

Complex Integrative Morphological and Mechanical Contributions to ACL Injury Risk

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MCLEAN, S.G. and M. L. BEAULIEU. Complex integrative morphological and mechanical contributions to ACL injury risk. *Exerc. Sport Sci. Rev.*, Vol. 38, No. 4, pp. 192–200, 2010. By failing to consider the integrative impact of key morphological and neuromechanical factors within the anterior cruciate ligament injury mechanism, we consider the current injury prevention model to be flawed. Critical links between these factors continue to be identified, suggesting that a successful prevention model should entrench neuromuscular control strategies that can successfully cater to individual morphological vulnerabilities. **Key Words:** morphology, biomechanics, injury mechanism, injury prevention, joint structure

INTRODUCTION

Anterior cruciate ligament (ACL) injury is a common and potentially traumatic sports-related injury, typically arising via a noncontact episode during landing, cutting, or pivoting maneuvers (30). Approximately 300,000 new ACL injuries are suggested to occur annually within the United States alone, with most requiring surgical reconstruction and lengthy rehabilitation at a cost of almost \$3 billion (8,30). Of particular concern is the large sex disparity in ACL injury rates, with women having two to seven times the risk for injury compared with men in high-participation sports such as soccer and basketball (8,30). Apart from the obvious short-term implications, the injury also presents with substantial longer-term morbidities. Radiological signs of osteoarthritis, for example, appear in more than 50% of ACL-deficient knees as early as 5 to 15 yr after injury (27). Within the coming decades, therefore, a large number of otherwise healthy young individuals, particularly women, will likely have severe joint debilitation and a reduced quality of life. With these facts in mind, elucidating and ultimately countering the mechanism of ACL injury is paramount.

Proposed risk factors for ACL injury have been broadly categorized as either modifiable or nonmodifiable (30). Current research focuses primarily on modifiable factors and, in particular, neuromuscular control, as it demonstrates sex-dimorphic behaviors, directly impacts the joint mechanical profile, and is amenable to targeted intervention (8,30). Neuromuscular modification strategies aimed at preventing ACL injuries have evolved in line with these findings, with reported early successes (7). Despite these efforts, however, noncontact ACL injury rates and their associated sex-based disparity have endured (1). We contend that the current prevention strategy is severely flawed, as it fails to consider the integrative contributions of key additional risk factors within the ACL injury mechanism.

A number of key morphological variables have been identified as potential risk factors for ACL injury, with many also demonstrating sex-dimorphic behaviors (10,36). Because the contributions of these factors to ACL injury are largely nonmodifiable (8), they are rarely considered within current screening and/or prevention modalities. As a result, and despite ongoing speculation (10), limited knowledge exists regarding how such factors may contribute explicitly to injury risk. Our own work (23,24,26) and that of several others (29,34) have begun to bridge this knowledge gap, demonstrating explicit links between morphological, knee joint biomechanical, and resultant ACL loading factors. Based on outcomes of this evolving research, it is our fundamental tenet that morphological-mechanical interactions during high-risk landing maneuvers are critical to ACL injury potential and must be considered for successful ACL injury prevention to prevail. The current review establishes and supports the vital need for this consideration within ongoing ACL injury

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research. In doing so, it will also provide potential methodological frameworks through which ACL injury causality may be best identified and countered based on individual morphological and neuromechanical vulnerabilities. In particular, the need to assess evolving knee joint morphologies and resultant neuromechanics along the maturational pathway, where the potential for catastrophic developments may be greatest, and for innovative modeling methods that can successfully examine the impact of such interactions are proposed.

NEUROMUSCULAR-BASED ACL INJURY PREVENTION METHODS — PITFALLS AND LIMITATIONS

Neuromuscular-based training strategies aimed at preventing ACL injuries have been developed with the primary goal of modifying risky lower limb biomechanics during sports movement execution (8). In particular, an emphasis has been placed on altering what has been considered to be the “higher-risk” female biomechanical profile (8,30). Sex-based differences in landing neuromechanics are consistently identified, which are viewed to directly impact injury rates. Females, for example, land more extended, are quadriceps dominant, and demonstrate altered quadriceps-hamstrings coactivation strategies compared with males, resulting in larger anterior tibial shear loads following impact (8,30). They also elicit greater knee abduction motions and loads (20) during landings compared with males, which increase ACL loading (16) and prospectively predict injury risk (14). It is this group of “high-risk” neuromechanical traits that the current prevention model commonly aims to modify.

To date, training modalities based on common rationale derived from performance enhancement training and physical rehabilitation methods seem to demonstrate the greatest potential to modify male and particularly female lower limb biomechanical profiles. Failure of such methods to retard ACL injury rates (1), however, suggests that they possess limited global efficacies. A lack of athlete participation in, as well as athlete compliance to, these programs may limit their success in countering high ACL injury rates (12,30). Limited success also may stem from a lack of insight into the inherent motor learning strategies that underpin “trained” neuromechanical behaviors, thus minimizing the potential for consistency and repeatability (25). Over the past decade, we also have proposed a number of pitfalls and limitations that compromise the prevention model’s potential to truly “prevent” ACL injuries (17,22,25). Current efforts, for example, base their success on promoting safe landing mechanics via systematic neuromuscular modifications within a controlled laboratory setting. Such efforts may not promote the level of coupled perception-action necessary to successfully adapt to the inherently random sports movement environment (25). Our research has demonstrated that integrating “sports-relevant” factors within the movement environment, such as fatigue and decision making, promotes substantial and potentially high-risk adaptations in landing biomechanics, particularly in females (25) (Fig. 1). The ability of the current prevention model to successfully cater to the complex central and peripheral processing modulations driving these changes has thus been questioned (25).

