Biomechanical risk factors for ACL injury

Development of analysis methods specific to injury mechanism

Haraldur B. Sigurðsson

Thesis for the degree of
Philosophiae Doctor

Supervisor:
Prof. Kristín Briem

Advisor:

Prof. Kristín Briem

Doctoral committee:
Prof. Þórarinn Sveinsson – Prof. Lynn Snyder-Mackler – Prof. Jón Karlsson – Associate Prof. Árni Árnason

December, 2019

UNIVERSITY OF ICELAND
SCHOOL OF HEALTH SCIENCES

FACULTY OF MEDICINE

Lífaflfræðilegir áhættuþættir krossbandaslita

Þróun sértækrar nálgunar á úrvinnslu gagna

Haraldur Björn Sigurðsson

Ritgerð til doktorsgráðu

Umsjónarkennari:
Kristín Briem, Prófessor

Leiðbeinandi:
Kristín Briem, Prófessor

Doktorsnefnd:
Þórarinn Sveinsson, Prófessor
Lynn Snyder-Mackler, Prófessor
Jón Karlsson, Prófessor
Árni Árnason, Dósent

Desember, 2019

UNIVERSITY OF ICELAND
SCHOOL OF HEALTH SCIENCES
FACULTY OF MEDICINE

ISBN 978—9935-9516-0-1

Printing by Háskólaprent.

Reykjavik, Iceland 2019

Ágrip

Markmið: Markmið doktorsverkefnis var að þróa og meta aðferðir til að vinna úr gögnum sértækt fyrir slit á fremra krossbandi. Markmið vísindagreinar I var að meta mun á tímasetningum krafta sem verka á fremra krossband, milli drengja og stúlkna. Markmið vísindagreinar II var að kanna hagkvæmni þess að nota aðferð til klasagreiningar sem þróuð var fyrir verkefnið til að flokka bylgjuform kiðvægis í hné. Markmið vísindagreinar III var að kanna tengsl milli bylgjulögunar með snemmbúinn tind, og hreyfinga sem sem eiga sér stað fyrir eða við slit á fremra krossbandi.

Aðferðir: Allar vísindagreinarnar nota gögn úr hreyfigreiningu þátttakenda sem fengnir voru úr handbolta- og fótboltafélögum á höfuðborgarsvæði og framkvæmdar ýmist við 9-12 ára (fyrsti fasi) og/eða 14-18 ára (seinni fasi) aldur. Viðföng framkvæmdu við hvort tilefnið 5 endurtekningar á hvorum fæti af gabbhreyfingu, fyrir og eftir æfingarinngrip. Endurskinsmerki voru notuð til að fylgja hreyfingum líkamshluta, kraftplötur mældu gagnkraft jarðar, og hreyfingar og kraftvægi um liðamót voru síðan reiknuð út. Fyrir vísindagrein I voru gögn endurskinsmerkja síuð með lágpassasíu með 6 Hz tíðnimörk, en kraftplötugögn síuð með lágpassasíu með 20 Hz tíðnimörk. Fyrir vísindagrein II og III voru hrágögn notuð til að reikna liðhreyfingar og kraftvægi, sem voru því næst síuð með 6 Hz lágpassasíu.

Tilgátuprófanir voru gerðar með marktektarmörk sett á 0,05. Vísindagrein III notaði Bonferroni leiðréttingu fyrir endurtekna samanburði. Vísindagrein I notaði blandaða línulega aðhvarfsgreiningu fyrir endurteknar mælingar. Vísindagreinar II og III notuðu tveggja þrepa klasagreiningu þar sem gögnum var fyrst umbreytt í formerki diffraðs merkis og myndaðir klasar með Ward.d2 aðferð byggðri á fjarlægðum Euclids. Þeir klasar sem mynduðust voru aftur klasagreindir með upprunalega merki innan hvers klasa og myndaðir undirklasar sem aðskildir voru á magni kraftvægis, einnig með Ward.d2 aðferð og fjarlægðum Euclids.

Í vísindagrein III voru gögn fyrir hreyfingar sem rannsóknir hafa sýnt að eigi sér stað við áverka á fremra krossbandi dregin út. Hvort fyrsta snerting við jörð var með hæl eða ekki var tvíþátta breyta, en fyrir samfelldar breytur voru reiknuð ROC gröf og hágildi stuðuls Youden notaður til að velja þröskuld sem breytur voru flokkaðar eftir sem tvíþátta í tilgátuprófanir. Vísindagreinar II og III prófuðu tilgátur varðandi tíðnidreifingu á snemmbúnum toppum eftir kyni og aldri (vísindagrein II, próf McNemar) eða liðferlum (vísindagrein III, próf Fisher).

Niðurstöður: Í vísindagrein I var munur eftir kyni, en stúlkur höfðu seinni tind í kiðvægi en strákar (P < 0,001) sem skilaði sér í minni meðaltíma milli tinda kiðvægis og innsnúningsvægis (0 ms hjá stúlkum, 5 ms hjá drengjum, P < 0,001), og milli kiðvægis og lóðrétts gagnkrafts jarðar (1 ms hjá stúlkum, 5 ms hjá drengjum, P < 0,001).

Í vísindagrein II var mögulegt að flokka bylgjugerð kiðvægis í sex flokka; snemmbúna tinda, snemmbúna dali, tinda, dali, brekku upp, og brekku niður. Það var tíðnimunur eftir kyni (P < 0,001) þar sem drengir í fasa I höfðu tíðari snemmabúna tinda (575 sáust, von á 464) heldur en stúlkur (642 sáust, von á 768). Í fasa II höfðu stúlkur tíðari snemmbúna toppa (178 sáust, von á 129) heldur en drengir (78 sáust, von á 112).

Í vísindagrein III fundust tengsl milli snemmbúna tinda kiðvægis og fyrstu snertingu við jörð með hæl (Áhættuhlutfall (ÁH) 1,5; P = 0,01), fjarlægðar milli þungamiðju bols og fótar í breiðskurði (ÁH 3,7; P < 0,01), hné beygju eftir lending (ÁH 1,9; P < 0,01), hné beygju við fyrstu snertingu (ÁH 2,2; P < 0,01), og fráfærslu í hné eftir lending (ÁH 2,2; P < 0,01).

Ályktanir: Tímasetning krafttinda í upphafi stöðufasa er mismunandi milli drengja og stúlkna í þá átt sem við er búist (minni tími milli tinda hjá stúlkum), en ekki er mögulegt að staðsetja tind í öllum mælingum og því gefa gögnin ekki rétta mynd af atburðarrás snemma í stöðufasa. Klasagreining bylgjulögunar leiddi af sér flokkun á kiðvægi við upphaf stöðufasa, og amk einum flokki (snemmbúnum tindum) ber saman við það ferli sem veldur áverkum á fremra krossbandi. Snemmbúnir tindar eru tíðari hjá táningsstúlkum, og hafa tengsl við þær hreyfingar sem sést hafa við greiningu á áverkum á fremra krossband. Flokkanir úr klasagreiningu ættu að vera sannreyndar á tíðni krossbandaslita. Niðurstöðurnar styðja notkun inngripa sem hvetja íþróttamenn til að lenda á tábergi í stað hæls með fótinn nálægt bol og meiri beygju í hné til að koma í veg fyrir snemmbúna tinda kiðvægis.

Lykilorð:

Fremra krossband, forvarnir gegn meiðslum, klasagreining, lífaflfræði, hreyfigreining

Abstract

Aims: The aim of the doctoral project was to develop and assess data extraction and analysis methods specific to the anterior cruciate ligament injury mechanism. The aim of paper I was to evaluate differences in the timing of the peak knee valgus moment in the first 100 ms of a cutting maneuver between boys and girls. The aim of paper II was to explore the feasibility of using a cluster analysis protocol developed for this project to categorize the waveforms of the early stance phase knee valgus moment. The aim of paper III was to test associations between kinematics observed during anterior cruciate ligament injury, and the early peak knee valgus moment waveform extracted with the cluster analysis protocol.

Methods: All papers used motion analysis data of subjects recruited from local handball and soccer clubs tested at 9-12 years old (phase I) and/or 14-18 years old (phase II). Subjects performed 5 cutting maneuvers on each leg, before and after an exercise intervention at each visit (phase I and phase II). Reflective markers and force plates were used to calculate kinematic and kinetic data. For paper I, marker trajectories were low pass filtered at 6 Hz and force plate data at 20 Hz. For papers II & III, raw marker trajectories and force plate data were used to calculate kinematics and kinetics, and the calculated signal low pass filtered at 6 Hz.

All hypothesis testing used an alpha of 0.05. Paper III used a Bonferroni adjustment for multiple comparisons. Paper I used a generalized mixed linear model for hypothesis testing. Papers II & III used a two-step cluster analysis process; knee valgus moment data was transformed into signed differences, which were clustered using the Ward.d2 method on Euclidean distances. The clusters were then merged according to visual appearance (six categories for paper II, two categories for paper III) and then then sub-clusters representing the knee valgus moment magnitude created using non-transformed signals and the Ward.d2 method and Euclidean distances.

Paper III extracted data for kinematics which have been previously reported from analysis of anterior cruciate ligament injuries. A heel strike landing posture was a binary variable. For continuous kinematic data, a ROC curve was calculated and the Youden’s index used to select a cut-off value which was then used for hypothesis testing.

Paper II tested the frequency distribution of the early peak cluster between sex and phase using McNemar’s test. Paper III tested the association between the early peak cluster and kinematics above / below the cut-off using the Fisher’s exact test.

Results: In paper I girls had a later mean knee valgus moment peak ($P < 0.001$) which resulted in a lower mean time between peak knee valgus moment and peak knee internal rotation moments (0 ms for girls, 5 ms for boys, $P < 0.001$), as well as a lower mean time between peak knee valgus moment and peak vertical ground reaction force (1 ms for girls vs 7 ms for boys, $P < 0.001$).

In paper II the knee valgus moment waveforms could be categorized into six discrete shapes; early peak, early trough, peak, trough, upslope, and downslope. There was a difference in relative frequencies ($P < 0.001$) between boys and girls in phase I where boys had more frequent early peaks (575 observed, 464 expected) compared with girls (642 observed, 768 expected). In phase II, however, girls had more frequent early peaks (178 observed, 129 expected) compared with boys (78 observed, 112 expected).

In paper III, there was an association between the early peak knee valgus moment, and a heel strike landing posture (Odds ration (OR) 1.5, $P = 0.01$), medio-lateral distance between trunk and foot center of mass (OR 3.7, $P < 0.01$), knee flexion excursion (OR 1.9, $P < 0.01$), knee flexion at initial contact (OR 2.2, $P < 0.01$), and knee abduction excursion (OR 2.2, $P < 0.01$).

Conclusions: Timing of peak forces during the early stance phase is different between boys and girls in the expected direction (less time between peaks for girls), however not every trial has a peak value and extacting those peaks will therefore not be a complete dataset. Cluster analysis of early stance phase knee valgus moment waveforms produces discrete categories one of which (the early peak) is consistent with the injury mechanism. The early peak is more frequent for adolescent females and is associated with multiple kinematics reported from analysis of ACL injuries. The clusters produced by cluster analysis should be validated against the end-point of ACL injury. The results support strategies to promote forefoot landing postures with more knee flexion to prevent the early peak knee valgus moment waveform.

Keywords:

Anterior cruciate ligament, injury prevention, cluster analysis, biomechanics, motion analysis

Acknowledgements

This thesis is truly a team effort. Although I wrote the manuscripts and conducted the scientific work required to complete this thesis, I acknowledge the essential contributions of my team members.

Professor Kristín Bríem, my supervisor, advisor, and mentor has provided invaluable support and guidance throughout this process, often going above and beyond to provide timely feedback on materials and opportunities for career development. Without her, there would be no ACL project and definitely no thesis.

While I stand responsible for all statistical errors which the thesis may contain, Professor Þórarinn Sveinsson has provided patient guidance and fertile discussions in this area, especially regarding generalized mixed linear modelling.

Professors Jón Karlsson and Lynn Snyder-Mackler have provided insights from their decades of experience. This has especially proven valuable in placing my research in its external context. They have also provided guidance on the publication process, journal selection, and more.

I thankfully acknowledge financial support from Rannís, the University of Iceland Research Fund, the University of Iceland Doctoral travel fund, and the Icelandic Football Association for a travel grant.

Ólafur Sverrir Kjartansson wrote custom software to convert exported files to spreadsheet format, and his eye for design regarding figures, graphs, and posters.

Professor Ólafur Pétur Pálsson and his student, Ragnar Leví Guðmundarson consulted with me on time series analysis, which later led to the idea to use cluster analysis.

The research was conducted at the University of Iceland, where I have been provided with a desk and a biomechanics lab.

Last but not least; while I have attempted to reach the shoulders of giants, my loving wife, Tobba, has built the ladder to climb with while doing so. She and our children; Björn, Eldrún, and Ágústa, haven given me loving support, somewhere to look forwards to going after the setbacks, and ears to listen to my ramblings about clusters and timings.

Contents

List of abbreviations

ACL = Anterior Cruciate Ligament

VM = Valgus Moment, of the knee unless otherwise stated

IC = Initial Contact

GRF = Ground Reaction Force

List of figures

List of tables

List of original papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I-V [as needed]):

I. H. B. Sigurðsson, Þ. Sveinsson, and K. Briem, “Timing, not magnitude, of force may explain sex-dependent risk of ACL injury,” *Knee Surgery, Sport. Traumatol. Arthrosc.*, vol. 26, no. 8, 2018.

II. H. B. Sigurðsson and K. Briem, “Cluster analysis successfully identifies clinically meaningful knee valgus moment patterns: frequency of early peaks reflects sex-specific ACL injury incidence,” *J. Exp. Orthop.*, vol. 6, no. 1, p. 37, 2019.

III. H. B. Sigurðsson, J. Karlsson, L. Snyder-Mackler and K. Briem. ”Kinematic variables observed during ACL injury are associated with early peak knee abduction moments during cutting in healthy adolescents,” *Under peer-review in the Journal of Orthopaedic Research.*

Papers I & II of this thesis build upon are published Open Access which allows reproduction of all materials presented within them without explicit permission of the publisher. Paper III is currently under peer-review, and material from paper III is reproduced here from the manuscript submitted for peer review.

Declaration of contribution

As part of the work for this thesis I have been involved in all parts of the research process. During data collection, I have contacted and recruited some of the subjects. I led data collections for all phase II subjects, usually with the help of 1-2 assistants or students. I have processed part of the phase I and phase II data, which involves e.g. labelling marker trajectories, gap-filling trajectories, and applying the musculoskeletal model. I formulated the research questions together with my supervisor and committee members, conducted the data analysis and statistical analysis required for the papers. I developed the two-step cluster analysis process. I drafted the manuscripts and revised based on co-author feedback.

1 Introduction

1.1 The Anterior Cruciate Ligament injury

The anterior cruciate ligament (ACL) is one of four key ligaments of the knee. Its primary purpose is to constrain against anterior translation of the tibia relative to the femur [1], and in this manner it acts as a tibiofemoral stabilizer against the anterior translation produced by the quadriceps muscle during gait [2]. When the ACL is torn through sports participation, other knee structures such as the mensicii or the medial collateral ligament are commonly torn as well [3]. Recovery requires lengthy rehabilitation often in combination with reconstructive surgery [4]. Even after rehabilitation and surgery, athletes are commonly unable to resume their sports activities due to the injury [5] and when they do, may have reduced performance and a shorter career [6].

For the athlete, long-term consequences of an ACL injury include tibiofemoral and patellofemoral osteoarthritis [7], [8], and reduced quality of life [9]. The societal burden includes the cost of treating the acute injury, as well as for subsequent knee OA and lost work hours [10]. The high cost and serious consequences of ACL injuries have resulted in extensive research efforts to reduce the incidence of ACL injuries.

1.2 Epidemiology of anterior cruciate ligament injuries

In Iceland the annual incidence of ACL injuries is 72 per 100.000 individuals [11]. This rate is comparative to both Sweden, where the rate is estimated at 85 per 100.000 [12], and the United States, where the incidence is 69 per 100.000 [13]. The majority of ACL injuries are accompanied by injuries to other knee structures such as the menisci [14] and occur during sports participation [15]. The injury rate per sports exposure has been reported to range from 0.08 to 0.32 per 1000 exposures depending on the sport [16], making ACL injuries twice as common as fractures in soccer [17], and one fifth as common as ankle sprains in basketball [18].

There are sex-dependent differences in the incidence of ACL injuries which differ by sports. A meta-analysis on soccer athletes showed that compared to males, female athletes have a 2.2x higher risk of suffering ACL injuries when adjusted for participation hours [19]. Other meta-analyses have estimated that the sex-specific incidence is 3.5x higher for female athletes in basketball, but only 1.18x higher in lacrosse [16]. In Iceland, women make up 34% of all athletes over age 16 [20], but 51% of ACL tears in the age bracket 10-19 yeas old are females [11].

The higher incidence for females has led researchers to search for risk factors that may explain the disparity between the sexes. It's been found that the female ACL is less stiff, absorbs less force and has a smaller circumference compared with the male ACL, and even when adjusted for subject height and weight, show lower loads at failure [21]. The ligament's tensile properties and a steeper tibial slope [22] likely account for a significant portion of the sex-specific incidence. However, a meta-meta analysis has shown that preventative training reduces non-contact ACL injury rates by 60% [23] which strongly indicates that there exist an unknown number of biomechanical modifiable risk factors which are being influenced by these training programs.

1.3 ACL loading and injury mechanism

Early studies using cadvers found that anterior shear force directly loads the ACL [1]. A knee valgus moment (VM), a knee varus moment, and both internal and external rotation moments will also result in strain on the ACL, and combining forces over different planes of loading can have a larger effect than the sum of its parts and is variable by joint position [24]. The tibial plateu has a posterior slope which results in anterior translation of the tibia relative to the femur under compression [25], and partial or complete ACL ruptures have been induced in cadaveric knees by isolated tibiofemoral compression or internal rotation [26], and simulated Quadriceps muscle contractions [27]. While VM loading in isolation is unlikely to cause an ACL rupture [28], the addition of a VM load to a simulated landing impact has been shown to result in 30% higher strain values compared with an equal impact without the VM [29].

Cadaveric landing simulators have shown that applying either an internal rotation moment, or a VM influences the bone bruise location during ACL injury [30]. Recently a cadaveric landing simulator has been developed that can produce a similar pattern of ACL and concomitant injuries as is observed clinically by combining VM, internal rotation moments, and an axial impact [14]. This reproduced the location of the rupture and the frequency of e.g. MCL or medial meniscus injuries [14].

The mechanism by which VM increases ACL loading is that valgus loading increases tibiofemoral compression on the lateral tibial plateu which has a more gradual incline compared to the medial plateu [22], [31]–[33]. Tibiofemoral compression will therefore produce an anterior tibial translation and external tibial rotation. However under valgus loading the increased compression on the lateral plateu will produce a net internal rotation moment on the tibia [32]. As females have a steeper posterior tibial slope [22], they may be affected by combined VM and axial compression loading to a larger degree than males.

Cadaveric studies have also found that the peak ACL loading occurs very quickly after ground contact, with a mean of 54 ms after initial contact [34]. This timing is consistent with an ACL injury being induced by a sudden impact with the ground. Video analysis of athletes while sustaining an ACL injury has corroborated the cadaveric models. Leading up to the ACL rupture, athletes make contact with the ground with relatively low knee flexion angles, undergo knee valgus and knee internal rotations, and sustain the injury 40 - 60 ms after initial contact [35], [36]. Subsequent to the injury, a tibial external rotation is observed, indicating that the joint geometry under VM loading causes the internal rotation moment while the ACL is intact and not necessarily the internal rotation moment calculated in motion analysis studies [35]. In contrast, video analysis of similar gameplay situations without injury have shown that the knee valgus and internal rotations do not normally occur [37].

Other aspects of the athletic movement can contribute indirectly to the injury mechanism. Non-knee kinematics can affect the loading of the knee by altering the orientation of the ground reaction force (GRF) vector [38]. Landing on the heel [39], [40], with a large distance between base of support and center of mass [39], hip internal rotation at initial contact [39] and lateral flexion of the trunk [41] have all been observed during an ACL injury.

In summary, ACL injuries most likely occur as a result of a forceful axial impact with the ground combined with a large VM, causing knee valgus rotations and internal rotations, within 60 ms after initial contact with the ground.

1.4 Kinetic and kinematic risk factors

Prospective studies have focused on the forces that are known to load the ACL and evaluated if kinetic or kinematic factors can predict future ACL injury. A study from 2005 found that magnitude of the knee VM during the weight acceptance phase of a drop-jump landing was significantly higher in those that would tear an ACL compared to those that would not [42].

While promising, the study suffers from numerous methodological issues which are important to consider when interpreting prospective biomechanical studies. With a small number of injured athletes (9 subjects tore their ACL [42]) the study is under-powered resulting in a higher likelihood of false positive results [43]. The first author of that study recently wrote in a letter to an editor regarding a different paper, that more statistical analyses had been performed on the data of the 2005 study without reporting the results of that additional analysis [44], indicating an exploratory nature of the published results. Results from exploratory studies, especially those with small sample sizes, need to be validated by conducting follow-up studies replicating the analysis. Two subsequent prospective studies did not find a difference in VM between injured and healthy cohorts [45], [46].

A noteworthy problem with the three prospective cohort studies that employed motion analysis techniques [42], [45], [46], is that their analyses were not performed in a manner consistent with the ACL injury mechanism [47]. All three studies used peak VM during the weight acceptance phase of a bilateral drop jump landing as their outcome measure [42], [45], [46]. The weight acceptance phase of a drop jump is much wider than the timespan where ACL injuries occur [36] and most ACL injuries occur during unilateral movements [48].

1.5 Injury prevention programs

The earliest large scale study to evaluate the effects of a preventative intervention was published in 1996 [49]. Six hundred athletes underwent a proprioception training intervention using different unstable surfaces, for 20 minutes daily for 30 days, and 3 times weekly for the rest of the year. They showed a remarkable reduction in ACL injury incidence, with the intervention group suffering 0.15 injuries per team per season compared to 1.15 in the control group [49]. However, the total time investment for one year on the program is, according to my calculations, 720 hours of training to prevent one ACL injury [49], which is certainly a considerable time investment.

Recently, numerous studies on various interventions to reduce ACL injuries have been performed leading to an increasing number of meta-analyses demonstrating their effectiveness. A meta-analysis of meta-analyses recently combined all of them to demonstrate a 67% reduction of non-contact ACL injuries with prevention programs [23], and the effectiveness of these programs is therefore well established.

Researchers have implemented prevention programs as a structured warm-up in order to facilitate uptake [50]. Despite this, the rate at which ACL injury prevention programs are implemented by sports teams has been low with most performing a reduced number, and modified versions, of preventative exercises due to conflicting priorities and scheduling constraints [51]. The numbers needed to treat (NNT) to prevent an ACL injury have been reported to be as low as 70 [52] and as high as 120 [53]. For an athlete to gain more time from prevention than is lost by injury with NNT of 70 requires that the time spent performing the program with 70 athletes outweighs the time loss of an injury, which is commonly stated as being one year [5]. This simple equation reveals that a prevention with NNT of 70 can require only 1:70 of the total training time or 1.4%. Preventative programs commonly take an hour per week to perform meaning that athletes need to train for 70 hours per week to see benefits. In other words, an athlete that trains for 2 hours, 5 times per week can allot 7.5 hours *per year* to preventative training to “break even” on the time investment.

A meta-analysis of the contents of different intervention programs showed that the effective components were strength training and training to prevent specific postures [54]. However, the studies administering these components of interventions are the same studies [54]. The FIFA-11 program was an early program developed by the F-Marc [55], which included very low-level strengthening exercises along with balance exercises. The program was later updated to include a more strenuous strengthening component and progressions for the exercises [55]. A meta-analysis was conducted examining the efficacy of both programs and found that the FIFA-11 was not effective, but the more strenuous FIFA-11+ was effective [56]. However, intervention studies examining the effects of specific components or exercises are lacking.

1.6 Mechanism, risk, and prevention interdependencies

Studies on the ACL injury mechanism, risk factor studies, and preventative intervention studies form a chain where study results can inform each subsequent level of study. The injury mechanism studies describe the kinetics, kinematics, and external situations that lead to injury. Risk factor studies then find aspects of the injury mechanism that is observable without observing the injury. Preventative interventions target risk factors. I will argue that if this chain of research would have been followed, it could have prevented the inefficiencies observed with current study results.

Exploratory risk factor studies [42], [45], [46] that do not adequately account for the injury mechanism [47] in deciding which factors should be tested inflate the chance of false positive results and lead to weak risk factors. Broad range interventions that target multiple possible aspects of the injury mechanism [57] without strong risk factors lead to inefficient interventions and very costly research design to test effectiveness. Without prior testing on risk factors large scale intervention studies need hundreds of athletes over multiple seasons to see the benefits of prevention [23].

As prevention programs do reduce risk of ACL injuries, their biomechanical effects may lead to new discoveries regarding risk factors for ACL injuries. A meta analysis on the effects of intervention programs on side step cutting biomechanics found that the programs primarily affected sagittal plane mechanics including increased knee angle, reduced hip angles, and reduced knee flexion moments, with no change in knee valgus moments or angles [58]. However, all three studies included in the meta analysis extracted peak moments during either the whole weight acceptance phase [59], [60] or the first 40% of stance [61]. Two studies have been conducted since the meta analysis, that also report knee VM during the weight acceptance phase [62], [63] with little or no reductions of the VM during change of direction tasks.

1.7 Motion capture limitations

As the VM is likely a key component in the ACL injury mechanism [14], it is surprising that biomechanical studies have not found the VM to be affected by effective intervention programs. However, these studies suffer the same pitfalls as the prospective studies that the analysis conducted is not specific to the ACL injury mechanism since they report peak moments during the entire weight acceptance phase which is not consistent with the timing of ACL injuries [35].

The early weight acceptance phase of sporting maneuvers is dominated by the impact between the foot and the ground, which forms a high-frequency signal superimposed on the lower frequency signal that is the normal human movement [64]. Motion capture data are traditionally filtered using low-pass filters on both the marker and force plate data due to soft tissue artifacts [65] and measurement errors [66] which have high frequency contents. This severely attenuates the signal of the foot-ground impact [67], a high frequency signal that is not a source of error. The 2005 study of Hewett et al. used an uneven filter strategy of their data where force data were filtered at a higher frequency than the marker data [42]. Uneven filtering frequencies produce exaggerated impact peaks as the high frequency segment accelerations that accompany high frequency GRF components are reduced [68]. Figure 1 shows the effects of different filtering strategies on the knee valgus moment of a single trial. If the aim is to idenfity early peak knee valgus moments, the choice of filtering strategy greatly impacts the results of this example. It’s possible that the uneven filtering strategy used by Hewett et al. [42] resulted in some motion trials where an impact peak VM consistent with injury is exaggerated and thus the peak of the weight acceptance phase is consistent with the timing of ACL injury, similar to the example shown in Figure 1. These artifacts may therefore have resulted in this study being the only study where the peak VM is associated with injury risk, even though the observed moment is likely exaggerated.

The fact that motion analysis studies extract peak values for their analyses represents another problem. Using peak values requires consistently finding them across different motion trials, despite multiple potential movement strategies being used by athletes [69]. While knee VM peaks are consistent across trials during drop jump landings [61], there is likely variability in how the ground impact forces are distributed across the different planes, meaning that there is no guarantee that a “peak” occurs during the timeframe where ACL injuries occur [35].

There is a need to develop methods that can work around the technological limitations of motion capture in order to analyze the data in a manner specific to the ACL injury mechanism.

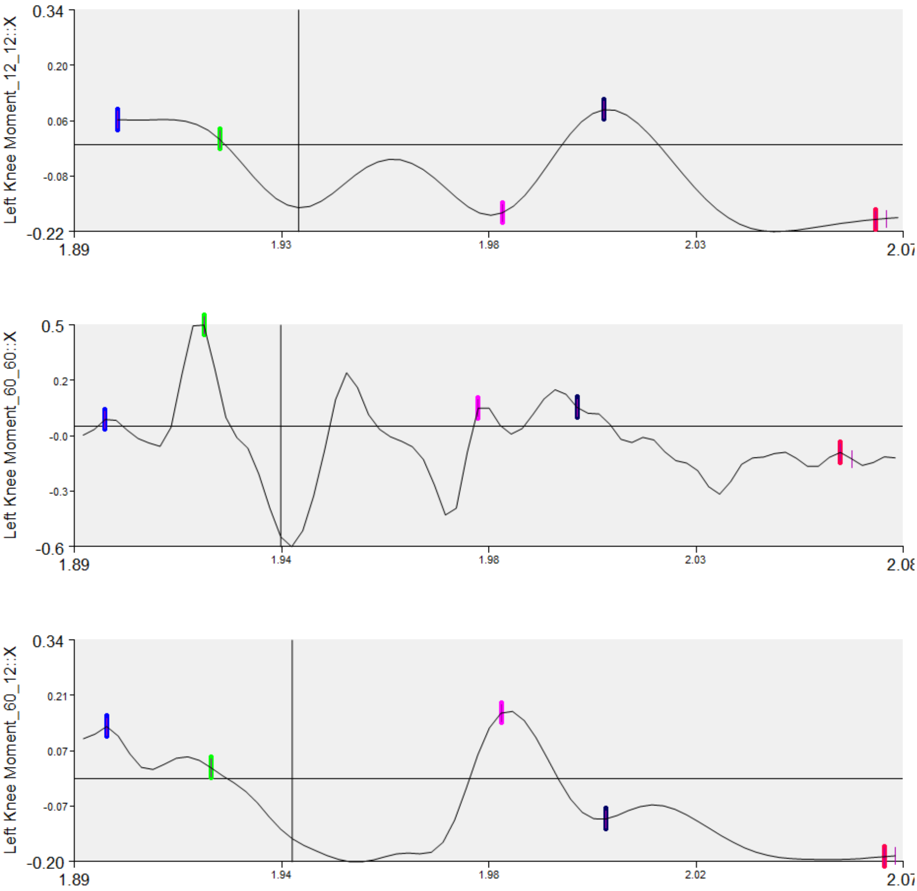


Figure 1 Example trial showing effects of different filtering strategies on knee valgus moments. The top graph shows both forces and markers filtered using 12 Hz, middle shows both filtered using 60 Hz and the bottom graph shows uneven filtering at 60 Hz for forces and 12 Hz for markers. The blue and red marks show the start and 50% of the stance phase duration of a cutting manuever. The green, pink and dark blue marks show the peaks from each filtering strategy. In this example, the 60_60 peak is the only one that occurs within 60 ms after ground contact.

2 Aims

The overall aim of this doctoral thesis was to analyze motion capture data in a manner specific to the ACL injury mechanism, focusing specifically on the forces observed during the early stance phase of the cutting manuver in order to identify potential new risk factors and targets for interventions aimed at preventing ACL injuries.

2.1 Specific aims & Hypotheses

2.1.1 Paper I

The specific aims of paper I were to examine the timing of peak VM and peak internal rotation moment during the first 100 ms of stance during a change of direction movement in pre- or early adolescent (phase I) athletes and compare their absolute and relative timing between the sexes.

The rationale was that at-risk athletes would show timing consistent with ACL injury such as earlier force peaks, and less time between peaks of different forces.

The following hypotheses were tested in paper I:

a. There is a sex-dependent difference in the timing and/or relative timing of peak VM, peak internal rotation moment, or peak vertical GRF within the first 100 ms of the stance phase during a change of direction task.
b. The weight acceptance peak VM, peak internal rotation moment, and/or peak vertical GRF occur after 100 ms and show less co-occurance compared with the early peak VM and internal rotation moment.

2.1.2 Paper II

The specific aims of paper II were to develop a cluster analysis method that could distinguish between different waveforms of the VM, and to conduct a preliminary validation study by comparing the relative frequency of an early peak VM waveform between sexes in early-/pre- adolescence and late adolescence.

The rationale was that not all attempts have an early peak consistent with the timing of ACL injury, and therefore the waveforms must have variable shapes that can be identified with cluster analysis.

The following hypotheses were tested in paper II:

a. VM waveforms are classifiable into a small number of discrete shapes using a cluster-analysis algorithm and at least one cluster will be an early-peak shape
b. Sex-dependent differences in the frequency of the early-peak shape are observed in phase 2, but not phase 1, athletes

2.1.3 Paper III

The specific aims of paper III were to establish concurrent validity of the cluster analysis methods developed in paper 2 by describing the relationship between kinematics commonly observed during ACL injuries, and the frequency of early peak VM waveforms in adolescents.

The rationale was that if a relationship exists between the early peak VM waveform and risk of injury, one would also expect a relationship between the early peak VM waveform and the kinematics observed during ACL injury. Logically, the kinematics of the movement would lead to high forces on the ACL, including the early peak VM.

The following hypotheses were tested in paper III:

a. The following variables are associated with more frequent early-peak VM during a change of direction task in adolescents:
    i. A heel strike landing pose
    ii. Greater anterior-posterior distance between base of support and trunk center of mass
    iii. Greater medio-lateral distance between base of support and trunk center of mass
    iv. Lower knee flexion angle at initial contact with the force plate
    v. Greater peak knee valgus excursion within the first 15% of the stance phase
    vi. Greater peak knee flexion excursion within the first 15% of the stance phase
    vii. Greater peak knee extension excursion within the first 15% of the stance phase
    viii. Greater peak trunk lateral flexion excursion over the stance leg within the first 15% of the stance phase

3 Materials and methods

3.1 Subjects

The national bioethics committee provided ethical approval for the study (approval code VSNb2012020011/03.07).

Subjects for the project were recruited from 5 local soccer and team handball clubs. At recruitment, the athletes were 9-12 years old (phase I). The 5 participating clubs provided contact information for the childrens' guardians, who were then contacted and asked whether they would consent to their child's participation. The consent forms that participants and guardians signed, included explicit consent to be contacted again for the second phase of the study, with expected follow up time being 5 years (phase 2). In phase 2, athletes still participating in their chosen sport as well as those who had ceased participation were asked to repeat the measurements. Participants in phase 2 were offered a 5000 ISK gift certificate for participation.

