Relative Risk of Cervical Neoplasms Among Copper and Levonorgestrel Intrauterine Device Users

Matthew E. Spotnitz, M.D., M.P.H.[1,2], Karthik Natarajan Ph.D.[1,2], Patrick B. Ryan, Ph.D.[1,2], and Carolyn L. Westhoff, M.D., M.Sc.[1]
[1] Columbia University Medical Center, New York, NY; [2]Observational Health Data Sciences and Informatics, New York, NY

Background

As early as the 1980's studies suggested a reduced risk of cervical cancer among women who has used an intrauterine contraceptive. A 2017 systematic review of 17 case-control studies found that intrauterine devices (IUDs) were protective against cervical cancer. The summary odds ratio was 0.64 (95% confidence interval 0.53, 0.77). Those authors suggested that the traumatic manipulation of the cervical canal may clear human papillomavirus (HPV) infection from a combination of acute and chronic inflammatory effects. That study did not differentiate users of a copper intrauterine device (Cu-IUD) from users of hormonal intrauterine devices such as a levonorgestrel intrauterine system (LNG-IUS).

Methods

We implemented a retrospective, observational, cohort study that compared a target cohort of Cu-IUD to a comparator cohort of LNG-IUS users. We used the date of a first IUD placement as the index date for the study. All patients had continuous observation in our database for at least 365 days prior to IUD insertion. We restricted our cohorts to female patients who were 45 years old or younger at the time of IUD placement. We excluded women with a history of endometrial or cervical neoplasms or who had a prior IUD placement. By default, women were in the Cu-IUD cohort unless exposure to an LNG-IUS occurred. The outcome was a high-grade cervical neoplasm diagnosis. The time at risk was from 30 days to 15 years after IUD placement. The study window was restricted to all IUD placements that occurred on or after 01/01/2003. We also performed a subgroup analysis including only those cervical neoplasm diagnoses that occurred at least 1 year following IUD placement.

OHDSI Software Packages:

- -Propensity Score Stratification: http://www.ohdsi.org/web/atlas/#/estimation/cca/138
- -Propensity Score Matching: http://www.ohdsi.org/web/atlas/#/estimation/cca/140
- -Subgroup Analysis: http://www.ohdsi.org/web/atlas/#/estimation/cca/186

Results

Covariate balance was achieved. The relative risk for cervical neoplasms by propensity score stratification was 0.49 [0.32-0.76], p<0.01, and by matching was 0.38 [0.16-0.78], p<0.02. A subgroup analysis with a study window from 365 days following IUD placement post was not statistically significant 0.64 [0.27-1.31], p = 0.31

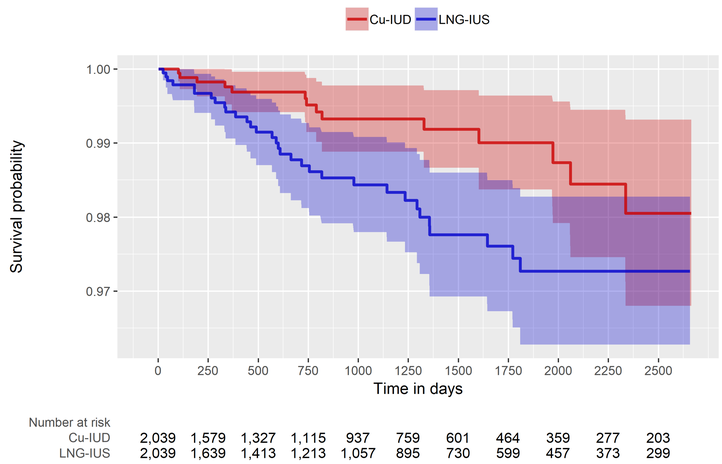

Figure 1: Kaplan-Meier Plot of High Grade Cervical Neoplasm Free Survival vs. Time (days) by IUD type as calculated by propensity score 1:1 matching with confidence interval shading. The time at risk was from 30 to 2530 days. Cu-IUD = Copper IUD (Cu-IUD) Cohort, LNG-IUS Levonorgestrel IUS (LNG-IUS) cohort.

Conclusions

Cu-IUD users have a lower risk of high-grade cervical neoplasms compared to LNG-IUS users. The relative risk of cervical neoplasms of LNG-IUS users compared to the general population is unknown.

Contact: mes2165@cumc.columbia.edu