Null Results in Brief

Cancer Epidemiology, Biomarkers & Prevention

History of Comorbidities and Survival of Ovarian Cancer Patients, Results from the Ovarian Cancer Association Consortium

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Abstract

Background: Comorbidities can affect survival of ovarian cancer patients by influencing treatment efficacy. However, little evidence exists on the association between individual concurrent comorbidities and prognosis in ovarian cancer patients.

Methods: Among patients diagnosed with invasive ovarian carcinoma who participated in 23 studies included in the Ovarian Cancer Association Consortium, we explored associations between histories of endometriosis; asthma; depression; osteoporosis; and autoimmune, gallbladder, kidney, liver, and neurological diseases and overall and progression-free survival. Using Cox proportional hazards regression models adjusted for age at diagnosis, stage of disease, histology, and study site, we estimated pooled HRs and 95% confidence intervals to assess associations between each comorbidity and ovarian cancer outcomes.

Results: None of the comorbidities were associated with ovarian cancer outcome in the overall sample nor in strata defined by histologic subtype, weight status, age at diagnosis, or stage of disease (local/regional vs. advanced).

Conclusions: Histories of endometriosis; asthma; depression; osteoporosis; and autoimmune, gallbladder, kidney, liver, or neurologic diseases were not associated with ovarian cancer overall or progression-free survival.

Impact: These previously diagnosed chronic diseases do not appear to affect ovarian cancer prognosis. *Cancer Epidemiol Biomarkers Prev; 26(9); 1470–3. ©2017 AACR.*

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Introduction

Preexisting chronic diseases among ovarian cancer patients can result in the use of nonstandard treatment regimens (1) or intolerance to the standard treatments (2), therefore limiting cancer therapy or affecting prognosis in these patients (3). Despite the likely role of comorbidities in ovarian cancer prognosis, detailed evidence regarding associations with particular comorbidities is limited, and results of earlier studies conducted to explore such associations are not consistent (1–6). These studies either did not distinguish among individual comorbidities or had insufficient statistical power to examine associations, particularly for histologic subtypes.

Previously, we reported on the association between histories of hypertension, heart disease, and diabetes in relation to overall survival (OS) and progression-free survival (PFS) among ovarian cancer patients (7). In this study, using a large multinational sample of studies participating in the Ovarian Cancer Association Consortium, we explore the relationship between other selected common comorbidities and OS and PFS among women diagnosed with ovarian cancer. We hypothesize that these comorbidities are associated with poor ovarian cancer prognosis.

Materials and Methods

Our analyses use pooled data from 23 studies. Characteristics of the included studies are shown in Supplementary Table S1. Patient-related data were collected by either self- or interviewer-administered questionnaires and/or medical records reviews. These data were obtained from the participating study centers, cleaned, and harmonized. Comorbidities of interest comprise endometriosis, asthma, autoimmune diseases (dermatomyositis, polymyositis, rheumatoid arthritis, Sjögren syndrome, scleroderma, systemic lupus erythematosus, inflammatory bowel disease, Hashimoto disease, Grave disease, and type I diabetes), depression/anxiety, osteoporosis, and any kidney, liver, gallbladder, and neurologic diseases. For the analyses, the study sample was limited to women with invasive epithelial ovarian cancer and no missing information on vital status, length of follow-up at the time of last contact or the comorbidity of interest (number varies for each disease).

We used age-, stage-, histology-, and site-adjusted Cox proportional hazards models to explore associations between each comorbidity and ovarian cancer outcomes by calculating pooled HRs and their 95% confidence intervals (CI). We were not able to assess heterogeneity among study-specific HRs due to limited numbers of cases in some studies. No other etiologically or prognostically important available factors appreciably changed observed estimates of age- and stage-adjusted study-specific or overall HRs; therefore, they were not included in any of the models.

In all the models, OS was defined as the time from the date of diagnosis to the date of death or end of follow-up, whichever occurred first. PFS was defined as the time from the date of diagnosis to the date when progression status (persistence, recurrence, or death) was determined, or the end of follow-up for cases without identified progression. Cases with no history of the comorbidity of interest were the referent.

We also examined whether or not associations differed according to the main histologic subtypes (high-grade serous, low-grade serous, mucinous, endometrioid, and clear cell), overweight status [18.5 kg/m^2 < body mass index (BMI) < 25.0 kg/m^2 vs. BMI $\geq$ 25.0 kg/m^2], age at diagnosis (<65 vs. $\geq$65 years), and stage of disease (local/regional vs. advanced). In addition, we examined possible multiplicative interactions by likelihood ratio statistics.

