Review Article

International Journal of Research in Pharmaceutical Sciences

Published by JK Welfare & Pharmascope Foundation

Journal Home Page: www.ijrps.com

Gender difference in cruciate ligament of the knee in normal condition and the risk to its injury; an updated review

Yasser Alharbi*

Department of Basic Medical Sciences, College of Medicine, King Saud Bin Abdul Aziz University for Health Sciences, (KSAU-HS, King Abdullah International Medical Research Center (KAIMRC), National Guard Health Affair (NGHA), King Abdulaziz Medical City, Jeddah, Saudi Arabia

Article History:

Received on: 20 Apr 2021
Revised on: 23 May 2021
Accepted on: 24 May 2021

Keywords:

Cruciate Ligament,
Knee,
Risk,
Trauma,
Females,
Injury

Abstract

Anterior cruciate ligament is a broad intracapsular stabilising ligament in the knee joint. Anterior cruciate ligament tears are one of the commonest injuries occurring to athletes. Numerous studies have investigated the epidemiology and risk factors to anterior Cruciate Ligament injury. It has been documented that anterior Cruciate Ligament tears are more common among females. In this review, we presented a collective summary of cruciate ligaments variations between genders in normal conditions and in different illnesses. Moreover, we illustrated the different response between genders to trauma and stressors as regards the effect on the cruciate ligaments. We also presented a summary of the risk factors and types of injury to the cruciate ligaments in response to different modes of trauma. We summarized the most prevalent, recent and evidence-based risk factors of anterior Cruciate Ligament injuries which include genetic, hormonal, anatomical, environmental, biomechanical and neuromuscular risk factors. We emphasized on the relationship between age, hormones and the incidence of anterior cruciate ligament injuries during puberty, older ages and changes accompanying menstrual cycles. We conclude that risk factors are numerous, but the higher prevalence in females can be predictable based on these factors and therefore preventable. However, further studies are required to deeper investigate the recovery predictive factors after injury and determine better approaches to tackle these risk factors.

*Corresponding Author

Name: Yasser Alharbi
Phone: +966555343831
Email: Algaidyy@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v12i3.4836

Production and Hosted by

IJRPS | www.ijrps.com

INTRODUCTION

A broad intracapsular stabilising ligament in the Knee joint is the anterior cruciate ligament (ACL). Factors external and internal to the ACL non-contact injury are suspected to lead and are well investigated (Hewett *et al.*, 2007). The major biomechanical risk factor for ACL non-contact wounds is indicated to be increased hip adduction, greater internal hip rotation, knee valgus and internal knee rotation during working activities (Olsen *et al.*, 2004).

The anterior cruciate ligament (ACL) injuries are more common in women 2 to 8 times when compared to males. Yet the etiology is not well known for this gender difference. Variabilities in the size of the ligament as well as the orientation of the lower limbs, in addition to hormonally induced improvements in the generalized laxity of ligaments and the functions related to the neuromuscular system have been due to a variety of interrelated causes (Anderson *et al.*, 2001).

The return to previous playing standard is also recorded at 65 in five years and in women in same sports is slightly lower than in men (Hewett *et al.*, 2007). The significant risk factors for non-contact ACL injury in females were an abnormal lower limb morphology and an abnormal neuromuscular control, Increased knee valgus allegedly leads to an increased risk of ACL in women through the quatman's team's systematic study (Quatman *et al.*, 2010).

To date, magnetic resonance imaging (MRI) was mainly used to diagnose tears of ACL. The MRI was developed with a sensitivity of 93 and 100% as an incredibly useful tool to correctly determine the integrity of the ACL. However, there wasn't significant use of picture to recognize risk factors which could lead to injuries; magnetic resonance (MR) was used to examine these architectural variations in gender in the knee. In comparison to ACL tears, the occurrence of PCL accidents does not vary according to gender even though they are much less frequent than ACL tears (Fayad *et al.*, 2008).

In this review, we present a collective summary of cruciate ligaments variations between genders in normal conditions and in different illnesses. Moreover, we illustrate the different response between genders to trauma and stressors as regards the effect on the cruciate ligaments. We also present a summary of the risk factors and types of injury to the cruciate ligaments in response to different modes of trauma.

Gender Differences in the morphology of ACL

In past years, imagery has examined the gender-based variabilities when it comes to the size of the ACL, but more distinct detail has been given in recent research. Initially, the previous calculations of ACL scale were presumably faulty due to the geometric structure of the ACL. The 0.2T ACL volume measurements were reported, but other ACL widths were obtained in subsequent experiments at an axial plane. The slice thickness was multiplied by 2.5 mm with the measured area, and a volume was estimated. Other experiments are limited to ACL distance or area rather than volume measurements (Anderson *et al.*, 2001). Measure the ACL in coronal, coronal, oblique, axial and sagittal planes were used in the above studies at 1.5T. A noble research by Fayad et al. was done at 1.5T and used both ACL bundles for a genuinely reliable calculation of volume (Fayad *et al.*, 2008).

In contrast with male athletes, Anderson et al. found that women have a narrower ACL region and indicated that greater muscle strength in female athletes contributes to more tension in a small ACL, which leads to a ligament tear in turn (Anderson *et al.*, 2001). This latter research failed, in order to create a true association between ACL size (area) and sex, with height, weight, and BMI parameters. In the Fayad's team analysis, the ACL volume and height, and ACL measurements were closely correlated, but there wasn't statistically significant difference in BMI (Fayad *et al.*, 2008).

