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Why do girls sustain more anterior cruciate ligament injuries than boys? A review of the changes in oestrogen and musculoskeletal structure and function during puberty

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Abstract

Sport is the leading cause of injury among adolescents and girls incur more non-contact anterior cruciate ligament (ACL) ruptures than boys, with this gender disparity in injury incidence apparent from the onset of puberty. Although the mechanisms for this gender disparity in ACL injuries are relatively unknown, hormonal, anatomical and biomechanical factors have been implicated. Puberty is associated with rapid skeletal growth and hormonal influx, both of which are thought to contribute to alterations in ACL metabolic and mechanical properties, as well as changes in lower limb strength and flexibility, ultimately influencing landing technique. Therefore, the aim of this review is to explain (i) the effects of changes in estrogen levels on the metabolic and mechanical properties of the ACL; (ii) changes in musculoskeletal structure and function that occur during puberty, including changes in knee laxity, and lower limb flexibility and strength; and (iii) how these hormonal and musculoskeletal changes impact upon the landing technique displayed by pubescent girls. Despite evidence confirming estrogen receptors on the ACL, there are still conflicting results as to how estrogen affects the mechanical properties of the ACL, particularly during puberty. However, during this time of rapid growth and hormonal influx, unlike their male counterparts, girls do not display an accelerated muscle strength spurt and the development of their hamstring muscle strength appears to lag behind that of their quadriceps. Throughout puberty, girls also display an increase in knee valgus when landing, which is not evident in boys. Therefore, it is plausible that this lack of a defined strength spurt, particularly of the hamstring muscles, combined with the hormonal effects of estrogen in girls, may contribute to a more 'risky' lower limb alignment during landing, in turn, contributing to a greater risk of ACL injury. There is, however, a paucity of longitudinal studies specifically examining the lower limb musculoskeletal structural and functional changes experienced by girls throughout puberty, as well as how these changes are related to estrogen fluctuations characteristic of puberty and their effects on landing biomechanics. Therefore, further research is recommended to provide greater insight as to why pubescent girls are at an increased risk of non-contact ACL injuries during sport compared with boys. Such information will allow the development of evidence-based training programmes aimed at teaching girls to land more safely and with greater control of their lower limbs in an attempt to reduce the incidence of ACL ruptures during puberty.

Why Do Girls Sustain More Anterior Cruciate Ligament Injuries Than Boys?

A Review of the Changes in Estrogen and Musculoskeletal Structure and Function during Puberty

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Contents

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Despite evidence confirming estrogen receptors on the ACL, there are still conflicting results as to how estrogen affects the mechanical properties of the ACL, particularly during puberty. However, during this time of rapid growth and hormonal influx, unlike their male counterparts, girls do not display an accelerated muscle strength spurt and the development of their hamstring muscle strength appears to lag behind that of their quadriceps. Throughout puberty, girls also display an increase in knee valgus when landing, which is not evident in boys. Therefore, it is plausible that this lack of a defined strength spurt, particularly of the hamstring muscles, combined with the hormonal effects of estrogen in girls, may contribute to a more 'risky' lower limb alignment during landing, in turn, contributing to a greater risk of ACL injury. There is, however, a paucity of longitudinal studies specifically examining the lower limb musculoskeletal structural and functional changes experienced by girls throughout puberty, as well as how these changes are related to estrogen fluctuations characteristic of puberty and their effects on landing biomechanics. Therefore, further research is recommended to provide greater insight as to why pubescent girls are at an increased risk of non-contact ACL injuries during sport compared with boys. Such information will allow the development of evidence-based training programmes aimed at teaching girls to land more safely and with greater control of their lower limbs in an attempt to reduce the incidence of ACL ruptures during puberty.

1. Introduction

The highest prevalence of sports injuries in children and adolescents occurs at the onset of and during puberty, corresponding with the adolescent growth spurt.[1-3] When comparing the incidence of sport-related injuries during puberty, girls appear to be at a greater risk of incurring injuries such as non-contact anterior cruciate ligament (ACL) ruptures than their male counterparts,[4] particularly in sports involving repetitive running, jumping and landing movements.[5] In fact, females are greater than two-times more likely to rupture their ACL compared with males,[6] with ACL ruptures accounting for 37% and 23% of all knee injuries in females and males, respectively, from 11 to 18 years of age.[4] This gender disparity in ACL injury incidence becomes evident from 11 to 12 years of age, coinciding with the onset of puberty.[4,6] However, no gender difference in ACL injury rate is apparent prior to the onset of puberty,[7] contributing to only 0.2% of all knee injuries in girls and boys aged 5–10 years.[4,7]

ACL injury risk is multifactorial in nature with several potential risk factors having been identi-fied and widely discussed in the literature.[8-17] Some of these potential risk factors include hormonal (including the effects of estrogen on the ACL), anatomical (including knee laxity, lower limb strength and anthropometric variables) and biomechanical factors (including the effects of altered landing biomechanics on the ACL).[8-17] We postulate that differences in estrogen levels between males and females, particularly from the onset of puberty, as well as the rapid changes in growth during puberty (including anthropometry, knee laxity, lower limb flexibility and strength), may play a role in the between-gender disparity in non-contact ACL injury incidence during dynamic landing movements.

This review aims to discuss published research that has investigated the hormonal, anatomical and biomechanical factors thought to predispose pubescent girls to a higher risk of non-contact ACL injuries. More specifically, this review will focus on (i) the effects of changes in estrogen levels on the metabolic and mechanical properties of the ACL; (ii) changes in musculoskeletal structure and function that occur during puberty, including changes in knee laxity, and lower limb flexibility

and strength; and (iii) how these estrogen and musculoskeletal changes impact upon the landing technique displayed by pubescent girls. The purpose of the review is to gain greater insight into factors that might contribute to the between-gender disparity in non-contact ACL injuries from the onset of puberty, as well as to provide recommendations for future research in this important field of sports medicine.

