



Prognostic significance of positive peritoneal cytology in endometrial carcinoma based on ESGO/ESTRO/ESP risk classification: A multicenter retrospective study

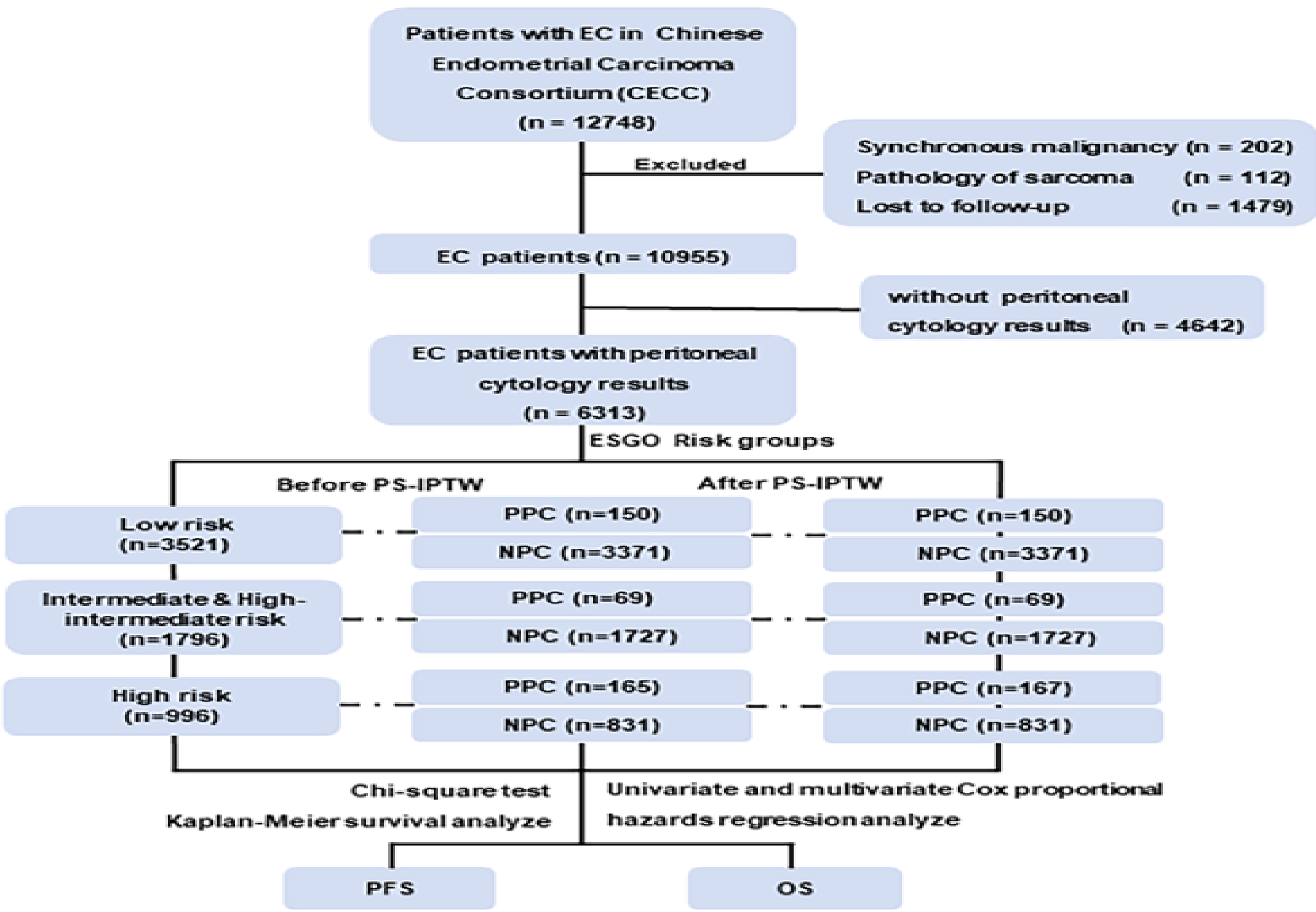
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Background

- Due to the lack of sufficient evidence to prove that PC is an independent risk factor for endometrial carcinoma (EC) patients’ prognosis, the International Union of Obstetrics and Gynecology (FIGO) excluded PC from stage IIIA in 2009.
- This study aimed to determine the prognostic significance of positive peritoneal cytology (PC) on endometrial carcinoma (EC) patients under the ESGO/ESTRO/ESP risk classification.

