Clinical Observations of Anterior Cruciate Ligament (ACL) Lesions in Patients with Chronic Fatigue

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Abstract

**Purpose** To explore how chronic fatigue impacts on anterior cruciate ligament (ACL) lesion and observe related clinical characteristics.

**Methods** A retrospective study conducted from December 2015 to December 2019, includes 86 males who involved chronic fatigue determined by the fatigue self-assessment scale and present symptoms of knee pain with no trauma. For those who diagnosed with ACL lesion, we recorded their basic characteristics such as age, BMI $\text{kg/m}^2$, daily training time, etc. and carried out some tests on them to evaluate their clinical performance and observed their manifestations under X-ray, MRI and arthroscopy around the treatment procedure.

**Results** Of all 86 males with ACL lesion, 59 patients were injured in the left knee while 27 in the right knee. Age, weekly training intensity, BMI, and knee hyperextension are independent influence factors for ACL lesion through multivariate analysis. Physical examinations and radiologic features included resting pain(23[26.7%]); standing pain(56[65.1%]); exercising pain(86[100%]); “powerless knee“(34[39.5%]); anterior patellar pain(41[47.7%]); knee axis tenderness(38[44.2%]); first degree positive in ADT test(34[39.5%]); second to third degree positive in ADT test(23[26.7%]); positive in Lachman test(73[84.9%]); positive in pivot shift test(5[5.8%]); ACL cyst(15[17.4%]); ACL thickness change(75[87.2%]); PCL tortuosity(35[40.7%]); synovitis(80[93.0%]); intra-articular effusion(79[91.9%]).

**Conclusion** The main risk factor of ACL lesion is patients’ training experience time. Knee pain, mild anterior instability of knee joint, synovitis and intra-articular effusion are the most typical clinical manifestations of ACL patients.

Introduction

Anterior cruciate ligament (ACL) lesion is a clinically common knee lesion, especially among military personnel and athletes. More than 70% of ACL lesions are caused by the participants' own activation, change of direction, and twisting of the knee joint when jumping to the ground. They are non-contact injuries which are closely related to the deformation of the knee joint during exercise. The annual incidence of ACL lesion among the athlete population is 0.06 to 3.70 cases per 1,000 hours of competition. According to data from the US Centers for Disease Control and Prevention, the number of ACL reconstruction operations is about 100,000 per year, ranking sixth among the most common types of surgery performed in the United States. ACL lesion is a common intra-knee lesion that occurs in young sporty people. Acute ACL lesion is the most common type. Chronic ACL lesion is mostly developing from undiagnosed or untreated trauma-caused acute type, then turned into long-term meniscus and cartilage damage. Primarily, we assume this is a chronic, insidious ACL fatigue lesion, which is another type of ACL lesion classified by time rather than acute or chronic. There are 6810 active athletes in China, including 3983 males and 2827 female athletes. Among various sports injuries, the incidence of ACL
lesion is as high as 0.47. The sport that caused the most ACL damage was basketball, followed by football, and young people accounted for 75.5% of the injured.

According to the currently known ACL lesion typing, it can be categorized into contact lesion and non-contact lesion according to the cause of lesion [6]. The lesion site is categorized into tendon-bone interface lesion at ligament insertion, avulsion fracture, and ligament body fracture [7]. Complete ACL fracture and partial lesion can be classified according to the degree of lesion. According to the time of onset, it can be divided into acute (less than 3 months after lesion), subacute (3 to 6 months after lesion) and chronic ACL lesion (more than 6 months after lesion) [8]. However, we found that a type of ACL failure patients without history of trauma has a clinical characteristic of years of fatigued training history, mainly manifested by knee pain, mild instability and abnormal MRI performance during exercise.

