Towards automated ligamentous injury evaluation in syndesmotic ankle lesions

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1. Abstract

Purpose
Forced external rotation is hypothesized as the key mechanism of syndesmotic ankle injuries. This complex trauma pattern ruptures the syndesmotic ligaments, inducing a three-dimensional deviation from the normal distal tibiofibular joint configuration. However, current diagnostic imaging modalities are impeded by a two-dimensional assessment, without taking into account ligamentous stabilizers. Therefore, our aim is two-fold: (1) to construct an articulated statistical shape model of the normal ankle with inclusion of ligamentous morphometry and (2) to apply this model in the assessment of a clinical cohort of patients with syndesmotic ankle injuries.

Methods
Three-dimensional models of the distal tibiofibular joint were analyzed in asymptomatic controls (N = 76; Mean age 63 +/- 19 years), patients with syndesmotic ankle injury (N = 13; Mean age 35 +/- 15 years), and their healthy contralateral equivalent (N = 13). Subsequently, the statistical shape model was generated after aligning all ankles based on the distal tibia. The position of the syndesmotic ligaments was predicted based on previously validated iterative shortest path calculation methodology. Evaluation of the model was described by means of accuracy, compactness and generalization. Canonical Correlation Analysis was performed to assess the influence of syndesmotic lesions on the distal tibiofibular joint congruency.

Results
Our presented model contained an accuracy of 0.23 +/- 0.028 mm. Mean prediction accuracy of ligament insertions was 0.53 +/- 12 mm. A statistically significant difference in anterior syndesmotic distance was found between ankles with syndesmotic lesions and healthy controls (95% CI [0.32, 3.29], p = 0.017). There was a significant correlation between presence of syndesmotic injury and the morphological distal tibiofibular configuration (r = 0.873, p <0.001).

Conclusion

In this study, we constructed a bony and ligamentous statistical model representing the distal tibiofibular joint. Furthermore, the presented model was able to detect an elongation injury of the anterior inferior tibiofibular ligament after traumatic syndesmotic lesions in a clinical patient cohort.

Keywords:
Statistical Shape Modelling, Computer-Aided Diagnosis, Distal Tibiofibular Syndesmosis, Ligament Injury, Threedimensional analysis
2. Introduction

Ankle sprains are among the most common sport injuries and compromise 5% of all emergency department visits (1, 2). Up to 24% involve injury to the ligaments stabilizing the ankle syndesmosis (3, 4). This anatomical complex is comprised by the distal tibiofibular joint (DTFJ) and the syndesmotic ligaments. Its intrinsic stability is provided by the inherent osseous congruence between the convex distal fibula and concave incisura fibularis.

The extrinsic stability is ensured by distinct ligamentous restraints. The anterior inferior tibiofibular ligament is the primary restraint to fibular external rotation, whereas the posterior inferior tibiofibular ligament restricts posterior translation. The interosseous ligament merges with the interosseous membrane proximally and provides resistance to lateral translation of the fibula (5-7). Injuries to these restraints are generally caused by forced dorsiflexion-external rotation during foot pronation. As the rotation moment of the talus within the mortise progresses, its wide anterior dome directly drives the distal fibula into supraphysiological external rotation and posterolateral translation, sequentially injuring the anterior inferior tibiofibular ligament, interosseous ligament and finally the posterior inferior tibiofibular ligament (8, 9). These lesions, especially when subtle, present a deceitful diagnostic challenge. Specific tests during clinical examination lack sufficient sensitivity, whereas plain radiographs are highly affected by foot rotation and do not correlate with presence of syndesmotic injury (10-12). Due to these flaws of traditional diagnostic modalities, syndesmotic lesions have a high propensity for misdiagnosis and subsequent mistreatment, potentially leading to long-term sequelae including chronic syndesmotic instability and post-traumatic osteoarthritis (8,9). Conventional Computed Tomography (CT) imaging provides three-dimensional (3D) assessment of bony syndesmotic geometry, which allows for precise evaluation of DTFJ configuration. Magnetic Resonance Imaging (MRI) boasts both outstanding sensitivity and specificity in diagnosing specific ligamentous damage (13, 14).
However, these traditional imaging modalities do not represent for weight-bearing conditions, potentially underestimating lesion severity. The recent advent of weightbearing cone-beam CT (WBCT) overcomes these drawbacks by imaging both ankles while in bipedal stance. Using WBCT, novel noninvasive 3D imaging methods have already shown to identify patients with a history of syndesmotic injuries (15, 16). However, the manner of assessment has been highly variable. Various methods have attempted to objectify DTFJ configuration, mostly by use of manual measurements on 2D axial slices (17). These 2D metrics, however, correlate poorly with the actual 3D deviation of the fibula. (18). Indicated by the drawbacks of previously described imaging modalities, an accurate diagnosis of syndesmotic lesions should involve 3D weightbearing osseous imaging in combination with – preferably automated- inclusion of patient-specific ligamentous information. This gap can be bridged by creating idealized generic musculoskeletal models, which allows for scaling, morphing and fitting into patient-specific ankle anatomy.

