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Recent changes in endometrial cancer trends among menopausal-age US women

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ABSTRACT

Background: Changes in endometrial cancer incidence rates after the precipitous decline in menopausal hormone therapy (MHT) use in 2002 have not been evaluated.
Methods: Using data from the Surveillance, Epidemiology, and End Results Program from 1992 to 2009 (SEER 13), we identified 63 428 incident endometrial cancer cases among women ages 20–74. We compared annual percent change (APC) in endometrial cancer incidence rates from 1992 to 2002 to rates from 2003 to 2009.
Results: In contrast to the constant endometrial cancer rate pattern observed from 1992 to 2002 (APC 0.0%), rates increased after 2002 in women 50–74 years old (2.5%; $P_{\text{APC comparison}} < 0.01$). Endometrial cancer incidence increased over the entire time period among women ages 20–49 (1992–2002: 1.1%; 2003–2009: 2.1%; $P_{\text{APC comparison}} = 0.21$). Post-2002 increases in incidence among women ages 50–74 were specific to Type I endometrial tumors (1992–2002: −0.6%; 2003–2009: 1.6%; $P_{\text{APC comparison}} < 0.01$).
Discussion: The increase in endometrial cancer incidence rates after 2002 may be related to the widespread decrease in estrogen plus progestin MHT use, which has been reported to lower endometrial cancer risk in overweight and obese women.

1. Introduction

Endometrial cancer is the fourth most common cancer among women and the most common gynecological cancer in the US [1]. Multiple lines of evidence suggest that endometrial cancer is related to excess exposure to estrogens relative to progesterone, especially for the most common type of endometrial cancers (termed Type I) [2]. Specifically, elevated endogenous estrogen levels may mediate the increased endometrial cancer risk associated with postmenopausal obesity [3], and use of estrogen-only menopausal hormone therapy (MHT) is contraindicated among women with intact uteri because of its link to marked increases in endometrial cancer incidence [3]. In contrast, continuous regimen estrogen plus progestin MHT (26 days or more of progestin per month) is associated with a decreased endometrial cancer risk relative to non-hormone use [4].

In 2002, the Women's Health Initiative (WHI) randomized trial was stopped early due to an increased risk of breast cancer and other adverse events [5]. As a result of extensive media coverage there was a subsequent precipitous decline in usage of estrogen plus progestin MHT [5]. Following the decrease in estrogen plus progestin MHT use, breast cancer incidence fell rapidly [6]. Endometrial cancer incidence rates after the decline in MHT use have not been comparably analyzed. Using data from the National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) we evaluated trends in endometrial cancer incidence before and after the early termination of the WHI trial and the resultant decrease in MHT use.

2. Materials and methods

Data on endometrial cancer incidence was obtained from the National Cancer Institute's SEER 13 registries for the years 1992–2009 [7]. SEER 13 data is estimated to cover 13.8% of the US population and includes the following cancer registries: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Utah, San Francisco-Oakland, Seattle-Puget Sound, Los Angeles, San Jose-Monterey, rural Georgia and the Alaska Native Tumor Registry. We identified endometrial cancer cases as primary tumors that demonstrated malignant behavior with site codes uterine corpus (C540–C549) or uterus, NOS (C559).

We further restricted our case definition to tumors with *International Classification of Diseases for Oncology, 3rd Edition* (ICD-O-3) codes that fell into one of three mutually exclusive categories: Type I (adenocarcinoma, NOS (8140), adenocarcinoma tubular

Abbreviations: APC, annual percent change; BMI, body mass index; MHT, menopausal hormone therapy; SEER, Surveillance, Epidemiology and End Results Program; WHI, Women's Health Initiative.

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(8210, 8211), papillary adenocarcinoma (8260, 8262, 8263), endometrioid (8380, 8381, 8382, 8383), mucinous adenocarcinoma (8480, 8481, 8482), adenocarcinoma with squamous metaplasia/adenosquamous (8560, 8570)); Type II (serous/papillary serous (8441, 8460, 8461), clear cell (8310)); and Other (small cell carcinoma (8041), squamous cell (8050, 8070, 8071, 8072, 8076), mixed cell adenocarcinoma (8323), malignant mixed mullerian tumors (8950, 8951, 8980, 8981, 8982)). A total of 63,428 endometrial cancer cases were reported among women ages 20–74 years.

3. Statistical analysis

Using SEER*Stat 8.0.10 software (National Cancer Institute, Bethesda, MD), incidence rates of endometrial cancer per 100 000 woman-years were age-standardized to the US population in 2000. The annual percent change (APC) was calculated for two time periods: before (1992–2002) and after (2003–2009) the early termination of the WHI trial. Rates were estimated for women ages 20–49 ($n = 10\ 936$) and 50–74 ($n = 52\ 492$), approximating pre- and postmenopausal groups.

For women 50–74 years old, we evaluated incidence rate trends by histologic type (as defined above) and race (white, black, American Indian/Alaska Native, Asian/Pacific Islander). Additionally, we conducted lag analyses excluding data 1, 2 and 3 years after the termination of the WHI trial and used the Joinpoint Regression Program 3.5.4 (National Cancer Institute, Bethesda, MD) to further evaluate change points in incidence trends.

