graft by managing persistent infections with two to four subsequent debridement procedures, but all four patients developed degenerative changes at a mean of 36 months²¹. One factor that is crucial for graft viability is an early diagnosis since patients diagnosed after 7 days from the onset of symptoms had a higher graft removal rate^{18,25}. Delayed treatment might weaken the graft, delay integration or lead to insufficiency²⁶.

Scheduled debridement should not be performed in patients with a favorable course after the first debridement.

Additional debridement is indicated if the clinical course is not favorable. Unfavorable determinants include increasing pain, fever or persistent or secondarily increased CRP without any other explanation (e.g., nosocomial infection), a persistent discharge from the portal or persistent local signs of inflammation. In cases with an uneventful course, repeated arthroscopic debridement is not needed. If the course is not adequate after the 3rd debridement, graft and hardware removal should be considered. MRI may help identifying the cause of persistent infection in those cases.

- **When can the new ACL-R be performed in cases of graft and hardware removal?**

Based on the available evidence of PJI and native septic arthritis, a new graft can be reconstructed after 6 weeks if the following considerations are fulfilled²⁷:

- No bone involvement (no osteomyelitis)
- Good clinical evolution
- Decreasing CRP (no need to be normal)
- No difficult-to-treat infections caused by a microorganism that is resistant to biofilm-active antibiotics

In the case of a new ACL-R, tissue cultures from the synovial membrane and bone tunnels must be obtained during surgery. Histopathology of the tunnels might be of help in ruling out osteomyelitis.

Keeping patients under antibiotics until the results of intraoperative diagnostics are available is recommended.

If these requirements are not met, the new ACL-R must be delayed, either after additional debridement procedures or when the prolonged antibiotic treatment (i.e. osteomyelitis treatment) is completed.

We recommend that graft reimplantation be performed after 6 weeks in selected cases in cases of graft and hardware removal.

SYSTEMIC ANTIMICROBIAL TREATMENT

- **What is the optimal treatment duration for ACL-R-infections?**

There is a controversy regarding the duration of antibiotic treatment and when to switch from intravenous to oral therapy. There are no randomized controlled studies addressing this issue. In native septic arthritis, the duration of antimicrobial treatment depends on the organism isolated and the clinical response to the chosen antibiotic. The duration of treatment is generally 2 to 6 weeks²⁸. In infections after ACL-R, it was 2 to 12 weeks in previously published case series^{3,18,29}. Intravenous treatment was given for 5 days to 6 weeks^{3,22,29}. In most reports, an adequate clinical response and a decrease in CRP are prerequisite for a switch to oral treatment or discontinuation of antibiotics^{1,10,18,22}. Overall, antibiotic treatment is maintained for a minimum of 4 to 6 weeks^{1-4,30}. In a recent study, a good clinical outcome was seen with oral treatment started at a mean of 5 days (range, 4–7) after surgery and a total antibiotic treatment lasting an average of six weeks²⁹. Recent landmark studies corroborated the trend towards shorter i.v. treatment durations in severe infections such as bone and joint infections and infective endocarditis^{31,32}.

A 1-week (up to 2 weeks) i.v. treatment regimen is suggested. It should be followed by oral treatment for another 4 to 5 weeks. It would be preferable to do it with bactericidal agents with good bioavailability and bone penetration as well as biofilm-activity if avascular tissue and fixation devices are in situ. The conditions for switching to an oral treatment are a good clinical response with a decrease in local inflammatory signs and CRP trending towards normal values.

We suggest a 1 week (up to 2 weeks) of intravenous treatment followed by oral treatment for another 4-5 weeks, preferably with bactericidal agents with good bioavailability and bone penetration as well as biofilm-activity if avascular tissue and fixation devices are in situ. The conditions for switching to oral treatment are a good clinical response with nearly normal CRP values.

Reference

1. **Mouzopoulos G, Fotopoulos VC, Tzurbakis M.** Septic knee arthritis following ACL reconstruction: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2009;17(9):1033–1042.
2. **Musso AD, McCormack RG.** *Infection after ACL reconstruction: what happens when cultures are negative? Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine.* 2005.
3. **Torres-Claramunt R, Gelber P, Pelfort X, Hinarejos P, Leal-Blanquet J, Pérez-Prieto D, et al.** Managing septic arthritis after knee ligament reconstruction. *Int Orthop* 2016;40(3):607–614.
4. **Bauer T, Boisrenoult P, Jenny JY.** Post-arthroscopy septic arthritis: Current data and practical recommendations. *Orthopaedics & traumatology, surgery & research : OTSR* 2015;101(8 Suppl).
5. **Cadet ER, Makhni EC, Mehran N, Schulz BM.** Management of septic arthritis following anterior cruciate ligament reconstruction: a review of current practices and recommendations. *J Am Acad Orthop Surg* 2013;21(11):647–656.
6. **Gobbi A, Karnatzikos G, Chaurasia S, Abhishek M, Bulgherhoni E, Lane J.** Postoperative Infection After Anterior Cruciate Ligament Reconstruction. *Sports Health* 2016;8(2):187–189.
7. **Torres-Claramunt R, Pelfort X, Erquicia J, Gil-Gonzalez S, Gelber PE, Puig L, et al.** Knee joint infection after ACL reconstruction: prevalence, management and functional outcomes. *Knee Surg Sports Traumatol Arthrosc* 2013;21(12):2844–2849.
8. **Indelli PF, Dillingham M, Fanton G, Schurman DJ.** Septic arthritis in postoperative anterior cruciate ligament reconstruction. *Clin Orthop Relat Res* 2002;(398):182–188.
9. **Judd D, Bottoni C, Kim D, Burke M, Hooker S.** Infections following arthroscopic anterior cruciate ligament reconstruction. *Arthroscopy* 2006;22(4):375–384.
10. **Van Tongel A, Stuyck J, Bellemans J, Vandenuecker H.** Septic arthritis after arthroscopic anterior cruciate ligament reconstruction: a retrospective analysis of incidence, management and outcome. *Am J Sports Med* 2007;35(7):1059–1063.
11. **Manadan AM, Block JA.** Daily needle aspiration versus surgical lavage for the treatment of bacterial septic arthritis in adults. *Am J Ther* 2004;11(5):412–415.
12. **Ravindran V, Logan I, Bourke BE.** Medical vs surgical treatment for the native joint in septic arthritis: a 6-year, single UK academic centre experience. *Rheumatology (Oxford)* 2009;48(10):1320–1322.
13. **Schollin-Borg M, Michaëlsson K, Rahme H.** Presentation, outcome, and cause of septic arthritis after anterior cruciate ligament reconstruction: a case control study. *Arthroscopy* 2003;19(9):941–947.
14. **Smith RL, Schurman DJ, Kajiya G, Mell M, Gilkerson E.** The effect of antibiotics on the destruction of cartilage in experimental infectious arthritis. *J Bone Joint Surg Am* 1987;69(7):1063–1068.