Acclaimed for their ability to reduce data dimensionality, statistical shape models (SSM) are well-suited for 3D shape correlation to predict patient-specific missing anatomical information (19). In this context, SSM has already been efficiently utilized for computer-assisted Anterior Cruciate Ligament (ACL) reconstruction (20), virtual reconstruction of acetabular bone defects (21) and planning of corrective osteotomies for malunited forearm bones (22).

In regard of ligament modelling, earliest techniques represent deformable soft-tissue structures as straight segments connecting commensurate points (23). This has been shown to yield inaccurate results, which can be explained by the fact that soft-tissues follow smooth curved paths due to bony prominences. Recent techniques (24-26) overcame these limitations by describing a novel methodology based on discrete element rigid body spring models to describe muscle and ligament wrapping paths.
Combining geometric statistical models and soft-tissue wrapping methodology has not yet been described in the ankle joint. Nevertheless, this could open the door for ligamentous injury prediction in ankle sprains. Therefore, we aim to build an articulated, multi-object statistical shape model representing ligamentous anatomy of the DTFJ. In addition, we hypothesize that by applying this model to the clinical entity of traumatic syndesmotic lesions, automatic ligament prediction can identify patterns in ligamentous injury.

3. Results

3.1 Model Validation

3.1.1 Accuracy

General accuracy of our skeletal shape model was 0.23 ± 0.028 mm. Mean prediction accuracy of the 5 ligament insertion points was as follows: Tibial insertion of the anterior inferior tibiofibular ligament 0.54 ± 0.12 mm; fibular insertion of anterior inferior tibiofibular ligament, 0.54 ± 0.12 mm; tibial insertion of the posterior inferior tibiofibular ligament, 0.51 ± 0.15 mm; fibular insertion of posterior inferior tibiofibular ligament, 0.61 ± 0.10 mm. Mean accuracy of the tibial vertices for calculation interosseous diastasis was 0.47 ± 0.16 mm (Fig. 1a).

3.1.2 Compactness

With 19 principal components included, our model was able to explain 90% of anatomical variance in the input data. Figure 1b shows the cumulative compactness of the model, for increasing number of modes of variation included. The amount of variance described by the
first principal component is 56%. Size was most pronounced present in this first component, as previously described. (27)

3.1.3 Generalization

Figure 1c depicts the generalization capability of the model with increasing amount of training shapes included. The generalization curve shows that with an increasing number of samples, the error of the model decreases and approaches the in-model accuracy. Accuracy of predicting ligament insertions on new, unseen cases is presented in Figure 1d.

3.2 Ligament Injury Evaluation

Mean length of the Anterior inferior tibiofibular ligament was 12.26 ± 1.89mm for the control cases, 12.32 ± 1.58 mm for the contralateral cases and 14.13 ± 1.48 mm for the cases with syndesmotic lesions. Statistically significant differences were found between the latter two (95% CI [0.32, 3.29], p = 0.017) (Fig. 2a). Mean length of the Posterior inferior tibiofibular ligament was 13.44 ± 0.84 mm for the control cases, 16.03 ± 0.90 mm for the contralateral cases and 15.99 ± 0.75 mm for the cases with syndesmotic lesions. No statistically significant differences were found between the latter two (95% CI [-1.42, 1.35], p = 0.96) (Fig. 2b). Mean length of the IOD was 3.78 ± 0.89 mm for the control cases, 4.97 ± 0.94 mm for the contralateral cases and 5.18 ± 0.92 mm for the cases with syndesmotic lesions. No statistically significant differences were found between the latter two (95% CI [-0.71, 1.12], p = 0.65) (Fig. 2c). Mean lengths of each fiber as well as p-values are listed in Table 1.

