Selection Criteria for Patients With Chronic Ankle Instability in Controlled Research: A Position Statement of the International Ankle Consortium

Epidemiology and Impact of Ankle Injury
Injuries to the ankle joint account for 20% of the population afflicted with joint injury.46 There are more than 3 million emergency room visits annually for ankle/foot injuries in the United States, and the largest percentage of self-reported musculoskeletal injuries (greater than 10%) are to the ankle.1 Each year, more than 628,000 ankle injuries, including ankle sprains and fractures, are treated in US emergency rooms, accounting for 20% of all injuries treated in emergency facilities.46 Ankle sprains account for an estimated 3% to 5% of emergency room visits in the United Kingdom, representing a significant amount of devoted healthcare resources. Additionally, it is estimated that as many as 55% of patients who sustain an ankle sprain do not seek evaluation or treatment from a healthcare professional.22 Subsequently, traumatic ankle sprains may be grossly underreported in healthcare statistics.

Short- and Long-Term Sequelae
Traumatic ankle injury represents a significant healthcare issue. Of further significance is the high rate of recurrence (as high as 80% in high-risk sports) of ankle sprains.44,49 Recent data indicate that ankle sprains are not just an innocuous injury primarily incurred by young athletes but also impact approximately 8% of the general population who report persistent symptoms following an initial ankle sprain.23 Chronic joint injury and degeneration are associated with over $3 billion in annual healthcare costs in the United States.9 Evidence for the relationship between acute and recurrent ankle joint trauma and the development of posttraumatic ankle joint osteoarthritis (OA) is growing.8,18 Saltzman et al36 reported that as many as 4 in 5 cases of ankle joint OA are the result of previous musculoskeletal trauma, with these patients being on average a decade younger than patients with primary ankle joint OA. Additionally, self-reported disability scores, assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey physical component summary score, were significantly lower in patients with ankle OA from the United States35 compared with the general population, and was also equal to or lower compared to those in patients with end-stage kidney disease,39 chronic heart failure,42 and Parkinson’s disease.30 Therefore, ankle joint sprains and their associated sequelae affect individuals across their lifespan and represent a large healthcare burden.

Advances in Research
The prevalence and impact of ankle sprains on society and healthcare systems support the need for continued research related to the prevention, treatment, and rehabilitation of ankle sprains and their associated sequelae. As mentioned above, an unfortunate and prominent consequence of acute ankle sprains is a very high recurrence rate. It has been reported that 32% to 74% of individuals with a previous history of ankle sprain have some type of residual and chronic symptoms, recurrent ankle sprains, and perceived instability.3,25 Evidence from peer-reviewed literature suggests that the characteristics of patients with recurrent ankle injury are not homogeneous. Many categorical descriptions have been used to define this pathology, including chronic ankle instability (CAI), functional ankle instability, mechanical ankle instability, and recurrent ankle instability.15,20,21 CAI
has been defined in a variety of ways, but is most predominantly described “as an encompassing term used to classify a subject with both mechanical and functional instability of the ankle joint.”15

INTERNATIONAL ANKLE CONSORTIUM POSITION STATEMENT

The International Ankle Consortium is an international community of researchers and clinicians whose primary scholastic purpose is to promote scholarship and dissemination of research-informed knowledge related to pathologies of the ankle complex. The constituents of the International Ankle Consortium and other similar organizations have yet to properly define the clinical phenomenon known as CAI and its related characteristics for consistent patient recruitment and advancement of research in this area. Although research on CAI and awareness of its impact on society and healthcare systems have grown substantially in the last 2 decades, the inconsistency in participant/patient selection criteria across studies presents a potential obstacle to addressing the problem properly. This major gap within the literature limits the ability to generalize this evidence to the target patient population. Therefore, there is a need to provide standards for patient/participant selection criteria in research focused on CAI, with justifications using the best available evidence. The primary rationale for documenting such standards is to outline specific inclusion criteria that should be reported on as a minimum when conducting research in the area of CAI. This will be of particular importance as research into CAI continues to grow and become more sophisticated, especially to enable high-fidelity synthesis and meta-analyses of data through future systematic reviews.