3.2 Preventative intervention

Representatives from one club agreed to adopt a coach led, physiotherapist assisted intervention program based on the FIFA-11 [56] where physical therapists would attend training sessions every three weeks, evaluate performance of exercises and progress athletes as they improved. A small (2-3) number of exercises was chosen for each three-week time block between sessions, and included only exercises aiming to improve an athletes' motor control through training a specific movement pattern. The effects of the intervention program are not evaluated further in this thesis. However, there is evidence that at least for short-term training the FIFA-11 does not reduce ACL injury rate [56].

3.3 Equipment

Two AMTI force plates collected GRF data at 2000 Hz. An 8 camera Qualisys Oqus system (Qualisys AB, Gothenborg, Sweden) was used to track reflective markers at 200 Hz (phase 1) or 400 Hz (phase 2). A hand-held dynamometer (Manual Muscle Tester, model 01163, Lafayette Instrument Company, Lafayette, USA) was used for isometric strength measurements. A custom-made slideboard with adjustable bank width was used for the exercise intervention.

3.4 Data collection procedure

Subjects reported to the Research Centre of Movement Science lab at the University of Iceland. After receiving information regarding the study, including the risks and benefits, each participant and their guardian signed an informed consent form. All tests were performed in fitted shorts and the subjects' own shoes. Boys were topless, and girls wore a sports bra.

Height, weight, and leg length (floor to iliac crest) were measured. After a 5-minute warm-up on a stationary bicycle, strength testing of the hip abductors was performed, using a belt secured dynamometer with the subject in a side-lying position and hips in 0-5° flexion and 0-5° abduction. Strength testing of the hip external rotators followed. For the hip external rotator strength test, the subject was seated with arms crossed and no backrest. Hip rotation was neutral and knees flexed to 90° and feet off the ground. Strength was measured with a belt-secured dynamometer. The order in which limbs were tested were randomized separately for each strength test. For each strength test, a familiarization attempt was performed, followed by recorded maximal trials.

Following strength testing, 46 reflective markers were placed on the athlete to define the musculoskeletal model (described under section 3.4). A static trial was recorded before removing 12 anatomic-only markers. Subjects performed drop-jump tests and change of direction tests in randomized order starting with 1-3 familiarization trials followed by at least 5 trials for each test.

For the cutting maneuver, the subject was located close to the force plate in a ready-position. When given a verbal signal, the subject performed an antero-lateral step on the force plate before pushing off into a sprint in the opposite direction (see Figure 2). Subjects were encouraged to perform the movement with maximal speed and explosiveness. The exact angle with which the cut was performed was not controlled, giving subjects the freedom to perform anything from roughly 170° to 10° cuts. Using 2-3 habituation trials, the position of the subjects was altered such that the preferred strategy and angle would result in the stance leg being placed on the force plate.

A 5-minute skateboard exercise intervention was performed with progressive intensity where the first minute was to familiarize with the movement, and intensity increased every minute such that the last minute was an all-out effort. A numerical rating scale was used to assess fatigue where 0 was no fatigue at all, and 10 was exhausted. After the exercise intervention, the motion trials were performed again in reverse order

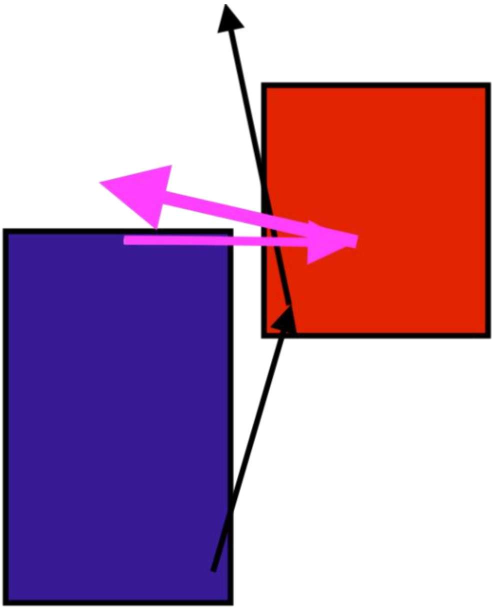


Figure 2 Experimental setup for cutting maneuver. The red box represents the force plate, the blue box represents the range of possible starting locations for a right-leg cut. The black arrows show the widest cut allowed by the setup, and the large pink arrows show the narrowest cut allowed by the setup.

3.5 .Data processing

Motion analysis data was captured with QTM (Qualisys, Gothenburg, Sweden). Raw marker trajectories were labelled by hand for one trial, and an automatic marker identification model was used to identify trajectories in other trials. Gaps of less than 30 frames were automatically gap filled using a spline function. Larger gaps were gap filled manually if possible, such that the marker trajectory appeared smooth and physiological. When trajectories were available for 2 or fewer markers on a segment and gap filling was unsatisfactory the trial was discarded.

3.5.1 Musculoskeletal model

An 8 segment musculoskeltal model was constructed in Visual3D (C-Motion, USA). The ankle joint center was the midway point between the malleoli (2 anatomic markers) and tracked by markers on heels (2) and base of toes 1 and 5 (2). The knee joint was defined as midway between markers placed on medial and lateral femoral epicondyles. Each shank and thigh was tracked by 4 markers secured on a cluster. The hip joint center was defined as 25% of the distance between markers placed on the greater trochanters. The pelvis was defined between markers placed on iliac crests and the greater trochanters, and tracked by 3 markers on the sacrum and 2 markers on the anterior superior iliac spines. The trunk was defined by markers on the lateral aspect of the acromion, and the iliac crest markers and tracked by markers on the 7th cervical vertebra, the sternum, and the posterior lower thorax.

Segment inertial properties were estimated based on the subjects' weight using the Visual 3D default settings. Net joint moments were calculated through inverse dynamics. Kinematics were calculated using the 6 degree of freedom method where each segment was individually calculated and no constraints were placed on joints.

3.5.2 Signal filters

For paper I, marker and force data were low-pass filtered using a digital single pass Butterworth filter with uneven cut-off frequencies similar to Hewett et al. [42], 6 Hz for markers and 20 Hz for force data, before calculating kinematics and kinetics. For papers II and III, kinematics and kinetics were calculated using raw marker and GRF data, before the resultant signal was low-pass filtered using a digital Butterworth filter with a cut-off frequency of 6 Hz.

3.6 Data extraction

3.6.1 Timing of early peak forces

For paper I, the timing of the peak VM, internal rotation moment, and the vertical GRF within the first 100 ms after initial contact was identified. An uneven filtering of force and marker data produced multiple joint moment peaks for each trial, and up to 3 local peaks, irrespective of magnitude or sign, were identified per trial. Using a spreadsheet calculator (Excel, Microsoft corporation), the largest peaks were identified and the timing of those peaks extracted for analysis.

3.6.2 Cluster analysis

For papers II and III a cluster analysis was performed in R [70]–[72] (see appendix for further details regarding the cluster analysis process). For paper II, data representing the frontal plane moment (VM and varus moment) during the first 30% of stance were extracted.

The cluster analysis procedure started by transforming the signal such that only the direction of the signal (increasing or decreasing) was retained. This represented the shape of the waveform. A Euclidean distance (sum of the distances in a straight line between each time point of the time series) was then calculated between each pair of observations. The result of the clustering process was expressed as the C-Index, calculated as the distance between observations within a cluster divided by the distances to other clusters. The number of clusters was decided using either the “elbow” of the C-Index graph, the point where adding more clusters results in smaller and smaller gains in the C-Index, or a 0.05 C-Index cut-off. The process created many clusters, some of whom were conceptually identical in terms of the ACL injury mechanism. Clusters were thus assigned one of 6 descriptive names based on visual inspection of their shapes; early peak, early trough, peak, trough, upslope, and downslope. The merged clusters differed slightly in terms of exact timing of the peaks and troughs. Within each of these 6 clusters a second cluster analysis step was performed on the non-normalized signal to extract sub-clusters based on the magnitude.

The analysis for Paper III only required identification of the early peak waveform. Analysis of the data from Paper II revealed that the early peak shape emerged within 10% of the stance phase. Therefore, it was sufficient to extract 15% of the stance phase for cluster analysis in paper III. The signal underwent the same transformation, and the early peak group was then sub-clustered for magnitude using the non-transformed signal. All cluster analyses used Euclidean distances, and the Ward-D2 process, which produces compact spherical clusters [73].

3.6.3 Kinematics

For paper III, kinematics that have been reported from analyses of videos of ACL injuries by other labs, were extracted. A heel strike ground contact [39] was defined as a negative angle of the foot segment to the floor. The distance between the trunk center of mass, and the stance foot center of mass was normalized by thigh length [39]. The knee flexion angle was extracted at initial contact with the ground [35], [40]. The peak excursion (change in rotation from initial contact within the first 15% of the stance phase) of the knee flexion [35], knee abduction [35], and trunk lateral flexion towards the stance leg [41] were extracted.

3.7 Hypothesis testing

For paper I, a mixed generalized linear model was constructed for each variable using SAS (SAS corporation) with the subject as a random effect, and the sex, limb, and exercise intervention status as fixed effects.

For Papers II & III, R was used for hypothesis testing [71]. For paper II, a McNemar test for paired data was performed. For paper III, a Fisher's exact test with 12 degrees of freedom was performed, and Fisher's exact test with 3 degrees of freedom was used for post-hoc tests. For continuous variables, ROC curves were calculated and the highest Youden's Index used to designate a cut-off value, which was then used in the Fisher's exact test.

All papers use an alpha of 0.05 for statistical significance. Paper III used a Bonferroni adjusted P due to multiple post-hoc comparisons.

4 Results

Results are summarized in this section, and figures and tables are reproduced from the original publications. For detailed results, the reader is referred to the original publications.

4.1 Paper I

4.1.1 Results of Paper I

Data was available for 129 participants. Data for two subjects and 153 other trials, were excluded due to measurement errors, leaving a total of 2387 captured trials available for analysis. The athletes were aged 10.5 years (SD 1.2 years), had a mean height of 1.50 m (SD 0.01 m), and a mean weight of 41 kg (SD 9 kg) with no differences in age, height, or weight between male and female participants. Results are presented in Tables 1 & 2. The main results were that females had later peak VM and knee internal rotation moments compared to males (Hypothesis 1 a, see Table 1), and less time between peak VM and knee internal rotation moment (hypothesis 1b, see Table 2). Notable, while the 95% confidence intervals for all three variable pairs included the zero for girls, the 95% confidence intervals for boys never included zero (Table 2).

Table 1 Time from initial contact with the ground to early (within 100 ms) and global stance phase peak force.

Early peak(ms)	Boys			Girls			Difference	
	Mean	95% CI Lower	95% CI Upper	Mean	95% CI Lower	95% CI Upper	Mean	P for difference
VM	32	30	33	37	36	38	-5	<0.001
IRM	36	35	37	38	37	39	-2	0.029
vGRF	38	37	40	37	36	38	1	n.s.
Global peak (ms)								
VM	204	195	213	238	230	245	-34	<0.001
vGRF	96	88	98	119	115	124	-23	<0.001
Abbreviations: VM = Valgus moment, vGRF = vertical Ground Reaction Force, IRM = knee Internal Rotation Moment.								

Table 2 The difference between force peaks during the first 100 ms after contact with the ground

Time between peaks (ms):	Boys			Girls			Difference	
	Mean	95% CI Lower	95% CI Upper	Mean	95% CI Lower	95% CI Upper	Mean	P for difference
VM & vGRF	-7	-9	-5	-1	-2	1	-6	<0.001
VM & IRM	-5	-6	-3	0	-2	1	-5	<0.001
IRM & vGRF	2	1	4	0	-1	2	2	n.s.
Abbreviations: VM = Valgus moment, vGRF = vertical Ground Reaction Force, IRM = knee Internal Rotation Moment.								

4.2 Paper II

4.2.1 Cluster analysis

Subject characteristics are summarized in Table 3. Data was available for over 5000 trials, of which 783 were from phase II subjects. There were 1025 unique VM waveforms, from which 39 clusters emerged with the C-Index below 0.05 (Figure 1). Visual inspection of the 39 clusters revealed 6 distinct groups which were named early peak, early trough, peak, trough, upslope, and downslope (hypothesis 2a). The second clustering step produced 2-3 magnitude based sub-clusters within each of the original six (Figure 2).

Analysis of cluster frequencies (Table 4) revealed that boys in phase I had a greater than expected frequency of early peaks while girls had a lower than expected frequency. In phase II, however, girls had a higher than expected frequency, and boys had a lower than expected frequency (hypothesis 2b). Analysis of the sub-cluster frequencies (Table 5) revealed that the higher frequency of phase II girls was due to a higher frequency of small early peaks.

Table 1 Descriptive statistics

		Boys		Girls		P
		Mean	SD	Mean	SD	
Phase 1	Age	10.6	0.7	10.8	1.1	0.148
	Height	149.0	7.9	149.9	8.2	0.721
	Weight	40.2	8.1	41.8	9.4	0.402
	N	1512		2502		
Phase 2	Age	15.8	0.8	16.0	0.8	0.500
	Height	180.7	9.1	167.4	4.0	< 0.001
	Weight	74.9	16.5	64.0	10.3	0.054
	N	364		419		

N is the total number of valid movement trials per group.

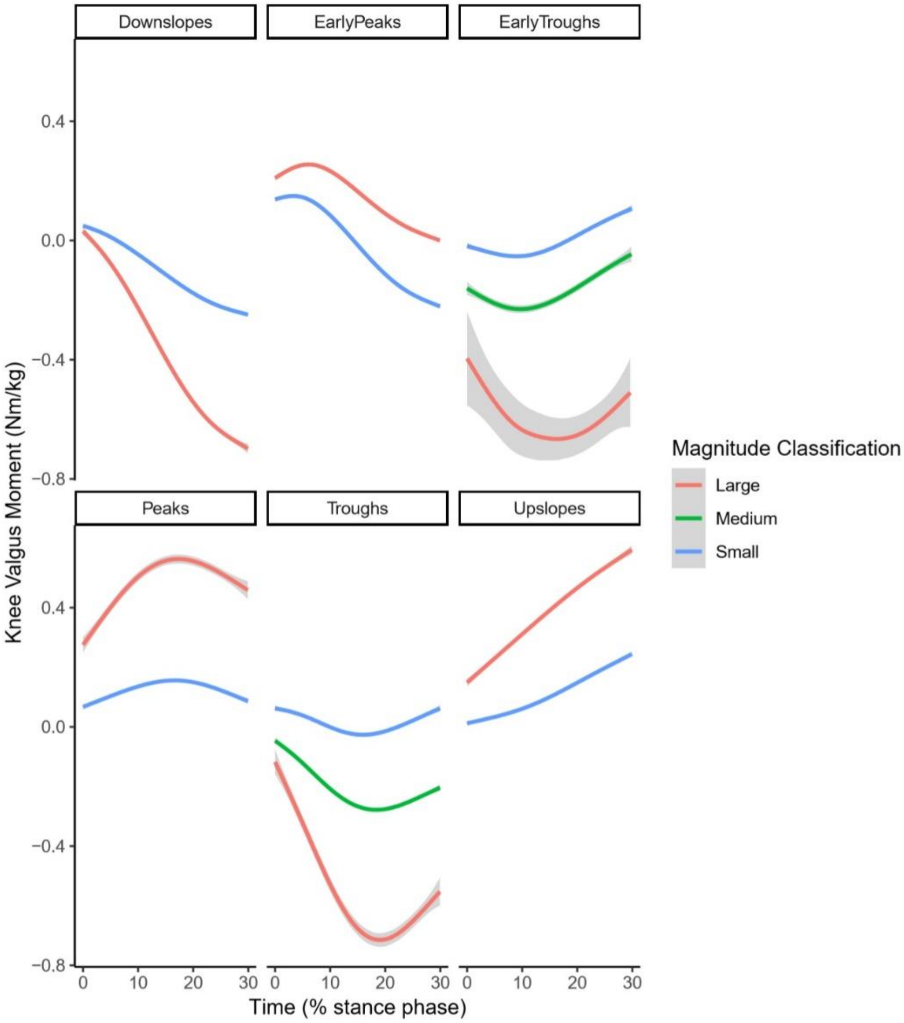


Figure 3 Six basic shapes and their sub-clusters (2-3 per shape) from a two step cluster analysis. Smoothed aggregates of the time series of the first 30% of the stance phase of all clusters generated with the two step cluster analysis. For each curve the gray shaded area denotes the 95% CI which is very narrow for some curves.

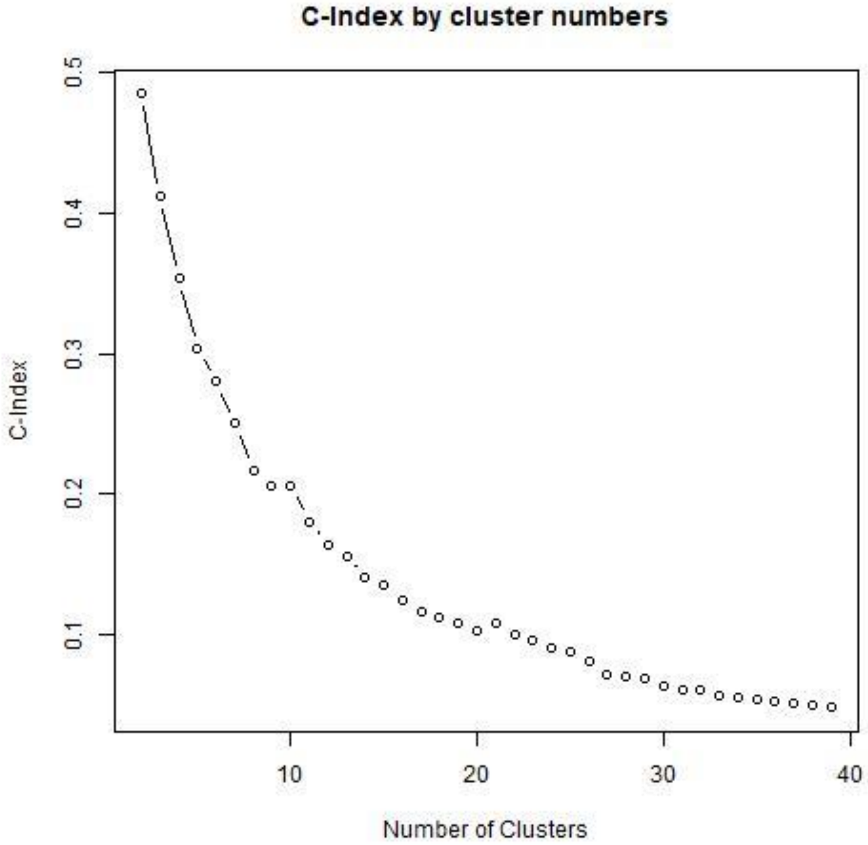


Figure 4 C-Index for up to 40 clusters in the first step clustering process. No clear elbow is present on the plot.

Table 4 The observed and expected frequencies and individual cell contribution to Chi-square value from the chi square test of each of the six basic waveforms.

		Observed (Expected)		Chi-square contribution	
		Boys	Girls	Boys	Girls
Phase 1	Downslopes	276 (420)	698 (695)	49.46	0.01
	EarlyPeaks	575 (464)	642 (768)	26.40	20.76
	EarlyTroughs	42 (41)	80 (67)	0.04	2.40
	Peaks	154 (149)	272 (247)	0.14	2.48
	Troughs	160 (164)	278 (272)	0.11	0.14
	Upslopes	305 (273)	532 (452)	3.68	14.08
Phase 2	Downslopes	207 (101)	152 (116)	110.77	10.87
	EarlyPeaks	78 (112)	178 (129)	10.20	18.92
	EarlyTroughs	4 (10)	3 (11)	3.42	6.07
	Peaks	10 (36)	38 (41)	18.75	0.28
	Troughs	55 (40)	28 (46)	6.05	6.74
	Upslopes	10 (66)	20 (76)	47.31	41.01

P-value for the Chi-Square test < 0.001

Table 5 Observed and expected frequencies for shape based clusters and magnitude based sub-clusters.

		Observed (Expected) Frequencies				Chi-Square contributions			
		Boys		Girls		Boys		Girls	
Curve shape	Magnitude cl	Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2
Early Peak	Small	291 (261)	58 (60)	335 (422)	130 (70)	3.4	0.1	18.0	51.0
	Large	284 (212)	20 (49)	307 (342)	48 (57)	24.8	17.1	3.5	1.4
Peak	Small	101 (112)	10 (26)	206 (182)	33 (30)	1.1	9.8	3.3	0.3
	Large	53 (40)	0 (9)	66 (64)	5 (11)	4.4	9.2	0.0	3.0
Downslopes	Small	198 (268)	83 (62)	478 (434)	77 (72)	18.4	7.1	4.6	0.3
	Large	78 (160)	124 (37)	220 (258)	75 (43)	41.7	205.8	5.5	24.1
Upslopes	Small	166 (167)	7 (39)	328 (269)	18 (45)	0.0	25.8	12.9	16.0
	Large	139 (112)	3 (26)	204 (180)	2 (30)	6.7	20.2	3.1	26.1
Troughs	Small	114 (110)	14 (25)	199 (177)	15 (29)	0.2	5.1	2.6	7.1
	Medium	43 (47)	24 (11)	70 (76)	9 (13)	0.3	16.0	0.4	1.0
	Large	3 (11)	17 (2)	9 (17)	4 (3)	5.4	86.5	3.8	0.5
Early Troughs	Small	31 (33)	3 (8)	67 (54)	3 (9)	0.2	2.9	3.2	4.0
	Medium	9 (7)	1 (2)	12 (11)	0 (2)	0.5	0.2	0.0	1.9
	Large	2 (1)	0 (0)	1 (2)	0 (0)	1.1	0.2	0.2	0.3

The Chi-Square value is 745 and the P value of a Monte-Carlo simulation significance test is < 0.001

4.3 Paper III

Subject characteristics are presented in Table 6. The cluster analysis produced six distinct clusters with a C-Index below 0.05 (Figure 3), of which three were classified as early peaks. During the second cluster analysis step, two magnitude based sub-clusters of early peaks were formed, and the large early peak was used for analysis. There was an association between the large early peaks and several of the kinematic variables (Figures 4 & 5) that have previously been observed during ACL injury . Out of all the odds ratios (Table 7), the largest (3.7 (95% CI 2.8 – 5.0, P < 0.01)) was for having a large early peak with a medio-lateral distance of over 95% of thigh length.

Table 6 Subject characteristics

Sex	Drop out	Height (mean, cm)	Weight (mean, kg)	Attempts (n)	Subjects (n)
Male	Yes	182	76.9	439	20
	No	177	71	871	38
Female	Yes	164	62.9	1128	53
	No	168	62	1234	59

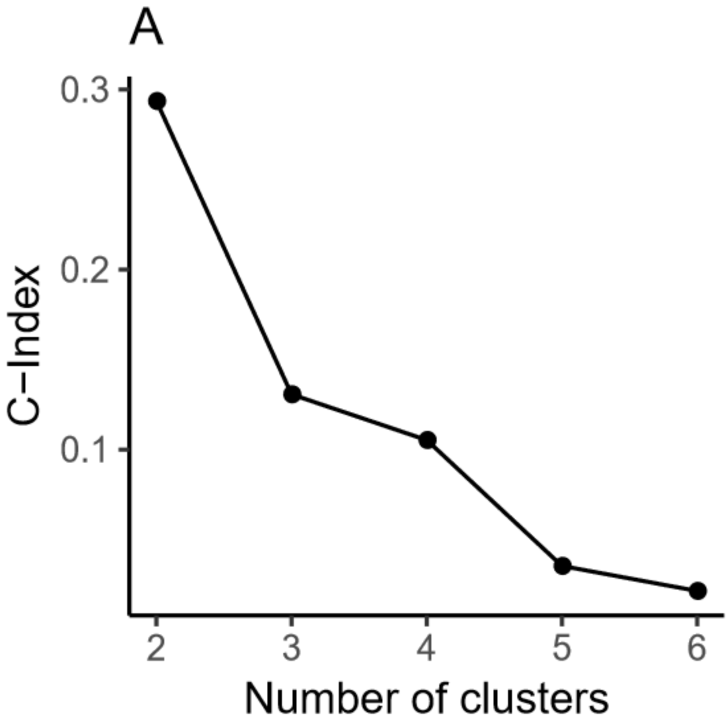


Figure 5 C-Index plot for first cluster analysis step

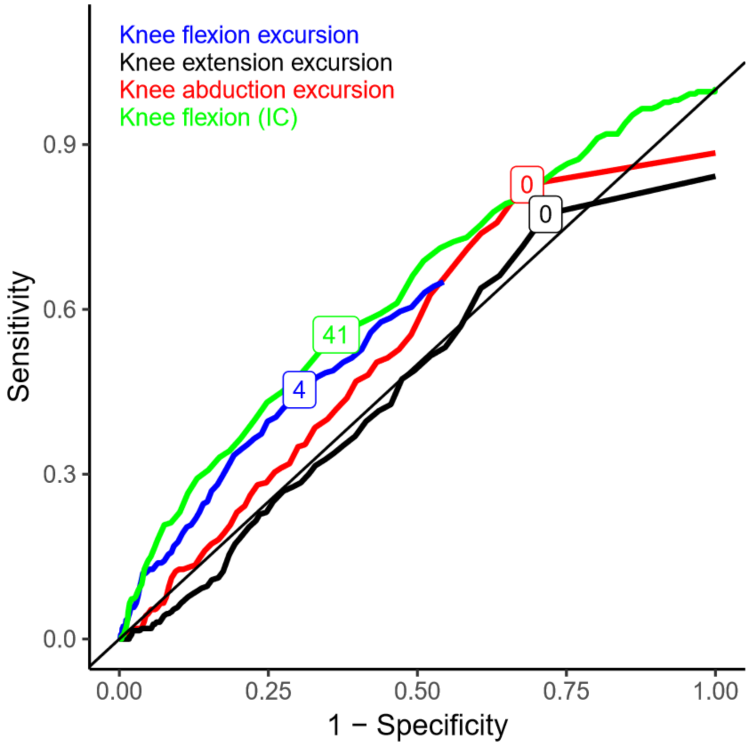


Figure 6 ROC curves for relationship between knee kinematics and early peak valgus moment waveforms. Abbreviations: IC = Initial contact. Excursion is the calculated change of an angle from initial to its peak during the first 15% of the stance phase.. Labels that show the variable value that has the the highest Youden‘s index are placed on each curve.

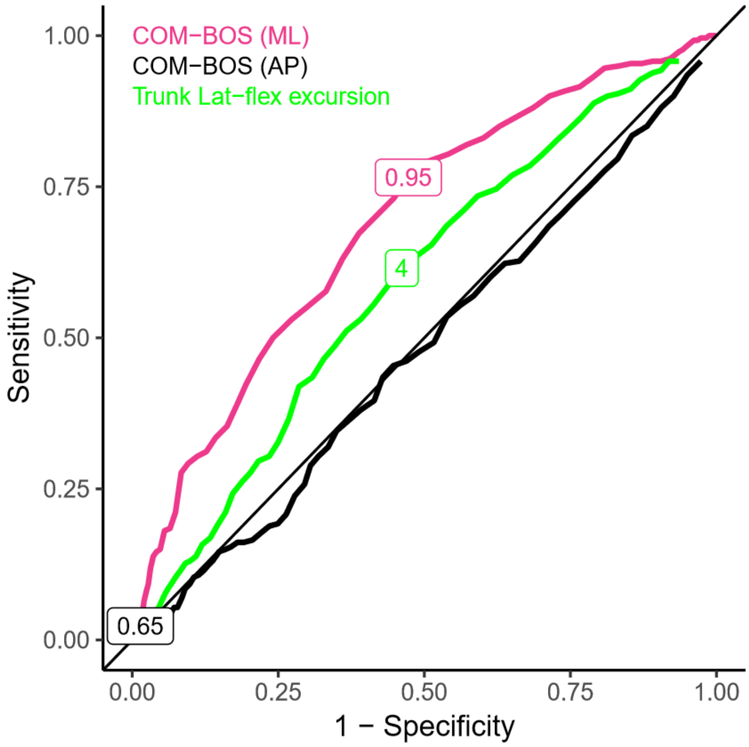


Figure 7 ROC for relationship between non-knee kinematics and large early peak valgus moment waveforms. Abbreviations: ML = medio-lateral. AP = Anterior-posterior. Lat-flex = lateral flexion. The excursion is calculated as the change in the angle from initial ground contact to its peak within 15% of the stance phase. Labels that show the variable value with the the highest Youden‘s index are placed on each curve.

Table 7 Odds ratios for kinematic variables

Variables	Odds ratio	Confidence interval		P-Value
		lower	upper	
Heel strike landing	1.7	1.2	2.3	0.01
COM ant-post	1.7	0.7	3.8	1.00
COM med-lat	3.7	2.8	5.0	<0.01
Knee extension excursion	1.4	1.0	1.8	0.34
Knee flexion excursion	1.9	1.5	2.5	<0.01
Knee flexion at IC	2.2	1.7	2.8	<0.01
Knee abduction excursion	2.2	1.6	3.1	<0.01
Trunk lateral flexion excursion	1.9	1.5	2.5	<0.01

P-values are Bonferroni adjusted. Abbreviations: COM = Center of mass. Ant-post = anterior-posterior direction. Med-lat = medio-lateral direction. IC = Initial contact with the ground.

5 Discussion

The overarching aim of this thesis was to develop and validate methods of analyzing motion capture data in a manner specific to the mechanism of ACL injury, especially with regards to the timing of the forces extracted [36]. Paper I analyzed the actual and relative timings of peak VM, knee internal rotation moment and the vertical ground reaction force themselves and highlighted the difficulty of this approach. Paper II described a cluster analysis method developed to extract information regarding the timing and magnitude of the VM. Paper III validated the method against kinematics previously reported to occur alongside ACL injury.

As the first step of the analysis, paper I used a straightforward approach of analyzing the timing of peak forces during the early stance phase. It was guided by the theory that the less time between the VM and IRM forces, the more likely a multi-planar loading event would occur. The hypotheses were confirmed, as female youth athletes had later VM peaks (Paper I, hypothesis a) and less time between IRM and VM peaks than males (Paper I, hypothesis b). This could indicate that even though girls at this age experience lower early peak VM magnitudes (Appendix B), females are more likely to experience multi-planar loading of the knee during a change of direction task.

However, there were some notable limitations to the analysis performed in paper I. An important limitation was that the uneven filtering of force and marker signals produces artifacts [64]. The magnitude of the exaggerated VM peaks produced by uneven filtering has been linked to risk of ACL injury [42]. The artifacts produced are potentially an exaggeration of a signal that is none the less present. Therefore, less time between VM and IRM peaks may still reflect a higher chance of multi-planar loading for females.

There are however problems that make interpretation of unevenly filtered data difficult. The signal is likely not physiological as computer simulations of muscle work based on those results are not able to account for the exaggerated peaks [68]. No filtering strategy preserves impact peaks while also removing errors from the signal [64]. Using an even filter cut-off of such as 15 Hz [45] for both force and marker data filters the forces too much [64] while marker trajectories are not filtered enough [74]. An alternative is to calculate the kinetics using raw marker and force data, and filter the resulting signal. This process produces smoother waveforms which are more likely to be physiological [68]. However, even when best case low pass filteres are used, not all trials have an identifiable peak VM during the timeframe where ACL injuries occur due to normal variability in human movement. This makes comparisons of timing or force magnitudes problematic. Peak extraction algorithms would either exclude trials without VM peaks or include values which are not relatable to the injury mechanism resulting in limitations as to evaluation and interpretation of the data.

Paper II presents a cluster analysis method which was developed to address the shortcomings of traditional peak extracting data processing methods by classifying the VM waveforms into different shapes rather than extract discrete data points. The results showed that the method was feasible and produces well defined clusters for the waveforms' shapes indicated by the low C-Index. The six shapes created with the cluster analysis method included an early peak shape (Paper II, hypothesis a) which had frequency distribution properties similar to the sex-dependant ACL injury incidence in adolescent athletes with female adolescents having twice as many early peak VM as male adolescents [19] and no sex-dependant difference in phase 1 athletes (Paper II, hypothesis b).

As a novel method, the clusters produced by paper II are not validated against the hard end-point of ACL injury. A similar incidence between the early peak waveform and the ACL injury may be regarded as a form of concurrent validity. Establishing concurrent validity can help determine which potential risk factors are worth testing with prospective studies. Paper III tested several hypotheses of association between early peak waveforms and kinematics that have been previously described by analyzing video footage of actual ACL injuries [35], [39]–[41]. Six out of the eight kinematic variables tested (Table 6) were associated with the early peak waveform (Paper III, hypotheses a-ii and a-vii were not confirmed), providing further concurrent validity.

Together, the three papers presented provide rationale in support of using cluster analysis of VM waveforms for producing clusters that are related to variables associated with ACL injury. The results indicate that the impact generated by ground contact interacts with the kinematics to produce a VM force peak which potentially contributes to the multi-planar loading that cause an ACL injury [14].

5.1 Implications for injury prevention

Preventative intervention studies have focused on exercises intended to affect the posture and orientation of the knee [54]. Paper III shows that joint angle excursions towards greater knee valgus are associated with greater knee VM early peak frequency. Static balance exercises, and exercises aimed at reducing peak knee valgus rotations do therefore potentially target the forces likely to contribute to ACL injuries. However, studies have not demonstrated that effect [62], possibly due to data extraction processes, such as identifying peaks over the entire weight acceptance phase, results of which do not reflect the ACL injury mechanism [47]. Using the cluster analysis method presented in this thesis has potential to elucidate if the interventions aimed at reducing the knee VM do in fact affect the early knee VM waveforms.

The results of this thesis highlight the importance of considering the physics of how the early peak VM is generated. The athlete seeks to create movement by pushing on the ground away from his center of mass. When the dominant factor is this push from the athlete, the knee valgus angle has a large effect towards determining the orientation of the GRF relative to the knee [75]. This effect dominates the movement after the initial impact of ground contact. During ground contact however, the downward and lateral motion of the athlete will result in a GRF vector which is oriented perpendicular to the direction of travel. This vector will be lateral to the knee no matter the knee valgus angle. This effect would be larger with a more laterally planted foot, since the lateral distance between the knee center of rotation and the GRF origin increases. This may be seen as a strategy to decelerate from high lateral velocity without effective use of hip abduction. This is corroborated by our results that greater distance between base of support and center of mass is associated with greater early peak VM frequency.