Another potential limitation of the current prevention model, central to our own evolving research track and to this review, is its emphasis on training individuals to adopt a homogeneous, “male-like” neuromuscular strategy. Such an assumption does not consider the potential for individual-specific morphological factors to contribute to equally divergent knee joint mechanical profiles. With sex-based differences presenting in many morphological factors linked to ACL injury (29,30,33), sex-dimorphic joint mechanics in response to a common overarching neuromuscular strategy seem plausible. Targeted assessments of explicit links between key morphological and joint mechanical parameters thus seem critical to extending risk screening and prevention strategies beyond an isolated and likely compromised sex-based focus.

PROPOSED MORPHOLOGICAL ACL INJURY RISK FACTORS

As noted, a number of key knee joint morphological variables have recently been identified as risk factors for ACL injury and as contributors to the sex-disparity in ACL injury rates. A small femoral notch, higher-than-normal body mass index, and increased knee joint laxity, for example, prospectively predicted ACL injury risk in a relatively large ($n = 895$) cohort of U.S. military cadets (36). Furthermore, possessing more than one of these factors greatly increased the relative risk of ACL injury, particularly in women, where an ACL injury always occurred if each factor was present. Interestingly, these prospective risk factors also demonstrate reasonable sex dependence, with females generally presenting with a femoral notch that is less round and narrower (8), reduced lean body mass, and increased general and knee joint laxity (33) compared with males. Individuals having previously experienced an ACL injury, again particularly females (10), also possess larger posterior tibial slope angles compared with matched controls. Hashemi *et al.* (10) also have demonstrated that a shallow medial tibial plateau depth in conjunction with a steep lateral posterior tibial slope in females and steep medial and lateral posterior tibial slopes in males may promote an even greater risk for ACL injury. They suggest that as additional morphological risk factors are considered (e.g., ACL size, knee laxity) within the injury model, sex-specific risk assessment tools may ultimately be necessary. Our own work, expanded upon later in this review, supports this evolving tenet. In fact, it suggests that extrapolating such efforts even further to examine risk variations within a sex may be critical.

Although not yet shown to directly contribute to injury causality, a number of other morphological factors have been indirectly linked to sex-based ACL injury risk. Females, for instance, possess ACL of smaller length, cross-sectional area, and volume, resulting in lower load to failure magnitudes (3). Concomitant sex-based differences in ligament ultrastructure, namely, collagen fibril number and size, are suggested to govern these geometric and structural differences (11). Knee joint articular surfaces also are reported to be 20% to 35% smaller in females (6), which we proposed may increase injury risk via a dangerously small lever arm between the tensile load on the ACL and compressive load on the lateral condyle