Existed evidence shows that neuromuscular fatigue can reduce athletes' performance and increase the anterior tibial translation. It also leads to decreased exercise endurance and quality, which may increase the risk of ACL lesion [9]. In the current related research, the researchers only compared the changes of lower limb biomechanics under two conditions: before and after fatigue. The drawback of this type of research is that due to differences in the individuals in the sample, each person's corresponding degree of fatigue after fatigue is different. There are also a few literatures that involve multiple levels of fatigue classification. For example, in the Mclean and Boro study, the fatigue rating is defined as 5 (pre-fatigue, 25%, 50%, 75%, 100%) [10]. In Tsai's research. The fatigue level is divided into four (pre fatigue, post fatigue, 20-min post fatigue, 40-min post fatigue) [11]. These studies aim to explore the difference in performance of different degrees of fatigue, and do not involve clinical observation.

In the beginning, for such patients we regarded them as chronic knee synovitis or obsolete ACL lesion. As the number of patients increased, symptoms with same characteristics such as knee pain, knee instability and abnormal ACL signal on MRI gradually attracted our attention. In the absence of studies on the clinical symptoms of ACL fatigue failure, we aim to observe the relevant epidemiological and corresponding treatment for ACL fatigue failure, evaluating the risk factors and manifestations of ACL fatigue failure patients, then provide basis for their treatment.

1. Methods And Analysis

1.1 Sample selection

From June 2015 to December 2019, 86 patients were selected from orthopedics clinic, who were treated for knee pain or knee instability on training. All males, aged 23 to 42 years, including policeman, fireman and those who maintain routine training. The selection criteria included patients' training experience (more than 1 year); no previous history of severe knee trauma and following swelling; the main symptom is knee pain when standing or exercising; probably some individuals showed "powerless knee(knees become weak when standing or walking)"; long-term of overwhelming training experience, such as long-distance running, high jump, obstacle training, competitive sports, etc.; aberrant ACL signal confirmed by
MRI. Patients’ fatigue levels were determined by the fatigue self-assessment scale (FSAS). Besides we excluded some samples with poor psychology or emotion.

1.2 Data collection

The medical records of all patients were analyzed by the research team of the department of orthopedics, Northern Theater General Hospital. Medical record, symptoms, clinical signs and radiologic features are collected from electronic records, and analyzed by a group of trained clinicians. Basic characteristics are collected by a designed form, and the information on forms included age, years of athlete training experience, body mass index (BMI), and weekly training time. Clinical data includes physical examination and radiologic features, such as knee pain degree, ADT test, Lachman test, pivot shift test, etc. ACL images shows MRI results and histogram shows all patients’ clinical manifestations.

1.3 Statistical analysis

Exploratory analysis of data is carried out first. The continuous variables of the normal distribution are described by mean ± standard deviation (SD), and the independent sample t-test is used for comparison between groups. The non-normal distribution continuity variables are described by maximum, minimum, and median values, P25, P75, and by non-parametric tests are used. Unidirectional ordered rank data uses Wilcoxon rank-sum test. Chi-square test for composition ratio. Pearson correlation coefficient is used to indicate the degree of correlation of continuous variables, and Spearman correlation coefficient is used to indicate the degree of correlation between classification/level variables and continuity variables. Compare the patient's demographic characteristics, disease-related items and other indicators, and analyze the impact of various factors on the patient's disease. P<0.05 was considered statistically significant.

2. Results

2.1 Basic characteristics of patients

A total of 86 patients were included in this study, all male, with an average age of 28±2.32 years and an average BMI index of 28.43±2.93 kg/m² (Table 1). For universities analysis results, ACL fatigue lesion is associated with the patient's age, routine training intensity, BMI, athlete training experience time, and knee hyperextension, all of which are p <0.05 (Table 1). According to multivariate analysis results, routine training intensity, BMI, and knee hyperextension are independent influencing factors (Table 1).