The results of paper III thus support at least two strategies of reducing the frequency of early peak knee valgus moments. The first, and obvious, method is to reduce the magnitude of the vGRF. Strategies such as doing more eccentric work of the knee and landing on the forefoot instead of the heel are supported by paper III. However, an intervention study emphasizing these exact strategies did not prove effective at reducing ACL injury frequency [76]. The second strategy is to focus on reducing the vGRF moment arm from the ground contact. Increasing the active push of the athlete into the ground can potentially reduce the moment arm, since the vGRF will then point more towards the athletes' center of mass. Active hip abduction [77], active quadriceps and active hamstrings contractions [63] during impact are examples of potentially effective strategies. Plyometric exercise interventions have been largely ineffective [54] despite strong mechanistic reasoning. This can in part be explained by a lack of focus on lateral plyometrics and specific training for the motion of changing directions. Strength is also the foundation of power. Studies have found that low sagittal plane strength [78] and low hip abduction strength [79] are associated with risk of ACL injury and that strength components are important for prevention programs [54]. Those results suggest that a good foundation of strength may be a pre-requisite to train effective change of direction movements.

5.2 Implications for motion analysis

A motion analysis study such as forms the basis of this thesis, collects an enormous amount of data. Coordinates of 34 markers are tracked along with force plate data and from it, numerous variables are calculated with differing precision. The data points from a single movement trial number in the thousands but traditional biomechanical studies reduce this enormous amount of data into a set of 3-10 values representing either peaks or means over a broad time [62], [80], [81]. It’s been stated that the biomechanical community would benefit from adopting methods commonly associated with “Big Data” [82], [83]. The difficulty of extracting the timing of peak values in Paper I highlights the difficulties in trying to perform analyses specific to the ACL injury mechanism. The presence of multiple peaks, or no peaks, makes automated identification of the timing difficult and can potentially result in a large number of incorrectly identified points or no identified points at all. The sheer amount of data that are collected but not used during motion capture studies lends itself well to “Big-Data” methods, and we have shown that cluster analysis or time series can yield clinically meaningful patterns and bypass many of the difficulties inherent in identifying peaks.

5.3 Limitations

5.3.1 Paper I

Paper I used a mixed generalized linear model to examine timing variables. The timing variables were calculated from discrete frame counts representing 5 ms per frame. As the sampling rate limits the accuracy of the timing, it can not be assumed that 5 ms is half of 10 ms (as both could be 7.5 ms), but it can be assumed that 5 ms is less than 15 ms (a full frame in between). With a 200 Hz sampling rate, only one out of every 5 ms is represented in the data. It’s therefore likely that the same proportion of peak timings are inexact.

The filtering strategy in paper I was an uneven filtering where the GRF was filtered at 20 Hz and the markers at 6 Hz. Uneven filtering results in exaggerated impact peaks [84]. Exaggerated impact peaks are likely reasons why so few trials in paper I had missing data (~5%), as the prevalence of true early peaks in the data, as reported in paper II is much lower than 95%. This filtering strategy is similar to the one used by the original study to demonstrate VM as a risk factor [42], while subsequent studies that have not found the VM to be predictive of risk have used an even filtering strategy [45], [46].

5.3.2 Paper II

The primary limitation of paper II was the low number of athletes available for the adolescent cohort. While the study was adequately powered to demonstrate the capabilities of cluster analysis techniques, it was under-powered to definitively conclude that adolescent females have more frequent VM early peaks. However, these preliminary findings were consistent with the difference in incidence of ACL injuries between male and female adolescent athletes [19]. Moreover, the results are consistent with cadaveric simulations wherein an axial impact with a VM loading produces clinically meaningful ACL injuries [14].

5.3.3 Paper III

Paper III used the large early peak waveform for the analysis. No clear distinction exists between the small and large early peaks, and due to the filtering of the data it is unclear whether each trial is affected to a similar extent by the filtering. While the waveform could be distorted with filtering, it is more likely that the magnitude is affected to a greater extent than its shape. It is unclear what a difference in magnitude witin the early peak cluster means. It could be a result of a more explosive movement from a more experienced athlete [85]. Therefore the small and large early peak waveforms could be close to equal in regards to what movement patterns they represent, and subsequently that they could have a similar relationship to the kinemtics. The choice to use the large early peak waveform was made on the basis that the relationship between waveform and kinematics would be most obvious for the cluster with a larger VM magnitude.

5.3.4 Papers II and III

Papers II and III use the same filtering strategy where the kinetics and kinematics are calculated using raw data, and the resultant signal is then filtered using a 6 Hz digital low pass butterworth filter. The cut-off is likely appropriate for mid-to-late stance variables, but during the ground impact likely overly reduces the joint moments. This affects the shape of the curve. In-house pre-testing revealed that the lower the cut-off frequency, the simpler the resulting signal. A signal filtered at 20 Hz produces an unphysiological rate of peaks and troughs [67], thus dramatically increasing the number of clusters which will be detected in the shapes while also reducing the shape difference between clusters. The 6 Hz cut-off frequency produces good clustering results with well discriminated clusters consistent with what would be expected of the physiological signal.

5.3.5 Reliability and validity of methods

The validity of motion analysis results has been tested in numerous publications. A study comparing marker based motion capture to concurrently collected dual fluoroscopy found that the validity of sagittal plane angles was high, lower for frontal plane angles, and worst for transverse plane [86]. In addition, a systematic bias was detected in frontal and transverse plane angles, which was dependent on the knee flexion angles [86]. The marker based motion capture produced knee frontal plane angles that ranged from -15° to 5°, while the radiostereometric analysis ranged from -5° to 5° [86].

The validity of the calculated joint moments depends on all inputs used to generate it. Errors in segmental kinematics, errors in estimates of segment center of mass and errors in location of the center of foot pressure all contribute to the inaccuracy of the result [87]. The most accurate signals are marker trajectories [88] and force plate data [66]. Segment coordinates are calculated from the marker trajectories, which are subject to systematic errors and soft tissue artifacts [86]. From these, inertial properties are estimated, in this case using anthropometric mean values which are the Visual3D default settings. As a result, the net joint moments calculated are unlikely to be accurate representations of the true net joint moments. However, the sources of error affect mostly the magnitude of the joint moments. It is reasonable that the timing of peak forces, and the shape of the VM waveform curve are not affected by these sources of error.

A study on the reliability of side cutting motion analysis reported errors of 5° for kinematics and 16 Nm – 31 Nm for the knee joint moments between sessions [89]. Variability within the individual in how the movement is performed is likely even higher in our subject pool due to their young age. While this variability is aknowledged, it’s not currently known how reliable the VM waveform is between sessions – or how many repetitions are required in order to accurately represent an athletes’ movement strategy and early peak waveform frequency.

6 Conclusions

The aim of this thesis was to develop methods of analyzing motion capture data that are specific to the injury mechanism of ACL injuries, most importantly regarding the timing of observed variables. Cluster analysis of VM waveforms accomplishes this, is feasible and results in a discrete number of distinct waveforms. The early peak VM waveform has a similar relative frequency between the sexes as the relative incidence of ACL injury between the sexes and is associated with kinematics that are observed using video analysis of ACL injuries.

There are numerous implications for future research. The early peak VM waveform is potentially a risk factor for ACL injury. The timing is consistent with the timing of injury, it represents a force that is crucial for the injury mechanism, and it has a relationship with kinematics observed during an ACL injury. Prospective studies are required to test the predictive value of cluster analyzed waveform patterns for future injury. The clinical relevance of the thesis lies in highlighting that impact-modifying landing techniques may be more important than modifying knee valgus rotations in preventing ACL injuries.

If its validity can be established, the cluster analysis of VM waveforms could be used to analyze the effects of exercise interventions. Current interventions, while effective, are time consuming and have a large number needed to treat, limiting their uptake. If the biomechanical changes induced by these programs are identified, shorter, more targeted, versions of interventions may be tested regarding their effectiveness to reduce the time investment for athletes. The early peak VM waveform is a variable that is potentially affected by such interventions and could prove to be a valuable marker for intervention effectiveness. Sex-specific decreases in the frequency of early peak VM occur for boys between the age of 12 and 15 but not for girls. This may be an ideal time for specific interventions aimed at reducing the frequency of early peak VM before injury occurs.

Cluster analysis, and similar methods, will allow researchers to make better use of collected motion analysis data. Demonstrating successful use of such techniques will facilitate further exploration of these methods by scientists which can open up new avenues of research into human movement.

References

[1] K. L. Markolf, J. F. Gorek, J. M. Kabo, and M. S. Shapiro, “Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique,” *J Bone Jt. Surg Am*, vol. 72, no. 4, pp. 557–567, 1990.

[2] L. F. Draganich and J. W. Vahey, “An in vitro study of anterior cruciate ligament strain induced by quadriceps and hamstrings forces,” *J Orthop Res*, vol. 8, no. 1, pp. 57–63, 1990.

[3] R. W. B. Wyatt, M. C. S. Inacio, K. D. Bellevue, A. L. Schepps, and G. B. Maletis, “Isolated ACL versus multiple knee ligament injury: associations with patient characteristics, cartilage status, and meniscal tears identified during ACL reconstruction,” *Phys. Sportsmed.*, vol. 45, no. 3, pp. 323–328, 2017.

[4] R. B. Frobell, E. M. Roos, H. P. Roos, J. Ranstam, and L. S. Lohmander, “A Randomized Trial of Treatment for Acute Anterior Cruciate Ligament Tears,” *N. Engl. J. Med.*, vol. 363, no. 4, pp. 331–342, 2010.

[5] S. Beischer, E. Hamrin Senorski, C. Thomee, K. Samuelsson, and R. Thomee, “Young athletes return too early to knee-strenuous sport, without acceptable knee function after anterior cruciate ligament reconstruction,” *Knee Surg Sport. Traumatol Arthrosc*, 2017.

[6] B. S. Kester, O. A. Behery, S. V Minhas, and W. K. Hsu, “Athletic performance and career longevity following anterior cruciate ligament reconstruction in the National Basketball Association,” *Knee Surg Sport. Traumatol Arthrosc*, vol. 25, no. 10, pp. 3031–3037, 2017.

[7] X. Xie *et al.*, “Increased incidence of osteoarthritis of knee joint after ACL reconstruction with bone–patellar tendon–bone autografts than hamstring autografts: a meta-analysis of 1,443 patients at a minimum of 5 years,” *Eur. J. Orthop. Surg. Traumatol.*, vol. 25, no. 1, pp. 149–159, 2015.

[8] A. Ajuied *et al.*, “Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: a systematic review and meta-analysis,” *Am J Sport. Med*, vol. 42, no. 9, pp. 2242–2252, 2014.

[9] B. E. Oiestad, I. Holm, L. Engebretsen, and M. A. Risberg, “The association between radiographic knee osteoarthritis and knee symptoms, function and quality of life 10-15 years after anterior cruciate ligament reconstruction,” *Br J Sport. Med*, vol. 45, no. 7, pp. 583–588, 2011.

[10] A. A. Kiadaliri, M. Englund, L. S. Lohmander, K. S. Carlsson, and R. B. Frobell, “No economic benefit of early knee reconstruction over optional delayed reconstruction for ACL tears: registry enriched randomised controlled trial data,” *Br J Sport. Med*, vol. 50, no. 9, pp. 558–563, 2016.

[11] M. Nicholls, T. Aspelund, T. Ingvarsson, and K. Briem, “Nationwide study highlights a second peak in ACL tears for women in their early forties,” *Knee Surg Sport. Traumatol Arthrosc*, 2017.

[12] R. B. Frobell, L. S. Lohmander, and H. P. Roos, “Acute rotational trauma to the knee: poor agreement between clinical assessment and magnetic resonance imaging findings,” *Scand J Med Sci Sport.*, vol. 17, no. 2, pp. 109–114, 2007.

[13] T. L. Sanders *et al.*, “Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study,” *Am J Sport. Med*, vol. 44, no. 6, pp. 1502–1507, 2016.

[14] N. A. Bates, N. D. Schilaty, C. V Nagelli, A. J. Krych, and T. E. Hewett, “Validation of Noncontact Anterior Cruciate Ligament Tears Produced by a Mechanical Impact Simulator Against the Clinical Presentation of Injury,” *Am J Sport. Med*, p. 363546518776621, 2018.

[15] J. Kvist, J. Kartus, J. Karlsson, and M. Forssblad, “Results from the swedish national anterior cruciate ligament register,” *Arthrosc. - J. Arthrosc. Relat. Surg.*, vol. 30, no. 7, pp. 803–810, 2014.

[16] C. C. Prodromos, Y. Han, J. Rogowski, B. Joyce, and K. Shi, “A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen,” *Arthroscopy*, vol. 23, no. 12, pp. 1320-1325 e6, 2007.

[17] E. Schiffner *et al.*, “Fractures in German elite male soccer players,” *J. Sports Med. Phys. Fitness*, pp. 110–115, 2019.

[18] S. L. Zuckerman, A. M. Wegner, K. G. Roos, A. Djoko, T. P. Dompier, and Z. Y. Kerr, “Injuries sustained in National Collegiate Athletic Association men’s and women’s basketball, 2009/2010-2014/2015,” *Br. J. Sports Med.*, vol. 52, no. 4, pp. 261–268, 2018.

[19] A. M. Montalvo *et al.*, “‘What’s my risk of sustaining an ACL injury while playing football (soccer)?’ A systematic review with meta-analysis,” *Br J Sport. Med*, 2018.

[20] Í. Ó. Íslands, “Tölfræði Íþróttahreyfingannar 2017,” 2018. [Online]. Available: http://www.isi.is/library/Skrar/Efnisveita/Tolfraedi/Tölfræðirit 2018.pdf?=. [Accessed: 21-Jun-2019].

[21] N. Chandrashekar, H. Mansouri, J. Slauterbeck, and J. Hashemi, “Sex-based differences in the tensile properties of the human anterior cruciate ligament,” *J Biomech*, vol. 39, no. 16, pp. 2943–2950, 2006.

[22] D. S. Weinberg, D. F. Williamson, J. J. Gebhart, D. M. Knapik, and J. E. Voos, “Differences in Medial and Lateral Posterior Tibial Slope: An Osteological Review of 1090 Tibiae Comparing Age, Sex, and Race,” *Am J Sport. Med*, vol. 45, no. 1, pp. 106–113, 2017.

[23] K. E. Webster and T. E. Hewett, “A Meta-analysis of Meta-analyses of Anterior Cruciate Ligament Injury Reduction Training Programs,” *J Orthop Res*, 2018.

[24] K. L. Markolf, D. M. Burchfield, M. M. Shapiro, M. F. Shepard, G. A. Finerman, and J. L. Slauterbeck, “Combined knee loading states that generate high anterior cruciate ligament forces,” *J Orthop Res*, vol. 13, no. 6, pp. 930–935, 1995.

[25] D. B. Lipps, Y. K. Oh, J. A. Ashton-Miller, and E. M. Wojtys, “Morphologic characteristics help explain the gender difference in peak anterior cruciate ligament strain during a simulated pivot landing,” *Am J Sport. Med*, vol. 40, no. 1, pp. 32–40, 2012.

[26] E. G. Meyer and R. C. Haut, “Excessive compression of the human tibio-femoral joint causes ACL rupture,” *J Biomech*, vol. 38, no. 11, pp. 2311–2316, 2005.

[27] G. DeMorat, P. Weinhold, T. Blackburn, S. Chudik, and W. Garrett, “Aggressive quadriceps loading can induce noncontact anterior cruciate ligament injury,” *Am J Sport. Med*, vol. 32, no. 2, pp. 477–483, 2004.

[28] C. S. Shin, A. M. Chaudhari, and T. P. Andriacchi, “The effect of isolated valgus moments on ACL strain during single-leg landing: a simulation study,” *J Biomech*, vol. 42, no. 3, pp. 280–285, 2009.

[29] T. J. Withrow, L. J. Huston, E. M. Wojtys, and J. A. Ashton-Miller, “The effect of an impulsive knee valgus moment on in vitro relative ACL strain during a simulated jump landing,” *Clin Biomech (Bristol, Avon)*, vol. 21, no. 9, pp. 977–983, 2006.

[30] J. W. Levine *et al.*, “Clinically relevant injury patterns after an anterior cruciate ligament injury provide insight into injury mechanisms,” *Am J Sport. Med*, vol. 41, no. 2, pp. 385–395, 2013.

[31] N. A. Bates, R. J. Nesbitt, J. T. Shearn, G. D. Myer, and T. E. Hewett, “Posterior Tibial Slope Angle Correlates With Peak Sagittal and Frontal Plane Knee Joint Loading During Robotic Simulations of Athletic Tasks,” *Am J Sport. Med*, vol. 44, no. 7, pp. 1762–1770, 2016.

[32] A. M. Kiapour *et al.*, “Uni-directional coupling between tibiofemoral frontal and axial plane rotation supports valgus collapse mechanism of ACL injury,” *J Biomech*, vol. 48, no. 10, pp. 1745–1751, 2015.

[33] A. Navacchia, N. A. Bates, N. D. Schilaty, A. J. Krych, and T. E. Hewett, “Knee Abduction and Internal Rotation Moments Increase ACL Force During Landing Through the Posterior Slope of the Tibia,” *J. Orthop. Res.*, 2019.

[34] A. M. Kiapour, C. E. Quatman, V. K. Goel, S. C. Wordeman, T. E. Hewett, and C. K. Demetropoulos, “Timing sequence of multi-planar knee kinematics revealed by physiologic cadaveric simulation of landing: Implications for ACL injury mechanism,” *Clin. Biomech.*, vol. 29, no. 1, pp. 75–82, 2014.

[35] H. Koga *et al.*, “Mechanisms for noncontact anterior cruciate ligament injuries: Knee joint kinematics in 10 injury situations from female team handball and basketball,” *Am. J. Sports Med.*, vol. 38, no. 11, pp. 2218–2225, 2010.

[36] T. Krosshaug *et al.*, “Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases,” *Am J Sport. Med*, vol. 35, no. 3, pp. 359–367, 2007.

[37] S. Sasaki, H. Koga, T. Krosshaug, S. Kaneko, and T. Fukubayashi, “Kinematic analysis of pressing situations in female collegiate football games: New insight into anterior cruciate ligament injury causation,” *Scand. J. Med. Sci. Sport.*, vol. 28, no. 3, pp. 1263–1271, 2018.

[38] E. Kristianslund, O. Faul, R. Bahr, G. Myklebust, and T. Krosshaug, “Sidestep cutting technique and knee abduction loading: Implications for ACL prevention exercises,” *Br. J. Sports Med.*, vol. 48, no. 9, pp. 779–783, 2014.

[39] H. Koga, A. Nakamae, Y. Shima, R. Bahr, and T. Krosshaug, “Hip and Ankle Kinematics in Noncontact Anterior Cruciate Ligament Injury Situations: Video Analysis Using Model-Based Image Matching,” *Am. J. Sports Med.*, vol. 46, no. 2, pp. 333–340, 2018.

[40] C. Montgomery, J. Blackburn, D. Withers, G. Tierney, C. Moran, and C. Simms, “Mechanisms of ACL injury in professional rugby union: a systematic video analysis of 36 cases,” *Br J Sport. Med*, vol. 52, no. 15, pp. 994–1001, 2018.

[41] T. E. Hewett, J. S. Torg, and B. P. Boden, “Video analysis of trunk and knee motion during non-contact anterior cruciate ligament injury in female athletes: Lateral trunk and knee abduction motion are combined components of the injury mechanism,” *Br. J. Sports Med.*, vol. 43, no. 6, pp. 417–422, 2009.

[42] T. E. Hewett *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 Sport. Med*, vol. 33, no. 4, pp. 492–501, 2005.

[43] R. M. Christley, “Power and Error: Increased Risk of False Positive Results in Underpowered Studies,” *Open Epidemiol. J.*, vol. 3, no. 1, pp. 16–19, 2010.

[44] T. E. Hewett, “Normalization influences knee abduction moment results: Could it influence ACL-injury research, too? A Letter to the Editor,” *J. Sci. Med. Sport*, vol. 22, no. 5, p. 502, May 2019.

[45] M. Leppanen *et al.*, “Stiff Landings Are Associated With Increased ACL Injury Risk in Young Female Basketball and Floorball Players,” *Am J Sport. Med*, vol. 45, no. 2, pp. 386–393, 2017.

[46] T. Krosshaug *et al.*, “The Vertical Drop Jump Is a Poor Screening Test for ACL Injuries in Female Elite Soccer and Handball Players: A Prospective Cohort Study of 710 Athletes,” *Am J Sport. Med*, vol. 44, no. 4, pp. 874–883, 2016.

[47] B. Dai, D. Mao, W. E. Garrett, and B. Yu, “Anterior cruciate ligament injuries in soccer: Loading mechanisms, risk factors, and prevention programs,” *J. Sport Heal. Sci.*, vol. 3, no. 4, pp. 299–306, 2014.

[48] M. Walden, T. Krosshaug, J. Bjorneboe, T. E. Andersen, O. Faul, and M. Hagglund, “Three distinct mechanisms predominate in non-contact anterior cruciate ligament injuries in male professional football players: a systematic video analysis of 39 cases,” *Br J Sport. Med*, vol. 49, no. 22, pp. 1452–1460, 2015.

[49] A. Caraffa, G. Cerulli, M. Projetti, G. Aisa, and A. Rizzo, “Prevention of anterior cruciate ligament injuries in soccer: A prospective controlled study of proprioceptive training,” *Knee Surgery, Sport. Traumatol. Arthrosc.*, vol. 4, no. 1, pp. 19–21, 1996.

[50] G. Myklebust, L. Engebretsen, I. H. Braekken, A. Skjolberg, O. E. Olsen, and R. Bahr, “Prevention of anterior cruciate ligament injuries in female team handball players: a prospective intervention study over three seasons,” *Clin J Sport Med*, vol. 13, no. 2, pp. 71–78, 2003.

[51] J. O’Brien, W. Young, and C. F. Finch, “The delivery of injury prevention exercise programmes in professional youth soccer: Comparison to the FIFA 11,” *J Sci Med Sport*, vol. 20, no. 1, pp. 26–31, 2017.

[52] H. J. Silvers-Granelli, M. Bizzini, A. Arundale, B. R. Mandelbaum, and L. Snyder-Mackler, “Does the FIFA 11+ Injury Prevention Program Reduce the Incidence of ACL Injury in Male Soccer Players?,” *Clin Orthop Relat Res*, 2017.

[53] K. R. Pfile and B. Curioz, “Coach-led prevention programs are effective in reducing anterior cruciate ligament injury risk in female athletes: A number-needed-to-treat analysis,” *Scand. J. Med. Sci. Sport.*, vol. 27, no. 12, pp. 1950–1958, 2017.

[54] D. Sugimoto, G. D. Myer, K. D. Foss, and T. E. Hewett, “Specific exercise effects of preventive neuromuscular training intervention on anterior cruciate ligament injury risk reduction in young females: meta-analysis and subgroup analysis,” *Br J Sport. Med*, vol. 49, no. 5, pp. 282–289, 2015.

[55] A. Junge *et al.*, “Countrywide campaign to prevent soccer injuries in Swiss amateur players,” *Am. J. Sports Med.*, vol. 39, no. 1, pp. 57–63, 2011.

[56] K. Thorborg, K. K. Krommes, E. Esteve, M. B. Clausen, E. M. Bartels, and M. S. Rathleff, “Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: a systematic review and meta-analysis of the FIFA 11 and 11+ programmes,” *Br J Sport. Med*, vol. 51, no. 7, pp. 562–571, 2017.

[57] T. Soligard *et al.*, “Comprehensive warm-up programme to prevent injuries in young female footballers: cluster randomised controlled trial,” *BMJ*, vol. 337, p. a2469, 2008.

[58] E. Pappas, E. J. Nightingale, M. Simic, K. R. Ford, T. E. Hewett, and G. D. Myer, “Do exercises used in injury prevention programmes modify cutting task biomechanics? A systematic review with meta-analysis,” *Br. J. Sports Med.*, vol. 49, no. 10, pp. 673–680, 2015.

[59] C. J. Donnelly, B. C. Elliott, T. L. A. Doyle, C. F. Finch, A. R. Dempsey, and D. G. Lloyd, “Changes in knee joint biomechanics following balance and technique training and a season of Australian football,” *Br. J. Sports Med.*, vol. 46, no. 13, pp. 917–922, 2012.

[60] A. R. Dempsey, D. G. Lloyd, B. C. Elliott, J. R. Steele, and B. J. Munro, “Changing sidestep cutting technique reduces knee valgus loading,” *Am. J. Sports Med.*, vol. 37, no. 11, pp. 2194–2200, 2009.

[61] L. J. Distefano, J. T. Blackburn, S. W. Marshall, K. M. Guskiewicz, W. E. Garrett, and D. A. Padua, “Effects of an age-specific anterior cruciate ligament injury prevention program on lower extremity biomechanics in children,” *Am. J. Sports Med.*, vol. 39, no. 5, pp. 949–957, 2011.

[62] J. A. Thompson *et al.*, “Biomechanical Effects of an Injury Prevention Program in Preadolescent Female Soccer Athletes,” *Am J Sport. Med*, vol. 45, no. 2, pp. 294–301, 2017.

[63] M. K. Zebis *et al.*, “Effects of evidence-based prevention training on neuromuscular and biomechanical risk factors for ACL injury in adolescent female athletes: A randomised controlled trial,” *Br. J. Sports Med.*, vol. 50, no. 9, pp. 552–557, 2016.

[64] R. W. Bisseling and A. L. Hof, “Handling of impact forces in inverse dynamics,” *J Biomech*, vol. 39, no. 13, pp. 2438–2444, 2006.

[65] T. Y. Tsai, T. W. Lu, M. Y. Kuo, and C. C. Lin, "Effects of soft tissue artifacts on the calculated kinematics and kinetics of the knee during stair-ascent," *J Biomech*, vol. 44, no. 6, pp. 1182–1188, 2011.

[66] S. T. McCaw and P. DeVita, "Errors in alignment of center of pressure and foot coordinates affect predicted lower extremity torques," *J Biomech*, vol. 28, no. 8, pp. 985–988, 1995.

[67] S. Shin, B. Yoo, and S. Han, "Automatic spline smoothing of non-stationary kinematic signals using bilayered partitioning and blending with correlation analysis," *Digit. Signal Process.*, vol. 39, pp. 22–34, 2015.

[68] S. S. Tomescu, R. Bakker, T. A. C. Beach, and N. Chandrashekar, "The Effects of Filter Cutoff Frequency on Musculoskeletal Simulations of High-Impact Movements," *J Appl Biomech*, vol. 34, no. 4, pp. 336–341, 2018.

[69] A. Franklyn-Miller *et al.*, "Athletic groin pain (part 2): a prospective cohort study on the biomechanical evaluation of change of direction identifies three clusters of movement patterns," *Br J Sport. Med*, vol. 51, no. 5, pp. 460–468, 2017.

[70] M. Charrad, N. Ghazzali, V. Boiteau, and A. Niknafs, "Nbclust: An R Package for Determining the Relevant Number of Clusters in a Data Set," *J. Stat. Softw.*, vol. 61, no. 6, pp. 1–36, 2014.

[71] R. C. Team, "R: A Language and Environment for Statistical Computing," 2018.

[72] P. Montero and J. A. Vilar, "TSclust: An R Package for Time series clustering," *J. Stat. Softw.*, vol. 62, no. 1, pp. 1–43, 2014.

[73] F. Murtagh and P. Legendre, "Ward's Hierarchical Agglomerative Clustering Method: Which Algorithms Implement Ward's Criterion?," *J. Classif.*, vol. 31, no. 3, pp. 274–295, 2014.

[74] L. Ren, R. K. Jones, and D. Howard, "Whole body inverse dynamics over a complete gait cycle based only on measured kinematics," *J Biomech*, vol. 41, no. 12, pp. 2750–2759, 2008.

[75] J. Bencke, D. Curtis, C. Krogshede, L. K. Jensen, T. Bandholm, and M. K. Zebis, "Biomechanical evaluation of the side-cutting manoeuvre associated with ACL injury in young female handball players," *Knee Surg Sport. Traumatol Arthrosc*, vol. 21, no. 8, pp. 1876–1881, 2013.

[76] J. Gilchrist *et al.*, "A randomized controlled trial to prevent noncontact anterior cruciate ligament injury in female collegiate soccer players," *Am J Sport. Med*, vol. 36, no. 8, pp. 1476–1483, 2008.

[77] N. Maniar, A. G. Schache, P. Sritharan, and D. A. Opar, "Non-knee-spanning muscles contribute to tibiofemoral shear as well as valgus and rotational joint reaction moments during unanticipated sidestep cutting," *Sci Rep*, vol. 8, no. 1, p. 2501, 2018.

[78] S. Ryman Augustsson and E. Ageberg, "Weaker lower extremity muscle strength predicts traumatic knee injury in youth female but not male athletes," *BMJ Open Sport &amp; Exerc. Med.*, vol. 3, no. 1, 2017.

[79] K. Khayambashi, N. Ghoddosi, R. K. Straub, and C. M. Powers, "Hip Muscle Strength Predicts Noncontact Anterior Cruciate Ligament Injury in Male and Female Athletes: A Prospective Study," *Am J Sport. Med*, vol. 44, no. 2, pp. 355–361, 2016.

[80] K. Briem, K. V Jonsdottir, A. Arnason, and T. Sveinsson, "Effects of Sex and Fatigue on Biomechanical Measures During the Drop-Jump Task in Children," *Orthop J Sport. Med*, vol. 5, no. 1, p. 2325967116679640, 2017.

[81] M. Baggaley, B. Noehren, J. L. Clasey, R. Shapiro, and M. B. Pohl, "Frontal plane kinematics of the hip during running: Are they related to hip anatomy and strength?," *Gait Posture*, vol. 42, no. 4, pp. 505–510, 2015.

[82] E. Halilaj, A. Rajagopal, M. Fiterau, J. L. Hicks, T. J. Hastie, and S. L. Delp, "Machine learning in human movement biomechanics: Best practices, common pitfalls, and new opportunities," *J Biomech*, vol. 81, pp. 1–11, 2018.

[83] R. Ferber, S. T. Osis, J. L. Hicks, and S. L. Delp, "Gait biomechanics in the era of data science," *J Biomech*, vol. 49, no. 16, pp. 3759–3761, 2016.

[84] N. E. Bezodis, A. I. Salo, and G. Trewartha, "Excessive fluctuations in knee joint moments during early stance in sprinting are caused by digital filtering procedures," *Gait Posture*, vol. 38, no. 4, pp. 653–657, 2013.

[85] S. Sigward and C. M. Powers, "The influence of experience on knee mechanics during side-step cutting in females," *Clin Biomech (Bristol, Avon)*, vol. 21, no. 7, pp. 740–747, 2006.

[86] R. Tranberg, T. Saari, R. Zugner, and J. Karrholm, "Simultaneous measurements of knee motion using an optical tracking system and radiostereometric analysis (RSA)," *Acta Orthop*, vol. 82, no. 2, pp. 171–176, 2011.

[87] V. Camomilla, A. Cereatti, A. G. Cutti, S. Fantozzi, R. Stagni, and G. Vannozzi, “Methodological factors affecting joint moments estimation in clinical gait analysis: A systematic review,” *Biomed. Eng. Online*, vol. 16, no. 1, 2017.

[88] A. M. Aurand, J. S. Dufour, and W. S. Marras, “Accuracy map of an optical motion capture system with 42 or 21 cameras in a large measurement volume,” *J. Biomech.*, vol. 58, pp. 237–240, 2017.

[89] S. P. Sankey *et al.*, “How reliable are knee kinematics and kinetics during side-cutting manoeuvres?,” *Gait Posture*, vol. 41, no. 4, pp. 905–911, 2015.

Paper I

Knee Surgery, Sports Traumatology, Arthroscopy (2018) 26:2424–2429
https://doi.org/10.1007/s00167-018-4859-9

KNEE

Timing, not magnitude, of force may explain sex-dependent risk of ACL injury

Haraldur B. Sigurðsson[1] · **Þórarinn Sveinsson**[1] · **Kristín Briem**[1]

Received: 9 October 2017 / Accepted: 2 February 2018 / Published online: 10 February 2018

Abstract

Purpose The anterior cruciate ligament is loaded through valgus moment, vertical ground reaction force, and internal rotation moment. The aim of this study was to compare the timing of force peaks during early stance between youth girls and boys.
Methods One-hundred and twenty-nine team sport athletes aged 9–12 completed a total of 2540 cutting maneuvers captured with an 8-camera motion capture system. Timing of early force peaks was analyzed within 100 ms after ground contact.
Results Genders showed different mean (95% CI) time to peak valgus—(32 ms (30–33 ms) vs 37 ms (36–38 ms), $P < 0.001$) and time to peak internal rotation moments (36 ms (35–37 ms) vs 38 ms (37–39 ms), $P = 0.029$) but not time to peak vertical ground reaction force [38 ms (37–40 ms) vs 37 ms (36–38 ms, n.s.)]. Girls showed a smaller time between vertical ground reaction force and valgus moment peaks (mean (95% CI) of 1 ms (1–2 ms) vs 7 ms (5–9 ms), $P < 0.001$), and valgus- and internal rotation moment peaks (0 ms (− 2 to 1.0 ms) vs − 5 ms (− 6 to − 3 ms), $P = 0.0003$) but not between internal rotation moment and vertical ground reaction force.
Conclusions Concurrent force peaks are more common for girls compared with boys, leading to more frequent multi-planar loading of the knee. Timing may explain sex-dependent risk of ACL injuries. Exposure to repeated cutting movements may result in greater ACL injury risk due to timing of knee forces as well as magnitude. Such exposure should be minimized for at-risk athletes.
Level of evidence III.

Keywords Knee · ACL · Biomechanics · Injury prevention · Motion analysis

Abbreviations

VM	Knee valgus moment
IRM	Knee internal rotation moment
vGRF	Vertical ground reaction force
ACL	Anterior cruciate ligament
IC	Initial contact with the ground

Introduction

One of the more serious knee injuries that team sports athletes suffer are anterior cruciate ligament (ACL) injuries which can result in significant time loss for the athlete [26], decreased sports performance and career longevity for adult athletes [11], high risk of re-rupture [27], and rapid progression of knee osteoarthritis [1]. The result is a high economic price tag on every injury [20] and decreased long-term knee-related quality of life [8]. Young athletes who sustain an ACL injury have been found to return prematurely to sports [3] with functional deficits persisting for years after injury [10]. The incidence of ACL injuries in soccer matches has been reported to be 0.2 for every 1000 h for men, and up to three times higher for females [36]. Females and young athletes have an increased risk of sustaining a contralateral ACL injury following the first injury [33], and recent reports indicate that frequency of ACL injuries in athletes aged 5–14 years is increasing [29].

