Author’s response to reviews

Title: The effects on calcaneofibular ligament function of differences in the angle of the calcaneofibular ligament with respect to the long axis of the fibula: A simulation study

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Author’s response to reviews:

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Prof Alan Borthwick and Prof Hylton Menz
Editors-in-Chief
Journal of Foot and Ankle Research

Dear Profs. Borthwick and Menz:

Ms. Ref. No.: JFAR-D-17-00115
“The effects on calcaneofibular ligament function of differences in the angle of the calcaneofibular ligament with respect to the long axis of the fibula: A simulation study” by Mutsuaki Edama

Thank you for your letter. We are grateful for the detailed feedback provided by the reviewers, whose comments have helped us to significantly improve the paper. Attached are our point-by-point responses to the reviewers’ comments and our revised manuscript, which we hope will now meet with your approval. For your convenience, we have attached a copy of the manuscript with all revisions highlighted in red font. We believe that our revisions have addressed the issues raised by the reviewers and trust that the manuscript is now suitable for publication in the Journal of Foot and Ankle Research.

Thank you again for your thoughtful comments, and we look forward to hearing from you soon.

Sincerely,

Mutsuaki Edama

RESPONSES TO REVIEWER 1

1. How long has it become cadaver?

→ All cadavers were examined on average 2 to 3 years after death.

2. Whether the same preservation technique on all cadaver?

→ The same preservation techniques were used for all cadavers; they were fixed in 10% formalin, followed by alcohol substitution at our institution.
3. There was no known activity in life of those cadavers, which may affect the elasticity of the ligaments

→ We had no information about activities prior to death. However, none showed signs of previous major surgery around the ankle.

4. Need a more detailed explanation of the data in table 2 and table 3, namely:

What is the mean of value of each plantar flexi -30, -20 and -10?

→ Table 2 has been corrected as suggested.

The new title is "Table 1. Changes in strain for each category during dorsiflexion and plantarflexion".

Value: Strain at plantarflexion and dorsiflexion

CFL20°, angle of the CFL with respect to the long axis of the fibula from 20° to 29°; CFL30°, angle of the CFL with respect to the long axis of the fibula from 30° to 39°; CFL40°, angle of the CFL with respect to the long axis of the fibula from 40° to 49°; CFL50°, angle of the CFL with respect to the long axis of the fibula from 50° to 59°; CFL2, CFLs with two crossing fiber bundles.

Table 3 has been corrected as suggested.

The new title is "Table 2. Changes in strain when ankle varus (20°) and valgus (20°) were added at the ankle joint with plantarflexion/dorsiflexion for each calcaneofibular ligament category".

Value: Strain at Inversion/Strain at Eversion

Average: Values presented as means ± SD.

CFL20°, angle of the CFL with respect to the long axis of the fibula from 20° to 29°; CFL30°, angle of the CFL with respect to the long axis of the fibula from 30° to 39°; CFL40°, angle of the CFL with respect to the long axis of the fibula from 40° to 49°; CFL50°, angle of the CFL with respect to the long axis of the fibula from 50° to 59°; CFL2, CFLs with two crossing fiber bundles.

5. In the discussion it should be mentioned that the assessment technique, does not consider the element of gravity, weight bearing, and muscle activity
6. It should be mentioned also that the posture of foot during life, can affect the degree of CFL (pes planus/pes cavus)

The text has been corrected as suggested (Pg 10, Lns 37-45).

This study did have a number of limitations. First, it involved simulations with cadavers. Therefore, gravity, weight bearing, muscle activity, and the posture of the foot were not considered. In the future, we believe that it will be necessary to perform biomechanical research using our basic data with in vivo samples.

7. A tool used to assess the flexibility of the ligaments, is less clearly described

It should be described the shape and how was the tool work.

We have added Figure 1 (Pg 6, Ln 18).

8. In discussion need to be added whether the difference of result of this research with research which has been done by: P. Kitsoulis, A. Marini, A. Pseftinakou, concerning Morphological study of the calcaneofibular ligament in cadavers.