3.3 DTFJ configuration in syndesmotic lesions
As defined by use of canonical correlation analysis (CCA), there was a significant correlation between sustaining a high ankle sprain and the DTFJ configuration ($r = 0.873$, $p < 0.001$).

Figure 3 provides a visual representation of the reduced data, mapped into 2D space by use t-SNE. It demonstrates that t-SNE was able to cluster WBCT syndesmotic ankles as a separate entity, apart from their contralateral counterpart and non-weightbearing controls. Additionally, t-SNE was able to cluster the contralateral (weightbearing) controls on the periphery of the control group. This is presumably due to a difference in posterior inferior tibiofibular ligament distance between the weightbearing and non-weightbearing controls, as described previously (section 3.3). Difference in anterior inferior tibiofibular ligament length results in separate clustering of the WBCT syndesmotic injured ankles versus their contralateral counterpart.

4. Discussion

Syndesmotic ankle injuries are associated with a prolonged time to recovery and progression to early onset ankle osteoarthritis (28, 29). One of the main reasons for these debilitating sequela are the current diagnostic modalities, which contain marked shortcoming in the identification and quantification of syndesmotic ligament injuries. Previous studies analyzing this clinical enigma were based on discrete measurements of the DTFJ and did not assess its correlation with distinct ligamentous lesions. Therefore, our study focused on building an articulated, multi-object shape model of the DTFJ including syndesmotic ligamentous restraints. In addition, we applied the presented model to unravel specific ligamentous injury patterns in patients with syndesmotic ankle sprains.

With regard to the first aim, our constructed shape model boasted an excellent accuracy describing the included bones and ligament insertions. Also, it was capable of adapting to
unseen shapes and predicting corresponding syndesmotic ligaments, hence the generalization metric of our model. Previous shape models, by Tümer et al. (30) and Quintens et al. (31), focused mainly on anatomical variance of the separate tibia and fibula rather than the morphological variance of their articular congruence. Regarding compactness, these previous models show a high amount of variance in the first components. This did not apply to our study since the bones were scaled, which eliminated size differences. Also, only the distal part of the tibia and fibula were used, further reducing the influence of size. Prominent shape variance in these previous models were attributed to differences in shape of the proximal or middle third of the tibia and fibula. Consequently, these shape variations could not contribute to the variance of our model. Evidently, we suspect that both the scaling and cutting procedure are the cause of the different compactness curve of our models compared to previous shape models including the tibia/fibula.

Concerning our second aim, syndesmotic ankle injuries are typically caused by a dorsiflexion external rotation force transmitted through the ankle and injures the Anterior inferior tibiofibular ligament as first of the ligamentous stabilizers (32). In accordance to this mechanical hypothesis, the presented automated ligament prediction was capable of depicting an increased length of Anterior inferior tibiofibular ligament fibers in westpoint grade II syndesmotic lesions, with similar Interosseous/Posterior inferior tibiofibular ligament distance. This represents an elongation/rupture of the Anterior inferior tibiofibular ligament, resulting in an ‘anterior open-book injury’, which could also be confirmed during arthroscopy (Fig. 4). Additionally, these findings are supported by previous cadaveric studies. Xenos et al. (33) found the fibula to rotate externally 2.7 degrees on average after sectioning the Anterior inferior tibiofibular ligament. The observation of anterior diastasis in patients with syndesmotic instability are further reinforced by the investigations of Hagemeijer et al. (34)
Our study additionally showed a tendency of increased anterior inferior tibiofibular ligament length, posterior inferior tibiofibular ligament length and interosseous diastasis of healthy ankles after weight-bearing. These findings are similar to those of Malhotra et al (35), describing external rotation, lateral and posterior translation of the loaded fibula.