4. Results

In contrast to the constant endometrial cancer incidence rate pattern observed from 1992 to 2002 in women ages 50–74 (APC, 0.0%; 95% CI, −.5%, 0.5%), rates increased after 2002 among this age group (APC, 2.5%; 95% CI, 1.4%, 3.6%; $P_{\text{APC comparison}} < 0.01$) (Fig. 1). A different pattern was observed among women ages 20–49, with rates increasing over the entire time period (1992–2002: APC, 1.1%; 95% CI, 0.3%, 2.0%; 2003–2009: APC, 2.1%; 95% CI, 0.7%, 3.5%; $P_{\text{APC comparison}} = 0.21$). In lag analyses, the increase in incidence among women ages 50–74 strengthened (APC 2004–2009: 2.8%, 2005–2009: 3.3%, 2006–2009: 4.2%).

Among white women ages 50–74, endometrial cancer incidence rates followed the same pattern as in all races; incidence rates were constant between 1992 and 2002 (APC, 0.0%; 95% CI, −0.6%, 0.5%), followed by an increase after 2002 (APC, 1.8%; 95% CI, 1.0%, 2.6%; $P_{\text{APC comparison}} < 0.01$) (Table 1). Among black women and Asian/Pacific Islanders, increases were seen over the entire time period; however, the increase accelerated after 2002 ($P_{\text{APC comparison}} = 0.03$ and 0.01, respectively). The endometrial cancer incidence rates for American Indians/Alaska Natives were suggestive of a constant pattern from 1992 to 2002 (APC, 0.0%; 95% CI −5.3%, 5.7%) followed by an increase in incidence after 2002 (APC, 8.4%; 95% CI, −4.5%, 23.0%); however, the APC comparison did not achieve statistical significance likely because of small numbers ($P_{\text{APC comparison}} = 0.13$).

For Type I endometrial cancers in women 50–74 years old, the incidence rate pattern changed from decreasing between 1992 and 2002 (APC, −0.6%; 95% CI, −1.2%, −0.1%), to increasing after 2002 (APC, 1.6%; 95% CI, 1.0%, 2.3%); $P_{\text{APC comparison}} < 0.01$). In Joinpoint analyses, endometrial cancer incidence rates showed a marked increase circa 2006 for women ages 50–74 and circa 2004 for type I tumors in this age group (results not shown).

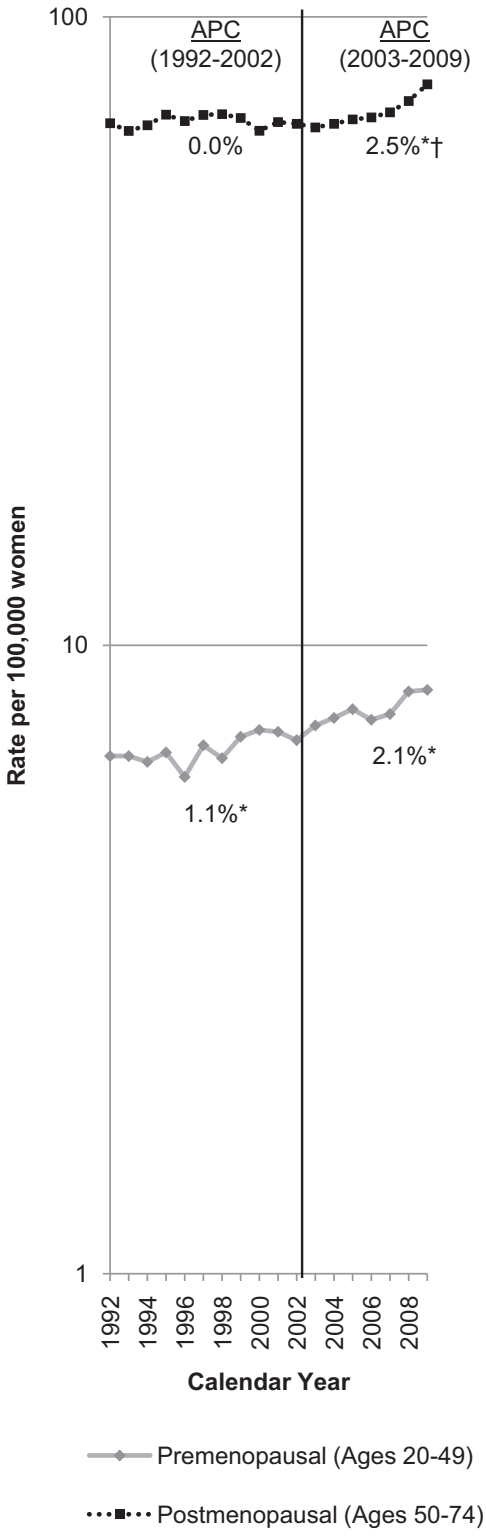

Fig. 1. Age-adjusted endometrial cancer incidence and annual percent change (APC) among US women, 1992–2009, SEER 13. APC = annual percent change. *: APC is significantly different from zero ($P < 0.05$). †: APC for 2003–2009 is significantly different from APC for 1992–2002 ($P < 0.05$).

5. Discussion

We observed increases in endometrial cancer incidence rates following the early termination of the WHI trial in 2002. This pattern was strongest among women in the age group most likely