An initial search in MEDLINE (1950+), CINAHL (1982–2011) and SPORTDiscus™ (1982–2011) in December 2011, limited to articles published in English, was conducted. Specific keywords were entered into the databases, including 'anterior cruciate ligament', which was combined ('AND') with the following keywords: 'mechanical properties', 'metabolic properties', 'gender'. Other keywords included 'puberty' combined ('AND') with: 'flexibility', 'knee', 'laxity', 'strength', 'landing' and this yielded a total of 1202 papers. These results were further limited by combining ('AND') with the specific keywords of 'estrogen', 'lower limb', 'girls'. Papers were only included in this review if they investigated the association between estrogen and properties of the ACL, as well as if they investigated changes in lower limb flexibility or strength, knee laxity or landing technique in girls throughout puberty. Papers investigating upper limb flexibility or strength, for example, were therefore excluded from this review. Additional relevant papers were obtained from the reference lists of these primary sources (located in the databases), with unpublished studies excluded, leaving a total of 41 papers for review. Whilst only 41 papers were systematically reviewed, additional articles have been included to help explain and support information presented throughout the review.

2. Anthropometric and Hormonal Changes in Girls during Puberty

Puberty is the transitional period from childhood to adulthood, accompanied by the appearance of secondary sex characteristics, maturation of the reproductive system and the adolescent growth spurt.[18] Pubertal onset is often determined by measuring factors such as skeletal age,[19-21]

secondary sex characteristics,[21-23] time of menarche in girls,[18,21,22,24] as well as peak height velocity (PHV; peak growth in height during the adolescent growth spurt) and time from PHV (referred to as maturity offset).[25] As some children develop faster than others, chronological age is not a valid or reliable indication of maturation or the onset of puberty, particularly given that the growth spurt for boys lags 2 years behind that of girls.[18,21,22,26] In fact, due to the range of variability in anthropometric growth parameters and biological development (physiological growth) between individuals of the same chronological age during the growth spurt, chronological age has been suggested to be of limited use in assessing maturity.[22,24,25,27] Therefore, several methods have been developed to determine biological rather than chronological age. These methods, as well as advantages and major limitations of each method, are outlined in table I.

During the adolescent growth spurt, from the onset to the cessation of growth, girls grow approximately 25 cm.[22] The period of most rapid growth in height is referred to as PHV, and is reported to be approximately 8–10 cm/year in girls.[21,22] This occurs around the ages of 11–12 years in girls,[25] corresponding with Tanner stages II–III (figure 1).[28] The peak velocity for leg length growth during the growth spurt occurs before PHV, whereas peak velocity for sitting height growth occurs after PHV, corresponding with Tanner stages III–IV (figure 1).[22,25] Tanner et al.[22] reported peak velocities of leg length and sitting height of 4.25 and 4–4.5 cm/year, respectively, measured in 90 girls and boys throughout their adolescent growth spurt. In addition to increases in height and limb length during puberty, girls have been shown to display an increase in body mass of approximately 5.5 kg/year from 8 to 18 years of age,[24] reflecting the growth in muscle mass and fatty tissue.[24] Furthermore, limb mass and, specifically lower limb mass, increases by more than 3-fold in boys and girls from 6 to 14 years of age.[29]

Due to rapid growth of the long bones leading up to PHV, a rapid increase in both length and mass of the lower limbs occurs at this time, contributing to changes in the moment of inertia of

Table I. A summary of methods used to indicate puberty in girls, as well as the advantages and major limitations of these methods

Puberty indicator	Method	Advantages	Major limitations	References
Chronological age	Age determined from birth date	Quick, non-intrusive, non-invasive	Widely variable between individuals,[18,21,22,26] poorly correlated with skeletal age[20]	Faust,[24] Hauspie et al.,[20] Iuliano-Burns et al.,[27] Tanner et al.,[22]
Pubertal development (development of secondary sex characteristics)	Tanner stages (I–V) determined through pictures and modified diagrams[21-23]	Non-invasive, can be self-assessed	Intrusive and embarrassing (when examined by a clinician)	Tanner et al.,[21] Tanner et al.,[22] Taylor et al.[23]
Skeletal age (epiphyseal fusion of radius)	Hand and wrist radiographs[20,21] and MRI[19]	Most accurate and reliable indicator of pubertal/biological age[19,20,24,25]	Expensive equipment required, exposure to radiation (radiographs)	Dvorak et al.,[19] Hauspie et al.,[20] Tanner[21]
Time from PHV (maturity offset)	Measured retrospectively from height measurements.[21,22,24,27] Regression equation (using mass, standing and sitting height, age and gender)[25]	Regression equation is quick, accurate and correlates highly with skeletal age	Time consuming if tracking longitudinally	Faust,[24] Iuliano-Burns et al.,[27] Tanner,[21] Tanner et al.[22]
Menarche (time of first menstruation)	Time of menarche[21,22,24]	Non-invasive, easily determined	Menarche is a late event during puberty, variable among individuals	Faust,[24] Tanner,[21] Tanner et al.[22]

MRI = magnetic resonance imaging; **PHV** = peak height velocity.

the limbs.[29-31] This requires an increase in muscular torque to accelerate the limbs for a given movement, ultimately affecting muscle strength requirements during the performance of dynamic movement tasks, such as landing.[30,32] Jensen and Nassas[29] reported that lower limb moment of inertia relative to the transverse axis increases 10-fold from 6 to 14 years of age. Furthermore, differential timing of growth also exists within the limb segments whereby the more distal segments, such as the foot, experience their peak growth velocity before the more proximal segments, such as the shank and thigh,[21] again altering the inertial properties of the lower limbs.[30] Therefore, rapid changes in stature and limb dimensions throughout the adolescent growth spurt, particularly around the time of PHV, may affect functional parameters such as lower limb flexibility and strength, and ultimately performance during dynamic movements. Given that landing from a jump is a common non-contact ACL injury mechanism,[33] these rapid growth changes may possibly contribute to the greater number of ACL injuries sustained by females during this time.

