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Investigation of the Causes of Inflammatory Reaction after Arthroscopic Anterior Cruciate Ligament Reconstruction

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A**bstract:** *Objective*: To analyze the data of local inflammatory storm after anterior cruciate ligament reconstruction under knee arthroscopy, and to understand the causes and countermeasures. *Methods*: A retrospective analysis was performed on 135 patients who underwent anterior cruciate ligament reconstruction in the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force from September 2020 to September 2023. The gender, age, injury time, operation time, blood loss, postoperative anticoagulant drug application time, drainage tube application, and other items were collected. The causes of postoperative local inflammatory storm in patients were obtained by binary logistic regression analysis. *Results*: There were no significant differences in gender, age, injury time, operation time, and blood loss ($P > 0.05$), but there were significant differences in the placement of drainage tubes and the initiation time of anticoagulant drugs ($P < 0.05$). Early application of anticoagulants for one day increased the risk of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction by 0.305 times, and the occurrence of inflammatory reaction without a drainage tube was 5.994 times higher than that with a drainage tube. *Conclusions*: Premature use of anticoagulant drugs and inadequate drainage may be the main causes of local inflammatory storm in these patients.

Keywords: Arthroscopic anterior cruciate ligament reconstruction; Local inflammatory storm; Anticoagulants; Drainage tube

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1. Introduction

Anterior cruciate ligament (ACL) injury is one of the most common knee ligament injuries. ACL rupture is often accompanied by bone contusion, other ligaments, and meniscus injuries, which can affect the stability of the knee joint, and long-term joint instability will lead to premature degeneration of the knee joint [1]. Due to the very low chance of self-healing after ACL rupture and the poor effect of conservative treatment, the current treatment of ACL rupture is still mainly based on surgical treatment. Arthroscopic anterior cruciate ligament reconstruction is a minimally invasive surgical procedure under the arthroscope to replace the injured ligament to re-stabilize the knee

joint, which is the gold standard for the treatment of ACL rupture.

In 2020, according to statistics, China has more than 100000 cases of anterior cruciate ligament reconstruction under arthroscopy. With ACL reconstruction surgery gradually rising, its postoperative complications also attract more attention. Although the infection rate after ACL reconstruction is less than 1%, delayed treatment may lead to graft failure, articular cartilage destruction, secondary osteoarthritis, and other consequences [2], which seriously affect the knee joint function. Although there was no purulent infection in this study, the symptoms found are very similar to infection, and the possibility of further development of infection cannot be excluded, so it has attracted full attention.

In this study, the clinical manifestations resembled those of a knee joint infection; however, no pathogenic organisms were detected in the synovial fluid obtained via joint puncture. Following arthroscopic anterior cruciate ligament reconstruction, patients developed knee effusion and swelling within three days. Subsequently, redness appeared in the calf area, accompanied by a low-grade fever, increased skin temperature, and a moderate elevation in white blood cell count. After joint puncture and administration of antibiotics, the patients' symptoms quickly resolved [3]. A review of the relevant literature and medical texts revealed no prior reports of such a phenomenon. Therefore, this condition is temporarily referred to as a "local inflammatory storm." In order to understand the causes of this phenomenon and explore its coping methods, this study collected the data from the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force, from September 2020 to September 2023.

2. Materials and methods

2.1. Study subjects

A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction from September 2020 to September 2023 in the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of Joint Logistics Support Force were selected for retrospective analysis. Inclusion criteria: (1) patients met the diagnostic criteria of ACL rupture. (2) arthroscopic anterior cruciate ligament reconstruction; (3) complete medical records. Exclusion criteria: (1) patients with intra-articular fractures; (2) patients with joint infection and rheumatoid arthritis; (3) gouty arthritis; (4) patients with immune diseases and abnormal coagulation.

2.2. Clinical data

The general data of 135 patients included in this study were collected, including gender, age, injury time, operation time, blood loss, postoperative antibiotic application time, postoperative anticoagulant drug application time, drainage tube application, and other items. When the patients had clinical manifestations such as effusion and swelling of the knee joint, redness and swelling of the upper leg, low-grade fever, and elevated skin temperature after anterior cruciate ligament reconstruction under knee arthroscopy, blood routine, erythrocyte sedimentation rate, C-reactive protein, and other blood tests were performed immediately, and the joint cavity puncture fluid was collected for bacterial culture. According to the clinical manifestations, hematological examination, and joint fluid examination, it is necessary to quickly identify whether the knee joint infection is caused by pathogens [4]. After excluding pathogenic infection, the clinical manifestations are attributed to a local inflammatory storm.