15. **Stutz G, Gächter A.** [Diagnosis and stage-related therapy of joint infections]. *Unfallchirurg* 2001;104(8):682–686.
16. **Stutz G, Kuster MS, Kleinstück F, Gächter A.** Arthroscopic management of septic arthritis: stages of infection and results. *Knee Surg Sports Traumatol Arthrosc* 2000;8(5):270–274.
17. **Peres LR, Marchitto RO, Pereira GS, Yoshino FS, Castro Fernandes M de, Matsumoto MH.** Arthrotomy versus arthroscopy in the treatment of septic arthritis of the knee in adults: a randomized clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2016;24(10):3155–3162.
18. **Wang C, Ao Y, Wang J, Hu Y, Cui G, Yu J.** Septic arthritis after arthroscopic anterior cruciate ligament reconstruction: a retrospective analysis of incidence, presentation, treatment, and cause. *Arthroscopy* 2009;25(3):243–249.
19. **Calvo R, Figueroa D, Anastasiadis Z, Vaisman A, Olid A, Gili F, et al.** Septic arthritis in ACL reconstruction surgery with hamstring autografts. Eleven years of experience. *Knee* 2014;21(3):717–720.
20. **Binnet MS, Başarir K.** Risk and outcome of infection after different arthroscopic anterior cruciate ligament reconstruction techniques. *Arthroscopy* 2007;23(8):862–868.
21. **McAllister DR, Parker RD, Cooper AE, Recht MP, Abate J.** Outcomes of postoperative septic arthritis after anterior cruciate ligament reconstruction. *Am J Sports Med* 1999;27(5):562–570.
22. **Abdel-Aziz A, Radwan YA, Rizk A.** Multiple arthroscopic debridement and graft retention in septic knee arthritis after ACL reconstruction: a prospective case-control study. *Int Orthop* 2014;38(1):73–82.
23. **Vertullo CJ, Quick M, Jones A, Grayson JE.** A surgical technique using presoaked vancomycin hamstring grafts to decrease the risk of infection after anterior cruciate ligament reconstruction. *Arthroscopy* 2012;28(3):337–342.
24. **Pogorzelski J, Themessl A, Achtnich A, Fritz EM, Wörtler K, Imhoff AB, et al.** Septic Arthritis After Anterior Cruciate Ligament Reconstruction: How Important Is Graft Salvage? *Am J Sports Med* 2018;46(10):2376–2383.
25. **Saper M, Stephenson K, Heisey M.** Arthroscopic irrigation and debridement in the treatment of septic arthritis after anterior cruciate ligament reconstruction. *Arthroscopy* 2014;30(6):747–754.
26. **Schuster P, Schlumberger M, Mayer P, Raoulis VA, Oremek D, Eichinger M, et al.** Lower incidence of post-operative septic arthritis following revision anterior cruciate ligament reconstruction with quadriceps tendon compared to hamstring tendons. *Knee Surg Sports Traumatol Arthrosc* 2020;
27. **Zimmerli W, Trampuz A, Ochsner PE.** Prosthetic-joint infections. *N Engl J Med* 2004;351(16):1645–1654.
28. **Conen A, Borens O.** Septic Arthritis. In: Kates SL, Davos BO, eds. *Principles of Orthopedic Infection Management*. edn. Switzerland: AO Publishing, 2016:213–226.
29. **Pérez-Prieto D, Trampuz A, Torres-Claramunt R, Eugenia Portillo M, Puig-Verdié L, Monllau JC.** Infections after Anterior Cruciate Ligament Reconstruction: Which Antibiotic after Arthroscopic Debridement? *J Knee Surg* 2017;30(4):309–313.

30. **Williams RJ, Laurencin CT, Warren RF, Speciale AC, Brause BD, O'Brien S.** Septic arthritis after arthroscopic anterior cruciate ligament reconstruction. Diagnosis and management. *Am J Sports Med* 1997;25(2):261–267.
31. **Iversen K, Ihlemann N, Gill SU, Madsen T, Elming H, Jensen KT, et al.** Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis. *The New England journal of medicine* 2019;380(5):415–424.
32. **Li HK, Rombach I, Zambellas R, Walker AS, McNally MA, Atkins BL, et al.** Oral versus Intravenous Antibiotics for Bone and Joint Infection. *The New England journal of medicine* 2019;380(5):425–436.