Methods

- This is a retrospective study from 27 medical centers in China during 2000 to 2019.
- Three key ESGO risk groups:
 - 1) Low-risk groups
 - 2) Intermediate and high-intermediate risk groups
 - 3) High-risk groups
- Statistical analysis:
 - 1) Propensity score-based inverse probability of treatment weighting (PS-IPTW)
 - 2) Univariate and multivariate Cox analysis
 - 3) Kaplan-Meier analysis



Results

- A total of 6313 EC patients with PC results were included and positive PC was reported in 384 women (6.1%). The multivariate Cox analysis in all patients showed the positive PC was significantly associated with decreased PFS (hazard ratio [HR] 2.23, 95% confidence interval [CI] 1.57-3.14, $P < 0.001$) and OS (HR 2.29, 95%CI 1.53-3.44, $P < 0.001$).
- The Kaplan-Meier curves also showed a poor survival in the intermediate and high-intermediate risk group (5-year PFS: 75.5% vs. 93.0%, $P < 0.001$; 5-year OS: 78.3% vs. 96.4%, $P < 0.001$);
- While in the low-risk group, there were no significant differences in PFS and OS between different PC status (5-year PFS: 93.1% vs. 97.3%, $P = 0.124$; 5-year OS: 98.6% vs. 98.2%, $P = 0.823$);
- In the high-risk group, significant difference was only found in PFS (5-year PFS: 62.5% vs. 77.9%, $P = 0.033$).

Conclusion

- Positive PC was an adverse prognostic factor for EC, especially in the intermediate and high-intermediate risk patients.
- Gynecologic oncologists should reconsider the effect of positive PC on different ESGO risk groups.

Table 1. Characteristics of patients in the before and after PS-IPTW cohorts

Characteristics	Before IPTW (N=6313)			After IPTW (N=6309)		
	Negative (N=5929)	Positive (N=384)	P	Negative (N=5929)	Positive (N=385)	P
Age (year)			0.068			0.416
<60	4367 (73.7)	266 (69.3)		4356 (73.5)	292 (75.8)	
≥60	1562 (26.3)	118 (30.7)		1573 (26.5)	94 (24.4)	
BMI (kg/m2)			<0.001			0.634
<24	1667 (28.1)	100 (26.0)		1654 (27.9)	104 (27.0)	
≥24	2186 (36.9)	112 (29.2)		2157 (36.4)	133 (34.5)	
Unknown	2076 (35.0)	172 (44.8)		2118 (35.7)	149 (38.7)	
Hysteroscopy			0.016			0.969
No	3241 (54.7)	191 (49.7)		3222 (54.3)	208 (54.0)	
Yes	1125 (19.0)	66 (17.2)		1118 (18.9)	72 (18.7)	
Unknown	1563 (26.4)	127 (33.1)		1590 (26.8)	106 (27.5)	
Surgical route			0.001			0.798
Laparoscopy	2908 (49.0)	223 (58.1)		2941 (49.6)	188 (48.8)	
Open	3021 (51.0)	161 (41.9)		2988 (50.4)	197 (51.2)	
Hysterectomy			0.020			0.830
Simple	4247 (71.6)	272 (70.8)		4245 (71.6)	278 (72.2)	
Supracervical	886 (14.9)	44 (11.5)		873 (14.7)	52 (13.5)	
Radical	796 (13.4)	68 (17.7)		812 (13.7)	56 (14.5)	
BSO			0.119			0.730
No	462 (7.8)	21 (5.5)		454 (7.7)	32 (8.3)	
Yes	5467 (92.2)	363 (94.5)		5476 (92.4)	353 (91.7)	
Grade			0.001			0.574
Low grade(G1/2)	4840 (81.6)	284 (74.0)		4812 (81.2)	315 (81.8)	
High grade(G3)	1054 (17.8)	96 (25.0)		1081 (18.2)	69 (17.9)	
Unknown	35 (0.6)	4 (1.0)		36 (0.6)	1 (0.3)	
Myometrial invasion depth			<0.001			0.960
<1/2	4766 (80.4)	268 (69.8)		4725 (79.7)	304 (79.0)	
≥1/2	1084 (18.3)	104 (27.1)		1119.0 (18.9)	75 (19.5)	
Unknown	79 (1.3)	12 (3.1)		85 (1.4)	6 (1.6)	
FIGO (2009) Stage			<0.001			0.965
IA	4048 (68.3)	179 (46.6)		3970 (67.0)	260 (67.5)	
IB	653 (11.0)	27 (7.0)		639 (10.8)	44 (11.4)	
II	469 (7.9)	19 (4.9)		458 (7.7)	25 (6.5)	
IIIA	213 (3.6)	34 (8.9)		232 (3.9)	16 (4.2)	
IIIB	72 (1.2)	16 (4.2)		83 (1.4)	5 (1.3)	
IIIC	385 (6.5)	60 (15.6)		419 (7.1)	27 (7.0)	
IV	89 (1.5)	49 (12.8)		129 (2.2)	8 (2.1)	
Histology			<0.001			0.330
Endometrial	5561 (93.8)	321 (83.6)		5526 (93.2)	363 (94.3)	
Non-endometrial	368 (6.2)	63 (16.4)		403 (6.8)	22 (5.7)	
LVS			<0.001			0.943
No	5335 (90.0)	303 (78.9)		5294 (89.3)	345 (89.6)	
Yes	407 (6.9)	63 (16.4)		443 (7.5)	29 (7.5)	
Unknown	187 (3.2)	18 (4.7)		193 (3.3)	11 (2.9)	
Cervix stroma involvement			0.017			0.538
No	5250 (88.5)	324 (84.4)		5236 (88.3)	345 (89.6)	
Yes	679 (11.5)	60 (15.6)		693 (11.7)	41 (10.6)	
Lymph node metastasis			<0.001			0.983
No	4026 (67.9)	218 (56.8)		3986 (67.2)	259 (67.3)	
Yes	408 (6.9)	79 (20.6)		459 (7.7)	29 (7.8)	
No resection	1495 (25.2)	87 (22.7)		1484 (25.0)	97 (25.2)	
Postoperative therapy			<0.001			0.788
None	3744 (63.1)	151 (39.3)		3659 (61.7)	247 (64.2)	
Radiotherapy	411 (6.9)	20 (5.2)		405 (6.8)	24 (6.2)	
Chemotherapy	1201 (20.3)	173 (45.1)		1291 (21.8)	81 (21.0)	
Radiotherapy+ Chemotherapy	573 (9.7)	40 (10.4)		575 (9.7)	32 (8.3)	