The injury is most often a non-contact injury during a landing or cutting maneuver [4]. Cadaver studies, simulating relevant knee joint forces, have demonstrated that the ACL is primarily loaded through anterior tibial translation in relation to the femur [17], external knee valgus moment (VM) and external tibial internal (medial) rotation moment (IRM) [18]. Tibiofemoral joint compression [24] results in anterior tibial translation and is thus a secondary ACL loading mechanism.

✉ Haraldur B. Sigurðsson
harbs@hi.is

[1] Department of Physical Therapy, Faculty of Health Sciences, University of Iceland, Hringbraut 31, 101 Reykjavík, Iceland

The resulting load on the ACL is additionally dependent on the knee joint position, most notably the flexion angle [17, 19], and anatomic factors such as the tibial slope [23, 37] and ACL structural properties, both of which are sex-dependant [22, 38]. A combination of forces results in greater strain on the ACL than individual forces [2, 12, 15], and the ACL injury is, therefore, likely a multi-planar event. Prospective risk factor studies have shown conflicting results of whether the VM and/or the vertical ground reaction force (vGRF) can predict injury [9, 14]. Although female athletes are at greater risk of injury, our laboratory has reported that boys, and not girls, demonstrate greater VM [30]. Furthermore, the magnitude of forces has been shown to increase with greater training [31], whereas the incidence of ACL injury is greater in younger athletes who have had less training compared to the older athletes [36].

The ACL has been shown to mechanically weaken with fatigue [16]. Lipps et al. subjected cadaveric knees to repeated loading of 3 or 4 times the bodyweight during a simulated pivoting motion and found that a large proportion of the ACLs ruptured, with loading magnitude a key determinant to the number of load repetitions to failure [16]. Under these conditions, subject sex or tibial slope did not result in fewer cycles to failure; however, the researchers applied compressive and internal rotation loading concomitantly while also using relatively few loading cycles at greater loads compared to soccer match play [16]. If repeated multi-planar loading resulting in fatigue-failure of the ACL is the primary injury mechanism, the sex-dependent risk of ACL injury may be due to females having more frequent multi-planar loadings due to anatomic or neuromuscular factors rather than high magnitude of loading. The aim of this study was, therefore, to identify the timing of early peak VM, IRM, and vGRF for boys and girls during early stance, at the age where ACL injuries are beginning to occur [29]. The primary focus was to investigate whether differences would be found between male and female youth athletes with respect to the timing of peaks as well as the occurrence of coincident multi-planar loading. The primary hypothesis is that at this age, as it is not known if sex-dependent risk of injury has manifested, both sexes would have similar timing of peak forces. A secondary aim was to evaluate if the global stance-phase peak VM and vGRF, which have previously been linked to risk of ACL injury [9, 14], showed similar timing and co-occurrence as the early peak VM and vGRF. The secondary hypothesis is that these peaks would occur later in the movement and show less co-occurrence compared with the early peak forces.

Materials and methods

This is a cross-sectional laboratory study investigating characteristics of a potential risk factor for ACL injury.

Participants

Participants were recruited from five local soccer and team handball clubs. Recruitment and measurements took place between 2012 and 2014 spanning three consecutive seasons.

Data collection

The study is from the baseline measurements of a prospective controlled trial. Each athlete performed five repetitions of the cutting maneuver on each leg, before and after a 5-min fatigue protocol, for a total of ten attempts per leg. Both fatigue conditions were pooled for this analysis. In addition to cutting maneuvers, biomechanical data collection included bilateral drop jumps and strength testing not included in this report. The methods of data collection are described in detail elsewhere [5]. An 8-camera motion capture system (Qualisys Corporation, Göteborg, Sweden) sampling at 200 Hz was used. Marker placement was performed by experienced physiotherapists who received hands-on training from the primary investigator (KB) to increase reliability. The reliability for 3D kinematic analysis has been established for a running task, similar to our protocol [32]. The accuracy of external marker-based kinematic analysis has been evaluated compared with radiostereometric analysis and found to be good for flexion–extension movements, but the error of measurements of rotations are large but systemic, increasingly so as flexion angles increase [35]. No study has compared marker-based kinematics and radiostereometric analysis during rotational movements such as the cutting maneuver, and the cutting maneuver mostly involves low flexion angles ($< 50°$). While the accuracy of the rotational estimates may be lacking, the reliability is still excellent and allows for between-group comparisons. The accuracy of positioning the ground reaction force vector has been reported to be around 0.5–1.0 cm which can result in around 7–14% errors when estimating the joint moments [21].

Data processing

Selection of variables to study

In line with the multi-planar nature of ACL injuries, variables shown to produce strain on the ACL in cadaveric studies were assessed. All moments are reported as external moments, normalized by body mass. The variables are knee VM (N*m/kg), IRM (N*m/kg) [18], and vertical GRF (N/kg) [24].

Data synthesis

Recorded trials were digitized using the Qualisys track manager software (Qualisys AB, Göteborg, Sweden) and exported for further analysis in Visual-3D (C-motion Inc., Germantown, Maryland, USA). A pipeline of commands was programmed to identify the following events: (a) Initial contact (defined as the first frame with vGRF > 15N), (b) 100 ms after IC (defined as 20 frames after IC), (c) up to three peaks for each variable of interest between initial contact and 100 ms. The data were exported as ASCII files and converted into spreadsheet format using a custom made computer program. This method has an effective detection window of 85 ms, from 10 ms after IC until 95 ms after IC. Using excel, the highest early force peaks were sorted from the three peaks recorded. Using a three-peak system was necessary, as often each variable would display multiple local maxima, the largest of which could be any one of them and the use of the absolute highest value within the 100-ms window often resulted in high values occurring at exactly 100 ms and thus not accurately represented the time frame of ACL injury. The study was approved by the Icelandic National Bioethics Committee, approval code VSNb2012020011/03.07.

Statistical analysis

Statistical analysis was done using the SAS statistical package (SAS Institute, Copenhagen, Denmark). A mixed-models ANOVA was used to compare sexes and control for fatigue conditions, limb-differences*, and repeated measurements. An alpha of 0.05 was used to determine statistical significance. A post-hoc power analysis was performed using G*Power [6], which showed that with an alpha = 0.05 and power of 0.8 the current study is powered to detect a Cohen's $f = 0.26$. Results are reported as means with 95% confidence interval (CI) instead of standardized effect sizes because CIs are better to evaluate if the zero difference (force summation) is likely.

Results

Data on 129 athletes (60% female) were processed and available for analysis, of whom two were excluded due to processing errors for a total of 127 athletes. Participants' mean (SD) weight, height, and age was 41 (9) kg and 1.5 (0.01 m), 10.5 years (1.2), respectively. Out of 2540 trials, 153 were excluded due technical errors. A total of 2387 trials entered the analysis, including both limbs, and both pre- and post-fatigue trials. The following results are presented as means with 95% CI.

Time to peak – time between peaks

The timing of the force peaks is reported in Table 1. Most importantly, females show later force peaks with less spread compared with males. The time between peaks is reported in Table 2; most importantly females show lower mean times between peaks compared with males for the VM and IRM peaks. There was no difference between sexes in time between global stance phase peak VM and vGRF [120 ms (125–110 ms) vs 110 ms (120–100 ms), n.s.].

Discussion

The key findings of this study are that all three forces displayed peaks during the first 100 ms after IC with the ground, with differences between sexes where girls' peaks occurred later than the boys and with a smaller time between peak forces compared with boys, but not between global stance-phase peak VM and vGRF. This is to our knowledge the first study to report a sex-dependent difference in the

Table 1 Time from initial contact with the ground to peak force

	Boys			Girls			Difference	
	Mean	95% CI		Mean	95% CI		Mean	*P* for difference
		Lower	Upper		Lower	Upper		
Early peak (ms)								
VM	32	30	33	37	36	38	− 5	< 0.001
IRM	36	35	37	38	37	39	− 2	0.029
vGRF	38	37	40	37	36	38	1	ns
Global peak (ms)								
VM	204	195	213	238	230	245	− 34	< 0.001
vGRF	96	88	98	119	115	124	− 23	< 0.001

Early peaks occur within 100 ms after initial contact with the ground. Global peaks are maximum of whole stance phase

VM Valgus moment, *vGRF* vertical Ground Reaction Force, *IRM* knee Internal Rotation Moment

Table 2 The difference in timing between force peaks during the first 100 ms after ground contact

Time between peaks (ms):	Boys			Girls			Difference	
	Mean	95% CI		Mean	95% CI		Mean	*P* for difference
		Lower	Upper		Lower	Upper		
VM and vGRF	− 7	− 9	− 5	− 1	− 2	1	− 6	< 0.001
VM and IRM	− 5	− 6	− 3	0	− 2	1	− 5	< 0.001
IRM and vGRF	2	1	4	0	− 1	2	2	n.s

VM Valgus moment, *vGRF* vertical Ground Reaction Force, *IRM* knee Internal Rotation Moment

timing of these events. A multi-planar load of anterior tibial translation, VM, and IRM has been proposed as the mechanism of ACL rupture [28]. Prospective risk factor studies have hitherto reported single peak variables as risk factors, most notably VM and vGRF [9, 14], which we have shown here to occur later in the movement than the ACL injury [13]. The same studies have also used the drop landing test, while ACL injuries more commonly occur during pivoting movements [7] such as the movement used in the current trial. The results presented here show that early force peaks are more likely to result in multi-planar load events during the estimated time of ACL injuries than are the global stance phase peaks. Cadaveric studies using repeated loading have demonstrated a fatigue-effect on the ACL resulting in a clinically relevant rupture type [16]. Recent studies using fluoroscopy have found that neither VM [34] nor vGRF [25] correlate with anterior tibial translation, but that increased Quadriceps muscle demand leads to higher anterior tibial translation although within a safe range [25]. Combined with recent reports from our lab that show that boys, and not girls, demonstrate higher peak forces during the first 100 ms after IC, it stands to reason that these peaks are not useful risk factors.

The frequency with which VM, IRM, and vGRF coincide may be one factor that predisposes athletes to more frequent high loading on the ACL contributing to a fatigue-effect to a greater extent than these loads do in isolation. Our results show that girls have a lower time between peak forces, indicating a greater frequency of multi-planar loads occurring at the knee. The variable timing of forces can be the missing link between training load, force magnitudes, and ACL injury risk.

There are some limitations related to the data collection and analysis process. The global peak values are easy to identify but occur later in the movement than an ACL injury. To extract the relevant data points required a more complex data extraction system due to the inherent variability of the data. Often, there would be multiple early peaks detectable, out of which only the largest was used in the analysis. The method we used is successful in extracting the largest early peak, however, by doing so secondary peaks large enough to be relevant for ACL injury risk may have been missed.

The sampling frequency of 200 Hz used in this study results in a 5-ms interval between frames of measurements. The results we report here are at the extreme of what a 5-ms interval can detect, but as no prior study has looked at the timing of these events, the sampling rate was estimated to be sufficient. A higher sampling frequency is required to clarify the temporal relationships between these variables.

The task was performed without a running approach and, therefore, the force peaks involved are likely of a smaller magnitude than would be seen during a sporting event. This is evident in that the early vGRF in the current study averaged 17 N/kg whereas Leppanen et al. [14] reported an average of 18.5 N/kg (calculation based on the reported sample mean weight). When scaling the speed and power of the movement up, it is reasonable to make the assumption that all forces would scale in a similar fashion. We argue that this results in a systematic bias where at best all variables are scaled down, and at worst the early peak forces increase more in comparison to the global peaks. The temporal relationships between variables are likely not affected by the running start to the same extent as the forces, and the results as reported are unlikely to be affected by this bias.

Conclusions

The primary results are that coincidental summation of early force peaks are more common in girls compared with boys aged 9–12 years. Timing of force peaks, most importantly the co-occurrence, may be a crucial link in a multi-planar loading event as the cause of ACL injury. Clinically, these results indicate that athletes at-risk for ACL injury, such as those previously injured, should limit their exposure to repetitive cutting movements, as although they may demonstrate unremarkable magnitudes of forces acting on the knee joint, the timing of those forces may be important in the risk of ACL injury.

Acknowledgements We would like to thank Ólafur Sverrir Kjartansson from the Department of Engineering and Computer Science for donating his time for writing the custom computer program to convert data.

Author contributions KB and ÞS were involved in planning and execution of the project. HBS wrote the research hypotheses, performed the data analysis and wrote the manuscript. All authors were involved in revising the manuscript and have approved the submitted version of the manuscript. The work submitted is not under consideration elsewhere, and will not be submitted elsewhere while under consideration at the Knee Surgery, Sports Traumatology, Arthroscopy journal.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest.

Funding Funding for salaries (funding code 120410021) and equipment to conduct measurements [Qualisys motion capture cameras and software (funding code 903271305), and AMTI force plates (funding code 1203250031)] was provided by The Icelandic Centre for Research (Rannís—Rannis.is). The Football Association of Iceland has provided travel funds to the lead author to present findings at a conference. No funding source was involved in the study design, the execution of the study, the data analysis, writing the report, the decision to publish the results, or writing the article.

Ethical approval The study was approved by the Icelandic National Bioethics Committee, approval code VSNb2012020011/03.07.

Informed consent Upon arrival participants and their legal guardian were informed about the study protocols and risks, after which they signed an informed consent.

References

1. Ajuied A, Wong F, Smith C, Norris M, Earnshaw P, Back D et al (2014) Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: a systematic review and meta-analysis. Am J Sports Med 42:2242–2252
2. Bates NA, Schilaty ND, Nagelli CV, Krych AJ, Hewett TE (2017) Novel mechanical impact simulator designed to generate clinically relevant anterior cruciate ligament ruptures. Clin Biomech (Bristol Avon) 44:36–44
3. Beischer S, Hamrin Senorski E, Thomee C, Samuelsson K, Thomee R (2017) Young athletes return too early to knee-strenuous sport, without acceptable knee function after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc. https://doi.org/10.1007/s00167-017-4747-8
4. Boden BP, Dean GS, Feagin JA Jr, Garrett WE Jr (2000) Mechanisms of anterior cruciate ligament injury. Orthopedics 23:573–578
5. Briem K, Jonsdottir KV, Arnason A, Sveinsson T (2017) Effects of sex and fatigue on biomechanical measures during the drop-jump task in children. Orthop J Sports Med 5:2325967116679640
6. Faul F, Erdfelder E, Lang AG, Buchner A (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 39:175–191
7. Fauno P, Wulff Jakobsen B (2006) Mechanism of anterior cruciate ligament injuries in soccer. Int J Sports Med 27:75–79
8. Filbay SR, Culvenor AG, Ackerman IN, Russell TG, Crossley KM (2015) Quality of life in anterior cruciate ligament-deficient individuals: a systematic review and meta-analysis. Br J Sports Med 49:1033–1041
9. Hewett TE, Myer GD, Ford KR, Heidt RS Jr, Colosimo AJ, McLean SG et al (2005) 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 33:492–501
10. Ithurburn MP, Altenburger AR, Thomas S, Hewett TE, Paterno MV, Schmitt LC (2017) Young athletes after ACL reconstruction with quadriceps strength asymmetry at the time of return-to-sport demonstrate decreased knee function 1 year later. Knee Surg Sports Traumatol Arthrosc. https://doi.org/10.1007/s00167-017-4678-4
11. Kester BS, Behery OA, Minhas SV, Hsu WK (2017) Athletic performance and career longevity following anterior cruciate ligament reconstruction in the National Basketball Association. Knee Surg Sports Traumatol Arthrosc 25:3031–3037
12. Kiapour AM, Demetropoulos CK, Kiapour A, Quatman CE, Wordeman SC, Goel VK et al (2016) Strain response of the anterior cruciate ligament to uniplanar and multiplanar loads during simulated landings: implications for injury mechanism. Am J Sports Med 44:2087–2096
13. Krosshaug T, Nakamae A, Boden BP, Engebretsen L, Smith G, Slauterbeck JR et al (2007) Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. Am J Sports Med 35:359–367
14. Leppanen M, Pasanen K, Kujala UM, Vasankari T, Kannus P, Ayramo S et al (2017) Stiff landings are associated with increased ACL injury risk in young female basketball and floorball players. Am J Sports Med 45:386–393
15. Levine JW, Kiapour AM, Quatman CE, Wordeman SC, Goel VK, Hewett TE et al (2013) Clinically relevant injury patterns after an anterior cruciate ligament injury provide insight into injury mechanisms. Am J Sports Med 41:385–395
16. Lipps DB, Wojtys EM, Ashton-Miller JA (2013) Anterior cruciate ligament fatigue failures in knees subjected to repeated simulated pivot landings. Am J Sports Med 41:1058–1066
17. Markolf KL, Burchfield DM, Shapiro MM, Shepard MF, Finerman GA, Slauterbeck JL (1995) Combined knee loading states that generate high anterior cruciate ligament forces. J Orthop Res 13:930–935
18. Markolf KL, Gorek JF, Kabo JM, Shapiro MS (1990) Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. J Bone Joint Surg Am 72:557–567
19. Markolf KL, Jackson SR, Foster B, McAllister DR (2014) ACL forces and knee kinematics produced by axial tibial compression during a passive flexion-extension cycle. J Orthop Res 32:89–95
20. Mather RC, 3rd, Koenig L, Kocher MS, Dall TM, Gallo P, Scott DJ et al (2013) Societal and economic impact of anterior cruciate ligament tears. J Bone Joint Surg Am 95:1751–1759
21. McCaw ST, DeVita P (1995) Errors in alignment of center of pressure and foot coordinates affect predicted lower extremity torques. J Biomech 28:985–988
22. McLean SG, Mallett KF, Arruda EM (2015) Deconstructing the anterior cruciate ligament: what we know and do not know about function, material properties, and injury mechanics. J Biomech Eng 137:020906
23. McLean SG, Oh YK, Palmer ML, Lucey SM, Lucarelli DG, Ashton-Miller JA et al (2011) The relationship between anterior tibial acceleration, tibial slope, and ACL strain during a simulated jump landing task. J Bone Joint Surg Am 93:1310–1317

24. Meyer EG, Haut RC (2008) Anterior cruciate ligament injury induced by internal tibial torsion or tibiofemoral compression. J Biomech 41:3377–3383
25. Myers CA, Torry MR, Peterson DS, Shelburne KB, Giphart JE, Krong JP et al (2011) Measurements of tibiofemoral kinematics during soft and stiff drop landings using biplane fluoroscopy. Am J Sports Med 39:1714–1722
26. Nagelli CV, Hewett TE (2017) Should return to sport be delayed until 2 years after anterior cruciate ligament reconstruction? Biological and functional considerations. Sports Med 47:221–232
27. Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE (2012) Incidence of contralateral and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL reconstruction and return to sport. Clin J Sport Med 22:116–121
28. Quatman CE, Kiapour AM, Demetropoulos CK, Kiapour A, Wordeman SC, Levine JW et al (2014) Preferential loading of the ACL compared with the MCL during landing: a novel in sim approach yields the multiplanar mechanism of dynamic valgus during ACL injuries. Am J Sports Med 42:177–186
29. Shaw L, Finch CF (2017) Trends in pediatric and adolescent anterior cruciate ligament injuries in Victoria, Australia 2005–2015. Int J Environ Res Public Health. https://doi.org/10.3390/ijerph14060599
30. Sigurðsson HJ (2016) Trunk and knee biomechanics in boys and girls during sidestep cutting maneuver: effect of fatigue and side. [MSc Thesis]. Reykjavík: School of Health Sciences, University of Iceland. http://hdl.handle.net/1946/25867. Accessed 15 Dec 2017
31. Sigward S, Powers CM (2006) The influence of experience on knee mechanics during side-step cutting in females. Clin Biomech (Bristol Avon) 21:740–747
32. Sinclair J, Hebron J, Taylor PJ (2014) The influence of tester experience on the reliability of 3D kinematic information during running. Gait Posture 40:707–711
33. Snaebjornsson T, Hamrin Senorski E, Sundemo D, Svantesson E, Westin O, Musahl V et al. (2017) Adolescents and female patients are at increased risk for contralateral anterior cruciate ligament reconstruction: a cohort study from the Swedish National Knee Ligament Register based on 17,682 patients. Knee Surg Sports Traumatol Arthrosc. https://doi.org/10.1007/s00167-017-4517-7
34. Torry MR, Shelburne KB, Myers C, Giphart JE, Pennington WW, Krong JP et al (2013) High knee valgus in female subjects does not yield higher knee translations during drop landings: a biplane fluoroscopic study. J Orthop Res 31:257–267
35. Tranberg R, Saari T, Zugner R, Karrholm J (2011) Simultaneous measurements of knee motion using an optical tracking system and radiostereometric analysis (RSA). Acta Orthop 82:171–176
36. Walden M, Hagglund M, Werner J, Ekstrand J (2011) The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. Knee Surg Sports Traumatol Arthrosc 19:3–10
37. Wang YL, Yang T, Zeng C, Wei J, Xie DX, Yang YH et al (2017) Association between Tibial plateau slopes and anterior cruciate ligament injury: a meta-analysis. Arthroscopy 33:1248–1259.e1244
38. Weinberg DS, Williamson DF, Gebhart JJ, Knapik DM, Voos JE (2017) Differences in medial and lateral posterior tibial slope: an osteological review of 1090 Tibiae comparing age, sex, and race. Am J Sports Med 45:106–113

Paper II

Sigurðsson and Briem *Journal of Experimental Orthopaedics* (2019) 6:37
https://doi.org/10.1186/s40634-019-0205-5

Journal of
Experimental Orthopaedics

RESEARCH Open Access

Cluster analysis successfully identifies clinically meaningful knee valgus moment patterns: frequency of early peaks reflects sex-specific ACL injury incidence

Haraldur B. Sigurðsson* and Kristín Briem

Abstract

Background: Biomechanical studies of ACL injury risk factors frequently analyze only a fraction of the relevant data, and typically not in accordance with the injury mechanism. Extracting a peak value within a time series of relevance to ACL injuries is challenging due to differences in the relative timing and size of the peak value of interest.

Aims/hypotheses: The aim was to cluster analyze the knee valgus moment time series curve shape in the early stance phase. We hypothesized that 1a) There would be few discrete curve shapes, 1b) there would be a shape reflecting an early peak of the knee valgus moment, 2a) youth athletes of both sexes would show similar frequencies of early peaks, 2b) adolescent girls would have greater early peak frequencies.

Methods: $N = 213$ (39% boys) youth soccer and team handball athletes (phase 1) and $N = 35$ (45% boys) with 5 year follow-up data (phase 2) were recorded performing a change of direction task with 3D motion analysis and a force plate. The time series of the first 30% of stance phase were cluster analyzed based on Euclidean distances in two steps; shape-based main clusters with a transformed time series, and magnitude based sub-clusters with body weight normalized time series. Group differences (sex, phase) in curve shape frequencies, and shape-magnitude frequencies were tested with chi-squared tests.

Results: Six discrete shape-clusters and 14 magnitude based sub-clusters were formed. Phase 1 boys had greater frequency of early peaks than phase 1 girls (38% vs 25% respectively, $P < 0.001$ for full test). Phase 2 girls had greater frequency of early peaks than phase 2 boys (42% vs 21% respectively, $P < 0.001$ for full test).

Conclusions: Cluster analysis can reveal different patterns of curve shapes in biomechanical data, which likely reflect different movement strategies. The early peak shape is relatable to the ACL injury mechanism as the timing of its peak moment is consistent with the timing of injury. Greater frequency of early peaks demonstrated by Phase 2 girls is consistent with their higher risk of ACL injury in sports.

Keywords: ACL, Biomechanics, Cluster analysis, Data mining, Injury risk

Background

Anterior cruciate ligament (ACL) injuries result in considerable societal burden (Kiadaliri et al., 2016), explaining extensive and ongoing research efforts to prevent them. Cadaver studies have demonstrated that the ACL can be loaded through a knee valgus moment (VM) (Markolf et al., 1990), and that the VM is an important contributor to the multi-planar loads that produce clinically meaningful injury patterns (Bates et al., 2018). A landmark study by Hewett et al. (Hewett et al., 2005) revealed that the knee valgus moment was a risk factor for ACL injury, but had important limitations. The total number of injured players was low ($N = 9$), leading to a high chance of false discoveries (Christley, 2010; Colquhoun, 2014). Furthermore, the study used a bilateral drop-jump, a movement which typically does not result in athletic ACL injuries (Montgomery et al., 2018; Walden et al., 2015).

---

* Correspondence: harbs@hi.is
Research Centre for Movement Sciences, University of Iceland, Reykjavík, Iceland

Table 1 Descriptive Statistics

		Boys		Girls		P
		Mean	SD	Mean	SD	
Phase 1	Age	10.6	0.70	10.8	1.06	0.148
	Height	149.0	7.87	149.9	8.20	0.721
	Weight	40.2	8.10	41.8	9.38	0.402
	No. of Trials	1512		2502		
Phase 2	Age	15.8	0.81	16.0	0.77	0.500
	Height	180.7	9.11	167.4	3.99	< 0.001
	Weight	74.9	16.54	64.0	10.27	0.054
	No. of Trials	364		419		

No. of Trials are the number of trials collected that entered the cluster analysis process

Recent studies using similar methodology (Krosshaug et al., 2016; Leppanen et al., 2017) have not replicated the results of the Hewett study (Hewett et al., 2005) and the observation has been made that biomechanical risk factor studies seldom account for the ACL injury mechanisms in their analyses (Dai et al., 2014) which may explain their inconsistent results. While ACL injuries occur shortly after contact with the ground (Koga et al., 2010; Krosshaug et al., 2007), prospective studies have extracted peak values over the complete weight acceptance phase (Hewett et al., 2005; Krosshaug et al., 2016; Leppanen et al., 2017). The timing of global peaks occur during mid- to late weight acceptance phase, which is inconsistent with that of ACL injury (Sigurethsson et al., 2018). A key difficulty in extracting the peak value of the knee VM during the critical early contact phase is the variability in the waveform of the calculated VM signal, which doesn't always have a discrete peak in the early phase (Sigurethsson et al., 2018).

Augmenting traditional biomechanical approaches with machine learning tools, such as cluster analysis (Halilaj et al., 2018) has been suggested as a means for opening new avenues of research. Identifying a waveform consistent with the mechanism of ACL injury is a classification problem that may be solved with cluster analysis. To date, no method has been published that clusters joint moment waveforms into different shapes.

The primary aim of this study was to test the feasibility of using cluster analysis to identify different shapes of VM waveforms in the early weight acceptance phase of a change of direction task, a movement during which ACL injuries occur (Walden et al., 2015). Our hypotheses were; 1a) the waveforms may be classified into a small number of categories, 1b) at least one of the resulting clusters will have an early peak consistent with the timing of ACL injury (Krosshaug et al., 2007).

A secondary aim was to compare the frequency of the early peak waveform between the sexes before and after puberty. Our hypotheses were that; 2a) before adolescence, athletes will show an identical frequency of early peaks, 2b) after adolescence girls will have greater frequency of early peaks, consistent with the 2-3x greater risk of sports related ACL injuries reported in the literature (Montalvo et al., 2018; Nicholls et al., 2018).

Methods

Design and setting

Prospective cohort laboratory study.

Subjects

Athletes were 9–12 years old at baseline (phase 1) and recruited from local soccer and team handball clubs. This

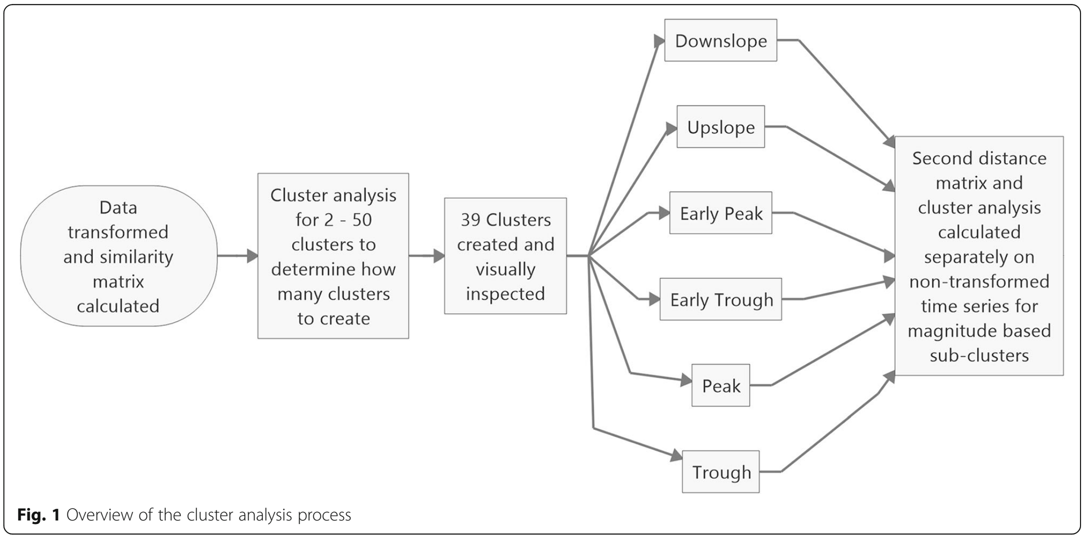


Fig. 1 Overview of the cluster analysis process

age range has been shown to have identical ACL injury rates (Nicholls et al., 2018) in the country where the study is performed. At the follow up data collection (phase 2), these same athletes (some of whom have changed, or departed from, sports) were aged 14–17 years old for a mean time from baseline to follow up of 5 years. Athletes' characteristics for phase 1 (*N* = 213, 39% boys) and phase 2 (*N* = 35, 45% boys) are summarized in Table 1.

Data collection

Data collection methods have been previously described by Briem et al. (Briem et al., 2017). In short, height and weight were measured before a short warm-up on a stationary bike. Strength testing of hip muscles in abduction and external rotation was performed.

After strength testing, 46 reflective markers were placed on the subject, 4 on each foot, one per malleolus, a 4 marker cluster on each shank, one per femoral condyle, a 4 marker cluster on each thigh, a 3 marker cluster on the sacrum, one on each greater trochanter of the femur and on the highest point of each iliac crest, on bilateral anterior superior iliac spines, on the thorax (approximately t10-t12), on the c7, on the sternum, and on the lateral aspects of each scapular acromion.

A static trial was recorded, and anatomical markers were removed (trochanteric, malleolar, condylar, and iliac crests) before the dynamic movement trials. Subjects performed 5 repetitions of a change of direction

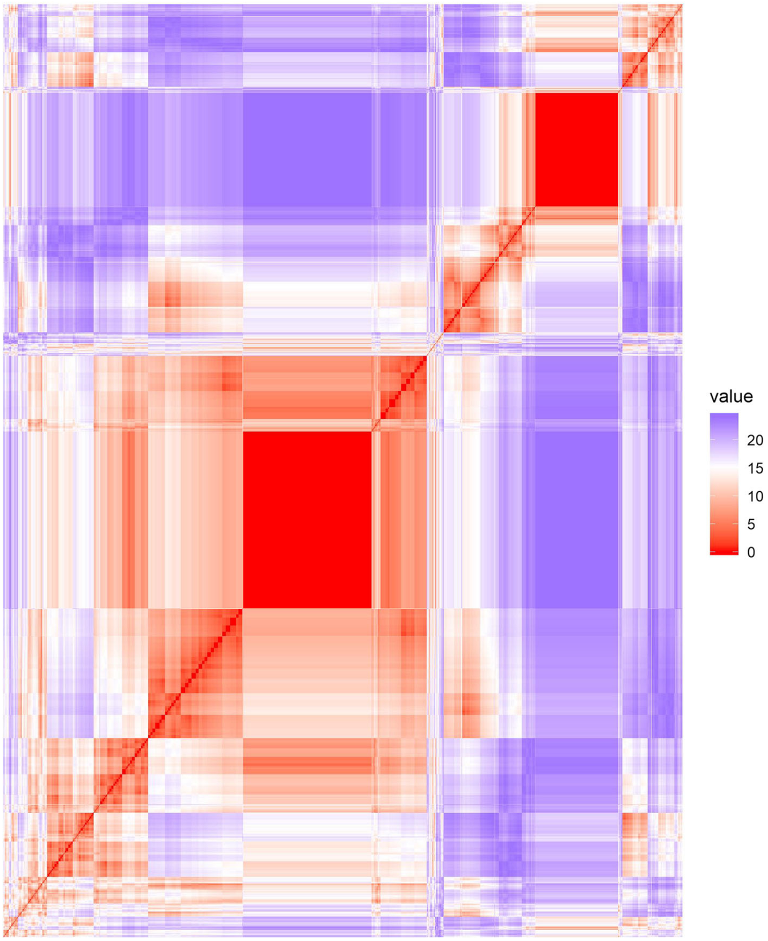


Fig. 2 Heat map of the Euclidean distances of the time series after reduction to the signs of the differenced curve. Two large solid red boxes are present, indicating a number of identical time series (distance = 0)

task on each leg, and 5 repetitions of a bilateral drop-jump from a 23 cm (youth) or 30 cm (adolescents) box. Movement tasks were repeated after a 5 min skateboard exercise protocol and all conditions were pooled for this analysis. The order of movement trials was randomized with an online randomizer in phase 2 (Random.org, 2016), and a coinflip in phase 1.

Data processing and statistical analysis

An 8 segment, 48 degree of freedom, musculoskeletal model was constructed in Visual3D (C-Motion) consisting of feet, shanks, and thighs of both lower extremities, in addition to a pelvis and a trunk. Ankle joint centers were defined as midway between malleolar markers, knee joint centers as midway between femoral condyle markers, hip joint centers as 25% of the distance between trochanteric markers, and the pelvis-trunk joint as midway between the iliac crest markers. Visual3D default settings were used for all segment inertial parameters.

Calculations of kinematics were performed using the 6 degree-of-freedom method and inverse kinetics were calculated for joint moments. Joint moments were normalized by subject body weight, since the tensile strength of the ACL ligament also scales with body weight (Chandrashekar et al., 2006). Time series data of the stance phase of a change of direction task was exported from Visual3D (C-Motion) and imported into R (Team, 2018) for analysis. Video analysis of ACL injuries have revealed that ACL injuries occur in the initial 50 ms after contact with the ground (Krosshaug et al., 2007). However, these descriptions of ACL injuries most often involve high level athletes (Koga et al., 2018) due to the availability of match video recordings. With that in mind, we observed that the fastest athletes in our cohort who displayed an early peak knee VM did so close to the 50 ms mark, which was generally within the first 25% of the stance phase. In order to ensure that slopes on either side of the peak waveform would be captured, data from the first 30% of stance were selected for the cluster analysis.