Development of the external primary and secondary sex characteristics, such as breasts, genitals and pubic hair development, accompanies puberty, and are best determined using the Tanner stages of pubertal development.[21] There are five Tanner stages whereby stage I is representative of the prepubescent individual and stage V represents the adult or more mature individual.[21] The development of secondary sex characteristics is, in part, the external expression of hormonal changes that occur during puberty.[18] One of the major events occurring at the onset of puberty (Tanner stage II) is the large influx of hormones, particularly the sex-steroid hormones such as estrogen and testosterone.[18] In girls there is a substantial influx of estrogen at the onset of puberty. Estrogen levels then continually rise throughout puberty, before reducing again during adulthood (figure 2).[18] Similarly, boys experience a rapid increase in testosterone levels from the onset of puberty, an increase that is not apparent in girls (figure 2).[18] Overall, it can be seen that the influx of estrogen, as well as the vast differences in hormonal concentrations in girls and boys during
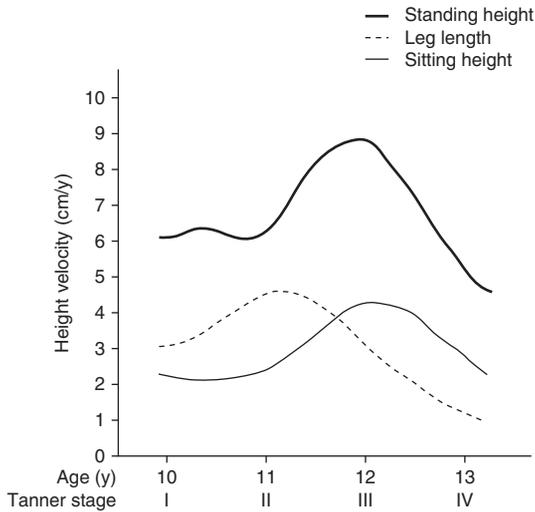
Fig. 1. The timing of peak height velocity, according to chronological and pubertal stage, in relation to peak leg length and sitting height in girls (modified from Mirwald et al.,[25] with permission, and Kanbur et al.[28]). Peak leg length occurs prior to peak height velocity, at the age of 11.2 years, corresponding with Tanner stage II. After peak height velocity is attained, at a mean age of 11.8 years in girls (Tanner stage II–III), sitting height reaches a peak at a mean age of 12.2 years,[22] which coincides with Tanner stage III–IV.

puberty, may play a role in the high incidence of ACL injuries incurred by pubescent females.[17,34,35]

3. Effects of Changes in Estrogen Levels during Puberty on Anterior Cruciate Ligament (ACL) Injury Risk

3.1 Fibroblast Proliferation and Collagen Synthesis

Fibroblasts are crucial for maintaining the integrity of ligaments as they are responsible for preventing or repairing ongoing microscopic damage to ligamentous tissues.[36] Collagen is produced by fibroblasts and forms the major load-bearing structure of the ACL.[37] The main types of collagen referred to in this review are type I collagen, responsible for providing mechanical strength to connective tissues, and type III collagen, responsible for tissue elasticity.[38]

It has been proposed that the hormonal differences between males and females may be one factor to explain the greater number of ACL injuries displayed by females.[35,39] Reports have

found both estrogen and testosterone receptors on the fibroblasts of the human ACL[35,39] with no difference in the number of these receptors in young adult males and females.[40] Given the higher estrogen concentration in females compared with males, sex hormones, particularly estrogen, may have the potential to directly affect the structure, composition, and ultimately the mechanical integrity of the human ACL, contributing to the higher injury risk in females, particularly at the time of the pubertal estrogen influx.

A study performed in the late 1990s exposed the ACL from a 32-year-old female to physiological and supra-physiological levels of exogenous estrogen (0.0029–25 ng/mL) for 2 weeks.[41] Results showed an initial up-regulation of fibroblasts in the first 3 days of estrogen exposure.[41]
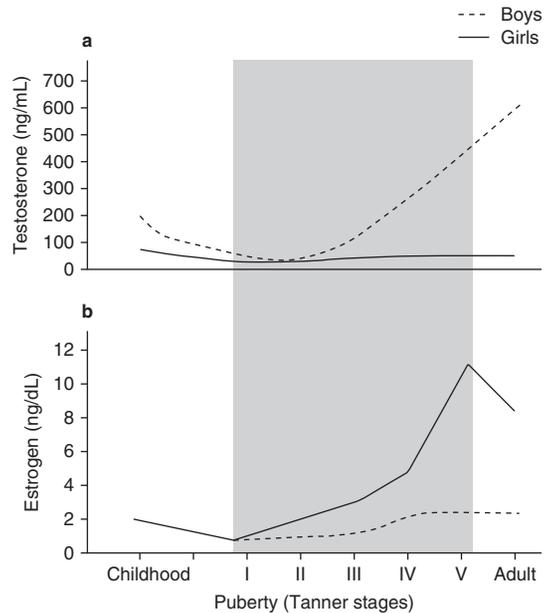
Fig. 2. Levels of (**a**) testosterone and (**b**) estrogen in boys and girls from childhood to adulthood. During puberty, boys experience a rapid influx in the levels of testosterone from Tanner stage II, continually increasing throughout puberty into adulthood. Similarly, girls experience an increase in estrogen levels from the onset of puberty (Tanner stage II of pubertal development) to Tanner stage III, a further increase from Tanner stage III to IV and a final increase from stage IV to V leading up to epiphyseal closure. Girls, however, do not experience the rapid testosterone influx that boys do, and boys do not experience the higher levels of estrogen that girls do throughout puberty (adapted, with permission from Malina et al.[18] Data from Esoterix, Inc., 2000 Endocrinology: expected values and SI unit conversion tables, 5th ed. [Calabasas Hills, CA: Esoterix]).

From day 7, however, a dose-dependent decrease in the proliferation of fibroblasts and rate of type I pro-collagen synthesis was evident, with increasing levels of estrogen.[41] These results were confirmed by Yoshida et al.[42] and Liu et al.[34] (table II). Contrary to these results, Seneviratne et al.[43] exposed sheep ACL to estrogen levels similar to previous studies[34,41] and found no change in fibroblast proliferation or collagen synthesis with increasing levels of estrogen. These results imply that estrogen does not have a negative effect on the metabolic properties of the ACL, such that there must be other underlying factors that pre-

dispose females to the greater number of ACL injuries compared with their male counterparts. It is important to note, however, that the ligament tissues in the Seneviratne et al.[43] study were only exposed to estrogen for 4–6 days, and so it is unknown whether the rates of collagen synthesis and fibroblast proliferation would have also decreased after 6 days, as it had in previous studies.[34,41,42]

As the ACL tissue in the studies described above was harvested from different species (human, rabbit and sheep), between-study comparisons are difficult. However, there is more evidence suggesting that, regardless of the concentration, estrogen

Table II. A summary of the major findings and limitations of the literature investigating the effects of estrogen on the anterior cruciate ligament