However the BMI is not inherently associated with muscle bulk, such results may contradict the suggestion that the more powerful the muscles get and the increased weight of sportswomen causes a CLA injury, as their small CLAs are stressed more frequently. There is also a fair need for analysis of gender variances in cross ligament volume for patients with the corresponding height and weight because body weight and height were reported as variables confounding in the volume of ACL measurement (Fayad *et al.*, 2008).

Besides ACL, tests were conducted on each cadres, imaging films, computed tomography (CT) and Magnetic Resonance Imaging(MRI) and were analyzed on the gender structural differences in the knee. Other anatomical anomalies so far found could involve gender-based differences in the femoris quadriceps angle (Q angle) as well as discrepancies in the distance of the femoral notch (Fayad *et al.*, 2008). The Q angle for women is greater than for men and in principle raises the medial tension in the knee given the stronger action of the quadriceps muscle laterally, possibly contributing to ACL injuries. In this research, it has been seen that the anteromedial bundle (AMB), which is smaller than the posterolateral bundle (PLB) of ACL, may be predicted to lead to an unconscionable tear due to the larger Q angle and the tension among women.

The latest data indicate that the space between both femoral condyles, which is measured as a whole size, is considerably bigger for men than females, although it is possible that the difference depends on the person's height rather than sex. Furthermore, the number of intercondylar notches correlates equally with the volume of the ACL of women and men both, which disproportionately refutes the fact that an inconsistent size of that notch (mismatch) and ACL (narrowing of the notch) could be triggering tears of the ACL in women (Fayad *et al.*, 2008).

In short, there are gender disparities in the amount of ACL. However, this can only be attributed to the disparities in height between men and women. Moreover, with progressive study, the idea that the difference between the volume of the femoral notch and the ACL becomes more problematic as a contributor to the production of ACL injuries among women. The AMB, which is the smaller component of both sets of the ACL, but it also has an effect on tear production in the ACL of women.

Effect of gender on the femoral kinematics axis location and ACL injury

The efficiency of athletic activities after normal movement has crossed the amount of ACL injury can be viewed as a worse situation for ACL charge by a combination of extreme transverse plane movement and injurious frontal and/or sagittal plane dynamics (Quatman *et al.*, 2010). Therefore, irregular or anomalous cinematics on several planes may be an acceptable indication of a growing risk of ACL injury during the mission results.

The ACL primary risk factor is noted for synchronization of the Valgus during the completion of athletic activities. During the execution of sporting activities analyzed for both I C and peak values, the ranges measured in this analysis indicate a degree of valgus. The excessive valgus presence may, however, suggest an increased risk of injury. The only cinematic variables which are clarified to anticipate ACL tears in females among the samples are knee valgus measurements (IC and peak values) throughout the execution of an upward jumping mission. Hewett et al. observed the mean values of KVAR/VALG at IC and max, respectively, for subjects sustaining ACL injury to land at -5,0° and-9,0°, compared with 3,4° and -1,4° for uninjured persons. The following records were accessible (Hewett *et al.*, 2007).

Both cohorts in the Hewett et al. analysis displayed KVAR/VALG angles within typical ranges as defined for the double-legged, vertical jumping challenge by this examination (-5.3° to 4.7°) and peak values (-17.79° to 0.37 °). This could derive from the variations found in the IC and peak KVAR/VALG values in tests, which may be due to methodological variations among Hewett's team's study and further investigations mentioned in the current analysis (eg. decrease in height and the cohorts investigated) (Hewett *et al.*, 2007). However, it is important to remember that in contrast with uninjured individuals, ACL-injured subjects landed with IC corners closer to irregular movement. These values can mean that near to the end areas of natural motion, in particular for KVAR/VALG at IC, can be an indication of an elevated risk of injury (Fox *et al.*, 2014).

In the area of cinematic sagittal aircraft, all the physical activities studied covered the usual spectrum of hip and knee flexion. But for the cutting activity of side steps, hip and knee bending values improved from IC to max. During the execution of athletic activities, a state of hip and knee flexion is required, since flexion of the joint is a method in attenuating forces and control the activity while the knee is in contact with the ground. If the hip and knee have inadequate bending, passive joint braces are important (e.g., ACL), so that the joint load on the knee is stabilized and counteracted further. Consequently, reduced motion is often known as an ACL injury risk factor on the sagittal plane (Yu and Garrett, 2007). Interestingly, many of the flexion angles proposed to raise the likelihood of ACL in women fell beyond the usual range of cuts and landings found in this study (Fox *et al.*, 2014).

Cross-cutting plane cargoes were also occurs alongside an enhanced ACL strain and were thus proposed to increase the risk of ACL injury (Hewett *et al.*, 2007). With respect to KINT/EXT, the most dominating movement was identifiable, with the highest range values are usually on any side of the neutral posture for those factors, either internal (such as internal shank rotation in relation to femur) or external (such as the external shank rotation relative to the femur). While external shank rotation would lead to minor increases in ACL tension, movements in this direction are still found in cases of ACL injury and may therefore also contribute to injury (Olsen *et al.*, 2004). Therefore, the elevated risk for ACL damage can be considered as an excess or irregular tibial or knee rotation (Fox *et al.*, 2014).

Effects of Puberty on Anterior Cruciate Ligament (ACL) and Injury Risk

Effect on fibroblast proliferation and collagen synthesis

Fibroblasts are essential to preserving ligament integrity, as they prevent or restore the continued damage to the ligamentous tissue from becoming microscopic. Collagen is derived from fibroblasts and constitutes the ACL's principal load-bearing structure. Form I collagen, which is in charge of supplying support to connective tissues during motion or stability and collagen type III in charge of elasticity of the tissue are the major types of collagen alluded to throughout this study (Lee *et al.*, 2004a).