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Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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Table 1. Associations between history of selected comorbidities and OS and PFS: Ovarian Cancer Association Consortium

	Deceased			Progression		
Comorbidity	**Yes**	**No**	**HR (95% CI)[a,b]**	**Yes**	**No**	**HR (95% CI)[a,b]**
Endometriosis						
No	6,356	4,824	1.00 (ref)	2,554	1,329	1.00 (ref)
Yes	571	853	0.92 (0.84–1.01)	203	184	1.06 (0.91–1.24)
Asthma						
No	2,117	1,393	1.00 (ref)	1,446	640	1.00 (ref)
Yes	125	101	1.00 (0.84–1.20)	89	50	0.93 (0.75–1.16)
Depression						
No	2,731	1,647	1.00 (ref)	1,669	741	1.00 (ref)
Yes	439	308	0.97 (0.87–1.08)	202	98	0.90 (0.76–1.07)
Osteoporosis						
No	2,043	1,405	1.00 (ref)	1,093	445	1.00 (ref)
Yes	170	85	0.95 (0.81–1.12)	76	21	0.96 (0.73–1.27)
Autoimmune disease						
No	907	579	1.00 (ref)	784	386	1.00 (ref)
Yes	242	178	0.94 (0.73–1.22)	162	76	0.95 (0.74–1.23)
Kidney disease						
No	1,739	1,317	1.00 (ref)	1,004	516	1.00 (ref)
Yes	48	37	1.19 (0.89–1.60)	18	9	1.04 (0.65–1.67)
Liver disease						
No	2,186	1,461	1.00 (ref)	1,485	664	1.00 (ref)
Yes	31	15	0.98 (0.68–1.41)	15	10	0.86 (0.54–1.38)
Gallbladder disease						
No	2,433	1,626	1.00 (ref)	1,483	645	1.00 (ref)
Yes	438	205	1.06 (0.96–1.18)	254	88	1.09 (0.94–1.26)
Neurological disease						
No	1,156	1,031	1.00 (ref)	547	250	1.00 (ref)
Yes	17	11	1.32 (0.79–2.21)	9	8	0.82 (0.41–1.68)

[a]Models adjusted for age (continuous), stage (localized, regional, or advanced), histology, and study site.
[b]Studies included for each comorbidity as presented in Supplementary Table S1.

We had 80% power to detect the following risk estimates for OS and PFS, respectively: 1.11 and 1.20 for endometriosis, 1.28 and 1.34 for asthma, 1.15 and 1.23 for depression, 1.26 and 1.41 for osteoporosis, 1.22 and 1.27 for autoimmune disease, 1.50 and 1.95 for kidney disease, 1.71 and 1.97 for liver disease, 1.16 and 1.21 for gallbladder disease, and 2.08 and 2.29 for neurologic diseases.

Results

Results of the analyses are presented in Table 1. No significant associations were observed between histories of endometriosis, asthma, depression, osteoporosis, autoimmune, gallbladder, kidney, liver, and neurologic diseases and OS or PFS. Results were also not significant and not different in strata defined by histologic subtype, overweight status, age, and stage of disease. No evidence of multiplicative interaction was observed.

Discussion

In this large international sample of women diagnosed with invasive ovarian cancer, we did not observe associations between histories of endometriosis, asthma, depression, osteoporosis, and autoimmune, kidney, liver, gallbladder, and neurologic diseases and OS and PFS. Results of our study are similar to others reporting no association between presence of comorbidity and survival among ovarian cancer patients (1, 4, 6). Our results are also consistent with those from Hemminki and colleagues (8) that showed no association between autoimmune disease and survival (HR = 1.09; 95% CI, 0.99–1.20). These results suggest that various comorbidities have little impact on survival for a disease that is already characterized by poor prognosis (4).

Strengths of our study include the large sample of patients with ovarian cancer, allowing for the assessment of associations within histologic subtypes as well as potential effect modification. Limitations of this research include the possibility of residual confounding, particularly due to the absence of information on treatment regimen and on comorbidities diagnosed after ovarian cancer diagnosis.

In conclusion, we did not observe evidence of the relationship between selected chronic diseases and OS and PFS among cases diagnosed with invasive epithelial ovarian carcinoma.

Disclosure of Potential Conflicts of Interest

A. deFazio reports receiving commercial research support from AstraZeneca. P.A. Fasching is a consultant/advisory board member for Amgen, Celgene, Novartis, Pfizer, and Roche. D.W. Cramer has provided expert testimony for Ashcraft and Gerel and Beasley Allen. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The authors assume full responsibility for analyses and interpretation of these data.

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