Cluster analysis

Cluster analysis is a mathematical method which seeks to form groups of discrete data points such that they are more similar to other members within the cluster than they are to those outside the cluster. How well a data set has been clustered can be calculated as the C-Index (Hubert & Levin, 1976), which is the ratio of distances within clusters divided by distances outside a cluster. A requirement for cluster analysis is that the similarity or dissimilarity is calculated between each pair of observations. For the cluster analysis technique presented here (Fig. 1), each recorded trial entered the process separately (at most 20 trials for each athlete and phase)

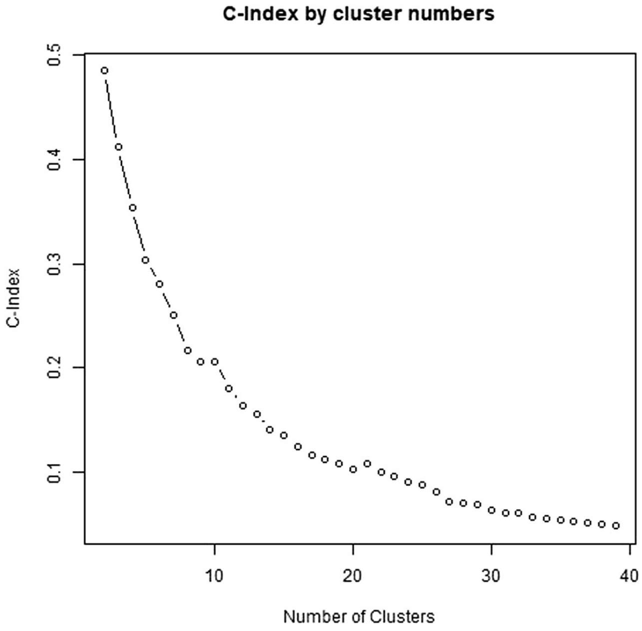


Fig. 3 C-Index plot of initial cluster analysis step

and the dissimilarity metric was calculated as the Euclidean distance (Montero & Vilar, 2014) between the waveforms. The method requires that each time series contains equally many data-points, and thus each time series was first interpolated to lengths equal to the longest series + 2 frames.

A transformation was then performed by calculating the lagged differences of the series and taking its sign. Thus, if a VM data point was higher than that found in the prior frame it was given the value 1, whereas if the data point was lower than that in the prior frame, a value of − 1 was given. Each time series was therefore reduced to its directional changes (increasing or decreasing), representing its waveform. The Euclidean distances between the transformed waveforms were calculated (Montero & Vilar, 2014) and clusters formed using the Ward.D2 (Charrad et al., 2014; Murtagh & Legendre, 2014) method which produces compact spherical clusters.

To decide on a number of clusters to produce, the C-Index (Hubert & Levin, 1976) was calculated for total cluster numbers from 2 to 50 clusters. As there was no distinct elbow in the C-Index plot, a number of clusters was selected based on a C-Index cut-off value of 0.05. The resulting clusters were visually examined and assigned to groups based on similarities in their appearance. Individual curves within a cluster were examined when the aggregated cluster appearance was unclear.

In order to differentiate between different magnitudes of similar shapes of knee VM data, a second cluster

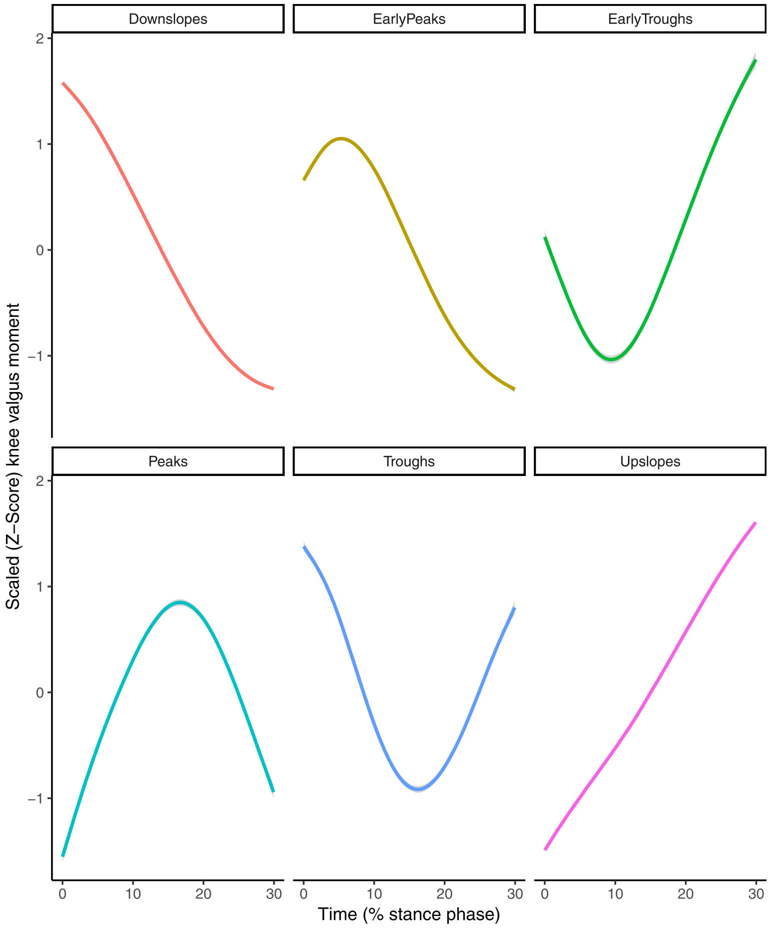


Fig. 4 Smoothed aggregate time series' of the six basic shapes of the scaled knee valgus moment curves generated in the initial shape-based cluster analysis. Each time series is individually scaled. The gray shaded area denotes the 95% confidence interval of the smoothing process

analysis step was performed. All curves within each shape were interpolated and divided by bodyweight in kg. The Euclidean distances between them were calculated and using the Ward.D2 method (Murtagh & Legendre, 2014), 2–4 sub-clusters based on force magnitude were formed. The lowest C-Index value out of the result was selected. Each of the resulting sub-clusters were then examined and classified as either a small, medium, or a large magnitude.

Statistical analysis

No specific cut-offs have been commonly accepted to determine the quality of clusters formed with cluster analysis. Instead, the cluster analysis process was visually inspected to confirm that the intended goal of discrete shapes in the VM waveform was reached. For the secondary aims of determining sex- and age-dependent differences in the frequency of the early peak VM shape, a chi-square test was performed on the frequency distribution of the clusters by sex and maturity where each individual trial was the unit of study. Significance level was set at 0.05.

Results

After screening for errors in performing the side-step maneuver as well as removing trials with large artifacts, 4903 attempts out of the 5080 collected were available for analysis.

Clustering process

After reducing each time series to the signs of a lagged difference, a total of 1025 unique shapes were present with a median of 1 trials per shape but with two large groups of identical shapes (Fig. 2). A total of 39 clusters

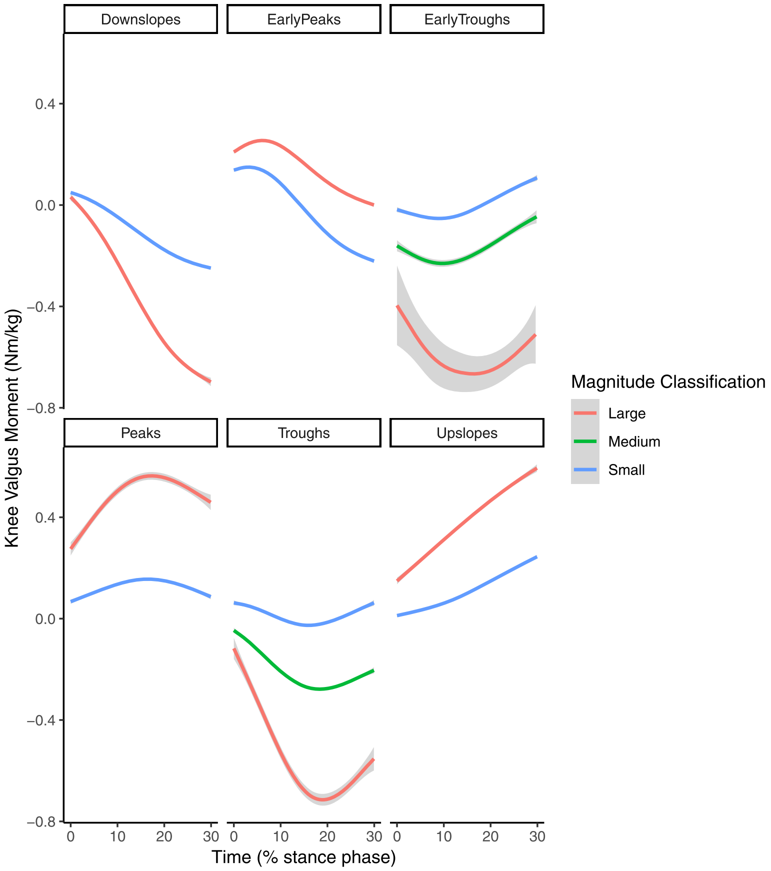


Fig. 5 Smoothed aggregates of the time series of the first 30% of the stance phase of all clusters generated with the two step cluster analysis. The gray shaded area denotes the 95% confidence interval from the smoothing process

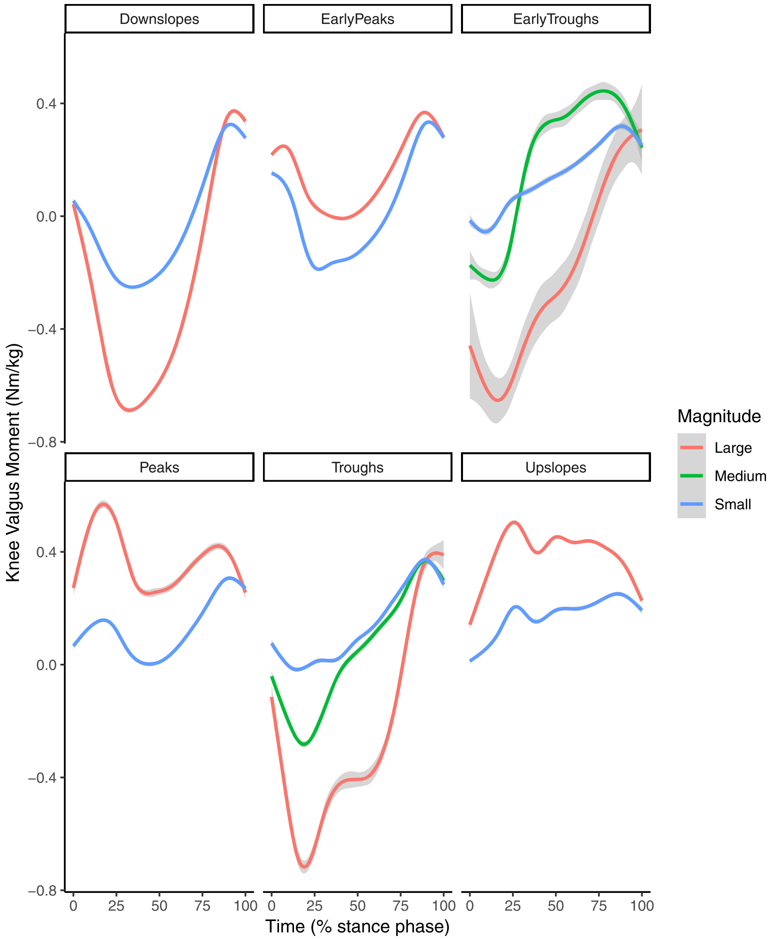


Fig. 6 Smoothed aggregates of the time series of the whole stance phase of all clusters generated with the two step cluster analysis. The gray area denotes the 95% confidence interval from the smoothing process

were formed in the initial cluster analysis step. No elbow was observed in the C-Index plot and the C-Index for 39 clusters was 0.049 (Fig. 3). From those 39 clusters, 6 distinct shapes were identified (Fig. 4); early peaks, peaks, upslopes, downslopes, early troughs, and troughs. From the six basic shapes, a total of 14 magnitude based sub-clusters were formed (Figs. 5 & 6).

Chi-squared test

The chi-squared test for the six basic shapes revealed that in phase 1, boys had a greater than expected frequency of early peaks, while girls had a lower than expected frequency (chi-square contributions of 26.4 and 20.8, respectively). In phase 2, boys had a lower than expected frequency while girls had a greater than expected frequency of early peak shapes (chi-square contributions of 10.2 and 18.9, respectively). The total Chi-Square value of the test was 400.1 with $P < 0.001$. The frequencies, expected frequencies and chi-square contributions for shapes are reported in Table 2.

The relative frequency of the early peak shape overall was 32% in phase 1 and 32% in phase 2. The relative frequencies of the sexes were such that in phase 1 boys showed an early peak in 38% of trials while girls showed an early peak in 25% of trials. In phase 2 boys showed an early peak frequency of 21% (decreased from phase 1) while girls showed an early peak frequency of 42% (increased from phase 1). The relative frequency of each shape by sex and phase are shown in Fig. 7.

Table 2 The observed and expected frequencies of the six shape-based clusters representing the knee valgus moment

		Observed (Expected)		Chi-square contribution	
		Boys	Girls	Boys	Girls
Phase 1	Downslopes	276 (420)	698 (695)	49.46	0.01
	Early Peaks	575 (464)	642 (768)	26.40	20.76
	Early Troughs	42 (41)	80 (67)	0.04	2.40
	Peaks	154 (149)	272 (247)	0.14	2.48
	Troughs	160 (164)	278 (272)	0.11	0.14
	Upslopes	305 (273)	532 (452)	3.68	14.08
Phase 2	Downslopes	207 (101)	152 (116)	110.77	10.87
	Early Peaks	78 (112)	178 (129)	10.20	18.92
	Early Troughs	4 (10)	3 (11)	3.42	6.07
	Peaks	10 (36)	38 (41)	18.75	0.28
	Troughs	55 (40)	28 (46)	6.05	6.74
	Upslopes	10 (66)	20 (76)	47.31	41.01

Chi-square contribution is the individual cell contribution to Chi-square value from the chi square test. *P*-value for the Chi-Square test < 0.001

During further analysis of shape and magnitude based clusters, expected frequencies for early troughs and some groups of troughs were below 5 indicating that the assumptions of the Chi-square test are violated. A Monte-Carlo simulation procedure was used as a significance test (Adery, 1968) instead. Analyses focusing on the knee VM demonstrated that phase 2 boys had fewer than expected large early peaks, while phase 2 girls had the expected frequency (chi-square contributions of 17.1 and 1.4, respectively). For small early peaks, phase 2 boys had the expected frequency while phase 2 girls had greater than expected (chi-square contributions of 0.1 and 51, respectively). The total Chi-Square value of the test was 745 with $P < 0.001$. The observed and expected frequencies with chi-square contributions for shapes and magnitudes are reported in Table 3.

Discussion

The main results of this study are in line with hypothesis 1a, i.e. that the two-step clustering process reported can differentiate between six different curve shapes of the knee VM during the early stance phase, and 2–3 different magnitudes within each shape. Moreover, one of the shapes identified was the early peak, consistent with hypothesis 1b. In phase 1 boys had a greater relative frequency of early peaks, in contrast to hypothesis 2a. However, consistent with hypothesis 2b, girls in phase 2 did have a greater relative frequency of early peaks with a ratio of 2:1, consistent with the reported 2-3x higher incidence of ACL injuries for adult females (Montalvo et al., 2018; Walden et al., 2011).

The Van Mechelen model of injury prevention is an established framework to guide preventative research (van Mechelen et al., 1992). The model emphasizes the need to first establish the aetiology and mechanisms of injury before implementing interventions. Extensive research has been conducted on the mechanism of injury, including cadaver models of ACL injuries (Bates et al., 2018), but very little work has been done to discover how components of injury mechanisms are manifested in non-injury movements. This dearth of cross-sectional research has resulted in prospective studies that are largely exploratory (Hewett, 2019). The relatively low incidence of ACL injuries (Montalvo et al., 2018) means that the ACL-injured cohort in prospective risk factor studies is likely to be small, with a resulting elevated risk of both false positive and false negative results (Christley, 2010; Colquhoun, 2014). Rather than exploration, risk factors tested in prospective studies should be grounded by theory to produce more robust findings.

That is the context in which this study is placed. We present cluster analysis of knee VM waveforms as a novel method to identify the existence of an important component of the ACL injury mechanism, the early peak VM (Bates et al., 2018). Although ACL injuries are more common for female athletes than for male athletes (Montalvo et al., 2018), the injury mechanism is likely the same (Owusu-Akyaw et al., 2018). Therefore, a factor that is related to the injury mechanism in addition to being more common for female athletes has potential to be a true risk factor. Future research should examine a connection of the early peak VM waveform to kinematics observed during ACL injury, and conduct prospective cohort studies to establish a connection to injury risk.

Strengths

This is to our knowledge the first study to have used cluster analysis techniques on 3D motion capture data. During motion capture, a number of different time series are calculated resulting in thousands of data points per measurement. Traditionally, these thousands have been reduced to a small number of single values such as local or global peaks (Leppanen et al., 2017; Torry et al., 2011) which can be input into a statistical model. Our results show that reducing different curve shapes of the knee VM to a single data point in such a manner results in many of the extracted data points being essentially unrelated to the timing of ACL injury. This likely weakens data analysis of such studies in terms of statistical power and the clinical relevance of the results.

Limitations

Assessment of homogeneity of shape within each cluster was performed via visual inspection. This requires a certain level of clinical judgement which may not be reliable between different assessors. The reader is encouraged to

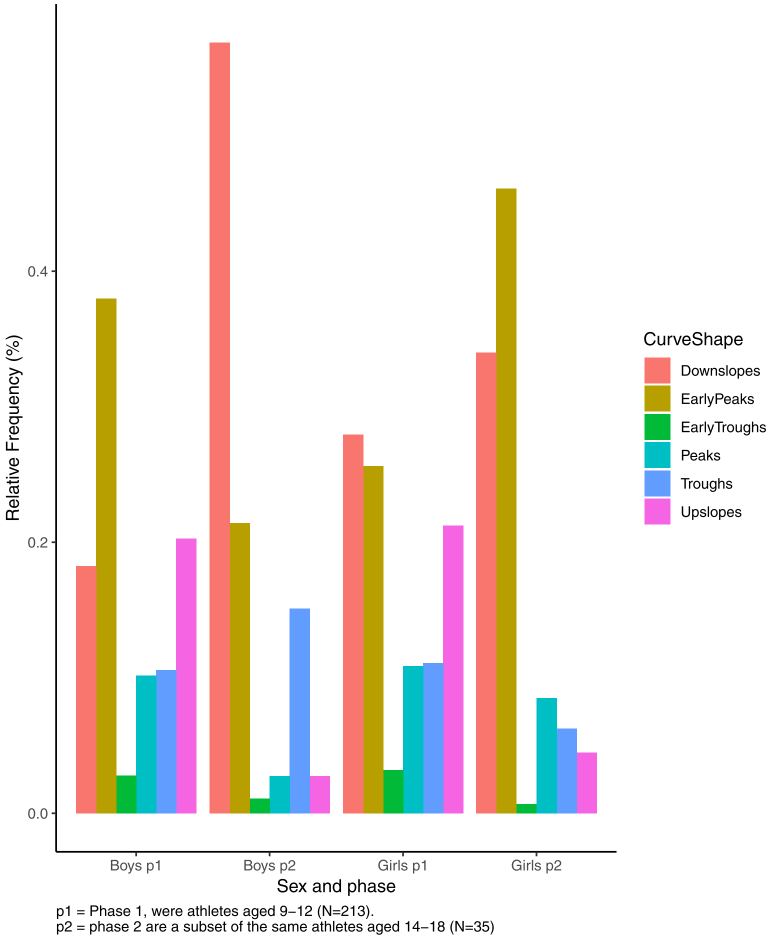


Fig. 7 Relative frequencies of each shape according to sex and phase

examine the results of the clustering process using our data and analysis script from the online depository (see data availability statement).

The C-Index of our cluster analysis is reported, but currently there is no consensus on what constitutes a good C-Index or how the number of clusters should be decided. We used the first elbow of the C-Index graph, or a 0.05 cut-off of a smooth graph. The potential number of clusters in our data is 1025 unique shapes, some of which likely differ only in the exact location of local maxima or minima. It's possible, but in our opinion unlikely, that using 6 initial clusters would yield the same 6 shapes presented as the basic shapes in the present study, or that using 100 initial clusters would yield superior results.

We have reported results from only 35 athletes in the adolescent cohort. The choice to use a subset of the available data was made due to the exploratory approach undertaken. A sample size of 35 is common in biomechanical studies, and since 20 trials are collected from each athlete the study is adequately powered for the chi-squared test. Future studies with larger cohorts are required to confirm the frequency of the early peak VM waveform.

Conclusions and clinical relevance

This is to our knowledge the first study that demonstrates that clustering techniques are feasible to extract meaningful information from biomechanical data with relevance to a specific injury mechanism. A small number of distinct shapes of early stance phase knee VM curves exist and can be identified with a cluster analysis procedure. The early peak knee VM shape is

Table 3 Observed and expected frequencies for shape based clusters and magnitude based sub-clusters

		Observed (Expected) Frequencies				Chi-Square contributions			
		Boys		Girls		Boys		Girls	
Curve shape	Magnitude classification	Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2	Phase 1	Phase 2
Early Peak	Small	291 (261)	58 (60)	335 (422)	130 (70)	3.4	0.1	18.0	51.0
	Large	284 (212)	20 (49)	307 (342)	48 (57)	24.8	17.1	3.5	1.4
Peak	Small	101 (112)	10 (26)	206 (182)	33 (30)	1.1	9.8	3.3	0.3
	Large	53 (40)	0 (9)	66 (64)	5 (11)	4.4	9.2	0.0	3.0
Downslopes	Small	198 (268)	83 (62)	478 (434)	77 (72)	18.4	7.1	4.6	0.3
	Large	78 (160)	124 (37)	220 (258)	75 (43)	41.7	205.8	5.5	24.1
Upslopes	Small	166 (167)	7 (39)	328 (269)	18 (45)	0.0	25.8	12.9	16.0
	Large	139 (112)	3 (26)	204 (180)	2 (30)	6.7	20.2	3.1	26.1
Troughs	Small	114 (110)	14 (25)	199 (177)	15 (29)	0.2	5.1	2.6	7.1
	Medium	43 (47)	24 (11)	70 (76)	9 (13)	0.3	16.0	0.4	1.0
	Large	3 (11)	17 (2)	9 (17)	4 (3)	5.4	86.5	3.8	0.5
Early Troughs	Small	31 (33)	3 (8)	67 (54)	3 (9)	0.2	2.9	3.2	4.0
	Medium	9 (7)	1 (2)	12 (11)	0 (2)	0.5	0.2	0.0	1.9
	Large	2 (1)	0 (0)	1 (2)	0 (0)	1.1	0.2	0.2	0.3

The Chi-Square value is 745 and the *P* value of a Monte-Carlo simulation significance test is < 0.001

consistent with the ACL injury mechanism, since the injury occurs early and the knee VM can strain the ACL. The sex-specific frequencies of the early peak shape in adolescence is consistent with the sex-specific difference in ACL injury incidence and may be a predisposing factor to injury. These findings should inform prospective risk factor studies as well as studies on kinematics related to the early peak waveform.

Abbreviations

ACL: Anterior cruciate ligament; VM: Valgus moment

Acknowledgements

The authors would like to acknowledge Prof. Ólafur Pétur Pálsson and Ragnar Leví Guðmundarson for valuable input regarding the data analysis.

Authors' contributions

HBS collected phase 2 data, designed and performed the data analysis and wrote the manuscript. KB designed the study, participated in planning of the data analysis, and provided substantial revision of the manuscript. Both authors read and approved the final manuscript.

Funding

Funding for the study was provided by The Icelandic Centre for Research (Rannís – Rannis.is), funding codes 120410021, 903271305, 1203250031, and 185359051. The Football Association of Iceland has provided travel funds to the lead author to present findings at a conference. No funding source was involved in the study design, the execution of the study, the data analysis, writing the report, the decision to publish the results, or writing the article.

Availability of data and materials

A number of decisions have to be made by the authors during data processing and analysis. The field of cluster analysis has not reached consensus on how to select many important parameters during the cluster analysis process, including the number of clusters. In order to facilitate replication and auditing of the results presented, a data set that can be used to replicate the cluster analysis is available https://doi.org/10.5061/dryad.v8n3gv3. The data set includes the R code used to perform the cluster analysis, but no other information such as sex or age.

Ethics approval and consent to participate

Ethics approval granted by the Icelandic National Bioethics committee, approval code VSNb2012020011/03.07. All participants, together with a legal guardian, received information regarding the study protocol, including known risks and benefits, and signed an informed consent statement.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 26 February 2019 Accepted: 25 July 2019

References

Adery CAH (1968) A simplified Monte Carlo significance test procedure. J R Stat Soc Ser B Methodol 30:582–598

Bates NA, Schilaty ND, Nagelli CV, Krych AJ, Hewett TE (2018) Validation of noncontact anterior cruciate ligament tears produced by a mechanical impact simulator against the clinical presentation of injury. Am J Sports Med 46:2113–2121

Briem K, Jonsdottir KV, Arnason A, Sveinsson T (2017) Effects of sex and fatigue on biomechanical measures during the drop-jump task in children. Orthop J Sports Med 5:2325967116679640

Chandrashekar N, Mansouri H, Slauterbeck J, Hashemi J (2006) Sex-based differences in the tensile properties of the human anterior cruciate ligament. J Biomech 39:2943–2950

Charrad M, Ghazzali N, Boiteau V, Niknafs A (2014) Nbclust: an R package for determining the relevant number of clusters in a data set. J Stat Softw 61:1–36

Christley RM (2010) Power and error: increased risk of false positive results in underpowered studies. Open Epidemiol J 3:16–19

Colquhoun D (2014) An investigation of the false discovery rate and the misinterpretation of p-values. R Soc Open Sci 1:140216

Dai BY, Mao DW, Garrett WE, Yu B (2014) Anterior cruciate ligament injuries in soccer: loading mechanisms, risk factors, and prevention programs. J Sport Health Sci 3:299–306

Halilaj E, Rajagopal A, Fiterau M, Hicks JL, Hastie TJ, Delp SL (2018) Machine learning in human movement biomechanics: best practices, common pitfalls, and new opportunities. J Biomech 81:1–11

Hewett TE (2019) Normalization influences knee abduction moment results: could it influence ACL-injury research, too? A letter to the editor. J Sci Med Sport 22:502

Hewett TE, Myer GD, Ford KR, Heidt RS Jr, Colosimo AJ, McLean SG et al (2005) 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 33:492–501

Hubert LJ, Levin JR (1976) A general statistical framework for assessing categorical clustering in free recall. Psychol Bull 83:1072–1080

Kiadaliri AA, Englund M, Lohmander LS, Carlsson KS, Frobell RB (2016) No economic benefit of early knee reconstruction over optional delayed reconstruction for ACL tears: registry enriched randomised controlled trial data. Br J Sports Med 50:558–563

Koga H, Nakamae A, Shima Y, Bahr R, Krosshaug T (2018) Hip and ankle kinematics in noncontact anterior cruciate ligament injury situations: video analysis using model-based image matching. Am J Sports Med 46:333–340

Koga H, Nakamae A, Shima Y, Iwasa J, Myklebust G, Engebretsen L et al (2010) Mechanisms for noncontact anterior cruciate ligament injuries: knee joint kinematics in 10 injury situations from female team handball and basketball. Am J Sports Med 38:2218–2225

Krosshaug T, Nakamae A, Boden BP, Engebretsen L, Smith G, Slauterbeck JR et al (2007) Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. Am J Sports Med 35:359–367

Krosshaug T, Steffen K, Kristianslund E, Nilstad A, Mok KM, Myklebust G et al (2016) The vertical drop jump is a poor screening test for ACL injuries in female elite soccer and handball players: a prospective cohort study of 710 athletes. Am J Sports Med 44:874–883

Leppanen M, Pasanen K, Kujala UM, Vasankari T, Kannus P, Ayramo S et al (2017) Stiff landings are associated with increased ACL injury risk in young female basketball and floorball players. Am J Sports Med 45:386–393

Markolf KL, Gorek JF, Kabo JM, Shapiro MS (1990) Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. J Bone Joint Surg Am 72:557–567

Montalvo AM, Schneider DK, Silva PL, Yut L, Webster KE, Riley MA et al (2018) What's my risk of sustaining an ACL injury while playing football (soccer)?' a systematic review with meta-analysis. Br J Sports Med. https://doi.org/10.1136/bjsports-2016-097261

Montero P, Vilar JA (2014) TSclust: an R package for time series clustering. J Stat Softw 62:1–43

Montgomery C, Blackburn J, Withers D, Tierney G, Moran C, Simms C (2018) Mechanisms of ACL injury in professional rugby union: a systematic video analysis of 36 cases. Br J Sports Med 52:994–1001

Murtagh F, Legendre P (2014) Ward's hierarchical agglomerative clustering method: which algorithms implement Ward's criterion? J Classif 31:274–295

Nicholls M, Aspelund T, Ingvarsson T, Briem K (2018) Nationwide study highlights a second peak in ACL tears for women in their early forties. Knee Surg Sports Traumatol Arthrosc 26:648–654

Owusu-Akyaw KA, Kim SY, Spritzer CE, Collins AT, Englander ZA, Utturkar GM et al (2018) Determination of the position of the knee at the time of an anterior cruciate ligament rupture for male versus female patients by an analysis of bone bruises. Am J Sports Med 46:1559–1565

Random.org. True random number service. www.random.org. Accessed June 2016

Sigurethsson HB, Sveinsson T, Briem K (2018) Timing, not magnitude, of force may explain sex-dependent risk of ACL injury. Knee Surg Sports Traumatol Arthrosc 26:2424–2429

Team RC. R: a language and environment for statistical computing. 2018; https://www.R-project.org/

Torry MR, Shelburne KB, Peterson DS, Giphart JE, Krong JP, Myers C et al (2011) Knee kinematic profiles during drop landings: a biplane fluoroscopy study. Med Sci Sports Exerc 43:533–541

van Mechelen W, Hlobil H, Kemper HC (1992) Incidence, severity, aetiology and prevention of sports injuries. A review of concepts. Sports Med 14:82–99

Walden M, Hagglund M, Werner J, Ekstrand J (2011) The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. Knee Surg Sports Traumatol Arthrosc 19:3–10

Walden M, Krosshaug T, Bjorneboe J, Andersen TE, Faul O, Hagglund M (2015) Three distinct mechanisms predominate in non-contact anterior cruciate ligament injuries in male professional football players: a systematic video analysis of 39 cases. Br J Sports Med 49:1452–1460

Publisher's Note

Paper III

Journal of Orthopaedic Research

Kinematic variables observed during ACL injury associated with early peak knee abduction moments during cutting in healthy adolescents

Journal:	*Journal of Orthopaedic Research*
Manuscript ID	JOR-19-0565
Wiley - Manuscript type:	Research Article (Non-Member)
Date Submitted by the Author:	09-Aug-2019
Complete List of Authors:	Sigurðsson, Haraldur; Haskoli Islands, Physical Therapy Karlsson, J.; Sahlgrenska University Hospital (Ostra), Dept. of Orthopaedics Snyder-Mackler, Lynn; Univ. of Delaware, Briem, Kristin; University of Iceland, Physical Therapy; University of Delaware, Biomechanics and Movement Science
Keywords:	ACL, Kinematics and Kinetics, Gait, Biomechanics
Areas of Expertise:	Biomechanics, Cluster analysis, kinematics, gait analysis

Title: Kinematic variables observed during ACL injury associated with early peak knee abduction moments during cutting in healthy adolescents

Haraldur B. Sigurðsson (1, 2, 3), Jón Karlsson (4), Lynn Snyder-Mackler (5) & Kristín Briem (2, 3)

1: Corresponding author. Address: Hringbraut 31, 101 Reykjavík, Iceland. Tel: 00354-8564558.

E-mail: Harbs@hi.is

2. Research Centre for Movement Sciences, University of Iceland

3. Department of Physical Therapy, University of Iceland

4. Department of Orthopaedics, Sahlgrenska University Hospital, Sahlgrenska Academy, Institute of Clinical Sciences, Gothenborg University, Gothenburg, Sweden

5. Department of Physical Therapy, University of Delaware

Running title: Kinematics and early peak moments

Author contribution statements:

HBS collected the data, performed data analysis, and drafted the manuscript. KB designed the study and critically revised the manuscript. JK and LSM critically revised the manuscript.

Abstract:

Studies have shown that cluster analysis of knee abduction moment waveforms may be useful to examine biomechanical data. The aim of this study was to analyze if the knee abduction moment waveform of early peaks, consistent with anterior cruciate ligament injury mechanisms, were associated with foot-trunk distance, knee kinematics, and heel strike landing – all of which have been observed during anterior cruciate ligament injuries. Methods: One-hundred-and-seventy-seven adolescent athletes performed cutting maneuvers, marker-based motion capture collected kinetic and marker data and an 8-segment musculoskeletal model was constructed. Knee abduction moment waveforms were clustered as either a large early peak, or not a large early peak using a two-step process with Euclidean distances and the Ward-d2 cluster method. Results: Medio-lateral distance between foot and trunk were associated with the large early peak waveform with an odds ratio (95% CI) of 3.7 (2.8 – 5.0). Knee flexion angle at initial contact and knee abduction excursions had an odds ratio of 2.2 (1.7 – 2.8) and 2.2 (1.6 – 3.1), respectively. Heel strike landings showed an odds ratio of 1.7 (1.2 – 2.3). Knee flexion excursions and antero-posterior distance between foot and trunk were not associated with the large early peak waveform, odds ratios of 1.4 (1.0 – 2.8) and 1.7 (0.7 – 3.8), respectively. Conclusions and clinical relevance: The knee abduction moment waveform is associated with several kinematic variables observed during ACL injury. The results support intervention programs that can modify these kinematics and thus reduce early stance phase knee abduction moments.

