Clin Orthop Relat Res (2012) 470:2930–2940
DOI 10.1007/s11999-012-2440-2

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SOCIETY AWARDS

The 2012 ABJS Nicolas Andry Award

The Sequence of Prevention: A Systematic Approach to Prevent Anterior Cruciate Ligament Injury

Timothy E. Hewett PhD, Gregory D. Myer PhD, Kevin R. Ford PhD, Mark V. Paterno PhD, PT, Carmen E. Quatman MD, PhD

Received: 1 November 2011 / Accepted: 7 June 2012 / Published online: 29 June 2012

Abstract

Background ACL injuries are common, often devastating injuries that lead to short-term disability and long-term sequelae, many of which lack effective treatment, such as osteoarthritis. Therefore, prevention of ACL injury is currently the only effective intervention for these life-altering sequelae, while much of the literature has a rehabilitative focus.

Questions/Purposes The primary long-term purpose of our multidisciplinary collaborative research team has been to develop ACL injury prevention programs by determining which factors related to ACL injury should be altered, followed by how and when they should be altered.

Methods Our primary study objectives were to determine: (1) modifiable risk factors; (2) how these factors can best be modified; and (3) when is the best time to diminish these risk factors. Throughout the course of various studies, we determined the modifiable factors related to increased ACL injury risk. Our research team then focused on exploring numerous ways to augment these factors to maximize prevention efforts. We developed a sequence of prevention models that provide a framework to monitor progress toward the ultimate goal of preventing ACL injuries.

Results The modifiable factors shown in our work include biomechanical and neuromuscular functionality. When targeted in physical training, we have determined that these factors can be enhanced to effectively aid in the prevention of ACL injuries. Preliminary data have shown that

One of more of the authors has received funding from the National Institutes of Health grants R01-AR049735 (TEH), R01-AR056259 (TEH), R01-AR055563 (TEH), and R03-AR057551 (KRF); The Orthopaedic Research and Education Foundation (OREF) (TEH); National Football League Charities (TEH); University of Toledo College of Medicine Pre-Doctoral Fellowship (CEQ); and the American College of Sports Medicine Foundation Plus One Active Research Grant on Wellness Using Internet Technology (CEQ).
All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request.
This work was performed at Cincinnati Children's Hospital Medical Center, Sports Medicine Biodynamics Center and Human Performance Laboratory, Cincinnati, OH, USA.

T. E. Hewett (✉), G. D. Myer, C. E. Quatman
Departments of Physiology & Cell Biology and Orthopaedic Surgery, The Ohio State University Sports Medicine Sports Health & Performance Institute, 2050 Kenny Road, Suite 3100, Columbus, OH 43221-3502, USA
e-mail: Timothy.Hewett@osumc.edu; tim.hewett@osumc.edu

T. E. Hewett
Family Medicine, School of Allied Medical Professions and Biomedical Engineering, The Ohio State University, Columbus, OH, USA

T. E. Hewett, G. D. Myer
Athletic Training Division, School of Allied Medical Professions and Biomedical Engineering, The Ohio State University, Columbus, OH, USA

T. E. Hewett, G. D. Myer, K. R. Ford, M. V. Paterno, C. E. Quatman
Cincinnati Children's Hospital Medical Center, Sports Medicine Biodynamics Center and Human Performance Laboratory, Cincinnati, OH, USA

T. E. Hewett, G. D. Myer
Departments of Pediatrics, Orthopaedic Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA

T. E. Hewett
Department of Biomedical Engineering, University of Cincinnati College of Medicine, Cincinnati, OH, USA

childhood and early adolescence may be valuable periods to implement such training.

Conclusions Current evidence has led to the evolution of clinical assessment tools for high-risk athletes and interventions for large populations and specific high-risk individuals. Targeted intervention implemented at the specified developmental stage of highest risk may be the final step toward the maximal reduction of ACL injury risk in young athletes.

Introduction

ACL injury is a devastating injury to the knee that leads to short-term disability, possible loss of scholarship funding, and serves as a precursor to the development of osteoarthritis in young athletes [1, 2]. Radiographic studies indicate athletes who sustain an ACL rupture are at high risk for development of knee osteoarthritis as early as 10 years after the injury [23, 25, 50, 51, 81]. During the past two decades, conservative estimates indicate that more than 1.5 million ACL reconstructions were performed in the United States [47]. Historically, ACL reconstructions were aimed to salvage meniscal injuries and prevent risk of further joint degeneration with restoration of joint stability [47, 57]. Using a conservative cost of $17,000 (US dollars) per patient for surgery and rehabilitation, the estimated cost for treatment of patients with ACL injuries in the United States likely exceeds three billion dollars annually [30, 47, 57].

Despite advances in surgical technique and rehabilitation programs, long-term followup studies indicate that recovered anterior-posterior (AP) knee stability does not appear to correlate with an asymptomatic knee [5, 50] and 10% to 90% of patients with ACL injuries have clinical symptoms and radiographic findings of knee osteoarthritis at 10 to 20 years, regardless of treatment [50, 81]. Thus, the degenerative changes associated with ACL injury may be related to the trauma that occurs at the time of ACL injury and may not be only the result from knee instability subsequent to ligament disruption [81]. Prevention of ACL injury is paramount to allow many young adults to safely receive the health benefits of sports participation and recreational activity, and to avoid the greatly increased long-term risk of having osteoarthritis develop.

The 'Sequence of Prevention' model reported by van Mechelen et al. provides a framework to monitor progress toward the ultimate goal of preventing ACL injuries in athletes [103]. In this model of injury prevention, modifiable factors (ie, biomechanical and neuromuscular) related to injury mechanisms likely provide the best opportunity for the development of effective interventions.

The current article summarizes the findings of more than 80 of our reports related to the sequence of ACL injury prevention published by our research team from 1996 to 2011. Our work during the past decade has focused on defining (1) the underlying risk factors and mechanisms for ACL injury, and determination of (2) how to predict and assess individuals at risk. In addition, we have targeted how to prevent ACL injury by identifying (3) which prevention strategies are most effective and (4) when implementation of these strategies offer the greatest benefit to young athletes.

Risk Factors and Mechanisms

Epidemiologic studies show female athletes have a two- to eightfold greater ACL injury rate compared with male athletes, and approximately one in 20 female high school varsity athletes per year sustains a primary ACL injury [6, 10, 30, 53]. Before the onset of puberty, ACL injuries are relatively rare and no sex-related differences in ACL ruptures have been observed [4, 22]. During the pubertal process, many anatomic, hormonal, and neuromuscular factors differ between males and females which may contribute to the sex disparity in injury rates after puberty [35, 90, 96]. Some studies suggest females have a different mechanism of ACL injury than males [49, 92]. Sex differences including hormones, maturation, joint laxity, neuromuscular, biomechanical, and genetic risk factors for ACL injury have been explored extensively by our group and are summarized below.

