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Anterior Cruciate Ligament Injury: Risk Factors and Injury Mechanisms. A Systematic Review

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ABSTRACT

Introduction: Anterior cruciate ligament (ACL) rupture is a highly prevalent injury, particularly among athletes, and poses significant physical and psychological challenges that negatively impact quality of life. Numerous risk factors (RFs) and injury mechanisms (IMs) have been described. However, the validity of many studies in this field is questionable, underscoring the need for a critical evaluation of the existing research. This systematic review (SR) aims to assess the quality of the recent literature on ACL ruptures and identify the primary evidence based RFs and IMs.

Methods: This SR included review article published within the last five years and indexed in the PubMed database. Eligible studies focused on potential RFs and IMs associated with ACL rupture. Studies focusing on surgical or conservative treatments, concomitant injuries, or exclusively post-surgical populations were excluded. The selection process followed PRISMA guidelines, and the quality of the included articles was evaluated using the AMSTAR-2 tool.

Results: A total of 10 SRs, encompassing findings from 218 individual studies, were included. Of these, 8 reviews were rated as "critically low quality," 1 as "low quality," and 1 as "moderate quality." The analysis identified 13 potential RFs and 3 primary IMs associated with ACL rupture.

Conclusions: The overall methodological quality of the research is low, with the majority of SRs rated as "critically low." Key RFs identified include sport-specific demands, sex, neuromuscular characteristics, and a family history of ACL injury. Primary IMs associated with ACL rupture include stiff landings, heel-strike landings, knee hyperextension, valgus collapse, and internal rotation. These findings underscore the urgent need for higher-quality research to improve understanding of ACL risks and inform the development of effective prevention programs.

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Introduction

An anterior cruciate ligament (ACL) rupture is a highly prevalent injury and is widely regarded as one of the most severe traumatic knee injuries. The primary function of the ACL is to provide mechanical stability to the knee during movement, preventing anterior translation and rotation of the tibia relative to the femur. This ligament plays a crucial role in maintaining proper biomechanics of the knee joint.

ACL injuries are common in sports environments, affecting athletes across all age groups and levels of competition. These injuries have significant consequences for the individual, including knee instability, meniscal damage, and an increased risk of secondary osteoarthritis. Additionally, such injuries often have a profound psychological impact on athletes, compromising knee functionality and negatively affecting their perception of health-related quality of life.

Numerous risks factors (RFs) for ACL injuries have been identified in the literature, typically categorized into extrinsic and intrinsic RFs. Extrinsic factors are external to the individual, while intrinsic factors pertain to personal characteristics and are further classified as modifiable or non-modifiable. Modifiable intrinsic factors, which can be altered, are the primary focus of prevention programs. In contrast, non-modifiable intrinsic factors, being inherent to the individual, cannot be influenced or changed.

Understanding these RFs and their underlying mechanisms is essential not only for accurate diagnosis and effective treatment but also for developing targeted prevention strategies to reduce both the incidence and clinical impact of ACL injuries.

The mechanisms behind ACL injuries are generally analyzed and categorized into two types: contact and non-contact mechanisms. Contact mechanisms involve direct trauma, while non-contact mechanisms result from forced movements of the knee. Notably, over 70% of ACL ruptures are attributed to non-contact mechanisms.

The primary objective of this systematic review (SR) is to evaluate the quality of existing literature on ACL RFs and injury mechanisms (IMs). It aims to systematically organize the most discussed elements in the field, synthesize the latest evidence, and provide a comprehensive, up-to-date review on the topic.

Methods

To develop this review, existing SR articles published between 2018 and 2023 were included to ensure a broad range of evidence and diversity. These studies, involving men and/or women, focused on evaluating potential RFs or underlying IMs related to ACL injury. The research framework, including the definition of inclusion criteria, was structured using the PICO tool (Table 1). The exclusion criteria were as follows:

- Studies exclusively examining concomitant injuries associated with ACL rupture.
- Studies addressing surgical or conservative treatments for ACL rupture.
- Studies involving populations exclusively post-surgery.

Table 1: Inclusion criteria according to the PICO strategy

Definition	Inclusion criteria
Population/Problem	ACL rupture
Intervention	Exploration of the RF and mechanisms associated with ACL rupture
Comparison	Not applicable
Outcome	Identification of FRs that contribute to ACL rupture and their underlying mechanisms

An electronic search was conducted in the PubMed database, utilizing a combination of keywords with Boolean operators (Table 2).

