Knee Surgery, Sports Traumatology, Arthroscopy (2020) 28:1154–1158
https://doi.org/10.1007/s00167-019-05820-9

KNEE

Soaking of autografts in vancomycin is highly effective in preventing postoperative septic arthritis after revision anterior cruciate ligament reconstruction

Philipp Schuster[1,2] · Michael Schlumberger[1,3] · Philipp Mayer[1] · Martin Eichinger[1,3] · Markus Geßlein[2] · Jörg Richter[1]

Received: 12 August 2019 / Accepted: 27 November 2019 / Published online: 3 December 2019

Abstract

Purpose To determine and compare the incidence of postoperative septic arthritis following revision anterior cruciate ligament reconstruction (R-ACLR) with and without soaking of the graft in vancomycin solution prior to implantation in a large single-centre series.

Methods A total of 2155 isolated R-ACLR with autologous tendons were performed from 2004 to 2019 and were reviewed with regard to the occurrence of postoperative septic arthritis. From February 2017 onwards, all grafts were wrapped in a vancomycin-soaked (5 mg/ml) gauze swab between harvest and implantation (517 patients, treatment group (2), prospectively followed). These were compared to 1638 patients before that date (control group (1), retrospectively evaluated). The technique of R-ACLR did not significantly change during the years of the study. Hamstring tendons were used in 1310 patients (60.8%) and quadriceps tendons with patellar bone block were used in 845 patients (39.2%), respectively, with no difference between the groups (n.s.). Routine follow-up examination was performed 6 weeks postoperatively (follow-up rate 96.5%), and patients with no treatment for septic arthritis until that time were classified as non-infected.

Results There were 14 cases of postoperative septic arthritis in group 1 (incidence 0.9%), and none in group 2 (incidence 0.0%), respectively. The difference was significant ($p = 0.029$).

Conclusion Soaking of the graft in vancomycin solution prior to implantation dramatically reduces the incidence of postoperative septic arthritis in R-ACLR.

Level of evidence III.

Keywords Infection · ACL · Anterior cruciate ligament · Septic arthritis · Complication · Prevention · Antibiotics · Vancomycin · Local · Revision · Failure · Arthroscopy

Introduction

Septic arthritis following anterior cruciate ligament reconstruction (ACLR) has a reported incidence rate between 0.14 and 1.8% [11, 14, 21, 24, 25, 27]. Beside individual patient-specific factors such as diabetes, tobacco use and increased comorbidity, a longer operation time, higher complexity of the procedure and preceding surgical procedures have been reported to generally increase the risk for postoperative infection [3, 7, 12]. It has been shown that revision anterior cruciate ligament reconstruction (R-ACLR) generally has a higher incidence of postoperative septic arthritis compared to primary ACLR with a reported odds ratio of 2.5 [12, 21]. Although good results for the treatment of this complication with arthroscopic irrigation and debridement have been

Investigation performed at the Centre for Sports Orthopedics and special joint surgery, Orthopedic Hospital Markgroeningen, Germany.

✉ Philipp Schuster
philipp_schuster@gmx.de

[1] Centre for Arthroscopy and Special Joint Surgery, Orthopedic Hospital Markgroeningen, Kurt-Lindemann-Weg 10, 71706 Markgroeningen, Germany

[2] Department of Orthopedics and Traumatology, Paracelsus Medical Private University, Clinic Nuremberg, Nuremberg, Germany

[3] Department of Trauma Surgery, Medical University Innsbruck, Innsbruck, Austria

reported, there is a need for the prevention of this complication [5, 21, 27].

Recently, it has been shown that the soaking of the graft in vancomycin solution effectively prevents postoperative septic arthritis following primary ACLR [15, 17, 18, 26]. To date, no data are available if this technique is also comparably effective in R-ACLR.

Therefore, the purpose of this study was to determine the incidence rate of septic arthritis following R-ACLR with and without pre-soaking of the graft in vancomycin solution in a large single-centre series. The hypothesis was that local vancomycin treatment effectively reduces the incidence rate of this complication.