The intrinsic risk factors that differ between sexes are likely multifactorial with anatomic, hormonal, neuromuscular, and biomechanical sex differences theorized to contribute to the injury rate disparity [35]. We have explored numerous sex differences including: laxity, muscle strength and coordination, dynamic hip and knee control, lower extremity joint stiffness, and force attenuation during landing [11, 15–19, 26, 33, 37, 39, 68, 90, 91, 109]. The current literature indicates that ACL injury

G. D. Myer
Rocky Mountain University of Health Professions, Departments of Athletic Training, Sports Orthopaedics, Pediatric Science and Health Promotion and Wellness, Provo, UT, USA

K. R. Ford
Department of Physical Therapy, School of Health Sciences, High Point University, High Point, NC, USA

K. R. Ford
Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

M. V. Paterno
Department of Occupational Therapy and Physical Therapy, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

occurs within 30 to 100 ms of initial contact between the foot and the ground during landing, deceleration, and lateral pivoting maneuvers [48, 49]. The ability to safely attenuate large forces, recruit muscular restraints to resist perturbations, and control loads driving dangerous lower extremity movements during initial contact is critical for prevention of lower extremity injury. Our work showed that, compared with males, mature females exhibit decreased force attenuation abilities during landing (greater landing forces and force loading rates), lower hamstrings to quadriceps torque ratios at high angular velocities, altered quadriceps and hamstrings activation strategies that may increase dynamic knee abduction, and greater frontal plane motion and loads during dynamic tasks [1, 15, 17–19, 26, 33, 39, 45, 68, 90, 99]. A recent systematic review [55] showed there are sex differences in trunk and hip motion in all planes (sagittal, coronal and transverse). Decreased force attenuation abilities and altered landing strategies coupled with increased generalized joint laxity, anterior knee laxity, and decreased torsional stiffness in females may partially explain their increased risk for ACL injuries compared with males [26, 76, 91, 109].

In addition to the anthropomorphic strength and power differences between males and females, the hormonal milieu, particularly after the onset of puberty is considerably different between sexes. Cyclic fluctuations in sex hormones, particularly female hormones associated with the follicular and ovulatory phases of the menstrual cycle, have been theorized to affect the mechanical properties of ligaments and ACL injury risk [7, 27, 39, 100, 104, 105]. Systematic reviews [108] and aggregated analyses by our group [42] provide further evidence the menstrual cycle may be associated with increased AP knee laxity and incidence of ACL injury. Thus, the precise mechanisms by which hormonal factors may contribute to ACL injury risk, particularly in females, and the extent to which they can be modified remain unclear.

As children mature, their anatomy, hormonal milieu, and gait patterns change. After the onset of puberty, there is a sex divergence in these factors during maturation with a concomitant increased rate of ACL injury in females [8, 33, 90]. During the pubertal process, adolescents undergo rapid increases in height and body mass that result in a higher center of mass and longer levers (femur and tibia) in the lower extremity. Longitudinal and cross-sectional studies in our laboratory indicate males and females experience neuromuscular and biomechanical differences in variables such as hamstrings to quadriceps peak torque ratios and knee abduction moment during maturation [16, 19, 37, 65]. Systematic reviews by our research team indicate many aspects of neuromuscular function continue to mature throughout adolescence, and at least some children experience delays or regressions in some neuromuscular control mechanisms [20, 96]. Deficits, delays, or regressions in neuromuscular function such as reduced frontal plane lower extremity control (particularly related to lower extremity movement tasks) appear to be associated with increased ACL injury risk in female athletes [19, 85, 109].

Before puberty, minimal lower extremity biomechanical and neuromuscular differences are detectable between the sexes [8, 33, 52]. However, after the onset of maturation and after puberty, females show measurable neuromuscular imbalances of quadriceps dominance, ligament dominance, leg dominance (lower extremity asymmetry), and trunk dominance compared with males [15, 40, 41]. Our studies showed that in contrast to males, after the onset of puberty, females have an increase in knee abduction angles, knee abduction motions, knee abduction moments, and decreased passive joint stiffness with apparent relative reductions in active knee stiffness [19, 33, 65, 91]. Increased knee abduction, generalized joint laxity, and active joint stiffness are purportedly potential neuromuscular risk factors that may help explain the sex discrepancy in ACL injuries [2, 35, 36, 62, 76].

Males also appear to have a neuromuscular spurt in strength, power, and coordination during puberty, whereas females show little change throughout and after puberty [33, 90]. In the absence of a sufficient neuromuscular adaptation to control the longer bony levers and greater mass that accompany the maturation process, neuromuscular imbalances may increase torque and injury risk at the knee. The development of neuromuscular imbalances and failure to have a neuromuscular spurt after the onset of puberty may be linked to the increased ACL injury risk in females relative to males [33, 37, 65, 90]. Sex differences in landing mechanics, force absorption, muscle recruitment, and joint stability that occur during maturation can be modified with neuromuscular training programs [41, 60, 83]. Induction of a neuromuscular spurt in pubertal and postpubertal females may be important for ACL prevention strategies.

Increased generalized joint laxity and joint laxity are potential factors that have been linked to greater risk of knee and ACL injury [76, 97]. A systematic review from our research team indicates the downstream effects of sex hormones associated with the menstrual cycle may affect AP joint laxity of the knee at the ovulatory (peak estrogen) phase, and female athletes may be more predisposed to ACL injuries during the preovulatory phase of the menstrual cycle [42]. Increased joint laxity measures in females after the onset of puberty, coupled with the associations of the menstrual cycle to increased joint laxity and ACL injury, suggest laxity may be an important contributing risk factor for ACL injury [39, 42, 76]. Athletes with increased generalized joint laxity also show increased midfoot loading that may alter lower extremity force distribution and proximal transfer of forces up the kinetic chain [21]. Although laxity may not be directly modifiable for ACL injury prevention strategies, increased strength and enhanced neuromuscular control may reduce the risk of injury for athletes who have increased knee and generalized joint laxity.

The risk of ACL injury in either limb is substantially greater in individuals with a previous ACL injury compared with the risk of initial ACL injury, particularly in young, active athletes [87, 98, 106]. The reported risk for initial ACL injuries is between one in 60 to one in 100 athletes [24, 56]. In contrast, the reported estimates of subsequent ACL injury (either reinjury or contralateral injury) can be 25 times greater with ranges between one in four and one in 17 for athletes who return to sports participation after ACL reconstruction. Identifying modifiable risk factors that predict a second ACL injury is important to reduce this high risk for subsequent injury. A prospective study showed that altered neuromuscular control of the knee and hip and deficits in postural stability predict a second ACL injury after return to sport from ACL reconstruction [82].

We have repeatedly observed asymmetry in loading of limbs during landing after ACL reconstruction. Patients who have had ACL reconstruction often unload the involved limb relative to their contralateral limb at the time of return to sport, and this deficit appears to persist 2 years after ACL reconstruction [82, 84, 85]. Limb-loading asymmetry has been identified as a potential ACL injury risk factor in healthy female athletes [15]. Persistent abnormal neuromuscular and biomechanical risk factors, such as lower limb motion and loading asymmetries, may increase risk for future injury and suggest patients who have had ACL reconstruction may require more targeted interventions before return to sports participation.