Study	Animal vs human models	Major findings	Major limitations
Liu et al.[35]	Human model 13 females, 4 males	Estrogen and progesterone receptors were located in the fibroblasts of human ACL	Large age range (18–78 y) for only 17 participants
Faryniarz et al.[40]	Human (cadaver) 8 females, 7 males	4–10% of ACL cells expressed estrogen receptors No significant difference between males and females	All subjects were ACL injured patients
Yu et al.[41]	Human (live, *in vitro*) 1 female (32 y)	Day 1–3: decreased fibroblast and procollagen synthesis with increasing estradiol	Only 1 participant, limits the generalizability of results
Yoshida et al.[42]	Animal model (rats) 40 females	Decreased type 1 collagen expression in rat ACL exposed to endogenous estrogen vs ovariectomized rats	Animal model limits direct application of results to humans
Liu et al.[34]	Animal model (rabbits) 6 females	Decrease (40%) in fibroblast and collagen synthesis with increasing estrogen (physiological levels)	Small cohort size (n=6) and no control group
Seneviratne et al.[43]	Animal model (ovine) 6 females	Estrogen receptors located on ACL No change in fibroblast or collagen synthesis with increased estrogen levels	Estrogen exposure was short (only 4–6 days) Animal model limits direct application of results to humans
Toyoda et al.[44]	Animal model (rabbits) n=18	20% increase in collagen synthesis when cyclic tensile load applied to ACL	Gender NS Animal model limits direct application of results to humans
Lee et al.[45]	Animal model (porcine) n=NS	Tensile load: increased mRNA expression of type I collagen. Estrogen+tensile load: decreased mRNA expression of type I and III collagen	Number and gender of subjects NS Animal model limits direct application of results to humans
Lee et al.[46]	Animal model (porcine) n=NS	Tensile load: increased mRNA expression of type I and III collagen. Estrogen+tensile load: decreased mRNA expression of type I and III collagen	Number and gender of subjects NS Animal model limits direct application of results to humans
Romani et al.[47]	Animal model 10 females, 9 males	Female vs male ACL: greater stiffness (8.35 vs 4.23 N/mm/g) and failure loads (11.18 vs 5.67 N/g)	Animal model limits direct application of results to humans
Woodhouse et al.[48]	Animal model (rats) 40 females	High vs low estrogen: decreased deformation to failure (0.19 vs 0.79 mm) and increased energy prior to failure	Animal model limits direct application of results to humans
Slauterbeck et al.[17]	Animal model (rabbits) 16 females	Decreased load at failure in ACL of estrogen group (446 N) vs control (non-estrogen; 503 N)	Animal model limits direct application of results to humans

ACL = anterior cruciate ligament; **mRNA** = messenger ribonucleic acid; **N** = Newtons; **NS** = not specified.

may affect the metabolic properties, and thus composition of, the ACL.[34,41] As these effects may reduce the ligament's ability to withstand load and increase the risk of injury, it is important to examine the effects of estrogen and loading on the ACL.

3.2 Effects of Estrogen and Loading on the Metabolic Properties of the ACL

The ACL is continually subjected to tensile loads during walking, running and other activities of daily living and it is thought that this load is essential in maintaining integrity of the ACL fibres.[44] Toyoda et al.[44] exposed the ACL of rabbits to a cyclic tensile load of 80 mmHg vacuum force for 24 hours and found a 14% increase in type I collagen fibres in the ACL that was subjected to loading, compared with the control (unloaded) ACL. This result was supported by Lee et al.[45,46] who reported an increase in the messenger RNA (mRNA) expression of type I collagen[45] and an increase in type I and type III collagen[46] when porcine ACL were subjected to a cyclic tensile load (table II). It is postulated that an increase in the number of type I collagen fibres in the ACL would provide greater strength to the ligament,[37] thus increasing the ability of the ACL to withstand high loads. As the ACL experiences tensile loads of up to 300 Newtons (N) during normal walking,[49] it can be assumed that the repeated application of this load, independent of estrogen, may be beneficial to ACL health.

When the porcine ACL was subjected to cyclic tensile loads in an estrogen environment (representative of the follicular, ovulatory and luteal phases of the female menstrual cycle), results showed a downregulation of the mRNA expression of type I and type III collagen.[45,46] Consequently, the presence of estrogen may decrease the strength, and in turn the integrity, of the ACL. These results imply that the higher estrogen levels in females negate the positive effects of everyday loading of the ACL, possibly placing females at an increased injury risk. This may be due to downregulation of fibroblasts, which might result in reduced ligament strength.[37] However, it is important to determine whether these changes in the metabolic

properties and fibre composition of the ACL affect the mechanical properties of the ligament, thereby making it more susceptible to rupture.

3.3 Mechanical Properties of the ACL in an Estrogen Environment

Common sporting movements, such as jumping and landing, expose the lower limb, including the ACL, to forces up to 2–10 times body weight (BW).[50] In order to withstand these high loads generated during sport, the ACL must have adequate ultimate tensile strength and stiffness. As discussed in section 3.2, although controversial, there is support to show that estrogen affects the metabolic properties of the ACL, irrespective of whether the ligament is loaded or unloaded.[34,41,42,45,46] These changes in the collagen (type I and III) content of the ligament will also affect the mechanical properties of the ACL, compromising factors such as ultimate tensile strength and stiffness, and its ability to withstand high loading.[38]

Romani et al.[47] showed that female rats displayed significantly less type III and substantially lower type I mRNA collagen expression compared with male rats. Therefore, it was hypothesized that the female rats would display reduced stiffness and failure loads, as a result of reduced collagen synthesis, relative to their male counterparts. Interestingly, however, female rats displayed greater normalized ACL stiffness and failure loads compared with the male rats (table II), indicating the female rats were better able to withstand load,[47] contradicting the results of previous studies on human ACL tissue.[9,51,52]

In contrast, a recent study[48] examined the effects of high- and low-estrogen environments, manipulated using the contraceptive pill, on mechanical properties of rat ACL. Higher estrogen levels in the control group (no contraceptive pill; 46.7 pg/day/mL) resulted in the ACL displaying lower deformation to failure, as well as less energy absorbed prior to failure compared with ACL harvested from the experimental group, who had lower estrogen levels of 32.9 pg/day/mL (contraceptive pill). Estrogen levels were representative of those experienced during a normal human menstrual cycle,[34,41] as well as estrogen levels of

females using the contraceptive pill.[48] Slauterbeck et al.[17] reported a decreased load to failure in the ACL of ovariectomized rabbits treated with an estrogen supplement (serum estrogen level 52 pg/mL) compared with ovariectomized rabbits not exposed to estrogen (serum estrogen level 15 pg/mL; table II). The results of these studies[17,34,41,48] indicate that the structural and mechanical integrity of the ACL is compromised in a high-estrogen environment (such as estrogen levels similar to that experienced at the onset of puberty in girls), compared with a lower-estrogen environment (estrogen levels similar to males or pre-pubescent females). Therefore, changes in the mechanical properties of the ACL throughout puberty and how this affects joint laxity may provide further insight into the increased ACL injury risk characteristic in girls following the onset of puberty.

