Comorbidity and survival of ovarian cancer among patients in the U.S. Midwest

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1. Background

- Ovarian cancer (OC) is the fifth leading cause of cancer death among women in the U.S. Midwest states, including Missouri, Iowa and Kansas, have among the highest rates of OC in the nation and relatively poorer survival in the country.
- Comorbidity may negatively influence survivorship among patients with OC. However, evidence supporting comorbidity as a prognostic factor for OC survival while accounting for other known clinical prognostic factors is inconclusive.

Table 1 Sample Characteristics by Comorbidity Category

	CCI=0 (n, %)	CCI=1 (n, %)	CCI=2+ (n, %)	P-value
Age at diagnosis				**<.0001**
<40	44 (5.8)	1 (0.7)	0	
40 to 49	94 (12.3)	11 (7.2)	2 (2.3)	
50 to 59	185 (24.3)	21 (13.7)	10 (11.5)	
60 to 69	204 (26.7)	50 (32.7)	19 (21.8)	
70 to 79	150 (19.7)	41 (26.8)	24 (27.6)	
80 +	86 (11.3)	29 (19.0)	32 (36.8)	
Census tract education				.41
≤30% high school	245 (32.2)	55 (36.0)	33 (37.9)	
>30% high school	517 (67.8)	98 (64.0)	54 (62.1)	
Census track median Income				.11
≤50,999	366 (48.4)	80 (52.3)	52 (59.8)	
≥51,000	390 (51.6)	73 (47.7)	35 (40.2)	
Rural vs. urban residence				**.003**
Rural	391 (51.5)	53 (34.6)	36 (41.4)	
Urban	369 (48.5)	100 (65.4)	51 (58.6)	
Cytoreductive surgery outcomes				**.017**
Optimal (residual not visible or <1cm)	350 (62.1)	56 (55.5)	28 (71.8)	
Suboptimal (residual ≥1cm)	18 (3.2)	11 (10.9)	1 (2.6)	
Size NOS	107 (19.0)	17 (16.8)	7 (18.0)	
Unknown	89 (15.8)	17 (16.8)	3 (7.6)	
Chemo therapy type				**<.0001**
No chemo and/or definitive surgery	222 (29.1)	55 (36.2)	51 (58.6)	
Pre-surgery/neoadjuvant	67 (8.8)	17 (11.2)	5 (5.8)	
Post-surgery/adjuvant	456 (59.7)	80 (52.6)	31 (35.6)	
Unknown	18 (2.4)	0	0	
Stage				**<.0001**
I	182 (23.9)	29 (18.9)	9 (10.3)	
II	53 (6.9)	10 (6.5)	4 (4.6)	
III	317 (44.5)	61 (39.9)	29 (33.3)	
IV	185 (24.3)	49 (32.0)	33 (37.9)	
Unknown	26 (3.4)	4 (2.6)	12 (13.8)	
Grade				**<.0001**
I (well differentiated)	56 (7.3)	12 (7.8)	1 (1.1)	
II (moderately differentiated)	98 (12.8)	15 (9.8)	6 (6.9)	
III (poorly differentiated)	334 (43.8)	49 (32.0)	22 (25.3)	
IV (undifferentiated)	118 (15.5)	27 (17.6)	15 (17.2)	
Unknown	157 (20.6)	50 (32.7)	43 (49.4)	
Histology				**<.0001**
Serous	444 (58.2)	77 (50.3)	31 (35.6)	
Endometrioid	52 (6.8)	7 (4.6)	3 (3.4)	
Mucinous	47 (6.2)	11 (7.2)	4 (4.6)	
Clear cell	43 (5.6)	4 (2.6)	2 (2.3)	
Epithelial NOS	92 (12.1)	37 (24.2)	21 (24.1)	
Others	85 (11.1)	17 (11.1)	26 (29.9)	
Surgeon specialty				0.22
Gynecological oncologist (GO)	26 (4.0)	5 (4.4)	6 (13.3)	
General surgeon	63 (9.6)	12 (10.6)	4 (8.9)	
OB/GYN	544 (83.1)	92 (81.4)	33 (73.3)	
Other	5 (0.8)	0	0	
Unknown	17 (2.6)	4 (3.5)	2 (4.4)	
Length of follow up (mean week, SD)	34.9 (25.7)	32.5 (26.2)	21.1 (23.8)	**<.0001**

2. Purpose

- To examine the role of comorbidity in OC survival using a population-based sample from three Midwestern states

3. Methods

- ***Sample:*** The Missouri, Kansas and Iowa cancer registries participated in a CDC and Westat-led project to collect more detailed data about OC patients diagnosed 2011-2012 (Iowa&Missouri) or 2010-2012 (Kansas). OC cases (N=1,003) were randomly selected from the state-specific sample that met selection criteria. Vital status was obtained through linkage to National Death Index through 31 December 2016.
- ***Measures:*** Comorbidity was measured using the Charlson Comorbidity Index (CCI), which includes 19 chronic conditions that are weighted based on their association with mortality. CCI was categorized into 0 (none), 1 (mild) or 2+ (moderate/severe). Demographic covariates included age at diagnosis, education, income and urban vs. rural residence. Tumor characteristics included stage, grade and histology. Treatment variables include cytoreduction status, chemotherapy type and surgeon specialty.
- ***Analysis:*** We used Chi-square tests to detect differences between comorbidity categories, Kaplan-Meier product-limits estimates to produce survival curves and Cox-proportional hazards regression models to estimate hazard ratio (HR) and 95% confidence intervals (CIs) of comorbidity for all-cause mortality among patients with OC.