Materials and methods

A total of 2155 revision ACLR were performed in a 15-year period from 2004 to 2019, with multi-ligament reconstructions and allografts excluded. From February 2017 onwards, the grafts were pre-soaked in vancomycin solution after harvest and before implantation. There were 1638 patients in group I (controls, no vancomycin treatment), and 517 patients in group II (treatment group, vancomycin-treated). The control group was analysed retrospectively and the treatment group was prospectively followed. Medical charts of all patients were reviewed by a database search whether there was a readmission at any time postoperatively. All patients with readmission were manually reviewed with focus on the occurrence of septic arthritis. In 50 consecutive patients of group II, the period of soaking (from the end of preparation until implantation) was obtained.

Routine follow-up examinations after revision ACLR reconstructions were scheduled at 6 weeks, 6 months and 12 months after the index operation. Postoperative septic arthritis is extremely unlikely 6 weeks or more after surgery; therefore, patients with uneventful follow-up examination at 6 weeks or beyond were considered non-infected [14, 27].

Medical records of patients with septic arthritis were analysed in terms of microbiological findings, if eradication was achieved, the number of necessary arthroscopic reoperations that were conducted and if the graft could be retained.

Technique of revision ACLR

The technique of revision ACLR was standardized and did not significantly change over the years of the study. Surgery was performed with single-dose antibiotics 30–60 min before surgery (cephalosporin group I or II or clindamycin in cases of allergy or intolerance) in both groups. A tourniquet was used (250 mmHg). All reconstructions were performed arthroscopically with independent (anatomic) femoral tunnel placement through an anteromedial portal.

Graft choice was dependent on available grafts as well as tunnel placement and widening resulting from preceding surgical interventions: Autologous hamstring tendons were the preferred graft (four stranded or six stranded, semitendinosus and gracilis tendon, either ipsi- or contralateral). In patients with no hamstrings available (e.g. after bilateral ACLR), quadriceps tendons were used. In patients with marginal tunnel malpositioning or tunnel widening, the quadriceps tendon (ipsilateral, if not available contralateral) was preferably used instead of hamstrings, because the bone block provides a better option of slightly correcting the former malpositioning of a tunnel or to overcome the problem of slight tunnel widening. The quadriceps tendon was generally harvested using a 3–4-cm incision slightly proximal to the patella and with an attached patellar bone block of approx. 20 mm in length. Mean surgical time was 54 ± 15 min (18–110) for reconstructions with hamstring tendons and 64 ± 18 min (30–128) for reconstructions with quadriceps tendons, respectively. In patients with no autologous hamstring or quadriceps tendons available, allografts were used, but these cases were excluded from this study. No patellar tendons were used because of a significant higher morbidity [23]. If tunnel positioning or widening did not allow single-stage revision, debridement of the tunnels and filling with autograft bone from the iliac crest (until 2012) or allograft bone (from 2012) was performed. R-ACLR was then performed after 3–6 months. Table 1 gives an overview of used tendons. There was no difference in the distribution of used grafts between the groups (n.s.). Aperture fixation with interference screws was performed on the femoral side (usually biodegradable or PEEK for hamstrings, titanium for bone block fixation of the quadriceps tendon) except for patients with open epiphyseal plates. For these, a cortical fixation was used. On the tibial side, a hybrid fixation with interference screw (biodegradable or PEEK) and non-absorbable sutures fixed to a cortical button or screw was used. Preparation of the tendons was done on a graft preparation table. After preparation, the graft was wrapped in a sterile moist gauze swab, which was soaked with saline

Table 1 Used tendon grafts in the control and treatment groups

	Group I (no vancomycin treatment)	Group II (vancomycin treatment)	Total
Hamstring tendons	1004 (61.3%)	306 (59.0%)	1310 (60.8%)
Quadriceps tendons	634 (38.7%)	211 (41.0%)	845 (39.2%)
Total	1638	517	2155
Follow-up	1577 (96.3%)	503 (97.1%)	2080 (96.5%)

There were no significant differences between the groups (n.s.)