3.4 Changes in Knee Joint Laxity during Puberty

The ACL is one of the primary passive restraints responsible for stability of the knee joint.[53,54] It is thought that greater knee joint laxity may contribute to increased ACL injury risk due to an associated decrease in joint stability.[14] For example, an increase in anterior tibial translation of one or more standard deviation above the mean has been found to significantly increase the risk of ACL injury in 1198 male and female army cadets.[55] Given the association between estrogen levels and mechanical properties of the ACL (section 3.3), the steep rise in estrogen levels in girls during puberty (figure 2) may contribute to altered ligament properties and, in turn, knee joint laxity and ACL injury risk.

Whilst increased knee joint laxity is associated with greater ACL injury risk,[55] only five papers[15,56-59] reporting changes in joint laxity in girls throughout puberty were located (table III). Quatman et al.[15] reported that 28% of pubescent females displayed knee hyperextension, compared with only 10% of pubescent males. Girls also displayed greater generalized joint laxity, assessed using the Beighton and Horan Joint Mobility Index, throughout puberty compared with their

male counterparts.[15] Varying results, however, have been reported in other studies, whereby some have found an increase in generalized knee joint laxity[15] or anterior knee laxity[58] with increasing age or Tanner stage, whilst others have found a decrease in knee laxity with age or Tanner stage (table III).[56,57] It is important to note that of the five studies reporting changes in joint laxity in girls throughout puberty, only two grouped or tracked their participants according to pubertal development or Tanner stage,[15,57] whilst the remaining studies assessed their participants purely based on chronological age.[56,58,59] Whilst it is acknowledged that previous reports assessed girls according to menarche status,[58,59] this is a late event during puberty and does not reflect the differences in Tanner stage between individuals (section 2). Therefore, how the substantial influx in estrogen in girls from the onset and throughout puberty affects knee laxity requires further investigation. Furthermore, given the rapid anthropometric changes during puberty (section 2), musculoskeletal structural and functional changes during puberty may provide further insight into the greater risk of ACL injuries in pubescent girls.

4. Musculoskeletal Structural and Functional Changes in Girls during Puberty

4.1 Lower Limb and Trunk Flexibility during Puberty

Flexibility is defined as the extensibility of periarticular tissues to allow physiological motion of a joint or limb,[53] and may be of fundamental importance during sport.[62] It is thought that there is an optimum range of joint flexibility that can prevent injury in the event that muscles or joints are overstretched during sport or activities.[53]

During the adolescent growth spurt, around the time of PHV (11–12 years and Tanner stages II–III in girls; figure 1), the skeleton grows at a faster rate than the supporting musculature. This growth differential between the skeleton and muscles is thought to lead to reduced flexibility or joint range of motion of the lower limbs and trunk. Only four[60-63] studies were located in the literature

Table III. A summary of the literature highlighting changes in knee joint laxity and lower limb and trunk flexibility in girls and boys throughout puberty

Study	Study design	Participants	Age[a]	Test	Results
Joint laxity					
Quatman et al.[15]	Cross sectional (according to TS)	275 girls 143 boys	11–18 Pre-pubertal (TS I) Pubertal (TS II–III) Post-pubertal (TS IV–V)	Generalized joint laxity using the Beighton and Horan Joint Mobility Index	Girls: increase (p = 0.042) in generalized joint laxity with puberty Boys: no change (p = 0.582)
Baxter et al.[56]	Cross sectional (according to age)	122 girls 110 boys	7–14	Anterior/posterior, varus/valgus and internal/external rotation displacement using knee arthrometer	Progressive decrease in knee laxity with age in boys and girls
Falcigllia et al.[57]	Longitudinal (tracked annually for 3 y)	61 girls 62 boys	10.5–14.5 (TS I–IV)	Anterior tibial translation using KT2000 knee arthrometer at 134 N	Boys and girls: decrease (p = 0.03) in laxity with TS Girls: increase in laxity (>1 mm) from TS I–II
Costello et al.[58]	Longitudinal (tracked annually for 3 y)	22 girls	8–12 (pre-menarche)	Anterior tibial translation using KT1000 knee arthrometer at 133 N	Significant increase in knee laxity (>2 mm; p = 0.002) with age
Ahmad et al.[59]	Cross sectional (according to age and menarche status)	53 girls 70 boys	10–18 G1, G2, B1, B2	Anterior tibial translation using KT1000 knee arthrometer at 20 and 30 lb (89 and 133 N)	G1, G2 and B1 displayed significantly greater knee laxity (1.5 mm greater; p < 0.05) than B2
Lower limb and trunk flexibility					
Loko et al.[60]	Cross sectional (according to age)	902 girls	10–17	Lower limb flexibility (touching fingertips to floor)	Decline in flexibility just before PHV
Heras Yague et al.[61]	Longitudinal (measured biannually for 3 y)	453 girls 509 boys	10–13 (measured according to height velocity)	Lower limb flexibility (touching fingertips to floor)	Decline in flexibility at PHV, with a peak increase in flexibility 8 mo after PHV
Merni et al.[62]	Cross sectional (according to age)	360 girls 460 boys	6–18	Standing hip extension (knee extended) and hip flexion ROM (knee flexed)	Peak decrease in hip extension ROM at PHV; hip flexion ROM decreased throughout puberty
Volver et al.[63]	Cross sectional (according to TS)	77 girls	11–14 (TS I–V)	Trunk flexibility (distance of the fingertips past the toes)	Increase in flexibility from TS II–III, followed by a decrease from TS III–IV

a   Ages are presented in year ranges, mean or TS where stated.

