INTRODUCTION

Despite noteworthy advances in understanding the mechanobiology as well as various neuromuscular aspects of the anterior cruciate ligament (ACL) injury over the past decades, the exact cause(s) of non-contact ACL injuries still eludes the scientific community. Consequently, the existing sex-based based disparity in ACL failure rates also remains inscrutable. There is a need for model-based approaches that produce quantitative insight into the structural properties of the ACL and loads placed upon it during various activities. These models would be more effective if they concurrently incorporated a variety of established risk factors. With this approach one could examine the impact of various risk factors and exclude spurious or redundant ones. Such an approach would guide the community’s research efforts in a more efficient manner. In this abstract, we build upon a previously developed model to predict, for the first time, the structural properties of the human anterior cruciate ligament. We focus on development of a linear multivariate regression model to predict linear stiffness of a subject’s ACL based on key covariates that are associated with a subject’s increased risk of suffering ACL injury. We hypothesize that the linear stiffness of an ACL may be predicted with reasonable accuracy based on age, sex, and anthropometric measurements of the subject and his/her ACL. Aside from its intriguing possibilities of identifying subjects at increased risk of suffering injury, such a model could serve as an important tool for future scientific research in the areas of risk factor analysis, risk management (estimating the probability of ACL injury), tissue engineering, and can be included in inverse dynamics simulations to understand subject-specific responses to ACL loading.

METHODS

This study was designed to test our hypothesis by performing novel analyses using models presented in our previous publication. A linear model was used to determine whether a general linear relationship exists between the response variables (structural properties) and the explanatory variables (age, sex, height, body mass, BMI, ACL length, minimum area, and volume). The following units were selected for each covariate: age (yrs), body mass (kg), height (m), and BMI (kg/m$^2$), ACL length (mm), ACL area (mm$^2$), and ACL volume (mm$^3$). Although this approach can be applied to all structural properties, due to lack of space, we presently focus only on linear stiffness of the ACL. We devised a new technique to present the predictions from the linear model (with its 8 dimensional nature that accounts for the 8 explanatory variables) and its corresponding 95% prediction intervals. Using Equation 1 (below), we calculated the 17 predicted values (in this application linear stiffness of 17 ACLs) based on the measurements of the covariates obtained from each corresponding donor. The predicted linear stiffness values were ranked (lowest to highest) in ascending order and the percentile for each value was calculated as $\frac{n_{\text{subject}} \times (\text{percentile} - 1)}{100}$ where $n$ is the number subjects or measurements. Finally, the contributions of both body anthropometry and ACL geometry risk factors to the prediction of linear stiffness were evaluated. This was done by excluding ACL geometry variables, re-evaluating the model, and comparing the reduced model $R^2$ to the original (geometry included) model $R^2$.

RESULTS AND DISCUSSION

Sex, age, height, and ACL minimum area were found to be significant contributors to the linear stiffness model ($p < 0.05$). The volume of the ACL was not found to be significant. Accordingly, the
estimated regression model for linear stiffness (LS) is presented below:

$$
LS = 0.925 + 21.2 \cdot \text{sex} - 5.3 \cdot \text{age} - 15 \cdot m - 110.3 \cdot ht - 105.6 \cdot \text{vol} - 62 \cdot \text{area}
$$

(1)

where \( m \) is mass, \( ht \) is height, \( \text{vol} \) is ACL volume and \( \text{area} \) is the minimum cross-sectional area of the ACL. The Pearson coefficient of correlation between the experimentally measured values of linear stiffness and their respective predictive values is \( r = 0.87 \). The test for the overall fit of this model is significant with \( p \)-value < 0.029 and \( R^2 = 0.756 \) indicating that 75.6% of the variability of the predicted linear stiffness value is explained by the model.

If ACL geometry is removed from the model, the overall fit suffers substantially, as \( R^2 \) is reduced to 0.575, the overall model remains significant (\( p = 0.03 \)), but only sex and age remain significant contributors to the model (\( p < 0.05 \)). The prediction curve (Figure 1) for linear stiffness of the ACL (blue) and the corresponding 95% prediction limits (red), are presented in Figure 1. In this figure, the data points represent the actual measured values of linear stiffness. Figure 1 presents the smoothing spline fit to the predicted values of linear stiffness (blue line) and their respective prediction limits (red lines) plotted against rank. In this figure, the vertical axis is the predicted linear stiffness, and the horizontal axis represents the corresponding rank of the predicted value within the full population that was tested.

Figure 1, in conjunction with Equation (1), can be used to obtain the 95% prediction intervals for given values of the explanatory variables (age, sex, body and ACL anthropometric measurements). For example, application of equation (1) to a 30 year old male subject with body mass = 84.4 kg, height = 1.7 m, and BMI = 30.9 kg/m², and ACL-min-area = 70 mm², produces a corresponding linear stiffness of 262.5 N/mm. This value can be identified on the vertical axis of Figure 1 and from that point a horizontal line (dashed) that intersects the blue prediction line can be constructed. Then a perpendicular line that intersects the prediction interval lines (red lines showing lower and upper confidence limits of 41.2 and 483.8 N/mm, respectively) and the horizontal axis (showing the rank of 8.9 out of 17 or approximately the 50th percentile) can be formed. This indicates that the predicted value of 262.5 N/mm falls very close to the middle of the given range in the population that was studied.

CONCLUSIONS

The applications for predictive models like the one presented here are myriad, but an example is that one could possibly associate knee laxity with the linear stiffness of subjects. Additionally, this type of model can be utilized in conjunction with other probabilistic techniques to provide a comprehensive method to estimate overall risk of ACL injury. Predictive models like the one presented here are of tremendous importance to the research community including sports injury and athletic training specialists. Other structural properties such as failure load, elongation at failure, and energy at failure can also be determined by similar models. Currently, no other models exist for non-invasively determining structural or material properties of the ACL.

REFERENCES