Table 2: Search Strategy

Database	Search number	Keywords
PubMed	1	(risk factor) OR (mechanism)
	2	((injury) OR (tear)) OR (rupture)
	3	(anterior cruciate ligament) OR (ACL)
	4	((#1) AND (#2)) AND (#3)
	5	Systematic review [Publication Type]
	6	(#4) AND (#5)

The review articles identified were selected using the methodology outlined in Figure 1, which adheres to the PRISMA guidelines. The initial selection was conducted independently by two authors, based on the titles and abstracts of the articles, achieving an 80% agreement rate. For articles where there was uncertainty about initial inclusion, the decision of the more experienced author in the field prevailed. Subsequently, two specialists in ACL trauma performed a detailed analysis of the articles from the initial selection to determine which met the predefined inclusion and exclusion criteria. In cases of disagreement regarding the relevance of the studies, the three authors engaged in a discussion until consensus was reached. The full text of the initially selected articles was carefully reviewed to extract relevant parameters for this analysis. Data extraction was performed independently by one author and subsequently verified by two ACL trauma specialists. The following information was extracted from each article: author, year of publication, number of studies included, study description, presence of a meta-analysis (MA), and risk factors (RFs) and/or injury mechanisms (IMs) potentially associated with ACL rupture. The RFs were further categorized as extrinsic or intrinsic, with intrinsic factors subdivided into sex, age, biomechanical, neuromuscular, and family history. Injury mechanisms were classified as either contact or non-contact.

The risk of bias (RoB) assessment of the selected studies was conducted using the AMSTAR-2 tool. This instrument is based on a set of 16 domains, subdivided into critical and non-critical domains. Depending on the number of parameters met, each domain is classified as: "Yes" (S), "Partially Yes" (SP), or "No" (N). Subsequently, based on the number of domains met and their category, each SR is classified regarding the overall confidence in the results as: "High," "Moderate," "Low," or "Critically Low."

Ethical approval was not required due to the nature of the study.

Results

Ten articles were included in this SR, which in turn included results from 218 studies. Figure 1 summarizes the selection process. Intrinsic RFs were addressed in 9 articles, while extrinsic RF were identified in 3 articles and injury mechanisms in 2 articles [1-6].

All the collected data were organized and presented in Table 3.

