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Mapping current research trends on anterior cruciate ligament injury risk against the existing evidence: In vivo biomechanical risk factors.

Mapping Current Research Trends on Anterior Cruciate Ligament Injury Risk Against the Existing Evidence: In Vivo Biomechanical Risk Factors

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Clinical Biomechanics

Abstract

Background: Whilst many studies measure large numbers of biomechanical parameters and associate these to anterior cruciate ligament injury risk, they cannot be considered as anterior cruciate ligament injury risk factors without evidence from prospective studies. A review was conducted to systematically assess the *in vivo* biomechanical literature to identify biomechanical risk factors for non-contact anterior cruciate ligament injury during dynamic sports tasks; and to critically evaluate the research trends from retrospective and associative studies investigating non-contact anterior cruciate ligament injury risk.

Methods: An electronic literature search was undertaken on studies examining *in vivo* biomechanical risk factors associated with non-contact anterior cruciate ligament injury. The relevant studies were assessed by classification; level 1 -a prospective cohort study, level 2 -a retrospective study or level 3 -an associative study.

Findings: An initial search revealed 812 studies but this was reduced to 1 level 1 evidence study, 20 level 2 evidence studies and 175 level 3 evidence studies that met all inclusion criteria. Level 1 evidence showed that the knee abduction angle, knee abduction moment and ground reaction force were biomechanical risk factors. Nine level 2 studies and eighty-three level 3 studies used these to assess risk factors in their study. Inconsistencies in results and methods were observed in level 2 and 3 studies.

Interpretation: There is a lack of high quality, prospective level 1 evidence related to biomechanical risk factors for non-contact anterior cruciate ligament injury. More prospective cohort studies are required to determine risk factors and provide improved prognostic capability.

Keywords: Anterior Cruciate Ligament, ACL Injury, Biomechanics, Sports Medicine, Level of Evidence

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Glossary

Abbreviation	*Description*
2D	Two dimensional
ACL	Anterior cruciate ligament
ACLD	ACL deficient
ACL_{INT}	ACL intact
ACLR	ACL reconstruction
CoM	Centre of mass
CoP	Centre of pressure
BoS	Base of support
DVJ	Drop vertical jump
EMG	Electromyography
F	Female
GRF	Ground reaction force
INJ	injured
KAA	Knee abduction angle
KAM	Knee abduction moments
M	Male
pGRF	Peak ground reaction force
RoM	Range of motion
UNINJ	uninjured

Introduction

Anterior cruciate ligament (ACL) injuries are highly debilitating and commonly occur in sporting activities [10-12]. Up to 70% of primary ACL injuries are non-contact in nature and occur during rapid dynamic activities such as sudden stops, change of direction, jump landings, pivoting and side cutting manoeuvres [11, 13]. The occurrence of non-contact ACL injury during such tasks is multi-factorial, likely including hormonal, environmental, anatomical, psychological, neuromuscular and biomechanical factors [14]. An understanding of non-contact ACL injury aetiology is therefore vital for effective screening, treatment, and injury prevention. The high incidence [15] of the ACL injury itself is not only devastating but could also have long-term effects on the knees such as through osteoarthritis [16]. On account of the high cost of surgical ACL reconstruction, it not only effects on the patient's health but also yields a heavy economic burden [17, 18].

Over the last decade, a large number of studies have used *in vivo* biomechanical methods to investigate links between specific biomechanical parameters and risk of non-contact ACL injury. One advantage being that these parameters have been shown to be modifiable [19]. Typically observed parameters include whole body kinematics, lower limb joint moments, and knee and hip kinematics at key events e.g. impact. Understanding the biomechanics of the dynamic movement is crucial in investigating the risk factor of the non-contact ACL injury. Biomechanical risk factors have been proposed in all three planes but inconsistency in methods and techniques of evaluating risk factors however have not been examined in detail. Two dimensional (2D) kinematic video recording [20, 21] has also been used to inform the injury mechanism, but its accuracy and precision are still uncertain. A recent review [22] implicated a number of biomechanical "risk factors" such as reduced lateral trunk flexion and knee flexion angle, yet it would seem that such measures have only been associated to ACL injury risk and cannot therefore be considered as ACL injury risk factors *per se*. Risk factors are predictive parameters established from prospective cohort studies, where the parameters showed meaningful differences between ACL injured athletes compared to uninjured athletes. It is perhaps therefore a misconception that there are a large number of established biomechanical risk factors for non-contact ACL injury.

Once risk factors have been established from prospective cohort studies they may be further supported by evidence from retrospective studies which can identify differences between ACL injured and controls, and further understood through associative studies by investigating what can influence risk factors, e.g. approach speed influences knee abduction moments [23]. As outlined in the ‘Translating Research into Injury Prevention Framework’ [24], these types of studies are needed to strengthen the development of intervention and prevention programs as the success of these programs is underpinned by a solid understanding of the risks associated with sustaining the injury as opposed to any surrogate or any indirect measure of injury. Retrospective studies therefore provide weaker evidence relating to the identification of risk factors than prospective cohort studies, and associative studies build on the evidence rather than generating it. As the field of research progresses, it is desirable that the number of independent studies with a high level of evidence increases [25]. The research trends relating to the biomechanical risk factors of non-contact ACL injury are unknown and therefore critical examination of the existing evidence is required.