Keywords: Anterior cruciate ligament; cluster analysis; knee; biomechanics; injury prevention

Introduction

Anterior cruciate ligament (ACL) injuries are serious injuries that result in a large societal burden due to the high treatment cost and disease progression [1]. Consequently, efforts to prevent ACL injuries have led to the development of effective intervention programs [2; 3]. These programs have not been widely adopted at least partly due to the time they take [4], and research has yet to identify a plausible biomechanical effect of these programs that is linked to the ACL injury mechanism [5; 6].

Cadaveric impact simulators have reproduced the clinical presentation of ACL rupture by using a combination of an external knee abduction moment (KAM), anterior tibial shear, and internal tibial rotation moment together with an axial impact [7]. Consistent with being an impact injury, both cadaveric studies [8] and video analyses of injuries in-vivo [9] have demonstrated that the ACL injury occurs within 100 ms after initial contact with the ground. The KAM is likely a key component of the injury [7; 10-12], as it leads to greater compression of the femur on the lateral tibial plateau and subsequently to an anterior tibial shear force and internal rotation of the tibia [8; 13]. Studies analyzing video recordings of ACL injuries in-vivo have identified kinematics associated with the ACL rupture such as a heel strike landing [14] and a large base of support to center of mass distance [15]. These kinematics may increase the likelihood of high impact forces that are subsequently transmitted to the ACL.

There is a methodological gap between studies on the ACL injury mechanism and prospective studies evaluating the risk of injury [16], resulting in heterogeneous results. The KAM has been identified as a potential risk factor for ACL injury in a prospective study [17]. However replication studies have failed to corroborate that finding [18; 19]. Prospective biomechanical studies [17-19] have focused on peak values over the whole weight acceptance phase, despite evidence indicating that the injury results from an impact during early stance [20]. The peak KAM during weight acceptance only moderately correlates with the KAM observed during the first 100 ms [21], indicating that the prospective studies have not analyzed impact forces such as those that lead to injury.

One reason for this discrepancy is the technical difficulty in extracting biomechanical data from ground impact forces using traditional 3D motion analysis. The ground impact is a high-frequency signal, but it also generates high frequency artifacts from marker oscillations and movement of the skin relative to the bone [22]. In order to calculate joint moments, the segmental position is derived twice leading to an amplification of the high frequency component of the signal [23]. With respect to filtering strategies, marker data requires a much lower cut-off frequency than force plate data [24], but filtering them unevenly produces artificially large impact artifacts while filtering both signals equally removes the impact peak [23]. The only prospective study that found a link between knee KAM and ACL injury risk used an uneven filtering strategy [17] that produces artificially large impact artifacts, and was therefore more likely to identify the KAM peak in the early stance that is consistent with the timing of injury [25].

An alternative to the magnitude of peak KAM is to categorize the different waveforms of KAM according to the presence or absence of a peak KAM using cluster analysis [26]. Using this method, it's possible to identify which trials present with an early peak KAM with timing consistent with ACL injury [25]. Analyses using videos of actual ACL injuries have identified particular postures associated with the time and occurrence of ACL rupture. If the early peak KAM waveform identified with cluster analysis is associated with ACL injury, it might also be associated with kinematics observed during ACL injury, even in non-injury situations. The aim of this study was to assess if kinematics associated with ACL injury would also be associated with an early peak KAM waveform.

We hypothesized that the following positions at initial contact (IC) would be associated with an early peak knee KAM; 1a) a heel strike landing pose [14], 1b) greater antero-posterior (AP) distance between the base of support and the trunk center of mass [15], 1c) the medio-lateral (ML) distance between the base of support and the trunk center of mass [15], 1d) the knee flexion angle [14]. We further hypothesized that the following kinematics during the first 15% of the stance phase would be associated with the early peak KAM; 2a) knee abduction excursion [27], 2b) knee flexion excursion [20], 2c) knee extension excursion [28], and 2d) trunk lateral flexion excursion [27].

Methods

This is a cross-sectional laboratory study (level of evidence: III). Subjects were recruited from local handball and soccer clubs aged 9-12 (first phase) years, and followed up 5 years later at 14-18 (second phase) years of age. Of the 293 subjects originally recruited, 174 (59%) consented to the follow-up investigation and were used for this analysis. All participants, together with a guardian, signed an informed consent. The study was approved by the Icelandic national bioethics committee, approval code VSNb2012020011/03.07.

The data collection process has been previously reported [29]. In short, participants wore shorts and girls additionally wore athletic tops. A 5-minute stationary bicycle warm-up preceded isometric strength measures of the hip abductors and external rotators. A total of 46 markers were placed on participants and a static measurement was captured to define the musculoskeletal model after which 12 markers were removed. Participants performed bilateral drop jumps and cutting maneuvers in randomized order with 2 familiarization attempts and 5 recorded trials. Cutting maneuvers were performed in a planned direction against a dummy opponent using a self-selected angle from a ready position without a running start. Participants then underwent a 5-minute progressive skateboard exercise intervention before the drop-jumps and cutting maneuvers were repeated in reverse order. An optical motion capture system was used where reflective markers were tracked using the QTM software (Qualisys AB, Gotherborg) and an 8 camera Oqus 300 system sampling at 400 Hz. Ground reaction force data were collected using an AMTI force plate (AMTI, Watertown) sampling at 2000 Hz. For this analysis, only the cutting maneuver task was used, and attempts before and after the skateboard intervention were pooled.

Data analysis:

Data were exported from the QTM software to the c3d file format, which was imported to Visual3D (C-Motion, Germantown) where model construction and calculations were performed. An 8 segment skeletal model was constructed where ankle joint centers were placed midway between malleolar markers [30], knee joint center midway between epicondylar markers [31], the hip joint center was located as 25% of the distance between trochanter markers [32], and trunk motion was simplified as one segment connected to the pelvis by a joint located midway between the iliac crest markers. Segment inertial parameters were assigned using the Visual3D defaults.

Signal processing was done with the aim of retaining the waveform of the KAM during the early stance phase. Unfiltered markers were used to calculate kinematics using the 6-DOF method, and unfiltered force plate data and kinematics were used for kinetics using the inverse dynamics method and normalized by body weight. Joint moments are reported as external moments such that the KAMis the force acting to abduct the knee. Using unfiltered signals for the calculations preserves both the impact peak data and congruity between force data and segmental accelerations [24]. The resulting calculated signals were then lowpass filtered using a single bidirectional pass Butterworth filter at 6 Hz. Using a low-frequency cut-off creates a smooth signal that can be used to cluster analyze the curve shape even though it does introduce an under-estimation of the force magnitudes [23; 33].

The cluster analysis method has been previously described [26]. The initial 15% of the time series of the stance phase was first transformed into the sign of lagged differences and then clustered into discrete shape and then magnitude clusters using Euclidean distances and the Ward-D2 [34; 35] method. The resulting clusters were categorized as either small or large early peaks, or other (non-early peak).

The joint angles, and segment center of mass positions were identified at the time of IC, defined as the time when the vertical ground reaction force crossed a 10N threshold. The distance between the center of mass of the trunk and stance leg foot was calculated as the distance in either the AP or ML directions and normalized by the participants' thigh length. The joint excursions were calculated as the difference between the joint angle at IC, and the peak value observed within 15% of the stance phase duration. To identify a heel strike landing, the angle between the floor and the foot was calculated and negative values in the sagittal plane were taken to be a heel strike landing.

Statistical analysis:

To analyze the relationship between the kinematic variables and the large early peak KAM, sensitivity and specificity were calculated. For continuous variables, a ROC curve was calculated by separating the range of the variable into 100 equally sized parts and calculating the sensitivity and specificity for each cut-off value. The value with the highest Youden's Index [36] was used for hypothesis testing and calculation of the odds ratio. Each trial was classified as either a heel strike landing or not, and the sensitivity and specificity calculated where a heel strike landing was a true positive. The Fisher's exact test with a Bonferroni adjustment for multiple comparisons was used for hypothesis testing, with an alpha of 0.05.

Results

A total of 174 participants completed data collection, of which 73 had discontinued sports participation at the time of initiation of this investigation. Four subjects had incomplete follow-up data and were excluded. The remaining 170 participants provided a total of 3,672 trials that were used for analysis. Subject characteristics are summarized in table 1.

Table 1: Subject characteristics at the follow-up data collection and number of valid trials analyzed (attempts)

Sex	Drop out	Height (mean, cm)	Weight (mean, kg)	Attempts (n)	Athletes (n)
Male	Yes	182	76.9	439	20
	No	177	71.0	871	38
Female	Yes	164	62.9	1128	53
	No	168	62.0	1234	59

Cluster analysis:

A heat map of the Euclidean distances between transformed waveforms is displayed in figure 1. In the initial step, six clusters were formed (figure 2), out of which 3 were classified as having an early peak KAM. In the second clustering step, two clusters were found in the early peak clusters and classified as small or large (figure 3). C-indices for step one and two were < 0.05 and 0.15, respectively (figure 4).

Risk factors for large early peaks:

Descriptive statistics of the kinematic variables are presented in table 2. A total of 260 trials (8% of the total) had the large early peak waveform. ROC curves for the continuous variables are presented in figures 5 (knee kinematics) & 6 (trunk related kinematics). A heel strike landing had a sensitivity of 0.22 and specificity of 0.85 ($P < 0.0001$) for predicting a large early peak KAM. Six of the eight kinematic variables analyzed were associated with the large early peak KAM (table 3), notably a knee flexion angle below 41° at IC had a sensitivity of 0.55 and specificity of 0.63 (figure 5). Knee abduction excursions greater than 0° had the highest sensitivity at 0.82, and a specificity of 0.31 ($P < 0.0001$, figure 5). Knee extension excursions greater than 4° had a sensitivity and specificity of 0.45 and 0.69, respectively ($P < 0.001$, figure 5). The only variables not associated with the frequency of large early peak KAM ($P > 0.05$) were AP distance between stance leg and trunk center of mass (figure 6), and knee flexion excursion (figure 5). Odds-ratios and their confidence intervals and P values are presented in table 4.

Table 2: Means, standard deviations (SD) and number of valid trials (n) for study variables

Variables	Mean	SD	n
COM latero-medial (% thigh length)	0.2	0.16	3,647
COM antero-posterior (% thigh length)	1.0	0.15	3,647
Ankle dorsiflexion (IC) (°)	7	8.89	3,672
Knee flexion (IC) (°)	45	10.96	3,672
Knee abduction excursion (°)	-1	1.26	3,672
Trunk lateral flexion excursion (°)	4	2.95	3,646

Knee flexion excursion (°)	3	4.12	3,672
Knee extension excursion (°)	-2	2.60	3,672
Thigh length (m)	0.41	0.03	3,672

Table 3: Odds ratios and P-values for variables

	Odds ratio	95% Confidence Interval		P-value	Adjusted P
		Lower	Upper		
Heel strike landing	1.7	1.2	2.3	0.00	0.01
COM ant-post	1.7	0.7	3.8	0.25	1.00
COM med-lat	3.7	2.8	5.0	0.00	<0.01
Knee extension excursion	1.4	1.0	1.8	0.04	0.34
Knee flexion excursion	1.9	1.5	2.5	0.00	<0.01
Knee flexion at IC	2.2	1.7	2.8	0.00	<0.01
Knee abduction excursion	2.2	1.6	3.1	0.00	<0.01

Trunk lateral flexion excursion	1.9	1.5	2.5	0.00	<0.01

Abbreviations: COM = Center of mass. Ant-post = anterior to posterior. Med-lat = medial to lateral. IC = initial contact with the ground. Adjusted P value was calculated using a Bonferroni correction.

Discussion

A landing posture with a heel strike (hypothesis 1a), larger ML distance between foot and trunk center of mass (hypothesis 1c), and less knee flexion (hypothesis 1d) were associated with a greater frequency of large early peak knee KAM. Furthermore, during the first 15% of the landing phase, movement into greater knee abduction (hypothesis 2a), knee flexion (hypothesis 2b), and trunk lateral flexion (hypothesis 2d) was associated with a greater frequency of large early peak KAM. Contrary to our hypotheses, a landing posture with a greater AP distance between foot and trunk center of mass was not associated with large early peak KAM (hypothesis 1b), nor was movement into greater knee extension during the initial 15% of the stance phase (hypothesis 2c).

The results of the study show that although a heel strike landing does not guarantee the occurrence of a large early peak KAM, it is, as hypothesized, associated with a greater frequency of large early peaks. A heel strike landing pattern may lead to reduced ability of the joints to absorb the impact force during dynamic movements, and has previously been associated with a greater frequency of impact peaks during running [37].

A larger distance between the foot and trunk center of mass in the ML direction were associated with greater frequency of large early peak KAM (hypothesis 1c), while AP direction distance was not (hypothesis 1b). Sheehan et al. [15] found that during ACL injury, athletes landed with a greater AP distance between the foot and trunk center of mass, however, the change of direction task in the current study is more of a ML movement and this is reflected in our findings. In order to minimize the early stance KAM, the athlete must push actively into the ground away from the body center of mass. When a relatively greater downwards force is acting, consistent with less push laterally into the ground, an early peak KAM is more likely. As the distance between the foot and trunk center of mass increases, it may be increasingly demanding to push laterally into the ground and thus the chance of an early peak KAM may increase. As opposed to a landing or rapid deceleration, an ACL injury during side-stepping may be a predominantly valgus collapse injury mechanism and unaffected by the AP distance between foot and trunk center of mass.

Lower flexion angles at IC were associated with a greater frequency of large early peak KAM (hypothesis 1d) and this is consistent with cadaver studies showing higher strains on the ACL with less knee flexion [38], likely due to tibiofemoral geometry promoting a posterior femoral translation under compression [39]. Stiffer landings, usually defined as lower knee flexion angles at IC and larger first peak vertical ground reaction force, have been associated with greater force absorption at the ankles and less at the knee [40] and greater risk of ACL injury [18]. However, knee extension excursions, indicating a concentric quadriceps contraction immediately after IC and a stiffer landing, were not associated with increased large early peak KAM frequency (hypothesis 2c), supporting a complex relationship between the stiff landing and valgus collapse mechanisms of injury.

Knee flexion excursions during the first 15% of the stance phase were associated with greater large early peak KAM frequency (hypothesis 2b). Lower limb strength has been associated with ACL injury risk [41], and rapid deceleration requires muscular capacity for both high forces and a high rate of force development. A low knee flexion angle at IC may allow for greater knee flexion excursions, and this was supported by a post-hoc calculation that revealed a correlation of -0.57 (Pearson's r) between knee flexion angles at IC and knee flexion excursions. Lower flexion at initial contact and increased flexion excursion may be indicative of a strategy attempting to give the quadriceps muscles more time to decelerate and is associated with more frequent large early peak KAM.

A valgus collapse mechanism has been proposed to explain ACL injuries [42]. The valgus collapse movement pattern is the combination of ankle pronation, knee abduction, hip adduction and internal rotation, and lateral trunk flexion towards the stance leg. The resulting KAM will stretch the ACL and compress the lateral compartment of the tibiofemoral joint, leading to an internal tibial rotation due to the lateral tibial plateau being more posteriorly rotated compared with the medial tibial plateau [43]. We found that knee abduction excursion and trunk lateral flexion excursion were indeed associated with greater frequency of large early peak KAM (hypotheses 2a and 2d). Rather than increasing the landing impact, the knee abduction and lateral trunk flexion excursions can increase the moment arm of the landing force and may therefore result in a larger early peak KAM.

Limitations:

This is the second study to use cluster analysis to classify joint moment waveforms. While it has been proposed that research in the area of biomechanics can benefit from data mining techniques (systematically searching data sets for previously unknown relationships) such as a cluster analysis [44], it is a technique that has not been validated against a hard end-point such as an ACL injury. The present study demonstrates that cluster analysis of the KAM results in categories that have an association with kinematics observed during ACL injury and is congruent with the proposed mechanism of ACL injury. However, prospective studies that examine the relationship between the early peak waveform and subsequent injury are needed.

The use of digital filters on biomechanical data is a source of continued debate [45; 46] and may have affected the shape of the curve. Rather than focus on the accuracy of inverse dynamics joint moment magnitudes, we propose that data should be processed in a way that preserves the usefulness of the data. The usefulness of any biomechanical variable of interest, and the experimental procedures that generated the variable, ultimately needs to be validated against meaningful endpoints such as an ACL injury.

Visual-3D default settings were used for segment inertial properties. The magnitude of joint moments are dependent on inertial properties, but it is unknown to what extent, if any, the KAM waveform is altered.

A decision was made to use the large early peak as the reference group for the calculation of sensitivity and specificity. The large early peak pattern emerged from the cluster analysis method, and no clear point of differentiation exists between the early peak categories, which is reflected in the higher C-Index. The large early peak may not be the only shape of importance in light of the multi-planar nature of an ACL rupture, and a small peak observed during laboratory testing may translate to more frequent and larger KAM early peaks during sports. The choice of using the large early peaks was to create the best conditions to test for the relationship between the kinematic factors and the KAM waveform. To validate a certain magnitude or shape requires the use of hard end-points such as an ACL injury.

Conclusions and clinical relevance

The main findings of this study show that kinematic factors that have been observed during ACL injury are associated with an early peak KAM waveform in a mixed cohort of teenagers performing a change of direction task - a movement where a large portion of ACL injuries occur [47].

These findings provide convergent validity to cluster analysis of the KAM waveform in the early stance phase and support the use of interventions that train athletes to change direction on the balls of the feet, with the foot close to the trunk, with a flexed knee, and to minimize lateral trunk flexion excursions and knee flexion excursions.

Aknowledgements

The authors have no conflicts of interests that would bias or otherwise affect the current study, but would like to acknowledge The Icelandic Centre for Research (http://rannis.is) for funding through the following grants: 120410021, 903271305, 1203250031, and 185359051. The Football Association of Iceland has supported the lead author (HBS) with a travel grant. No funding source was involved in the design or execution of the study, the data analysis, interpretation of results, or the decision to publish the results.

References

1. Kiadaliri AA, Englund M, Lohmander LS, et al. 2016. No economic benefit of early knee reconstruction over optional delayed reconstruction for ACL tears: registry enriched randomised controlled trial data. British journal of sports medicine 50:558-563.
2. Myklebust G, Engebretsen L, Braekken IH, et al. 2007. Prevention of noncontact anterior cruciate ligament injuries in elite and adolescent female team handball athletes. Instructional course lectures 56:407-418.
3. Thorborg K, Krommes KK, Esteve E, et al. 2017. Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: a systematic review and meta-analysis of the FIFA 11 and 11+ programmes. British journal of sports medicine 51:562-571.
4. O'Brien J, Finch CF. 2017. Injury Prevention Exercise Programs for Professional Soccer: Understanding the Perceptions of the End-Users. Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine 27:1-9.
5. Thompson JA, Tran AA, Gatewood CT, et al. 2017. Biomechanical Effects of an Injury Prevention Program in Preadolescent Female Soccer Athletes. The American journal of sports medicine 45:294-301.
6. Zebis MK, Andersen LL, Brandt M, et al. 2016. Effects of evidence-based prevention training on neuromuscular and biomechanical risk factors for ACL injury in adolescent female athletes: a randomised controlled trial. British journal of sports medicine 50:552-557.

7. Bates NA, Schilaty ND, Nagelli CV, et al. 2018. Validation of Noncontact Anterior Cruciate Ligament Tears Produced by a Mechanical Impact Simulator Against the Clinical Presentation of Injury. The American journal of sports medicine 46:2113-2121.

8. Kiapour AM, Quatman CE, Goel VK, et al. 2014. Timing sequence of multi-planar knee kinematics revealed by physiologic cadaveric simulation of landing: Implications for ACL injury mechanism. Clinical Biomechanics 29:75-82.

9. Krosshaug T, Nakamae A, Boden BP, et al. 2007. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. The American journal of sports medicine 35:359-367.

10. McPherson AL, Bates NA, Schilaty ND, et al. 2018. Ligament Strain Response Between Lower Extremity Contralateral Pairs During In Vitro Landing Simulation. Orthopaedic journal of sports medicine 6:2325967118765978.

11. Markolf KL, Burchfield DM, Shapiro MM, et al. 1995. Combined knee loading states that generate high anterior cruciate ligament forces. Journal of orthopaedic research : official publication of the Orthopaedic Research Society 13:930-935.

12. Markolf KL, Gorek JF, Kabo JM, et al. 1990. Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. The Journal of bone and joint surgery American volume 72:557-567.

13. Navacchia A, Bates NA, Schilaty ND, et al. 2019. Knee Abduction and Internal Rotation Moments Increase ACL Force During Landing Through the Posterior Slope of the Tibia. Journal of orthopaedic research : official publication of the Orthopaedic Research Society.

14. Montgomery C, Blackburn J, Withers D, et al. 2018. Mechanisms of ACL injury in professional rugby union: a systematic video analysis of 36 cases. British journal of sports medicine 52:994-1001.

15. Sheehan FT, Sipprell WH, 3rd, Boden BP. 2012. Dynamic sagittal plane trunk control during anterior cruciate ligament injury. The American journal of sports medicine 40:1068-1074.

16. Dai BY, Mao DW, Garrett WE, et al. 2014. Anterior cruciate ligament injuries in soccer: Loading mechanisms, risk factors, and prevention programs. Journal of Sport and Health Science 3:299-306.

17. Hewett TE, Myer GD, Ford KR, et al. 2005. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. The American journal of sports medicine 33:492-501.

18. Leppanen M, Pasanen K, Kujala UM, et al. 2017. Stiff Landings Are Associated With Increased ACL Injury Risk in Young Female Basketball and Floorball Players. The American journal of sports medicine 45:386-393.

19. Krosshaug T, Steffen K, Kristianslund E, et al. 2016. The Vertical Drop Jump Is a Poor Screening Test for ACL Injuries in Female Elite Soccer and Handball Players: A Prospective Cohort Study of 710 Athletes. The American journal of sports medicine 44:874-883.

20. Koga H, Nakamae A, Shima Y, et al. 2010. Mechanisms for noncontact anterior cruciate ligament injuries: knee joint kinematics in 10 injury situations from female team handball and basketball. The American journal of sports medicine 38:2218-2225.

21. Sigurethsson HB, Sveinsson T, Briem K. 2018. Timing, not magnitude, of force may explain sex-dependent risk of ACL injury. Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA 26:2424-2429.

22. Tsai TY, Lu TW, Kuo MY, et al. 2011. Effects of soft tissue artifacts on the calculated kinematics and kinetics of the knee during stair-ascent. Journal of biomechanics 44:1182-1188.

23. Bisseling RW, Hof AL. 2006. Handling of impact forces in inverse dynamics. Journal of biomechanics 39:2438-2444.

24. Ren L, Jones RK, Howard D. 2008. Whole body inverse dynamics over a complete gait cycle based only on measured kinematics. Journal of biomechanics 41:2750-2759.

25. Koga H, Nakamae A, Shima Y, et al. 2018. Hip and Ankle Kinematics in Noncontact Anterior Cruciate Ligament Injury Situations: Video Analysis Using Model-Based Image Matching. The American journal of sports medicine 46:333-340.

26. Sigurðsson HB, Bríem K. 2019. Cluster analysis successfully identifies clinically meaningful knee valgus moment patterns: Frequency of early peaks reflects sex-specific ACL injury incidence. Medical Archives.

27. Hewett TE, Torg JS, Boden BP. 2009. Video analysis of trunk and knee motion during non-contact anterior cruciate ligament injury in female athletes: lateral trunk and knee abduction motion are combined components of the injury mechanism. British journal of sports medicine 43:417-422.

28. DeMorat G, Weinhold P, Blackburn T, et al. 2004. Aggressive quadriceps loading can induce noncontact anterior cruciate ligament injury. The American journal of sports medicine 32:477-483.

29. Briem K, Jonsdottir KV, Arnason A, et al. 2017. Effects of Sex and Fatigue on Biomechanical Measures During the Drop-Jump Task in Children. Orthopaedic journal of sports medicine 5:2325967116679640.

30. Davis RB, Õunpuu S, Tyburski D, et al. 1991. A gait analysis data collection and reduction technique. Human Movement Science 10:575-587.

31. Sinclair J, Hebron J, Taylor PJ. 2015. The test-retest reliability of knee joint center location techniques. Journal of applied biomechanics 31:117-121.

32. Weinhandl JT, O'Connor KM. 2010. Assessment of a greater trochanter-based method of locating the hip joint center. Journal of biomechanics 43:2633-2636.

33. Shin S, Yoo B, Han S. 2015. Automatic spline smoothing of non-stationary kinematic signals using bilayered partitioning and blending with correlation analysis. Digital Signal Processing 39:22-34.

34. Murtagh F, Legendre P. 2014. Ward’s Hierarchical Agglomerative Clustering Method: Which Algorithms Implement Ward’s Criterion? Journal of Classification 31:274-295.

35. Charrad M, Ghazzali N, Boiteau V, et al. 2014. Nbclust: An R Package for Determining the Relevant Number of Clusters in a Data Set. Journal of Statistical Software 61:1-36.

36. Hajian-Tilaki K. 2018. The choice of methods in determining the optimal cut-off value for quantitative diagnostic test evaluation. Stat Methods Med Res 27:2374-2383.

37. Nordin AD, Dufek JS, Mercer JA. 2017. Three-dimensional impact kinetics with foot-strike manipulations during running. J Sport Health Sci 6:489-497.

38. Mizuno K, Andrish JT, van den Bogert AJ, et al. 2009. Gender dimorphic ACL strain in response to combined dynamic 3D knee joint loading: implications for ACL injury risk. The Knee 16:432-440.

39. Sturnick DR, Van Gorder R, Vacek PM, et al. 2014. Tibial articular cartilage and meniscus geometries combine to influence female risk of anterior cruciate ligament injury. Journal of orthopaedic research : official publication of the Orthopaedic Research Society 32:1487-1494.

40. Devita P, Skelly WA. 1992. Effect of landing stiffness on joint kinetics and energetics in the lower extremity. Medicine and science in sports and exercise 24:108-115.

41. Ryman Augustsson S, Ageberg E. 2017. Weaker lower extremity muscle strength predicts traumatic knee injury in youth female but not male athletes. BMJ Open Sport &amp; Exercise Medicine 3.

42. Kiapour AM, Demetropoulos CK, Kiapour A, et al. 2016. Strain Response of the Anterior Cruciate Ligament to Uniplanar and Multiplanar Loads During Simulated Landings: Implications for Injury Mechanism. The American journal of sports medicine 44:2087-2096.

43. Kiapour AM, Kiapour A, Goel VK, et al. 2015. Uni-directional coupling between tibiofemoral frontal and axial plane rotation supports valgus collapse mechanism of ACL injury. Journal of biomechanics 48:1745-1751.

44. Halilaj E, Rajagopal A, Fiterau M, et al. 2018. Machine learning in human movement biomechanics: Best practices, common pitfalls, and new opportunities. Journal of biomechanics 81:1-11.

45. Roewer BD, Ford KR, Myer GD, et al. 2014. The 'impact' of force filtering cut-off frequency on the peak knee abduction moment during landing: artefact or 'artifiction'? British journal of sports medicine 48:464-468.

46. Kristianslund E, Krosshaug T, van den Bogert AJ. 2012. Effect of low pass filtering on joint moments from inverse dynamics: implications for injury prevention. Journal of biomechanics 45:666-671.

47. Walden M, Krosshaug T, Bjorneboe J, et al. 2015. Three distinct mechanisms predominate in non-contact anterior cruciate ligament injuries in male professional football players: a systematic video analysis of 39 cases. British journal of sports medicine 49:1452-1460.

Figure 1: Heat map of Euclidean distances between direction reduced knee valgus moment time series. The x and y axis contain each of the time series and the distance between each observation pair is represented by the color.

Figure 2: Six shapes from initial clustering of transformed time series. Clusters 4, 5 and 6 were classified as an early peak. Gray shaded area is the 95% confidence interval of the graph smoothing process.

442

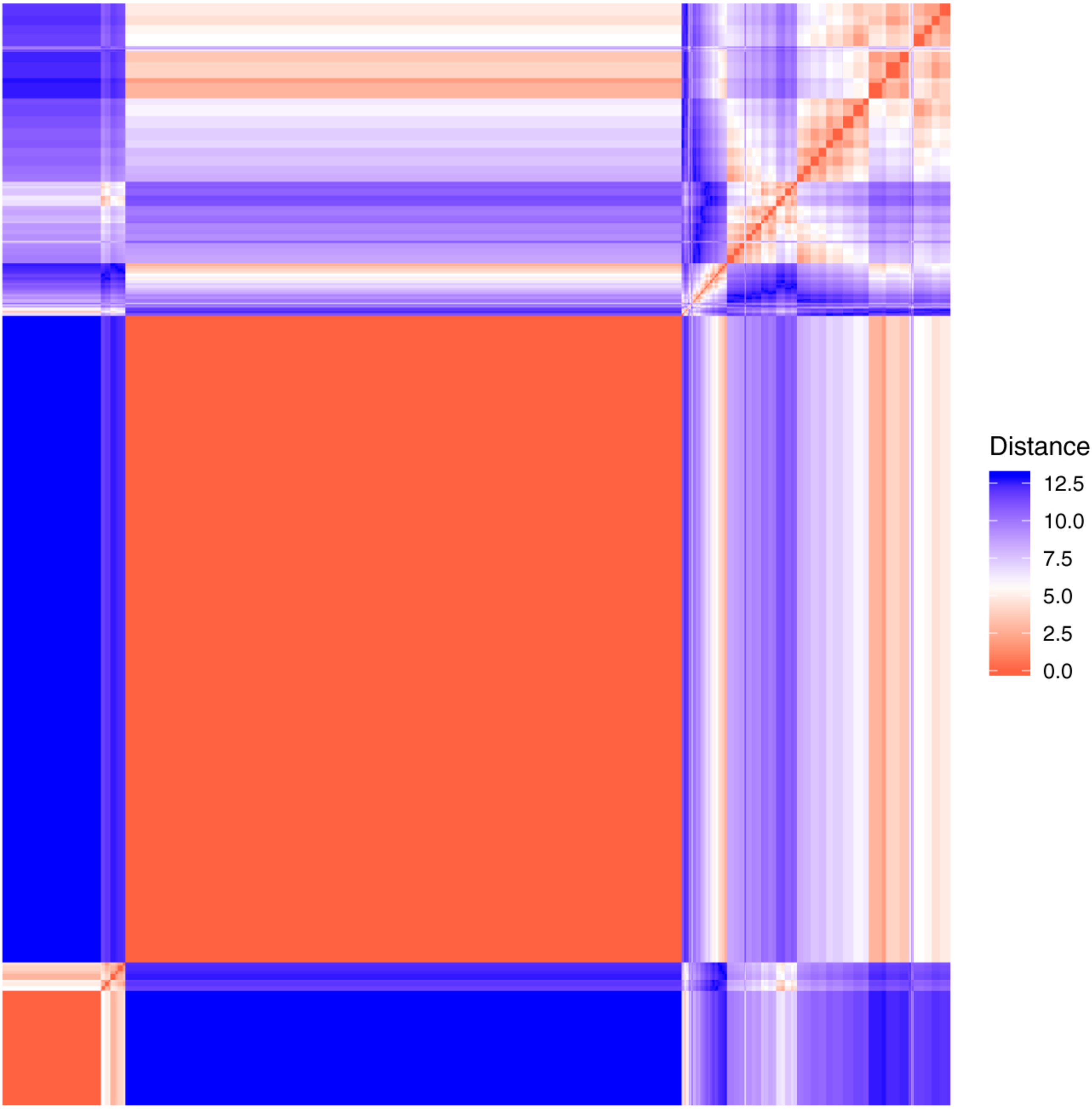
Figure *3*: Clusters based on Euclidean distances of non-transformed time series of clusters classified as an early peak. Cluster #2 was classified as the large early peak.