The fibroblast of human ACL has demonstrated that the number of these receptors is not the same for young adult men and women both as estrogens and testosterone receptors. Given the greater concentration of estrogens in females than in men, sex steroids, specifically estrogens, could directly influence the synthesis, components and, eventually, the mechanical wellbeing of the ACL in humans which results in an increased likelihood of injury in women, especially during the estrogens' influx surge during puberty (Wild *et al.*, 2012).

In an analysis done in the late nineties of the past century, the ACL for a 32-year-old woman was subjected for two weeks to exogenous estrogen physiological and supra physiological (0.0029–25ng/mL). The first 3 days of exposure to estrogen revealed initial up-regulation of fibroblasts. However, the dose-dependent decline in fibroblast proliferation and rate of prokollagen-Type I synthesis with rising estrogen levels became clear in day 7 (Yu and Garrett, 2007).

As the tissue ACL from various species (human, rabbit and sheep) is harvested in the studies mentioned above, it is difficult to make distinctions between these species. However, there is further evidence that estrogen may influence the metabolic specifications and thus the structure of ACL, regardless of its concentration. As this could decrease the potentiality of the ligament to resist loads and increase the risk of damage, the effects of estrogen and loads on ACL should be studied (Wild *et al.*, 2012).

Effects on the metabolic properties of the ACL

During walking, running and other everyday exercise, the ACL is continuously exposed to tensile pressures and is considered to be important for the integrity of ACL fibers (Lee *et al.*, 2004a). In contrast to the control ACL (unloaded), Toyoda and others subjected the rabbits' ACL to a cyclical 80 mmHg of vacuum power for a one-day duration and observed an increase of 14% regarding collagens of type I in the ligament, which were subject to heavy loads. This finding was confirmed by Lee and colleagues, who documented elevated levels of type I collagen messenger RNA activity (mRNA) and an elevation of collagens type I and III in cyclic tensile load of porcine ACL (Lee *et al.*, 2004b).

A rise in the amount of collagen of form I within the ACL will give the ligament greater resilience, thereby broadening the capacity of the ACL to stand heavy objects. During regular walking, the ACL undergoes train loads, which could measure up to three hundred newtons(N), so the frequent use of this load, irrespective of estrogen, may be supposed to support ACL's wellbeing (Shelburne *et al.*, 2004).

The findings showed inhibition of the expression of mRNA responsible for synthesizing type I and type III collagen, when the porcine ACL was undergoing cyclic loads of the estrogens (represents the follicular, ovulatory and luteal process of menstrual cycle in females) in an estrogen setting. The involvement of estrogen will also decrease the ACL's strength and integrity. These findings suggest that the higher levels of estrogen in women deny the beneficial benefits of ACL loading every day, which can contribute to a rising risk of injuries for women. This could be attributed to fibroblast downregulation, which could contribute to lower ligament strength. It is necessary, however, to decide whether these metabolic and the ligament fiber changes influence the mechanical characteristics of the ACL and make it more liable to tear or rupture (Wild *et al.*, 2012).

Effect on mechanical properties of the ACL

The lower limb, like the ACL, is subjected to 2–10 times body weight through ordinary sports activities, including jumping and landing (BW). The ACL must be of ample tensile strength and rigidity in order to cope with the high charges produced during sport. It is supported that estrogens have an effect on the ACL's metabolic characteristics, regardless of whether the ligament has been primed or unloaded (Lee *et al.*, 2004b).

Furthermore these improvements in the ligament's collagen content (type I and III) will impact the mechanical characteristics of ACL, jeopardize aspects (for example: the strength end-point and rigidity, as well as their capacity to survive intense processing (Lee *et al.*, 2004a). It was noteworthy that the ACL stiffness was higher than the male rat, suggesting that the female rat had the potential to handle loads better, and that the findings of previous human ACLtissue experiments defied this (Pollard *et al.*, 2006).

In comparison, a recent study investigated the mechanical properties of ACL rat manipulated in conditions, where estrogen levels were low or high using contraceptive pills. In a test sample, higher estrogens (not taking the pills; 46,7 pg/day/mL) showed better outcome regarding the defect deformity and less pre-failure energy absorption than in experimental ACL, which had lower estrogen concentrations of 329pg/day/mL (the contraceptive pills). Estrogen levels were indicative of the levels of people with contraceptive pills during the normal human menstrual period (Yu and Garrett, 2007).

Ovariectomized rabbits treated with estrogen supplement (52 pg serum estrogen levels/mL) were decreased to load due to failure in the ACL, relative to ovariectomized estrogen-not exposed rabbits (14 pg serum estrogen/mL). These findings show that in an extremely estrogenous setting (such as estrogen levels that arise in puberty in girls) the structural and functional stability of the ACL is impaired compared with the lowest estrogen condition (the levels of estrogen were similar to pre-puberty females or male athletes). There is also an opportunity for more insights on the increased risk of ACL injury for girls after puberty to alter the mechanical characteristics of the ligament during puberty as well as how puberty changes could make joints more lax (Wild *et al.*, 2012).

Effect on knee joint laxity

The ACL is considered of the key factors controlling the knee joint stabilization. More laxity in the knee joint is believed to result in an increased susceptibility of ACL injury as the joint flexibility is decreased. For example, the incidence of AC L injury in 1 98 military cadets was shown to rise dramatically in anterior tibial translation of one or two standard deviations higher than normal (Myer *et al.*, 2008). Due to the combination of the estrogen concentrations and ACL mechanical properties, a sharp increase in the estrogen levels of girls during puberty will lead to altered ligament properties (Uhorchak *et al.*, 2003).

