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A study on the outcome of autograft soaking of vancomycin for anterior cruciate ligament reconstruction surgeries

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***Abstract*---**Background: In Anterior Cruciate Ligament (ACL) reconstruction surgery the rate of development of infection or septic arthritis is an uncommon but devastating condition. Presoaking of autografts into the vancomycin has also shown to be effective in reducing the rate of infection in ACL reconstruction patients. This present study thus assessed the efficacy of vancomycin presoaking autograft in decreasing the rate of infection in ACLR patients. Material and methods: This is a hospital-based prospective study conducted in the A.J. Institute of Medical Sciences, Mangalore starting from August 2017 to January 2020 for 3 years. In this study patients from the age group of 18 years to 40 years were included. The vancomycin-soaked grafts were used in these patients. After the operation, the patients were discharged after 10 days. The follow-up was done for 12 months postoperatively. The presence of infection was done and the improvement in the patient's activity was further evaluated using two scores International Knee Documentation Committee (IKDC) score and the Lysholm knee scoring scale. The result of this study was tabulated and then evaluated using SPSS software. Result :In this study total of 100 patients were included with a mean age of 28.1 ± 7.1 years. The majority of participants (95%) received Hamstring grafts while only 5%

received the patellar tendon bone (PTB) graft. In only 1 case of the ACLR, the surgery patient reported the presence of post-operative complications. In 1% of cases, graft failure happened because of septic arthritis. In this patient, positive growth of *Staphylococcus aureus* was noted. Only one case of Arthrofibrosis was reported (1%). Conclusion: Autograft pre-soaking with vancomycin in combination with classical intravenous antibiotic prophylaxis reduces the rate of knee joint infection following an ACLR, without increasing the incidence of postoperative complications like arthrofibrosis.

***Keywords*---**autograft, vancomycin, anterior cruciate ligament, reconstruction.

Introduction

In Anterior Cruciate Ligament (ACL) reconstruction surgery the rate of development of infection or septic arthritis is an uncommon but devastating condition that can lead to the unpleasant outcome of the surgery [1]. In the past studies have reported infection in the reconstruction surgeryranges from 0.14% to 1.87% [2]. Apart from the graft misalignment, bacterial infections after the surgery are still a concern. The majority of infections occur within 30 days of receiving the reconstruction [3].

The Anterior Cruciate ligament is part of the most complex joint in the human body, the knee joint.This ligament originates from the anterior aspect of the tibial plateau and is placed in a crisscross pattern in the knee joint. This ligament is mainly responsible for providing support to the knee in both transverse and also in frontal planes. These ligament bundles are prone to teat whenever there is a sudden stop in the motion of the leg [4]. In approximately 64% of the athletic knee injuries, ACLtears have been reported [5].

The gold standard for treating the anterior cruciate ligament is surgery. The surgery is characterized by removing the old torn ones with a new one using grafts such as quadriceps tendon, bone-patellar tendon bone, etc. All these tendons can be taken from cadavers (allograft) it can be acquired from the patient (autograft) [4]. The rate of infection after the ACL reconstruction surgery depends on several factors including different socio-demographic parameters including the history of pre-surgical procedures, diabetes, smoking, or type of surgical procedures [3]. The most common type of pathogenic organism that isshown to be associated with the infection is the Staphylococci species. Almost 90% of the cases this is the causative organism and half of the organisms are coagulase-negative species. Other than this pathogens such as Enterobacter species and Propionibacterium acnes are also showed to causeinfection after the reconstruction surgery [6,7].

Production of biofilms by the bacterial species shields Staphylococcus against antimicrobials, opsonization, and phagocytosis, making eradication difficult. This contamination of the harvest presents a possible vehicle for infection of the knee joints [8]. Studies have shown that the use of prophylactic antibiotics along with proper hair removal can significantly decrease the chance of developing septic

arthritis in ACL reconstruction patients [9]. Presoaking of autografts into the vancomycin has also shown to be effective in reducing the rate of infection in ACL reconstruction patients [1,6,10].