Data presented in number (%)

solution in group 1 and vancomycin solution (5 mg/ml) in group 2, respectively. It was then set aside until implantation. The vancomycin solution was prepared by dissolving 500 mg of vancomycin powder in 100 ml of sterile solution in a bowl and the gauze swab was soaked in this solution. The graft was not rinsed before implantation.

Postoperative rehabilitation protocol consisted of full range of motion with a brace without limitation and partial weight bearing (10–20 kg) for 10–14 days. In patients with concomitant meniscus repair or cartilage procedures, rehabilitation protocol was adapted.

Management of septic arthritis

In patients with septic arthritis, arthroscopic reoperation was performed on the day of admission. Irrigation and debridement was performed arthroscopically (> 10–15 L of fluid) using anterior standard portals [21, 27]. The approach was focused on graft retention. Antibiotic therapy (empiric) was started after arthroscopic reoperation and was reevaluated and changed if necessary depending on microbiological findings. Clinical evaluation was performed every day, and inflammatory lab parameters (c-reactive-protein, CRP) were obtained every other day. In patients with deterioration another arthroscopic irrigation and debridement procedure was performed. Graft removal was only considered in graft insufficiency or loosened fixation. Patients were discharged with oral antibiotics. Follow-up examinations were performed on a weekly basis, and antibiotic therapy was stopped when CRP value is within normal range.

The study protocol was approved by the competent research ethics board (Landesärztekammer Baden-Württemberg, Germany, F-2018-037).

Statistical analysis

Data from the control group were obtained retrospectively. Data from the treatment group were obtained prospectively but analysed retrospectively. Statistical analysis was performed using IBM SPSS Statistics for Windows (version 24, IBM Corp., Armonk, NY). For statistical evaluation of categorial variables, Fisher's exact test was used. All reported p values are two tailed, with an alpha level < 0.05 considered as significant.

Results

The follow-up rate was 96.5% (Table 1), and did not significantly differ between the groups (n.s.).

There were 14 patients with postoperative septic arthritis in group 1 (incidence rate 0.9%) and no patients with postoperative septic arthritis in group 2 (incidence rate 0.0%), respectively. The difference was significant ($p = 0.029$).

The presoaking time in a consecutive sample series of 50 patients was 15 ± 9 min (2–31) for hamstring tendons ($n = 27$, 54%) and 19 ± 6 min (9–28) for quadriceps tendons ($n = 23$, 46%), respectively, with no difference between the groups (n.s.). The type of infection-causing bacteria was identified in 11 of 14 cases of group 1. The most common bacteria were coagulase-negative staphylococci in seven cases (63.6%) and *Staphylococcus aureus* in three cases (27.3%), respectively. In all patients with septic arthritis, eradication was achieved after 2.4 ± 1.4 (1–6) arthroscopic reoperations with irrigation and debridement. Graft retention was possible in thirteen patients (92.9%). In one case of a *Staphylococcus epidermidis* infection, the graft and hardware were removed within the sixth reoperation because of graft insufficiency and loosened femoral fixation.

Discussion

The major finding of this study is that the incidence of postoperative septic arthritis in R-ACLR can be reduced dramatically by pre-soaking of the graft in vancomycin solution prior to implantation. Therefore, the hypothesis of this study was confirmed.

The technique of vancomycin presoaking of tendons for ACLR was first described by Vertullo et al. [26]. In their series, no postoperative septic arthritis occurred in 870 consecutive primary ACLRs. Phegan et al., Perez-Pietro et al. and Offerhaus et al. confirmed these findings in several similar investigations with 700–1300 patients [15, 17, 18]. The effectiveness of this treatment has, therefore, been clearly shown.

No studies have so far investigated the effectiveness of local vancomycin in R-ACLR. It is well known that the incidence of septic arthritis is higher in this group, but the bacterial spectrum is the same [12, 21]. Against this background, the effectiveness of this local antibiotic treatment appears logical, and this hypothesis has been confirmed by the present study.