Given the greater ACL injury risk in individuals with a previous ACL injury compared with healthy individuals, the collagenase composition of the ACL and associations with inheritable features such as joint laxity, it is probable that risk factors for ACL injury are inheritable. Although limited information is available in the literature regarding the genetic factors that may contribute to an athlete's risk for ACL injury [14, 88, 89], there is evidence that there may be a familial predisposition [14, 88, 89]. Fraternal twin sisters we screened before their subsequent ACL injuries showed multiple potential risk factors including increased knee abduction angles, decreased knee flexion angles, increased generalized joint laxity, decreased hamstrings/quadriceps torque ratios, and smaller femoral condylar notch widths may be subject to familial predisposition [31]. Although ACL rupture is likely multifactorial, a pleiotropic genetic predisposition is likely. Delineation of genetic traits that may increase risk for ACL injury may potentially help identify at-risk athletes, target specific risk factors in family members, and help develop prevention programs to minimize ACL injury risk.

Identifying biomechanical and neuromuscular risk factors for ACL injury has been a goal and is the primary initiative of our laboratory, as these components likely offer the most modifiable means for prevention strategies [27, 32, 40]. As described above, many biomechanical and neuromuscular differences are apparent between males and females, particularly after the onset of puberty. We have examined the entire lower kinetic chain (trunk to foot) relative to knee biomechanics, neuromuscular function, and their associations to ACL injury risk. Neuromuscular and biomechanical factors such as muscle activation strategies, strength, proprioception, and lower extremity biomechanics as they relate to sex differences, puberty, and ACL injury risk have been investigated extensively and systematically published in the medical literature.

Muscle strength and activation are important for lower extremity neuromuscular control during dynamic tasks, and synergistic muscular coordination is likely an important consideration when evaluating ACL injury risk in young athletes [43]. Hamstrings and quadriceps cocontraction may contribute substantially to dynamic knee stabilization. Female athletes who have a combination of decreased relative hamstrings and high relative quadriceps strength may be at increased risk for ACL injury [62]. In addition, hip muscular recruitment strategies differ between males and females which may predispose females to knee abduction moments and motions that put them at greater risk for ACL injury [16, 18, 55, 61, 109].

Proprioception (ie, balance, coordination) is important for neuromuscular control of the lower extremity, particularly during perturbations, landing, and cutting tasks [107]. Increased trunk displacement after sudden perturbations is highly sensitive for prediction of knee, ligament, and ACL injury [107]. Proprioceptive deficits in control of the body's core predict knee injury with 90% sensitivity and 56% specificity [107]. In addition, our studies indicate deficits in single-leg postural stability in patients after ACL reconstruction substantially increase an athlete's risk for a second ACL injury [85]. Thus, deficits or alterations in proprioception are important clinical signs that should be considered in ACL injury screening assessments and prevention strategies.

Our coupled biomechanical-epidemiologic studies show knee abduction measures, hip external rotation, and limb asymmetry predict ACL injury [36, 85]. In a prospective study, we prescreened 205 female athletes with three-dimensional kinematics and joint loads during a jump landing task. The nine athletes who experienced subsequent ACL injury after testing had greater knee abduction angles (8°), 2.5 times greater knee abduction moments, and 20% greater ground reaction forces at landing compared with control teammates who did not sustain ACL injuries [36]. Our studies evaluating cutting tasks suggest neuromuscular mechanisms that increase knee abduction are primarily coronal plane motions at the hip [46]. Trunk- and hip-focused neuromuscular training programs that reduce coronal plane hip motion may be important for injury prevention strategies aimed to decrease knee abduction measures [46].

The modifiable factors described above are of importance as deficiencies in them may leave athletes more susceptible to the knee motions that are considered mechanisms of ACL injury. Tibiofemoral joint motions occur in six degrees of freedom (three rotations, three translations) in the sagittal, frontal, and transverse planes. Joint loads that result in motions beyond the normal physiologic range in any plane potentially could lead to ACL injury. Despite the abundance of literature related to ACL injury, few studies evaluate the ACL injury mechanism and inciting injury event. A robust systematic review showed that in almost 1000 studies evaluating ACL injury, only 34 were identified that directly induced or observed an ACL injury [95]. Collectively, these studies indicate ACL injuries are more likely to occur during multiplanar rather than uniplanar mechanisms, and there is evidence suggesting females may have different injury mechanisms than males [35, 49, 92, 95]. Video studies of ACL injury mechanisms in athletes indicate lateral trunk motion, knee abduction motions, either flatfooted or hind foot initial ground contact, and increased hip flexion are often components of the inciting ACL injury event [9, 49]. Females tend to land with substantially greater knee and hip flexion and have a 5.3 times greater relative risk of exhibiting valgus knee collapse during ACL injury compared with males [49].

The methodologic approaches that have been used to investigate ACL injury mechanisms include athlete interviews, arthroscopic studies, video analyses, cadaveric studies, in vivo laboratory studies, and mathematical modeling. Each of these methods has multiple, inherent limitations that make it difficult to fully define ACL injury mechanisms [95]. We therefore developed a new research paradigm that incorporates a multifaceted, multidisciplinary, integration of in vivo, in vitro (cadaveric), and in silico (computer modeling methods) that we term "in sim" [94]. In sim approaches may provide a platform for more comprehensive understanding of the complex relations between joint biomechanics and observed ACL injury mechanisms. We have used this technique of multiple cross-validations to analyze tibiofemoral cartilage pressure distributions during normal and injurious landing scenarios. We compared our findings from simulations with in vivo bone bruise patterns that occur in greater than 80% of patients who sustain ACL injuries [93, 102]. In vivo landing data from young female athletes who had subsequent ACL injury were incorporated into a computer model (validated by in vitro data) to analyze landing mechanics [107]. Injury simulations also were conducted based on in vivo video data of female athletes during an ACL injury event [48, 49]. The resultant articular cartilage load distributions compared with bone bruise patterns associated with ACL injury support a valgus collapse injury mechanism that results from tibial abduction combined with anterior tibial translation or external or internal tibial rotations [93]. Incorporation of new research methods, such as in sim techniques, may facilitate further elucidation of the primary modifiable risk factors and inciting mechanisms associated with the ACL injury event.

Prediction and Assessment of At Risk Individuals

During the past decade we have performed prospective, longitudinal, biomechanical-epidemiologic studies of female and male athletes. More than 3000 athletes have been prescreened in our laboratory for biomechanical, anatomic, and neuromuscular measures before their athletic seasons and followed to determine who had subsequent ACL injury. From this robust sampling, we observed that athletes who had subsequent injury after testing had greater knee abduction angles, knee abduction moments, and higher ground reaction forces than uninjured teammates [36]. In addition, subjects who experienced ACL injury had a 16% shorter stance time at landing than uninjured control subjects, which resulted in more rapid occurrence of motion, forces, and moments at the knee [36]. Logistic regressions showed knee abduction moments and angles at initial contact and peak values during landing predicted ACL injury with 78% sensitivity and 73% specificity [36]. In addition, for every 1.3-mm increase in side-to-side difference in AP knee displacement (measured by KT-2000, MEDmetric, San Diego, CA, USA) the odds of ACL injury increased fourfold and positive knee hyperextension increased ACL injury odds fivefold [76]. Females who experienced subsequent ACL injury had decreased hamstrings strength but similar quadriceps strength compared with male control subjects [63].

