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Anatomical Study of the Cuboid and Its Ligamentous Attachments and Its Implications for a Cuboid Osteotomy

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Abstract

Background: Lateral column lengthening (LCL) for flexible flatfoot is an effective surgery with powerful correction of deformity because it tightens only the lateral third of the long plantar ligament (LPL). However, LCL has been associated with joint damage at the osteotomy site and loss of foot flexibility owing to joint fixation. We focused on the cuboid and investigate a novel anatomical LCL osteotomy site that effectively tightens the LPL without damaging any joints.

Methods: We studied 24 feet of 12 cadavers (mean age, 80.8 years). The lengths of the LPL and short plantar ligament, locations of the attachments, and shape and location of the cuneocuboid joint on the medial side of the cuboid were studied. ImageJ software was used to measure the osteotomy angle.

Results: The lateral cuboid attachment of the LPL on average was located 4.6 mm from the calcaneocuboid joint, and the cuneocuboid joint on average was located 6.7 mm from the cuboid-metatarsal joint on the medial surface of the cuboid. The direct line connecting the anterior cuneocuboid joint and the oblique crest of the cuboid on average was at a 10.3-degree inclination posterior to the cuboid-metatarsal joint.

Conclusion: A straight line must be selected between a point 4 mm from the calcaneocuboid joint laterally and 6 mm from the cuboid-metatarsal joint medially at a 10-degree posterior tilt to the cuboid-metatarsal joint to perform a cuboid osteotomy LCL without damaging the articular surface.

Clinical Relevance: We investigated a potential novel cuboid osteotomy method for LCL.

Keywords: lateral column lengthening, flatfoot, cuboid osteotomy

Introduction

Flatfoot is the general term for diseases of the foot involving eversion of the posterior foot, lowered or flattened medial longitudinal arch, and abduction of the forefoot caused by stretched or ruptured plantar ligaments, such as the spring ligament. Surgery for flexible flatfoot without osteoarthritis typically combines soft tissue surgeries, such as spring ligament repair, transfer of the flexor digitorum longus tendon, and Achilles tendon lengthening with bone and joint surgeries, such as medial displacement calcaneal osteotomy and lateral column lengthening (LCL).[4] In particular, LCL is a powerful correctional surgery, which tightens the lateral third of the long plantar ligament (LPL), the lateral extension of the inferior calcaneocuboid ligament (ICCL),[3] which results in adduction anterior to and supination posterior to osteotomy.[1] However, its mechanism is not completely understood.[11] There are 2 parts of the ICCL: the LPL and short plantar ligament (SPL).[8] The LPL attaches posteriorly to the inferior surface of the calcaneus between the posterior and anterior tubercles. The LPL comprises deep fibers and superficial fibers. The deep fibers attach across the calcaneocuboid joint from the cuboid tuberosity to the oblique crest of cuboid. Further anterior, the superficial fibers form the roof of the groove of the peroneus