2.3. Treatment methods

Antibiotics were given within 24 hours after anterior cruciate ligament reconstruction under knee arthroscopy,

and low-molecular-weight heparin anticoagulation therapy was given 24 hours after surgery. In case of effusion, swelling, redness, low-grade fever, and elevated skin temperature in the upper leg, joint puncture was given in time. In order to relieve the patient's symptoms and avoid the occurrence of septic arthritis, antibiotic treatment was continued [5]. After treatment, the degree of knee joint effusion and swelling, the recovery of local symptoms such as calf skin temperature, and the recovery of hematological examination such as white blood cell count were used as evaluation indicators to evaluate the therapeutic effect, and then determine the subsequent treatment plan.

2.4. Statistical methods

SPSS 22.0 statistical software was used to process and analyze the data. The measurement data were expressed as mean ± standard deviation (SD) and *t*-test was used. Count data were expressed as rate or constituent ratio, and χ^2 test was used. Using the Hosmer-Lemeshow test, the goodness of fit of the regression model was assessed; $P > 0.05$ means not statistically significant for binary logistic regression. $P < 0.05$ indicates a statistically significant difference.

3. Results

3.1. General information

A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction from September 2020 to September 2023 in the Third Surgical Group of Department of Orthopedics, 988th Hospital of Joint Logistics Support Force were selected, including 112 males and 23 females, aged from 15 to 61 years, with an average age of 29.39 ± 8.79 years. There were 35 cases of local inflammatory storm in the knee joint after operation, including 57 cases of old injury, 78 cases of fresh injury, 56 cases of drainage tube placement, and 79 cases of no drainage tube placement. See **Table 1** for details.

Table 1. Basic clinical data of 135 patients after anterior cruciate ligament reconstruction

Clinical data	***n* = 135**	**Percentage (%)**
Gender		
Male	112	83%
Female	23	17%
Age (mean ± SD)	29.39 ± 8.79	-
Nature of injury		
Fresh	57	42%
Old	78	58%
Operation time (mean ± SD)	121.61 ± 41.09	-
Amount of bleeding (mean ± SD)	28.19 ± 26.28	-
Antibiotic application time (mean ± SD)	4.65 ± 3.30	-
Anticoagulant initiation time (mean ± SD)	4.41 ± 3.44	-
Whether to place a drainage tube		
Yes	56	41%
No	79	59%

3.2. Binary logistic regression analysis

Logistic regression analysis of local inflammatory storm after anterior cruciate ligament reconstruction is presented in **Table 2**. A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction were selected as cases. The data on gender, age, injury type, operation time, blood loss, antibiotic application time, anticoagulation initiation time, and drainage tube placement were analyzed. Hosmer-Lemeshow test showed that $\chi^2 = 8.776$, $P = 0.362$. $P > 0.05$ indicated that the regression model fitted the data well, and the regression model was established. Through binary logistic regression model test results analysis, the initiation time of anticoagulation and whether to place a drainage tube were statistically significant ($P < 0.05$), and the odds of local inflammatory storm increased by 0.305 times when the initiation time of anticoagulation was used one day earlier. The risk of local inflammatory storm in patients without drainage tube placement was 5.994 times higher than that in patients with drainage tube placement.

Table 2. Results of binary logistic regression analysis.