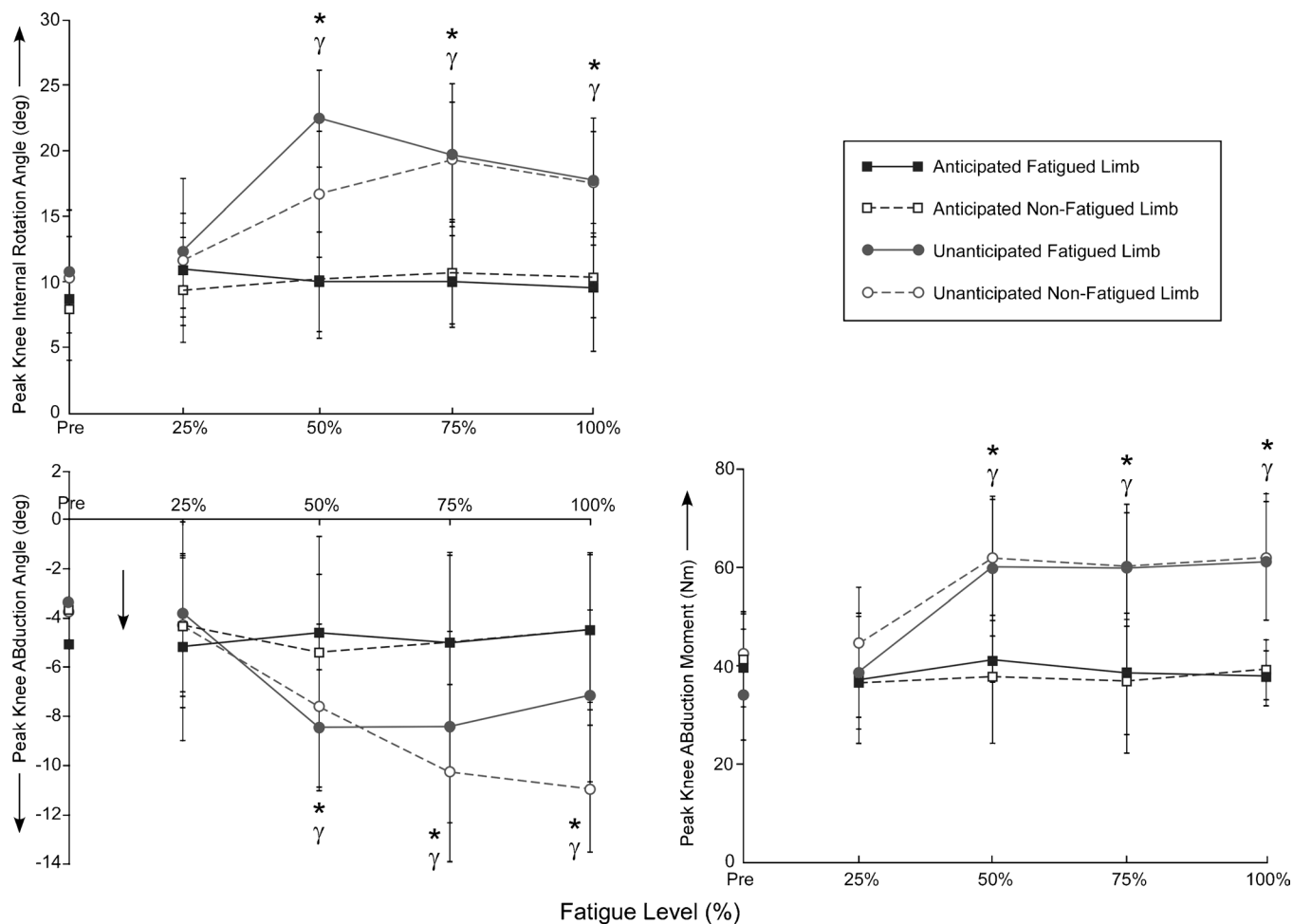


Figure 1. Combined effects of fatigue and decision making on key knee joint biomechanical parameters during a high-impact single leg landing task. As fatigue progressed, statistically significant ($P < 0.01$) increases in peak stance knee internal rotation and knee abduction angles and peak stance knee abduction moment were observed (*) in both the fatigued and non-fatigued limb. Bilateral fatigue-induced increases in each of these mechanical parameters were also more pronounced in unanticipated compared to anticipated landings (γ). [McLean SG, Samorezov JE. Fatigue-induced ACL injury risk stems from a degradation in central control. *Med Sci Sports Exerc.* 2009; 41(8):1661–72. Copyright © 2009 Lippincott Williams & Wilkins. Used with permission.]

during external knee abduction loading (23). Females also demonstrate specific lower limb alignment characteristics, such as increased anterior pelvic tilt, femoral anteversion, static quadriceps angle, and genu recurvatum compared with males (30), which are posited to increase knee joint and resultant ACL loading during high-impact landing tasks (30).

Despite increased evidence and speculation linking morphological parameters to ACL injury risk, they are rarely considered within the prevention model, as they possess limited potential for direct modification. Thus, the means through which these factors contribute directly to injury risk remain largely unknown. Again, we consider this knowledge gap to be a critical limiting factor in the current and future success of ACL injury prevention. Specifically, we propose that individual-specific morphologies directly impact the resultant knee joint biomechanical profile and hence the extent to which a trained neuromuscular strategy can protect the ACL. In the following section, we review our recent work and that of several others, which we feel consolidates this tenet. In doing so, we establish that integrative morphological and neuromuscular control contributions to knee joint and

ACL loading must be considered if noncontact ACL injuries are to be ultimately prevented.

INTEGRATIVE MORPHOLOGICAL AND MECHANICAL CONTRIBUTIONS TO ACL INJURY RISK

Despite morphological parameters being increasingly linked to ACL injury, the precise means through which they contribute to injury risk has remained largely unknown. Speculation continues to evolve for some factors, stemming primarily from basic mechanical principles. A larger-than-normal posterior tibial slope, for example, is posited to increase the anterior shear component of the impact-induced knee joint reaction force, precipitating similarly large and potentially risky peak ACL loads (10). Increased knee laxity similarly has been suggested to compound ACL injury risk via the promotion of ineffective joint stability and lower limb control during high-impact landing tasks (30,31). Although such outcomes indeed seem plausible, an imprecise understanding of morphological

contributions to injury substantially compromises the potential to successfully counter their deleterious impact. Fortunately, research is now taking this important step, with explicit links between knee neuromechanics and knee laxity, postural alignment, and joint anatomical factors being explored (Table).