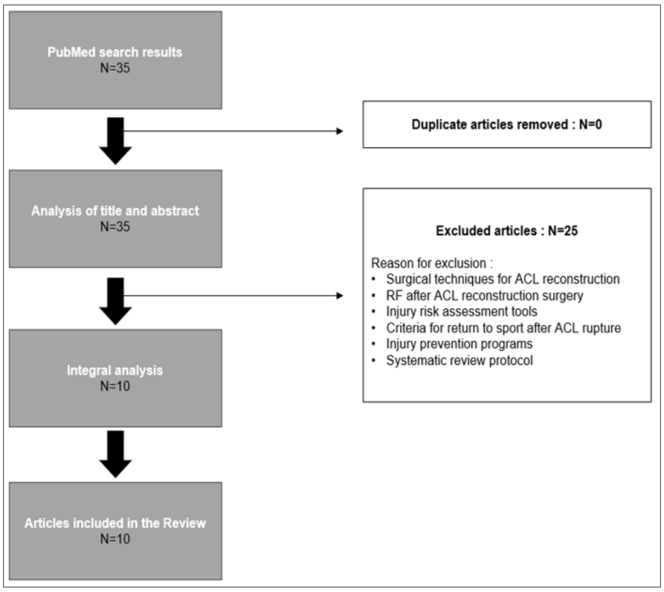

Figure 1: PRISMA Flowchart

Table 3: Study Characteristics

Author	Publication Year	Number of studies included	Study description	MA	Potentially significant mechanism/FR for ACL rupture	Categories
Aiello et al [6]	2022	12	Evaluation of specific activities at the time of ACL rupture.	No	Movements inherent to the practice of soccer	Injury mechanism - Non-contact
Chia et al [5]	2022	45	To determine the incidence and proportion of non-contact ACL injuries based on sex, age, type of sport, type of exposure, and level of participation in team ball sports.	Yes	Sex	Intrinsic - Sex
					Age	Intrinsic - Age
					Type of exposure (competition vs. training)	Extrinsic
					Level of participation (Amateur vs. Intermediate vs. Professional)	
					Level of contact inherent to a sports activity	
Kellis et al [7]	2023	5	To determine whether the hamstrings to quadriceps strength ratio (H:Q) is a key factor in ACL injury.	No	Hamstrings to quadriceps strength ratio	Intrinsic - Neuromuscular
Montalvo et al [6]	2019	36	To assess the sex differences in ACL injury based on the level of contact inherent to a sport (collision vs. contact vs. limited contact vs. non-contact vs. sports with fixed objects and high-impact rotational landing).	Yes	Sex	Intrinsic – Sex
					Level of contact inherent to a sports activity	Extrinsic
Larwa et al [2]	2021	18	To determine the biomechanical RFs that contribute to ACL injury.	No	Stiff landings	Injury mechanism - Non-contact
					Heel strike landings	
					Hip abduction strength deficit	Intrinsic - Neuromuscular
					Deficit of gastrocnemius strength	
					Core instability	
					Increased valgus/abduction angle of the knee	Intrinsic - Biomechanical
Cronström et al [1]	2020	9	To evaluate the impact of the knee abduction angle on ACL injury.	Yes	Increase in knee abduction angle	Intrinsic - Biomechanical
Hasani et al [8]	2022	5	To evaluate the impact of family history on ACL injury.	Yes	Positive family history of ACL tear	Intrinsic - Family History
Piskin et al [9]	2022	2	To determine CNS changes through neurofunctional evaluation prior to ACL injury.	No	Decreased functional connectivity between different cortical areas	Intrinsic - Neuromuscular
Montalvo et al [4]	2019	28	To evaluate the incidence proportion and incidence rate of ACL injury in soccer players based on sex.	Yes	Sex	Intrinsic - Sex
Montalvo et al [4]	2019	58	To determine the incidence rate of ACL injury in athletes based on sex and participation level (amateur vs. intermediate vs. professional).	Yes	Sex	

According to the AMSTAR-2 tool, 8 articles were classified as having "Critically Low" quality, 1 with "Low" quality, and 1 with "Moderate" quality [1-6,10]. The detailed analysis of each article and the resulting evaluation are summarized in Table 4.

Table 4: Quality of SR (AMSTAR-2)

Author	Domain																
	1	2*	3	4*	5	6	7*	8	9*	10	11*	12	13*	14	15*	16	Quality
Aiello et al [6]	Y	Y	N	Y	Y	Y	Y	PY	Y	N	NA	NA	Y	Y	NA	S	Moderate
Chia et al [5]	Y	Y	N	N	Y	Y	N	Y	Y	N	Y	Y	Y	Y	S	S	Critically Low
Kellis et al [7]	Y	N	N	N	Y	Y	N	PY	Y	N	NA	NA	Y	Y	NA	S	Critically Low
Montalvo et al [3]	Y	N	N	PY	Y	Y	N	PY	Y	N	N	N	N	N	N	N	Critically Low
Larwa et al [2]	Y	N	N	N	Y	Y	N	PY	PY	N	NA	NA	N	N	NA	S	Critically Low
Cronström et al [1]	Y	S	N	PY	Y	N	N	Y	Y	N	Y	Y	Y	Y	S	S	Low
Hasani et al [8]	Y	S	N	PY	Y	N	N	Y	Y	N	Y	N	Y	N	N	S	Critically Low
Piskin et al [9]	Y	N	N	PY	N	Y	N	PY	N	N	NA	NA	N	N	NA	N	Critically Low
Montalvo et al [4]	Y	N	N	PY	Y	Y	N	N	Y	N	Y	Y	Y	Y	S	S	Critically Low
Montalvo et al [4]	Y	N	N	PY	Y	Y	N	N	Y	N	Y	Y	Y	Y	S	S	Critically Low

NA: Not applicable; *: Critical domains

Extrinsic Risk Factors

A total of 3 extrinsic RFs for ACL rupture were identified. The exposure type was analyzed by Chia L et al., who concluded that athletes are more likely to experience ACL rupture without contact during competitions than in training [5]. Regarding participation level, Chia L et al. found that intermediate-level athletes have a higher risk of injury than amateur athletes, while Montalvo A concluded that amateur athletes have a 2.1 times greater risk of injury compared to intermediate and professional athletes [4,5]. Lastly, contact level was explored by two studies. Montalvo A et al. identified that sports involving fixed objects and high-impact rotational landing movements have a higher ACL injury rate in both sexes when compared to collision, contact, limited contact and non-contact sports. On the other hand, Chia L et al. did not consider the level of sport contact as a significant FR [3,5].

Intrinsic Risk Factors

Sex: Female sex is widely identified as a RF, with several studies showing that women have a higher risk of ACL injury compared with men. Montalvo A et al. indicates that the risk of rupture is up to 3 times higher in women, especially in contact and fixed-object sports [3]. In another study by Montalvo A et al., it was found that, in any sport, the risk of ACL rupture is 1.5 times higher in women, regardless of participation level [4]. However, it is at the amateur level in most sports where the discrepancy is greatest, as women have a 2.1 times higher risk compared to men. Additionally, Chia L et al. observed that women have a higher risk of injury from non-contact mechanisms [5].