While CAI is a multifaceted condition, there have been research developments to capture functional deficits associated with those who have recurrent issues. Freeman16 was among the first to recognize measurable differences in clinical outcomes in patients who had a history of ankle joint injury. Recognition of prolonged deficits in single-limb balance after ankle ligament sprains led to a theory of changes in neural signaling following trauma to the ankle joint, and to the categorization of these patients as having functional ankle instability. Several decades later, Hertel19 presented a model that recognized the contributions from functional and mechanical insufficiencies associated with an acute ankle sprain that may interact to precipitate the development of CAI. The development of this model was a seminal step in facilitating an understanding of why many patients incur repeated ankle joint dysfunction. The use of the term CAI, according to the Hertel19 model, represented the initial attempt to define and provide potential contributions from functional and mechanical insufficiencies, which helped in the development of a more comprehensive approach to researching and treating individuals with this pathology.

Research related to ankle joint instability evolved over the decade following the publication of the Hertel CAI model,20 with the primary aim of much of the research devoted to understanding exactly which combinations of functional and mechanical insufficiencies best define CAI. Many recent reviews and multifactorial studies have provided important information out-
lining the multiple potential contributing mechanical, neuromuscular, functional, and/or perceived deficits that may persist long after physiological tissue healing times have elapsed and interventions have been completed following an acute ankle joint sprain. Consistently, these reviews and multifactorial studies support the proposition that CAI is a multifaceted and complex condition, requiring further in-depth interdisciplinary study.

While the volume and quality of this research grew substantially, it became more evident that individuals with CAI were quite heterogeneous in their presentation of impairments, leading the research toward consideration of a possible conglomeration of subgroups. Recently, Hiller et al.22 introduced an update of Hertel’s CAI model20 that suggests there may be as many as 7 different subsets of patients who incur persistent symptoms following an initial ankle joint sprain, which are dependent on the complex interaction of mechanical insufficiencies, perceived instability, and frequency of recurrent sprains.

Rationale

Examining the body of work related to repeated and recurrent ankle joint injury and instability, one finds a spectrum of patient characteristics that have been used within the ankle instability (including CAI and functional ankle instability) research literature from the last 2 decades.15,23 Delahunt et al.23 systematically investigated these issues in the research relating to recurrent ankle joint sprain and the resulting inconsistent definitions and use of terms such as CAI, functional ankle instability, etc. They concluded that CAI was the most commonly used term to describe individuals who report ongoing symptoms after an initial ankle sprain, and the most commonly reported deficits associated with CAI were frequent/recurrent sprains and episodes of, or the reporting of, feelings of ankle joint “giving way.” Subsequently, the authors advocated that research in this area could be improved if consistent terminology and a specific set of patient selection criteria could be established.

Statement Objectives

It is the opinion of the International Ankle Consortium that some of the inconsistency in defining the factors and characteristics that best explain recurrent ankle sprains and instability may be attributed to inconsistent inclusion criteria among this literature. The International Ankle Consortium proposes the establishment of an accepted set of selection criteria that should be used in this area of research, as it will provide consistency to the future data synthesis devoted to improving the understanding of CAI and enhance external validity of findings for this patient population. The purpose of this position statement is to present and discuss an endorsed set of selection criteria for patients with CAI, based on the best available evidence, to be used in future research and study designs. Our group wishes to advocate for the pursuit of the strongest and most appropriate evidence that will improve the understanding and management of CAI.

CRITERIA RECOMMENDATIONS

Standard inclusion and exclusion criteria endorsed by the International Ankle Consortium, as a minimum, for enrolling patients who fall within the heterogeneous condition of CAI in controlled research are listed in TABLES 1 and 2. Additionally, the International Ankle Consortium encourages the reporting of critical information found in TABLE 3 for patients with CAI to provide a comprehensive description of the study participants who have been enrolled in controlled research studies.