Despite knee joint laxity being a documented risk factor for ACL injury (36), the means through which it contributes to injury has remained largely unknown. Recent studies have provided important insights here, demonstrating strong links between knee joint laxity and risky knee joint biomechanical profiles (28,29,34,35). Increased anterior knee laxity, for example, correlated with higher knee joint abduction and axial rotational loads during cutting and stop-and-jump maneuvers (28). Along with general joint laxity, it also related to increased work absorption and stiffness about the knee during similar tasks (35). Greater abduction/adduction and internal/external rotational knee joint laxity additionally predicted increased out-of-plane hip and knee rotations and loads during landings in both males and females (34). Less clear, however, is the role that hormonal changes, particularly across the female menstrual cycle, may have on laxity contributions to the neuromechanical response. There is evi-

dence suggesting that knee laxity is directly governed by menstrual cycle phase (33), which may in turn modulate the knee loading response during high-impact landings (29). Associations between menstrual cycle phase, general and/or knee joint laxity, and knee loading, however, remain inconclusive (4). Further research into how such associations may impact ACL injury risk and the associated sex disparity in injury rates thus seems warranted.

In research conducted over the past decade, we have begun to establish the sensitivity of the joint mechanical profile during high-impact landing maneuvers to individual-specific alignment and structural factors. Outcomes of this work have strongly suggested that a successful neuromuscular prevention strategy must cater to variations in such factors (17). Several early studies, for example, highlighted the likely critical role of postural alignment at impact during dynamic single-leg landing maneuvers. Specifically, initial contact hip internal rotation posture predicted peak stance phase knee abduction moments arising during stance (20). Furthermore, this relation was more sensitive in females compared with males, suggesting that the former may require more consistent hip control strategies during landings to accommodate for

TABLE. Research studies investigating explicit links between morphological and knee joint biomechanical factors associated with anterior cruciate ligament (ACL) injury risk.

Study	Morphological Outcome Measures	Biomechanical Outcome Measures	Study Outcome
McLean <i>et al.</i> , 2010 (23)	Medial posterior tibial slope (MTS) Lateral posterior tibial slope (LTS) MTS:LTS ratio Tibial plateau width (TPW) Intercondylar distance (ICD) TPW:ICD ratio	Peak stance anterior tibial shear force Peak stance knee abduction angle Peak stance knee internal rotation angle ► During a single-leg landing	Positive correlation between ► Anterior tibial shear force load and LTS ► Internal rotation angle and MTS:LTS Negative correlation between ► Knee abduction angle and TPW:ICD ► Knee abduction angle and MTS:LTS
McLean <i>et al.</i> , 2010 (24)	Posterior tibial slope (PTS)	Peak anterior tibial acceleration Peak relative anteromedial bundle (AMB)-ACL strain ► During a cadaveric simulated impact	Positive correlation between ► AMB-ACL strain and anterior tibial acceleration ► Anterior tibial acceleration and PTS ► PTS and AMB-ACL strain
Park <i>et al.</i> , 2009 (28)	Anterior knee joint laxity	3D knee angles, moments ^a and impulses ► During a cutting maneuver and a jumping/stopping task	Positive relation between ► Knee laxity and knee abduction impulse (cutting) ► Knee laxity and knee abduction moment (jump) ► Knee laxity and knee internal rotation moment and impulse (jump)
Park <i>et al.</i> , 2009 (28)	Change (Δ) in anterior knee joint laxity between menstrual cycle phases	Change (Δ) in 3D knee angles, moments ^a and impulses between menstrual cycle phases ► During a cutting maneuver	Positive correlation between ► Δ Knee laxity and knee abduction moment and impulse ► Δ Knee laxity and knee external rotation impulse and moment
Shultz and Schmitz, 2009 (34)	Rotational knee joint laxity ► Abduction/adduction ► Internal/external rotation	Frontal- and transverse-plane hip and knee angles and moments ^a ► During a double-leg landing	High knee laxity group ► Greater hip adduction and knee abduction angles ► Longer duration of hip and knee abduction moments

^aRefers to external moments.

underlying structural variations. A follow-up investigation, using subject-specific sidestep cutting model simulations, consolidated these *in vivo* observations, with peak knee abduction loads being sensitive to both initial contact sagittal plane hip and knee and transverse plane hip postures (21). “Training” the models to land with decreases in each of these parameters also drastically reduced the number of ACL injuries via a knee abduction load mechanism (21).

As noted, the current prevention model promotes a homogeneous and typically “male-like” neuromuscular strategy as a means of countering ACL injury risk. Such efforts have been driven by the rationale that males demonstrate significantly lower ACL injury rates and hence “less risky” neuromuscular patterns than females (8). To test the plausibility of this rationale, we used male and female cadaveric

data to develop sex-specific mathematical models that predicted anteromedial bundle (AMB) ACL strain in response to any combined 3-dimensional (3D) knee joint load state (26). Applying a consistent “sports relevant” 3D loading scenario to both male and female models resulted in significantly larger peak AMB strain predictions for the latter (Fig. 2). Sex-dimorphic ACL load behaviors were posited to arise via concomitant joint and/or ligament structural differences. These outcomes also imply that, for the same external load state, the ability for the overarching neuromuscular strategy to successfully restrain resultant joint and ACL loads may vary greatly between men and women because of key morphological differences. Movement away from a homogeneous neuromuscular-based interventional strategy to one that similarly demonstrates sex specificity may thus be necessary.