Further analyzing our data, t-SNE was performed to investigate whether this algorithm is able to distinguish syndesmotic DTFJ anatomy from the control anatomy. As demonstrated, the 2D scatter plot depicts a distinct clustering of the syndesmotic lesion group, compared to the controls, indicating an underlying anatomical dissimilarity.

We acknowledge that our study has several important limitations. Firstly, control patients were collected from a database of angio-CT images, ordered for clinical suspicion of vascular disease and presumably do not represent the general population. Secondly, our clinical cohort consisted of a small amount of patients with syndesmotic lesions included, which might impair the generalizability of the findings. However, all patients were carefully selected after a detailed arthroscopic examination, which is currently considered as the gold standard in detecting syndesmotic ankle injuries (36, 37). With regard to confirm the findings of our study, future research should therefore focus on the inclusion of more patients with high ankle sprains, as well as inclusion of healthy asymptomatic control patients from similar age groups. Thirdly, ligamentous insertion sites were based on description in anatomical atlases, and our ligament modelling algorithm was not validated to the true subject-specific anatomy. However, a previous anatomical study by Williams et al. (38) has shown limited variance in ligament insertions between subjects. Finally, t-SNE clusters represent non-linear reductions in dimensionality, which remain difficult to interpret (39). Nevertheless, rapid evolving technology in this field has high potential for future algorithms interpreting these low-dimensional data clusters. (40, 41)
The present tibiofibular shape model has a high propensity for application in various settings. Our ligament modelling algorithm could be used for computer-aided ligament reconstruction anatomy, e.g. anatomical lateral ankle ligament reconstruction or ACL reconstruction. Since contralateral ankle anatomy is not always available to template asymptomatic anatomy, our model opens the door for virtual reconstruction of a ‘healthy twin’, including population variance. Especially since syndesmotic malreduction has been reported in up to half of ankle fractures with syndesmotic lesions, resulting in concomitant functional consequences (42), virtual reconstruction of healthy anatomy could aid in anatomical reduction, significantly improving current diagnostic and therapeutic standards of syndesmotic injuries.

5. Materials and methods

5.1 Study Population and Design

Control data consisted of healthy ankles (N=76, Mean age 63 +/- 19 years), without history of previous syndesmotic pathology. The imaging database was constructed from living subjects receiving angio-CT scanning for vascular work-up between 2012 and 2016. Every image domain included the full lower limb anatomy ranges from rib 12 to toes. The participating subjects were not exposed to additional radiation for the present study. The local institutional ethics commission of the university hospital Ghent approved this study and all patients gave informed consent (reference B670201111480). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. CT-images of the control subjects were obtained in a Siemens SOMATOM® (Siemens Healthineers, Erlangen Germany) CT scanner. Each scan data set consisted of an
average of 1864 slices with a pixel size between 0.575 mm to 0.975 mm. The following imaging protocol and settings were used: tube voltage (KVP) = 140 kV; tube current = 156 mAs; CTDIvol = 16.07 mGy; matrix = 512 × 512; and slice thickness = 0.6 mm.

Patient data consisted of 16 patients after sustaining syndesmotic injury (Age 35 +/- 15 years). Inclusion criteria consisted of presence of bilateral CT-imaging and age between 18 and 60 years. CT imaging was requested if there was clinical suspicion of syndesmotic injury (dorsiflexion-external rotation injury mechanism, local tenderness over the anterior inferior tibiofibular ligament, positive external rotation and squeeze test and/or if the tibiofibular clear space on plain radiography was increased). Exclusion criteria were osteoarthritis of the DTFJ, motion artefacts or CT-images of inferior quality, and CT-images lower than 10 cm above the tibiotalar joint. Image domain consisted out of the distal tibia, fibula and foot. A PedCAT weightbearing cone beam CT was used (Curvebeam, Warrington, PA, USA) containing following imaging protocol and settings: tube voltage (KVP) = 96 kV; tube current = 7.5 mAs; CTDIvol = 4.3 mGy; matrix = 160 × 160 × 130; and slice thickness = 0.4 mm. At the department of radiology, patients were asked to assume a natural stance with both feet parallel to each other at shoulder width apart. After exclusion, our dataset contains 76 unilateral ankle CT’s from healthy controls and 13 weightbearing ankle CT’s from patients with syndesmotic ankle injuries. Twelve patients were diagnosed with a high ankle sprain-west-point grade II (43), whereas one patient was diagnosed with a Maisonneuve fracture and concomitant syndesmotic injury. Syndesmotic injury and instability was confirmed during arthroscopy by a senior foot-and ankle surgeon.

