GYNECOLOGY

Survival differences in women with serous tubal, ovarian, peritoneal, and uterine carcinomas

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OBJECTIVE: The fallopian tube has been implicated as the primary origin of pelvic serous cancers. We proposed to determine the survival outcomes of serous tubal, ovarian, peritoneal, and uterine cancer patients.

STUDY DESIGN: Data were obtained from the National Cancer Institute between 2004 and 2009. Kaplan-Meier and Cox proportional hazards models were used for analysis.

RESULTS: Of 12,336 high-grade serous cancer patients, 563 were tubal (TC), 8560 ovarian (OC), 1037 primary peritoneal (PPC), and 2176 uterine cancer (USC). The median ages of these patients were 63 vs 62 vs 67 vs 68 years, respectively. The majority were white (89% vs 88% vs 91% vs 74%). The overall 5 year, disease-specific survival was 37%. The survivals of those with TC, OC, PPC, and USC were 50%, 37%, 26%, and 40% ($P < .01$). There was no detailed staging on PPC cancers. Adjusted for stage, the survival of those with stage I, II, III, and IV TC were 73%, 62%, 44%, and 22% ($P < .01$), OC were 83%, 64%, 34%, and 15% ($P < .01$), and USC were 88%, 72%, 55%, and 17% ($P < .01$). On multivariate analysis, younger age, white race, earlier stage, and tubal origin were independent predictors for improved survival.

CONCLUSION: In advanced-staged serous cancer patients, tubal cancer patients have better survivals compared with ovarian, peritoneal, and uterine cancer.

Key words: cancer origin, endometrial cancer, ovarian cancer, serous cancer, survival analysis

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Serous carcinomas comprise 46% of ovarian cancers, 40% of tubal cancers, 70% of peritoneal cancers, and 6% of uterine cancers.[1,2] Serous cancers are associated with more advanced stage and poorer prognosis compared with other cell types.

The origin of serous cancers in the pelvis has received significant attention. Although the ovary, peritoneum, and uterine corpus do not natively contain serous cells, serous cancers are a significant proportion of these diseases. Because the adjacent fallopian tubes have native serous cells, it became the site of interest as the potential neoplastic origin of these cancers.[3]

Crum et al[3] found that women with BRCA mutations have a 50% likelihood of developing tubal intraepithelial carcinoma (TIC), a precursor for serous tubal carcinoma (TC). They found that the precursor lesion could then lead to TC, with potential to spread to the uterus, ovaries, and peritoneum. Furthermore, Przybycin et al[4] showed that up to 60% of TICs may be responsible for pelvic tubal carcinomas. Although these organs are in close proximity to each other, serous cancers of the ovary and uterus differ on a molecular level. In fact, Zorn et al[5] found different expression patterns of serous ovarian and endometrial cancers based on their site of origin. However, on a clinical level, the differential survival outcomes of serous pelvic cancers have not been well documented.

The clinical outcomes of cancer based on histology vs site of origin remain unclear. Researchers using the Swedish Cancer Registry highlighted the importance of histology in survival outcomes.[6] Alternatively, other investigators found that the site of origin was the strongest predictor for survival rate in anal vs rectal melanoma.[7] However, most of these previously reported findings were from small, homogenous groups of patients and lacked supporting data from a hypothesized biological

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TABLE 1
Patient demographic and clinicopathologic characteristics

Factor	Total (n = 12,336)	TC (n = 563)	OC (n = 8560)	USC (n = 2176)	PPC (n = 1037)	*P* value
Median age, y (range)	64 (24–97)	63 (32–91)	62 (24–97)	68 (27–96)	67 (30–91)	< .01
Race						
White	10,511 (86%)	497 (89%)	7466 (88%)	1607 (74%)	941 (91%)	< .01
Black	970 (8%)	24 (4%)	506 (6%)	400 (18%)	40 (4%)	
Asian	804 (7%)	38 (7%)	551 (6%)	160 (7%)	55 (5%)	
Surgery						
Yes	11,859 (96%)	563 (100%)	8302 (97%)	2029 (93%)	965 (93%)	< .01
No	469 (4%)	0 (0%)	253 (3%)	144 (7%)	72 (7%)	
Stage						
I	1313 (12%)	101 (19%)	558 (7%)	654 (32%)	—	< .01
II	912 (8%)	86 (16%)	615 (7%)	211 (10%)	—	
III	5652 (52%)	250 (46%)	4720 (57%)	682 (33%)	—	
IV	3014 (28%)	103 (19%)	2382 (29%)	529 (25%)	—	

OC, ovarian carcinoma; *PPC*, primary peritoneal carcinoma; *TC*, tubal carcinoma; *USC*, uterine serous carcinoma.

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model of pathogenesis as in pelvic serous cancers.[4,8]

Given the limited data on the clinical outcomes of serous pelvic cancers, we proposed a large, population-based study to investigate the survival outcomes of serous tubal, ovarian, peritoneal, and uterine carcinomas.

Materials and Methods

Information of women diagnosed with high-grade serous cancers was obtained from the Surveillance, Epidemiology, and End Results (SEER) (accessed Aug. 21, 2012) of the National Cancer Institute. Because SEER is a nationwide, deidentified database, our study was not covered by an institutional review board application. Patient demographic data, cancer data (such as histology, stage, and grade), diagnosis date, surgical treatment and radiation therapy, follow-up of vital status, and cause of death (if applicable) were recorded. Serous cancer was defined using *International Classification of Disease*, third revision, codes (8441, 8442, 8460, 8461, and 9014) between the years 2004 and 2009.

The SEER program encompasses approximately 26% of the US population in varied demographic areas. A Kaplan-Meier and Cox proportional hazards model were used to investigate survival statistics. The outcome of interest was survival rate with regard to the original site of origin of cancer. Two-tailed tests at values of $P < .05$ were considered significant. All data were analyzed using R 3.0.2 using the package survival for survival analyses (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics

Of 12,336 patients with high-grade, serous carcinoma, the median age was 64 years (range, 24–97 years) (Table 1). Of these women, 563 had TC, 8560 had ovarian carcinoma (OC), 1037 had primary peritoneal carcinoma (PPC), and 2176 had uterine serous carcinoma (USC). Subjects with USC and PPC were older than patients with TC and OC (68 and 67 vs 63 and 62 years, $P < .01$), whereas a greater proportion of PPC and TC patients reported being white than OC and USC patients (91% and 89% vs 88 and 74%, $P < .01$).

In the overall study group, 96% of patients (n = 11,859) underwent primary surgery, which comprised 563 with TC, 8302 with OC, 965 with PPC, and 2029 with USC. Of all patients, 12% had stage I, 8% had stage II, 52% had stage III, and 28% had stage IV disease. Based on stage at presentation (Figure 1), those with TC and USC had more than a 2-fold higher proportion of early-stage cancers as compared with ovarian cancer ($P < .01$). More specifically, 35% of TC and 42% of USC patients presented with stage I and II disease, compared with 14% of ovarian cancer patients. Those with OC presented with advanced cancers at 86%, whereas TC and USC patients had 65% and 58% advanced cancers, respectively. There was no staging diagnosis available for PPC cancers.

Survival outcomes based on patient characteristics

In the overall study group, the 5 year survival rate was 37%. Those with stages I, II, III, and IV disease had survival rates of 73%, 62%, 44%, and 22% ($P < .01$) (Table 2).

Outcomes based on site of origin

Based on the tumor site of origin, the survivals of those with TC, OC, PPC, and