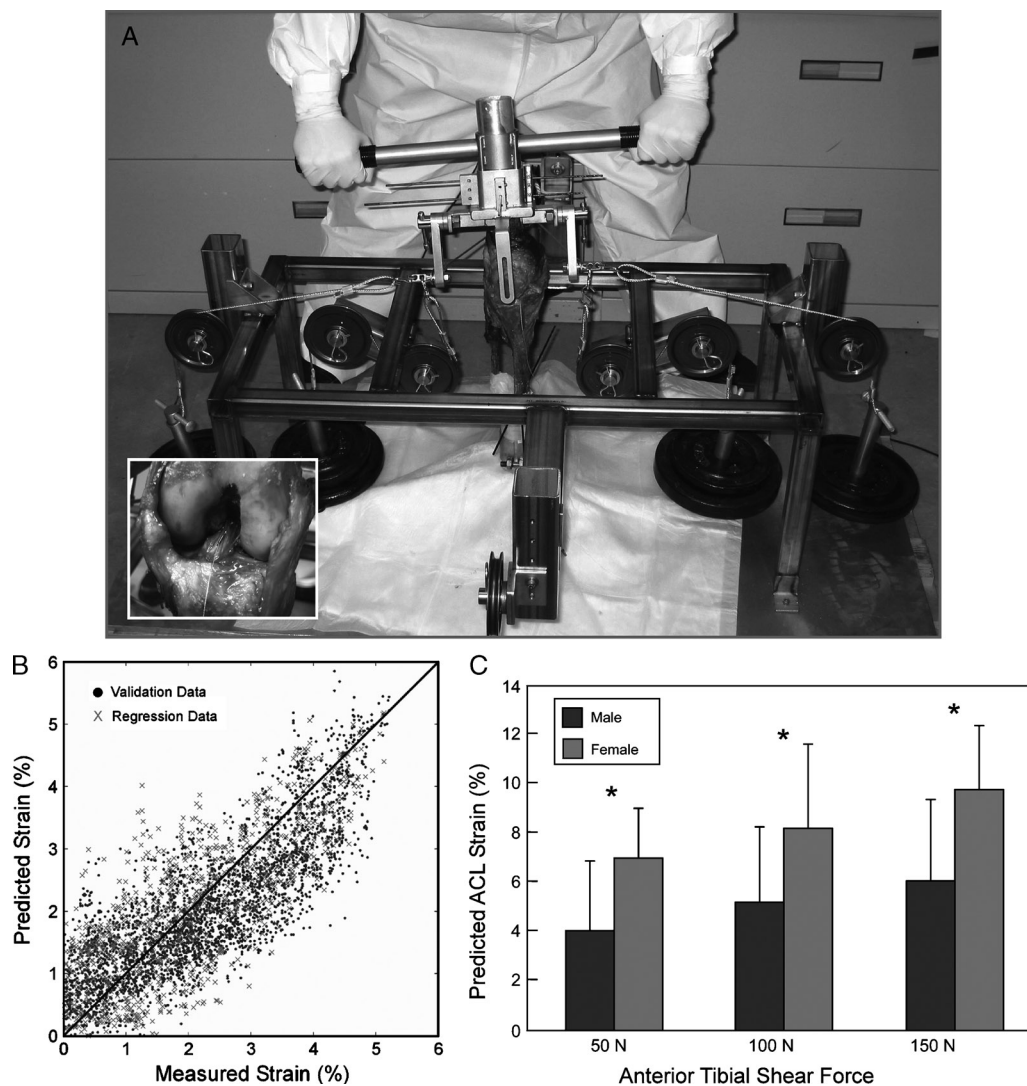


Figure 2. A custom designed manual loading device was used to apply combined 3D loads to male and female cadaveric knee specimens (A). Using these and resultant ligament strain data, specimen-specific regression models were developed that could predict peak anterior cruciate ligament (ACL) strain magnitudes to within $0.51\% \pm 0.01\%$ and $0.52\% \pm 0.06\%$ of measured data, and within $0.61\% \pm 0.11\%$ and $0.57\% \pm 0.05\%$ of validation data (not used in model development) respectively (B). Application of combined valgus (45 Nm), internal rotation (20 Nm) and compressive (300 N) loads at a fixed knee flexion angle (40 deg) and three discrete anterior tibial shear load magnitudes (50 N, 100 N and 150 N) resulted in predicted peak female ACL strains that were significantly greater than male ACL strain values (C). [Adapted from Mizuno K, Andrich JT, van den Bogert AJ, McLean SG. Gender dimorphic ACL strain in response to combined dynamic 3D knee joint loading: implications for ACL injury risk. *Knee*. 2009; 16(6):432–40. Copyright © 2009 Elsevier. Used with permission.]

The large within-sex variations evident in many of these morphological parameters additionally suggest that sex-specific intervention models, although indeed a step in the right direction, may still be unable to accommodate for individual-specific morphological contributions to ACL injury.