Table 2. Multivariate Cox regression analysis for PFS and OS in the before and after PS-IPTW cohorts

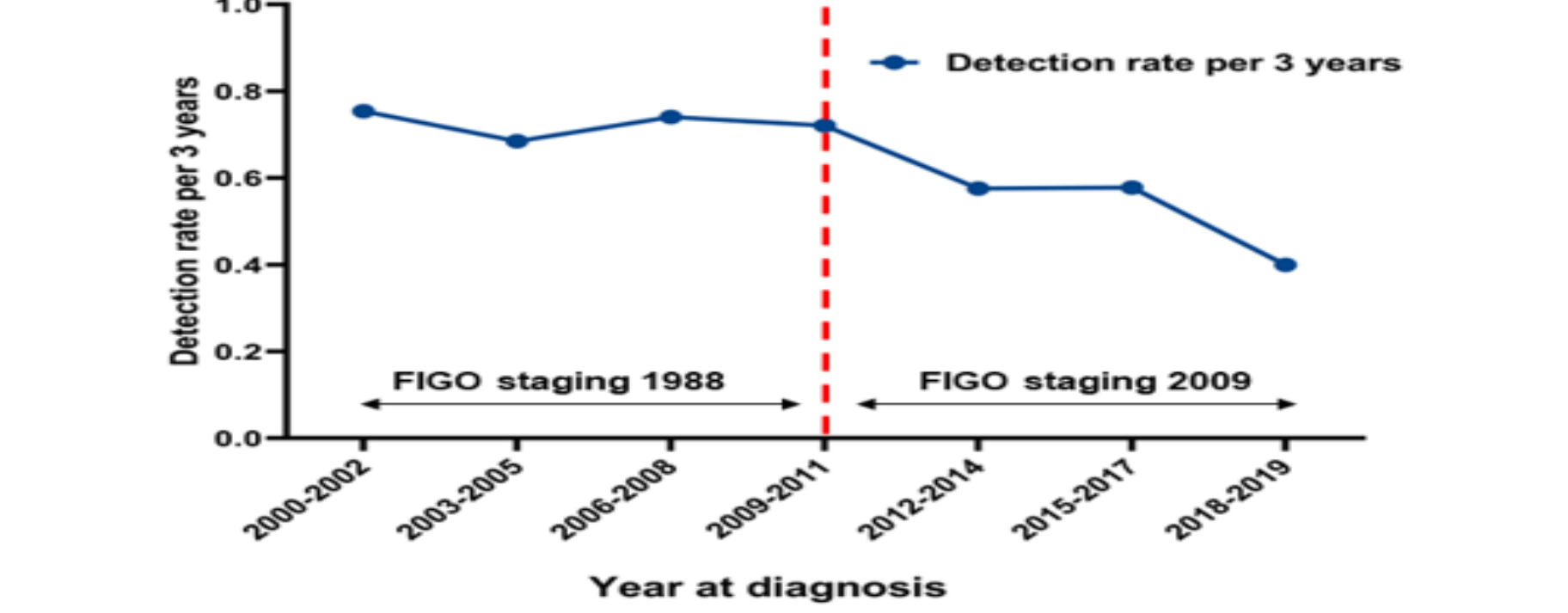
Characteristic	Univariable analysis				Multivariate analysis			
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Age (year)								
<60	Reference		Reference		Reference		Reference	
≥60	2.85 (2.33-3.48)	<0.001	3.58 (2.80-4.56)	<0.001	2.43 (1.96-3.02)	<0.001	2.94 (2.25-3.85)	<0.001
Surgical route								
Laparoscopy	Reference		Reference		Reference		Reference	
Open	0.68 (0.54-0.86)	0.001	0.50 (0.37-0.68)	<0.001	0.90 (0.72-1.13)	0.370	0.65 (0.48-0.87)	0.005
Extent of hysterectomy								
Extrafascial	Reference		Reference		Reference		Reference	
Supracervical	0.74 (0.55-1.00)	0.051	0.68 (0.47-0.98)	0.036	0.68 (0.50-0.92)	0.014	0.60 (0.41-0.87)	0.008
Radical	1.20 (0.93-1.55)	0.167	1.22 (0.90-1.65)	0.197	0.75 (0.56-1.01)	0.062	0.71 (0.50-1.01)	0.058
Grade								
Low grade(G1/2)	Reference		Reference		Reference		Reference	
High grade(G3)	3.49 (2.85-4.28)	<0.001	3.52 (2.76-4.50)	<0.001	1.91 (1.45-2.52)	<0.001	1.69 (1.20-2.37)	0.003
Unknown	1.61 (0.53-4.90)	0.401	1.92 (0.70-5.26)	0.207	1.67 (0.53-5.20)	0.378	1.81 (0.63-5.15)	0.268
Myometrial invasion								
≤1/2	Reference		Reference		Reference		Reference	
>1/2	4.07 (3.32-4.99)	<0.001	4.66 (3.65-5.95)	<0.001	1.81 (1.31-2.50)	<0.001	1.89 (1.30-2.76)	<0.001