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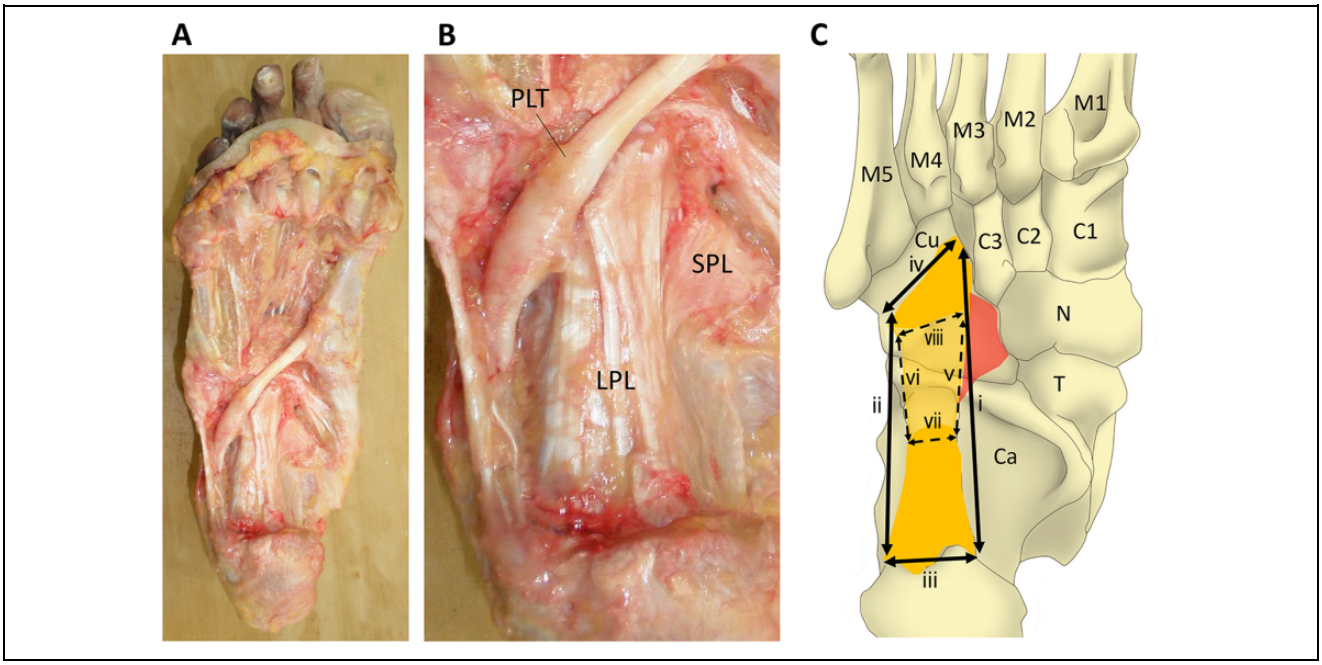

Figure 1. Anatomy of the inferior calcaneocuboid ligament from the plantar view. (A) Overall view. (B) Enlarged view of LPL and SPL. (C) Schematic diagram and measurement items. i, LPL medial length; ii, LPL lateral length; iii, LPL calcaneus attachment width; iv, LPL cuboid attachment width; v, LPL attachment medial length; vi, LPL attachment lateral length; vii, LPL attachment calcaneus width; and viii, LPL attachment cuboid width. Ca, calcaneus; Cu, cuboid; T, talus; N, navicular; C1-3, cuneiform; M1-5, metatarsal; PLT, peroneus longus tendon; LPL, long plantar ligament; SPL, short plantar ligament.

longus and continue to the bases of the second, third, fourth, and fifth metatarsal bones.[8,14] The SPL is attached in front of the calcaneus tuberosity across the calcaneocuboid joint and is attached to the cuboid tuberosity posterior to the oblique crest of cuboid. This contributes to the stability of the calcaneocuboid joint and formation of the lateral longitudinal arch.

Conventional LCLs are broadly classified into 2 types: those that involve lengthening by osteotomy in the anterior portion of the calcaneus, such as Evans osteotomy[5] and Hintermann osteotomy,[6,7] and those that lengthen and fix the ligament at the calcaneocuboid joint, namely, calcaneocuboid distraction arthrodesis (CCDA).[1] Each of these types is associated with its own risks: lengthening in the anterior portion of the calcaneus in which the site of osteotomy matches the anterior and middle talocalcaneal joints,[4] which causes the risk of osteoarthritis related to talocalcaneal joint injury, and decreased flexibility owing to fixing the joint in CCDA[1,2] have been noted.

In this study, we focused on the cuboid and ICCL for anatomical investigation of novel LCL osteotomy that could effectively tighten the LPL without damaging any joints to possibly solve these issues with conventional surgeries.