DISCUSSION

The preceding endorsed criteria for selection of individuals with CAI in research are based on the best available evidence, and the International Ankle Consortium recommends adherence to produce consistent population characteristics for improved outcomes and external validity in future research of this clinical phenomenon. These recommendations will enhance the validity of research conducted in this clinical population, with the end goal of bringing the research evidence to the clinician and patient. Additional rationale for the
The International Ankle Consortium acknowledges the work of Delahunt et al, which provided the framework for this position statement, and recommends consultation of and familiarization with that work by all researchers with an interest in CAI. The aims of the systematic investigation by Delahunt and colleagues were (1) to identify the definition of ankle instability used by authors publishing research papers pertaining to ankle joint sprain and its subsequent sequelae, (2) to identify the terminology utilized by authors to classify subjects who report ongoing symptoms after an initial ankle sprain, and (3) to identify the specific inclusion criteria used by authors publishing research papers pertaining to ankle joint sprain and subsequent sequelae. This was the first published paper to systematically investigate the aforementioned issues that may lead to inconsistencies in research results relating to ankle joint sprain and its subsequent sequelae. The results of this systematic investigation indicated that CAI was the most commonly used term to describe subjects who report ongoing symptoms after an initial ankle sprain. Furthermore, the most commonly used descriptors relating to CAI were frequent/recurrent sprains and episodes of, or the reporting of, feelings of ankle joint giving way. Based on their findings, Delahunt et al recommended that consistent terminology and a specific minimum set of criteria be reported, as this would improve research endeavors pertaining to CAI. As such, Delahunt et al devised a set of operational definitions related to ankle joint sprain and its subsequent sequelae, as well as a specific set of criteria that should be reported when undertaking research on individuals with CAI. These definitions and the criteria set formed the basis of discussion at the International Ankle Symposium, from which the International Ankle Consortium formed a consensus statement relating to operational definitions pertaining to ankle joint sprain and its subsequent sequelae and a minimum set of criteria to be reported when conducting CAI research.

At the Fifth International Ankle Symposium (Lexington, KY, 2012), the International Ankle Consortium executive committee discussed the concepts of this position paper based on the existing work and the new information being presented at the meeting. Consistent with the work by Delahunt et al, new papers presented at the International Ankle Symposium emphasized the strength of reported episodes of giving way and patient-reported instability in defining CAI. Snyder et al, using the Delphi method to gather input from expert clinicians and researchers, reported that “recurrent sense of giving way” was the strongest characteristic in defining CAI. However, there are other characteristics, such as feelings of instability and recovery from a “rolling-over” incident, that are important in both identifying who has CAI and establishing the severity of the condition that are not obtained through the reporting of giving way alone. A series of papers support the use of condition-specific self-report questionnaires to identify those with the minimal accepted criteria for ankle instability. It is critical to utilize condition-specific questionnaires that are both valid and reliable in the collection of this information. This recent work highlights the increasing evidence for the selected criteria we introduce in this position paper.

Additionally, measurement of self-reported instability should be differentiated from measurement of resulting change to physical function or quality of life. Changes to physical function may be a result of insufficiencies, self-reported instability, and recurrent sprains. Therefore, if investigators are interested in the deficits present in participants with CAI, such as strength, neuromuscular, or proprioception deficits, measures of self-reported function may not be a necessary inclusion criterion for this type of study. However, if functional impairment is relevant to the proposed project or intervention, then validated ankle-specific
questionnaires designed to evaluate self-reported function should be used to create the necessary inclusion criteria.\textsuperscript{15,27}

Our recommended inclusion criteria are based on assessments of injury history, function, and disability, but we recognize the lack of definitive selection criteria based on an assessment of joint integrity or laxity. Although an initial ankle sprain often threatens the integrity of ligamentous structures and some authors have reported lingering ankle laxity, hypomobility, and hypermobility, these outcomes do not appear to be observed consistently in patients with CAI. Previous authors have considered mechanical instability as an explanatory factor for lingering ankle instability, but there has not been a definitive association of ankle laxity with CAI.\textsuperscript{6,8,15,20,21,24,28,29,47}

Hertel’s\textsuperscript{20} original model differentiated mechanical instability from functional instability. More recently, Hiller et al.,\textsuperscript{23} refining the model of categorizing CAI, suggested as many as 7 subgroups of individuals with CAI that would likely provide better homogeneity in describing the pathology. Of the 3 primary separation factors, the authors suggested that mechanical instability provided the weakest contribution. Additionally, hypomobility, rather than joint laxity, contributed more to the subgroup model creation. It appears that in some patients mechanical instability may be a factor that leads to recurrent ankle injury and measures of perceived ankle instability, but these are not necessarily dependent on the presence of ankle hypermobility. Data from other multifactorial studies that have included measures of mechanical instability in patients with CAI suggest that mechanical instability alone may not be a consistent identifier of this pathology.\textsuperscript{28,47}