The aims of this study are firstly, to systematically review the *in vivo* biomechanical literature that has identified risk factors for non-contact ACL injury during dynamic sports tasks and secondly, to critically evaluate the research trends from retrospective and associative studies investigating non-contact ACL injury risk. Risk factors and studies relating to either sex are considered for completeness.

Methods

The Cochrane Handbook [26] and the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) [27] guidelines were used in conducting this systematic review.

Electronic Literature Search

A systematic electronic database search of PubMed, SCOPUS, Web of Science, CINAHL and SPORTDiscus was conducted for studies between January 1990 and 10th August 2015. The search terms were constructed and tested prior to the initial search for their appropriateness. Search terms were divided into five groups (Table 1) and when searching the groups were connected with AND. Depending on the search database, the appropriate search term notation technique was applied.

Table 1 Electronic database literature search strategy for key terms used

Step	Strategy	PubMed	Scopus	Web of Science	CINAHL	SPORTDiscus
#1	Search "ACL injur*" OR "anterior cruciate ligament injur*"	2,413	3,861	7,483	4,599	1,974
#2	Search knee OR hip OR ankle OR trunk OR torso OR valgus OR varus OR abduction OR adduction OR flexion OR extension OR "ground reaction force*" OR "internal rotation" OR "external rotation"	485,043	659,671	1,364,572	99,867	67,865
#3	Search #1 AND #2	2,111	3,351	6,260	3,129	1,435
#4	Search biomechanic* OR kinematic* OR kinetic* OR angle* OR moment* OR load* OR torque* OR sagittal OR frontal OR transverse	985,113	3,336,664	4,912,796	83,466	83,973
#5	Search #3 AND #4	1,025	1,506	1,441	1,180	765
#6	Search risk OR prevent* OR predict* OR screening OR associate* OR sensitivity OR specificity OR reproducibility OR reliability OR validity	7,380,702	9,622,122	21,467,428	1,206,876	209,644
#7	Search #5 AND #6	776	940	969	649	561
#8	Search side* OR cut* OR hop* OR land* OR jump* OR sprint* OR run*	894,257	2,867,571	4,688,133	121,429	184,408
#9	Search #7 AND #8	348	520	590	336	399

Study selection

EndNote® (version X7.0.1, Thomson Reuters) was used to select titles and abstracts based on the inclusion and exclusion criteria; and prospective cohort studies, retrospective studies and associative studies were classified as level 1, 2 and 3 evidence, respectively (Table 2). Any duplicates found were excluded. A prognostic article was included if the study (i) measured biomechanical variables (e.g. kinetic, kinematic); (ii) measured other variables (e.g. neuromuscular or physiological variables) but still contained biomechanical assessments; (iii) contained risk factors or associations with non-contact ACL injury; (iv) was published in English; (v) involved participants of dynamic sports i.e. those involving rapid dynamic movements such as sudden stops, changes of direction, jump landings, pivoting and side cutting (e.g. basketball, football, hockey, volleyball, handball); (vi) was an *in vivo* study. Articles were excluded if (i) no abstract was available; (ii) they were a review, systematic review, technical note or meta-analysis; (iii) the study focused on the effect of treatment or training; (iv) their sole focus was on ACL deficient or reconstructed populations; (vi) they were *in vitro* studies, (vii) there was a non-dynamic sport setting.

Initially, title and abstract selection was completed by authors 2 and 6 independently, in order to avoid risk of bias in identifying potentially relevant papers for full review. If there were discrepancies between the two reviewers, there were discussions between the two to reach a consensus. If consensus could not be reached, the article was referred to author 1 or 7. Next, the full text assessment was reviewed by authors 1 and 7 and if there were any disagreements between the two reviewers, consensus was again sought through discussions between themselves, and a moderator if needed (author 6). Study classifications and the inclusion / exclusion criteria were implemented within this process.

Table 2 Classification of studies (Level of Evidence)

Level of Evidence	Prognostic Studies—Investigating the Effect of a Patient Characteristic on the Outcome of Disease
Level 1	*Prospective Cohort Study* Observe a large number of uninjured athletes and then monitor their injury status over a period of time. Those athletes that become injured can then be compared to the uninjured group in an attempt to identify differences with a predictive value commonly called risk factors.
Level 2	*Retrospective Study* A study design that takes a look back at the effect of an event that occurred in the past and typically makes comparisons to a control group. In a typical retrospective ACL study, investigators would compare ACL injured or reconstructed athletes to an uninjured control group.
Level 3	*Associative Study* Provides a lower level of evidence because these cannot measure risk factors directly and so instead associates other variables with known risk factors. They can help to understand how known risk factors are influenced by other variables that have not yet been shown prospectively as risk factors themselves.