Table 1 general information of chronic ACL fatigue lesion patients
| Variables                              | n  | Questionnaire score/average | T value or $\chi^2$ value | $P$ value |
|---------------------------------------|----|----------------------------|---------------------------|-----------|
| Age                                   | 41 | 58.23                      | 23.134                    | 0.001     |
| Under 30                              | 45 | 47.32                      |                           |           |
| Over 30                               |    |                            |                           |           |
| Routine training intensity/1 week     | 20 | 60.34                      | 45.341                    | 0.001     |
| ≤15 hours                             | 32 | 52.34                      |                           |           |
| 15-25 hours                           | 34 | 45.67                      |                           |           |
| ≥25 hours                             | 3  |                            |                           |           |
| BMI (kg/m²)                           | 42 | 63.34                      | 54.234                    | 0.001     |
| ≥28                                   | 44 | 47.12                      |                           |           |
| Athlete training experience           | 50 | 56.12                      | 28.134                    | 0.001     |
| ≥3 years                              | 36 | 49.34                      |                           |           |
| ≥3 years                              |    |                            |                           |           |
| Knee hyperextension ≥5°               | 45 | 46.77                      | 32.144                    | 0.001     |
| yes                                   | 41 | 53.12                      |                           |           |
| no                                    |    |                            |                           |           |

### 2.2 Physical examination and radiologic features

The outcomes of major clinical symptoms, physical examination and MRI features are shown in Chart 1. Of all 86 patients, 23 have resting pain; 56 have standing pain; 86 have exercising pain; 34 have powerless knee; 41 have anterior patellar pain; 38 show knee axis tenderness; 34 show first degree positive in ADT test; 23 show second to third degree positive in ADT test; 73 show positive in Lachman test; 5 show positive in pivot shift test; 15 have ACL cyst; 75 show ACL thickness change; 35 show PCL tortuosity; 80 show synovitis; 79 show intra-articular effusion.

As shown in the histogram analysis image (Figure 1), knee pain and positive Lachman test are the primary clinical manifestations of chronic ACL fatigue failure. ACL thickness change, joint effusion and synovitis are most common signs on MRI scan (Figure 1).

### 3. Discussion
The etiological features are no serious trauma history and long-term overwhelming training history. In the clinical manifestation, the histogram display mainly shows feeling pain during exercise, the Lachman test is positive and MRI image changes. In addition, this MRI changing needs to pay more attention. ACL fatigue lesion is mostly combined with a small amount of effusion in joints and synovitis in MRI. The ACL signal is mainly manifested as thinning, thickening, tension change, etc. And can also incorporate the adaptive change of PCL. We believe that thinner ACLs would be injured easier at the same training intensity, which will lead to blurred ACL edges and tension changes. The partial ACL damage has led to changes of biomechanical structure in the joint, which has caused synovitis and joint effusion. Further research on ACL fatigue lesion image changes will be carried out by our team soon.

Some research has pointed that fatigue could cause acute ACL lesion, but the definition of ACL fatigue lesion has not been revealed completely from academic field. Until 2013, Ashton-Miller ‘s biomechanical study based on knee model through donated human corpses has demonstrated that repetitive pressure-applying jump is likely to cause ACL fatigue damage, but Miller ‘s research is only limited in biomechanical field, not involved with clinical research. For two of the cases, arthroscopy surgery was performed and concluded that ACL fatigue lesion without trauma history manifested as ligament relaxation and partial femoral end damage.

Regarding the causes of chronic ACL fatigue lesion, the exploring is still on process. However, with the academic theory, there are many ACL lesion-causing factors that can explain its development from different aspects. For example, the signal receptor on ligament surface hypothesis, abundant mechanical receptors exist on ACL surface, especially the ligament end points and synovial folds. Dhillon MS's analyzed the risk of the cruciate ligament damage within the changes of mechanical receptors. His research confirmed that the number of mechanical receptors was related to the prolonged ligament lesion, the longer the damage, the less the number of mechanical receptors. After reviewing the literature and considering clinical observations, we state a hypothesis that fatigue can weaken the muscle force surrounding the knee, thereby weakening the dynamic stability of the knee. At the same time, knee static stability structure most relied on ligament stands outranged tension, secondly makes ligaments deformed, mechanical receptors decreased, eventually the chronic ACL lesion happens. More importantly, this process can also lead to another kind of positive feedback cycle, that is, chronic lesion leads to static damage, and static damage exacerbates chronic lesion. This also theoretically explains the root cause of that one case who was diagnosed with chronic ACL fatigue lesion, he was admitted to our hospital again for acute complete ACL rupture due to sprain during training after discharging in six months. Other research groups had also clarified their views based on other case-control studies and biomechanical analysis, under fatigue, the flexion and valgus angles of the hip, knee and ankle joints are different from the normal state, so that it changed the force from ground to the body, converting the knee torque in various directions, further proving fatigue condition induces ACL lesion.