Methods

The protocol of the present study was approved by the ethics committee of the St Marianna University School of Medicine (approval no. 4094). This study was carried out in accordance with the World Medical Association Declaration of Helsinki. Specimens were obtained with the cooperation of the Department of Anatomy of the St Marianna University School of Medicine. Preserved cadaveric feet were obtained and used according to institutional guidelines and approval. Twenty-four feet were obtained from 12 cadavers (mean age, 80.8 years; age range, 72-92 years) for dissection with 12 feet from 6 men and 12 from 6 women. All feet were fixed in formalin and did not have any fractures or deformities. After excising soft tissues such as skin and plantar fascia, the deep fibers and SPL of the LPL were exposed (Figure 1A, B). The medial and lateral lengths of the deep fibers of the LPL, calcaneus attachment width, and cuboid attachment width were measured (Figure 1C: i-iv). The deep fibers of the LPL have a width such that they can attach to both the calcaneus and cuboid. Thus, we measured the medial and lateral lengths between the attachments of the deep fibers of the LPL, width of the calcaneus attachment, and width of the cuboid attachment (Figure 1C: v-viii). Next, the LPL was excised (Figure 2A), and the medial and lateral lengths of the SPL, calcaneus attachment, and cuboid attachment were measured (Figure 2B: i-iv). In addition, the SPL was resected (Figure 3A) to measure the medial and lateral distances of the SPL and LPL attachment from the calcaneocuboid joint to the calcaneus side (Figure 3B: i-iv). Because the lateral side of the SPL and medial side of the LPL overlap on the cuboid side, the SPL and LPL attachments were measured at 3 points: medial, central, and lateral (Figure 3B: v-vii). Next, the cuboid was removed (Figure 4A) and the location of the cuneocuboid joint was measured on the medial side of

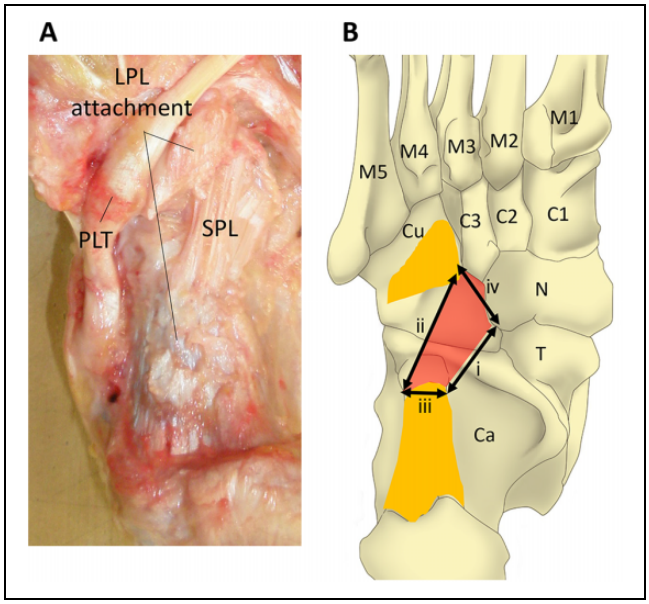

Figure 2. Anatomy of the short plantar ligament after resecting the long plantar ligament. (A) Anatomical chart. (B) Schematic diagram and measurement items. i, SPL medial length; ii, SPL lateral length; iii, SPL calcaneus attachment width; iv, SPL cuboid attachment width. Ca, calcaneus; Cu, cuboid; T, talus; N, navicular; C1-3, cuneiform; M1-5, metatarsal; PLT, peroneus longus tendon; LPL, long plantar ligament; SPL, short plantar ligament.

