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Executing a Collaborative Prospective Risk-Factor Study: Findings, Successes, and Challenges

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Moderate evidence[1] demonstrates that injury-prevention training programs can substantially reduce the risk of anterior cruciate ligament (ACL) injury in athletes. Yet the current literature[2–4] contains both positive and negative results for ACL injury prevention. Researchers must identify the prospective risk factors for noncontact/indirect-contact ACL injury to ultimately improve the effectiveness of existing ACL injury-prevention programs.

PROSPECTIVE RISK FACTORS VERSUS MECHANISMS OF INJURY

A critical distinction needs to be made when describing prospective risk factors for ACL injury. This involves differentiating between ACL injury mechanisms and prospective risk factors. An ACL injury *mechanism* can be defined as the combinations of joint forces, moments, and movements that cause failure of the ACL and occur at the time of injury. However, ACL injury *prospective risk factors* are variables that are useful for screening purposes. Also, prospective risk factors for ACL injury are not necessarily the same as mechanisms of ACL injury or loading. Prospective risk factors are variables that can be identified years before an ACL injury mechanism is experienced. Therefore, prospective risk factors for ACL injury can be defined as those variables (eg, signature movement patterns, age, sex, injury history) that identify individuals who will later experience an ACL injury mechanism.

Risk factors and injury mechanisms are related in 2 ways. First, risk factors may work in a synergistic manner to raise the probability that a certain individual is exposed to high-risk biomechanical forces that create injury mechanisms. For example, knee laxity and poor neuromuscular control of the hamstrings muscles are independent risk factors that might interact to increase the probability of an injury mechanism occurring. Second, risk factors might be ''proxies'' or ''markers'' for unknown factors that predispose an individual to injury mechanisms; for example, sex may be a proxy for poor neuromuscular control in high school-aged athletes.

Improving our understanding of mechanisms for ACL injury has been accomplished through cadaver-based and computer-simulation research. Cadaver-based research has provided insight into how internal and external loads at the knee may facilitate stress and strain on the ACL.[5–7] Recently, computer simulations of ACL loading mechanisms have enhanced our understanding of the loading combination most likely to facilitate an ACL injury mechanism.[8–13] Even though cadaver-based and computer-simulation–based research has greatly improved our understanding of ACL injury mechanisms, this research does not identify prospective risk factors. Thus, we still have a very limited understanding of prospective risk factors for ACL injury because injury mechanisms and prospective risk factors, although related, are not identical.

The prospective cohort design is considered the strongest method for identifying prospective risk factors for ACL injury.[14] This design requires testing of participants before they experience an ACL injury mechanism, which allows for a preinjury profile of each participant to be established. Only 2 prospective cohort studies[15,16] have been performed to investigate biomechanical and neuromuscular characteristics related to ACL injury. Hewett et al[15] demonstrated that increased external knee abduction (valgus) moment during a drop-landing task was a prospective risk factor for ACL injury. The sensitivity and specificity of increased external knee-abduction moment were 78% and 67%, respectively. Zazulak et al[16] showed that increased trunk motion after a sudden force release was also a prospective risk factor for sustaining an ACL injury mechanism. The associated sensitivity and specificity for increased trunk motion after a sudden force release were 83% and 76%, respectively. These studies provide significant insight into prospective risk factors for ACL injury involving biomechanical and neuromuscular characteristics; however, a major limitation is the small number of injury events reported in both studies. Hewett et al[15] observed a total of 9 ACL injuries, whereas Zazulak et al[16] observed only 6 ACL injuries. Thus, more prospective cohort studies investigating biomechanical and neuromuscular characteristics associated with ACL injury are critically needed.

Overall, the occurrence of noncontact/indirect-contact ACL injuries is relatively rare. In the general population, the rates of these injuries are 0.52 and 0.62 per 100 000 athlete-hours in females and males, respectively.[17] The incidence of ACL injuries is greater when considering specific populations. For example, the incidence of ACL injuries in female youth soccer players is 1 per 1000 athlete-hours.[17] However, even in young, physically active populations, a large number of participants (approximately 5000) would be required to record enough ACL injury events to effectively identify prospective risk factors. Collaborative multisite studies are needed to efficiently test a sample size of this magnitude in a reasonable time period.