Items	B	SE	Wals	df	Sig.	Exp (B)	95% CI of Exp (B)	
							Lower limit	Upper limit
Gender (1)	0.574	0.701	0.669	1	0.413	1.775	0.449	7.018
Age	0.015	0.030	0.249	1	0.618	1.015	0.957	1.077
Nature of injury (1)	0.086	0.480	0.032	1	0.857	1.090	0.425	2.794
Duration of surgery	0.003	0.006	0.189	1	0.663	1.003	0.990	1.015
Amount of blood loss	0.008	0.008	0.930	1	0.335	1.008	0.992	1.025
Duration of antibiotics	0.057	0.072	0.634	1	0.426	1.059	0.920	1.219
Initiation time of anticoagulation	-0.363	0.101	13.028	1	0.000	0.695	0.571	0.847
Placing a drain (1)	1.791	0.571	9.849	1	0.002	5.994	1.959	18.341

4. Discussion

4.1. Definition and clinical significance of local inflammatory storm

The Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force found that a part of the patients who underwent arthroscopic anterior cruciate ligament reconstruction had knee joint hemorrhage after surgery, followed by redness and swelling of the upper leg, elevated skin temperature, and low-grade fever. Blood routine examination showed a slight increase in white blood cells and C-reactive protein. After multiple cultures, no bacteria grew. After 7–10 days, the above symptoms gradually disappeared, and there was no long-term effect on the patients. The third surgical group began to pay attention to this phenomenon and began to search the literature and books, and found that this phenomenon had not been reported. Only Babalola *et al.* [6] reported a case of microbridge allergy with similar symptoms, but this situation excluded allergic reactions. After discussions, this phenomenon was named as local inflammatory storm after anterior ACL reconstruction, and relevant clinical data were collected for further analysis.

A total of 135 patients undergoing arthroscopic anterior cruciate ligament reconstruction were routinely treated with antibiotics and anticoagulant drugs after surgery, but the study found that 35 patients developed local inflammatory storm after surgery, with an inflammation rate of 26%. The patients presented with effusion and

swelling of the knee joint, redness and swelling of the upper leg, low-grade fever, and increased skin temperature. There were no obvious systemic symptoms, and the blood routine test showed mild leukocytosis. This local inflammatory storm is different from joint infection. From the perspective of etiology, the occurrence of this local inflammatory storm is not caused by the invasion of bacteria, viruses, and other microorganisms, which belongs to non-infectious local inflammatory storm [7]. From the perspective of clinical symptoms, the local symptoms of this local inflammatory storm are obvious, and no systemic symptoms of infection occur. From the auxiliary examination, it can be found that the white blood cell count in the blood routine of these patients is increased, while other blood test indexes are in the normal range, and the bacterial culture of synovial fluid puncture is negative. From the perspective of the outcome of the disease, this local inflammatory storm is self-limited and can be clinically cured, but the appearance of local symptoms such as knee joint swelling and pain delays the recovery process. Although the outcome is good, it increases the course of the disease, hospitalization costs, and pain of the patient, which still needs to be paid attention to.

4.2. Cause analysis of local inflammatory storm

This study found that a total of 35 patients developed local inflammatory storm after surgery. To explore the causes of this phenomenon, in this study, binary logistic regression was used to analyze the correlation between gender, age, complications, operation time, blood loss, postoperative antibiotic application time, postoperative anticoagulant drug application time, and drainage tube application and postoperative local inflammatory storm, in order to determine the cause of postoperative local inflammatory storm. The results showed that the risk of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction was increased by 0.305 times when anticoagulant drugs were used one day earlier after surgery, and the risk of local inflammatory storm in patients without a drainage tube was 5.994 times that in patients with a drainage tube. However, there was no significant correlation between the patient's gender, age, operation time, intraoperative blood loss, and postoperative antibiotic application time and the postoperative local inflammatory storm. The results showed that the timing of anticoagulant use and the placement of a drainage tube were significantly correlated with the occurrence of local inflammatory storm, which further indicated that postoperative local hemorrhage may be the main cause of postoperative local inflammatory storm.

After anterior cruciate ligament reconstruction under knee arthroscopy, patients often have knee joint swelling, which is usually caused by knee joint effusion. The reasons may include rupture of local capillaries due to trauma caused by own ligaments and surgery, increased permeability of blood vessel wall, and interstitial edema caused by intravascular fluid penetration into the soft tissue space. During the operation, soft tissue traction and blunt dissection lead to postoperative soft tissue reactive swelling. When a large amount of normal saline is used to flush the joint cavity during the operation, swelling is caused by the absorption of normal saline by the nearby soft tissue.

