Gynecologic Oncology 136 (2015) 205–211

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

The prognostic value of dividing epithelial ovarian cancer into type I and type II tumors based on pathologic characteristics

Kira Philipsen Prahm [a,*], Mona Aarenstrup Karlsen [b], Estrid Høgdall [b], Nikolai Madrid Scheller [c], Lene Lundvall [a], Lotte Nedergaard [d], Ib Jarle Christensen [e], Claus Høgdall [a]

[a] Dept. of Gynecology, Juliane Marie Centre, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
[b] Molecular Unit, Dept. of Pathology, Herlev Hospital, University of Copenhagen, Copenhagen, Denmark
[c] Dept. of Epidemiologic Research, Statens Serum Institute, Copenhagen, Denmark
[d] Dept. of Pathology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
[e] Finsen Laboratory, Copenhagen Biocenter, University of Copenhagen, Copenhagen, Denmark

HIGHLIGHTS

- The prognostic significance of type I and type II ovarian cancer was investigated.
- No difference in survival was observed within the first two years of follow-up.
- After two years of follow-up type II tumors had an increased risk of death.

ARTICLE INFO

Article history:
Received 30 October 2014
Accepted 16 December 2014
Available online 27 December 2014

Keywords:
Epithelial ovarian cancer
Type I and type II
Prognostic value
Pathologic characteristics

ABSTRACT

Objective. To investigate the prognostic significance of dividing epithelial ovarian cancer (EOC) in type I and type II tumors based on pathologic variables.

Methods. We used the Danish Gynecologic Cancer Database to identify all patients diagnosed with EOC from 2005 to 2012. Information on histologic type and grade were used to classify tumors as either type I or type II. Death, and several prognostic factors were used in the multivariate Cox regression, and Landmark analysis was used to estimate hazard ratios of all-cause mortality.

Results. Among 2660 patients diagnosed with EOC, 735 were categorized as type I tumors, and 1925 as type II tumors. Patients with type II EOC were more frequently diagnosed in late FIGO stages (stages III–IV) than patients with type I EOC (78.1% vs. 32.1% respectively; $P < 0.001$). Time dependent multivariate Cox analysis, adjusted for known prognostic variables, showed no significant difference in survival within the first two years after diagnosis, however, after 730 days of follow-up a significantly increased overall survival for type I tumors was observed (hazard ratio 1.72, 95% confidence interval: 1.28–2.31, $P < 0.001$). Similarly the Landmark analysis for survival confirmed the increased overall survival for type I tumors after two years of follow-up (hazard ratio: 1.85, 95% confidence interval: 1.35–2.54, $P < 0.001$).

Conclusion. Classification of EOC in type I and type II tumors based on pathologic variables was associated with an increased risk of death for type II tumors after two years of follow-up, while no increased risk was seen during the first two years of follow-up.

Introduction

Ovarian cancer (OC) is the seventh most common cancer among women worldwide, and the leading cause of death from gynecologic malignancies with an estimated 200,000 incident cases and 125,000 deaths annually [1,2]. Previously EOC was believed to originate primarily from the surface epithelial cells covering the ovaries and lining subserosal cysts [3]. However, recent morphologic, immunohistochemical and molecular studies have led to a new paradigm for the pathogenesis and origin of EOC, dividing EOC into two groups designated as type I and type II [4,5]. This new understanding of the carcinogenesis of EOC suggests that EOC may also originate from the fimbriated part of the fallopian tube, from endometriotic lesions (endometrioid, and clear cell tumors), or from the epithelial nests at the tubal–mesothelial junction (mucinous, and Brenner tumors) [5–10]. From this new evidence on ovarian tumorigenesis, the major histologic subtypes are divided into type I

* Corresponding author at: Department of Gynecology, Juliane Marie Centre, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen, Denmark.
E-mail address: kira@prahm.dk (K.P. Prahm).

http://dx.doi.org/10.1016/j.ygyno.2014.12.029
0090-8258/

Table 1
Baseline characteristics of 2660 patients with EOC and further classified by type I and type II EOC.