Unknown	2.38 (1.21-4.70)	0.012	2.68 (1.23-5.84)	0.013	0.71 (0.34-1.46)	0.351	0.87 (0.38-2.02)	0.754
FIGO (2009) Stage								
IA	Reference		Reference		Reference		Reference	
IB	3.00 (2.21-4.09)	<0.001	3.22 (2.20-4.71)	<0.001	1.08 (0.61-1.92)	0.793	1.03 (0.50-2.10)	0.939
II	2.89 (2.02-4.10)	<0.001	2.85 (1.80-4.50)	<0.001	1.90 (1.04-3.47)	0.036	1.57 (0.75-3.31)	0.231
IIIA	3.78 (2.52-5.67)	<0.001	4.18 (2.55-6.86)	<0.001	2.57 (1.10-5.98)	0.029	2.01 (0.75-5.38)	0.165
IIIB	4.95 (2.92-8.39)	<0.001	7.14 (4.05-12.59)	<0.001	3.09 (1.21-7.88)	0.018	2.90 (1.00-8.42)	0.051
IIIC	7.38 (5.62-9.69)	<0.001	9.37 (6.78-12.97)	<0.001	2.72 (0.83-8.91)	0.098	3.06 (0.76-12.31)	0.115
IV	12.48 (8.39-18.56)	<0.001	18.07 (11.42-28.60)	<0.001	3.57 (1.33-9.57)	0.011	3.89 (1.26-12.02)	0.018
Peritoneal cytology								
Negative	Reference		Reference		Reference		Reference	
Positive	2.16 (1.52-3.06)	<0.001	2.25 (1.49-3.38)	<0.001	2.23 (1.57-3.14)	<0.001	2.29 (1.53-3.44)	<0.001
Adjuvant therapy								
None	Reference		Reference		Reference		Reference	
Radiotherapy	2.70 (1.92-3.8)	<0.001	2.65 (1.77-3.95)	<0.001	1.35 (0.93-1.98)	0.118	1.09 (0.69-1.72)	0.710
Chemotherapy	2.51 (1.95-3.22)	<0.001	2.47 (1.83-3.34)	<0.001	1.24 (0.92-1.67)	0.156	1.14 (0.80-1.62)	0.479
Radiotherapy+chemotherapy	4.42 (3.39-5.76)	<0.001	4.46 (3.26-6.10)	<0.001	1.68 (1.19-2.36)	0.003	1.35 (0.88-2.05)	0.165