B1 = boys <13 y; **B2** = boys >14 y; **G1** = girls pre-menarche group; **G2** = girls post-menarche group; **N** = Newtons; **PHV** = peak height velocity; **ROM** = range of motion; **TS** = Tanner stage.

that assessed flexibility changes displayed by girls during puberty (table III). Overall, these studies showed that girls displayed a decrease in flexibility just before or at the time of PHV,[60-62] indicating that the rapid growth at the time of PHV may be a contributing factor to reduced flexibility during puberty. One study,[63] however, indicated that the girls displayed an increase in flexibility throughout puberty. These between-study differences in results may be due to discrepancies in the types of tests performed to quantify flexibility, as well as the joints examined. For example, two studies measured lower limb flexibility by asking the participants to try and touch their fingertips to the floor,[60,63] whereby the results may be confounded by tightness in the lower back rather than the lower limbs. Furthermore, only one of these studies was longitudinal in design. Given the lack of research in this field, further research is recommended to quantify changes to flexibility displayed by girls during puberty, using longitudinal study designs and valid and reliable flexibility

assessment tests, to determine whether changes in flexibility during puberty play a role in the high incidence of non-contact ACL injuries in pubescent girls.

4.2 Quadriceps and Hamstring Muscle Strength during Puberty

As outlined in section 2, puberty is accompanied by rapid growth, including a substantial increase in the moment of inertia of the limbs and, in turn, greater muscle strength to control the limbs during dynamic movements.[30] Given that the ACL is commonly ruptured during abrupt landing tasks,[6,33] the role of muscles controlling the knee during landing, such as the hamstring and quadriceps muscles, and changes in the development of these muscles during puberty, are of vital importance. Furthermore, due to vast differences in circulating hormones in boys and girls during puberty (figure 2), it is postulated that between-gender differences in lower-limb strength will also be evident during puberty.

The quadriceps muscles apply an extensor moment to the knee prior to landing in order to prevent the knee from collapse upon landing.[64] A total of eight papers investigating changes in quadriceps strength in girls throughout puberty were located (table IV). Every 4 months over 5 years, Round et al.[16] monitored changes in height, quadriceps strength and testosterone levels displayed by boys and girls, recruited from 8 to 12 years of age. Results of this study highlighted that boys and girls displayed similar increases in strength as they developed until 1 year prior to PHV. Clear gender differences in the rate of strength increases were then evident from 0 to 2 years after PHV, whereby boys demonstrated an accelerated strength development whereas girls did not, instead displaying a consistent pattern of strength gain (table IV).[16] The authors concluded that the consistent increase in quadriceps strength in girls was proportional to the general increases in height and weight throughout the growth spurt. In contrast, the increased testosterone levels explained the greater increase in quadriceps strength displayed by the boys. These results have been confirmed by similar studies that have reported accelerations in

the development of isokinetic (concentric and eccentric)[66,68] and isometric[58,59,65] quadriceps strength after PHV and throughout puberty in boys, but not in girls (table IV). This highlights the androgenic role of testosterone in promoting increased muscle mass and strength.[16,18] Although estrogen has some androgenic properties,[18] it is not as potent as testosterone and, therefore, may explain why no accelerated development of muscular strength is evident in girls during puberty.[16,58,65,66]

In contrast to the studies described above, Ramos et al.[67] reported a significant increase in muscle strength with increasing age for both boys and girls, with no gender differences in strength (table IV). However, when normalized to body mass, boys showed an increase in strength of approximately 75 Nm/kg with age, whereas girls reported an increase of only 1–2 Nm/kg. Therefore, despite a lack of statistical difference between genders, a between-group difference of approximately 70–100 Nm of both absolute and relative torque could be considered clinically relevant. Also, the mean age of the boys and girls in group one (11–12-years-of-age group; table IV) of this study were 11.8 and 11.9 years, respectively, with the boys in Tanner stage II and the girls in Tanner stage III. It is difficult therefore to make valid between-gender comparisons with respect to strength gains when the pubertal stages differed between the gender groups.

The hamstring muscles also play a vital role during landing movements by imparting a posterior drawer force to the tibia, thus acting as a synergist to the ACL.[54] Many studies reporting changes in lower limb strength in girls throughout puberty focus on development of quadriceps strength,[16,65-67] with only four papers located that investigated changes in hamstring strength throughout puberty in girls (table IV).[12,58,59,68] Similar to changes in quadriceps strength, a significant increase in peak concentric[12,68] and isometric[59] hamstring muscle torque is typically displayed by males throughout puberty, with no significant increases in torque displayed by females.[58] Furthermore, females display significantly weaker hamstring muscles relative to their quadriceps muscles with age when compared with their male counterparts.[59] In fact, Barber-Westin et al.[68]

Table IV. A summary of the literature highlighting changes in quadriceps and hamstring muscle strength in girls and boys throughout puberty

Study	Study design	Participants	Age[a]	Test	Results
Round et al.[16]	Longitudinal (tracked every 4 mo for 5 y)	50 girls 50 boys	8–12 (measurements were relative to PHV)	MVC of quadriceps, seated in 90° of knee flexion	Boys: 80–90 N/y increase in strength; girls: 20–30 N/y increase in strength 0–2 y after PHV
Parker et al.[65]	Cross sectional (according to age)	284 girls 267 boys	5–17	MVC of quadriceps, seated in 90° of knee flexion	Boys: 55 N/y increase in strength; girls: 25 N/y increase in strength from 12 y
Segar and Thorstensson[66]	Longitudinal (tracked annually for 5 y)	7 girls 9 boys	11.5 Pre- vs post-puberty (according to TS)	Concentric and eccentric quadriceps strength at 45°, 90° and 180° sec (isokinetic dynamometer)	Boys: increased concentric (71–94%) and eccentric (87–100%); girls: increased concentric (53%) and eccentric (56%)
Ramos et al.[67]	Cross sectional (according to age)	42 girls 45 boys	1. 11–12 (TS II–III) 2. 13–14 (TS IV) 3. 17–18 (TS V)	Concentric quadriceps strength at 60° sec using (Cybex 340)	Increase (p < 0.001) in quadriceps strength in boys (130 Nm) and girls (34 Nm) with age
Hewett et al.[12]	Cross sectional (according to TS)	100 girls 81 boys	11–18 Pre-pubertal (TS I) Pubertal (TS II–III) Post-pubertal (TS IV–V)	Concentric quadriceps and hamstring strength at 300° sec	Quadriceps and hamstrings: significant (p < 0.05) in males, not females across puberty
Costello et al.[58]	Longitudinal (tracked annually for 3 y)	22 girls	8–12 (pre-menarche)	MVC of quadriceps and hamstrings, seated in 20–30° of knee flexion	Quadriceps: increase of 2 kg from 9.5 to 10.5 y of age, decrease of 4 kg from 10.5–11.5 y Hamstrings: no change with age
Ahmad et al.[59]	Cross sectional (according to age and menarche status)	53 girls 70 boys	10–18 G1, G2, B1, B2	MVC of quadriceps and hamstrings, seated in 45° and 90° of knee flexion	B2 vs B1: increased quadriceps (148%) and hamstring strength (179%); G2 vs G1: increased quadriceps (44%) and hamstring (27%) strength
Barber-Westin et al.[68]	Cross sectional (according to age)	853 girls 177 boys	9–17	Concentric quadriceps and hamstring strength at 300° sec	Boys: increase in quadriceps (40%) and hamstring strength (23%); girls: increase in quadriceps (20%) but not hamstring strength (16%)