Assessment of the risk of bias

Risk of bias assessment was undertaken for level 1 evidence studies (Table 3). The Risk of Bias Tool for Cohort Studies by the Cochrane Bias Methods Group was used to review the selected articles. The retrospective and associative studies were not quality assessed as these studies were retrieved only to map current trends of the field. Authors 1 and 7 assessed the risk of bias independently and then reached a consensus. For each item answered ‘Yes’, one point was given other responses scored 0 points. The total score of the methodological quality ranged between 0 – 9 for the prospective cohort study. If an item was not present, not reported or insufficient information was given, no points were given. An item might not be applicable to a study, so these items were excluded from calculation for quality assessment. Scoring ‘Yes’ shows that the study has a low risk of bias and ‘No’ means that the study has a high risk of bias.

Results

Search results

A total of 3698 studies were identified (Figure 1) with the database breakdown as follows: PubMed (348), Scopus (520), Web of Science (590), CINAHL (336) and SPORTDiscus (399). When duplicates and unrelated articles (2886) were removed 812 studies remained. After careful screening of titles, abstracts and classification of level of evidence 605 studies were excluded as they did not meet the inclusion criteria and 207 studies remained and underwent full evaluation. Twelve prospective cohort studies were selected for full text assessment of the inclusion and exclusion criteria. A total of 20 retrospective and 175 associative studies were also identified.

Full text assessment of the 12 prospective cohort studies meant that eleven further studies were excluded for the following reasons: (1) one had no full text available [1], (2) one did not meet the requirement of participation in dynamic sports [2], and (3) nine did not focus specifically on investigating or finding new ACL injury risk factors as they were observing other injuries (e.g. patellofemoral pain syndrome) [4, 8], gender differences [7, 9], perfecting screening tools [3, 6, 7], effect of maturation or joint laxity effects [5, 7]. Hence, only one level 1 evidence study [28] was quality assessed.