The above tenets have driven the subsequent examination of more detailed associations between knee morphologies and resultant knee biomechanics during high-impact landings. We initially examined such relations in a young healthy female test population and found that “high-risk” knee joint biomechanics during landings could be predicted by several knee joint anatomical indices (23) (Fig. 3). Specifically, peak anterior knee joint reaction forces and internal tibial rotations elicited during these tasks were particularly sensitive to the lateral posterior tibial slope and the ratio between lateral and medial slopes, respectively. These biomechanical param-

eters typically demonstrate sex dependence during landings (18,39) and have been shown *in vitro* to increase ACL loading (15,16). Ratios between tibial plateau width and the intercondylar distance also predicted peak stance knee abduction magnitudes, which, as noted earlier, directly impact female ACL injury risk (14). The apparent critical role of the posterior tibial slope in dictating high-risk knee joint biomechanical states has been further highlighted in our recent cadaveric work examining knee joint anatomical-mechanical interactions (24). Using an apparatus that could simulate, in the presence of muscle forces, impulsive loading typical of unipedal landings (38), we demonstrated that peak relative AMB-ACL strain significantly correlated with the peak impact-induced anterior tibial acceleration magnitude. Moreover, this relation, and hence the potential for risky acceleration states, was governed by the posterior tibial slope angle.

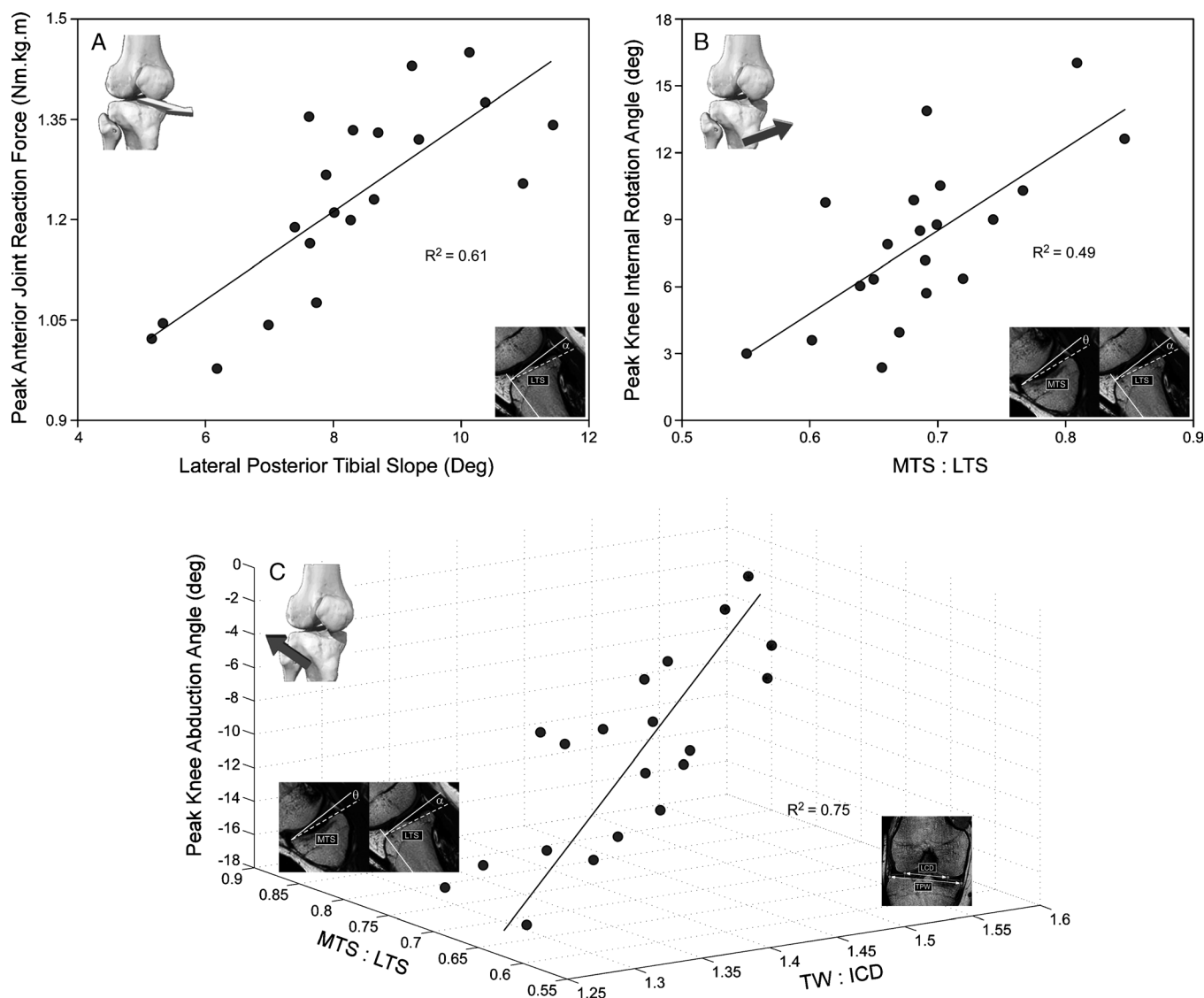


Figure 3. Associations between key knee joint anatomical indices and peak stance phase knee joint biomechanical variables during a single-leg landing task. Specifically, peak anterior knee joint reaction force was significantly positively correlated with lateral posterior tibial slope (LTS) (A). Peak knee joint internal rotation angle was significantly positively correlated with the ratio between medial and lateral posterior tibial slopes (MTS:LTS) (B). Peak knee abduction angle was significantly positively correlated with both MTS:LTS and the ratio between the tibial plateau width and the intercondylar distance (TPW:ICD) (C). [Adapted from McLean SG, Lucey SM, Rohrer S, Brandon C. Knee joint anatomy predicts extreme *in vivo* knee joint mechanics during single leg landings. *Clin Biomech.* 2010;In press. Copyright © 2010 Elsevier. Used with permission.]