The text has been corrected as suggested (Pg 5, Lns 1-3; Pg 8, Lns 57-60; Pg 9, Lns 1-3).

Kitsoulis found 52 subjects (72.2%) with one band forming the CFL, 16 with two bands (22.2%), and 4 with three bands (5.6%)[7].

Unlike the previous study, though, the present sample did not include specimens with fan-shaped morphology or with an angle with respect to the long axis of the fibula of 0° and 80–90°[6] or with three bands[7].


RESPONSES TO REVIEWER 2

1. The title needs clarification, as well as the abstract and throughout the text, on what "running angles" means. To the audience interested in this journal it would be fair to say that the initial
thought is that this term is related to running gait. I think the term should clarify that this is fibre orientation, if I am understanding this correctly?

→ The title has been corrected as suggested (Pg 1, Ln 1-3).

The new title is “The effects on calcaneofibular ligament function of differences in the angle of the calcaneofibular ligament with respect to the long axis of the fibula: A simulation study”.

In other parts, also changed "running angles" to "angle of the CFLs with respect to the long axis of the fibula" (Pg 2, Ln 5; Pg 2, Ln 11; Pg 2, Ln 18; Pg 2, Lns 56-58; Pg 4, Lns 39-42; Pg 5, Lns 8-11; Pg 5, Ln 14; Pg 5, Ln 19; Pg 5, Lns 57-60; Pg 6, Lns 3-7; Pg 10, Ln 6; Pg 10, Lns 24-26; Pg 10, Ln 32; Figure 2; Table 1, Table 2).

2. Check throughout the manuscript on the journal referencing style and rectify accordingly. Similarly review the language format of tense and reduce 1st person.

→ The reference has been corrected as suggested (REFERENCES).

Introduction

3. ATFL is introduced first and then quickly moved on to CFL - it may be worth revisiting how this is written as it distracts from the main topic.

→ The text has been corrected as suggested (Pg 4, Lns 3-9).

Many studies have investigated the functional role of the CFL in addition to the ATFL because the ATFL and CFL are largely involved in ankle inversion restriction[1,2]. However, consensus has yet to be reached on the functional role of the CFL.


4. Grond JT? I assume this is an author - ref correctly

→ The text has been corrected as suggested (Pg 4, Lns 54-60).
Analyzing data from autopsies and operations, Ruth identified four categories of CFLs based on angles relative to the long axis of the fibula and morphology: 0° (14 feet, 18.7%), 10–45° (56 feet, 74.7%), 80–90° (three feet, 4%), and fan-shaped CFLs (two feet, 2.6%)[6].


Methods

5. Expand the ethical judgement of this paper and acknowledge that ethical protocols were adhered to. Who consented to this work being completed? Expand the statement about ethical approval to assure the readers that this project was suitably approved.

→ The text has been corrected as suggested (DECLARATIONS).

Ethics approval and consent to participate

Informed consent was obtained from the families of all subjects. This study was approved by the Ethics Committee at the Mutsuaki Edama, Niigata, Japan.

6. Why did the specimens have to be dissected above the knee for CFL assessment?

→ In our study, the talocrural joint, the line connecting the inferior borders of the medial and lateral malleoli, and the subtalar joint, the line connecting the lateral border of the calcaneal tuberosity and the midpoint of the talar head, were designated as the joint axes. For the setting of the joint axes, the medial condyles and lateral epicondyles of the femur are required as bone landmarks. Therefore, the lower limbs were cut 10 cm above the knee to produce isolated specimens.

7. Who dissected the CFL?

→ The text has been corrected as suggested (Pg 5, Ln 49).

One author (first author) dissected the CFL ligaments alone.