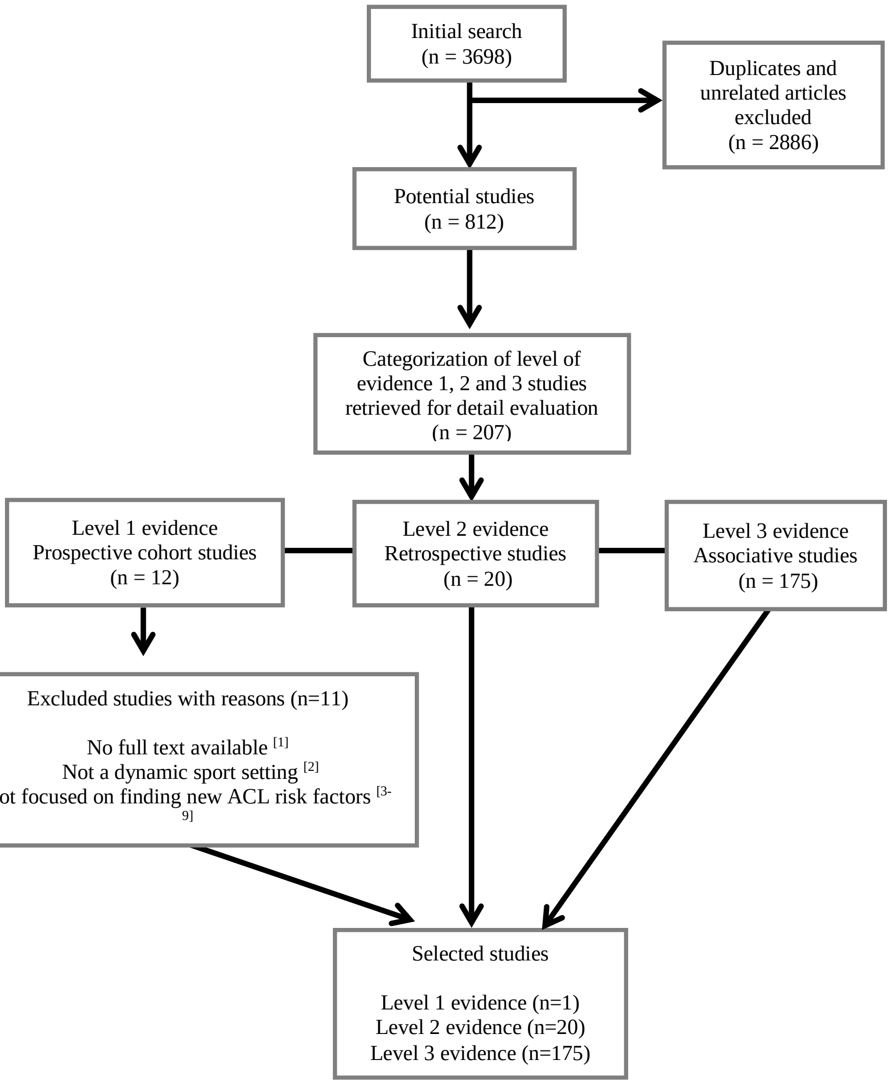

Fig. 1 Flow diagram of search strategy

Level 1 evidence

The selected level 1 evidence study [28] scored 7/8 points in the risk of bias assessment (Table 3) hence, this study has a low risk of bias and key information has been summarized. This study was an exploratory prospective study as the authors did not know which variables might predict ACL injury. They observed 9 ACL injuries in a sample of 205 female adolescent basketball, volleyball and football players (14-18 years). The drop vertical jump (DVJ) was used to examine landing biomechanics during the first contact phase. A range of biomechanical variables were measured and they found that the group that subsequently had an ACL injury had higher knee abduction angles (KAA) at landing (9° vs. 1.4°), higher peak knee abduction moments (KAM, -45.3 vs. -18.4 Nm) and higher vertical ground reaction forces (GRF) (1266 vs. 1057 N) which distinguished them from the uninjured group. The KAM predicted ACL injury status with 73% specificity and 78% sensitivity.

Table 3 Methodological Quality Assessment (Risk of Bias Assessment)

Description scores		Hewett et al. 2005
a.	Was selection of the prospective cohorts drawn from the same population	Y
b.	Can we be confident in the assessment of activity exposure in subjects	Y
c.	Can we be confident that any injury was not present at start of the study (prospective) or had suffered from ACL injury and controls had not (case-control)?	Y
d.	Were the cases (those who acquired ACL injury) appropriately selected?	Y
e.	Were the controls appropriately selected?	N/A
f.	Did the study match injured and uninjured subjects (prospective) or cases and controls (case-control) for all variables that are associated with the potential risk factor or did the statistical analysis adjust for these prognostic variables?	N
g.	Was the nature/cause of the ACL injury well defined?	Y
h.	Can we be confident in the assessment of the ACL injury?	Y
i.	Was the follow up of cohorts adequate?	Y
Total score		7/8

** N/A not applicable, N no or insufficient information, Y yes*

Level 2 evidence

Of the 20 retrospective level 2 evidence studies (Table 4), 14 compared an ACL reconstruction (ACLR) group and 6 compared an ACL deficient (ACLD) group to either a healthy control group or to the individual’s uninjured side. Nine studies observed the variables KAM or KAA to assess the ACL injury based on the risk factors found by Hewett *et al.*. An increased KAA was found both in the ACLR [29, 30] and ACLD [7] group during side cutting and DVJ, compared to control groups.

Concerning sex differences, KAA was seen to be higher in females compared to males in both injured and uninjured leg [31]. However, other studies observed no significant difference in KAA when comparing ACLD [32] and ACLR [33, 34] individuals compared to controls. While comparing female subjects to male subjects, Miranda et al. [35] observed the amount of KAA found in their study did not seem to resemble to a valgus collapse position. Only one study [36] observed a greater KAM in an ACLR group during a side hop (6.96 vs. 1.16 N·m/KgBW) and a lower KAM during crossover hopping (1.31 vs. 5.59 N·m/KgBW) compared to a healthy control group.

The other eleven studies investigated biomechanical variables in the context of stability and postural control [37-40], gait [41], vision [42], limb asymmetry [43], walk and jog patterns

[44], gender differences [45], as well as neuromuscular aspects [46]. Landing strategies and medio-lateral control of the ACLD and ACLR patients were also investigated by Roos et al. [47] and found that these groups had not fully recovered.

ACLD and ACLR subjects showed significantly poorer clinical and biomechanical results compared to controls [44, 38, 45]. However no differences were found in knee joint kinematics and kinetics during gait [41]. Distinguishing characteristics of ACLD groups included posterior centre of mass (COM) changes [39], increased time to stabilization [40], postural sway and other unique adaptations aimed at stabilizing the knee [46]. Distinguishing characteristics of ACLR groups included greater postural sway [37] and altered responses to visual disruption [42].

Level 3 evidence

A total of 175 associative studies were retrieved from the search. We identified that 57% of these associative studies involved both sexes a further 30% investigated females only with only 11% of studies investigating males. The remaining 2% was unknown as it was not specified in the abstract or the full text. Only 19% of the papers studied adolescent athletes (between 10 – 18 years old) while the rest of the studies included adults. Out of the 175 associative studies, 30 studies used KAM and KAA to assess non-contact ACL injury risk, all of which were published after Hewett et al.'s prospective study [28] which included athletes aged ranging between 14 to 17 years old. There are a wide variety of other biomechanical factors assessed in level 3 studies including the association of risk factors with sex, maturational development, sport type, fatigue, task and neuromuscular aspects.

Studies have shown that females tend to have a greater risk of getting an ACL injury [28, 48]. This is supported by the findings found in the associative studies where females are more likely to have poorer landing technique such as reduced hip and knee flexion at initial contact [49, 50]; higher knee abduction [51, 52] and less knee flexion throughout landing [50] compared to males. Landing with a more erect posture and greater angular velocities than males has also been speculated to contribute to non-contact ACL injury in females [53].