We observed deficits in active proprioception to control the body's core in females who subsequently had ligament or meniscal knee injuries [107]. Proprioception deficits predicted knee injury with 90% sensitivity and 56% specificity in female athletes whereas no similar association was apparent in male subjects [107]. Trunk displacement and more specifically lateral trunk displacement, after a sudden perturbation was greater in athletes who subsequently had a knee injury. A logistic regression model that consisted of the variables of trunk displacement, proprioception, and history of low back pain predicted knee ligament injury with 91% sensitivity and 68% specificity in all athletes and predicted ACL injury risk in females with 91% accuracy [107].

In addition to the variables explored above for first ACL injury prediction, biomechanical-epidemiologic studies of athletes who return to sport after ACL reconstruction suggest biomechanical and neuromuscular deficits may predict a second ACL injury after return to sport after ACL reconstruction [85]. Net hip rotation torque impulse, frontal plane knee ROM during landing, asymmetries in sagittal plane knee moments at initial contact during landing, and postural stability predict second ACL injury (92% sensitivity, 88% specificity) during return to sport after ACL reconstruction [82]. Cumulatively, the evidence indicates it may be possible to predict who is at risk for first and second ACL injuries. This step of identifying at-risk athletes is critical for targeting prevention programs for athletes who will benefit most from intervention strategies.

To develop the most efficacious ACL injury prevention programs, it is paramount that valid and reliable clinical assessment tools identifying at-risk athletes be developed to target the populations that will benefit most from intervention. Measures of high knee abduction moment during landing tasks predict ACL injury with high specificity and sensitivity [36]. However, until recently, expensive biomechanical laboratories that use costly measurement tools (eg, motion analysis systems, force plates), labor-intensive data collection, and reduction techniques were necessary to obtain knee abduction measurements.

We have developed several clinician-friendly assessment tools to help identify at-risk athletes with techniques that require less expensive and labor-intensive measures [59, 69, 71–73, 78]. Clinical correlates to laboratory-based measures identify and predict high knee abduction moments with 73% sensitivity and 70% specificity [72]. These clinical correlates include simplified screening systems that use a calibrated physician's scale, a standard measuring tape, standard camcorder, ImageJ software (National Institutes of Health, Bethesda, MD, USA), and an isokinetic dynamometer, which predict high knee abduction moments status with 84% sensitivity and 67% specificity [70, 73]. A clinical-based nomogram tool is now available that identifies athletes who have high knee abduction moments with greater than 75% prediction accuracy [70, 73]. These clinical prediction tools may help facilitate entry of female athletes with high ACL injury risk into appropriate injury prevention programs.

Our current projects are aimed at the development of neuromuscular screening techniques to identify high-risk athletes and target these athletes with the most appropriate training for their specific deficits. This necessitates the augmentation of clinical assessment tools that reliably and accurately assess high-risk neuromuscular deficits. Widespread adoption and use of such tools require that the assessment tools be inexpensive, easy to use, with objective criteria that can be used to identify deficits and monitor improvement with time. We have evaluated common assessment tools such as the star excursion balance test, functional hop tests, stabilometry, and dynamometry, in addition to developing new techniques to help identify lower extremity asymmetry and high-risk landing and cutting techniques [13, 44, 69, 72, 78, 83].

Real-time assessment tools that can be used to provide immediate biofeedback may provide direction for targeted neuromuscular training to reduce ACL injury risk [70]. We have developed a tuck jump assessment tool that measures important landing techniques, such as limb symmetry, foot positioning, knee abduction, technique degradation, coordination, and landing forces during a high-level effort movement [69]. We also have modified agility training tests and developed techniques to assess frontal and sagittal plane biomechanics using inexpensive tools [44, 54, 84]. We have been able to use these techniques for individual assessments and large-scale screening techniques similar to what occurs during National Football League combine testing [44, 72, 78, 84].

The potential use of clinical assessment tools for function is not limited to screening and training for neuromuscular deficits in at-risk athletes. These tools also may prove useful during rehabilitation after injury to monitor functional improvements and determine level of readiness to meet the functional demands of sports with minimal risk of reinjury or compensatory injury.

Prevention Strategies and Techniques

Neuromuscular-based injury prevention measures necessitate identification of risk factors and mechanisms of injury that are potentially modifiable. ACL injury prevention strategies have been a high priority in our laboratory for the past 15 years and we have published more than 25 papers in peer-reviewed journals dedicated to neuromuscular training strategies to identify and address neuromuscular control deficits related to ACL injury [27–30, 32, 34, 38, 40, 41, 58, 60, 61, 64, 66, 67, 69, 70, 74, 77–79, 84].

Neuromuscular control deficits are defined as muscle strength, power, coordination, or activation patterns that potentially increase injury risk owing to increased joint loads [67]. Females often have one or more neuromuscular control deficits such as ligament, quadriceps, trunk, or leg dominance and these deficits likely play a role in ACL injury risk [67]. During landing, pivoting, or deceleration, the motion of the female athlete's trunk is often excessive and directed, to a greater extent, by that body segment's inertia, than by the athlete's core muscle function. This decreased core control and ability to dissipate force results in excessive trunk motion, especially in the frontal plane, and high ground reaction forces and knee abduction torques (knee load) [59].

Neuromuscular control deficits may persist or develop during puberty and if left unaddressed, may continue into adulthood and place many females at increased risk for ACL injury [16, 19, 33, 36, 90]. It is well established that neuromuscular training programs can result in increased strength, power, and coordination [41, 60, 64]. Induction of a neuromuscular spurt and reduction of neuromuscular control deficits may be possible with training, particularly in females [29, 64]. Coincident with increased performance measures, neuromuscular training has shown potential for approximately 50% reduction of ACL injury risk in female athletes [29, 30, 64]. Neuromuscular training protocols that integrate biomechanical, proprioceptive, and strength training techniques have shown induction of an appreciable neuromuscular spurt, positive performance enhancements, and improved biomechanical techniques that lower ACL injury risk [29, 30, 64, 74]. However, training protocols that target single-component training approaches have had limited success at reducing knee injuries in female athletes [86, 101]. The assessment and training of power (via plyometrics), strength (via resistance training), and coordination of muscle recruitment (via dynamic stabilization/balance training) individually and in combination are important considerations to enhance potential ACL injury prevention strategies.

The comprehensive interventions currently used in ACL injury prevention programs [29] often involve an extensive time commitment, player and coach involvement, and training volumes. Each of these can deter widespread acceptance of and commitment to the training necessary to reduce injury risk. Our research has focused on identifying targeted training protocols to more effectively and efficiently alter high-risk landing and cutting biomechanics and improve neuromuscular deficiencies. We compared the effects of maximum-effort plyometric training versus dynamic stabilization exercises, trunk- and hip-focused training, and functional proprioceptive training on power, strength, coordination, and high-risk lower extremity biomechanics (ie, limb asymmetry, high ground reaction forces, knee abduction measures, and knee flexion measures) [13, 29, 58, 60, 64, 74, 83]. In relation to high-risk lower extremity biomechanics, plyometric and balance training can reduce high-risk knee abduction and flexion measures [29, 64, 74]. Trunk-focused neuromuscular training increases hip abduction strength which may improve neuromuscular control of lower limb alignment and decrease knee loads that occur as a result of increased trunk displacement during sports activities [58]. Neuromuscular training programs that target core and lower extremity strength can improve single-limb postural stability and neuromuscular control [13, 83]. In addition, female athletes categorized as high risk based on knee abduction measures are more responsive to neuromuscular training than teammates who do not exhibit high-risk measures [64]. However, even after 4 to 7 weeks of training, the mean high-risk values were not reduced to values similar to those of the low-risk group. Although training improves high-risk lower extremity biomechanics, isolated preseason or in-season training in short doses may not provide the training dosage necessary to reduce ACL injury risk in females [64].