8. And how were the angles determined?
The CFLs were carefully dissected after removal of skin, subcutaneous tissue, muscle-tendon tissue, and crural fascia. With reference to a previous study [6], the CFLs were categorized according to the angles of the CFLs with respect to the long axis of the fibula and the number of fiber bundles, using a stainless 180 goniometer (300 mm CK-S4305-300, Chin Kou Medical Instrument Ltd, New Taipei City, Taiwan). Five categories were established: CFL20° (angle of the CFL with respect to the long axis of the fibula from 20° to 29°); CFL30° (range 30–39°); CFL40° (range 40–49°); CFL50° (range 50–59°); and CFL2 (CFLs with two crossing fiber bundles). All measurements were done in an intermediate position of ankle plantarflexion/dorsiflexion of 0°.


9. Diagrams of the methodology would enhance the understating of this work as the audience reading it would not necessarily have knowledge of the descriptive techniques used.

→ We added Figure 1.

10. Expand what was examined statistically.

→ This study simulated each category of CFLs. Therefore, there was no need for statistical analysis.

Discussion

11. Do not repeat the results in the opening paragraph.

→ The text has been corrected as suggested (Pg 8, Lns 52-60; Pg 9, Lns 1-3).

In the present study, five categories were identified. The present sample comprised 65 feet (80.3%) with an angle respect to the long axis of the fibula between 10° and 50°, which was similar to the finding of 56 feet (74.7%) reported in the previous study[6]. Unlike the previous study, though, the present sample did not include specimens with fan-shaped morphology or with an angle with respect to the long axis of the fibula of 0° and 80–90°[6] or with three bands[7].
12. The acknowledgment of their being variations between ethnicities in the second paragraph is a relevant discussion point, however I feel that it should be at the end of the discussion as it is a limitation of the study really and distracts from the main message at the beginning of this work.

This section needs complete revision as it is an extension of all literature review with your results popped in. There is no discussion about why you got the results you did or what significance this has. Build on what you have written in a way that delves into the work and discusses why there is such variation in a population and why the ligament behaves differently.

→ The text has been corrected as suggested (Pg 8, Lns 52-60; Pg 9, Lns 1-3; Pg 10, Lns 44-55).

In the present study, five categories were identified. The present sample comprised 65 feet (80.3%) with an angle respect to the long axis of the fibula between 10° and 50°, which was similar to the finding of 56 feet (74.7%) reported in the previous study[6]. Unlike the previous study, though, the present sample did not include specimens with fan-shaped morphology or with an angle with respect to the long axis of the fibula of 0° and 80–90°[6] or with three bands[7].

Second, all cadavers used in this study were Japanese. It is not certain whether the present findings apply to cadavers from other ethnicities. Many studies have raised the possibility of skeletal muscle and tendon variations across ethnicities [19-23], and this could be true for ligaments as well. Thus, future studies will need to investigate variations based on ethnic origin.


RESPONSES TO REVIEWER 3

Abstract

1. I would question the main conclusion that ankle function may change in relation to various CFL angles. The study demonstrated that CFL strain varies according to sagittal and frontal plane positioning of the ankle not vice versa.

→ The text has been corrected as suggested (Pg 2, Lns 56-59).

CFL function changed according to the difference in the angles of the CFLs with respect to the long axis of the fibula.

Background: Page 1

2. Line 16: Sentence begins with "Since", please consider an alternative start for the sentence

→ The text has been corrected as suggested (Pg 4, Lns 3-9).

Many studies have investigated the functional role of the CFL in addition to the ATFL because the ATFL and CFL are largely involved in ankle inversion restriction[1,2]. However, consensus has yet to be reached on the functional role of the CFL.


3. Lines 26-32: This sentence is confusing

→ The text has been corrected as suggested (Pg 4, Lns 11-17).
For example, Ozeki et al. examined cadavers to explore the functional role of the CFL and observed that the CFL becomes taut at dorsiflexion angles ≥18°, and it is nearly relaxed at other angles[3].


4. Line 47: Sentence starts with "on the other hand", please consider an alternative start for the sentence

→ The text has been corrected as suggested (Pg 4, Lns 31-40).