A deep knee infection can be severe, necessitating the removal of grafts and hardware, as well as, in many cases, a second reconstruction surgery after 4 to 6 months. Graft failure and long-term graft function, as well as an elevated risk of long-term osteoarthritis, are two main concerns following deep knee infection after ACL-R. Hence, in the present study, we assessed the efficacy of pre-soaking the hamstring graft with an appropriate antibiotic at the time of harvest and whether this can decrease the rate of septic arthritis after ACL reconstruction. Moreover, this study will also try to evaluate whether this was associated with an increased rate of complications, includinggraft failure or arthrofibrosis.

Material and Methods

This is a hospital-based prospective study conducted in the A.J. Institute of Medical Sciences, Mangalore starting from August 2017 to January 2020 for 3 years. At the beginning of the study ethical clearance of the study was taken from the Ethical committee of the institute. The patients with ACL injury treated by arthroscopic reconstruction in AJ Institute of Medical Sciences and Research Centre, Kuntikana, Mangalore were included in this study based on the inclusion criteria.

Inclusion Criteria

- Patients in the age group of 18 years to 40 years.
- Patients requiring clinically diagnosed ACL-R with an ACL tear confirmed by a positiveLachmann test, and an MRI.
- Both acute and chronic ACL deficient knees were included,

Exclusion Criteria

- Patients with chronic ACL insufficiency with osteoarthritis.
- Patients with pre-existing infections
- Patients who have comorbid conditions and are not fit for the procedure
- ACL injury associated with fractures
- Those undergoing simultaneous osteotomy, revision ACL reconstructions
- Patients who are not willing for the procedure due to financial problems

After the inclusion of the patients, informed consent was signed from all of them. A pre-tested semi-structured questionnaire was used for recording the medical history, sociodemographic parameters, and results of hematological and radiological investigations.

Surgical procedures

On the day of the surgery, all the patients were screened thoroughly for the presence of any preoperative infections if present. Before the surgery, all the rings or any other objects were removed from the patient. The hair from the operative site was removed and the site was cleaned with betadine solution. Intravenous antibiotics were administered to all the patients. New 2 portal ACL construction technique was used. The tunnel creation was done by the experienced surgeons and the tendon was freed from the distal end of the tendon with the scissors. Next, the tendon stripper is pushed up along the tendon to remove it from its muscular attachment. Meanwhile, assistants prepared the bone patellar tendon bone autograft. The graft soaking solution was prepared by dissolving and diluting the contents of 500 mg vancomycin hydrochloride vials with an appropriate volume of sterile normal saline to produce final concentrations. Sterile gauze swabs were immersed in soak solutions for 1 minute. Tendon grafts were wrapped tightly in impregnated gauze swabs and left to stand for 10 minutes. Before transplantation of the graft through the drill, the graft was washed with 20 mL of sterile saline solution.

The tibial tunnel drilled sequentially by 1 mm increments up to the desired size of the tunnel using an endoscopic drill bit. An accessory anteromedial portal (AAM) was created using an 18-gauge needle. The AAM portal should be located as low as possible above the medial joint line while avoiding the anterior horn of the medial meniscus. Rotate the arthroscope medially to determine if the needle is positioned too close to the medial femoral condyle. The ACL graft is passed into the knee joint using the graft passing sutures. All our patients were fixed with endobuton proximally and with aninterference screw distally.

Post-operative outcome

The patients were discharged after 10 days of the operation. The follow-up was done for 12 months postoperatively. All the patients were instructed to follow the same postoperative rehabilitation. All the patients were instructed to report in case they are facing any pain, fever, or swelling after they were discharged from the hospital. The postoperative infection was recorded as

- Positive culture on the aspiration of a painful knee
- Negative aspiration culture with a raised or rising serial CRP,
- Increased synovial white cell count with a painful effusion,

The improvement in the patient's activity was further evaluated using two scores International Knee Documentation Committee (IKDC) score and the Lysholm knee scoring scale. The result of this study was tabulated and then evaluated using SPSS software.

