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CLINICAL FEATURE
LETTER TO THE EDITOR

Adolescent combined hormonal contraceptives and surgical repair of anterior cruciate tears: a risky recommendation based on an unproven causal relationship

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ABSTRACT

A recent cross-sectional national USA registry of surgery to repair anterior cruciate ligament tears found that fewer adolescent women who reported using combined hormonal contraceptives (CHC) had the surgery. They reviewed a complex literature on ovarian steroidal relationships with connective tissues biology, physiology and clinical issues. They concluded, based on their data and that evidence shows the greatest gender imbalance for women's ACL injury during adolescence, that all adolescent athletic women should be treated with CHC to prevent ACL injury. We caution that this admonition is using association to imply causation, implies we understand the ovarian hormonal relationships with connective tissues while that remains unclear, the directive to use CHC in adolescent ignores the recent meta-analytic evidence that its use is associated with failure to achieve peak bone mass and that these authors have used erroneous inferential reasoning and ignored the other variables besides sex and age related to ACL injury and the convincing evidence that training strategies can prevent tears.

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ACL injury; risk factors; adolescent women; prevention; training

The DeFroda article [1] is important in calling attention to the increased risk of anterior cruciate ligament (ACL) knee injury in adolescent women in a surgically treated cohort study of women ages 15 to 44 years.

However, ***four things concern us related to this article***:

(1) Misrepresenting a cross-sectional association as causation;
(2) Implying we understand the hormonal etiology of ACL injuries when they remain unclear;
(3) Advocating adolescent combined hormonal contraceptives (CHC) use when it may impair ovulatory cycle development and prevent peak bone mass; and
(4) Attributing the decreased risk of ACL reconstruction to CHC use without accounting for established factors that protect against or increase the risk for ACL tears.

Cross-sectional data are not causal

DeFroda and colleagues' study [1] included 82,874 women who were either receiving CHC or not; the rate of ACL reconstruction was 0.56% in the CHC group and 0.69% in the non-CHC group – an absolute difference of 0.13%. Regardless of how large the database and how representative the underlying population (insufficient information provided to determine this), the only scientific inference that can be made from this cross-sectional data is that female sex and CHC prescription in persons that have undergone an ACL reconstruction are associated, not that CHC is a protective factor of ACL reconstruction surgery or ACL tear. Accordingly, the title is misleading in stating that 'Oral contraceptives provide protection against anterior cruciate ligament tears.'

Hormonal contributions to adolescent women's higher rates of ACL injury

An International Olympic Committee review of non-contact ACL injury in women athletes identified younger women as being at higher risk than men [2]. They further reported that injuries are higher in the early part of the menstrual cycle when estradiol levels are higher but progesterone levels are lower [2]. DeFroda and colleagues describe CHC as including 'a combination of estrogen and progesterone.' In fact, CHC preparations include high-dose synthetic estrogen (at ~4–5 times physiologically equivalent doses) and ***progestin*** at a dose that is approximately similar to the native progesterone hormone [3]. Since many women with regular cycles experience subclinical (silently) non-ovulatory ones [4], much of the quoted literature provides questionable support for the implication that higher estrogen in CHC will *protect* teens against ACL injury. It thus seems inappropriate to advocate a hormonal intervention when the hormonal pathophysiology of ACL injury is unclear (and non-hormonal training methods are highly effective – as discussed below).

New, negative reproductive and bone health information about CHC use in adolescent women

CHC were originally designed for, and most randomized controlled trials have been conducted in, mature adult women.

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However, CHC are increasingly used in adolescents and often for treatment of cramps or irregular cycles that may be normal in the first two post-menarcheal years [5,6]. Retrospective data noted that women given CHC to treat amenorrhea had a significantly lower likelihood of cycle or fertility recovery, and these took longer, than for those who declined treatment [7]. In addition, a recent meta-analysis of prospective, controlled studies in women ages 12–19 years showed that adolescents starting CHC had significant bone mineral density loss over two-years compared to increases in controls who were appropriately accruing bone mass [8]. Since peak bone mass is strongly related to later life fracture risk [9], early CHC use may predict a lifelong increased osteoporosis risk.

Established risk and protective factors for ACL injury in adolescent women

The two most established risk factors for ACL tears are exposure to sports that involve pivoting and cutting, plus previous knee injury. The established protective factor for ACL tears is participation in specific injury prevention programs that decrease women's ACL injury rates by two-thirds [10]. As these factors are not considered in the DeFroda study [1] it is plausible that the non-CHC group may have included women with a greater exposure to high-risk sports, who had experienced a previous knee injury, or had less opportunity to participate in ACL injury prevention training programs. Similarly, is it possible that adolescent women who choose to take CHC are less likely to have ACL reconstruction, or less likely to have non-Medicaid insurance coverage than non-CHC users? This is relevant given that the rate of surgical repair of ACL tears in youth and adolescents is estimated at 70% [11,12], and that there is a clear bias toward surgery in those with private insurance coverage [13]. Further, given the cross-sectional nature of the DeFroda study design and lack of information about the sampling technique, it is plausible that there are other unknown and unaccounted for differences between these two groups.

In summary, this paper is important in calling attention to the fact that fewer general population women (particularly in adolescence) undergoing ACL reconstruction are taking CHC. However, those data **do not** extrapolate to prescribing CHC to prevent ACL injury in athletic adolescent women. Many training-related strategies proven to decrease the incidence of ACL injury in active adolescent women are more constructive [2,10] and potentially less harmful [3,8].

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Declaration of interest

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