DVJ tasks have been combined with the influence of fatigue [54-58] to examine the effect on biomechanical variables. Around 13% of the associative studies examined the effect of fatigue on ACL injury risk factors. Fatigue has been observed to alter both the movement patterns and motor control [59, 54, 55]. Both males and females demonstrated reduced KAA moving closer to neutral and decreased knee flexion at initial contact after fatiguing [59, 54]. In addition, the KAM at peak stance and hip flexion angle was also decreased and a larger GRF was seen in females after fatigue [54, 56]. Knee and hip control also altered neuromuscular characteristics [60, 61].

Over a third (36%) of the level 3 studies observed cutting manoeuvres with the majority being anticipated rather than unanticipated tasks. The inclusion of unanticipated tasks increases the magnitude of joint loads and increases the KAA in females compared to males [49, 62-66]. Muscular activity imbalance and reduced hip flexion angles have also been associated with non-contact ACL injury [67, 66].

A filterable summary of the selected level 3 evidence papers research trend (Table S1) can be found in the supplementary material.

Table 4 Summary of the Selected Level 2 Evidence Papers

Subject condition	Author	Characteristics of subjects	Methodology of Data Collection / Task	Biomechanical Outcome Measure	Results/Findings
ACLR	Bjornaraa, J. and R. P. Di Fabio (2011)[42]	ACLR; 17 females (F) healthy controls; 17F	Vision – used electromagnetic sensor	- Absolute knee displacement, Peak and average absolute knee velocities, time to peak ground reaction force (pGRF) (% of cut).	- ACLR: < knee displacement, velocity, ↑ time to reach pGRF relative to healthy subjects' non-dominant knee. - Visual disruption: some effect on movements.
	Goerger, B. M., et al. (2015)[29]	ACLR-injured (ACLR-INJ); 8 males (M), 4F ACLR-uninjured (ACLR-UNINJ); 9M, 10F healthy controls, 20M, 19F	DVJ	- KAA, Knee adduction angle, Hip abduction angle, Hip adduction angle, Knee internal rotation angle, Knee extension moment, Hip flexion moment , Anterior tibial shear force	- ACL injury & ACLR altered lower extremity biomechanics - ACLR-INJ & ACLR-UNINJ: ↑ hip adduction and KAA. - ACLR- INJ: ↓ anterior tibial shear force, knee extension moment & hip flexion moment. - Control group: No high-risk biomechanical changes observed
	Holsgaard-Larsen, A., et al. (2014)[43]	ACLR; 23M healthy controls; 25M	Counter movement jump (CMJ), one-leg hop for distance	- Sagittal knee moment, Sagittal range of motion (RoM), Knee joint angle at transition point, Jump height, Asymmetry ratio	- Both types of CMJ: Between-limb asymmetry ratios for RoM differed between ACLR and controls - Jump for distance: ACLR > jump length asymmetry
	Lee, S. P., et al. (2014)[33]	ACLR; 3M, 8F healthy controls; 3M, 8F	Side-step cutting manoeuvre; with 3 pre-cutting approach (counter movement, one step and running)	- Knee flexion angle, Knee extension angle, KAA, Knee adduction angle, Internal and external rotation angles, Peak joint moments	- ACLR: > knee internal rotator moment - Inter-group comparisons; ACLR > abductor and internal rotator moments only in the running condition - ACLR: at ↑ risk of re-injury when participating in high-demand physical activities.
	Miranda, D. L., et al. (2013)[35]	ACL intact ($ACL_{INT)}$; 5M, 5F ACLR; 4M, 6F	Jump cut manoeuvre.	- GRF, Knee flexion, Knee extension, KAA, Knee adduction, Tibial internal - external rotation, Anterior - posterior knee translation, Medial - lateral knee translation, Anterior – posterior knee translation excursions, Medial – lateral knee translation excursions	- F: < knee flexion angle excursion during a jumpcut manoeuvre resulting in a ↑ pGRF & ↑ rate of anterior tibial translation. - ACLR: < GRF in jump cut manoeuvre than ACL_{INT} - ↑ landing stiffness leads to ↑ rate of anterior tibial translation while performing a jump-cut manoeuvre.
	Mohammadi, F., et al. (2012)[37]	ACLR; 22M, 8F healthy controls; 24M, 6F	Single-leg stance & single leg drop jump.	- Centre of pressure (CoP) anteroposterior amplitude and velocity, CoP mediolateral amplitude and velocity, Vertical GRF, Loading rate	- ACLR: > postural sway in operated leg compared with the non-operated side and matched limb of the control group - ACLR: > pGRF and loading rate on the uninvolved limb compared to control group at landing - Static & dynamic postural measures have high test–retest reliability, ranging from 0.73 to 0.88.
	Oberländer, K. D., et al. (2012)[38]	ACLR; 12 healthy controls; 13	Single leg hop.	- Margin of stability, CoM, GRF, Ankle dorsiflexion moments, Ankle plantarflexion moments, Knee flexion moments, Knee extension moments, Hip flexion / extension moments, Pendulum length, Trunk angle	- ACLD leg: < external knee flexion moments, > moments at the ankle & hip compared to controls - ACLD leg: joint moment redistribution > anterior position of the GRF vector, which affected the moment arms of the GRF acting about the joints