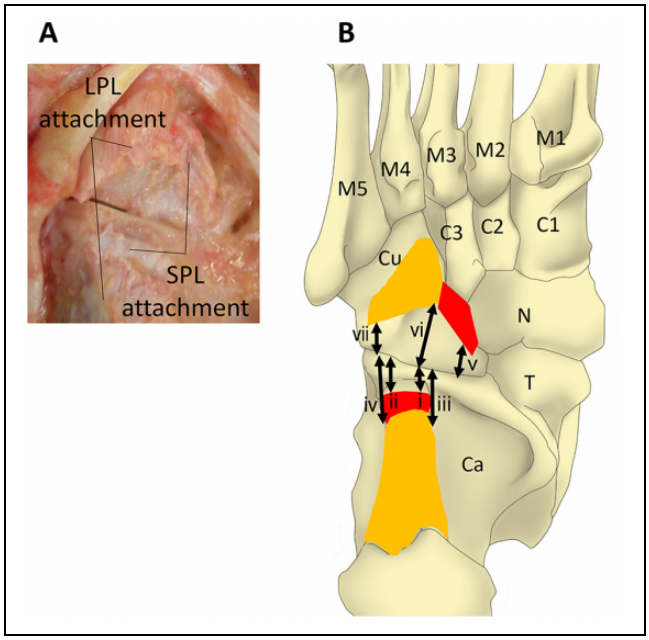

Figure 3. Distance from the calcaneocuboid joint to the attachment. (A) Anatomical chart. (B) Schematic diagram and measurement items. i, SPL distance to the medial calcaneus attachment; ii, SPL distance to the lateral calcaneus attachment; iii, LPL distance to the medial calcaneus attachment; iv, LPL distance to the lateral calcaneus attachment; v, distance to the medial cuboid attachment; vi, distance to the central cuboid attachment; vii, distance to the lateral cuboid attachment. Ca, calcaneus; Cu, cuboid; T, talus; N, navicular; C1-3, cuneiform; M1-5, metatarsal; PLT, peroneus longus tendon; LPL, long plantar ligament; SPL, short plantar ligament.

the cuboid relative to the cuboid-metatarsal joint and calcaneocuboid joint (Figure 4B: i, ii). A digital caliper (Mitutoyo Corporation, Kawasaki, Japan) was used for all measurements, and all measurements were obtained by the same individual 3 times. The mean value of these 3 measurements was used, and the standard deviation of measurements was calculated. ImageJ image processing software (National Institutes of Health, Bethesda, MD) and a photograph with the cuneocuboid joint surface on the medial surface of the cuboid horizontal were used to measure the straight line between the anterior border of the cuneocuboid joint and the oblique crest of the cuboid, as well as the angle it created with the cuboid-metatarsal joint (Figure 4B: α). Furthermore, measurements from the 2 sexes were compared to account for differences in foot size between men and women. Statcel 4[15] was used for statistical analysis. A P value less than .05 was considered statistically significant. F test was used. In addition, Student t test was used for normal distributions, and Welch t test was used for the lateral and medial length of the SPL; these were non-normal distributions.

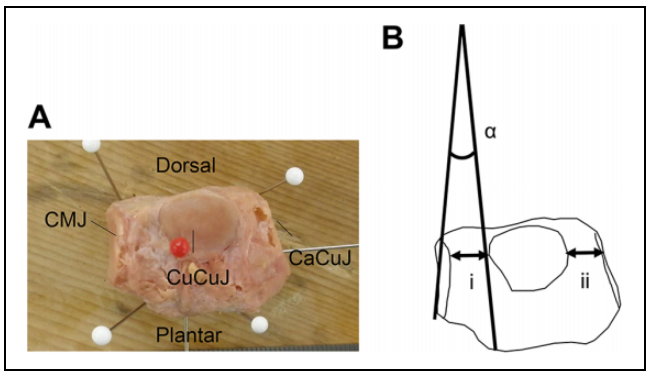

Figure 4. Medial facet of the cuboid. (A) Anatomical chart. (B) Schematic diagram and measurement items. i, Distance from the cuboid-metatarsal joint to the cuneocuboid joint; ii, distance from the calcaneocuboid joint to the cuneocuboid joint. α, osteotomy angle; CMJ, cubometatarsal joint; CaCuJ, calcaneocuboid joint; CuCu joint, cuneocuboid joint.