Age: Age was not conclusively identified as a RF, according to the study by Chia L et al., which did not find a clear relationship between age and ACL injuries [5].

Neuromuscular Factors: Weakness in hip abductors, especially the gluteus medius, is associated with a higher risk of ACL injury, particularly in women due to delayed activation of the vastus medialis during landing. Larwa J et al. highlighted that this factor may lead to dynamic knee valgus, increasing the risk [2]. Additionally, weakness in the gastrocnemius muscles also appears to increase the risk of injury, as it decreases the ability to absorb impact forces during landing, along with core instability. Kellis A et al. found that the quadriceps-to-hamstring strength ratio does not influence ACL rupture risk [7]. Meanwhile, a decrease in the brain connection between the left primary sensory cortex and the right posterior lobe of the cerebellum was considered in one study, along with poorer connectivity between the left secondary somatosensory cortex and the left supplementary motor area and between the left primary somatosensory cortex and the left primary motor cortex, as predictors of future ACL injury [9].

Biomechanical Factors: The knee abduction angle was analyzed in different studies, but the results were contradictory. While Cronström A et al. did not find an association with injury risk, Larwa J et al. suggested that dynamic knee valgus, especially when combined with other neuromuscular factors, increases the risk of injury [1,2].

Family History: A family history of ACL injury increases the likelihood of primary injury by 2.5 times, regardless of sex, as per the study by Hasani S et al. [8].

Injury Mechanisms

Aiello F. et al., through video analysis of injury moments in football, determined that most injuries occur during pressure on the ball carrier, as well as during shooting and dribbling. According to the author, these results can be explained by movements of knee valgus, internal rotation, and hyperextension that the knee is exposed to during these actions.

On the other hand, Larwa J. et al. concluded that rigid landing after a jump increases the risk of ACL rupture due to the hyperextension mechanism of the knee underlying this movement. In addition to rigid landings, the study also considered that landings on the heel increase the risk of injury compared to landings with plantar flexion of the foot.

Discussion

This SR evaluated the existing literature on RFs and IMs associated with ACL injuries using the standard methodology defined in the PRISMA guidelines. Although a structured approach was implemented to conduct this review, the conclusions are limited by the intrinsic quality of the existing evidence. According to the AMSTAR-2 framework assessment, most articles included in this review were of low quality. For example, we found that none of the included studies met the non-critical domains 3 and 10, and only one study met the critical domain 7. Indeed, studies on ACL rupture face many challenges in their design and, as a result, are more likely to be subject to bias. One of these challenges is that most studies use populations composed exclusively of athletes, which limits the generalization of the results to the general population. Additionally, the difficulty of following individuals over long periods means that most studies are retrospective, making them more susceptible to confounders and dependent on the quality of the records. Therefore, the results of studies on the topic of ACL rupture should always be interpreted cautiously and critically, as they are highly susceptible to bias and tend to have lower quality. Nevertheless, the existing literature can provide important cues on the most relevant RFs and IMs, particularly in areas where there is a clear conversion of results across a wide range of studies.

We found that extrinsic RFs are mainly related to characteristics inherent to the type of sports practice. And, in this context, the competitive environment is more conducive to ACL injuries compared to training. This can be explained by the higher levels of internal and external stress to which the athlete is exposed, as well as the fatigue resulting from the increased intensity of exercise, which leads to a decrease in motor coordination and decision-making ability. Therefore, it is extremely important to ensure the training environment replicates as closely as possible to the realities and challenges faced by the athletes in the competitive moment. Contrary to what would be expected, the risk of ACL injury is not directly proportional to the level of contact the athlete experiences in their sport, which explains why non-contact ACL ruptures account for more than half of all ACL injuries. This is supported by Aiello F. et al., who concluded that in football (a contact sport), most injuries occur during the movement of pressuring the ball carrier, during shooting and dribbling, in other words, actions where the level of contact is minimal but where non-contact injury mechanisms such as hyperextension, dynamic valgus, and internal rotation of the knee are at play [6]. Although it would be expected that activities like landing or rapid changes of direction would also have a significant impact on ACL injuries in football, this does not appear to be the case. In fact, it is primarily in sports involving fixed objects, such as obstacle racing, where the risk of injury appears to be higher, as the athlete repeatedly performs landing movements after jumps, making them more vulnerable to injury mechanisms such as stiff landings or heel strikes. Similarly to the competitive level, athletes in lower levels (amateur and intermediate) are at higher risk for ACL injuries, though there is no consensus in existing studies on which of the two has the greatest risk. Theoretically, in amateur or intermediate levels, the frequency and effectiveness of training is substantially lower, leaving the athlete even more exposed during competitive moments.