It remains unclear how long the grafts should be presoaked in the vancomycin solution. However, because of the usually more complex procedure of an R-ACLR, the period from harvest to implantation is consequently longer in most cases compared to primary ACLR. There are currently two paths that might explain the effectiveness of this simple practice: either decontamination of a contaminated graft, intraarticular elution of a loaded reservoir or both contribute to this highly effective treatment [8, 16, 22]. There have been different technical details described, how exactly the graft should be 'wrapped', how long this should be and if it

should be rinsed off with saline before implantation [5, 15, 17, 18, 22, 26]. It has been reported that graft contamination occurs during harvest and preparation in up to 22% [1, 9]. Perez-Pietro et al. showed that this contamination can be completely eradicated by pre-soaking in vancomycin solution for 10–15 min [16]. In contrast, Schuettler et al. found a high rate of persistent contamination after iatrogenic contamination with *Staphylococcus epidermidis* in an in vitro investigation after 10 min of vancomycin application [22]. In the presented study, most grafts were pre-soaked for 10 to 25 min, and no minimum time for pre-soaking was given. With no observed cases of infections, it seems appropriate to integrate this simple technique in the routine workflow, as this seems to be sufficient. It might even be enough only to drizzle the graft with vancomycin solution, but there is still paucity on this issue. However, there is still discussion on how exactly and how long the graft should be 'wrapped'.

There have been studies discussing different rates of postoperative septic arthritis depending on graft choice, and in most studies, bone–patellar–tendon bone grafts have been reported to have a lower incidence compared to hamstrings [2, 13]. This might be attributed to graft harvesting; however, quadriceps tendon grafts have so far not been investigated in regard of this complication. Further, the presented study is the first to include quadriceps tendons with vancomycin treatment. To date, there are no data available if different tendons react different to vancomycin treatment, e.g. in terms of uptake of the agent or elution kinetics.

While there is some evidence on the effectiveness of local vancomycin in terms of prevention of septic arthritis, there is significantly less data regarding clinical consequences and outcome. Although no serious complications have been reported in any of the available studies, only one study compared clinical outcomes of primary cases with and without vancomycin treatment [15]: Offerhaus et al. randomly selected 500 patients of their cohorts and found similar results for subjective outcome measurements and the rate of arthrofibrosis. Interestingly, they noted an even lower graft failure rate in their group with vancomycin treatment, but the reason therefore is unclear. Although the described technique appears safe in this regard, future studies should focus on clinical outcome and surely long-term follow-up data of larger cohorts (including subgroups with regard to graft choice; R-ACLR) are necessary.

Further, attention should be given to an effect which has been reported in spine surgery where local vancomycin has been used long before it was used in ACL surgery: Though a distinct reduction of Gram-positive infections was reported, there is controversy if this treatment also affects the rate of Gram-negative infections, which are by far more common in spine compared to knee surgery [4, 10]. Vancomycin is generally ineffective against Gram-negative bacteria. However, it has been reported that the topical use of vancomycin powder may increase (or even double) the rate of Gram-negative and polymicrobial surgical site infections because of selection pressure effects [6]. Gram-negative infections following ACLR are very rare, but have been reported, and should, therefore, not be forgotten [15].

Generally, this study confirms that in the rare event of septic arthritis, the graft can be retained in the majority of patients, even in the special setting of R-ACLR. This is in line with previous studies and should be seen as the standard treatment of this complication nowadays [19–21, 24, 27].

In daily clinical practice, the pre-soaking of autograft tendons in vancomycin solution can dramatically reduce septic arthritis, which is a rare but serious complication of these procedures. Therefore, the authors strongly recommend using this technique also in patients undergoing R-ACLR, analogously to how it has been recommended for primary ACLR [15, 16, 18, 26].