A recent advancement in the CAI literature has been the stratification of individuals, based on structural and functional impairments associated with ankle instability. Multiple studies by Brown et al\textsuperscript{28} compared sensorimotor and biomechanical measures between patients classified as having mechanical ankle instability, functional ankle instability, and no measurable ankle instability or repeated injury (copers). Although the presence of mechanical laxity was associated with some proximal joint sensorimotor alterations and increases in ground reaction forces during landing tasks compared with the other groups, these differences were not observed consistently. It is also interesting to note that the mechanical ankle instability groups had more self-reported disability and no differences in the number of episodes of giving way compared with the functional ankle instability groups, suggesting that the mechanical ankle instability groups had similar, if not more, functional instability than the functional ankle instability groups did. The design of these studies to separate mechanical ankle instability and functional ankle instability represents the comparisons required to glean the factors that best define CAI. The information would seem to lend support to the strength of the contribution of functional instability measures, rather than mechanical instability, to defining CAI.

\textbf{Future Considerations}

We have provided recommendations for selection of patients with CAI to improve the quality of research on this pathology. The healthcare burden associated with ankle instability necessitates increased research and clinical outcomes that can be used to reduce the disability and recurrence rates associated with CAI. It is clear from the body of literature that there are many contributing factors to CAI that can create a host of impairments\textsuperscript{15,20,21,24,29,39,47}; however, this condition is more heterogeneous than many realize.\textsuperscript{15,23} Therefore, researchers need to be cognizant of criteria that are best associated with CAI based on current available evidence. Based on the collective expertise of the International Ankle Consortium, we feel that the specified selection criteria should be incorporated in all future research on CAI.

The selection criteria are based on history of initial injury, history of ongoing bouts of instability, and ratings of patient-perceived function and disability gathered from validated survey instruments. In addition, to study CAI in patients, concomitant issues such as fracture and surgery and other significant lower extremity joint injury should be absent, and an appropriate amount of time should have passed since suffering acute, inflammatory symptoms, all for the purpose of eliminating confounding influence on the outcomes that researchers choose to employ.

We have provided our list of additional patient information that we feel should be reported and look forward to evaluating and utilizing the evidence that continues to grow from this work to modify our recommendations moving forward. In the future, consistency among these suggested reported measures will only help to strengthen the description and understanding of CAI. In the meantime, researchers should strive to report as many of these data to create clearer descriptions of CAI, which may lead to the enrollment of more homogeneous subgroups in studies. The rationale for this is to improve the understanding of the consequences of repetitive ankle injury and lingering instability, leading to development of more effective interventions to decrease the acute and chronic ankle injury rates in physically active populations.

\textbf{Statement and Background of Creation of the Position Statement}

The International Ankle Consortium, formed in 2004, is an international community of researchers and clinicians whose primary scholastic purpose is to promote scholarship and dissemination of research-informed knowledge related to pathologies of the ankle complex. We are a collegial network that strives to support the ongoing growth of scientific and clinical evidence to elucidate the mechanisms, characteristics, and interventions related to ankle complex/joint pathologies. The International Ankle Symposium is the primary venue by which the International Ankle Consortium dis-
semianates the work of its constituents in an effort to present and discuss the most contemporary theories and research related to ankle joint clinical phenomena and related interventions, with a primary focus on CAI.

Another focus of the International Ankle Consortium is to provide endorsement for standards of clinical research related to ankle joint pathologies. The International Ankle Consortium endorses the summary statements from past International Ankle Symposia that have presented the major findings and updates from the content of the meetings. Additionally, the International Ankle Consortium establishes position statements, such as this one, to endorse consistent standards for research and clinical management of ankle joint conditions in the physically active. This position statement provides background and discusses the existing evidence to support a set of specific selection criteria for patients with chronic/functional ankle instability, with the goal to improve the quality of research and outcomes related to this specific ankle condition.

REFERENCES

33. Munn J, Sullivan SJ, Schneiders AG. Evidence of
43. Snyder K, Evans T, Neibert P, Weiss W, Haak T. Development of an ankle instability model. Fifth International Ankle Symposium; October 17-20, 2012; Lexington, KY.