Results

Table 1 displays the results of ICCL measurement. The medial length of the LPL was 42.7 mm (range: 33.4-59.2 mm), the lateral length was 30.9 mm (range: 15.9-40.5 mm), and the medial and lateral lengths between the attachments were 26.9 mm (range: 20.4-43.2 mm) and 20.7 mm (range: 8.1-34.9 mm), respectively. The total medial and lateral lengths of the attachments on the calcaneus and cuboid sides were 15.8 mm (range: 1.5-30.2 mm) and 10.2 mm (range: 0.5-24.4 mm), respectively. Table 2 displays the distances from the calcaneocuboid joint to the attachments on the sides of the calcaneus and cuboid. There was a region on the cuboid where neither the LPL nor SPL were attached on

Table 1. Measurements of the Inferior Calcaneocuboid Ligament.

			Mean, mm	SD	Maximum, mm	Minimum, mm
LPL	Length	Medial	42.7	6.9	59.2	33.4
		Lateral	30.9	6.8	40.5	15.9
	Width	Calcaneus	19.2	3.6	26.0	11.2
		Cuboid	22.9	3.1	29.2	16.9
LPL attachment	Length	Medial	26.9	5.4	43.2	20.4
		Lateral	20.7	7.3	34.9	8.1
	Width	Calcaneus	13.1	3.4	20.5	6.7
		Cuboid	18.6	2.8	22.3	10.7
SPL	Length	Medial	15.9	3.2	22.2	9.2
		Lateral	21.4	3.8	31.0	15.2
	Width	Calcaneus	13.6	2.8	18.0	5.7
		Cuboid	13.6	4.1	19.2	7.2

Abbreviations: LPL, long plantar ligament; SD, standard deviation; SPL, short plantar ligament.

Table 2. Distance Between the Calcaneocuboid Joint and Attachment to the Inferior Calcaneocuboid Ligament.

			Mean, mm	SD	Maximum, mm	Minimum, mm
Calcaneus	CaCuJ to SPL	Medial	4.9	1.6	8.4	2.8
		Lateral	5.9	2.2	9.9	2.1
	CaCuJ to LPL	Medial	12.6	5.4	28.2	4.7
		Lateral	14.1	6.0	26.9	6.3
Cuboid	CaCuJ to SPL and LPL	Medial	4.4	1.1	7.9	2.2
		Middle	10.0	1.7	12.9	6.6
		Lateral	4.6	0.9	6.2	2.9

Abbreviations: CaCuJ, calcaneocuboid joint; LPL, long plantar ligament; SD, standard deviation; SPL, short plantar ligament

Table 3. Location of the Cuneocuboid Joint.

	Mean, mm	SD	Maximum, mm	Minimum, mm
CMJ to CuCuJ	6.7	1.2	9.2	4.3
CaCuJ to CuCuJ	4.7	2.6	8.7	0.7

Abbreviations: CaCuJ, calcaneocuboid joint; CMJ, cubometatarsal joint; CuCuJ, cuneocuboid joint; SD, standard deviation

the medial and central sides at approximately 4 mm and 10 mm, respectively, from the calcaneocuboid joint. Next, the cuboid was removed. Table 3 displays the distance of the cuneocuboid joint measured from the cuboid-metatarsal and calcaneocuboid joints on the medial side of the cuboid. The cuneocuboid joint touched the cuboid dorsally in shapes ranging from reverse triangles to ellipses. The distance between the cuboid-metatarsal joint and cuneocuboid joint was 6.7 mm (range: 4.3-9.2 mm). In all feet, the interosseous cuneocuboid ligament was present between the cuboid-metatarsal and cuneocuboid joints. The distance between the calcaneocuboid joint and cuneocuboid joint was 4.7 mm (range: 0.7-8.7 mm). In 18 of the 24 feet, the surface of the joint with the navicular bone was found between these joints, but there was a sex difference (12 of 12 men and 6 of 12 women). Among these 18 feet, the cuneocuboid joint and cuboid-navicular joint were fused in 10 feet (Figure 5B) and separated in 8 feet (Figure 5C). In one of the feet with fused cuneocuboid and cuboid-navicular joints, the articular facet was shared with the head of the talus (Figure 5D). There was no articular facet in 6 feet (Figure 5A). The angle formed by the direct line connecting the anterior border of the cuneocuboid joint and the oblique crest of the cuboid and the plane of the cuboid-metatarsal joint was the inclination of the potential osteotomy in the sagittal plane (α, 10.3 ± 4.1 degrees; range, 4.0-21.4 degrees). The groove of the peroneus longus was anterior to the oblique crest of the cuboid, and the straight line between the anterior border of the cuneocuboid joint and oblique crest of the cuboid was at an approximately 10-degree inclination to the cuboid-metatarsal joint. Table 4 displays the statistical analysis examining differences between men and women. Significant sex differences were found in the following parameters: calcaneus attachment width, medial length of the LPL, and lateral and medial sides of the distance from the calcaneocuboid joint to the calcaneus attachment along the SPL. All of these were significantly longer in men than in women. However, the distance from the calcaneocuboid joint to the cuneocuboid joint on the medial surface of the cuboid was significantly shorter in men than in women ($P < .05$).