1.1 Generation of 3D Models

CT scan segmentation in Mimics® (version 20.01, Materialise, Leuven, Belgium) was used to generate 3D bone models. Semi-automatic segmentation was performed using build-in
software tools, based on manual landmarking, Hounsfield Unit thresholding and gap filling. After initial segmentation, manual correction of each CT slice on top of the other one was performed manually to ensure accurate anatomical reproduction. From these segmentation masks each bony structure was rendered to form a binary formatted 3D stereolithography volume. Three-dimensional volumes of the control patients consisted of full tibia and fibula bones. In custom-made MATLAB® (MathWorks, Natick, Massachusetts, USA) script, each of these bones were separately non-rigidly registered to an anthropometric mask of fibula and tibia by use of a selection of readily available point/surface matching techniques (27, 44). As such, each control case was represented uniformly by an isometric triangular mesh. Meshes were defined as homologous, meaning each vertex corresponds to the identically numbered vertex over all meshes. Subsequent, each control bone was consistently virtually osteotomized Meshlab open source software (Meshlab, Pisa, Italy) software (45) by selecting only faces and vertices of the distal tibia and fibula, just above the apex of the incisura fibularis of the tibia. The cutting plane was chosen parallel to the tibial plafond. Since all bones were composed similarly, each bone was cut at corresponding height. After osteotomy, control bones were composed of 7244 vertices and 14365 faces, average inter-point distance as described by the edge length of the faces, in these point distribution models was 1mm(+/- 0.15).

1.2 Construction of the SSM

1.2.1 Skeletal Anatomy

Construction of the statistical shape model was based on previously described methodology (27). First, Iterative Procrustes (i.e. Robust Least Squares) superimposition of all homogenously arranged ankle meshes was performed to account for undesired scaling and
rotational and translation information. Since the specific hypothesis to analyze changes in DTFJ configuration, all ankles were aligned based on the tibia. The Procrustes transformation matrix of each tibia was subsequently used on the corresponding fibula, in order to retain the subject-specific anatomical configuration of the DTFJ. In doing so, variance in fibular positioning relative to the tibia could be visualized. Although the dataset consisted of mixed right and a left ankles, Procrustes analysis resulted in a perfectly ‘mirrored’ configuration.

Model evaluation was then performed following Principal Component Analysis (PCA). Theoretically, PCA decomposes a multivariate dataset into its mean and corresponding covariance matrix. The eigenvectors of the covariance matrix are usually referred to as principal components or eigenmodes, whereas the eigenvalues indicate their relative importance. An overview of the SSM construction is depicted in Figure 5.

1.2.2 Ligament Prediction and Modelling

Anatomical ligament insertions were qualitatively and quantitatively derived from anatomical studies (7, 38) and translated to our model. Each ligament insertion and origin was represented as 5 points. Included Relevant ligaments were the anterior inferior tibiofibular ligament, posterior inferior tibiofibular ligament and Interosseous ligament. A custom-made ligament wrapping algorithm was used for the anterior inferior tibiofibular ligament and posterior inferior tibiofibular ligament, based on earlier work by Audenaert et al. (24) In this algorithm, corresponding insertions and origin vertices are connected by elastic line segments and each arbitrarily divided into 11 equidistant nodes (Fig 6 A-B). These elastic lines are progressively released to a position of lesser potential energy without penetration of the surrounding bony contours resulting in a piecewise linear approximation to the true path. By doing so, a computational efficient solution can be obtained. In case the algorithm results in
node penetration of any local obstacle, the surface point on the obstacle closest to the local
minimum is withheld. Penetrating nodes are consequently penalized to return to the closest
point on the surface (Fig. 6 E-F). After calculation of each elastic line, nodes are
interconnected forming a flat mesh representing the ligament. For transition to a volumetric
model, each ligament was assigned a ligament-specific thickness, based on the literature (7).
interosseous ligament distance was modelled differently. Five insertion points were defined
on the anatomical location within the incisura. Each point was subsequently connected with
its geometrical closest neighbour on the fibula (Fig 6C). Ligaments could then automatically
be modeled on newly segmented cases by non-rigidly morphometric fitting its bony structures
onto their closest neighbor in the statistical shape model (Fig 7).