Collectively, our training studies [30, 41, 58, 63, 64, 74, 75] indicate a combination of plyometric, resistance, and balance training with technique biofeedback may further maximize the effectiveness of preseason training and ACL injury prevention strategies. The additive effect of improved performance measures and neuromuscular function, particularly in athletes with specific deficits or altered biomechanics, may lead to more efficacious, efficient, targeted ACL injury prevention programs. Our goals are to develop programs for early identification of at-risk athletes and implement targeted, efficient ACL prevention programs to improve compliance with training and lead to more widespread acceptance and use of ACL injury prevention programs.

Timing of Intervention

The emergence of sex differences in laxity and neuromuscular control during maturation, coupled with a divergence in ACL injury rates between the sexes after the onset of puberty, indicates that preadolescence or early puberty seems to be a critical phase related to the increased ACL injury risk factors [16, 19, 90, 91, 96]. Preliminary data indicate integrative neuromuscular training protocols implemented in preadolescent and early adolescent stages may artificially induce the neuromuscular spurt, especially related to relative posterior chain strength, postural control, and neuromuscular power [60]. An induced neuromuscular spurt may decrease differences in neuromuscular control of the lower extremity between adolescent male and female athletes and has the potential to reduce the risk of sports-related injury in adolescent female athletes [30, 34, 41, 62]. These data provide further support that preadolescence may be an essential time to institute programs to reduce these deficits that accelerate during maturation and lead to increased musculoskeletal injury risk [70].

There has been movement to promote youth involvement in strength and conditioning activities, which has resulted in concern regarding the most appropriate age to safely incorporate strength training programs [3, 12, 80]. In addition, while resistance training is an integral part of most high school sports programs for males, females likely have not had similar access, desire, or available resources to incorporate strength training measures into their sports programs [44]. Resistance training can be safe, effective, and valuable for children and adolescent female athletes. Training sessions should be supervised by qualified professionals and age-appropriate instructions on lifting techniques and safety guidelines followed [44, 70, 71, 80]. Integrative neuromuscular training throughout childhood and adolescence may promote positive health outcomes, enhance sports performance, and reduce the risk of sports-related and more specifically, ACL injury in young athletes [60, 70, 71].

Discussion

Owing to the high risk for development of long-term osteoarthritis in the ACL-injured population, with or without surgical reconstruction, primary prevention of ACL injury is currently the only effective intervention for these life-altering injuries. During the last decade, ACL injury mechanisms and risk factors have been described in the work of our collaborative research team and used to target intervention for high-risk individuals. Although we have encompassed numerous risk factors, the bulk of our focus has been on identification of biomechanical and neuromuscular risk factors. Different strategies to assess and manipulate the identified factors have been explored to moderate an individual's predisposition to ACL injury. Exploration of the most advantageous timing of biomechanical and neuromuscular interventions has been included in our team's effort to develop the foundation for an effective ACL prevention program.

Our studies are subject to certain limitations. First, they are in large part, prospective, longitudinal, cohort studies and as such, are not necessarily Level I studies. Second, our prior intervention studies have not all been randomized controlled trials. Third, since we are working with human populations, these data are subject to highly intersubject variability. Finally, many of our later studies have not been repeated and corroborated. We currently are conducting these studies with higher-level research designs and encourage others to do so as well.

Through recognition of modifiable risk factors for primary and secondary ACL injuries, we developed and studied various techniques in prevention programs. There now is evidence that neuromuscular training not only reduces the levels of biomechanical risk factors for ACL injury, but also decreases general knee and ACL injury incidence in female athletes. In addition to training, data have shown that the timing of implementation of prevention training also may be valuable in reducing the risk of ACL injury. However, early reevaluation of ACL injury rates indicates that this important health issue has yet to be resolved. Continued studies should include the assessment of relative injury risk using widespread neuromuscular screening techniques. Additional work toward the development of more specific injury prevention protocols targeted to high-risk athletes with determination of the timing of when these interventions should most effectively be used is imperative. It may be that athletes before puberty or in early puberty may have the potential to achieve favorable biomechanics (ie, minimal knee abduction, low ground reaction forces, and neutral frontal plane alignment of the lower extremity with knees and feet approximately shoulder length apart and neutral foot progression angles during landing and cutting activities) and the greatest chance of injury-free sports participation throughout their entire sports careers. Although we have made substantial strides forward, the sequence of prevention must be continued until there is substantial epidemiologic evidence that ACL injury risk is definitively decreased in young athletes.

Acknowledgements This comprehensive body of research was the result of a large team of individuals who have helped contribute to the data collection process. We thank all coauthors and colleagues who helped us find solutions to the important and devastating ACL injury dilemma.

References

1. Ahmad CS, Clark AM, Heilmann N, Schoeb JS, Gardner TR, Levine WN. Effect of gender and maturity on quadriceps-to-hamstring strength ratio and anterior cruciate ligament laxity. *Am J Sports Med.* 2006;34:370–374.
2. Alentorn-Geli E, Myer GD, Silvers HJ, Samitier G, Romero D, Lazaro-Haro C, Cugat R. Prevention of non-contact anterior cruciate ligament injuries in soccer players Part 1: mechanisms of injury and underlying risk factors. *Knee Surg Sports Traumatol. Arthrosc.* 2009;17:705–729.
3. American Academy of Pediatrics Council on Sports Medicine and Fitness, McCambridge TM, Stricker PR. Strength training by children and adolescents. *Pediatrics.* 2008;121:835–840.
4. Andrish JT. Anterior cruciate ligament injuries in the skeletally immature patient. *Am J Orthop (Belle Mead NJ).* 2001;30:103–110.
5. Ardern CL, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med.* 2011;45:596–606.
6. Arendt E, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer: NCAA data and review of literature. *Am J Sports Med.* 1995;23:694–701.
7. Arendt EA, Bershadsky B, Agel J. Periodicity of noncontact anterior cruciate ligament injuries during the menstrual cycle. *J Gend Specif Med.* 2002;5:19–26.
8. Beunen G, Malina RM. Growth and physical performance relative to the timing of the adolescent spurt. *Exerc Sport Sci Rev.* 1988;16:503–540.