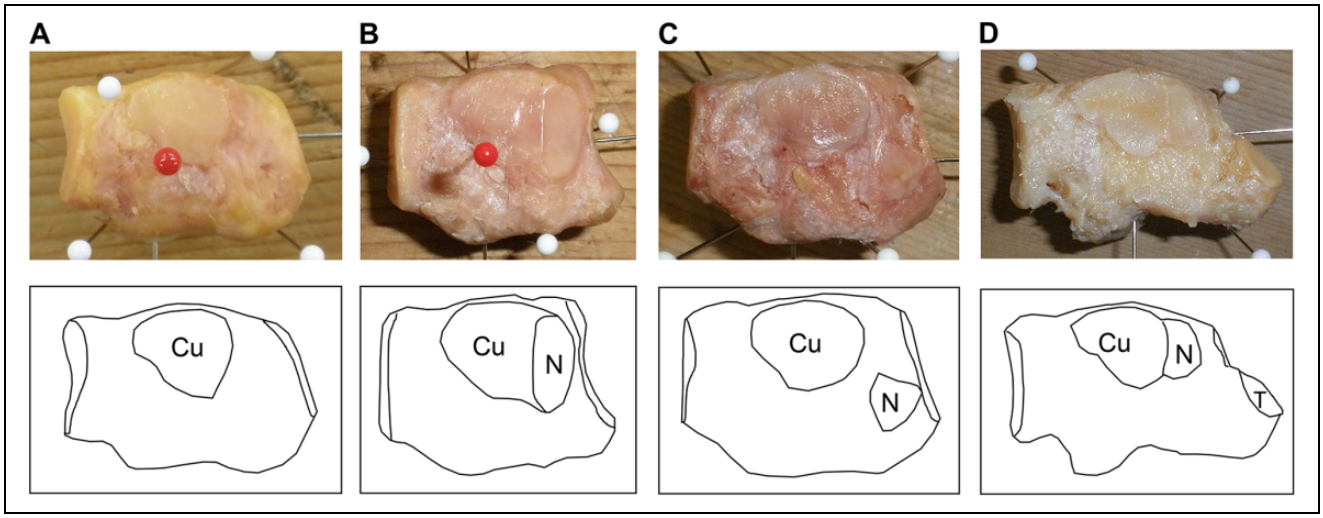

Figure 5. Joint on the medial facet of the cuboid. (A) No articular facet with the navicular bone. (B) Articular facet fused with the navicular bone. (C) Articular facet isolated from the navicular bone. (D) Articular facet with the head of talus. Cu, cuneocuboid joint; N, cuboideonavicular joint; T, talocuboid joint.

Table 4. Sex Comparison.