Result

In this study total of 100 patients were included with a mean age of 28.1 ± 7.1 years. In that 57% of the participants belonged to the 21-30 years of age,

followed by 26% of the participants belonging to 31-40 years of age. The number of male participants was higher compared with the female participants indicating a male predominance.

Three mechanisms of injury were recorded among the study participants, domestic, RTA, and sports injury. The majority of participants recorded domestic injury/ Non-contact injury (61%), followed by RTA (34%). A minor percentage of participants recorded sports injuries. 48% of the participants received Piperacillin, while both Cefixime (24%) and Ceftazidime (28%) made up a comparable participant population. The majority of participants (95%) received Hamstring grafts {Semitendinosus and Gracilis (ST-G)} while only 5% received the patellar tendon bone (PTB) graft. In only 1 case of the ACLR, the surgery patient reported the presence of post-operative complications. In 1% of cases, graft failure happened because of septic arthritis.

Only one patient presented with signs of deep knee infection wherein the positive growth of *Staphylococcus aureus* was noted. Arthrofibrosis is one of the concerns with the use of topical vancomycin. In our study, only one case of Arthrofibrosis was reported (1%). The patient who reported graft failure and deep knee infection showed features of arthrofibrosis as well.

Distribution of subjects based on Lysholm scores

All the patients reported an unsatisfactory Lysholm score pre-op. While improvement was recorded at subsequent time points, 52% of participants reported a fair score at 3-weeks, improving to 97% at 9-weeks. While at the 12-months majority of the patients reported excellent scores (55%). Lysholm's score at baseline was 46.71 which increased progressively to 90 at the end of 12 months. The mean improvement was significant at each follow up i.e. at 3 weeks, 9 weeks, and 12 months ($p<0.05$).

At 3-weeks a comparable number of participants receiving piperacillin and ceftazidime reported a fair score. While a higher number of patients receiving piperacillin reported unsatisfactory scores. While at 9 weeks, 43 participants receiving piperacillin reported a fair score. At 12-months highest number of participants recorded excellent scores, while an equal number of patients receiving cefixime and ceftazidime reported the outcome.

Distribution of subjects based on International Knee Documentation Committee (IKDC)

International Knee Documentation Committee (IKDC) score was used for subjective knee evaluation of difficulty in daily activities. It is the standard score used for the treatment of knee ligament injuries. The IKDC score at baseline was 36.87 which increased progressively to 92.91 at the end of 12 months. The mean improvement was significant at each follow up i.e. at 3 weeks, 9 weeks, and 20 weeks ($p<0.05$).

Discussion

In this present study, the effect of prophylactic graft saturation with vancomycin in reducing the rate of infection after the ACLR was reported. In this presents study either hamstrings or bone– patellar tendon–bone (BPTB) grafts were used. The present study showed that the maximum of patients was in 21 – 30 years of age (57%), with the mean age being 28.1 ± 7.1 years. Maximum of the patients were male indicating a male predominance. In a previous study, Baron et al showeda similar pattern of male dominance where 58% of the patients were male. This study reported a mean age of 27.7 ± 11.4 years which is similar to the present study findings [11]. In another study, Naendrup et al also reported the same study finding [10]. In a large study by Mei Y et al., a total of 4355 including 612 athletes and 3743 non-athletes were registered. Of all the 4355 cases, the meanage at the time of the first injury was 25.4 ± 8.8 years [12].

The most common mechanism of injury was domestic injury (61%), presenting equally in both left and right sides (50% each). The typical mechanism of injury is deceleration with twisting, pivoting, or a change of direction. At least 60 % of all ACL injuries sustained by patients are due to a non-contact mechanism of injury [13]. In our study, non-contact injuries like twisting injury slip and fall were classified as Domestic injuries, which were 61%. Road traffic accidents accounted for 34 cases (34%) and sports injuries were only seen in 5% of cases.