These outcomes affirmed prior speculation regarding tibial slope contributions to ACL injury (10), but also suggested that injury may arise via even more complex 3D anatomical-mechanical interactions. Such interactions may become even further complicated when considered in parallel with the laxity and postural alignment factors alluded to earlier. There is no question that this line of research, while evolving rapidly, still falls well short of understanding the intricate sensitivities of the knee biomechanical response to underlying morphological risk factors. Regardless, initial studies already strongly suggest that critical changes to current ACL injury risk screening and prevention models must be made. In particular, consideration of the neuromechanical response to individual-specific joint vulnerabilities based on key morphological risk factors seems paramount in the formulation of more targeted and individualized designs.

FUTURE DIRECTIONS

With links between morphology, knee mechanics, and ACL injury risk being increasingly identified, additional research examining these relations seems both timely and essential (Fig. 4). We propose that such efforts will be best served by targeting interactions between these factors at a time when their evolution and impact will be most pronounced; namely, during maturation. Sex-based differences in lower limb neuromuscular control arise after maturation onset, which are viewed as critical in evolving male and female ACL injury risk (13). Many morphological factors,

however, also change considerably during growth and development, with sex differences appearing coevally (32). Hence, although female neuromuscular control patterns that emerge across maturation may indeed contribute to their increased risk of ACL injury, they may conversely reflect a compensatory mechanism to accommodate for evolving and potentially hazardous morphological factors. Premature modification of the overarching neuromuscular strategy may thus be detrimental rather than protective. Detailed assessments of morphological-neuromuscular interactions in males and females along the maturational pathway now seem necessary to test these critical tenets.

Elucidating whether one can “redirect” an otherwise hazardous integrative morphological-mechanical pathway as maturation progresses also may drastically improve prevention model efficacies. The structural pathway progressing in line with maturation and its subsequent potential to become high risk is dictated primarily via combined endocrinal and mechanical mechanisms (37). Although manipulation of either is possible, the direct link between loading and structural adaptation renders the latter a primary intervention target. In the knee joint, for example, physical activity levels elicited across the life span directly modulate many joint factors linked to high-risk knee joint biomechanics in this review (5). Specific loading durations, frequencies, and intensities experienced across maturation, therefore, may dictate the likelihood of a deleterious lower extremity morphological and resultant neuromechanical outcome. If this is the case, then interventions that can strategically manipulate habitual load states and hence redirect this pathway may be possible. Correlating

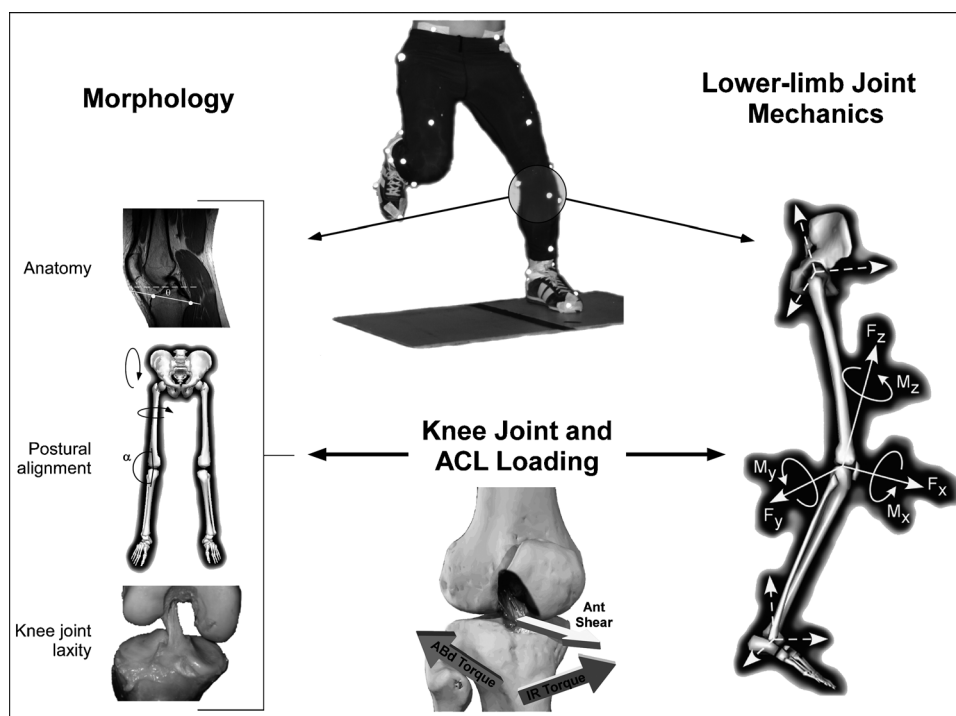


Figure 4. Conceptual model depicting integrative morphological and biomechanical contributions to knee joint and anterior cruciate ligament (ACL) loading during high-impact landing maneuvers. Explicit combinations of postural alignment and knee joint anatomical and laxity factors are posited to implicate within the ACL injury risk via the generation of large knee joint and resultant ACL load states. For the associated figure, ABd = abduction; IR = internal rotation; Ant Shear = anterior tibial shear; Fx = force in the x-axis direction; Fy = force in the y-axis direction; Fz = force in the z-axis direction; Mx = moment about the x-axis; My = moment about the y-axis; Mz = moment about the z-axis.