However, although Sarrafian and Kelikian found that the CFL is taut in dorsiflexion and relaxed in plantarflexion, they also noted that some specimens showed reversal of motions, whereas, in others, the tension in this ligament remained constant in all positions[5].


5. The word running angle was initially confusing and not a term I was familiar with. The running angle either needs to be defined earlier in the background or an alternative term used, e.g. anatomical orientation.

→ "Running angles" has been changed to "the angle of CFLs with respect to the long axis of the fibula" (Pg 2, Ln 5; Pg 2, Ln 11; Pg 2, Ln 18; Pg 2, Lns 56-58; Pg 4, Lns 39-42; Pg 5, Lns 8-11; Pg 5, Ln 14; Pg 5, Ln 19; Pg 5, Lns 57-60; Pg 6, Lns 3-7; Pg 10, Ln 6; Pg 10, Ln 24-26; Pg 10, Ln 32; Figure 2; Table 1, Table 2).

Background: Page 2

6. Line 6: Reference needs correction "Grond JT"

→ The text has been corrected as suggested (Pg 4 , Lns 54-60).

Analyzing data from autopsies and operations, Ruth identified four categories of CFLs based on angles relative to the long axis of the fibula and morphology: 0° (14 feet, 18.7%), 10–45° (56 feet, 74.7%), 80–90° (three feet, 4%), and fan-shaped CFLs (two feet, 2.6%)[6]. Kitsoulis found
52 subjects (72.2%) with one band forming the CFL, 16 with two bands (22.2%), and 4 with three bands (5.6%)[7].


7. Lines 21-27: The aim does not align with the study conclusions.

→ The text has been corrected as suggested (Pg 5, Lns 14-24).

Therefore, In the present study, CFLs harvested from cadavers were categorized according to the differences in the angle of the CFL with respect to the long axis of the fibula and the shape, and then three-dimensional reconstructions of the CFLs were used to simulate and examine the differences in the angles of the CFLs with respect to the long axis of the fibula and how they affect CFL function.

Methods: Page 1

8. Please add what institution granted ethical approval

→ The text has been corrected as suggested (Pg 5, Lns 42-44).

This study was approved by the Ethics Committee at our institution.

Methods: page 2

9. Lines 48-51: A previous study on what indicated reproducibility and reliability?

→ The text has been corrected as suggested (Pg 6, Lns 55-58; Pg 7, Lns 1-11).

The MicroScribe system is an instrument with high precision (manufacturer’s specifications, measurement precision of 0.23 mm). However, measurements must be performed manually. In addition, although the study cadavers were thoroughly fixed to the examination table such that they did not move, it was necessary to test whether they had moved, since the measurements entail dissection of the ligament tissue. A previous study by the authors found the intraclasse
correlation coefficient (1, 1) to be 0.97–0.99 [17], which indicates a high level of reliability and reproducibility.

[17] Edama M et al. Differences in the degree of stretching applied to Achilles tendon fibers when the calcaneus is pronated or supinated. Foot Ankle Online J. 2016;9: 5.

Statistical analysis

10. Was any adjustment considered for pooling the left and right feet?

→ The text has been corrected as suggested (Pg 7, Lns 34-60; Pg 8, Ln 1).

Sex and left-right differences

A comparison between males and females showed that, among men, 7 legs (8.6%) were CFL20°, 13 feet (16.1%) were CFL30°, 18 feet (22.2%) were CFL40°, 13 feet (16.1%) were CFL50°, and 0 feet (0%) were CFL2, while, among women, 7 feet (8.6%) were CFL20°, 9 feet (11.1%) were CFL30°, 11 feet (13.6%) were CFL40°, 2 feet (2.5%) were CFL50°, and 1 foot (1.2%) was CFL2. No significant differences were seen.