While increased laxity of the knee joint is accompanied with a higher risk of ACL tear, few literature records of alterations among girls' joint laxity during the process of puberty (Uhorchak *et al.*, 2003). Quatman and others estimated that around 28% of women had knee hyperextension during their puberty, in comparison with just 10% of men at the same age group. Women demonstrated higher general laxity during puberty, according to Beighton and Horan Joint Mobility Index measurements (Quatman *et al.*, 2010). However, other research reported varying findings, with some showing a decline in general laxity of the knee or anterior laxity of the knee with increasing ageing or the tanner period, while others showed a decline of knee laxity with ageing or tanner stage (Wild *et al.*, 2012). Although the previous studies recognize that girls have been tested for menarche status, this occurs later during the puberty period it doesn't show the discrepancies between persons according to the Tanner stage (Ahmad *et al.*, 2006).

Therefore, further study is required as the large influx of estrogens in females since the beginning and during puberty causes increased laxity of the knees. Find out more about the greater chance of ACL lesions in pubescents, because of accelerated anthropometric changes during adolescence, anatomical and alterations in the girls' musculoskeletal system throughout puberty.

Effects of menstrual cycle on ACL and injury risk

The risk of LCA damage, which happens 3 to 6 times more than adult males in both women and children, is especially high. The primary hormones investigated in the menstrual cycle related to ACL laxity are estradiol, progesterone and relaxin (Hewett *et al.*, 2007). At the start of the menstrual cycle Estradiol and progesterone are at their lowest levels of humans (days 1-6). Estradiol peaks at ovulation (days 12-14), and the latter extends the luteal duration by a second (days 20-24). Progesterone starts in the late follicular phase, but in the midluteal phase the peak level is attained (days 19-24). These normal hormonal variations were postulated in the menstrual cycle to induce ligament laxation, which raises the likelihood of ACL injury (Herzberg *et al.*, 2017).

Laboratory experiments have found, in particular, that the sensitivity of ACL to estradiol contributes to dose-dependent decreased synthesis of fibroblast and collagen and is attenuated by adding progestins. Relaxin is an ovarian and placental hormone that contributes in pregnancy and childbirth to the laxity of pubic symphysis and were suggested as well to induce a change on the ACL among non-pregnant females (Yu and Garrett, 2007).

To date, research has shown a possible correlation between menstrual cycle hormone levels and knee laxity and/or injury. There are various hypotheses surrounding the higher frequency of ACL breakdown in women versus men, including physiological variations, complex causes including leaping processes, and laxity of ligaments. Hormone variations were thought to probably play a part in the two latter. The hormones were hypothesized to impact ACL injury, either by the direct effect of the ligament laxity or rigidity on the ACL or through neuromuscular changes that affect knee alignment with collagen synthesis and tensile properties provided to the estrogen, progesterone, testosterone and relaxin receptor. Increased fibroblast proliferation and increases in collagen synthesis indicate ACLs in cell culture exposed to increased oestradiol while progesterone is linked to increasing proliferation of fibroblasts and increased collagen synthesis (Yu and Garrett, 2007).

Moreover, hormones have been speculated to alter knee orientation leading to neuromuscular shifts. The effect of hormonal variations on neuromuscular function was explored in two of these experiments. The neuromuscular activity of the quadriceps and hamstrings is measured all by electromyography (EMG). There were no discrepancies observed between one sample and another in increased follicular activity, while hemse activity increased in the ovulatory phase relative to follicular phase, with most pronounced effect in the lateral quadriceps (as measured by EMG activity). The medial hamstring has the highest pre-impact operation in particular. Khowailed et al. proposed that these variations lead to knee misalignment before impact and can contribute to increased ovulatory ACL injuries (Khowailed *et al.*, 2015).

If the ovulation's hormonal variations increase the risk of ACL rupture, follicular growth suppression and ovulation may be protective. While smaller studies have shown no effect, bigger studies have shown a possible 20% risk reduction for detecting a difference in the joint relationship between hormonal contraception and ACL injury. The relative dominance of progesterone in hormone contraceptives can reduce estradiol effects. The findings supporting this correlation were, however, based on administrative data from surgery patients. Although the experiments have tried to account for such big confounders as age, the retrospective nature of these studies makes it difficult to assign cause and effect. However, those fascinating results indicate that a large-scale, long-term analysis of elite women's athletes in and out of OCs or an interventional trial of hormonal contraception in elite athletes will be highly relevant (to monitor the stable consumer impact) (Herzberg *et al.*, 2017).

Other risk factors for ACL injury

It is apparent from reviewing the literature that the probability of contractual ACL tears is higher than it is for the primary ACL injury. Return to a high level of operation is the most significant risk factor for a contralateral ACL injury. There are some signs that the ACL reconstruction with auto-graft patellary tendon (compared to auto-graft hamstrings) and the small intercondylar notches will raise the likelihood of an ACL contralateral injury at the beginning of the ACL injury and subsequent ACL reconstruction. The female gender doesn't seem to be a risk factor of a contralateral ACL injury. Changed biomechanics and neuromuscular activity due to the original ACL fracture, which most likely impacts the affected leg as well as the uninjured leg, further raise the likelihood of an ACL counterpart injury. Further research is needed to explore the ability to decrease the probability of subsequent contractural ACL tears to restore normal biomechanics and neuro-muscular function after the first ACL injury.