When the accumulated blood reaches a certain pressure in the joint cavity, the accumulated blood will reach the other end of the bone tunnel along the tibia and femur [8]. As the femoral end is rich in muscle tissue and has a strong ability to absorb blood accumulation, there is generally no local heat absorption and local inflammatory storm. The external mouth of the tibial bone tunnel is the anterior-medial side of the tibia, where there is no muscle tissue, so the blood accumulation cannot be absorbed in time and spreads along the tibia, resulting in local inflammatory storm with redness and swelling, low-grade fever, and high skin temperature in the upper leg [9]. With a drainage tube placed at the end of the operation, the intra-articular blood can be drained out in time without

flowing out of the joint along the bone tunnel, and the occurrence of local inflammatory storm can be avoided. However, the placement of a drainage tube can also increase the risk of joint infection, and the drainage tube should be removed after 48 hours, so some patients may experience local inflammatory storm after the removal of the drainage tube [10].

4.3. Prevention and treatment of local inflammatory storm

The use of anticoagulant drugs to prevent venous thrombosis of the lower extremities after surgery has become an expert consensus [11]. As a small amount of blood accumulates in the joint after arthroscopic surgery, early use of anticoagulant drugs may increase the amount of blood in the joint cavity. However, if anticoagulant drugs are applied after the bleeding surface in the joint cavity has gradually healed, the chance of bleeding will be greatly reduced. Among the 35 patients with local inflammatory storm after surgery in this study, 30 patients (86%) were treated with anticoagulant drugs within 3 days after surgery, and 5 patients (14%) were treated with anticoagulant drugs after 3 days. Considering that most patients with anterior cruciate ligament injury are young adults, combined with the data, it is recommended to apply anticoagulant drugs to prevent thrombosis after 3 days of arthroscopic anterior cruciate ligament reconstruction [12]. If the patient is older than 40 years old or has a higher thrombosis risk assessment score, it is recommended to place a drainage tube during the operation and apply anticoagulant drugs immediately after the operation to prevent the formation of lower extremity venous thrombosis.

According to the current research data, there are no cases of septic arthritis, and the results of the patient's symptoms and laboratory tests are very similar to bacterial infection, and the possibility of bacterial infection cannot be excluded, because the blood accumulation in the joint is a very good medium for bacteria, so the prophylactic antibiotics are changed to therapeutic antibiotics. After this phenomenon occurs, patients often panic and may feel that their postoperative symptoms are worsening. They may suspect a postoperative infection. Therefore, doctors should provide appropriate psychological support, clearly explain the causes and prognosis to the patient, help ease their anxiety, and encourage active cooperation with the treatment. Based on the study and understanding of inflammatory storms, a standardized treatment plan should be developed: (1) Joint cavity puncture aims to relieve intra-articular pressure, and the aspirated fluid should be sent for bacterial culture. (2) Prolonged use of antibiotics: For example, in anterior cruciate ligament reconstruction, antibiotics are generally administered for 24 hours. To prevent purulent infection, the duration of antibiotic use should be appropriately extended. (3) Local cold compresses should be applied, along with medications that promote venous drainage, such as aescinate.

5. Conclusion

The occurrence of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction may be related to the starting time of postoperative anticoagulant drug application and whether to place a drainage tube [13]. The results of this study showed that the risk of local inflammatory storm increased by 0.305 times when anticoagulant drugs were used one day early after surgery. Therefore, attention should be paid to the initial application time of anticoagulant drugs in the routine treatment of anterior cruciate ligament reconstruction under knee arthroscopy. It is recommended to start anticoagulant drugs after 3 days [14,15], and try to avoid the risk of local inflammatory storm. The risk of local inflammatory storm in patients without drainage tube placement is

5.994 times that of patients with drainage tube placement. For patients with high thrombosis scores and timely application of anticoagulant drugs after surgery, drainage tubes should be placed during the operation. In case of local inflammatory storm, the differential diagnosis between infection and medical history, clinical manifestations, physical examination, hematological examination, and bacterial culture of synovial fluid puncture should be made as soon as possible. Meanwhile, anti-inflammatory antibiotics, anti-swelling drugs, and local cold compress treatment should be given immediately to relieve symptoms.

Disclosure statement

The authors declare no conflict of interest.

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