Some limitations of this study have to be considered: first, it is not a randomized controlled trial (RCT). The number of required patients for a RCT would be extremely high because of the rare incidence of this complication. With an assumed reduction of the incidence rate of 1.0% to 0.0% according to the available literature, a sample size calculation (alpha = 0.05 and power of 80%) revealed that a total of 1560 prospectively enrolled patients would be necessary, which is hardly realizable in a single-centre setting. Second, it cannot be completely excluded that patients with septic arthritis were treated elsewhere. However, this would be rather unusual and patients are advised to immediately contact their surgeon if they had signs of infection (increased pain, swelling, fever). Moreover, with the presented high follow-up rate of 96.5% this bias is minimized. Further, the groups might slightly differ in terms of individual factors such as sex, body mass index, comorbidities, cartilage damage, type and number of preceding surgeries, type of meniscus surgery, number of preceding ACLRs or other individual factors. It was not possible to obtain all of these factors in the partial retrospective setting of this study. However, both groups represent consecutive cohorts over given, long periods of time, with no substantial changes in indication, surgical technique or used implants in between. Therefore, it might be assumed that no substantial differences are present between the two groups.

Conclusion

Soaking of the graft in vancomycin solution prior to implantation dramatically reduces the incidence of postoperative septic arthritis in R-ACLR.

Compliance with ethical standards

Conflict of interest The authors declare they have no conflict of interest.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the competent Ethical committee.