a   Ages are presented in year ranges, mean or TS where stated.

B1 = boys <13 y; **B2** = boys >14 y; **G1** = girls pre-menarche group; **G2** = girls post-menarche group; **MVC** = maximal voluntary contraction; **N** = Newtons; **PHV** = peak height velocity; **TS** = Tanner stage.

reported that females displayed a significant increase in quadriceps but not hamstring muscle strength with age. It is speculated that this decreased hamstring strength relative to quadriceps strength with age may result in less protection of the ACL during dynamic movements, potentially increasing the risk of ACL injury in females.[59,68]

Despite differences in study design and strength assessment methods used in the studies described above (table IV), there is general consensus that muscle strength is continuously developing in girls throughout puberty without an obvious growth spurt, and the rate of strength development is delayed behind the rate of skeletal growth, compared with boys.[12,16,18,58,59,65,66,68] The greater increase in quadriceps compared with hamstring muscle strength in girls during development creates a potential over reliance of the quadriceps and an underutilization of the hamstrings,[12,59,68] with possibly insufficient hamstring muscular torque being available to act as an agonist and aid the ACL during dynamic movements such as landing. Therefore, it is important to investigate whether these changes in lower limb strength alter the landing biomechanics of girls throughout puberty.

5. Lower Limb Landing Biomechanics during Puberty

Landing is a dynamic movement that requires a knee extensor moment to be applied to prevent the lower limb from collapsing while the body's downward velocity is reduced to zero.[64] Louw et al.[69] stated that landing from a jump was a complex activity, not often mastered by adolescents, as it requires adequate muscle strength and coordination, which is continuously developing and changing throughout puberty.[18] In fact, poor landing technique, characterized by high ground reaction forces, increased knee joint valgus[70] and altered neuromuscular coordination,[71] is a common cause of knee injury, particularly ACL injury, in pubescent girls.[2,33,69] The ACL is also strained under knee abduction/valgus and rotational alignments that are commonly displayed by females during landing.[12,33,72,73]

Despite poor landing technique being a common cause of ACL injury, only seven studies were found that investigated the landing biomechanics displayed by girls during puberty or compared the landing technique of pubescent and pre-/post-pubescent individuals (table V).[11,12,68,74-77] Hewett et al.[74] reported no difference in the normalized peak vertical ground reaction forces generated by pubescent and post-pubescent boys and girls when the participants performed a box-drop landing manoeuvre. Similarly, Quatman et al.[75] reported females displayed no changes in the peak vertical ground reaction forces (normalized to body weight) generated across puberty. Girls, however, displayed significantly greater loading rates during Tanner stages II and III (45 BW/s) compared with during stages IV and V (40 BW/s), highlighting the importance of neuromuscular activation patterns during this period of growth. Girls also displayed greater overall

Table V. A summary of the literature highlighting changes in lower limb landing biomechanics in girls and boys throughout puberty

Study	Study design	Participants	Age[a]	Test	Results
Hewett et al.[74]	Cross sectional (according to TS)	87 girls 188 boys	TS II–V	GRF during box-drop landing	No significant changes in GRF over time or between-gender differences
Quatman et al.[75]	Longitudinal (measured annually for 2 y)	16 girls 18 boys	Y 1: TS II–III Y 2: TS IV-V	GRF during box-drop landing	Decrease in peak vertical GRF in post-pubescent vs pubescent males (0.2–0.4 body weight); no change in girls
Ford et al.[76]	Longitudinal (measured annually for 2 y)	265 girls 50 boys	Y 1: pre-pubertal Y 2: post-pubertal (according to TS)	Ankle, knee and hip joint stiffness during box-drop landing	Males > stiffness vs females (p = 0.001), and increased ankle (p = 0.001), knee (p = 0.043) and hip (p < 0.001) stiffness during pubertal growth vs females
Barber-Westin et al.[68]	Cross sectional (according to age)	853 girls 177 boys	9–17	Ankle and knee separation distance (cm) during box-drop landing	No change (p > 0.05) in ankle or knee separation distance with age in males or females
Hewett et al.[12]	Cross sectional (according to TS)	100 girls 81 boys	11–18 Pre-pubertal (TS I) Pubertal (TS II–III) Post-pubertal (TS IV–V)	Knee valgus and medial knee motion during box-drop landing	Girls display significant (p < 0.05) increase in knee medial motion and valgus with age, but not boys
Ford et al.[11]	Longitudinal (measured annually for 2 y)	265 girls 50 boys	Y 1: pre-pubertal Y 2: post-pubertal (according to TS)	Knee coronal plane motion during box-drop landing	Girls increased peak knee abduction angle (1.6°) and moment (0.07 Nm/kg^{-1}) during pubertal growth, but not boys
Wild et al.[77]	Cross sectional (according to age and time from PHV)	30 boys	Pre-pubertal (7–8 y) Pubertal (13–14 y) Post-pubertal (19–20 y)	Muscle activation of quadriceps and hamstrings during landing	Pubescent males displayed altered neuromuscular activation vs pre- and post-pubescent males

a   Ages are presented in year ranges, mean or TS where stated.