9. Boden BP, Torg JS, Knowles SB, Hewett TE. Video analysis of anterior cruciate ligament injury: abnormalities in hip and ankle kinematics. *Am J Sports Med.* 2009;37:252–259.
10. Chandy TA, Grana WA. Secondary school athletic injury in boys and girls: a three-year comparison. *Phys Sportsmed.* 1985;13:106–111.
11. Chaudhari AM, Lindenfeld TN, Andriacchi TP, Hewett TE, Riccobene JV, Myer GD, Noyes FR. Knee and hip loading patterns at different phases in the menstrual cycle: implications for the gender difference in anterior cruciate ligament injury rates. *Am J Sports Med.* 2007;35:793–800.
12. Faigenbaum AD, Kraemer WJ, Blimkie CJ, Jeffreys I, Micheli LJ, Nitka M, Rowland TW. Youth resistance training: updated position statement paper from the National Strength and Conditioning Association. *J Strength Cond Res.* 2009;23(5 suppl): S60–79.
13. Filipa A, Byrnes R, Paterno MV, Myer GD, Hewett TE. Neuromuscular training improves performance on the star excursion balance test in young female athletes. *J Orthop Sports Phys Ther.* 2010;40:551–558.
14. Flynn RK, Pedersen CL, Birmingham TB, Kirkley A, Jackowski D, Fowler PJ. The familial predisposition toward tearing the anterior cruciate ligament: a case control study. *Am J Sports Med.* 2005;33:23–28.
15. Ford KR, Myer GD, Hewett TE. Valgus knee motion during landing in high school female and male basketball players. *Med Sci Sports Exerc.* 2003;35:1745–1750.
16. Ford KR, Myer GD, Hewett TE. Longitudinal effects of maturation on lower extremity joint stiffness in adolescent athletes. *Am J Sports Med.* 2010;38:1829–1837.
17. Ford KR, Myer GD, Smith RL, Vianello RM, Seiwert SL, Hewett TE. A comparison of dynamic coronal plane excursion between matched male and female athletes when performing single leg landings. *Clin Biomech Bristol, Avon.* 2006;21:33–40.
18. Ford KR, Myer GD, Toms HE, Hewett TE. Gender differences in the kinematics of unanticipated cutting in young athletes. *Med Sci Sports Exerc.* 2005;37:124–129.
19. Ford KR, Shapiro R, Myer GD, Van Den Bogert AJ, Hewett TE. Longitudinal sex differences during landing in knee abduction in young athletes. *Med Science Sports Exerc.* 2010;42:1923–1931.
20. Ford KR, van den Bogert J, Myer GD, Shapiro R, Hewett TE. The effects of age and skill level on knee musculature co-contraction during functional activities: a systematic review. *Br J Sports Med.* 2008;42:561–566.
21. Foss KD, Ford KR, Myer GD, Hewett TE. Generalized joint laxity associated with increased medial foot loading in female athletes. *J Athl Train.* 2009;44:356–362.
22. Gallagher SS, Finison K, Guyer B, Goodenough S. The incidence of injuries among 87,000 Massachusetts children and adolescents: results of the 1980–81 Statewide Childhood Injury Prevention Program Surveillance System. *Am J Public Health.* 1984;74:1340–1347.
23. Gillquist J, Messner K. Anterior cruciate ligament reconstruction and the long-term incidence of gonarthrosis. *Sports Med.* 1999;27:143–156.
24. Gomez E, DeLee JC, Farney WC. Incidence of injury in Texas girls' high school basketball. *Am J Sports Med.* 1996;24:684–687.
25. Gray J, Taunton JE, McKenzie DC, Clement DB, McConkey JP, Davidson RG. A survey of injuries to the anterior cruciate ligament of the knee in female basketball players. *Int J Sports Med.* 1985;6:314–316.
26. Harrison AD, Ford KR, Myer GD, Hewett TE. Sex differences in force attenuation: a clinical assessment of single-leg hop performance on a portable force plate. *Br J Sports Med.* 2011; 45:198–202.
27. Hewett TE. Neuromuscular and hormonal factors associated with knee injuries in female athletes: strategies for intervention. *Sports Med.* 2000;29:313–327.
28. Hewett TE, Ford KR, Hoogenboom BJ, Myer GD. Understanding and preventing acl injuries: current biomechanical and epidemiologic considerations: update 2010. *N Am J Sports Phys Ther.* 2010;5:234–251.
29. Hewett TE, Ford KR, Myer GD. Anterior cruciate ligament injuries in female athletes: Part 2. A meta-analysis of neuromuscular interventions aimed at injury prevention. *Am J Sports Med.* 2006;34:490–498.
30. Hewett TE, Lindenfeld TN, Riccobene JV, Noyes FR. The effect of neuromuscular training on the incidence of knee injury in female athletes: a prospective study. *Am J Sports Med.* 1999;27: 699–706.
31. Hewett TE, Lynch TR, Myer GD, Ford KR, Gwin RC, Heidt RS Jr. Multiple risk factors related to familial predisposition to anterior cruciate ligament injury: fraternal twin sisters with anterior cruciate ligament ruptures. *Br J Sports Med.* 2010;44:848–855.
32. Hewett TE, Myer GD, Ford KR. Prevention of anterior cruciate ligament injuries. *Curr Womens Health Rep.* 2001;1:218–224.
33. Hewett TE, Myer GD, Ford KR. Decrease in neuromuscular control about the knee with maturation in female athletes. *J Bone Joint Surg Am.* 2004;86:1601–1608.
34. Hewett TE, Myer GD, Ford KR. Reducing knee and anterior cruciate ligament injuries among female athletes: a systematic review of neuromuscular training interventions. *J Knee Surg.* 2005; 18:82–88.
35. Hewett TE, Myer GD, Ford KR. Anterior cruciate ligamentiInjuries in female athletes: Part 1. Mechanisms and risk factors. *Am J Sports Med.* 2006;34:299–311.
36. Hewett TE, Myer GD, Ford KR, Heidt RS Jr, Colosimo AJ, McLean SG, van den Bogert AJ, Paterno MV, Succop P. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med.* 2005;33:492–501.
37. Hewett TE, Myer GD, Ford KR, Slauterbeck JR. Preparticipation physical examination using a box drop vertical jump test in young athletes: the effects of puberty and sex. *Clin J Sport Med.* 2006;16:298–304.
38. Hewett TE, Myer GD, Ford KR, Slauterbeck JR. Dynamic neuromuscular analysis training for preventing anterior cruciate ligament injury in female athletes. *Instr Course Lect.* 2007;56: 397–406.
39. Hewett TE, Myer GD, Zazulak B. Hamstring to quadriceps peak torque ratios diverge between sexes with increasing isokinetic angular velocity. *J Sci Med Sport.* 2008;11:452–459.
40. Hewett TE, Paterno MV, Myer GD. Strategies for enhancing proprioception and neuromuscular control of the knee. *Clin Orthop Relat Res.* 2002;402:76–94.
41. Hewett TE, Stroupe AL, Nance TA, Noyes FR. Plyometric training in female athletes: decreased impact forces and increased hamstring torques. *Am J Sports Med.* 1996;24:765–773.
42. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: a systematic review. *Am J Sports Med.* 2007;35:659–668.
43. Hewett TE, Zazulak BT, Myer GD, Ford KR. A review of electromyographic activation levels, timing differences, and increased anterior cruciate ligament injury incidence in female athletes. *Br J Sports Med.* 2005;39:347–350.
44. Hickey KC, Quatman CE, Myer GD, Ford KR, Brosky JA, Hewett TE. Methodological report: dynamic field tests used in an NFL combine setting to identify lower-extremity functional asymmetries. *J Strength Cond Res.* 2009;23:2500–2506.