In terms of graft used Hamstring grafts (Semitendinosus and Gracilis tendon (ST-G)) were placed in the majority of the patients. (95%) Bone patella tendon bone graft (BPTB) was used in only 5%of the cases. In previous studies, it was reported that Hamstring tendon autografts have a higher incidence of infection than BPTB autografts or allografts [7]. In our study, deep knee infection and graft failure was seen in one case where a Hamstring graft was used. Hence our study found that prophylactic vancomycin presoaking of hamstring autografts in addition to prophylactic IV antibiotics statistically reduced the infection rate after ACLR.

A previous study by Perez-Prieto et al reported that presoaking of autografts into vancomycin along with intravenous antibiotic prophylaxis can significantly reduce the incidence of infections in patients with ACLR surgery patients. This study reported 0% infection in patients who received intravenous antibiotics and the presoaked autograft [2]. Offerhaus et al reported that patients receiving only antibiotics had a higher infection rate (2%) compared to the patients antibiotic and undergoing vancomycin-soaked graft treatment (0%) [14]. Baron et al reported that vancomycin soaked grafts have a 10 times lower incidence of infection. This study reported an infection rate of 0.1% among patients who received vancomycin soaked grafts [11]. Similarly, a study by Vertullo et al, showed that among 1,135 ACLR surgeries, 870 patients underwent ACLR with a vancomycin-presoaked hamstring autograft and rest (group 2) with preoperative IV antibiotics. Ingroup 1 a total of 4 postoperative joint infections were documented (1.4%) and in group 2 no infections (0%) were recorded [15].

It was hypothesized that vancomycin pre-soaking of the graft would significantly reduce the rate of infection after ACLR without increasing adverse effects, including the rates of postoperative graft failure and arthrofibrosis. Few studies

have shown a slightly higher incidence of arthrofibrosis in vancomycin soaked grafts [16]. However in our study only 1% Arthrofibrosis was seen, which was in the patient who developed deep knee infection and graft failure. Hence arthrofibrosis in our study can be attributed to the infection and not particularly the vancomycin soaking.

In our study, there was an overall infection rate of 1 % (1 case) after ACLR. The following case presented as an acute infection that developed in the early postoperative period (5 weeks after surgery). The patient presented with increasing pain, large effusions, and rising or raised CRP. He later underwent Arthroscopic debridement and lavage 6 weeks post-operatively. Pus obtained was sent for culture and sensitivity. The bacteria isolated was Staphylococcus aureus and antibiotics were started based on the reports. As there wasn't a good response to washout and IV antibiotics, Patients underwent graft removal at a later stage. Patient follow-up was done until CRP value waswithin normal range.

Wang et al, recommends that in patients with septic arthritis, arthroscopic reoperation be performed on the day of admission. Irrigation and debridement should be performed arthroscopically (>10–15 L of fluid) using anterior standard portals [7]. Schuster et al, states that in patients with deterioration another arthroscopic irrigation and debridement procedure was performed. Graft removal was only considered in graft insufficiency or loosened fixation [17]. Follow-up examinations were performed every week, and antibiotic therapy was stopped when theCRP value is within the normal range.

Functional outcomes among the students were also evaluated in this present study. The lower rates of infection were reflected in improved Lysholm and IKDC scores, which are the measures of knee-specific symptoms. The average Lysholm score at baseline was 46.7 ± 3.83 which progressed to 90 ± 5.53 at the end of 12 months. The IKDC score at baseline was 36.85 ± 3.07 which progressed to 91.92 ± 5.89 at the end of 22 months. Also, the mean improvement was found to be significant at successive follow-ups of 3 weeks, 9 weeks, and 12/22 months ($p<0.05$). Additionally, all the patients reported unsatisfactory scores before treatment, while after treatment the percentage of patients reporting improvement in scores also progressed. At 3-weeks 52% of the patients reported fair scores, 9-weeks 97% of the patients reported fair scores, while at the end of 12 months 55% of patients reported excellent scores, while 38% patients reported good scores.