	Type I EOC $N = 735$ (%)	Type II EOC $N = 1925$ (%)	Overall $N = 2660$ (%)
Inclusion year			
2005	104 (3.9)	276 (10.4)	380 (14.3)
2006	103 (3.9)	290 (10.9)	393 (14.8)
2007	133 (5.0)	285 (10.7)	418 (15.7)
2008	92 (3.5)	281 (10.6)	373 (14.0)
2009	113 (4.2)	300 (11.3)	413 (15.5)
2010	97 (3.6)	263 (9.9)	360 (13.5)
2011	93 (3.5)	230 (8.6)	323 (12.1)
Age at inclusion			
<50	165 (6.2)	171 (6.5)	336 (12.6)
50–59	186 (7.0)	423 (15.9)	609 (22.9)
60–69	205 (7.7)	629 (23.6)	834 (31.4)
70–79	129 (4.8)	498 (18.7)	627 (23.6)
≥80	50 (1.9)	204 (7.7)	254 (9.5)
Median age at diagnosis	59.8	65.1	64
BMI group			
<18.5	32 (1.2)	77 (2.9)	109 (4.1)
18.5–24.9	344 (12.9)	1015 (38.2)	1359 (51.1)
25–34.9	282 (10.6)	691 (26.0)	973 (36.6)
≥35	49 (1.8)	72 (2.7)	121 (4.5)
Missing	28 (1.1)	70 (2.6)	98 (3.7)
ASA score			
1	330 (12.4)	635 (23.9)	965 (36.3)
2	302 (11.4)	956 (35.9)	1258 (47.3)
3	82 (3.1)	265 (10.0)	347 (13.0)
4	8 (0.3)	31 (1.2)	40 (1.5)
5	1 (0.0)	0 (0)	1 (0.0)
Missing	12 (0.5)	37 (1.4)	49 (1.8)
Performance status			
0	478 (18.0)	922 (34.7)	1400 (52.6)
1	173 (6.5)	670 (25.2)	843 (31.7)
2	47 (1.8)	222 (8.3)	269 (10.1)
3	20 (0.8)	62 (2.3)	82 (3.1)
4	6 (0.2)	27 (1.0)	33 (1.2)
Missing	11 (0.4)	22 (0.8)	33 (1.2)
Smoking status			
Former smoker	120 (4.5)	389 (14.6)	509 (19.1)
Never smoked	354 (13.3)	926 (34.8)	1280 (48.1)
Smoking	167 (6.3)	368 (13.8)	535 (20.1)
Missing	94 (3.5)	242 (9.1)	336 (12.6)
Comorbidity			
1) None	453 (17)	1169 (43.9)	1622 (61.0)
2) Cardiac-, vascular-, lung disease	183 (6.9)	465 (17.5)	648 (24.4)
3) Endocrine-, hematological-, neurological disease	35 (1.3)	86 (3.2)	121 (4.5)
4.) Liver-, kidney-, intestinal disease	5 (0.2)	14 (0.5)	19 (0.7)
5) 2 + 3	34 (1.3)	100 (3.8)	134 (5.0)
6) 2 + 4	2 (0.1)	13 (0.5)	15 (0.6)
7) 4 + 3	1 (0.0)	9 (0.3)	10 (0.4)
8) 2 + 3 + 4	1 (0.8)	7 (0.3)	8 (0.3)
9) Missing	21 (0.8)	62 (2.3)	83 (3.1)
Primary operation			
Yes	705 (95.9)	1702 (88.4)	2407 (90.5)
No (inclusive neoadjuvant chemo)	19 (2.6)	203 (10.5)	222 (8.3)
Missing	11 (1.5)	19 (1.0)	30 (1.1)
Radical surgery			
Yes	598 (22.5)	831 (31.2)	1429 (53.7)
No	127 (4.8)	1074 (40.4)	1201 (45.2)
FIGO stage			
I	435 (16.4)	251 (9.4)	686 (25.8)
II	64 (2.4)	170 (6.4)	234 (8.8)
III	177 (6.7)	1119 (42.1)	1296 (48.7)
IV	43 (1.6)	362 (13.6)	405 (15.2)
Missing	16 (0.6)	23 (0.9)	39 (1.5)
Total histological subtype	735 (27.6)	1925 (72.4)	2660 (100)
Serous adenocarcinomas	204 (7.7)	1501 (56.4)	1705 (64.1)
Endometrioid adenocarcinomas	112 (4.2)	188 (7.1)	300 (11.3)
Clear cell neoplasm	165 (22.4)	0 (0)	165 (6.2)
Mucinous adenocarcinomas	246 (33.5)	0 (0)	246 (9.2)
Transitional (Brenner) tumors	8 (0.3)	0 (0)	8 (0.3)
FIGO stage			