Body mass index, physical activity, and mortality in women diagnosed with ovarian cancer: Results from the Women's Health Initiative ☆

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HIGHLIGHTS

• Association of BMI, exercise and mortality among women diagnosed with ovarian cancer.
• Women with pre-diagnosis vigorous exercise showed lower risk of mortality.

ARTICLE INFO

ABSTRACT

Background. Ovarian cancer is often diagnosed at late stages and consequently the 5-year survival rate is only 44%. However, there is limited knowledge of the association of modifiable lifestyle factors, such as physical activity and obesity on mortality among women diagnosed with ovarian cancer. The purpose of our study was to prospectively investigate the association of (1) measured body mass index (BMI), and (2) self-reported physical activity with ovarian cancer-specific and all-cause mortality in postmenopausal women enrolled in the Women's Health Initiative (WHI).

Methods. Participants were 600 women diagnosed with primary ovarian cancer subsequent to enrollment in WHI. Exposure data, including measured height and weight and reported physical activity from recreation and walking, used in this analysis were ascertained at the baseline visit for the WHI. Cox proportional hazard regression was used to examine the associations between BMI, physical activity and mortality endpoints.

Results. Vigorous-intensity physical activity was associated with a 26% lower risk of ovarian cancer specific-mortality (HR = 0.74; 95% CI: 0.56–0.98) and a 24% lower risk of all-cause mortality (HR = 0.76; 95% CI: 0.58–0.98) compared to no vigorous-intensity physical activity. BMI was not associated with mortality.

Conclusions. Participating in vigorous-intensity physical activity, assessed prior to ovarian cancer diagnosis, appears to be associated with a lower risk of ovarian cancer mortality.

Introduction

Over 20,000 women are diagnosed with ovarian cancer in the United States each year [1]. Despite efforts to improve early detection and treatment, ovarian cancer is the most fatal gynecologic cancer with a 44% five-year survival rate [1]. Genetic and clinical factors including having a family history of ovarian cancer and a BRCA1/2 mutation have been shown to be associated with higher risk of

ovarian cancer [1]. In addition, lifestyle factors including physical activity and obesity may play a role in ovarian cancer risk and mortality [2,3].

Studies that have examined associations between obesity and mortality in women diagnosed with ovarian cancer have yielded inconsistent results. To our knowledge, seventeen studies have examined the association between obesity and mortality [4,20]. Eleven observed no association between obesity and mortality [10,20], one study suggested that obesity was associated with lower risk of mortality [9], and five studies observed that obesity was associated with higher risk of mortality [4,8]. Fourteen of these studies were included in a recent meta-analysis that showed a slightly higher mortality rate among obese women with ovarian cancer compared to non-obese women with ovarian cancer (HR = 1.17, 95% CI: 1.03–1.34) [21]. Another meta-analysis published in 2011 included 10 observational studies [22]. While no association was found for BMI at diagnosis and all-cause mortality, BMI in early adulthood (HR = 1.60, 95% CI: 1.10–2.34) and pre-diagnosis (HR = 1.45, 95% CI: 1.09–1.93) were associated with mortality in patients with ovarian cancer [22]. Despite the number of studies that has examined obesity and ovarian cancer mortality, none were prospective studies with measured BMI. Thus, there is a possibility of misclassification of obesity status when based on BMI derived from reported heights and weights. Furthermore, most of the studies were of limited sample size (<500 women) and often had a short follow-up period (<5 years).

Physical activity is another putative factor for ovarian cancer incidence and mortality. With mounting evidence that physical activity may help to reduce both the incidence and associated mortality of certain cancers, such as breast cancer, it is relevant to public health and clinical medicine to investigate whether ovarian cancer survivors would also obtain survival benefit from increased levels of physical activity [3,23]. Few studies have examined the association between physical activity and ovarian cancer mortality [6,10,24]. Two studies used retrospective self-report of physical activity collected after ovarian cancer diagnosis [6,24]. One study collected self-reported physical activity from healthy women who were followed for ovarian cancer outcomes [10]. No significant associations between physical activity before diagnosis and ovarian cancer mortality were found [6,10,24]. However, these studies were limited by retrospective physical activity data after cancer diagnosis and small sample sizes (<80 women).