Offerhaus et al also presented an IKDC score post long follow-up period of 37-months but no significant difference was reported between the vancomycin and no-vancomycin groups. Thus, such results demand an investigation following a larger sample size, however, the efficacy of vancomycin soaked ACLR graft was observed in the present study and corroborated with the findings reported by the previous results [14]. The main limitations of this study are its short follow-up period. Secondly, this study doesn't have a control group and hence might lead to overestimation of the efficacy. However, we have informed the patients to follow up with the hospital itself, therefore, decreasing this chance error.

Conclusion

Autograft pre-soaking with vancomycin in combination with classical intravenous antibiotic prophylaxis reduces the rate of knee joint infection following an ACLR, without increasing the incidence of postoperative complications like arthrofibrosis. Hence, Prophylactic pre-soaking of autografts in vancomycin during ACLR appears to be a viable, cost-effective, and safe option toreduce the rate of deep knee infection compared to systemic antibiotics alone.

Graphs and Tables

Table 1 Distribution of subjects based on age groups

Age		
	Frequency	Percent
15-20	11	11.0
21-30	57	57.0
31-40	27	27.0
Equal or more than 41	5	5.0

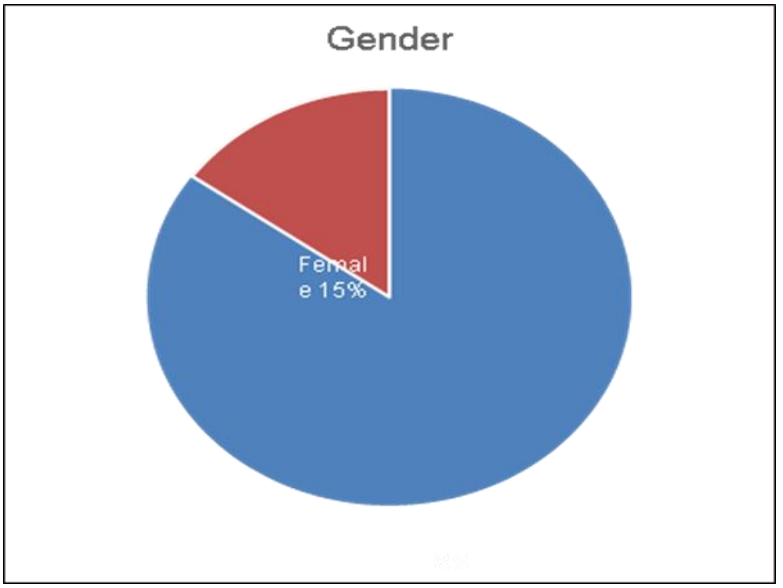

Figure 1: gender distribution

Table 2 Distribution of subjects based on side of injury

Site of Injury		
	Frequency	Percent
Right	50	50.0
Left	50	50.0

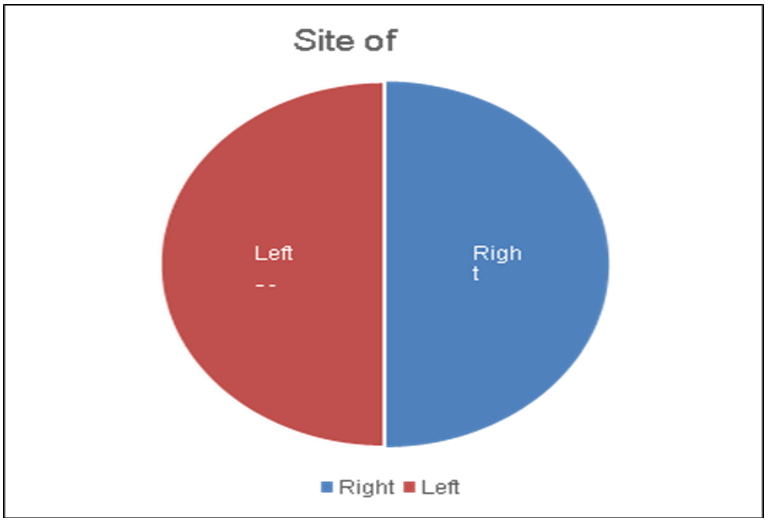

Table 3 Distribution of subjects based on mechanism of injury

Mechanism of Injury		
	Frequency	Percent
Domestic	61	61.0
RTA	34	34.0
Sports Injury	5	5.0

