

Supporting information CA-125 manuscript

Table S1. The searching strings

Database	
Embase.com	('ovary carcinoma'/exp OR ('ovary tumor'/de AND ('carcinoma'/de OR 'adenocarcinoma'/de)) OR (((epithelial* OR mucinous* OR serous* OR endometrioid*) NEAR/6 (ovar*) NEAR/6 (carcinoma* OR adenocarcinoma*))) :ab,ti,kw) AND ('cytoreductive surgery'/de OR (cytoreduc* OR debulking*) :ab,ti,kw) AND ('CA 125 antigen'/de OR 'cancer antigen 125'/de OR 'carcinoembryonic antigen'/de OR (ca-125 OR ca125 OR cancer-antigen-125 OR cancer-antigen125 OR carcinoembryonic-antigen* OR CEA OR Mucin-16*) :ab,ti,kw) AND (((advanced OR 2b OR 2c OR 3 OR 3a OR 3b OR 3c OR 4 OR iib OR iic OR iii OR iiia OR iiib OR iiic OR iv OR 2-b OR 2-c OR 3-a OR 3-b OR 3-c OR ii-b OR ii-c OR iii-a OR iii-b OR iii-c) NEAR/3 (stag*))) :ab,ti,kw NOT [conference abstract]/lim
Medline Ovid	(Carcinoma, Ovarian Epithelial/ OR (((epithelial* OR mucinous* OR serous* OR endometrioid*) ADJ6 (ovar*) ADJ6 (carcinoma* OR adenocarcinoma*))) :ab,ti,kf.) AND (Cytoreduction Surgical Procedures/ OR (cytoreduc* OR debulking*) :ab,ti,kf.) AND (CA-125 Antigen/ OR (ca-125 OR ca125 OR cancer-antigen-125 OR cancer-antigen125 OR carcinoembryonic-antigen* OR CEA OR Mucin-16*) :ab,ti,kf.) AND (((advanced OR 2b OR 2c OR 3 OR 3a OR 3b OR 3c OR 4 OR iib OR iic OR iii OR iiia OR iiib OR iiic OR iv OR 2-b OR 2-c OR 3-a OR 3-b OR 3-c OR ii-b OR ii-c OR iii-a OR iii-b OR iii-c) ADJ3 (stag*))) :ab,ti,kf. NOT (letter* OR news OR comment* OR editorial* OR congres* OR abstract* OR book* OR chapter* OR dissertation abstract*) :pt.
Web of science	TS=((((epithelial* OR mucinous* OR serous* OR endometrioid*) NEAR/5 (ovar*) NEAR/5 (carcinoma* OR adenocarcinoma*))) AND ((cytoreduc* OR debulking*)) AND ((ca-125 OR ca125 OR cancer-antigen-125 OR cancer-antigen125 OR carcinoembryonic-antigen* OR CEA OR Mucin-16*)) AND (((advanced OR 2b OR 2c OR 3 OR 3a OR 3b OR 3c OR 4 OR iib OR iic OR iii OR iiia OR iiib OR iiic OR iv OR 2-b OR 2-c OR 3-

	a OR 3-b OR 3-c OR ii-b OR ii-c OR iii-a OR iii-b OR iii-c) NEAR/2 (stag*))))
Cochrane Central	(((((epithelial* OR mucinous* OR serous* OR endometrioid*) NEAR/6 (ovar*) NEAR/6 (carcinoma* OR adenocarcinoma*))) :ab,ti,kw) AND ((cytoreduc* OR debulking*) :ab,ti,kw) AND ((ca NEXT 125 OR ca125 OR cancer NEXT antigen NEXT 125 OR cancer NEXT antigen125 OR carcinoembryonic NEXT antigen* OR CEA OR Mucin NEXT 16*) :ab,ti,kw) AND (((advanced OR 2b OR 2c OR 3 OR 3a OR 3b OR 3c OR 4 OR iib OR iic OR iii OR iiia OR iiib OR iiic OR iv OR 2 NEXT b OR 2 NEXT c OR 3 NEXT a OR 3 NEXT b OR 3 NEXT c OR ii NEXT b OR ii NEXT c OR iii NEXT a OR iii NEXT b OR iii NEXT c) NEAR/3 (stag*))) :ab,ti,kw
Google Scholar	“epithelial ovarian carcinoma adenocarcinoma” cytoreductive debulking “ca 125” ca125 “carcinoembryonic antigen” CEA “advanced 2b 2c 3a 3b 3c 4 stage staging”