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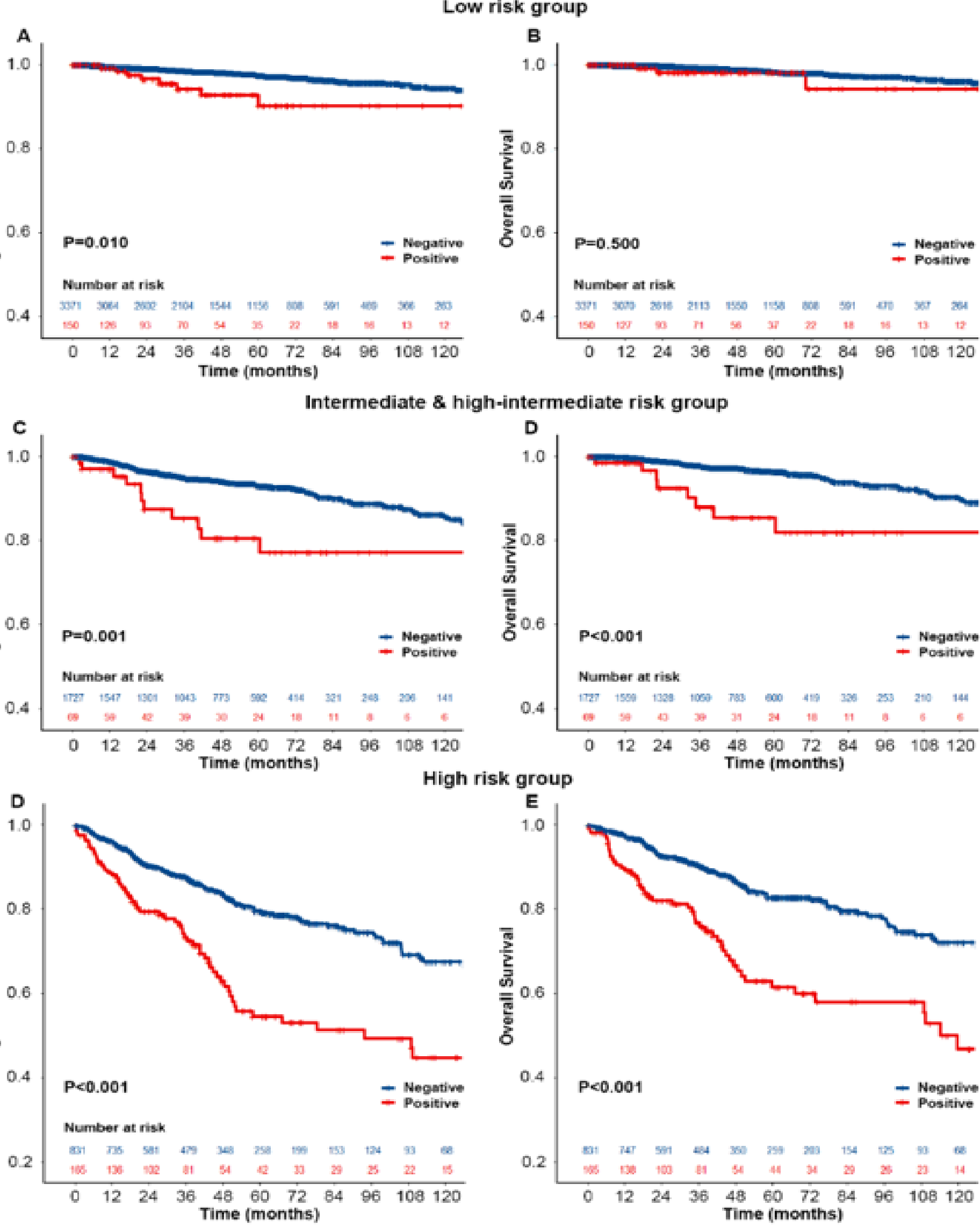
Conflict of interests: None

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Trends in peritoneal cytology evaluation in CECC project



The Kaplan-Meier curves in each ESGO risk group after PS-IPTW adjustment



Survival comparison of EC patients with or without positive PC

Groups	5-years PFS	5-years OS
Low-risk	93.1% vs 97.3%, P=0.124	98.6% vs 98.2%, P=0.823
Intermediate and high-intermediate risk	75.5% vs 93.0%, P<0.001	78.3% vs 96.4%, P<0.001
High-risk	62.5% vs 77.9%, P=0.033	71.3% vs 81.0%, P=0.071

Forest plots in different ESGO risk groups