References

1. Alomar AZ, Alfayez SM, Somily AM (2018) Hamstring autografts are associated with a high rate of contamination in anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 26:1357–1361
2. Bansal A, Lamplot JD, VandenBerg J, Brophy RH (2018) Meta-analysis of the risk of infections after anterior cruciate ligament reconstruction by graft type. Am J Sports Med 46:1500–1508
3. Clement RC, Haddix KP, Creighton RA, Spang JT, Tennant JN, Kamath GV (2016) Risk factors for infection after knee arthroscopy: analysis of 595,083 cases from 3 United States databases. Arthroscopy 32:2556–2561
4. Dodson V, Majmundar N, Swantic V, Assina R (2019) The effect of prophylactic vancomycin powder on infections following spinal surgeries: a systematic review. Neurosurg Focus 46:E11
5. Eriksson K, Karlsson J (2016) Local vancomycin in ACL reconstruction: a modern rationale (2016) for morbidity prevention and patient safety. Knee Surg Sports Traumatol Arthrosc 24:2721–2723
6. Gande A, Rosinski A, Cunningham T, Bhatia N, Lee YP (2019) Selection pressures of vancomycin powder use in spine surgery: a meta-analysis. Spine J 19:1076–1084
7. Gowd AK, Liu JN, Bohl DD, Agarwalla A, Cabarcas BC, Manderle BJ, Garcia GH, Forsythe B, Verma NN (2019) Operative time as an independent and modifiable risk factor for short-term complications after knee arthroscopy. Arthroscopy 35:2089–2098
8. Grayson JE, Grant GD, Dukie S, Vertullo CJ (2011) The in vitro elution characteristics of vancomycin from tendons. Clin Orthop Relat Res 469:2948–2952
9. Hantes ME, Basdekis GK, Varitimidis SE, Giotikas D, Petinaki E, Malizos KN (2008) Autograft contamination during preparation for anterior cruciate ligament reconstruction. J Bone Joint Surg Am 90:760–764
10. Hey HW, Thiam DW, Koh ZS, Thambiah JS, Kumar N, Lau LL, Liu KG, Wong HK (2017) Is intraoperative local vancomycin powder the answer to surgical site infections in spine surgery? Spine (Phila Pa 1976) 42:267–274
11. Indelli PF, Dillingham M, Fanton G, Schurman DJ (2002) Septic arthritis in postoperative anterior cruciate ligament reconstruction. Clin Orthop Relat Res 398:182–188
12. Maletis GB, Inacio MC, Funahashi TT (2013) Analysis of 16,192 anterior cruciate ligament reconstructions from a community-based registry. Am J Sports Med 41:2090–2098
13. Maletis GB, Inacio MC, Reynolds S, Desmond JL, Maletis MM, Funahashi TT (2013) Incidence of postoperative anterior cruciate ligament reconstruction infections: graft choice makes a difference. Am J Sports Med 41:1780–1785
14. Mouzopoulos G, Fotopoulos VC, Tzurbakis M (2009) Septic knee arthritis following ACL reconstruction: a systematic review. Knee Surg Sports Traumatol Arthrosc 17:1033–1042
15. Offerhaus C, Balke M, Hente J, Gehling M, Blendl S, Hoher J (2019) Vancomycin pre-soaking of the graft reduces postoperative infection rate without increasing risk of graft failure and arthrofibrosis in ACL reconstruction. Knee Surg Sports Traumatol Arthrosc 27:3014–3021
16. Perez-Prieto D, Portillo ME, Torres-Claramunt R, Pelfort X, Hinarejos P, Monllau JC (2018) Contamination occurs during ACL graft harvesting and manipulation, but it can be easily eradicated. Knee Surg Sports Traumatol Arthrosc 26:558–562
17. Perez-Prieto D, Torres-Claramunt R, Gelber PE, Shehata TM, Pelfort X, Monllau JC (2016) Autograft soaking in vancomycin reduces the risk of infection after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 24:2724–2728
18. Phegan M, Grayson JE, Vertullo CJ (2016) No infections in 1300 anterior cruciate ligament reconstructions with vancomycin pre-soaking of hamstring grafts. Knee Surg Sports Traumatol Arthrosc 24:2729–2735
19. Pogorzelski J, Themessl A, Achtnich A, Fritz EM, Wortler K, Imhoff AB, Beitzel K, Buchmann S (2018) Septic arthritis after anterior cruciate ligament reconstruction: how important is graft salvage? Am J Sports Med 46:2376–2383
20. Schuster P, Gesslein M, Mayer P, Schlumberger M, Mayr R, Richter J (2018) Septic arthritis after arthroscopic posterior cruciate ligament and multi-ligament reconstructions is rare and can be successfully treated with arthroscopic irrigation and debridement: analysis of 866 reconstructions. Knee Surg Sports Traumatol Arthrosc 26:3029–3038
21. Schuster P, Schulz M, Immendoerfer M, Mayer P, Schlumberger M, Richter J (2015) Septic arthritis after arthroscopic anterior cruciate ligament reconstruction: evaluation of an arthroscopic graft-retaining treatment protocol. Am J Sports Med 43:3005–3012
22. Schuttler KF, Scharm A, Stein T, Heyse TJ, Lohoff M, Sommer F, Spiess-Naumann A, Efe T (2019) Biomechanical and microbiological effects of local vancomycin in anterior cruciate ligament (ACL) reconstruction: a porcine tendon model. Arch Orthop Trauma Surg 139:73–78
23. Thompson SM, Salmon LJ, Waller A, Linklater J, Roe JP, Pinczewski LA (2016) Twenty-year outcome of a longitudinal prospective evaluation of isolated endoscopic anterior cruciate ligament reconstruction with patellar tendon or hamstring autograft. Am J Sports Med 44:3083–3094
24. Torres-Claramunt R, Pelfort X, Erquicia J, Gil-Gonzalez S, Gelber PE, Puig L, Monllau JC (2013) Knee joint infection after ACL reconstruction: prevalence, management and functional outcomes. Knee Surg Sports Traumatol Arthrosc 21:2844–2849
25. Van Tongel A, Stuyck J, Bellemans J, Vandenneucker H (2007) Septic arthritis after arthroscopic anterior cruciate ligament reconstruction: a retrospective analysis of incidence, management and outcome. Am J Sports Med 35:1059–1063
26. Vertullo CJ, Quick M, Jones A, Grayson JE (2012) A surgical technique using presoaked vancomycin hamstring grafts to decrease the risk of infection after anterior cruciate ligament reconstruction. Arthroscopy 28:337–342
27. Wang C, Lee YH, Siebold R (2014) Recommendations for the management of septic arthritis after ACL reconstruction. Knee Surg Sports Traumatol Arthrosc 22:2136–2144