

February 15, 2019  
Keio University School of Medicine

## Identifying the Warning Signs of Bone Stress Injuries in Japanese Female Athletes

### Hope for Effective Prevention of Stress Fractures

A group of researchers at Keio University School of Medicine, led by Project Associate Professor Takeshi Miyamoto, have attempted to identify biomarkers that may be able to predict future stress fractures in female athletes. The team evaluated 56 female athletes from Keio University, investigating the relationship between past stress fractures and dysmenorrhea, reduced food intake, and body weight loss, all of which are considered to be associated with stress injuries.

13 of those athletes (23.2%) answered that they had a history of stress fracture and more than half had experienced reduced food intake, dysmenorrhea, or shin splints (Note 1) (See Fig 1). Among these, dysmenorrhea was significantly associated with a history of stress fractures, the risk of stress injury by almost 8 times. In addition, the risk of stress injury was significantly higher in athletes who had a previous history of stress fracture.

In serum and urine, creatine kinase (CK) (Note 2) and lactic acid dehydrogenase (LDH) (Note 3) levels are generally known to increase following exercise. When we subdivided subjects into stress fracture and non-fracture groups, we found that levels of CK and LDH were significantly higher in the fracture group, while osteocalcin (OC) and uncarboxylated osteocalcin (ucOC), which are bone forming parameters, significantly decreased. This data indicates that increased serum CK and LDH and decreased serum OC and ucOC are useful as biomarkers of stress injuries.

This result is useful for the prevention of stress fractures in Japanese female athletes and is expected to also be useful in informing coaches about an individual's risk in order to prevent future stress fractures.

The results of this research were published in the international scientific journal *Scientific Reports* on December 21, 2018.

#### 1. Research Background

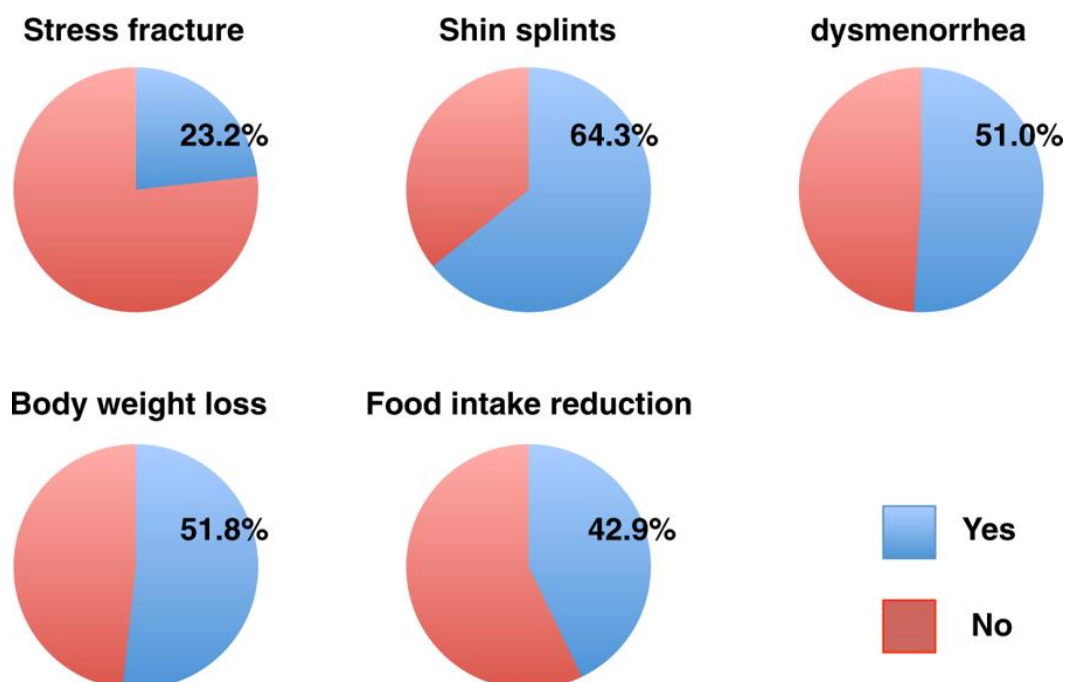
Stress fractures are a limitation for athletes not only in sports performance but in the course of daily life. Thus, preventing them is crucial. In female athletes, a triad of symptoms including low energy availability, functional hypothalamic amenorrhea and osteoporosis are considered risk factors for stress injuries, but biomarkers predictive of these outcomes are not available.

## 2. Research Significance and Future Development

In this study, we evaluated 56 female athletes from Keio University and identified that a history of dysmenorrhea including amenorrhea correlated with a history of stress injuries, with dysmenorrhea increasing the risk of stress injury by almost 8 times (see Fig. 2).

