Migraine History May Be Associated With Lower **Breast Cancer Risk**

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Several studies have previously reported that women with a history of migraine headaches have a lower risk of breast cancer, and have suggested that this reduction in risk is stronger for particular subtypes of breast cancer. Migraines, however, are a heterogeneous disorder, with varying presentation and characteristics. Additionally, only about half of migraine sufferers are aware their headaches are clinically-defined migraines. In order to better characterize the relationship between migraines and breast cancer, Drs. Sarah Lowry and Christopher Li, together with colleagues in the Public Health Sciences Division investigated the effect of specific characteristics of migraine history on molecular subtypes of breast cancer. Reporting their results in Cancer, Causes and Control, they found several differences in association between migraine history components and breast cancer risk that may suggest a dual role of estrogen exposure.

"This study builds upon previous findings by Dr. Chris Li and others that women who experience migraines are slightly less likely to be diagnosed with breast cancer," said lead author Dr. Lowry. To better characterize this relationship, the authors recontacted participants in the Seattle area Hormone And Reproductive Epidemiology (SHARE) breast cancer study. Participants were asked about specific characteristics of their migraines in order to establish the lifelong history of their migraine experience, including how old they were when they experienced their first migraine, how frequent and severe their migraine symptoms were over time, and whether any migraines included aura or were menstrually related. Rather than rely solely on self-reported migraines, as previous studies have done, these histories allowed the authors to more accurately classify migraine history according to clinical definitions. This is important because roughly half of migraine sufferers are unaware their headaches qualify as migraines, and roughly half of migraine sufferers have never been clinically diagnosed.

Using data from the Seattle-Puget Sound Surveillance Epidemiology and End Results (SEER) cancer registry, the authors were able to analyze these factors in relation to the estrogen receptor status (ER+ or ER-) and type (ductal or lobular) of breast cancer. Analyzing across these characteristics and subtypes, the authors found several differences in the relationship between migraines and breast cancer risk. "We observed that this relationship was limited to ER+ breast

cancer, and to certain migraine histories," said Dr. Lowry. "Specifically, women with longer-term (30+ years) and early onset (before age 20) of migraine history, as well as those who experienced migraines with aura, had a lower risk of ER+ breast cancer." Depending on their migraine history, these women had 30 to 60% lower risk of particular breast cancer subtypes (see figure).

Said Dr. Lowry, "these findings provide additional clues for understanding this association, while at the same time raising additional questions." While estrogen is known to influence risk of both migraines and breast cancer, the biological mechanism behind this relationship is not clear. Short-term increases or decreases in estrogen levels are thought to trigger migraines, while higher cumulative lifetime exposure to estrogen is associated with increased breast cancer risk (particularly ER+ breast cancer). Also suggestive is the timing of migraines with aura, which occur more frequently during points of the menstrual cycle when estrogen levels are higher.

"Or perhaps," said Dr. Lowry, "this association is explained by behavioral differences in women who experience migraines, such as avoiding alcohol consumption, which is a possible migraine trigger as well as a risk factor for ER+ breast cancer--though our data did not support that particular explanation." As such, further research will be needed to further explore the timing, duration, and biological mechanism behind this relationship. In the meantime, migraine sufferers can hope to find a silver lining to their plight.

Other PHS investigators contributing to this project were Drs. Kathleen Malone and Kara Cushing-Haugen.

<u>Lowry SJ, Malone KE, Cushing-Haugen KL, Li Cl.</u> 2014. The risk of breast cancer associated with specific patterns of migraine history. *Cancer Causes Control*. 25(12):1707-15.

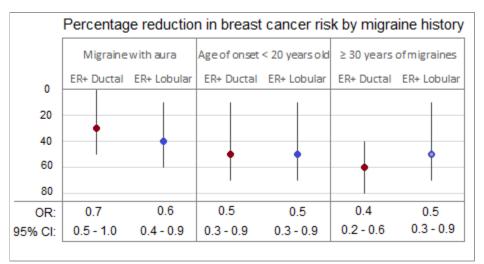


Image provided by Dr. Jonathan Kocarnik

Percentage reduction in breast cancer risk, according to characteristics of migraine history and type of breast cancer (location and estrogen receptor (ER) status). Odds ratios (OR) and 95% confidence intervals (95% CI) are compared to controls without a history of migraines.