Female gender

The most known risk factor for unilateral ACL injury is potentially female gender. Yet, there is no compelling indication that women are more likely to be negatively affected by ACL. There is clear evidence that pivoting and diagonal sports which include boxing, hockey, handball and basketball are so distinct. In French national skiers, the percentage of ACL tears contralaterally was greater for women than for men (Pujol *et al.*, 2007).

The disparity found was, however, not statistically important and is not addressed in the paper as to the degree of healing and competitiveness which sportsmen and women returned to after unilateral ACL injury. It is also impossible to assess whether women are a risk factor. Shelbourne et al. did not show substantial variations regarding the chances of contralateral ACL harm between males and females in a group balanced with their activity level. Another explanation for why there has been no reporting discrepancy between men's and women's risk of contractual ACL injury could be the environmental risk factors because of a single ACL injury outweigh classical ACL risk factors, including sex (Swärd *et al.*, 2010).

Age

Pinczewski et al. have found that young people are at higher risk of contralateral ACL damage during testing during ACL reconstruction. A ruptured ACL patient is expected to be more vulnerable to an ACL wound due to multiple intrinsical causes. In comparison, the risk of a young patient returning to a high operation is probably greater than the percentage of old individuals with ACL injuries at first, and their activity may be higher for a longer term (Pinczewski *et al.*, 2007).

Anatomic factor

Bone length

The knee torque increases with the rise in tibial and femoral bone thickness, which increases knee instability (Hewett *et al.*, 2007). In males, the strength and rigidity of their muscles will partially regulate this instability. This partial stabilization in women is not accomplished because of the smaller muscle density and the risk of ACL injury in women is thought to increase. A stronger ACL injury marker than the absolute length and breadth of the lower extremity limbs was seen for hip width to femoral length comparison (HLR) (Hewett *et al.*, 2005). However, in other research, this proportion did not vary greatly between sexes, with 0.73 in males and 0.77 in females, which indicates that the gender difference in ACL injuries cannot be justified (Cho *et al.*, 2014).

Q-angle and a valgus knee

The Q-angle is created by a crossing of the line imagined from the middle of the anterior superior iliac spine and the patella and an imaginary line drawn from the center of the patella to the tibial tuberosity. Males typically have Q-angles greater than females. The larger the pulling force of the quadriceps femoris muscle on the patella at the medial knee is greater than the lateral pulling power, the wider the Qangle. The risk of ACL lesions and other complications from the knee joint was increased by abnormal stress on the medial knee. In addition, the valgus knee was used as a predictor diagnosis for the ACL lesion (Griffin *et al.*, 2006). But since it cannot be used the static Q-angle in valgus or knee positions to estimate ACL injury. In the same manner, there is debate about whether the Q-angle and knee valgus should be used to provide a predictor of ACL injury (Myer *et al.*, 2008).

Intercondylar notch width and shape

Generally speaking, the higher you are, the greater the overall intercondylar. But at the same moment as you grow greater in males, the intercondylar clasp width reduces; this is not inherently larger than in your female height. In contrast with the larger intercondylar notch, females with a narrow intercondylar notch (<13 mm) are 16.8 times more likely to damage their ACL (Uhorchak *et al.*, 2003). This link between an intercondylar stitch and ACL was further illustrated by the fact that the narrower the stitch, the more significant the ACL injury was. Females with ACL injuries on one side had a broader intercondylar range than those without ACL wounds, and those with bilateral ACL wounds showed an intercondylar range much narrower than that of unilateral ACL wounds (Griffin *et al.*, 2006).

But it occurs that the difference in width between ACL-injured knee intercondylar and the uninfluenced contralateral knee is minor. As there are still debates as to whether intercondylar notch width is a sign of ACL injury because of the contra-sided knee, which has not yet had the knee predisposed to ACL injury (Cho *et al.*, 2014).

The Noch Width Index (NWI) has been stated to be a marker for an ACL injury by measuring the measurements of the distal femoral bone in the popliteal groove (Anderson *et al.*, 2001). However, findings were inconsistent, as Souryal and Freeman discovered that the scale of the distal femoral bone between the affected ACL and the uninjured cohort was not substantially different. While Griffin et al. found NWI to be greater in men than women, another analysis did not establish any association between NWI and ACL and no gender gap (Griffin *et al.*, 2006). The intercondylar shape varies, but it is unlikely the variation in shape will lead in ACL lesions (Smith *et al.*, 2012).

Anterior cruciate ligament size and mechanical property

Even if weight is considered, ACL scale is narrower in women than men. A smaller ACL was more related to ACL wound in several trials (Anderson *et al.*, 2001). Since a smaller ACL is more external than a larger ACL, it is unclear if these forces would be able to cause an injury(Uhorchak *et al.*, 2003). A further reason for the combination ACL injury is that a small ACL may also create a small intercondylar notch, which can lead to greater collision among the ligaments through movements such as climbing, landing, and cutting that involve extension of knee (Griffin *et al.*, 2006).

Posterior tibial slope

The tibial bone is positioned in the connection to the femoral bone at an earlier stage during the quadriceps femoris muscle contraction when the tibial pitch is increasing. This results in improved ACL loading. In females with ACL trauma, the posterior tibial pitch has been found to be higher than in females who have not. The angles were higher among ACL injuries in males than females, but there was no distinction between sexes in related research. A uniform method is important for comparison of posterior tibial pitch values along with other considerations such as a meniscal pitch angle, throughout the paper, with increasing reports on the corresponding tibial pitch (Hashemi *et al.*, 2010).