Table 4 Distribution of subjects based on IV antibiotics

IV Antibiotic		
	Frequency	Percent
Cefixime	24	24.0
Piperacillin	48	48.0
Ceftazidime	28	28.0

Table 5 Distribution of subjects based on graft failure

Graft Failure		
	Frequency	Percent
Yes	1	1.0
No	99	99.0

Table 6 Distribution of subjects based on deep knee infection

Deep Knee Infection		
	Frequency	Percent
Yes	1	1.0
No	99	99.0

Table 7 Distribution of subjects based on arthrofibrosis

ARTHROFIBROSIS		
	Frequency	Percent
Yes	1	1.0
No	99	99.0

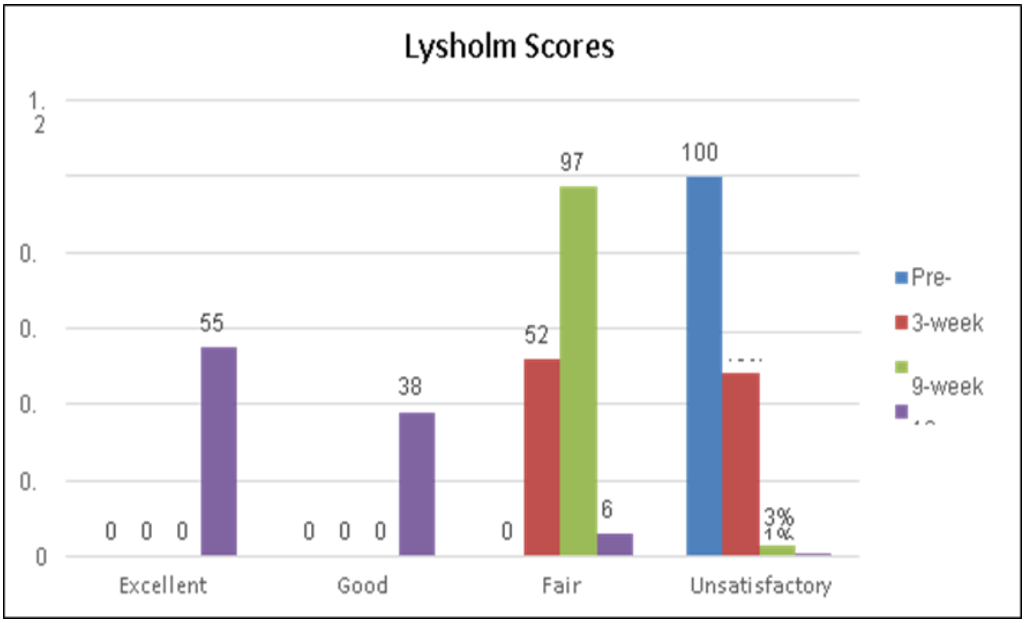

Figure 3: Comparison of Lysholm score

Table 8: Distribution of subjects based on mean pre- and post-op Lysholm Scores

	Mean	SD	N	SEM	P value
Pre-Op	46.71	3.83	100	0.38	P < 0.0001
3 weeks	65.31	4.91	100	0.49	P < 0.0001
9 weeks	71.15	3.93	100	0.4	P < 0.0001
12 months	90	5.5	100	0.54	P < 0.0001

Table 9: Distribution of subjects based on mean pre- and post-op IKDC Scores

	Mean	SD	N	SEM	
Pre-Op	36.87	3.07	100	0.31	P < 0.0001
3 weeks	51.71	3.45	100	0.34	P < 0.0001
9 weeks	62.55	3.85	100	0.38	P < 0.0001
12 months	92.91	5.15	100	0.58	P < 0.0001

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