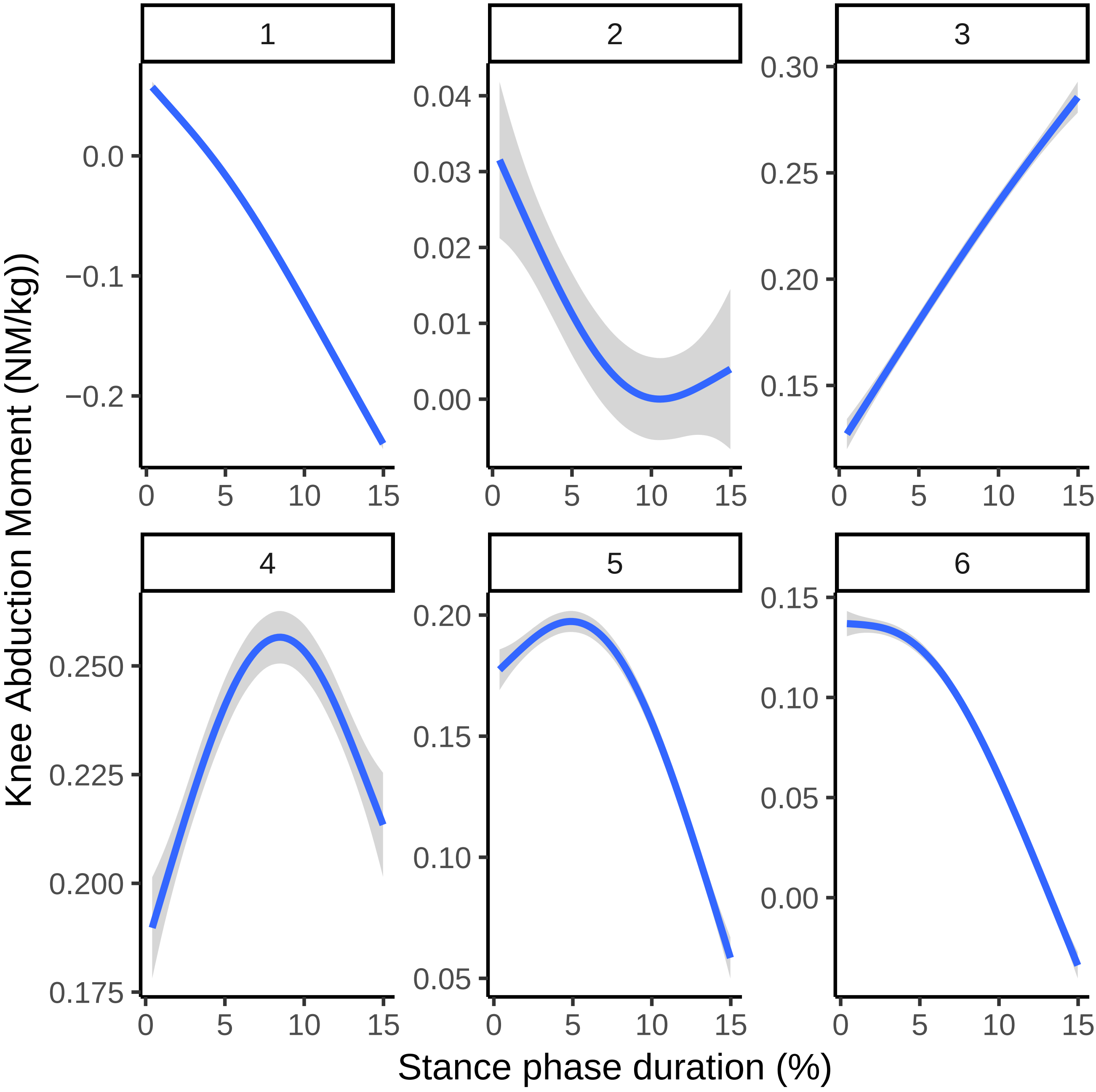
443

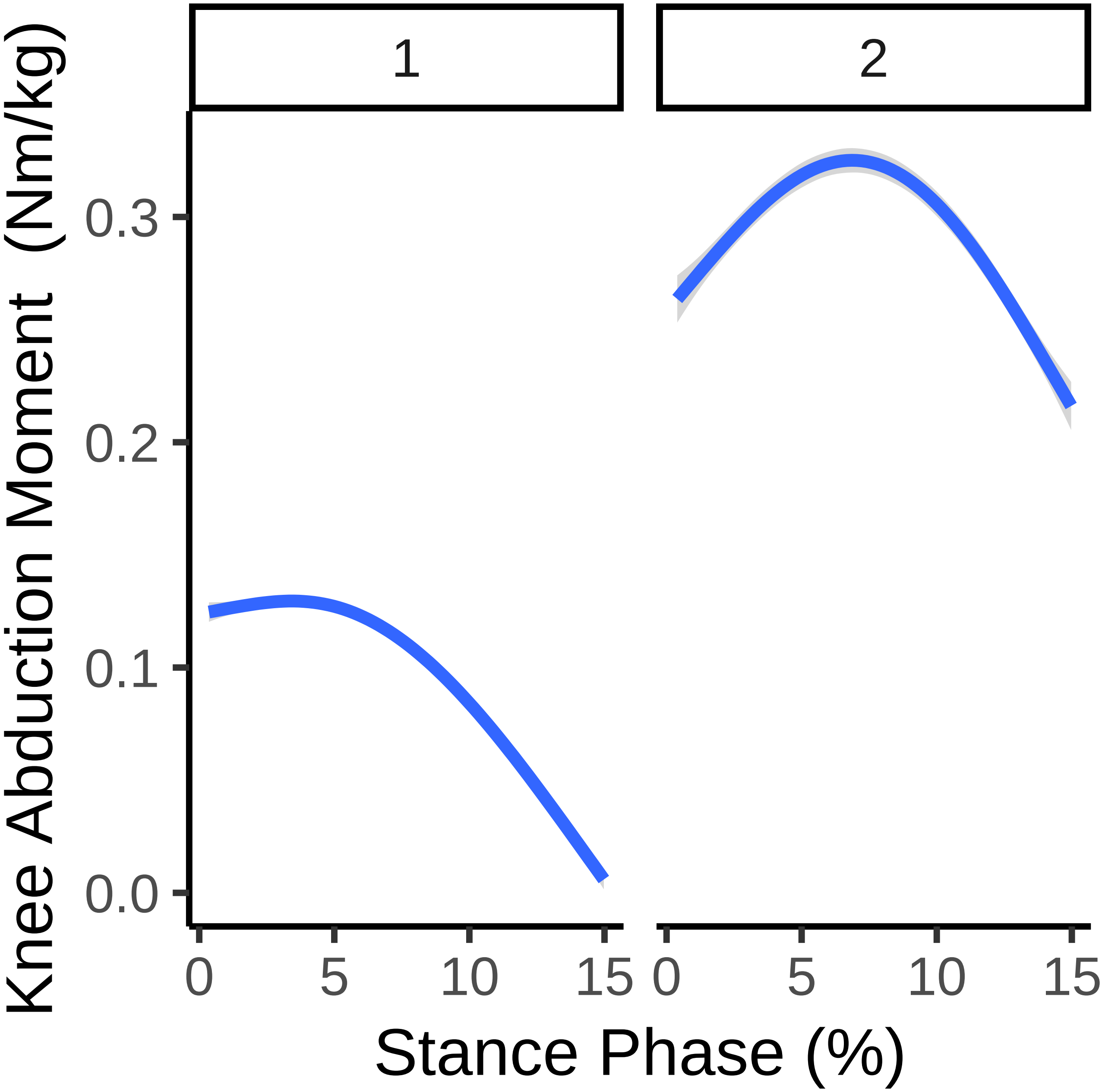
Figure 4: C-Index plots for the first (A) and second (B) cluster analysis steps. The C-Index is a ratio of how similar observations within a cluster are compared to how similar they are to other observations. A lower number indicates more clearly defined clusters.

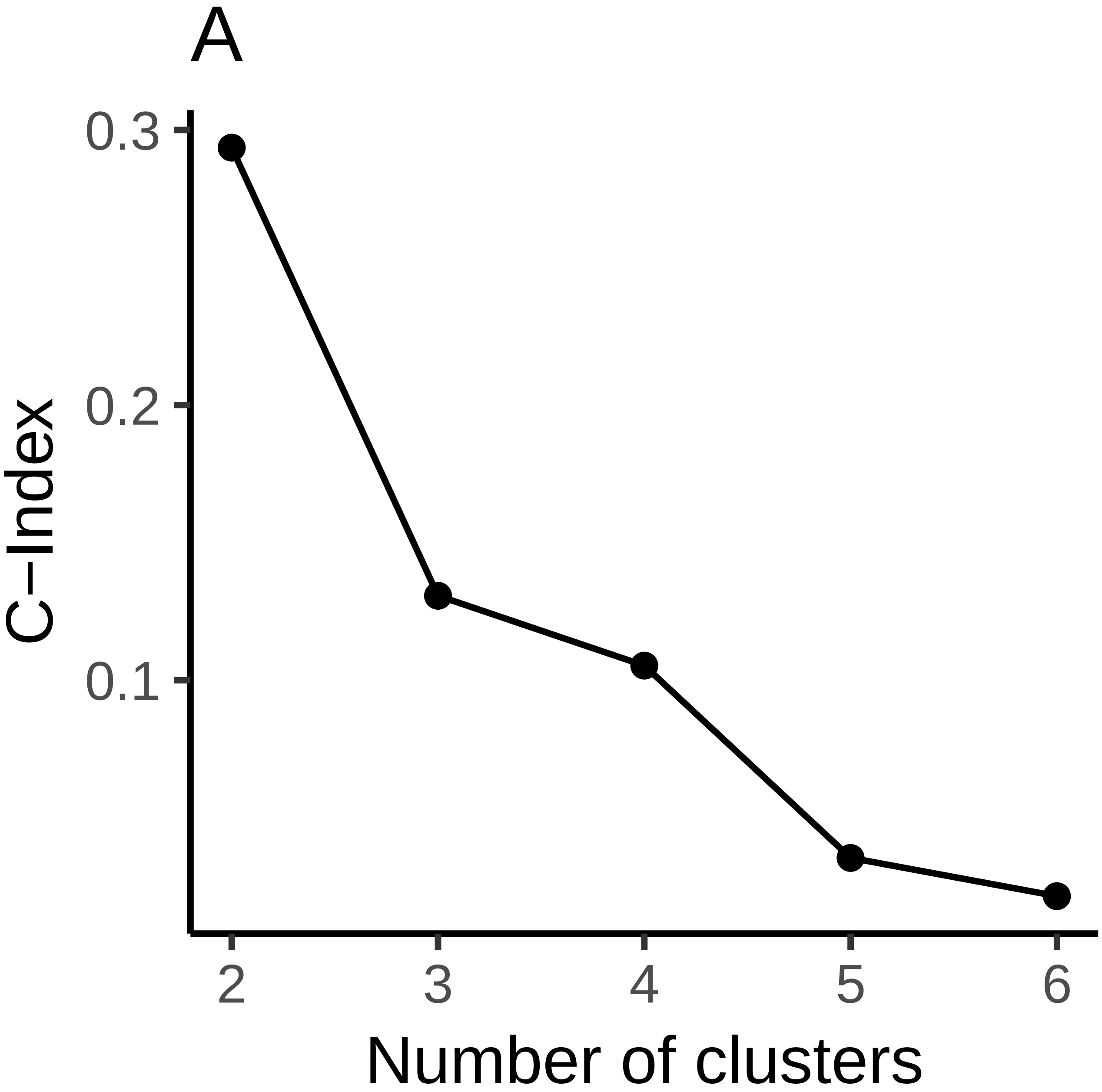
Figure 5: ROC of knee angles and excursions. Numeric labels on the line refers to the cut-off with the high Youden's Index. Abbreviations: IC = Initial contact

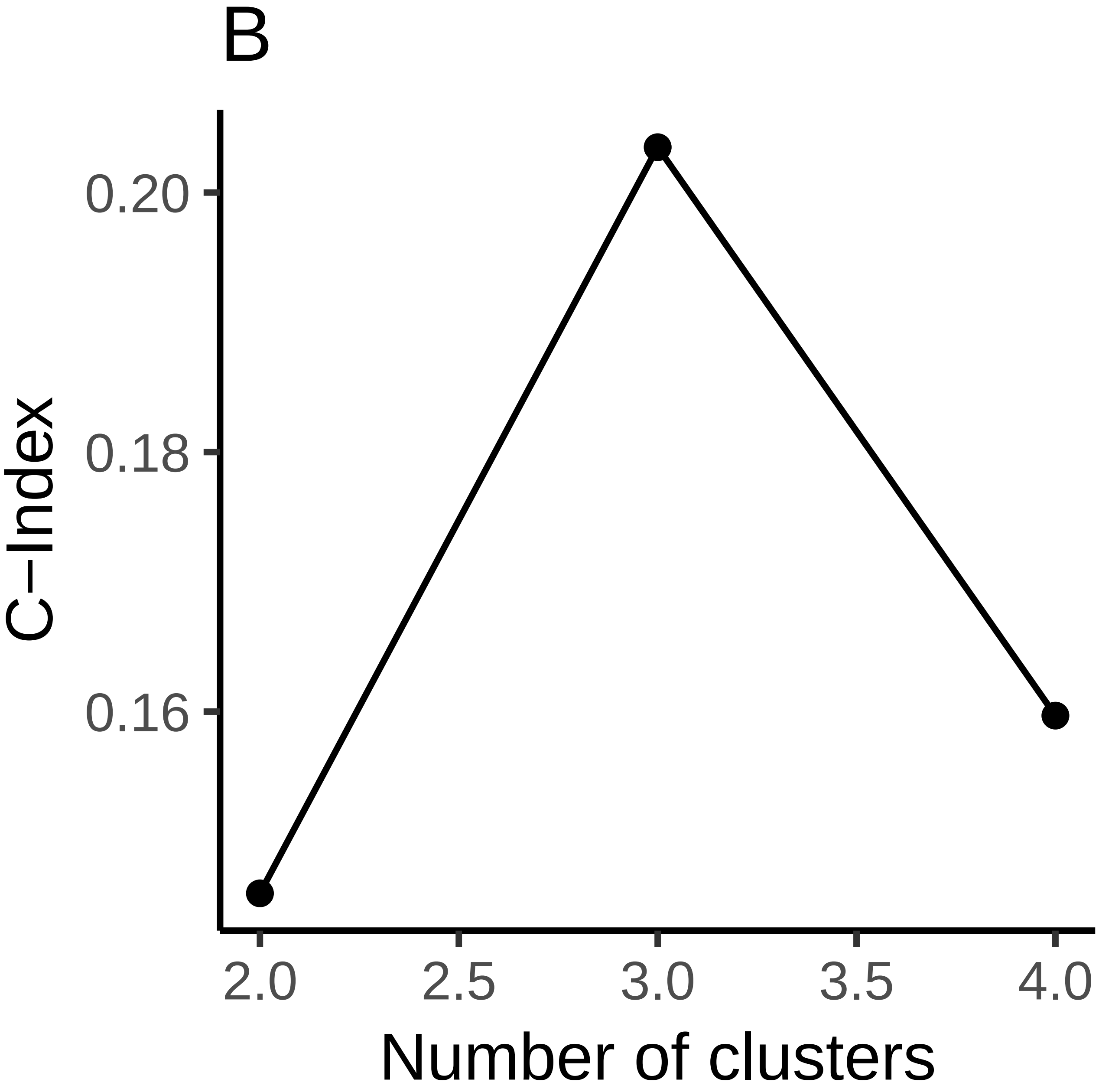
Figure 6: ROC of trunk related variables . Numeric labels on the line refers to the cut-off value with the highest Youden's Index. Distances expressed as % of thigh length. Abbreviations: COM = Center of Mass, BOS = Base of Support, ML = Medio-lateral, AP = Antero-Posterior, Lat-flex = Lateral flexion

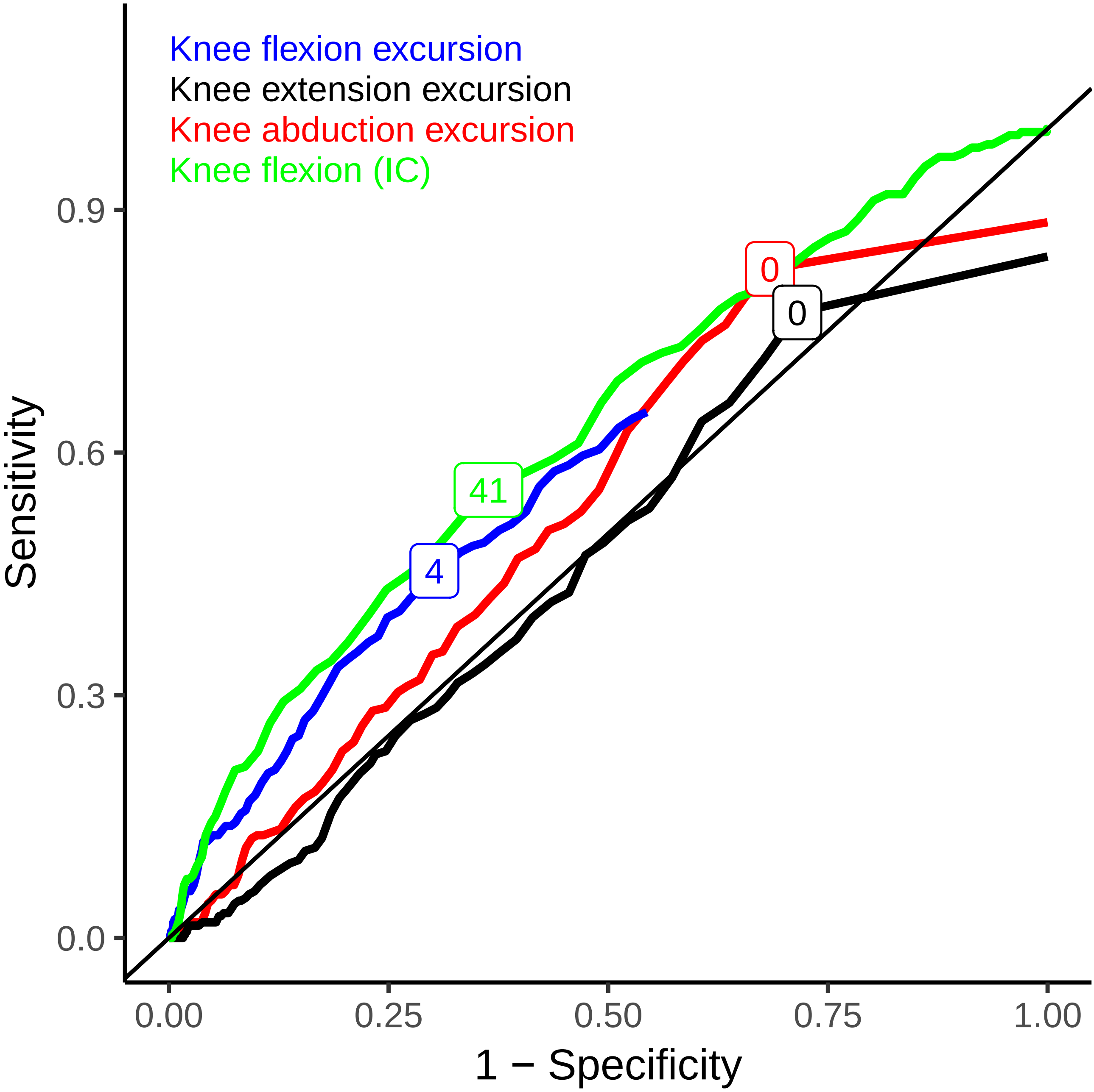

Distance
12.5
10.0
7.5
5.0
2.5
0.0

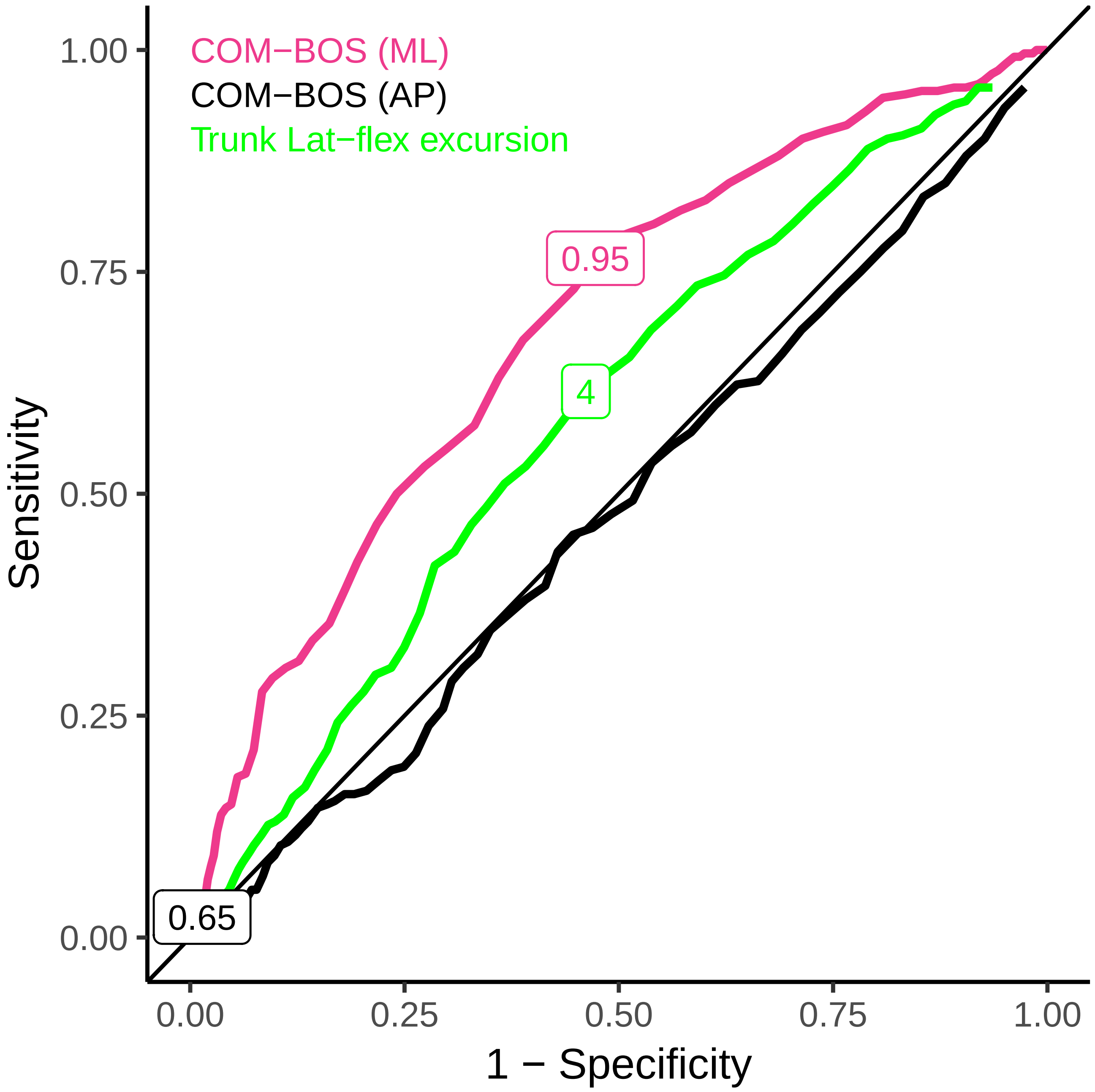

1
2
3
4
5
6
Knee Abduction Moment (NM/kg))
Stance phase duration (%)
0.0
−0.1
−0.2
0.04
0.03
0.02
0.01
0.00
0.30
0.25
0.20
0.15
0.250
0.225
0.200
0.175
0.20
0.15
0.10
0.05
0.15
0.10
0.05
0.00
0
5
10
15


1
2
Knee Abduction Moment (Nm/kg)
0.3
0.2
0.1
0.0
0
5
10
15
0
5
10
15
Stance Phase (%)


A
0.3
0.2
0.1
C−Index
2
3
4
5
6
Number of clusters


B
C−Index
0.20
0.18
0.16
2.0
2.5
3.0
3.5
4.0
Number of clusters


Knee flexion excursion
Knee extension excursion
Knee abduction excursion
Knee flexion (IC)
0.9
0.6
0.3
0.0
Sensitivity
0.00
0.25
0.50
0.75
1.00
1 − Specificity
41
4
0
0


COM−BOS (ML)
COM−BOS (AP)
Trunk Lat−flex excursion
0.95
4
0.65
Sensitivity
1.00
0.75
0.50
0.25
0.00
0.00
0.25
0.50
0.75
1.00
1 − Specificity

Appendix A – Cluster analysis method explained

Central to papers II & III is the cluster analysis method which was developed for this thesis. The method combines well known cluster analysis algorithms with data transformations which allow for good clustering results. The purpose of this appendix is to use a small data set to visualize the problems inherent in cluster analyzing the knee VM data and to visually demonstrate in greater detail the cluster procedure used for the thesis.

6.1 Selected data

Data was selected such that there were three early peaks and three non-early peaks. The early peaks were chosen at random. Since some of the methods presented require a non-0 standard deviation of the series, not all non-early peak series were usable. The non-early peak series were therefore selected at random from a subset of peaks. The series are presented in Figure 6.

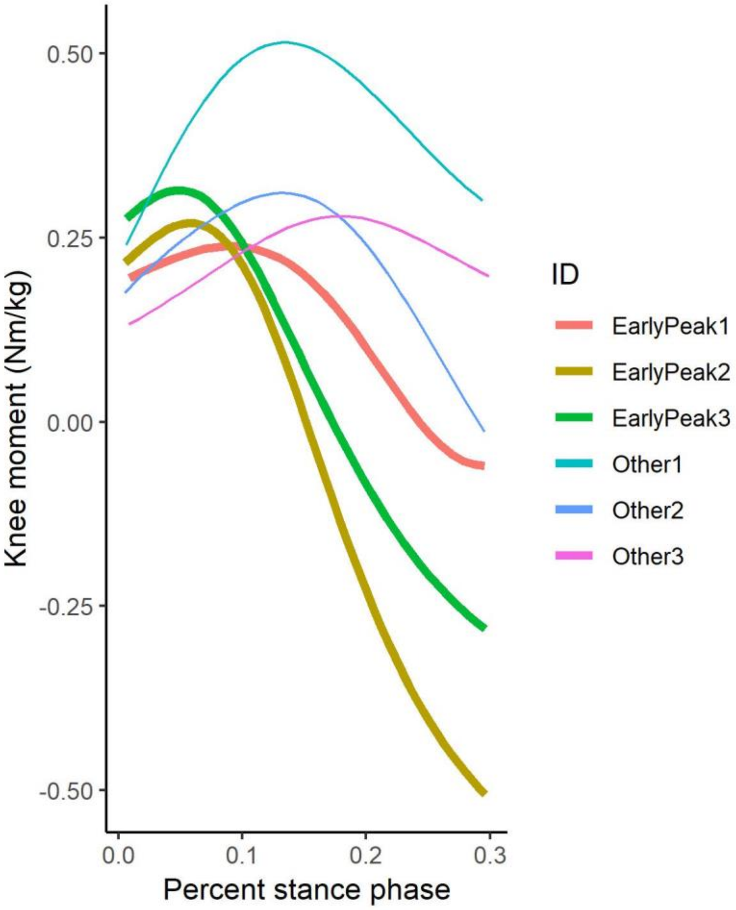


Figure 8 Simulated time series data. The early peaks (peak before 15% stance phase) are denoted by a thicker line for easier viewing.

6.2 Distance matrices

At least four different distance metrics could be useful to cluster the data set. In correlational distances (Figure 7, top left), the distance between two observations is represented with their correlation coefficient. With Euclidean distances (Figure 7, top right), the mean squared distance between every data point of each observation is the distance between them. Time warped distances (Figure 7, bottom left) are similar to Euclidean distances, but the time series are warped to minimize the distances. The minimum distance of a symbolically aggregated curve (Figure 7, bottom right) first transforms the data into four discrete symbols, and uses the lower bound of the Euclidean distance.

The ideal clustering method correctly identifies each shape as belonging with each other. This can be seen on order of observations on the axis of the heatmaps (Figure 7). Large red boxes represent good clusters, and ideally members of a group should be closer to other members of the same group, than to members of the other group (the C-Index).

The correlation distance metric creates good clusters for the series chosen, but Other2 is closer to the early peaks than to it’s own group. The Euclidean and timewarp distances do not form clusters on non-transformed data. The symbolically aggregated method produces the best clusters on non-transformed data forming the two groups, however the error rate (seen by Other2 having membership in both groups) was found to be high.

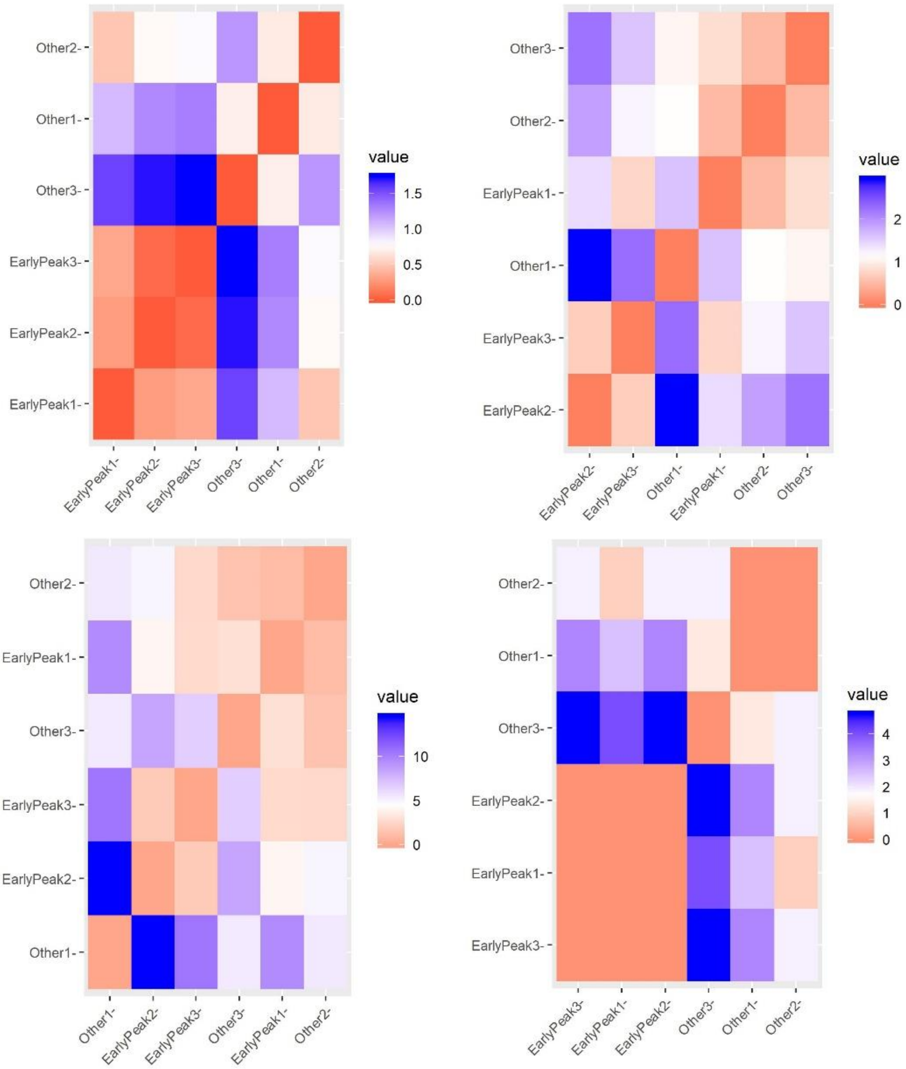


Figure 9 Heat map of distance matrices. Top left, correlational distance. Top right, Euclidian distance. Bottom left, time warp distance. Bottom right, minimum distance, symbolically aggregated.

6.3 Data transformation

None of the distance matrices with non-transformed data result in adequate clusters based on the waveform. A transformation of the data is required to improve the cluster analysis result, which retains all information regarding the shape of the curve, and discards other features.

The transformation used was to differentiate the curve and take the sign. So an increase in the signal for one frame is assigned “1”, while a decrease for one frame is assigned a “-1”. Figure 8 shows the same transformed time series.

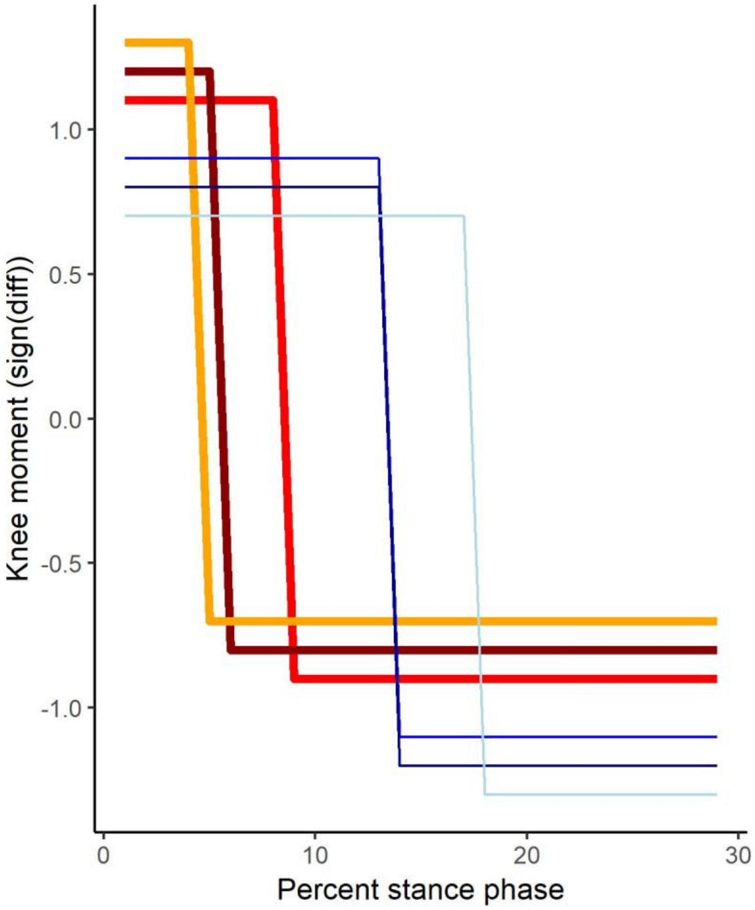


Figure 10 Transformed time series. Values range from -1 (decreasing) to 1 (increasing), but each series is nudged slightly to prevent them from overlapping. Thick lines denote the early peaks.

6.4 New distances matrices

Figure 9 shows the new distance matrices for the transformed data set. Most of the distance metrics have improved somewhat after the transformation. The correlation distance, the Euclidean distance, and the symbolically aggregated distance all correctly identify both groups. After the transformation, the time-warp distances produces are all equal to zero. This happens since all series can be laterally translated on top of each other after the transformation, and the timewarp distance metric indeed produces the minimum possible distance between series regardless of the time point. Before the transformation, the timewarp distances on scaled data produce good differentiation based on shape, but can not distinguish between early peaks and later peaks.

Since the transformation used in the thesis is similar to the transformation performed during the symbolic aggregation the results from those two methods are nearly identical. The difference is that symbolic aggregation uses four symbols while the transformation uses mainly two but up to three (since two equal values in a row produce a zero).

The correlation distance produces smaller distances within each cluster, but also smaller distances between the clusters. The Euclidean distances are greater between clusters and also greater within clusters. The Euclidean distances therefore will produce a larger amount of clusters (higher C-Index) but with fewer errors compared to the correlation distances. Both steps require a visual inspection step where clusters are combined based on the key element (presence of early peak). For this reason, the lower error rate of the Euclidean distances produces superior results.

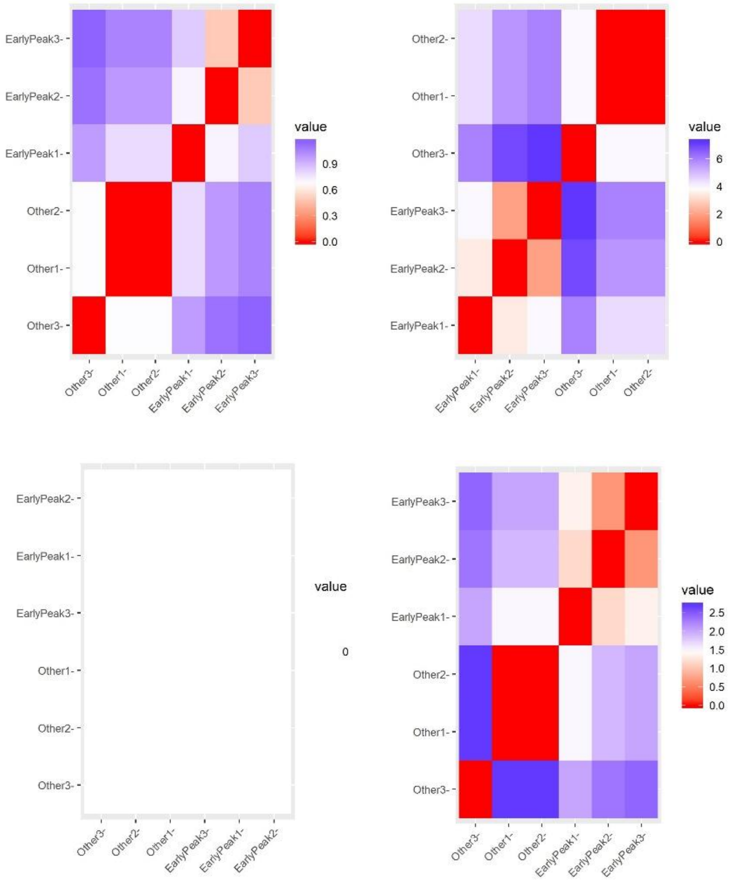


Figure 11 Distance matrices for transformed time series. Top left, correlational distance. Top right, Euclidian distance. Bottom left, time warp distance. Bottom right, minimum distance, symbolically aggregated.Note that the labels on top right, the Euclidian distances, are ordered such that earlypeaks are together, and peaks together.