Body mass index

The ACL damage is not clearly affected by BMI. The rise in BMI is attributed to a comparatively low energy material. A report on U.S. officer applicants The Military Academy has found that the incidence for women with ordinary BMIs is higher than that for those with less than normal BMIs. However, there was no sexual discrimination in BMI in a study of the impact of BMI on men and women who were educated in fundamental military activities (Uhorchak *et al.*, 2003).

Generalized ligament laxity

The incidence of general laxation of ligament has increased among females, while the incidence of non-contact ACL has not increased. Since the ACL fracture, knee dysfunction has increased by 2.7 (Uhorchak *et al.*, 2003). In addition to knee instability, the hamstring laxity of athletes with damaged ACL has been found to be significantly higher than that of regular ACL, but the same cannot be said where there has been a bilateral ACL lesion (Cho *et al.*, 2014).

Genetic and Familial factors

Very few genetic risk factors are known to increase ACL injury predisposition. While some anatomical components have been linked to an ACL injury (such as intercondylar noch width), there remain controversies. ACL injuries in women were linked to the

COL1A1 and COL5A1 genes. In specific restriction fragment length different configurations of the CC genotype, COL5A1 BstUI, is found to be less prevalent in females with ACL injury (Griffin *et al.*, 2006).

Environmental factor

In several research, environmental conditions have been involved in non-neutral ACL accidents (Griffin *et al.*, 2006). None of the environmental factors proposed to date, however, seems to be a gender risk factor. E.g. atmosphere, weather, boots, footwear resistances and prophylactic knee braces are environmental variables which may lead to ACL injuries (Cho *et al.*, 2014).

Climate conditions

The fact that research into this aspect is restricted relative to, for example, hormone and neuromuscular research meant that it was not predictable for temperature conditions. In Australian football players, ACL injury has been found to be more frequent than that of others. The consequence is repeated play on dry and hard ground caused by dry weather in Australia and the players are subsequently continuously subjected to high resistance to friction and torsion from sole to dirt. 0.82 Australian footballers, compared to just 0.12 American soccer players, are expected to experience ACL injury for every 1 000 Australian football players and American soccer players. While the climate conditions had a strong impact on the occurrence in some regions of ACL accidents, there was no indication that the climate conditions had a separate effect on gender (Cho *et al.*, 2014).

Ground surface

An elevated friction limit alongside an increase of the limit of friction and resisting player movement raises the risk of ACL injury. A dry soil creates a rubbing between the sole and ground surface, which is more readily ACL wounded on dry on wet soils than when soil is damp (Cho *et al.*, 2014). ACL wounds occur more rapidly. In the other side, whether concrete surfaces are more or less dangerous than natural surfaces is also not accepted. However, a new study of ACL-injured American football players found a 50% higher incidence of non-touch ACL injuries in those playing on natural grass than in those who played on man-made grass. However, another analysis found that natural grass is less toxic than artificial grass (Myer *et al.*, 2008).

Another research found that artificial indoor floors were less favourable than natural wood flooring, but the incidence of an ACL injury was not different in gender. Although the incidence of ACL injuries between the two styles of ground surfaces has not distinguished between males, this study finds that indoor artificial floors with ACL injury were more likely than in female natural wood floors (Olsen *et al.*, 2004).

Footwear

The decreased incidence of knee and ankle fractures was correlated with narrower and lower cleats in football players' exercise boots alone. In women there was no research to see what kind of shoes are defending them against ACL damage, but rather to prevent women in footwear, such as males, with long and uneven shoes. The torsional resistance of artificial and natural grass is improved by long and uneven cleat patterns which are why it can be associated with ACL lesions (Cho *et al.*, 2014).

Prophylactic knee brace

The risk of an ACL fracture in an athlete's normal is not impaired by prophylactic knee braces. The diminution of the medial collateral ligament and ACL lesions was not statistically important, when wearing the double-hinged, single, backward, knee brace off the shelf (Donjoy Inc., Carlsbad, Carlsbad, CA, USA). This research did not discuss differences between the sexes (Cho *et al.*, 2014).

Activity level

There have been shown a difference in the occurrence of ACL accidents across multiple sports and a greater chance of an ACL injury in turning and side-stepping sports is necessarily present. This was found for ACL injuries and in contralateral situations. For individuals who reported to engage in mild to demanding workout, the likelihood of a contralateral ACL injury was found to be much greater. The increasing incidence of contralateral ACL lesions in professional skiers also indicates the importance of a high degree of exercise (Pujol *et al.*, 2007).

Neuromuscular factor

The lack of mechanoreceptor afferent feedback which results in proprioceptive deficits (perceptions of activity and position) was also considered a contributing factor for the possibility of an ACL injury contralateral. Some people may also have inherently lower proprioceptive skills which make them vulnerable to bilateral ACL wounds. Apparent signals from multiple mechanoreceptors inside the joint in addition to the muscles and the skin are included within the proprioceptive sense (Fridén *et al.*, 2001).

Lastly, the absence of afferent feedback of ruptured ACL on the spinal cord relies on this. Moreover, the differed kinematics of the ACL injured knee can induce a different afferent impulses from the mechanoreceptors from the joint of injury, modify that response of the muscle spindle on both sides; therefore predispose persons to injury of the opposite ACL with unilateral ACL injury. Various experiments revealed the proprioceptive weakness of the injured leg, on comparing the group with injury to the normal group, at various time points after the ACL damage.