Intrinsic RFs were clearly the most commonly identified in the studies under review, with female sex being the most consistent factor for higher risk of ACL rupture. Women have up to three times the risk of men for ACL rupture. This discrepancy between sexes is particularly evident in contact sports (such as football) and sports involving fixed objects. As mentioned earlier, even in contact sports, most injuries result from non-contact mechanisms, and since women are at a higher risk than men for ACL ruptures due to non-contact mechanisms, this explains the increased risk in contact sports [5]. This higher risk of non-contact injuries may be explained by neuromuscular factors, such as lower thigh abduction strength in women compared to men, theoretically secondary to a larger pelvic bone structure, and delayed activation of the vastus medialis. Although lower thigh abduction strength leads to knee valgus, it is not sufficient to consider the knee abduction angle alone as a biomechanical RF. According to Cronström A et al., a greater knee abduction angle during vertical jumps and squats does not increase the risk of ACL injury [1]. On the other hand, Larwa J et al. states that dynamic knee valgus is an isolated RF, and when associated with neuromuscular RFs, it considerably increases the risk of injury [2]. Also, the deficit in core muscle strength, especially in women, and in the gastrocnemius muscles, seems to increase the risk of ACL rupture, in contrast to the hamstring-to-quadriceps strength ratio, which apparently does not influence the risk of ACL rupture. Since these factors are potentially modifiable, it is of utmost importance to invest in strengthening these muscle groups, emphasizing again the importance of training, especially in women, for knee joint stability.

Within neuromuscular RFs, there is also evidence that a decrease in functional brain connectivity, detected through neurofunctional assessment, between motor, sensory cortical areas, and the cerebellum increases the risk of injury. This is explained by a decrease in proprioception and, consequently, the ability and speed to recognize, adjust, and correct movements that predispose to injury. This leads not only to motor coordination limitations due to impaired precision and control of complex movements but also to joint instability. As is well known in sports, especially in the competitive environment, it is imperative for athletes to respond quickly to external stimuli, adjusting their movements in a coordinated, precise, and rapid manner to avoid risky postures that inevitably increase the likelihood of ACL rupture, which in this case is compromised by changes in the CNS. However, in practice, it seems unfeasible to perform neurofunctional assessments solely to assess the potential risk of ligament injury. Furthermore, the study from which this conclusion was drawn is based on an extremely small sample, which requires further confirmation for generalization of the results.

Family history of ACL rupture emerged as another significant RF for injury, as concluded by Hasani S et al [8]. According to their study, individuals with a family history of ACL injury are 2.5 times more likely to suffer a primary ACL injury, independent of sex. However, while there may be some genetic contribution to this fact, the risk is primarily explained by environmental factors. In athletic individuals, it is common for direct descendants to engage in physical activities from an early age, which increases exposure time to other RFs. The imitation of parents' behavior and the pressure to excel in sports competitions may create a vicious cycle, ultimately leading to ACL rupture. Even though genetic contribution cannot be ruled out and is not amenable to modification, preventive measures targeting other potentially modifiable factors to mitigate the impact of family history on the individual should be pursued.

This SR highlights the multifactorial nature of ACL injury risk, encompassing both extrinsic and intrinsic factors. Notably, many of these risk factors are modifiable, suggesting that targeted prevention programs could significantly reduce the incidence of ACL injuries. Future research should focus on developing and evaluating the effectiveness of such programs to provide evidence-based recommendations for injury prevention.

Conclusions

The quality of recent literature on RFs and IMs ACL injury is low, with all studies failing to meet at least two non-critical domains, and most being unable to fulfil all critical domains of the AMSTAR-2 assessment.

This review highlighted that the competitive environment is the most conducive to injuries, and the risk of injury is particularly high in sports with fixed objects and at amateur and intermediate participation levels. Female sex is consistently associated with a higher risk of ACL injury. Deficits in strength in the core muscles, hip abductors, and gastrocnemius, as well as alterations in the CNS, were also identified as RFs. Family history of ACL injury, in isolation, is considered a RF for this injury [11-13].

Regarding the mechanisms of injury, stiff or heel strike landings are described as harmful mechanisms for the ACL. Hyperextension, valgus, and internal rotation of the knee also contribute to the occurrence of ACL rupture.

These findings underscore the urgent need for higher-quality research to improve understanding of ACL risks and inform the development of effective prevention programs.

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