GRF = ground reaction forces; **PHV** = peak height velocity; **TS** = Tanner stage.

loading rates compared with the boys throughout puberty (40–45 BW/s and 30–35 BW/s), with this gender difference also evident among adult males and females.[70,78] Although interesting results, these studies only investigated vertical ground reaction forces.[74,75] As the ACL is commonly ruptured during landings involving a horizontal approach,[33] horizontal ground reaction forces may be a more appropriate variable to investigate. Furthermore, neither study examined how these forces generated at landing were affected by changes in lower limb kinematics or neuromuscular activation patterns across puberty or whether these factors predisposed adolescent girls to a higher ACL injury risk relative to their male counterparts.

A decline in the ability to maintain lower limb, and particularly knee, alignment occurs in girls but not boys throughout puberty.[12,68] Hewett et al.[12] collected coronal plane knee kinematic data for girls and boys, matched for pubertal development, while the participants performed a box-drop landing manoeuvre. Girls in Tanner stage IV and V exhibited greater peak knee valgus alignment compared with boys who were at the same Tanner stage of development (30° and 20° of peak knee valgus for females and males, respectively), whereas no gender differences in knee kinematics were evident prior to puberty. Ford et al.[11,72] also reported that pubescent females displayed greater total knee valgus motion compared with their male counterparts,[72] as well as an increased peak knee abduction angle in girls, but not in boys during pubertal growth.[11] In contrast to these previous studies, Barber-Westin et al.[68] reported no change in knee valgus motion with age in females or males when the participants performed a box-drop landing (table V). However, approximately 60% of all male and female participants in this study[68] landed with a valgus knee alignment, a knee alignment that has been shown to be predictive of ACL injury risk.[13]

Ford et al.[76] reported that pubescent boys displayed significant increases throughout puberty in overall lower limb (ankle, knee and hip) stiffness during landing, whereas this increased stiffness was not displayed by females (table V). It was suggested that decreased stiffness would be deleterious to landing, contributing to a decrease

in joint stabilization and ultimately greater risk of non-contact ACL ruptures.[76] However, given the rapid changes in growth during puberty,[21,22,25] the results of this study must be treated with caution as only two testing sessions, 1 year apart,[11,75,76] may not be sufficient to ascertain the changes in lower limb landing biomechanics during puberty.

Although the studies described in this section suggest that during landing tasks, pubescent girls display an increase in valgus angle and medial knee motion combined with decreased lower limb stiffness compared with boys,[11,12,76] these studies did not investigate the way the participants coordinated their lower limb muscles to align and stabilize the knee during landing. A recent study reported that pre-pubescent males tended to co-contract their quadriceps and hamstring muscles during a horizontal-leap landing movement,[77] a method thought to stabilize the knee joint during landing[79] (table V). However, post-pubescent males in the same study recruited their hamstring muscles before their quadriceps, most likely in an attempt to impart sufficient posterior tibial drawer to reduce the shear force imparted to the ACL by the subsequent quadriceps contraction.[80,81] Interestingly, the pubescent males co-contracted their lateral hamstrings and vastus medialis (medial quadriceps) muscles followed by co-contraction of their medial hamstring and rectus femoris muscles. The authors concluded that in transition from childhood to adulthood, activation of the thigh muscles to stabilize the knee joint during landing appears uncoordinated, possibly contributing to the higher incidence of injuries displayed by this pubescent population.[77] However, this study was only cross sectional in design and only included male and not female participants.

Overall, there is a paucity of research investigating changes in the landing biomechanics displayed by girls throughout puberty, particularly longitudinal studies. Interestingly, of the seven studies described in this section, only one examined a sport-specific landing movement,[77] whereas the other six studies examined a box-drop landing manoeuvre.[11,12,68,74-77,82] Given that sport is the leading cause of injury in pubescent girls,[83,84] and the ACL is predominantly ruptured during movements involving horizontal momentum,[33]

it seems that it would be more ecologically valid to examine the biomechanics of participants while they perform a sport-specific landing movement rather than a box-drop task. Research literature investigating entire lower limb biomechanics (ankle, knee and hip) during landing is also limited, with some studies focusing on only one joint (knee),[11,12] and predominantly in one plane of motion (coronal).[11,12,68] Given that foot placement, as well as trunk and hip motion, affect motion at the knee,[8,85,86] we recommend that future research should more comprehensively investigate the 3-dimensional biomechanics of the landing technique used by girls performing a sport-specific task and how this changes throughout puberty.

6. Conclusions and Directions for Future Research

Compared with boys, girls display a higher incidence of non-contact ACL injuries during sport at the onset of and during puberty. Although this between-gender difference in injury incidence is often attributed to the large estrogen influx that girls experience during puberty, there are conflicting results as to how or whether estrogen affects the metabolic and mechanical properties of the ACL, particularly in pubescent girls who have not yet begun menstruating. This is despite evidence confirming that estrogen receptors are located on the ACL. Therefore, estrogen still remains one factor in a multitude of other factors, which may play a role in the higher non-contact ACL injury incidence incurred by pubescent girls compared with boys.

There is a general consensus that, unlike boys, girls do not display an accelerated increase in muscle strength during puberty, and the development of their hamstring muscle strength appears to lag behind that of their quadriceps strength. Despite controversy in the literature, there is evidence to suggest that girls display an increase in knee valgus alignment throughout puberty, with this knee posture having been associated with an increased risk of ACL injury. It is plausible that the lack of a substantial increase in strength in girls, particularly of the hamstring muscles, may impede their ability to stabilize their knee and

protect the ACL during dynamic landing movements, contributing to a greater risk of ACL injuries. However, there is a paucity of longitudinal studies examining the lower limb musculoskeletal structural and functional changes (strength, flexibility and knee laxity) experienced by girls throughout puberty, as to how these changes are related to estrogen fluctuations characteristic of puberty, or how these changes affect the way these girls land. Furthermore, to our knowledge, no research has investigated changes in the neuromuscular activation patterns or lower limb biomechanics displayed by pubescent girls while they are performing a sport-specific, horizontal landing movement. Therefore, further research is recommended to fill these gaps in our knowledge and to provide greater insight to explain why pubescent girls incur more non-contact ACL injuries during sport compared with boys. Such information will allow the development of evidence-based training programmes aimed at teaching girls to land more safely and with greater control of their lower limbs in an attempt to reduce the incidence of lower limb injuries, particularly non-contact ACL ruptures, in pubescent girls.

Acknowledgements

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