The mean TDPM was seen to be substantially higher in the wounded knee 3 weeks and 6 weeks after surgery, but not for 3 or 6 months after surgery than in external checks. The TDPM was only much higher before procedure for the contralateral knee. Thus, following an ACL injury, proprioceptive defects in the contralateral knee appear to be easily rectified, rendering it unlikely that a contra-lateral ACL injury is a relevant risk factor. However, some patients may have lifelong proprioception defects following an ACL injury. The chances of a contralateral ACL injury can be significantly improved for these patients (Swärd *et al.*, 2010).

The risk of noncontact ACL accidents in both men and women is minimised by neuromuscular training services. To date, no detailed investigation has been made into the importance of neuromuscular care regimes to reduce the likelihood of contractual ACL injury. Given the evolving biomechanics and neuromuscular limitations after unilateral ACL injury, programmes like these may be particularly helpful in reducing the risk of a contralateral ACL damage for patients returning to a high level of operation after ACL injury (Swärd *et al.*, 2010).

Biomechanical factor

Changes in the biomechanic of the wounded leg as well as in the uninjured leg are a possible process by which the conditions gained secondary to the original ACL injury raise the likelihood of a reverse ACL injury. Knee cinematics and knee moments are complex factors which affect ACL pressure (Griffin *et al.*, 2006). It may be hypothesised that the possibility of an ACL contralateral injury can also be increased with a transition in the gait planned to stabilise the affected knee joint. Abnormal biomechanics is discovered both after ACL injury 3 weeks and after ACL injury 6 months. Moreover, several others reported improvements in the biomechanics of the healthy uninjured leg after ACL injuries, including Berchuck et al. who revealed that the contralateral side of any imbalance in the cinematic of the leg hurt, making a symmetrical but an irregular gait (Swärd *et al.*, 2010).

Importantly, the hamstrings cannot restrict the force of the ACL by simultaneous quadriceps contraction when the knee is at a bent angle of less than 30°. In reality, less flexion of the knee joint and enhanced contraction force ratio between quadriceps and hamstrings were suggested as two factors which make women more vulnerable than men to ACL injury (Ahmad *et al.*, 2006). This illustrates that the probability of a contralateral LCA injury can be raised by a slight bent angle in the knee joint secondary to a unilateral ACL injury.

The results of Myer's team's findings demonstrating that substantial side-by-side disparities of knee laxity were predisposed to an ACL tear were also an important, independent risk factors for the sustainability of an ACL contralateral injury (Myer *et al.*, 2008).

CONCLUSION

The anterior cruciate ligament (ACL) injury is one of the commonest injuries occurring to athletes. It has been documented that it's more common among female athletes, when compared to male athletes. Various studies investigated the risk factors for this discrepancy. In this review, we summarized the most vocal risk factors which make women more susceptible to this injury. We emphasized on the crucial role female hormones play in the pathogenesis of this injury especially during puberty and the monthly changes accompanying the menstrual cycle, which constitute a very important risk factor for this injury. These risk factors include anatomical risk factors due to larger bone length and muscle bulk in males, which protects against this injury. Moreover, due to the different anatomy of the femur bone itself, the articulation or the ligament is more stable. In addition, due to the higher estrogen levels, females experience generalized ligament laxity and higher BMI, which increases the risk for ACL tears. Further factors that induce this injury include footwear, ground surface, climate conditions and using knee braces. It's documented that these risk factors are more prevalent among females. In addition, different neuromuscular and biomechanical factors play an important role of the pathogenesis of such injury.

Funding Support

The author declares that there is no funding support for this study.

Conflict of Interest

The author declares that he has no conflict of interest.

REFERENCES

Ahmad, C. S., Clark, A. M., Heilmann, N., Schoeb, J. S., Gardner, T. R., Levine, W. N. 2006. Effect of Gender and Maturity on Quadriceps-to-Hamstring Strength Ratio and Anterior Cruciate Ligament Laxity. *The American Journal of Sports Medicine*, 34(3):370–374.

Anderson, A. F., Dome, D. C., Gautam, S., Awh, M. H., Rennirt, G. W. 2001. Correlation of Anthropometric Measurements, Strength, Anterior Cruciate Ligament Size, and Intercondylar Notch Characteristics to Sex Differences in Anterior Cruciate Ligament Tear Rates. *The American Journal of Sports Medicine*, 29(1):58–66.

Cho, Y., Lee, S., Lee, Y. S., Lee, M. C. 2014. Gender disparity in anterior cruciate ligament injuries. *Arthroscopy and Orthopedic Sports Medicine*, 1(2):65–74.

Fayad, L. M., Rosenthal, E. H., Morrison, W. B., Carrino, J. A. 2008. Anterior cruciate ligament volume: Analysis of gender differences. *Journal of Magnetic Resonance Imaging*, 27(1):218–223.

Fox, A. S., Bonacci, J., McLean, S. G., Spittle, M., Saunders, N. 2014. What is Normal? Female Lower Limb Kinematic Profiles During Athletic Tasks Used to Examine Anterior Cruciate Ligament Injury Risk: A Systematic Review. *Sports Medicine*, 44(6):815–832.

Fridén, T., Roberts, D., Ageberg, E., Waldén, M., Zätterström, R. 2001. Review of Knee Proprioception and the Relation to Extremity Function After an Anterior Cruciate Ligament Rupture. *Journal of Orthopaedic and Sports Physical Therapy*, 31(10):567–576.

