

Incidence of ACL Injuries in Females by Selective Use of Oral Contraceptive Pills

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INTRODUCTION: Females are more likely to experience anterior cruciate ligament (ACL) injuries compared to males¹. Relaxin, a collagenolytic hormone, among other biomechanical factors play a role in weakening the ACL, consequently increasing the risk of ACL tears in females. Oral contraceptive pills (OCPs) have been found to decrease relaxin in serum and increase ACL strength². The purpose of this study is to investigate the incidence of ACL injuries among females that use four different formulations of OCPs.

METHODS: In this retrospective cohort study, de-identified data were obtained from 14,664,162 female patients from 15 to 35 years of age between 2011-2023 from the Colorado Health Data Compass database. A total of 15,362 females who sustained an ACL injury, treated by arthroscopic ACL reconstruction, and 12,566,910 females without a history of ACL injury were included. Among these groups, non-OCP users and OCP users, including formulations norethindrone (NE) only, drospirenone (DS) + ethinyl estradiol (EE), etyodiol diacetate (ED) + EE, NE + EE, norgestimate (NG) + EE, were included in the analysis. Statistical analysis was completed using RStudio.

RESULTS SECTION: Comparing ACL injury incidence with and without OCP use, the proportion of ACL injury incidence with OCP use (0.08%; CI: [0.074, 0.086]) was less than the proportion of ACL injury incidence with no OCP use (0.125%; CI: [0.123,0.127]) (Table 1). Among females aged 15 to 18, the proportion of ACL injury incidence with OCP use (0.112%; CI: [0.085,0.114]) was comparable to ACL injury incidence with no OCP use (0.1%; CI: [0.096, 0.104]). Additionally, different OCP formulations showed similar ACL injury incidence, with a slightly lower proportion of ACL injuries in the NE only users group (0.029%; CI: [0.02, 0.042]) compared to NE+EE (0.083%; CI: [0.073, 0.094]), NG+EE (0.092%; CI: [0.081, 0.103]), and DS+EE (0.086%; CI: [0.067, 0.108]) users (Table 2). The average age was similar across groups of OCP formulations.

DISCUSSION: The confidence intervals (CI) comparing ACL injury incidence with and without OCP use did not overlap, suggesting the proportion of ACL injuries with OCP use is lower than no OCP use. After separating the groups by age, 15 to 18 years old and 19 to 35 years old, there was a significant decrease of ACL injury incidence with females using OCPs in the 19- to 35-year-old group. This suggests age may be a factor in the effects of OCP use on ACL injury incidence. Across different OCP formulations, the progestin only formulation (NE only) showed a lower incidence of ACL injury compared to the estrogen/progestin combination formulations, suggesting a role of progesterone in ACL injury prevention. Further research is warranted to explore additional variables impacting the association between OCP use and ACL injury, such as birth control formulation and method, mechanism of injury, and subject specific demographics.

SIGNIFICANCE/CLINICAL RELEVANCE: While past literature and our results suggest that females are at greater risk of ACL injury compared to males, investigating potential protective interventions to reduce ACL injury incidence is necessary. This study is an initial evaluation of associations between OCP use and ACL injury incidence and whether certain formulations of OCPs could serve protective effects against ACL injuries in females.

REFERENCES:

1. Wang CX, Kale N, Wu VJ, et al. Age, female sex, and oral contraceptive use are risk factors for ACL reconstruction: A nationwide database study. *The Knee*. 2023.
2. Konopka JA, Hsue LJ, Drago JL, et al. Effect of oral contraceptives on soft tissue injury risk, soft tissue laxity, and muscle strength: A systematic review of the literature. *Orthop J Sports Med*. 2019.

IMAGES AND TABLES:

Table 1. Incidence of ACL injuries in female OCP users compared to non-OCP users

Cohort Name	ACL Inj. Freq.	No ACL Inj. Freq.	Proportion ACL Inj.	95% CI	Row Overlap
Birth Control Use	620	776890	0.08%	[0.074, 0.086]	No Overlap
No Birth Control Use	14742	11790020	0.125%	[0.123, 0.127]	No Overlap

Table 2. Incidence of ACL injuries in female OCP users, categorized by different OCP formulations

Cohort Name	ACL Inj. Freq.	No ACL Inj. Freq.	Proportion ACL Inj.	95% CI	Row Overlap
NE+EE	255	305851	0.083%	[0.073, 0.094]	3, 4
NE only	29	98999	0.029%	[0.02, 0.042]	No Overlap
NG+EE	267	291398	0.092%	[0.081, 0.103]	1, 4
DS+EE	69	80642	0.086%	[0.067, 0.108]	1, 3