1.3 Model Validation

1.3.1 Accuracy

Model accuracy is defined as an average error between the original bone samples $S_i$ and their
model reconstruction of the bone $S'_i$ using the first principal components that describe 95% of
variance within the dataset. This is calculated as the Root Mean Squared Error (RMSE) of the
distances between the original and the reconstructed shape, averaged over all samples.
To evaluate the accuracy of ligament modelling, RMSE was separately calculated for each of
the ligaments insertion sites.

1.3.2 Compactness

A shape model should explain as much variance in the dataset as possible while keeping the
model relatively compact. Evaluation of the model’s compactness was done according to the
amount of components that account for a 95% of the accumulated variance. Considering the
variable impact of size of bones on the variance in the ankle, as described by Audenaert et al. (27), size dominance was reported as the percent variance described by the first principal component.

1.3.3 Generalization

The model generalization is the capacity of the model to accurately describe samples outside of the dataset. This can be calculated by the means of leave-one-out analysis. Shape models were built using an increasing numbers of samples ($K = 1, 5, 10, \ldots, 95, 99$). For each increment, the corresponding shape model was used to reconstruct the excluded samples. Subsequently, for each increment, the RMSE of the difference between the original shape $S^k$ and the reconstructions $S'_k$ was calculated and averaged. To assess the algorithm’s capability to consistently model ligament insertions on new samples, Leave-one-out analysis was performed by iteratively excluding one sample in the shape model. Of the excluded model, the nearest neighbor in the shape model was non-rigidly registered, after which shape-specific ligaments were modelled. Hereafter, RMSE was calculated between corresponding insertion points of the actual ligament and its modeled equivalent. RMSE was subsequently averaged over all iterations.

1.4 Ligament injury prediction

Ligaments were modelled for each of the 76 controls, 13 contralateral controls and 13 ankles with syndesmotic injury. Subsequently, the length of each ligament fiber was calculated. Difference in length of healthy contralateral versus syndesmotic injured ligaments were statistically analyzed by use of two-tailed Two-Sample student’s t-test.

1.5 DTFJ configuration in syndesmotic lesions
Since initial alignment was based solely on tibia anatomy and the corresponding fibula was transformed along the same transformation matrix, positional changes in the fibula between all meshes could be visualized. Aligned data were classified as control (+1) or syndesmotic lesion (-1). Statistical analysis of the relationship between syndesmotic injury and DTFJ anatomy was performed by means of canonical correlation analysis in the Euclidian subspace. CCA serves as a technique to find commonalities between two sets of multivariate data (46). In particular, the principal component values of the shape data, correlated to the presence of syndesmotic injury, were used as predictor variables and the observed positional change in DTFJ configuration measures as response variable.

Subsequent, clustering of control versus syndesmotic injured ankles was performed by use of t-distributed Stochastic Neighbor Embedding. t-SNE is an algorithm for non-linear dimensionality reduction, well suited for data exploration and visualizing high-dimensional data. Developed and described by Van der Maatens et al. (47) in 2008, it has recently become widespread in the field of machine learning. Previous applications include computer aided diagnosis of breast cancer (48), as well as classification of individuals with Parkinson’s Disease (49). After applying t-SNE, visualization of low-dimensional points allows for revealing of natural clusters in the original high-dimensional data.

Authors’ contributions
All Authors contributed equally to this article. MP designed, coordinated and drafted the manuscript. TH aided with the data collection and processing. AB co-designed the research hypothesis, helped with data collection and co-drafted the manuscript. SDM supervised drafting of the manuscript. MVW helped drafting the manuscript KB collected patient data, co-designed the research hypothesis and aided drafting the manuscript. JV supervised the final manuscript. EA supervised the research hypothesis, data processing, result analysis and drafting of the manuscript. All authors read and approved the final manuscript.

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