Appendix B – Effect of sex on ACL injury related biomechanics during the cutting manoeuvre in pre-adolescent athletes

Abstract

Background: Two movement patterns are associated with ACL injury, the dynamic valgus and the stiff landing. Although sex dependent differences have been identified for adults, less is known for preadolescent athletes regarding movement patterns known to load the ACL.

Purpose: We hypothesised that no sex-specific differences in the ACL loading movement patterns would be found in pre-adolescent athletes during a cutting manoeuvre.

Study Design: Cross-sectional laboratory study.

Methods: Male and female soccer and handball players (age 9-12 years; n=288) were recruited. A motion capture system synchronized to a force platform was used to record 5 trials of a cutting manoeuvre, before and after a 5-minute fatigue intervention. Linear mixed models were constructed and an ANOVA was used to analyse differences in outcomes associated with the sex of the athletes.

Results: Boys showed greater forces for peak knee valgus moments (boys: 0.26 Nm/kg, girls: 0.22 Nm/kg, P=0.048), peak knee internal rotation moment (boys: -0.13 Nm/kg, girls: -0.10 Nm/kg, P=0.021), knee rotation excursion (boys: -7.9°, girls: -6.9°, P=0.014) and knee extension excursion (boys: 2.7°, girls: 1.4°, P<.001), compared to girls. Sex*fatigue interaction was significant for the first peak vGRF (boys pre: 16.4 N/kg, post: 16.5 N/kg; girls pre: 15.3 N/kg; post: 16.0 N/kg, F = 7.6, P = 0.006).

Conclusion: Differences detected for biomechanical factors during the cutting manoeuvre do not point to greater ACL injury risk for pre- or early pubescent girls than for boys. Nonetheless, girls go on to develop more detrimental movement patterns than boys in terms of biomechanical risk factors. Implementation of preventive training may therefore be indicated during the early teens in order to influence movement patterns.

Clinical Relevance: Early adolescence is a good target age to learn and develop muscular control, balance, strength, flexibility, jumping, running and landing control. This time of physical

and athletic growth may therefore be an appropriate period to influence biomechanical factors and thereby task execution and injury risk.

What is known about the subject: (not included in word count): Adult female athletes have higher risk for ACL injury compared to males. Females have a greater peak knee valgus moment during drop jump landings, but prospective risk factor studies show mixed results for its predictive value.

What this study adds to existing knowledge (not included in word count): This study shows the differences between pre-pubertal boys and girls and for the first time explores the effects of fatigue protocol on lower limb neuromuscular function. The results indicate that early adolescence may be an appropriate time to introduce neuro-muscular training programs.

Keywords: ACL, injury prevention, cutting manoeuvre, biomechanics, sports medicine.

INTRODUCTION

Anterior cruciate ligament (ACL) injuries are one of the most serious injuries of the lower limb and can result in a relatively low rate of return to sport[1], decreased quality of life in later years[2], and a high rate of knee osteoarthritis[3]. It is an expensive injury, with surgical cost for ACL reconstruction alone reportedly lying between $5000 to $17 000[4].

The ACL is the primary restraint against anterior tibial translation[5] which is difficult to quantify with 3D movement analysis using reflective markers due to soft tissue artefacts[6]. However, the ACL has been demonstrated by cadaveric studies to be loaded through tibiofemoral compression[7] as well as tibial internal rotation (IRM) and knee valgus moments (VM)[8]. Furthermore, prospective studies have proposed the VM[9] and tibiofemoral compression (as per the vertical ground reaction force (vGRF))[10] as risk factors for ACL injuries, and these variables can be estimated with 3D motion analysis[11,12].

Compared to males, adult female athletes show a 2-3 fold increased incidence in ACL injury per hour of exposure[13]. Myer et al.[14] state in their review article that the most ACL injuries in female athletes occur during a non-contact episode, typically during deceleration, lateral pivoting, or landing tasks that are often associated with high external knee joint loads. The incidence of ACL injuries in youngsters has been rising over the last few years. A recent Australian study reported an almost 150% increase in hospital-treated ACL injuries from 2005-2015 in youngsters aged 5-14 years (from 2.74 to 6.79 per 100,000 person years)[15].

Although Briem et al[16] found girls and boys adopted different landing strategies during DJ performance and were differently affected by fatigue, others have not observed sex-related differences in ACL risk factors prior to puberty during the cutting maneuvre[17]. Several systematic reviews have examined the effects of fatigue and how fatiguing interventions affect the kinetics and kinematics of the lower extremity in older athletes[18–20]. However, fatigue protocols appear to have inconsistent effects on the lower limb kinematic or kinetic variables known to increase ACL injury risk[18].

Few studies have contrasted biomechanical risk factors of ACL injury of boy and girl athletes during the execution of a cutting manoeuvre task. Importantly, none have focused specifically on the timeframe of injury occurrence or attempted to induce fatigue to assess how this may influence performance. Therefore, the aim of this study was to compare kinematics and kinetics relevant to ACL injury of males and females aged 9-12 within the first 100 ms of the cutting manoeuvre, which is the time-frame where ACL injuries occur[21]. To the best of our knowledge this is the first study that investigates effects of both, sex and fatigue intervention, on ACL injury related biomechanics during the cutting manoeuvre in pre-adolescent athletes. Based on previous findings of DJ maneuver[16], we hypothesized that sex-specific biomechanical differences (kinematic and kinetic) would be found and that differences between the sexs would be observed for the fatigue intervention.

METHODS

Participants

After receiving ethical approval for the study from a National Bioethics Committee (approval code VSNb2012020011/03.07), a total of 293 participants were recruited from local handball and soccer clubs, but data from 288 athletes were used for the further analysis. Data for five participants were excluded due to technical errors or erroneous performance. Athletes were aged between 9 and 12 years and were recruited from the teams' age-based training groups. Exclusion criteria were history of torn knee ligaments or muscles of the lower extremities, intraarticular corticosteroid injection within the previous 3 months, neurological impairment, impaired balance, and any orthopaedic problems of the lower limb. Prior to participation, all procedures were explained to each athlete and informed consent was signed by the participant and a parent or guardian.

Table 1. Participant characteristics.

	Group	
Variable	**Boys (n=100)**	**Girls (n=188)**
Age (yr)	10.6 ± 0.7	10.8 ± 0.8
Height (cm)	150 ± 7.9	150 ± 7.9
Weight (kg)	40.9 ± 8.0	41.7 ± 8.8

Data are reported as mean ± SD. There were no statistically significant differences in any variable between males and females.

Data collection

Kinematics were collected at 200 Hz using a marker set with 46 markers and an 8-camera Qualisys motion capture cameras (Qualisys Corp, Sweden) positioned around a calibrated test area. Kinetics were simultaneously collected at 2000 Hz from a force platform (AMTI, Watertown, MA) embedded into the floor. Where possible markers were placed directly onto the skin, to minimize movement artefacts resulting from loose clothing. A static measurement was used to define segments and joint centres based on anatomic markers, while clusters of 3 to 4 markers tracked each segment during dynamic trials. Marker based kinematics and kinetics have been shown to be highly reliable[22] but display systematic errors in knee abduction angles, especially at higher flexion angles[12].

After warming up on a stationary bicycle for 5 minutes and performing preparatory cutting manoeuvres, participants performed 5 cutting manoeuvres against a dummy opponent. The movement was performed from a ready position without a run-up using a self-selected change of direction angle. Athletes took a quick sideways step on to the tested leg before accelerating to a maximal take-off away from the tested leg. Athletes were encouraged to use as much speed and explosiveness as they could. The order of testing was randomized with a coin flip and 5 valid trials were collected for each leg. A fatigue protocol described by Briem et al.[16], was then implemented, after which the subject performed another set of cutting tasks. The purpose of the fatigue intervention was to analyse how fatigue affected the execution.

Data synthesis and statistical analysis

Kinematic and kinetic outcome variables within the first 100 ms of stance were chosen as markers for ACL loading according to two proposed injury mechanisms supported by prospective risk factor studies[23]. The first cluster of outcome variables reflected dynamic valgus collapse based on the peak magnitude of knee VM and IRM, knee frontal and transverse plane excursions as well as knee valgus angle and knee rotation angle at IC. The second cluster of outcome variables reflected stiff landings[10] as determined by values of the first peak vGRF, knee flexion angle at IC, knee flexion excursion and knee extension excursion.

Force variables were normalized by body weight and presented as Nm/kg (VM & IRM) or N/kg (vGRF). The frontal and transverse plane knee moments are reported as peak external moments identified within the first 100ms as local maxima, the largest of which from each trial recorded was used for analysis. Joint angles (°) were extracted at IC and at the highest value identified within the first 100 ms, and excursions were calculated as the difference between the two. Knee angles in the frontal plane were defined as valgus (negative) or varus angles (positive), and in the transverse plane as internal (positive) and external (negative) rotation angles. Positive values of frontal plane knee moments are referred to as knee valgus moments, while negative values represent knee varus moment. Negative values of transverse plane knee rotation excursion indicate that knee rotated into greater internal rotation.

Inverse kinematics and inverse kinetics were performed in Visual 3D (C-Motion). Data were imported to R (R Foundation for Statistical Computing, Vienna, Austria) for analysis and processing. Jamovi, an R based program, was used for construction of linear mixed statistical models and creating figure. Power analysis was performed using G*Power.

An initial model was calculated to identify fixed main effects for sex, fatigue intervention and leg dominance, and interactions between i) Sex*fatigue intervention and ii) Sex*Leg Dominance. To obtain more accurate statistical models of sex dependent differences, leg dominance and fatigue intervention were included in the models to adjust for the effect of these variables. Subject was used as a random effect in all models to adjust for the repeated measure design of the study. For each of the fixed variables used, a random factor (random slope) was added in succession (fatigue intervention and leg dominance) to the linear mixed model and the best fit model selected according to -2 x Log Likelihood (using Chi-square distribution to test for a significant improvement for each successive addition of a random effects). Alpha was set at 0.05. Results are reported as least-squares means and difference between least-squares means with 95% confidence intervals. A power analysis revealed that an effect size of 0.25 had power of 0.83 in the study.

RESULTS

There were no differences in age, height or weight between the sexes (Table 1). Statistical results of the differences (ANOVA) are reported in Tables 2-4. The best model was always one that included random slopes for both fatigue intervention and leg dominance.

Dynamic valgus cluster

A statistically significant main effect of sex was found for three variables, as boys demonstrated greater peak knee VM and IRM, as well as greater excursion from an externally rotated position towards internal rotation (Table 2). Main effects of fatigue were observed in significant pre- to post-intervention increase in peak knee VM, greater post-intervention knee valgus angle at IC, and less knee external rotation angle at IC (Table 3). No statistically significant interaction between those two factors (sex*fatigue intervention) were found (Table 4).

Table 2. Results of ANOVA for Sex (main effects)

	Sex	
	Mean	**95% CI**
Dynamic valgus cluster		
Knee valgus moment (*F* = 3.9, *P* = **0.048**)		
Boys	0.26	0.23 to 0.29
Girls	0.22	0.20 to 0.25
Knee internal rotation moment (*F* = 5.4, *P* = **0.021**)		
Boys	–0.13	–0.15 to –0.11
Girls	–0.10	–0.11 to –0.08
Knee valgus at IC (*F* = 0.9, *P* = 0.342)		
Boys	–1.9	–2.7 to –1.0
Girls	–1.3	–2 to –0.7
Knee valgus excursion (*F* = 2.1, *P* = 0.151)		
Boys	2.9	2.5 to 3.3
Girls	3.3	3.0 to 3.6
Knee rotation at IC (*F* = 0.2, *P* = 0.64)		
Boys	–2.0	–3.3 to –0.7
Girls	–2.4	–3.3 to –1.4
Knee rotation excursion (*F* = 6.1, *P* = **0.014**)		
Boys	–7.9	–8.5 to –7.3
Girls	–6.9	–7.4 to –6.5
Stiff landing cluster		
First peak vGRF (*F* = 2.6, *P* = 0.108)		
Boys	16.5	15.7 to 17.3
Girls	15.7	15.1 to 16.3
Knee flexion at IC (*F* = 1.9, *P* = 0.164)		
Boys	39.4	37.4 to 41.4
Girls	37.6	36.1 to 39.1
Knee flexion excursion (*F* = 1.5, *P* = 0.226)		
Boys	14.1	13.2 to 15.1
Girls	14.8	14.1 to 15.5
Knee extension excursion (*F* = 15.4, *P* < **.001**)		
Boys	2.7	2.2 to 3.2
Girls	1.4	1 to 1.8

Table 3. Results of ANOVA for Fatigue Intervention (main effects)

	Fatigue Intervention	
	Mean	**95% CI**
Dynamic valgus cluster		
Knee valgus moment ($F = 14.3$, $P <$ **.001**)		
Pre	0.23	0.21 to 0.25
Post	0.25	0.23 to 0.27
Knee internal rotation moment ($F = 0.7$, $P = 0.419$)		
Pre	-0.11	-0.12 to -0.09
Post	-0.11	-0.12 to -0.10
Knee valgus at IC ($F = 59.1$, $P <$ **.001**)		
Pre	-2.1	-2.6 to -1.5
Post	-1.1	-1.7 to -0.6
Knee valgus excursion ($F = 0.2$, $P = 0.648$)		
Pre	3.1	2.9 to 3.4
Post	3.1	2.8 to 3.4
Knee rotation at IC ($F = 22.1$, $P <$ **.001**)		
Pre	-2.6	-3.4 to -1.7
Post	-1.8	-2.6 to -1.0
Knee rotation excursion ($F = 2.4$, $P = 0.122$)		
Pre	-7.3	-7.7 to -6.9
Post	-7.5	-8.0 to -7.1
Stiff landing cluster		
First peak vGRF ($F = 14$, $P <$ **.001**)		
Pre	15.9	15.8 to 16.8
Post	16.3	15.4 to 16.4
Knee flexion at IC ($F = 27.8$, $P <$ **.001**)		
Pre	37.6	38.0 to 40.7
Post	39.4	36.3 to 38.8
Knee flexion excursion ($F = 6$, $P =$ **0.015**)		
Pre	14.7	14.1 to 15.3
Post	14.2	13.6 to 14.9
Knee extension excursion ($F = 50$, $P <$ **.001**)		
Pre	1.7	1.4 to 2
Post	2.4	2.1 to 2.7

“pre” indicates before the fatigue intervention and “post” indicates after the fatigue intervention.

Table 4. Results of ANOVA for Sex*Fatigue Intervention (interaction)

	Sex* Fatigue Intervention	
	Mean	**95% CI**
Dynamic valgus cluster		
Knee valgus moment (*F* = 0.2, *P*= 0.645)		
Boys pre	0.26	0.23 to 0.30
Boys post	0.28	0.24 to 0.30
Girls pre	0.18	90.16 to 0.21
Girls post	0.23	0.18 to 0.24
Knee internal rotation moment (*F* = 1.5, *P* = 0.216)		
Boys pre	-0.13	–0.15 to –0.11
Boys post	-0.12	–0.14 to –0.10
Girls pre	-0.09	–0.11 to –0.08
Girls post	-0.10	–0.11 to –0.08
Knee valgus at IC (*F* = 1.8, *P* = 0.177)		
Boys pre	-1.5	–2.4 to –0.6
Boys post	-2.2	–3.2 to –1.3
Girls pre	-0.8	–1.5 to –0.1
Girls post	-1.9	–2.6 to –1.2
Knee valgus excursion (*F* = 0.9, *P* = 0.338)		
Boys pre	2.9	2.5 to 3.3
Boys post	3.0	2.5 to 3.5
Girls pre	3.3	2.9 to 3.6
Girls post	3.3	3.0 to 3.6
Knee rotation at IC (*F* = 1.4, *P* = 0.243)		
Boys pre	-2.3	–3.6 to –0.1
Boys post	-1.7	–3.0 to –0.3
Girls pre	-2.8	–3.8 to –1.9
Girls post	-1.9	–2.9 to –0.9
Knee rotation excursion (*F* = 0.3, *P* = 0.616)		
Boys pre	-7.8	–8.4 to –7.1
Boys post	-8.0	–8.7 to –7.4
Girls pre	-6.9	–7.4 to –6.4
Girls post	-7.0	–7.5 to –6.5
Stiff landing cluster		
First peak vGRF (*F* = 7.6, *P* = **0.006**)		
Boys pre	16.4	15.6 to 17.2
Boys post	16.5	15.7 to 17.3
Girls pre	15.3	14.7 to 15.9
Girls post	16.0	15.4 to 16.6
Knee flexion at IC (*F* = 0.4, *P* = 0.54)		
Boys pre	38.4	36.4 to 40.0
Boys post	40.4	38.2 to 42.5
Girls pre	36.8	35.3 to 38.3
Girls post	38.4	36.8 to 40.0
Knee flexion excursion (*F* = 0.1, *P* = 0.722)		
Boys pre	14.4	13.4 to 15.4
Boys post	13.8	12.9 to 14.8
Girls pre	15.0	14.3 to 15.8
Girls post	14.6	13.9 to 15.4
Knee extension excursion (*F* = 1.3, *P* = 0.257)		
Boys pre	2.2	1.7 to 2.8
Boys post	3.1	2.6 to 3.6
Girls pre	1.1	0.7 to 1.5
Girls post	1.7	1.3 to 2.1

Stiff landing cluster

There was a sex*fatigue intervention interaction (Table 4) where, although boys demonstrated higher peaks overall, a significant pre- to post-fatigue increase in the first peak vGRF was seen for girls (15.3 to 16 N/kg), while fatigue affected boys minimally (16.4 to 16.5 N/kg) (Figure 1). Overall, a main effect of sex was found for knee extension excursion, as boys showed significantly greater knee extension excursion during the first 100 ms compared to girls (Table 2). Main effects of fatigue intervention were found for all other variables, reflecting greater post-intervention knee flexion angle at IC (pre 37.6°; post 39.4°, P<.001), with a slight decrease in knee flexion excursion (pre 14.7°; post 14.2°, P=0.015) and greater extension excursion (pre 1.7°, post 2.4, P<.001) (Table 3).

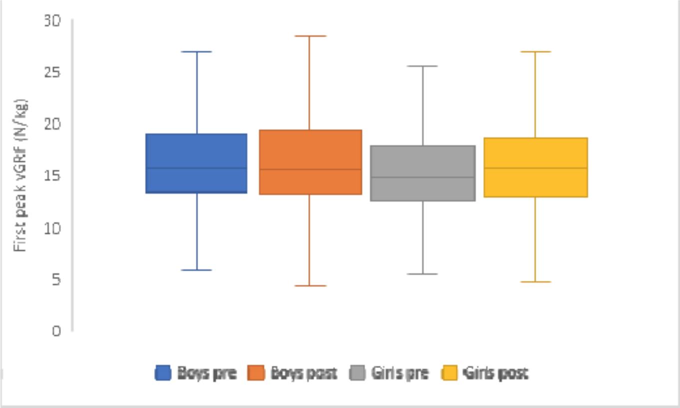


Figure 1. Mean (95% CI) magnitude of the vertical ground reaction force (Nm/kg) of boys and girls for the first 100 ms of the cutting manoeuvre, before (pre) and after (post) a five- minute fatigue intervention.

DISCUSSION

In the present study our main purpose was to investigate whether differences between pre-adolescent boys and girls would be identified for key biomechanical variables during their performance of the cutting manoeuvre. The main findings of this study demonstrate that in pre- or early- pubertal athletes, sex related differences are observed where, compared to girls, boys showed higher VM, IRM, first peak vGRF, rotation excursion and extension excursion.

Dynamic valgus cluster

Women are at greater risk for ACL injury than men[13] and the knee VM has been linked to risk of ACL injury[24]. Indeed, a study by Sigward et al.[25] involving 30 collegiate soccer players found that females showed higher VM than males in the early deceleration phase of a cutting manoeuvre, a time period very similar to our study. This is in contrast with the findings of the present study, which may be explained by the age difference. The athletes recruited for the present study were at an age where girls and boys have equal risk of ACL injury[26,27] and consequently one would expect them to demonstrate similar patterns of biomechanical risk factors. In a larger cross sectional study, Sigward et al.[25] compared age groups and did not find a sex*maturity interaction, but the number of subjects was low (n=19) indicating that the biomechanical differences between males and females were evident across all stages of maturation. Our results are in part consistent with those of Tanikawa et al.[28] who found that men (aged 25.4) had higher VM in a change of direction movement than women.

Stiff landing cluster

The results of the current study indicate that boys, not girls, demonstrate greater vGRF forces and greater knee extension excursion during the first 100 ms of the change of direction task, indicative of a stiffer landing strategy. The ACL is known to be loaded through tibiofemoral compression[29] and stiff landings as assessed via vGRF and knee flexion angles during DJ tasks have previously been associated with ACL injury risk in young female athletes, where the injured cohort displayed 30% higher peak vGRF compared to the uninjured group[10]. In comparison, our 95% CI support at most a 14% difference which in and of itself is unlikely to affect injury risk, but the timing of other contributing factors must be considered in this multi-factorial injury[30]. In contrast to the findings of the present study, analysis of data obtained during DJ performed by the same cohort showed that the girls had higher peak vGRF during the early landing phase compared to boys[16], indicating that results from DJ and cutting manoeuvres are not inter-changeable.

Although cutting and DJ are used for the screening of ACL injury risk, movement patterns are different and this may explain the differences in kinematics and kinetics[31]. Studies using the DJ test have demonstrated that compared to boys, girls show a higher peak VM[16] but studies have used different methodologies for analyses. We have recently shown that peak values during the complete deceleration phase occur much later in the movement compared to the time-frame during which ACL injury would occur[30]. A difference between sexes in mean knee abduction angles at IC has been reported for the DJ while in the current study no difference was found. Current prospective risk factor studies have exclusively used the DJ[16] and variations of it, while change of direction movements are far more often associated with the injury mechanism[30]. The current study demonstrated that even at this young age, biomechanical differences between the sexes are present. Direction of the difference is not towards higher risk for girls using currently reported risk factors, as would be expected, but a higher risk for boys instead. Studies show that adult females are 4 to 6 times more likely to sustain a non-contact ACL injury than males participating in the same sport[2]. Since within this age group there are no large epidemiological studies reporting ACL injuries and the incidence rate is very low[32], it is unlikely that these differences play a crucial role in ACL injuries in pre-adolescents. This does, however, seem an opportune time to start focusing on injury prevention, as there is a sharp rise in ACL injury incidence during the teen-age years[33].

A five-minute progressive skateboard fatigue intervention was employed in this study as a convenient way to induce fatigue. Statistical analysis revealed that a number of variables were affected by the fatigue intervention, with only one interaction by sex, which was an increase in the early peak vGRF for girls, not boys, which is consistent with results reported for DJ performance[16]. The direction of fatigue effects appears to always be towards greater risk; increased vGRF, a more extended position at IC, less flexion excursion and greater extension excursion during the first 100 ms of foot contact. The effects of fatigue on ACL injury incidence, however, are not clear. Recent publications as estimated by time of season and time in game do not indicate that this influences injury incidence[34]. Different fatigue protocols did not produce alterations in lower limb biomechanical factors that are believed to increase the risk of noncontact ACL injuries[20].

There are several strengths and limitations in the present study that should be acknowledged. Firstly, we have a large sample size (n=288) and therefore good statistical power. The data presented are baseline measures of a prospective cohort study and the athletes in our sample are younger than the age group where ACL injuries become more common. These findings may therefore not reflect sex specific differences that translate into a later increase in the risk of injury for girls. However, it is important to know when sex differences start to manifest, so the training parameters can be altered before the onset of increased risk. At this age, the kids' motor development is not complete, and the differences in the skill of execution between athletes may be greater in this age group compared to mature athletes, leading to a greater spread in the data. We account for this in our design by using a cutting manoeuvre without a running start. We propose that this decreases the potential confounding effect of maturity and motor development but acknowledge that it may lead to a systematic bias where the force of execution is lower compared to a running start. Similarly, it remains unclear if the execution speed is another possible confounding factor and that has not been discussed in this work. It is debatable whether the changes seen after the fatigue intervention are equally likely to be the result of increased movement speed due to a warm-up effect or that the five-minute progressive fatigue intervention was enough to induce fatigue in this group of athletes. Another novelty is the performance of the cutting manoeuvre, which is more likely to mimic an injury situation than a bilateral drop jump, and the exercise/fatigue intervention that, to the best of our knowledge, has not previously been introduced for this age group. The athletes who participate different sports can perform cutting and landing tasks differently. However, there are other factors that we cannot control for that may influence these results, including other sports, how often they attend practices and physical education in school, as well as their general lifestyle. The last limitation is that the maturity of each athlete remained unknown.

Conclusions and clinical relevance

The current study demonstrated that even at this young age, biomechanical differences between the sexes are present. However, the direction of the difference is not towards higher risk for girls using currently reported risk factors, as would be expected, but a higher risk for boys instead. We conclude that at this early age, girls do not demonstrate movement patterns associated with greater risk of ACL injuries during cutting manoeuvres. The age of 9-12 years may therefore be a good target age to start focusing on learning and developing muscular control, balance, strength and flexibility, which cumulatively can improve task execution and lower likelihood of ACL injury. These findings should help practitioners when to implement intervention programs aiming to reduce movement patterns associated with ACL injuries.

References

1. 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(7):596-606. doi:10.1136/bjsm.2010.076364
2. Arendt EA, Agel J, Dick R. Anterior Cruciate Ligament Injury Patterns among Collegiate Men and Women. *J Athl Train*. 1999;34(2):86-92.
3. Ajuied A, Wong F, Smith C, et al. Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: A systematic review and meta-analysis. *Am J Sports Med*. 2014;42(9):2242-2252. doi:10.1177/0363546513508376
4. Swart E, Redler L, Fabricant PD, Mandelbaum BR, Ahmad CS, Wang YC. Prevention and Screening Programs for Anterior Cruciate Ligament Injuries in Young Athletes: A

Cost-Effectiveness Analysis. *J Bone Joint Surg Am*. 2014;96:705-711.

5. Markolf K., Gorek J., Kabo J., Shapiro M. Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. *J Bone Jt Surg Am*. 1990;72(4):557-567. doi:10.1017/CBO9781107415324.004
6. Tsai TY, Lu TW, Kuo MY, Lin CC. Effects of soft tissue artifacts on the calculated kinematics and kinetics of the knee during stair-ascent. *J Biomech*. 2011;44(6):1182-1188. doi:10.1016/j.jbiomech.2011.01.009
7. Kolarz G, Kotz R, Hochmayer I. Long-term benefits and repeated treatment cycles of intra-articular sodium hyaluronate (Hyalgan) in patients with osteoarthritis of the knee. *Semin Arthritis Rheum*. 2003;32(5):310-319. doi:10.1053/sarh.2002.50013
8. Kiapour AM, Kiapour A, Goel VK, et al. Uni-directional Coupling between Tibiofemoral Frontal and Axial Plane Rotation Supports Valgus Collapse Mechanism of ACL Injury. *J Biomech*. 2015;48(10):1745-1751. doi:10.1016/j.jbiomech.2015.05.017.Uni-directional
9. Hewett TE, Lindenfeld TN, Riccobene J V., 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(6):699-706. doi:10.1177/03635465990270060301
10. Leppänen M, Pasanen K, Kujala UM, et al. Stiff Landings Are Associated with Increased ACL Injury Risk in Young Female Basketball and Floorball Players. *Am J Sports Med*. 2017;45(2):386-393. doi:10.1177/0363546516665810
11. Leigh RJ, Pohl MB, Ferber R. Does tester experience influence the reliability with which 3D gait kinematics are collected in healthy adults? *Phys Ther Sport*. 2014;15(2):112-116. doi:10.1016/j.ptsp.2013.04.003
12. Tranberg R, Saari T, Zügner R, Kärrholm J. Simultaneous measurements of knee motion using an optical tracking system and radiostereometric analysis (RSA). *Acta Orthop*. 2011;82(2):171-176. doi:10.3109/17453674.2011.570675
13. Waldén M, Hägglund M, Werner J, Ekstrand J. The epidemiology of anterior cruciate ligament injury in football (soccer): A review of the literature from a sex-related perspective. *Knee Surgery, Sport Traumatol Arthrosc*. 2011;19(1):3-10. doi:10.1007/s00167-010-1172-7
14. Myer G, Brent JL, Ford KR, Hewett TE. Real-time assessment and neuromuscular training feedback techniques to prevent ACL injury in female athletes Gregory. *Strength Cond J*. 2011;33(3):21-35. doi:10.1016/j.biotechadv.2011.08.021.Secreted
15. Shaw L, Finch CF. Trends in pediatric and adolescent anterior cruciate ligament injuries in Victoria, Australia 2005-2015. *Int J Environ Res Public Health*. 2017;14(6):1-10. doi:10.3390/ijerph14060599
16. Briem K, Jónsdóttir KV, Árnason Á, Sveinsson Þ. Effects of Sex and Fatigue on Biomechanical Measures During the Drop-Jump Task in Children. *Orthop J Sport Med*. 2017;5(1):1-7. doi:10.1177/2325967116679640
17. Sigward SM, Pollard CD, Havens K, Powers CM. The Influence of Sex and Maturation on Knee Valgus Moments During Cutting: Implications for Acl Injury. *Conf Proc Annu Meet Am Soc Biomech*. 2010;44(8):122-123. doi:10.1249/MSS.0b013e31824e8813.The
18. Bourne MN, Webster KE, Hewett TE. Is Fatigue a Risk Factor for Anterior Cruciate Ligament Rupture? *Sport Med*. 2019;49(11):1629-1635. doi:10.1007/s40279-019-01134-5
19. Benjaminse A, Webster KE, Kimp A, Meijer M, Gokeler A. Revised Approach to the Role

of Fatigue in Anterior Cruciate Ligament Injury Prevention: A Systematic Review with Meta-Analyses. *Sport Med*. 2019;49(4):565-586. doi:10.1007/s40279-019-01052-6

20. Barber-Westin SD, Noyes FR. Effect of Fatigue Protocols on Lower Limb Neuromuscular Function and Implications for Anterior Cruciate Ligament Injury Prevention Training: A Systematic Review. *Am J Sports Med*. 2017;45(14):3388-3396. doi:10.1177/0363546517693846

21. Krosshaug T, Nakamae A, Boden BP, et al. Mechanisms of anterior cruciate ligament injury in basketball: Video analysis of 39 cases. *Am J Sports Med*. 2007;35(3):359-367. doi:10.1177/0363546506293899

22. Sankey SP, Raja Azidin RMF, Robinson MA, et al. How reliable are knee kinematics and kinetics during side-cutting manoeuvres? *Gait Posture*. 2015;41(4):905-911. doi:10.1016/j.gaitpost.2015.03.014

23. Boden BP, Dean G, Feagin JJ, Garrett WE. Mechanisms of anterior cruciate ligament injury. *Orthopedics*. 2000;23(6):573-578.

24. 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. doi:10.1177/0363546504269591

25. Sigward SM, Powers CM. The influence of sex on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin Biomech*. 2006;21(1):41-48. doi:10.1016/j.clinbiomech.2005.08.001

26. Moksnes H, Grindem H. Prevention and rehabilitation of paediatric anterior cruciate ligament injuries. *Knee Surgery, Sport Traumatol Arthrosc*. 2016;24(3):730-736. doi:10.1007/s00167-015-3856-5

27. Hewett TE, Myer GD, Ford KR, Paterno M V., Quatman CE. The sequence of prevention: A systematic approach to prevent anterior cruciate ligament injury knee. *Clin Orthop Relat Res*. 2012;470(10):2930-2940. doi:10.1007/s11999-012-2440-2

28. Tanikawa H, Matsumoto H, Komiyama I, Kiriyama Y, Toyama Y, Nagura T. Comparison of knee mechanics among risky athletic motions for noncontact anterior cruciate ligament injury. *J Appl Biomech*. 2013;29(6):749-755. doi:10.1123/jab.29.6.749

29. Meyer EG, Haut RC. Anterior cruciate ligament injury induced by internal tibial torsion or tibiofemoral compression. *J Biomech*. 2008;41(16):3377-3383. doi:10.1016/j.jbiomech.2008.09.023

30. Sigurðsson HB, Sveinsson Þ, Briem K. Timing, not magnitude, of force may explain sex-dependent risk of ACL injury. *Knee Surgery, Sport Traumatol Arthrosc*. 2018;26(8):2424-2429. doi:10.1007/s00167-018-4859-9

31. Kristianslund E, Krosshaug T. Comparison of drop jumps and sport-specific sidestep cutting: Implications for anterior cruciate ligament injury risk screening. *Am J Sports Med*. 2013;41(3):684-688. doi:10.1177/0363546512472043

32. Faunø P, Jakobsen BW. Mechanism of anterior cruciate ligament injuries in soccer. *Int J Sports Med*. 2006;27(1):75-79. doi:10.1055/s-2005-837485

33. Nicholls M, Aspelund T, Ingvarsson T, Briem K. Nationwide study highlights a second peak in ACL tears for women in their early forties. *Knee Surgery, Sport Traumatol Arthrosc*. 2018;26(2):648-654. doi:10.1007/s00167-017-4807-0

34. Doyle T, Schilaty N, Webster K, Hewett TE. Time of Season and Game Segment Is Not

Related to Likelihood of Lower-Limb Injuries A Meta-Analysis. *Clin J Sport Med*. 2019;In print. doi:10.1097/JSM.0000000000000752