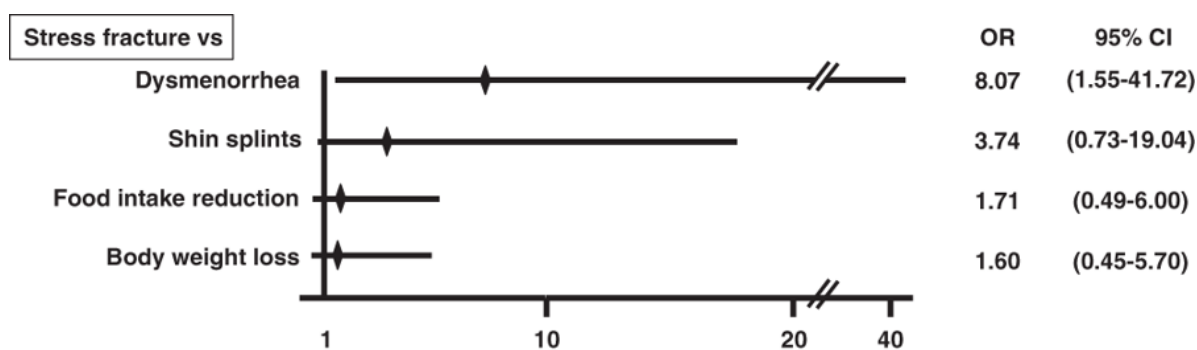
We also showed that risk of stress injury was significantly higher in athletes who had a previous history of stress fracture based on a chi-square test ( $X^2 = 4.99, p < 0.05$ ). In addition, we saw that stress injury was more likely to occur when energy consumption was high during periods of intense exercise.

Moreover, blood test results showed that serum levels of creatine kinase (CK) and lactic acid dehydrogenase (LDH) values were significantly higher (CK: $p < 0.05$ , LDH: $p < 0.01$ ) in athletes with a history of stress injuries, while osteocalcin (OC) and uncarboxylated osteocalcin (ucOC), which are bone forming parameters, significantly decreased (OC: $p < 0.05$ , ucOC: $p < 0.05$ ). This data indicates that these four variables are useful as biomarkers of stress injuries.



**Fig. 1: Previous Morbidity Related to Stress Fractures in Female Young Athletes**

Among subjects, 23.2% had a history of stress fracture. Around half of subjects reported past dysmenorrhea, body weight loss, or reduced food intake. We investigated the relationship between subjects' histories and stress fractures.



**Fig. 2: Correlation Between Stress Fractures and Risk Factors**

Dysmenorrhea caused the risk of fatigue fracture increase approximately 8 times, showing a strong correlation to stress fractures. Shin splints also showed a possible, though less significant, correlation to stress fractures. On the other hand, food intake reduction and body weight loss both showed little correlation to stress fractures.

In addition to biomarkers, it is expected that by monitoring dysmenorrhea, shin splints, past stress fractures, and energy consumption, we will be able to effectively prevent future stress fractures.

### 3. Notes

This research was made possible by JSPS Grant-in-Aid for Scientific Research JP15H04963.

### 4. Research Paper

Title: Elevated Creatine Kinase and Lactic Acid Dehydrogenase and Decreased Osteocalcin and Uncarboxylated Osteocalcin are Associated with Bone Stress Injuries in Young Female Athletes

Japanese Title : クレアチンキナーゼと乳酸デヒドロゲナーゼの上昇、オステオカルシンと低カルボキシル化オステオカルシンの低下は若い女性アスリートの疲労骨折に関連する

Authors: Takeshi Miyamoto, Yuko Oguma, Yuiko Sato, Tami Kobayashi, Eri Ito, Mayaka Tani, Kana Miyamoto, Yuji Nishiwaki, Hiroyuki Ishida, Toshiro Otani, Hideo Matsumoto, Morio Matsumoto, Masaya Nakamura

Publication: Scientific Reports

[Glossary]

Note 1 — Shin splints: acute pain in the shin and lower leg often caused by athletic activity

Note 2 — Creatine kinase: an enzyme found in skeletal and cardiac muscle tissue

Note 3 — Lactic acid dehydrogenase: an enzyme often found in the liver and skeletal muscle tissue

\*Please direct any requests or inquiries to the contact information provided below.

\*This press release has been sent to the MEXT Press Club, Science Press Club, MHLW Press Club, MHLW Hibiya Club, and society and education departments of other media outlets.

Research Inquiries

Keio University School of Medicine  
Department of Advanced Therapy for  
Musculoskeletal Disorders  
Project Associate Professor Takeshi Miyamoto

TEL: +81(0)3-5363-3812

FAX: +81(0)3-3353-6597

E-mail: miyamoto@z5.keio.jp

Press Release Inquiries

Office of General Affairs  
Shinanomachi Campus  
Keio University  
35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582

TEL: +81(0)3-5363-3611

FAX: +81(0)3-5363-3612

E-mail : med-koho@adst.keio.ac.jp

<http://www.med.keio.ac.jp/>