Swanik et al. also reported that athletes maintained a slower response and a slower processing speed in the non-contact ACL lesion compared with the control group. Many cases we saw in the clinic,
including the individual case with chronic ACL fatigue lesion reported this time, all of them have experienced long-term high-intensity overwhelmed training, besides, warm-up preparation before training, fatigue recovery status between training intervals and after training Stretching movements are all lack of scientific guidance. More reports confirm that during fatigue status, the neuromuscular control and coordination ability become inactive, neuromuscular control is weakened, ligament tension and joint pressure are altered, increasing the risk of ACL rupture.[30]

Furthermore, another theory is the cruciate ligament will gradually degenerate with the development of knee osteoarthritis by age growing, accompanied with decreasing ACL function[31] and knee proprioception[32]. The cruciate ligament degeneration is mainly associated with inflammation, which is an active, cell-mediated process of extracellular matrix reduction and remodeling[33]. The degeneration of ligaments and the weakening of proprioception of knee joint will promote the further development of osteoarthritis, which complement each other[34]. This theory could also explain our finding that chronic ACL fatigue lesion is more common in sporty people over the age of 30, while are rare in patients under the age of 25.

Certainly, chronic ACL injuries also share common risk factors with acute ACL injuries, such as ACL development defects, intercondylar fossa abnormalities, BMI, gender, and multiple joint relaxations[35-41]. Our study also supports this theory. Through univariate analysis, we know that ACL fatigue failure is related to the patient's age, daily training intensity, BMI, military service time, and knee hyperextension, such as knee function decreasing along with aging. Through multivariate analysis, it is known that weekly training intensity, BMI, and knee hyperextension all are independent influence factors for ACL fatigue lesion.

There are also some limitations in this report, due to the difference of individual physical quality and the complexity of qualifying fatigue, the evaluation of patients’ fatigue degree can’t be completely accurate. The content and intensity of the training vary with the occupation of the patients. This paper is only a preliminary clinical observation study, which can guide us to further understand the manifestations of such diseases and provide help for more targeted research in the future.

In conclusion, ACL fatigue lesion is mainly manifested by pain and instability of the knee joints, especially the exercising pain. In patients’ physical examinations, the positive proportion of Lachman test was as high as 84.9%, and very few (5) were positive in axial movement test, which proved that most patients presented with partial and mild lesions rather than severe ACL relaxation or even rupture. The high incidence of synovitis and intra-articular effusion was observed on MRI, both of which were the result of long-term high-intensity training.

## Abbreviations

ACL: Anterior cruciate ligament
Declarations

Ethics Approval and Consent to participate

This study was conducted according to the ethical guidelines and principles of the international Declaration of Helsinki.

Consent for Publication

Written informed consent for publication was obtained from all participants.

Availability of Data and Materials

Not applicable.

Competing Interests

The authors declare that they have no competing interest.

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Author’s Contribution

Wang Yu was the guarantor and designed the study, also participated in the acquisition, analysis, interpretation of the data, and drafted the initial manuscript. Liu Xianmin participated in the acquisition, analysis, interpretation of the data, and drafted the initial manuscript. Li Chunbao and Xiang Liangbi revised the article critically for important intellectual content. All authors read and approved the final manuscript.

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Figures
Cases calculation of various clinical manifestations. (a: resting pain; b: standing pain; c: exercising pain; d: powerless knee; e: anterior patellar pain; f: knee axis tenderness; g: ADT test(+); h: ADT test(++) i: Lachman test(+); j: pivot shift test; k: ACL cyst; l: ACL thickness change; m: PCL tortuosity; n: synovitis; o: intra-articular effusion). T2 image shows thin joint effusion in the suprapatellar capsule, medial and lateral joint space, tibial-femoral joint and meniscus space. The ACL signal in three consecutive layers
lacks continuity, and the posterior cruciate ligament is tortuous. T1 image mainly shows expansion and blur ACL signal.