IDENTIFYING PROSPECTIVE RISK FACTORS FOR NONCONTACT/INDIRECT-CONTACT ACL INJURY

The Joint Undertaking to Monitor and Prevent ACL Injury (JUMP-ACL) is a multisite prospective cohort study investigating biomechanical and neuromuscular risk factors for noncontact/indirect-contact ACL injuries. Approximately 5500 volunteers were tested between 2005 and 2008. For the JUMP-ACL study, we have developed testing methods to effectively collect valid and reliable biomechanical and neuromuscular data involving 3-dimensional motion analysis, strength, and postural alignment in a large number of participants across multiple testing sites. We propose 5 key steps to consider for successful data collection in this type of study:

1) Develop an Interdisciplinary Team

It is critical to develop an interdisciplinary research team that has expertise and experience in all areas important to your study. For the JUMP-ACL study, we included experts in the areas of epidemiology, public health, biostatistics, biomechanics, motor control, sports medicine, and orthopaedics. Each team member should provide insight into prioritizing the risk factors to study and refine your testing procedures. In multisite studies, it is vital to have members of your research team on-site at the testing location. These individuals play an important role in the study's day-to-day operations and serve as the ''public face'' of the study team during those time periods when data are not being actively collected on-site. The administrative burden of large, prospective, multisite studies is significant; thus, identifying someone to serve as the project manager or study coordinator is necessary for success. This person should have sufficient experience with large-scale studies performed across multiple sites. The final consideration for developing an interdisciplinary team is to identify research assistants who will invest in the study and consistently work as part of the study team throughout the study's duration. Retaining these key personnel will allow for consistency in data-collection procedures and a well-established chain of command.

2) Have a Clear (but Flexible) Plan

Before beginning data collection, each research team member should have a designated set of responsibilities. These responsibilities should include key tasks to be completed before, during, and after data collection on a daily basis. It is important to not only focus on those duties related to data collection but also to develop responsibilities related to administrative tasks associated with the study. These responsibilities and testing procedures should then be reviewed and confirmed with the on-site research team members to ensure that all parties understand and agree to the study procedures.

A unique aspect of multisite studies is that the plan for data collection will likely differ at each testing site. Each site has its own set of unique competing demands that the research team must consider. Thus, the research team must develop a site-specific set of testing procedures and responsibilities, which is best accomplished by conducting pilot testing at each site before full-scale data collection begins. This will enable the research team to identify the site-specific constraints at each testing site and to develop the most robust plan to ensure success.

3) Provide Extensive Training and Preliminary Testing

A detailed manual of operating procedures (MOOP) should be developed before preliminary testing and data collection. The MOOP should provide a step-by-step process of calibrating, testing, and troubleshooting for each of the testing procedures involved with the study. After developing the MOOP, the entire research team should attend a mandatory training session at which all information within the MOOP is reviewed. Preliminary testing should then be performed to ensure that all research team members are precisely following the testing procedures as outlined within the MOOP. As part of the preliminary testing schedule, the research team should develop methods to assess intertester reliability, both during preliminary testing and during actual data collection.

4) Establish Quality-Control Measures

The research team should put in place a series of quality-control measures cueing research assistants to review the data being collected to ensure validity and reliability. First, the research assistant performing data collection at each testing site should be identified on the data-collection form. This helps to ensure that the research assistant takes responsibility for the data he or she is collecting and allows the research team to identify the possibility of tester bias within the data. Second, a range of expected values for each variable should be listed on the data-collection form the research assistant uses to record the testing values. This permits the research assistant to compare the recorded data with preestablished normal ranges and to help ensure data quality. Third, the maximum allowable range between successive trials should also be listed on the data-collection form. This will allow the research assistant to ensure that participants are providing consistent data across trials. Our allowable range values between trials were established by determining the SDs for each measurement based on our preliminary data (approximately 1000 participants). We then set allowable range values across trials to be equal to the 1-SD value for each measurement. Fourth, create blank space on your data-collection form to allow the research assistant space for taking notes. Unexpected circumstances often arise when collecting data from a large number of volunteers; thus, providing blank space for field notes will allow the research team to later identify these cases. An on-site notebook for data-collection notes is also essential. Last, if large numbers of participants are to be tested, create a data-collection form that can be later scanned into a data spreadsheet, using software such as TeleForms (Teleforms Inc, Winnipeg, MB, Canada). This will help to eliminate expensive data-entry errors and minimize data-entry costs over the long term.

5) Develop Clear and Consistent Injury Definitions

The ultimate goal of a prospective cohort study is to identify individuals who go on to experience injury. Thus, the research team must establish clear operational defini-

tions for the injury and injury event. For the JUMP-ACL study, an *ACL injury* was defined as a tear or rupture of the ACL that was verified (1) during surgery or (2) by magnetic resonance imaging and clinical examination (in those cases where nonsurgical intervention was selected). Also, it is critical to collect full details of the injury event because the prospective risk factors for ACL injuries involving direct contact to the knee may be quite different than for ACL injuries that do not involve direct contact. For the JUMP-ACL study, the primary endpoint was a *noncontact/indirect-contact ACL injury*, defined as involving a cognitive or physical perturbation but not involving direct impact to the knee. An indirect contact event, in which the injured athlete was pushed or knocked off balance by an opponent but without forceful direct contact to the knee, is an example of a physical perturbation.