				- ACLD leg: trunk angle > flexed over the entire landing phase compared to controls - Significant correlation found between moment arms at the knee joint and trunk angle
Ortiz, A., et al. (2008)[34]	ACLR; 13F healthy controls; 15F	Single leg drop jump, up-down hop task. Electromyography (EMG).	- GRF, Hip flexion, Hip adduction, Hip internal rotation, Knee flexion, KAA, Knee external rotation, Knee extension moments, KAM, Anterior-posterior shear forces	- No differences between groups: peak hip & knee joint angles for the drop jump task. - ACLR: significant differences in neuromuscular activity & anterior-posterior knee shear compared with controls in drop jump task. - No differences between groups: for peak hip & knee joint angles, peak joint kinetics, or EMG during up-down hop task.
Ortiz, A., et al. (2011)[36]	ACLR; 13F healthy controls; 15F	Side to side hopping task. EMG.	- Hip flexion, Hip adduction, Knee flexion, KAA, Knee extension moments, KAM	- Controls & ACLR: similar hip & knee-joint angles during both types of hopping. - > Hip-joint angles: crossover hopping in both groups, & knee-joint angles did not differ between the groups or hops. - Knee-joint moments: group X manoeuvre interaction. - Control group: > knee extension & valgus moments during crossover hopping - ACL: > KAM during side hopping
Paterno, M. V., et al. (2011)[45]	ACLR; 21M, 5F healthy controls; 13M, 29F	DVJ.	- GRF	- After ACLR, M & F: at the time of return to sport demonstrated involved limb asymmetries in pGRF during landing from a bipedal task. - DVJ landing phase: significant side-by-group interaction for pGRF in the entire cohort. - ACLR involved limb: < Vertical GRF than the uninvolved & both the preferred limb & nonpreferred limb in the control group - No effect of sex was noted.
Roos, P. E., et al. (2014)[47]	ACLD; 18M, 3F ACLR; 19M, 4F healthy controls; 11M, 9F	Single leg hop.	- GRF, CoM velocity, Knee extensor moment, knee RoM, Knee flexion angle, Hop moment, Ankle moment, CoM angle	- ACLD: smallest hop distance - Control: largest hop distance - ACLR: used similar kinematic strategy to controls, but had a reduced peak knee extensor moment. - ACLD & ACLR: Fluency reduced
Stearns, K. M. and C. D. Pollard (2013)[30]	ACLR; 12F healthy controls; 12F	Sidestep cutting manoeuvre.	- KAA, KAM, Knee adductor moment, GRF	- ACLR: ↑ average KAA & peak knee adductor moments compared to controls.
Vairo, G. L., et al. (2008)[46]	ACLR; 5M, 9F healthy controls; 5M, 9F	Single leg drop jump. Neuromuscular, biomechanical &	- GRF, Hip & net summated extensor moments, Hip joint flexion, Knee joint flexion, Ankle joint flexion	- No significant differences in hip & net summated extensor moments within or between groups. - ISGA (ipsilateral semitendinosus and gracilis autograft) ACLR: ↓ decreased pGRF at landing for involved limb

			isokinetic strength & endurance evaluations.			compared to uninvolved & controls, > peak hip joint flexion angles at landing for involved compared to uninvolved limb & controls at initial ground contact, ↑ peak hip joint flexion angles at landing for involved limb compared to uninvolved & pGRF, > peak knee & ankle joint flexion angles when landing on involved limb compared to control at pGRF.
	Webster, K. A. and P. A. Gribble (2010)[40]	ACLR; 12F healthy; 12F	Single leg hop.	- Resultant vector of time to stabilization, GRF		- ACLR: longer time to stabilize than control
ACLD	Chmielewski, T. L., et al. (2001)[44]	ACLD; 9M, 2F healthy controls; 8M, 2F	Walking & jogging	- Knee flexion angle, Internal knee extension moment, Support moment (at peak knee flexion), GRF		- ACLD: flexed involved knee < than healthy subjects & uninvolved side during walking. - ACLD: < GRF during loading response, < knee support moment, & ↑ ankle support moment during walking compared to controls. In jogging, involved knee angle at initial contact > extended compared to controls, & < knee flexion than uninvolved side. - No differences in kinetics during jogging.
	Hewett, T. E., et al. (2010)[68]	ACLD; 2F, twins healthy controls; 72F	Jump distance, DVJ single leg hop.	- Knee abduction, Knee flexion, Side to side asymmetries, Anatomic & anthropometric: Femoral notch width height, weight, BMI, Side to side asymmetries, Vertical jump height		- ↑ KAA at one knee in both of the twins relative to uninjured controls at initial contact & at max displacement during landing. - ACL-INJ twin: ↓ peak knee flexion motion at both knees than controls during landing.
	Houck, J. R., et al. (2005)[32]	ACLD; 10M, 5F healthy controls; 7M, 7F	Straight-ahead task, crossover-cutting task, & a sidestep-cutting task.	- Knee flexion angles, KAA, Knee internal rotation, Hip flexion angle, Hip abduction angle, Hip internal rotation, KAM, Knee flexion moment, Knee internal rotation moment, Hip abduction moment, Hip flexion moment, Hip internal rotation moment, Stride length		- ACLD noncoper: 1.8° to 5.7° < knee flexion angle compared to control across tasks, used 22% to 27% < knee extensor moment during weight acceptance compared to control, 34% to 39% > sagittal plane hip extensor moments compared to control, hip frontal & transverse plane moments differ from the controls
	Sheehan, F. T., et al. (2012)[39]	Movie captures of 20 athletes; Movie captures of 20 athletes performing a similar manoeuvre that did not result in injury (controls)	1-legged landing manoeuvre that resulted in an ACL injury	- CoM_BoS (base of support)/femur, Limb angle (relative to the gravity vector), Trunk angle (relative to the gravity vector		- Landing with the CoM far posterior to the BoS may be a risk factor for noncontact ACL injury. - ACLD land with CoM far posterior to the BoS.
	von Porat, A., et al. (2006)[41]	ACLD; 12M healthy controls; 12M	Gait, step activity & cross over hop.	- GRF, Step length, Velocity, Stance phase, Peak knee flexion, Knee power absorption, Knee extensor moment, Knee power generation		- ACLD after 16 years < knee extension strength - No difference in knee joint kinematics & kinetics - ACL-INJ: < knee extension strength was associated with joint moment reductions during step activity & cross over hop.

