Oral Contraceptive Use Has Protective Effect Against Ankle Sprains in Women

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INTRODUCTION:

Ankle sprains are among the most common musculoskeletal injuries, with a high rate of recurrence and risk of chronic ankle instability. Women are especially predisposed to ankle sprains, with hormonal fluctuations related to the menstrual cycle thought to contribute to this sex disparity by affecting ligamentous laxity and muscle stiffness.

While oral contraceptives (OCPs) modulate hormone levels and have shown potential protective effects against anterior cruciate ligament (ACL) injuries, evidence regarding their impact on ankle sprains is limited. The current study investigated the potential association between OCP use and ankle sprains using a large, national, administrative database, aiming to inform preventive strategies in young women.

METHODS:

Data were abstracted from the M170Ortho PearlDiver Mariner Patient Claims Database, a national administrative claims database covering over 170 million patients across the United States. The database houses information on demographics, drug prescription records, medical procedures, diagnoses, and procedures.

The database was queried for female patients aged 15 to 50 years old to limit the study cohort to those of menstruating age. Patients with amenorrhea, oligomenorrhea, polycystic ovary syndrome, and using non-OCP sex hormone medications were excluded.

Those with ankle sprains were identified based on International Classification of Diseases (ICD) codes. A control cohort was derived from the broader PearlDiver control dataset, including patients without orthopedic conditions, as they are not represented in the M170Ortho subset; patients with a history of ankle sprains were excluded. The ankle sprain cohort and control cohort were matched based on age, Elixhauser Comorbidity Index (ECI), and body mass index (BMI) greater than 40 kg/m^2.

Each cohort was filtered based on OCP use using prescription records. In the ankle sprain cohort, OCP users were defined as patients prescribed OCPs within the year prior to ankle sprain. The OCP groups were further stratified into users of non-estrogen OCPs and estrogen-progesterone OCPs for secondary analysis.

Patient characteristics (age, ECI, BMI 40+) were compared between the matched and unmatched cohorts. Student's t-tests were used to compare continuous variables and Pearson chi-squared tests were used to compare categorical variables. Multivariate logistic regression was used to investigate independent predictors of ankle sprain.

RESULTS:

A total of 1,836,163 patients with ankle sprain who met the inclusion criteria were identified. The non-ankle sprain group consisted of 108,761 patients from the control dataset. The ankle sprain group was, on average, older (30.3 vs. 27.5, $p<0.001$), had a higher ECI (1.9 vs. 1.0, $p<0.001$), and had a higher proportion of patients with BMI 40+ (4.7% vs. 1.7%, $p<0.001$). Matching the ankle sprain and non-ankle sprain groups 1:1 eliminated these differences. After matching, both groups contained 108,761 patients.

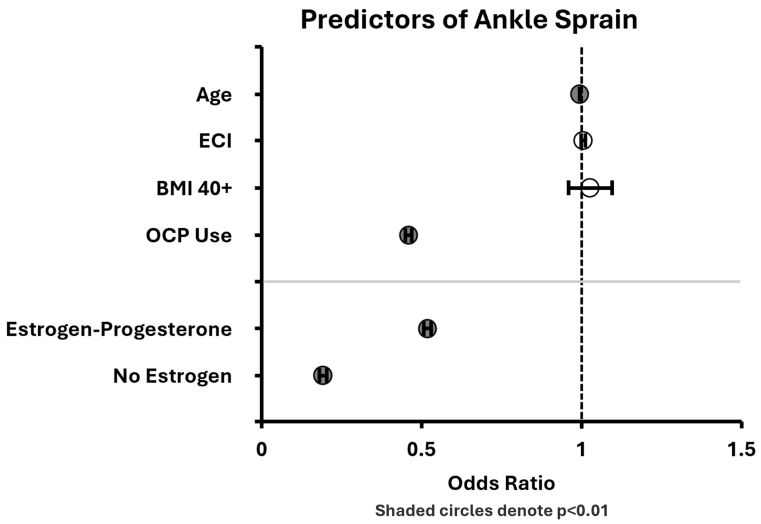
On univariate analysis, patients in the ankle sprain group were less likely to be on OCPs (15.3% vs. 27.6%, $p<0.001$). The univariate odds ratio (OR) of ankle sprain between non-OCP users and OCP users was 0.47 ($p<0.001$). Secondary analysis of estrogen-progesterone and non-estrogen OCP formulations versus non-OCP users showed ORs of 0.54 ($p<0.001$) and 0.20 ($p<0.001$), respectively.

On multivariate analysis, variables found to be significantly associated with ankle sprain were younger age (OR 0.99 per year increase) and OCP use (OR 0.46) (Figure 1). When considering type of OCP, non-estrogen OCPs were associated with a significantly greater reduction in ankle sprain odds (OR 0.19, 95% confidence interval [CI] 0.18-0.20) compared to estrogen-progesterone OCPs (OR 0.52, 95% CI 0.51-0.53).

DISCUSSION AND CONCLUSION:

Although hormonal factors have been proposed as contributing factors to musculotendinous injury in women, prior studies are limited by small sample sizes and often group ankle sprains with other injuries such as ACL tears and ankle dislocations, rather than analyzing ankle sprains in isolation. Prior research on the relationship between OCP use and ACL injuries has produced mixed results, with limited strength and quality of evidence.

The current study on ankle sprains complements the body of work on ACL injuries and establishes the correlation of OCP use with reduced odds of ankle sprains. Upon further analysis, this protective effect was especially emphasized in non-estrogen OCP users versus estrogen-progesterone OCP users. This may be valuable in counselling female athletes who are at greater risk of ankle sprains.


Predictors of Ankle Sprain
Age
ECI
BMI 40+
OCP Use
Estrogen-Progesterone
No Estrogen
0
0.5
1
1.5
Odds Ratio
Shaded circles denote p<0.01