Griffin, L. Y., Albohm, M. J., Arendt, E. A., Bahr, R., Beynnon, B. D., DeMaio, M., Dick, R. W., Engebretsen, L., Garrett, W. E., Hannafin, J. A., Hewett, T. E., Huston, L. J., Ireland, M. L., Johnson, R. J., Lephart, S., Mandelbaum, B. R., Mann, B. J., Marks, P. H., Marshall, S. W., Myklebust, G., Noyes, F. R., Powers, C., Shields, C., Shultz, S. J., Silvers, H., Slauterbeck, J., Taylor, D. C., Teitz, C. C., Wojtys, E. M., Yu, B. 2006. Understanding and Preventing Noncontact Anterior Cruciate Ligament Injuries. *The American Journal of Sports Medicine*, 34(9):1512–1532.

Hashemi, J., Chandrashekar, N., Mansouri, H., Gill, B., Slauterbeck, J. R., Schutt, R. C., Dabezies, E., Beynnon, B. D. 2010. Shallow Medial Tibial Plateau and Steep Medial and Lateral Tibial Slopes: New Risk Factors for Anterior Cruciate Ligament Injuries. *The American Journal of Sports Medicine*, 38(1):54–62.

Herzberg, S. D., Motu'apuaka, M. L., Lambert, W., Fu, R., Brady, J., Guise, J.-M. 2017. The Effect of Menstrual Cycle and Contraceptives on ACL Injuries and Laxity: A Systematic Review and Meta-analysis. *Orthopaedic Journal of Sports Medicine*, 5(7):1–10.

Hewett, T. E., Myer, G. D., Ford, K. R., Heidt, R. S., Colosimo, A. J., McLean, S. G., van den Bogert, A. J., Paterno, M. V., Succop, P. 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(4):492–501.

Hewett, T. E., Zazulak, B. T., Myer, G. D. 2007. Effects of the Menstrual Cycle on Anterior Cruciate Ligament Injury Risk. *The American Journal of Sports Medicine*, 35(4):659–668.

Khowailed, I. A., Petrofsky, J., Lohman, E., Daher, N., Mohamed, O. 2015. 17β-Estradiol Induced Effects on Anterior Cruciate Ligament Laxness and Neuromuscular Activation Patterns in Female Runners. *Journal of Women's Health*, 24:670–680.

Lee, C. Y., Liu, X., Smith, C. L., Zhang, X., Hsu, H. C., Wang, D. Y., Luo, Z. P. 2004a. The combined regulation of estrogen and cyclic tension on fibroblast biosynthesis derived from anterior cruciate ligament. *Matrix Biology*, 23(5):323–329.

Lee, C. Y., Smith, C. L., Zhang, X., Hsu, H. C., Wang, D. Y., Luo, Z. P. 2004b. Tensile forces attenuate estrogen-stimulated collagen synthesis in the ACL. *Biochemical and Biophysical Research Communications*, 317(4):1221–1225.

Myer, G. D., Ford, K. R., Paterno, M. V., Nick, T. G., Hewett, T. E. 2008. The Effects of Generalized Joint Laxity on Risk of Anterior Cruciate Ligament Injury in Young Female Athletes. *The American Journal of Sports Medicine*, 36(6):1073–1080.

Olsen, O.-E., Myklebust, G., Engebretsen, L., Bahr, R. 2004. Injury Mechanisms for Anterior Cruciate Ligament Injuries in Team Handball. *The American Journal of Sports Medicine*, 32(4):1002–1012.

Pinczewski, L. A., Lyman, J., Salmon, L. J., Russell, V. J., Roe, J., Linklater, J. 2007. A 10-Year Comparison of Anterior Cruciate Ligament Reconstructions with Hamstring Tendon and Patellar Tendon Autograft. *The American Journal of Sports Medicine*, 35(4):564–574.

Pollard, C. D., Braun, B., Hamill, J. 2006. Influence of gender, estrogen and exercise on anterior knee laxity. *Clinical Biomechanics*, 21(10):1060–1066.

Pujol, N., Blanchi, M. P. R., Chambat, P. 2007. The Incidence of Anterior Cruciate Ligament Injuries among Competitive Alpine Skiers. *The American*

Journal of Sports Medicine, 35(7):1070–1074.

Quatman, C. E., Quatman-Yates, C. C., Hewett, T. E. 2010. A 'Plane' Explanation of Anterior Cruciate Ligament Injury Mechanisms. *Sports Medicine*, 40(9):729–746.

Shelburne, K. B., Pandy, M. G., Anderson, F. C., Torry, M. R. 2004. Pattern of anterior cruciate ligament force in normal walking. *Journal of Biomechanics*, 37(6):797–805.

Smith, H. C., *et al.* 2012. Risk factors for anterior cruciate ligament injury: A review of the literature - part 1: Neuromuscular and anatomic risk. *Sports Health*, 4(1):69–78.

Swärd, P., Kostogiannis, I., Roos, H. 2010. Risk factors for a contralateral anterior cruciate ligament injury. *Knee Surgery, Sports Traumatology, Arthroscopy*, 18(3):277–291.

Uhorchak, J. M., Scoville, C. R., Williams, G. N., Arciero, R. A., Pierre, P. S., Taylor, D. C. 2003. Risk Factors Associated with Noncontact Injury of the Anterior Cruciate Ligament. *The American Journal of Sports Medicine*, 31(6):831–842.

Wild, C. Y., Steele, J. R., Munro, B. J. 2012. Why Do Girls Sustain More Anterior Cruciate Ligament Injuries Than Boys? *Sports Medicine*, 42(9):733–749.

Yu, B., Garrett, W. E. 2007. Mechanisms of noncontact ACL injuries. *British Journal of Sports Medicine*, 41(Supplement 1):i47–i51.