				- No significant differences in knee joint kinetics & kinematics in an ACL injured group 16 years after injury compared with a matched control group.
Yamazaki, J., et al. (2009)[31]	ACLD; 32M, 31F healthy controls; 14M, 12F	Single leg squat.	Relative angles between the body, thigh, & lower leg using an electromagnetic device: - Knee flexion, Knee adduction, Knee external rotation, Hip flexion, Hip adduction, Hip external rotation, KAA	- UNINJ leg of ACL-INJ M: < external knee rotation than M control dominant leg - UNINJ leg of ACL-INJ F: > external hip rotation & knee flexion & less hip flexion than F control dominant leg - M INJ leg: < external knee & hip rotation, less knee flexion, & > knee varus than UNINJ leg. - F INJ leg: > knee varus than UNINJ leg. - F > external hip rotation & knee valgus than M did in both the INJ & UNINJ legs.

ACL = Anterior cruciate ligament
ACLD = Anterior cruciate ligament deficient/injured
ACLR = Anterior cruciate ligament reconstructed
INJ = Injured
UNINJ = Uninjured
BoS = Base of support

M = Males
F = Females
GRF = Ground reaction force
pGRF = Peak ground reaction force
KAM = Knee abduction moment
KAA = Knee abduction angle

RoM = Range of motion
CoM = Centre of mass
DVJ = Drop vertical jump
EMG = Electromyography
ACL_{INT} = Anterior cruciate ligament intact

Discussion

This study reviewed the level of evidence with respect to the *in vivo* biomechanical literature to identify risk factors for non-contact ACL injury during dynamic sports tasks, and it critically evaluated research trends from retrospective and associative studies around non-contact ACL injury risk. The key findings of this review were a lack of level 1 evidence and a large number of level 3 evidence studies.

Ideally, associative studies are designed from a strong base of level 1 and level 2 evidence. Having observed only one level 1 evidence study and conflicting level 2 evidence, this appears not to be the case. A similarly skewed evolution of studies has also been observed in the more mature field of ACL reconstruction research [25] where studies with a lower level of evidence were published at a greater rate than level 1 or 2 evidence studies. Our study observed a large number of level 3 evidence studies that associated other variables to KAA and KAM. An important consequence of this is parameter bias, which is where only a limited number of parameters are used to inform retrospective or associative study designs. This was observed to some extent in the retrospective studies and to a greater extent in the associative studies. Parameter bias makes the results of these studies dependent on the reproducibility of the level 1 evidence and to our knowledge the findings of Hewett et al. [28] have as of yet not been confirmed independently. As long as that is the case, care should be taken using the KAA and KAM parameters only.

Recent level 1 evidence

Abstracts from two additional prospective-cohort studies were presented at the IOC 2014 World Conference Prevention of Injury & Illness in Sport, Monaco, France. The first study [69] collected prospective DVJ data from 708 Norwegian elite female football and handball players and observed 38 non-contact ACL injuries. This has recently been published [70] with 42 non-contact ACL injuries registered and neither KAM, KAA, knee flexion angle and peak GRF predicted ACL injury. The second study involved US military cadets [71], where 117 ACL injuries were observed in males and females from a cohort of 5758 cadets. They also found that KAM and KAA did not predict ACL injury but they did observe increased hip adduction and increased internal tibial rotation at contact in those who sustained an ACL injury. Both studies sampled larger cohorts and observed considerably more ACL injuries yet found that neither KAA nor KAM predicted ACL injury. This has important consequences for the large number of level 3 associative studies examining KAM and KAA only. The effect of parameter bias in this field therefore has important consequences for these studies and highlights the importance of having well-established level 1 evidence before conducting associative work. In the situation where conflicting level 1-evidence exists, it is clear that further prospective studies should be prioritized to develop a critical mass of biomechanical variables that predict ACL injury across studies. Researchers may wish to consider relevant factors identified from associative studies that may affect ACL injury risk yet have not been prospectively assessed including more dynamic tasks such as sidestepping, the influence of fatigue, and unanticipated movements.