			Male, mm	Female, mm	*P* value[a]
LPL	Length	Medial	45.9	39.4	.020
		Lateral	31.6	30.1	.593
	Width	Calcaneus	20.8	17.6	.035
		Cuboid	23.8	22.0	.162
LPL attachment	Lengths	Medial	27.7	26.0	.457
		Lateral	20.2	21.1	.787
	Widths	Calcaneus	13.6	12.6	.507
		Cuboid	19.6	17.7	.096
SPL	Lengths	Medial	16.7	15.1	.255[b]
		Lateral	22.1	20.7	.391[b]
	Widths	Calcaneus	14.6	12.7	.104
		Cuboid	14.7	12.5	.226
Calcaneus	CaCuJ to SPL	Medial	5.8	4.0	.003
		Lateral	6.9	4.9	.030
	CaCuJ to LPL	Medial	13.8	11.5	.336
		Lateral	15.0	13.2	.480
Cuboid	CaCuJ to SPL and LPL	Medial	4.6	4.3	.504
		Middle	10.2	9.8	.534
		Lateral	4.9	4.4	.130
CMJ to CuCuJ			7.1	6.2	.073
CaCuJ to CuCuJ			3.5	6.0	.021
Bone cutting angle			11.2	9.4	.300

Abbreviations: CaCuJ, calcaneocuboid joint; CMJ, cubometatarsal joint; CuCuJ, cuneocuboid joint; LPL, long plantar ligament; SPL, short plantar ligament.
[a]Student *t* test, unless otherwise noted.
[b]Welch *t* test.

Discussion

Deciding the treatment for flatfoot involves assessment of the severity of foot deformation and soft tissue conditions. Soft tissue procedures alone have limited corrective power or mechanical strength; thus, treatment often includes a combination of these procedures and osteotomy. One of these, LCL, provides powerful correction, and there have been reports of good outcomes.[9,13] However, one of the principles of correction by LCL requires that the lateral third of the LPL is tightened and the medial two-thirds loosened.[3] According to reports, this allows formation of the arch, relieving the load on medial soft tissues. Effectively tightening the LPL requires stretching the LPL within the segment between the calcaneus attachment and cuboid attachment. Evans[5] and Hintermann[6,7] place the osteotomy line at approximately 10 to 20 mm from the calcaneocuboid joint, on the side of the calcaneus. The lateral and medial calcaneus attachments of the LPL are

located on average 14.1 mm and 12.6 mm, respectively, from the calcaneocuboid joint, and stretching these tightens the LPL. However, when this distance exceeds 15 mm, the osteotomy line can come into contact with the LPL attachment, thereby preventing effective tightening of the LPL. In terms of the talocalcaneal joint, the Hintermann osteotomy corresponds to the middle talocalcaneal joints in 14.3% of cadaver feet, whereas in Evans osteotomy, it corresponds to the anterior and middle talocalcaneal joints in 57.1% and 28.6% of cadaver feet, respectively, resulting in dysfunction.[4] However, even if the osteotomy does not match, the extension will change the congruity of the subtalar joint. Thus, damage or extension to the talocalcaneal joint is inevitable as long as osteotomy is performed on the calcaneal side. Using CCDA, in which only the condylar side of the calcaneocuboid joint is resected for lengthening, the lateral LPL can be sufficiently tightened, but approximately 18% to 30% of the range of motion of the talocalcaneal joint is lost by articular fixation.[1,2]

These problems led us to focus on lengthening the cuboid, which would not have a direct impact on the talocalcaneal joint and would not require joint fixation. To date, there has been 1 report on lengthening of the cuboid,[16] but no one has reported a suitable osteotomy site and method. Measurements obtained in this study demonstrated that the deep fibers of the lateral and medial LPL are attached to the oblique crest of the cuboid at a mean distance of 4.6 mm and 10.0 mm, respectively, from the calcaneocuboid joint. This means that there was an area on the plantar side of the cuboid, 4 mm laterally and 10 mm medially, between the calcaneocuboid joint and the attachment of the LPL. Therefore, an osteotomy within 4 mm of the calcaneocuboid joint on the lateral cuboid would traverse this area proximal to the lateral attachment of the LPL and would tighten the lateral portion of the LPL, as desired. Furthermore, in terms of the medial facet of the cuboid, the cuneocuboid joint was located at a mean distance of 6.7 mm from the cuboid-metatarsal joint, and the cuneocuboid ligament was observed between them in all feet. Medially, the osteotomy should exit distal to the cuneocuboid articulation because 18 of 24 feet had an articulating facet with the navicular bone or head of the talus proximally, as demonstrated in Figure 5. Osteotomy site must be located within 6 mm of the metatarsal-cuboid joint to prevent the osteotomy site from overlapping the middle cuboid joint surface. As such, we found that the osteotomy line must connect a point approximately 4 mm from the calcaneocuboid joint laterally and approximately 6 mm from the cuboid-metatarsal joint medially to allow cuboid osteotomy to tighten the LPL effectively while preserving the articular surface. At the same time, the osteotomy should be performed at an approximately 10-degree posterior tilt to the cuboid-metatarsal joint to prevent damage to the peroneus longus tendon, which runs along the groove of the peroneus longus (Figure 6).