45. Hsu WH, Fisk JA, Yamamoto Y, Debski RE, Woo SL. Differences in torsional joint stiffness of the knee between genders: a human cadaveric study. *Am J Sports Med.* 2006;34:765–770.
46. Imwalle LE, Myer GD, Ford KR, Hewett TE. Relationship between hip and knee kinematics in athletic women during cutting maneuvers: a possible link to noncontact anterior cruciate ligament injury and prevention. *J Strength Cond Res* 2009; 23:2223–2230.
47. Kim S, Bosque J, Meehan JP, Jamali A, Marder R. Increase in outpatient knee arthroscopy in the United States: a comparison of National Surveys of Ambulatory Surgery, 1996 and 2006. *J Bone Joint Surg Am.* 2011;93:994–1000.
48. Koga H, Nakamae A, Shima Y, Iwasa J, Myklebust G, Engebretsen L, Bahr R, Krosshaug T. Mechanisms for noncontact anterior cruciate ligament injuries: knee joint kinematics in 10 injury situations from female team handball and basketball. *Am J Sports Med.* 2010;38:2218–2225.
49. Krosshaug T, Nakamae A, Boden BP, Engebretsen L, Smith G, Slauterbeck JR, Hewett TE, Bahr R. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. *Am J Sports Med.* 2007;35:359–367.
50. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med.* 2007;35:1756–1769.
51. Lohmander LS, Ostenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* 2004;50:3145–3152.
52. Malina RM, Bouchard C. Timing and sequence of changes in growth, maturation, and performance during adolescence. *Growth, Maturation, and Physical Activity*. Champaign, IL: Human Kinetics; 1991:267–272.
53. Malone TR, Hardaker WT, Garrett WE, Feagin JA, Bassett FH. Relationship of gender to anterior cruciate ligament injuries in intercollegiate basketball players. *J South OrthopAssoc.* 1993;2: 36–39.
54. McLean SG, Walker K, Ford KR, Myer GD, Hewett TE, van den Bogert AJ. Evaluation of a two dimensional analysis method as a screening and evaluation tool for anterior cruciate ligament injury. *Br J Sports Med.* 2005;39:355–362.
55. Mendiguchia J, Ford KR, Quatman CE, Alentorn-Geli E, Hewett TE. Sex differences in proximal control of the knee joint. *Sports Med.* 2011;41:541–557.
56. Messina DF, Farney WC, DeLee JC. The incidence of injury in Texas high school basketball: a prospective study among male and female athletes. *Am J Sports Med.* 1999;27:294–299.
57. Miyasaka KC, Daniel DM, Stone ML. The incidence of knee ligament injuries in the general popluation. *Am J Knee Surg.* 1991;4:43–48.
58. Myer GD, Brent JL, Ford K**R**, Hewett TE. A pilot study to determine the effect of trunk and hip focused neuromuscular training on hip and knee isokinetic strength. *Br J Sports Med.* 2008;42:614–619.
59. Myer GD, Brent JL, Ford KR, Hewett TE. Real-time assessment and neuromuscular training feedback techniques to prevent ACL injury in female athletes. *Strength Cond J.* 2011;33:21–35.
60. Myer GD, Brunner HI, Melson PG, Paterno MV, Ford KR, Hewett TE. Specialized neuromuscular training to improve neuromuscular function and biomechanics in a patient with quiescent juvenile rheumatoid arthritis. *Phys Ther.* 2005;85: 791–802.
61. Myer GD, Chu DA, Brent JL, Hewett TE. Trunk and hip control neuromuscular training for the prevention of knee joint injury. *Clin Sports Med.* 2008;27:425–448, ix.
62. Myer GD, Ford KR, Barber Foss KD, Liu C, Nick TG, Hewett TE. The relationship of hamstrings and quadriceps strength to anterior cruciate ligament injury in female athletes. *Clin J Sport Med.* 2009;19:3–8.
63. Myer GD, Ford KR, Brent JL, Hewett TE. The effects of plyometric vs. dynamic stabilization and balance training on power, balance and landing force in female athletes. *J Strength Cond Res.* 2006;20:345–353.
64. Myer GD, Ford KR, Brent JL, Hewett TE. Differential neuromuscular training effects on ACL injury risk factors in"high-risk" versus "low-risk" athletes. *BMC Musculoskelet Disord.* 2007;8:39.
65. Myer GD, Ford KR, Divine JG, Wall EJ, Kahanov L, Hewett TE. Longitudinal assessment of noncontact anterior cruciate ligament injury risk factors during maturation in a female athlete: a case report. *J Athl Train.* 2009;44:101–109.
66. Myer GD, Ford KR, Hewett TE. Methodological approaches and rationale for training to prevent anterior cruciate ligament injuries in female athletes. *Scand J Med Sci Sports.* 2004;14: 275–285.
67. Myer GD, Ford KR, Hewett TE. Rationale and clinical techniques for anterior cruciate ligament injury prevention in female athletes. *J Athl Train.* 2004;39:352–364.
68. Myer GD, Ford KR, Hewett TE. The effects of gender on quadriceps muscle activation strategies during a maneuver that mimics a high ACL injury risk position. *J Electromyogr Kinesiol.* 2005;15:181–189.
69. Myer GD, Ford KR, Hewett TE. Tuck jump assessment for reducing anterior cruciate ligament injury risk. *Athl Ther Today.* 2008;13:39–44.
70. Myer GD, Ford KR, Hewett TE. New method to identify athletes at high risk of ACL injury using clinic-based measurements and freeware computer analysis. *Br J Sports Med.* 2011; 45:238–244.
71. Myer GD, Ford KR, Khoury J, Hewett TE. Three-dimensional motion analysis validation of a clinic-based nomogram designed to identify high ACL injury risk in female athletes. *Phys Sportsmed.* 2011;39:19–28.
72. Myer GD, Ford KR, Khoury J, Succop P, Hewett TE. Clinical correlates to laboratory measures for use in non-contact anterior cruciate ligament injury risk prediction algorithm. *Clin Biomech Bristol, Avon.* 2010;25:693–699.
73. Myer GD, Ford KR, Khoury J, Succop P, Hewett TE. Development and validation of a clinic-based prediction tool to identify female athletes at high risk for anterior cruciate ligament injury. *Am J Sports Med.* 2010;38:2025–2033.
74. Myer GD, Ford KR, McLean SG, Hewett TE. The effects of plyometric versus dynamic stabilization and balance training on lower extremity niomechanics. *Am J Sports Med.* 2006;34:445–455.
75. Myer GD, Ford KR, Palumbo JP, Hewett TE. Neuromuscular training improves performance and lower-extremity biomechanics in female athletes. *J Strength Cond Res.* 2005;19:51–60.
76. Myer GD, Ford KR, Paterno MV, Nick TG, Hewett TE. The effects of generalized joint laxity on risk of anterior cruciate ligament injury in young female athletes. *Am J Sports Med.* 2008;36:1073–1080.
77. Myer GD, Paterno MV, Ford KR, Hewett TE. Neuromuscular training techniques to target deficits before return to sport after anterior cruciate ligament reconstruction. *J Strength Cond Res.* 2008;22:987–1014.
78. Myer GD, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior cruciate ligament reconstruction: criteria-based progression through the return-to-sport phase. *J Orthop Sports Phys Ther.* 2006;36:385–402.
79. Myer GD, Paterno MV, Hewett TE. Back in the game: a four-phase return-to-sport program for athletes with problem ACLS. *Rehab Manage.* 2004;17:30–33.