After developing clear definitions for injuries and injury events, it is important to ensure that these definitions are consistently applied over the course of the study. Multiple checks should be in place to ensure all injury cases are recorded. For example, injury cases can be captured by reports from the orthopaedic surgeon along with review of medical records. A respondent questionnaire should also be completed by all individuals who experience an ACL injury. This will allow the research team to review the injury events as described by the patient and better determine whether the mechanism of injury was direct contact or noncontact/indirect contact. In the JUMP-ACL study, we were able to use the Defense Medical Epidemiology Database (DMED) as an additional source to help identify injuries. Finally, a single person should be responsible for medical-record abstraction and verifying all injury cases and events. This will allow for consistency across multiple sites.

ROLE OF PROSPECTIVE RISK FACTORS AND INJURY MECHANISMS IN ACL INJURY PREVENTION

Following these 5 steps will help to facilitate successful data collection during a prospective cohort study across multiple sites. As previously stated, continued research in this area is needed to identify modifiable prospective risk factors for ACL injury. Both identifying prospective risk factors and understanding the mechanisms of ACL injury are necessary to develop effective ACL injury-prevention programs. Because prospective risk factors and mechanisms for ACL injury are related but are not identical, we must have a strong understanding of both. Successful ACL injury-prevention programs will likely need to address both the prospective risk factors and the mechanisms associated with ACL injury.

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REFERENCES

1. Padua DA, Marshall SW. Evidence supporting ACL-injury-prevention exercise programs: a review of the literature. *Athl Ther Today*. 2006;11(2):11–23.
2. Mandelbaum BR, Silvers HJ, Wantanabe DS, et al. Effectiveness of a neuromuscular and proprioception training program in preventing anterior cruciate ligament injuries in female athletes: a 2-year follow-up. *Am J Sports Med*. 2005;33(7):1003–1110.
3. Steffen K, Myklebust G, Olsen OE, Holme I, Bahr R. Preventing injuries in female youth football—a cluster-randomized controlled trial. *Scan J Med Sci Sports*. 2008;18(5):605–614.
4. 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(8):1769–1774.
5. Shimokochi Y, Shultz SJ. Mechanisms of noncontact anterior cruciate ligament injury. *J Athl Train*. 2008;43(4):396–408.
6. Fung DT, Hendrix RW, Koh JL, Zhang LQ. ACL impingement prediction based on MRI scans of individual knees. *Clin Orthop Relat Res*. 2007;460:210–218.
7. Markolf KL, Burchfield DM, Shapiro MM, Shepard MF, Finerman GA, Slauterbeck JL. Combined knee loading states that generate high anterior cruciate ligament forces. *J Orthop Res*. 1995;13(6):930–935.
8. Lin CF, Gross M, Ji C, et al. A stochastic biomechanical model for risk and risk factors of non-contact anterior cruciate ligament injuries. *J Biomech*. 2009;42(4):418–423.
9. Shin CS, Chaudhari AM, Andriacchi TP. The influence of deceleration forces on ACL strain during single-leg landing: a simulation study. *J Biomech*. 2007;40(5):1145–1152.
10. Shin CS, Chaudhari AM, Andriacchi TP. The effect of isolated valgus moments on ACL strain during single-leg landing: a simulation study. *J Biomech*. 2009;42(3):280–285.
11. McLean SG, Huang X, Su A, van den Bogert AJ. Sagittal plane biomechanics cannot injure the ACL during sidestep cutting. *Clin Biomech (Bristol, Avon)*. 2004;19(8):828–838.
12. McLean SG, Huang X, van den Bogert AJ. Investigating isolated neuromuscular control contributions to non-contact anterior cruciate ligament injury risk via computer simulation methods. *Clin Biomech (Bristol, Avon)*. 2008;23(7):926–936.
13. Pflum MA, Shelburne KB, Torry MR, Decker MJ, Pandy MG. Model prediction of anterior cruciate ligament force during drop-landings. *Med Sci Sports Exerc*. 2004;36(11):1949–1958.
14. Walter SD, Hart LE. Application of epidemiological methodology to sports and exercise science research. *Exerc Sport Sci Rev*. 1990;18:417–448.
15. Hewett TE, Myer GD, Ford KR, et al. 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(4):492–501.
16. Zazulak BT, Hewett TE, Reeves NP, Goldberg B, Cholewicki J. Deficits in neuromuscular control of the trunk predict knee injury risk: a prospective biomechanical-epidemiologic study. *Am J Sports Med*. 2007;35(7):1123–1130.
17. Marshall SW, Padua DA, McGrath M. Incidence of ACL injury. In: Hewett TE, Griffin LY, Shultz SJ, eds. *Understanding and Preventing Non-Contact ACL Injury*. Champaign, IL: Human Kinetics; 2007:5–29.

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