With respect to left-right differences, both legs could be measured in 37 cadavers (male 23, female 14; 74 feet). Among the right feet, 5 feet (6.7%) were CFL20°, 9 feet (12.2%) were CFL30°, 15 feet (20.3%) were CFL40°, 8 feet (10.8%) were CFL50°, and 0 feet (0%) were CFL2. Among the left feet, 7 feet (9.4%) were CFL20°, 11 feet (14.9%) were CFL30°, 11 feet (14.9%) were CFL40°, 7 feet (9.4%) were CFL50°, and 1 foot (1.4%) was CFL2. No significant differences were seen.

Results:

11. Please report P values

→ This study simulated each category of CFL. Therefore, no statistical analysis was needed.

12. Table 1: The title needs to be more descriptive. What are the differences in the table?

The in text description of the results section does not really match what Table 1 presents

→ The text has been corrected as suggested. I have omitted Table 1 (Pg 7, Lns 26-60; Pg 8, Ln 1).
CFL running angle categories (Figure 1)

Five categories were identified: CFL20° in 14 feet (17.3%); CFL30° in 22 feet (27.2%); CFL40° in 29 feet (35.8%); CFL50° in 15 feet (18.5%); and CFL2 in one foot (1.2%).

Sex and left-right differences

A comparison between males and females showed that, among men, 7 legs (8.6%) were CFL20°, 13 feet (16.1%) were CFL30°, 18 feet (22.2%) were CFL40°, 13 feet (16.1%) were CFL50°, and 0 feet (0%) were CFL2, while, among women, 7 feet (8.6%) were CFL20°, 9 feet (11.1%) were CFL30°, 11 feet (13.6%) were CFL40°, 2 feet (2.5%) were CFL50°, and 1 foot (1.2%) was CFL2. No significant differences were seen.

With respect to left-right differences, both legs could be measured in 37 cadavers (male 23, female 14; 74 feet). Among the right feet, 5 feet (6.7%) were CFL20°, 9 feet (12.2%) were CFL30°, 15 feet (20.3%) were CFL40°, 8 feet (10.8%) were CFL50°, and 0 feet (0%) were CFL2. Among the left feet, 7 feet (9.4%) were CFL20°, 11 feet (14.9%) were CFL30°, 11 feet (14.9%) were CFL40°, 7 feet (9.4%) were CFL50°, and 1 foot (1.4%) was CFL2. No significant differences were seen.

13. Table 2: There is some confusion between the in text description in the results section and table 2. The in text description is titled "changes in strain" but table 2 is titled "changes in degree of stretching"

→ Table 2 has been corrected as suggested (Table 1).

The new title is “Table 1. Changes in strain for each category during dorsiflexion and plantarflexion”.

14. Table 3: Same problem as Table 2 with regard to variation between in text and title.

The in text description of table 2 also needs some statistics presented in the results

→ Table 3 has been corrected as suggested (Table 2).

The new title is “Table 2. Changes in strain when ankle varus (20°) and valgus (20°) were added at the ankle joint with plantarflexion/dorsiflexion for each calcaneofibular ligament category”.

This study simulated each category of CFL. Therefore, no statistical analysis was needed.
Discussion

15. The authors need to acknowledge they only examined two planar motion (sagittal and frontal) components of ankle function. Incorporating varus and valgus motions at the hind foot also examined triplanar motion of the subtalar joint.

→ In our study, the talocrural joint, which is the line connecting the inferior borders of the medial and lateral malleoli, and the subtalar joint, which is the line connecting the lateral border of the calcaneal tuberosity and the midpoint of the talar head, were designated as the joint axes. Therefore, I think that movement of the subtalar joint can be included.

16. Conclusion: As mentioned in the abstract I feel the conclusion is not correct based on the results.

→ The text has been corrected as suggested (Pg 11, Lns 3-14).

The findings of the present study suggest that CFL function may change in relation to the angle of the CFL with respect to the long axis of the fibula and morphologies. We believe that it will be necessary in the future to perform biomechanical research using our basic data with in vivo samples and investigate whether individual anatomical differences may represent risk factors for CFL injury.