The paucity of prospective, well-powered studies examining obesity, physical activity, and ovarian cancer mortality warrants further research. The purpose of our study was to examine the prospective associations among obesity status based on measured BMI, self-reported physical activity and ovarian cancer mortality in a large sample of well-characterized postmenopausal women enrolled in the Women's Health Initiative (WHI) Study that were subsequently diagnosed with ovarian cancer post-enrollment.

Methods

Study population

Detailed enrollment methods have been published [25]. Briefly, the study enrolled 93,646 women into the WHI Observational Study (OS) and 61,132 women into the WHI Clinical Trials (CT), for a total of 161,808 women enrolled between October 1993 and December 1998 from 40 different centers across the United States. Postmenopausal women of all races and socioeconomic backgrounds, between the ages of 50 and 79 were recruited. Institutional review boards at all centers approved the study protocol and participants provided informed consent.

A total of 927 WHI women were diagnosed with ovarian cancer between October 1993 and September 2012. Women were included in this analysis if they: 1) had histology confirmed ovarian cancer (n = 35 with histology codes that indicated non-ovarian cancer were excluded);

2) did not have any previous cancer diagnosis (n = 67 with previous cancers were excluded); 3) were diagnosed with invasive epithelial ovarian cancer (n = 5 with in-situ ovarian cancer were excluded); 4) had clinical data associated with their ovarian cancer diagnosis (n = 130 diagnosed at death and/or had missing disease stage information were excluded); 5) had complete physical activity, BMI and covariate data (n = 33 with missing data were excluded); 6) were able to walk for one block (n = 7 unable to walk one block were excluded); 7) were alive one year following enrollment into WHI (n = 1 died within one year of enrollment was excluded); 8) had a date of last contact that was after diagnosis of ovarian cancer (n = 6 with censor date prior to date of diagnosis were excluded); and 9) had ovarian cancer diagnoses at least one year following enrollment into WHI (n = 43 were diagnosed within one year of enrollment were excluded) (Fig. 1). Thus, 600 women (65% of 927 women diagnosed with invasive ovarian cancer subsequent to WHI enrollment) were included in this analysis of BMI and physical activity on mortality.

Exposure assessment

Data collection was completed at each WHI center using a standardized protocol. Participants completed questionnaires on health and reproductive history, lifestyle factors and diet at enrollment. Height and weight were measured to the nearest one-tenth of a centimeter or kilogram. Height was measured using a wall-mounted stadiometer
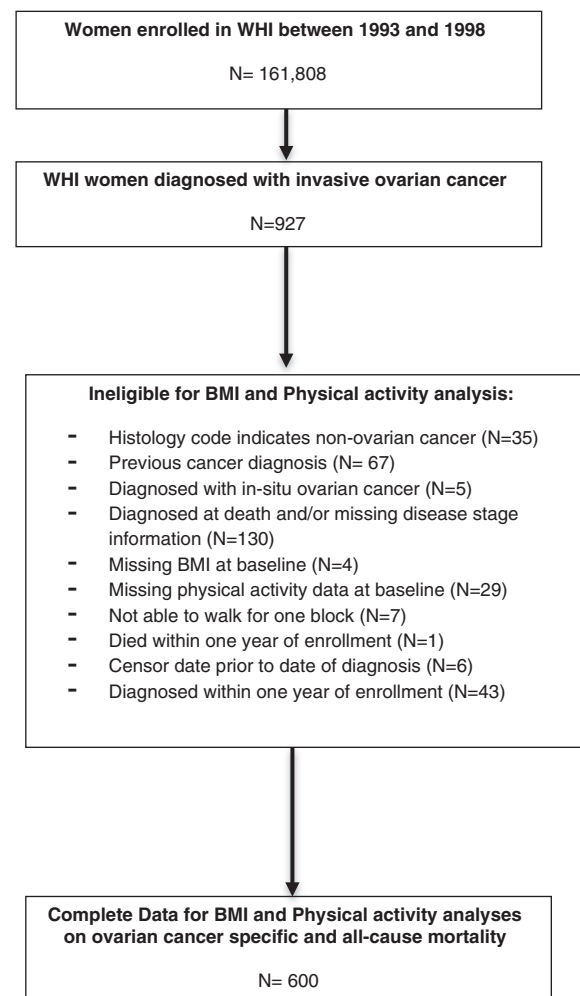

Fig. 1. Eligibility criteria for women in WHI included into the analysis of BMI and physical activity on ovarian cancer specific and all-cause mortality.