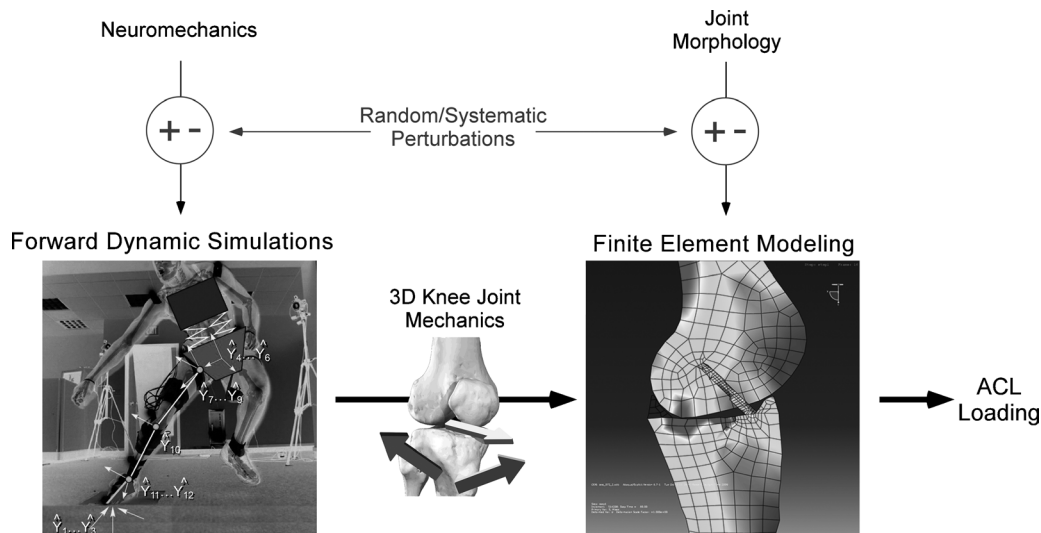


Figure 5. Surrogate (integrative forward dynamic and finite element) modeling techniques proposed to successfully investigate anterior cruciate ligament (ACL) causality based on integrative neuromechanical and morphological factors. Systematic and/or random perturbations can be applied at each level of the modeling pipeline, based on quantified variations in each measure, to determine ACL injury risk arising through individual-specific neuromechanical and morphological vulnerabilities.

loading histories with high-risk structural and mechanical interactions across maturation will provide valuable insights into the potential for such ambitious efforts to be successful.

In this article, we have highlighted that a number of key morphological factors are associated with high-risk knee joint biomechanical states. These same states, and hence ACL injury risk, however, also are governed by additional strength and lower limb control factors (8,30). As such, there is a growing consensus that the noncontact ACL injury mechanism is multifactorial (17). Injury causality may thus be truly elucidated only when the integrative impact of each of these modifiable and nonmodifiable risk factors is considered collectively. The inherent complexities associated with such an endeavor render *in vivo* experimental-based assessments virtually impossible. Applying innovative modeling methods to the ACL injury question, however, may circumvent these concerns. We have previously used valid subject-specific model simulations of landing maneuvers to examine the impact of realistic neuromuscular control perturbations on 3D knee load contributions to ACL injury risk (19,21). Recent surrogate modeling methods have extended this concept by coupling forward dynamic and structural relevant tissue deformation models (9). The finite element (FE) modeling method is a powerful and versatile modeling tool capable of reproducing highly complex joint tissue geometries and the mechanical behavior of constituent materials at discrete points throughout a system. These methods lend themselves directly to modeling the morphological complexities of the human knee joint in response to impact loading scenarios (2) and when coupled with the forward dynamic approach may successfully target the multifaceted ACL injury mechanism (Fig. 5). There is no question that developing models of this type represents a substantial and perhaps currently insurmountable computational challenge. Considering the potential long-term reward arising through these efforts, however, such novel and ambitious efforts should be encouraged.

SUMMARY AND CONCLUSIONS

Failure to reduce ACL injury rates and their associated sex disparity suggests that the current neuromuscular-based prevention model fails to counter key factors that contribute directly to ACL injury risk. We contend that morphological-mechanical interactions during high-impact landing maneuvers are critical to ACL injury risk and should thus necessarily be considered in a successful prevention strategy. Recent studies have highlighted critical links between explicit morphological factors and resultant high-risk knee joint biomechanical profiles. These initial outcomes suggest that current prevention methods would benefit substantially from developing neuromuscular control strategies that can successfully cater to individual joint vulnerabilities. More detailed assessments of 3D morphological-neuromechanical interactions, particularly as they evolve across the maturational pathway, are encouraged.

Acknowledgments

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