Extrapolation and standardization

Appropriate caution should be taken when extrapolating the results of level 1 evidence studies to retrospective and associative studies. Specifically altered KAA, KAM and GRF have only been found to predict ACL injury when calculated within the experimental protocol and sample of Hewett et al. [28]. Although this study is highly cited (1031 citations at time of submission), their low number of ACL injuries observed, and lack of familywise-error correction, means results require independent confirmation. The use of the KAA and KAM was observed in many studies involving different age-groups, demographics, males and other tasks such as single leg landings and sidestepping. Although in many cases, significant effects on the KAA and KAM have been found it is recommended that level 1 evidence studies inform their predictive value of ACL injury.

Many conflicting results were found in both level 2 and 3 evidence studies. This is likely due to the variety of tested samples e.g. males, females, ACLD, ACLR, pre and post-puberty, ages, the variety of tasks e.g. DVJ, side cutting, hopping, single leg landings. Whilst samples may be difficult to standardize given that most recruitment is governed by convenience, the choice of task and biomechanical methods, which can significantly affect the KAA and KAM [69, 72-75], could be standardized. The DVJ task is frequently chosen as it replicates the task from the prospective evidence [28]. It has the advantage that it is simple and reliable although its credibility as an ACL-injuring manoeuvre has been questioned [76]. Furthermore, the DVJ does not replicate sport specific landings, which are commonly only supported on one leg [76, 77]. The use of a more sport-specific movement as a measurement tool may produce more sensitive and specific ACL injury predictors. One interesting observation was that a large number of studies used non-prospectively assessed tasks to associate to prospectively identified variables. Side cutting or sidestepping in particular was widely used (36%). The use of tasks that are informed by prospective evidence should be considered.

Barriers to strengthen the available evidence

Prospective studies are known to be expensive, time consuming and challenging with the possibilities of dropouts and negative results. The challenges of such studies have been outlined in detail [78]. In particular, biomechanical techniques such as three-dimensional motion capture and analysis tend to be time consuming; often requiring ~ 2 hours per study participant for data capture. This is obviously inhibitive to testing large cohorts. These challenges could be mitigated through automated data capture and analysis software and routines, efforts to move towards multi-centre studies through conducting inter-laboratory reliability assessments and standardization of methods, including using the same biomechanical models and data processing techniques that could increase numbers of participants and observed injuries whilst reducing methodological inconsistency. One recently published attempt to standardize biomechanical analyses across three laboratories showed promising results [79]. Once methodological standardization is established and the number of prospective studies increase, a meta-analysis of prospective studies will provide additional means by which risk factors can be evaluated.

Samuelsson et al. [25] identified a trend that high level of evidence studies in ACL reconstruction research (including randomized controlled trials) increased over time. This trend has not been observed in the context of the biomechanical contributors to primary non-contact ACL injury risk. Although, with the publication of new prospective abstracts [69, 80] and a large new prospective cohort study [70] more high level of evidence studies are being conducted which is welcome. Yet, additional research efforts are needed. The lack of high level evidence may also be because this research is preventative rather than therapeutic which typically means that the direct benefit to individuals is less clear and hence financial resources are less readily available. In addition, evidence from a cost-effectiveness study [81] shows that prevention programs give a better outcome where it reduces the ACL injury incidence from 3% to 1.1% per season and are lower in cost to conduct.

Limitations

We specifically chose to focus on *in vivo* biomechanical studies. Whilst we acknowledge that other biomechanical research paradigms have made significant contributions to the understanding of ACL injury biomechanics including *in vitro* and *in silico* studies, it was our intention to focus on risk factors *in vivo* using participants of dynamic sports as these are most likely to inform injury prevention practice.

Conclusion

Our search revealed one prospective cohort study which aimed to determine how *in vivo* biomechanics can serve as a predictor of non-contact ACL injury. This study found that female athletes with increased dynamic knee abduction angle and with a high knee abduction moment are risk factors for ACL injury, albeit in a small sample of injuries. Many associative studies are based on these results alone and are therefore at risk of task and parameter bias. Though a reasonably large number of level 2 and 3 evidence studies are available, more prospective cohort studies are needed to drive on-going work with the purpose of developing prevention programs and clinical interventions. Generating a critical mass of high quality level 1 evidence should therefore be the priority for research to advance the understanding of *in vivo* biomechanical risk factors for non-contact ACL injury.

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