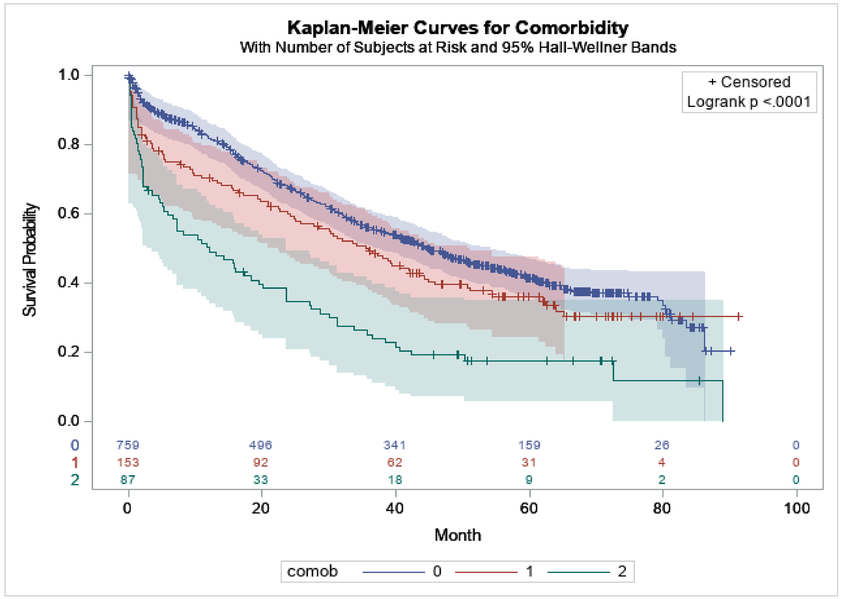

Table 2 Hazards of Death Associated with Comorbidity and Other Sociodemographic, Tumor and Treatment Characteristics

	Crude HR (95% CI)	Adjusted HR (95% CI)
Comorbidity		
CCI=0	1	1
CCI=1	**1.26 (1.00-1.59)**	0.76 (0.70-1.31)
CCI=2+	**2.39 (1.80-3.19)**	**1.74 (1.11-2.74)**
Age		
<40	1	1
40 to 49	**3.24 (1.41-7.45)**	**3.91 (1.47-10.39)**
50 to 59	**3.17 (1.40-7.16)**	**2.80 (1.07-7.26)**
60 to 69	**5.36 (2.40-11.97)**	**4.37 (1.68-11.37)**
70 to 79	**6.53 (2.91-14.63)**	**3.04 (1.19-7.76)**
80 +	**15.36 (6.82-34.60)**	**7.69 (2.91-20.32)**
Census tract education		
≤30% high school	1	1
>30% high school	1.16 (0.98-1.36)	1.10 (0.84-1.43)
Census tract median income		
≤50,999	1	1
≥51,000	**0.80 (0.68-0.94)**	0.95 (0.73-1.23)
Urban vs. rural residence		
Urban	1	1
Rural	**1.33 (1.12-1.57)**	1.17 (0.89-1.52)
Cytoreduction status		
<1cm	1	1
≥1cm	**2.64 (1.77-3.94)**	**1.90 (1.23-2.94)**
Size NOS	**2.28 (1.75-2.96)**	**1.67 (1.23-2.26)**
Unknown	**1.69 (1.26-2.27)**	**2.04 (1.46-2.84)**
Chemo therapy type		
No chemo/or definitive surgery	1	1
Pre-surgery/neoadjuvant	0.72 (0.46-1.10)	**0.28 (0.16-0.47)**
Post-surgery/adjuvant	0.87 (0.67-1.12)	**0.17 (0.10-0.26)**
Unknown	1.54 (0.47-5.08)	**0.39 (0.16-0.96)**
Stage		
I	1	1
II	**3.73 (2.22-6.27)**	**3.37 (1.55-7.33)**
III	**7.16 (4.90-10.46)**	**13.69 (6.53-28.74)**
IV	**15.71 (10.69-23.09)**	**20.45 (9.78-42.76)**
Unknown	**21.59 (11.64-40.03)**	**3.25 (1.13-9.38)**
Grade		
I	1	1
II	**2.12 (1.07-4.19)**	**3.57 (1.25-10.16)**
III	**4.88 (2.64-9.00)**	**4.48 (1.62-12.40)**
IV	**4.13 (2.20-7.76)**	**3.95 (1.40-11.10)**
Unknown	**10.79 (5.77-20.17)**	**3.25 (1.13-9.38)**
Histology		
Serous	1	1
Endometrioid	**0.35 (0.22-0.56)**	0.72 (0.34-1.57)
Mucinous	**0.33 (0.19-0.57)**	1.73 (0.75-3.95)
Clear cell	**0.44 (0.28-0.70)**	**2.74 (1.46-5.16)**
Epithelial NOS	**1.86 (1.45-2.49)**	0.99 (0.63-1.57)
Others	**1.85 (1.40-2.44)**	**2.34 (1.51-3.64)**
Surgeon specialty		
Gynecological oncologist (GO)	1	1
General surgeon	**1.74 (1.13-2.67)**	0.96 (0.56-1.66)
OB/GYN	**0.37 (0.23-0.61)**	**0.47 (0.28-0.79)**
Other	3.48 (1.32-9.19)	3.17 (0.76-13.12)
Unknown	0.84-2.96	0.74 (0.23-2.29)

4. Discussion

- Comorbidity is an important prognostic factor, independent of age, sociodemographic, tumor-specific and treatment factors, and has negative impact on the survival of OC in the U.S. Midwest.
- Our study highlights the importance of managing comorbidity in conjunction with cancer therapy among patients with OC.

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