Nonunion or dislocation, lateral column foot pain, and risk of osteoarthritis in nearby joints, including the calcaneocuboid and cuboid-metatarsal joints, are expected to occur

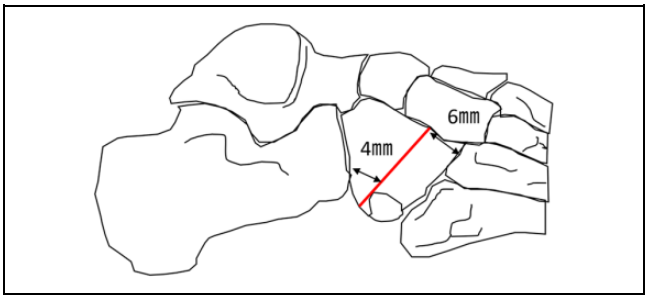

Figure 6. Osteotomy line. Osteotomy in a straight line connecting a point 4 mm from the calcaneocuboid joint laterally and a point 6 mm from the cuboid-metatarsal joint medially at a 10-degree posterior tilt to the cuboid-metatarsal joint.

with cuboid osteotomy lengthening, as in other LCLs. Therefore, optimal lengthening becomes crucial for preventing lateral foot pain owing to overcorrection or effects on nearby joints.[11,12] One study reported that the optimal length of the LCL should be determined as augmentation after repair of the spring ligament.[10] Zhou et al made a flatfoot model with fresh-frozen cadavers and reported that good correction was obtained with 3-mm LCL by cuboid osteotomy,[16] showing that even a small lengthening can effectively correct a deformity. Zhou et al performed osteotomy at a depth of 10 mm in the central cuboid, parallel to the calcaneocuboid joint. The present results showed that osteotomy at this location does not produce LPL tightening and it may cause cuneocuboid joint injury. Our method likely has more benefits for cuboid osteotomy LCL.

The present anatomical study has several limitations. First, the cadavers were formalin-fixed, not fresh-frozen, which may cause anatomical structural changes. Second, a digital caliper and ImageJ software were used for measurements. However, all measurements were obtained by a single person. As a result, intertester comparisons have not been made. Third, we have not been able to propose optimal lengthening after osteotomy or methods of fixation, which should be explored in more detail through biomechanics studies of the present osteotomy performed on fresh-frozen cadaveric feet.

Conclusion

Based on the results of this anatomic study, a safe LCL by cuboid osteotomy could be performed along a straight line connecting a point 4 mm from the calcaneocuboid joint laterally and a point 6 mm from the cuboid-metatarsal joint medially at a 10-degree posterior tilt to the cuboid-metatarsal joint in the sagittal plane.

Ethics Approval

The protocol of the present study was approved by the ethics committee of the St. Marianna University School of Medicine (approval no. 4094). This study was carried out in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the donor.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

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Appendix

Appendix 1. STROBE Statement—Checklist of Items That Should Be Included in Reports of Observational Studies.[a]

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-6

(continued)

Appendix 1. (continued)

	Item No.	Recommendation	Page No.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	NA
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8[b]	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA
Results			
Participants	13[b]	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-8
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14[b]	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15[b]	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8 Table4
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	NA
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

[a] An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of *PLoS Medicine* at http://www.plosmedicine.org/, *Annals of Internal Medicine* at http://www.annals.org/, and *Epidemiology* at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

[b] Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.