80. Myer GD, Quatman CE, Khoury J, Wall EJ, Hewett TE. Youth versus adult "weightlifting" injuries presenting to United States emergency rooms: accidental versus nonaccidental injury mechanisms. *J Strength Cond Res.* 2009;23:2054–2060.
81. Myklebust G, Bahr R. Return to play guidelines after anterior cruciate ligament surgery. *Br J Sports Med.* 2005;39:127–131.
82. Paterno MV, Ford KR, Myer GD, Heyl R, Hewett TE. Limb asymmetries in landing and jumping 2 years following anterior cruciate ligament reconstruction. *Clin J Sport Med.* 2007;17: 258–262.
83. Paterno MV, Myer GD, Ford KR, Hewett TE. Neuromuscular training improves single-limb stability in young female athletes. *J Orthop Sports Phys Ther.* 2004;34:305–316.
84. Paterno MV, Schmitt LC, Ford KR, Rauh MJ, Myer GD, Hewett TE. Effects of sex on compensatory landing strategies upon return to sport after anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 2011;41:553–559.
85. Paterno MV, Schmitt LC, Ford KR, Rauh MJ, Myer GD, Huang B, Hewett TE. Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport. *Am J Sports Med.* 2010;38:1968–1978.
86. Pfeiffer RP, Shea KG, Roberts D, Grandstrand S, Bond L. Lack of effect of a knee ligament injury prevention program on the incidence of noncontact anterior cruciate ligament injury. *J Bone Joint Surg Am.* 2006;88:1769–1774.
87. Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med.* 2007; 35:564–574.
88. Posthumus M, September AV, O'Cuinneagain D, van der Merwe W, Schwellnus MP, Collins M. The COL5A1 gene is associated with increased risk of anterior cruciate ligament ruptures in female participants. *Am J Sports Med.* 2009;37: 2234–2240.
89. Posthumus M, September AV, O'Cuinneagain D, van der Merwe W, Schwellnus MP, Collins M. The association between the COL12A1 gene and anterior cruciate ligament ruptures. *Br J Sports Med.* 2010;44:1160–1165.
90. Quatman CE, Ford KR, Myer GD, Hewett TE. Maturation leads to gender differences in landing force and vertical jump performance: a longitudinal study. *Am J Sports Med.* 2006;34:806–813.
91. Quatman CE, Ford KR, Myer GD, Paterno MV, Hewett TE. The effects of gender and pubertal status on generalized joint laxity in young athletes. *J Sci Med Sport.* 2008;11:257–263.
92. Quatman CE, Hewett TE. The anterior cruciate ligament injury controversy: is "valgus collapse" a sex-specific mechanism? *Br J Sports Med.* 2009;43:328–335.
93. Quatman CE, Kiapour A, Myer GD, Ford KR, Demetropoulos CK, Goel VK, Hewett TE. Cartilage pressure distributions provide a footprint to define female anterior cruciate ligament injury mechanisms. *Am J Sports Med.* 2011;39:1706–1713.
94. Quatman CE, Quatman CC, Hewett TE. Prediction and prevention of musculoskeletal injury: a paradigm shift in methodology. *Br J Sports Med.* 2009;43:1100–1107.
95. Quatman CE, Quatman-Yates CC, Hewett TE. A 'plane' explanation of anterior cruciate ligament injury mechanisms: a systematic review. *Sports Med.* 2010;40:729–746.
96. Quatman-Yates CC, Quatman CE, Meszaros AJ, Paterno MV, Hewett TE. A systematic review of sensorimotor function during adolescence: a developmental stage of increased motor awkwardness? *Br J Sports Med.* 2011 Apr 1. [Epub ahead of print]
97. Rozzi SL, Lephart SM, Gear WS, Fu FH. Knee joint laxity and neuromuscular characteristics of male and female soccer and basketball players. *Am J Sports Med.* 1999;27:312–319.
98. Salmon L, Russell V, Musgrove T, Pinczewski L, Refshauge K. Incidence and risk factors for graft rupture and contralateral rupture after anterior cruciate ligament reconstruction. *Arthroscopy.* 2005;21:948–957.
99. Shultz SJ, Shimokochi Y, Nguyen AD, Schmitz RJ, Beynnon BD, Perrin DH. Measurement of varus-valgus and internal-external rotational knee laxities in vivo: Part II. Relationship with anterior-posterior and general joint laxity in males and females. *J Orthop Res.* 2007;25:989–996.
100. Slauterbeck JR, Hardy DM. Sex hormones and knee ligament injuries in female athletes. *Am J Med Sci.* 2001;322:196–199.
101. Soderman K, Werner S, Pietila T, Engstrom B, Alfredson H. Balance board training: prevention of traumatic injuries of the lower extremities in female soccer players? A prospective randomized intervention study. *Knee Surg Sports Traumatol Arthrosc* 2000;8:356–363.
102. Speer KP, Spritzer CE, Bassett FH 3rd, Feagin JA Jr, Garrett WE Jr. Osseous injury associated with acute tears of the anterior cruciate ligament. *Am J Sports Med.* 1992;20:382–389.
103. van Mechelen W, Hlobil H, Kemper HC. Incidence, severity, aetiology and prevention of sports injuries: a review of concepts. *Sports Med.* 1992;14:82–99.
104. Wojtys EM, Ashton-Miller JA, Huston LJ. A gender-related difference in the contribution of the knee musculature to sagittal-plane shear stiffness in subjects with similar knee laxity. *J Bone Joint Surg Am.* 2002;84:10–16.
105. Wojtys EM, Huston LJ, Lindenfeld TN, Hewett TE, Greenfield ML. Association between the menstrual cycle and anterior cruciate ligament injuries in female athletes. *Am J Sport Med.* 1998;26:614–619.
106. Wright RW, Dunn WR, Amendola A, Andrish JT, Bergfeld J, Kaeding CC, Marx RG, McCarty EC, Parker RD, Wolcott M, Wolf BR, Spindler KP. Risk of tearing the intact anterior cruciate ligament in the contralateral knee and rupturing the anterior cruciate ligament graft during the first 2 years after anterior cruciate ligament reconstruction: a prospective MOON cohort study. *Am J Sports Med.* 2007;35:1131–1134.
107. Zazulak BT, Hewett TE, Reeves NP, Goldberg B, Cholewicki J. The effects of core proprioception on knee injury: a prospective biomechanical-epidemiological study. *Am J Sports Med.* 2007; 35:368–373.
108. Zazulak BT, Paterno M, Myer GD, Romani WA, Hewett TE. The effects of the menstrual cycle on anterior knee laxity: a systematic review. *Sports Med.* 2006;36:847–862.
109. Zazulak BT, Ponce PL, Straub SJ, Medvecky MJ, Avedisian L, Hewett TE. Gender comparison of hip muscle activity during single-leg landing. *J Orthop Sports Phys Ther.* 2005;35:292–299.