Table S2. Detailed methods of each platform used to analyze CA-125

	Roche	Abbott	Beckman Coulter	Siemens	Thermo Fischer
Platform	E601, E801	Architect i2000	DxI 800	Centaur	Kryptor Compact
Method	ECLIA	MEIA	CLEIA	CLEIA	TRACE
Signal technology	Ruthenium	AP	AP	Acrid-Fluor	Cryp-Acc

ECLIA = Electro-Chemiluminescent Immuno Assay; MEIA = Microparticle Enzyme Immuno Assay; CLEIA = Chemiluminiscent Enzyme Immuno Assay; AP = Alkaline Phosphatase; Acrid-Fluor = Acridinium-Fluorescein; TRACE = Time Resolved Amplified Cryptate Emission; Cryp-Acc = Cryptate-Acc

Table S3. Outcome of quality assessment

	Study participation	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Total
<i>Eltabbakh et al.</i> ⁽²⁵⁾	Green	Yellow	Green	Green	Green	Green
<i>Risum et al.</i> ⁽³³⁾	Yellow	Yellow	Green	Yellow	Yellow	Yellow
<i>Rodriguez et al.</i> ⁽³⁰⁾	Green	Green	Green	Green	Yellow	Green
<i>Furukawa et al.</i> ⁽²⁹⁾	Yellow	Green	Green	Green	Green	Green
<i>Jung et al.</i> ⁽²⁴⁾	Green	Yellow	Green	Yellow	Green	Green
<i>Pelissier et al.</i> ⁽²⁸⁾	Green	Green	Green	Green	Green	Green
<i>Karlsen et al.</i> ⁽²³⁾	Green	Green	Green	Green	Green	Green
<i>Morimoto et al.</i> ⁽³⁴⁾	Green	Yellow	Yellow	Yellow	Green	Yellow
<i>Zeng et al.</i> ⁽⁶⁾	Green	Green	Green	Green	Green	Green
<i>Matsuhashi et al.</i> ⁽²⁷⁾	Green	Green	Yellow	Yellow	Green	Green
<i>Ghisoni et al.</i> ⁽³¹⁾	Green	Yellow	Yellow	Green	Green	Green
<i>Gupta et al.</i> ⁽²⁶⁾	Green	Green	Green	Green	Yellow	Green
<i>Nakamura et al.</i> ⁽³²⁾	Green	Yellow	Green	Yellow	Green	Green
<i>Merlo et al.</i> ⁽³⁵⁾	Green	Yellow	Green	Yellow	Yellow	Yellow

Green = low risk of bias; Yellow = moderate risk of bias

Table S4. Univariable analysis of factors predicting normal levels of preoperative CA-125 before primary CRS

	Preoperative CA-125 ≤35 kU/L (n=4, 9.1%)	Preoperative CA-125 >35 kU/L (n=40, 90.9%)	Unadjusted OR [95%CI]	P-value
Median AGE (IQR), years	66 (22)	59 (17)	1.07 [0.96-1.20]	0.208
Median BMI (IQR), kg/m ²	22.2 (7.5)	24.8 (6.7)	0.89 [0.69-1.15]	0.373
WHO performance, n (%)				
0 (ref)	4 (100.0)	25 (62.5)		
1	0 (0.0)	11 (27.5)	N/A*	N/A*
≥2	0 (0.0)	3 (7.5)	N/A*	N/A*
FIGO stage, n (%)				
IIIB/IIIC (ref)	4 (100.0)	37 (92.5)		
IV	0 (0.0)	3 (7.5)	N/A*	N/A*
Histology, n (%)				
Serous (ref)	3 (75.0)	39 (97.5)		
Non-serous	1 (25.0)	1 (2.5)	13.00 [0.64-263.82]	0.095
Presence of peritoneal carcinomatosis on CT, n (%)	2 (50.0)	22 (55.0)	0.82 [0.11-6.40]	0.848
Presence of ascites, n (%)	1 (25.0)	30 (75.0)	0.11 [0.01-1.19]	0.070
Median ascites (IQR), ml	20 (-)	400 (700)	0.94 [0.76-1.17]	0.570
Presence of peritoneal carcinomatosis, n (%)	1 (25.0)	18 (45.0)	0.41 [0.04-4.26]	0.453
Surgical outcome, n (%)				
Complete CRS	4 (100.0)	28 (70.0)	N/A*	N/A*
Non-complete CRS (ref)	0 (0.0)	12 (30.0)		

CA-125 = Cancer Antigen 125, CI = confidence interval, CRS = cytoreductive surgery, IQR = interquartile range, N/A = not applicable, OR= odds ratio, REF = reference

* = odds-ratio or P-value could not be calculated

Table S5. Univariable analysis of factors predicting normalized preoperative CA-125 level before interval CRS

	Preoperative CA-125 ≤35 kU/L (n=85, 30.8%)	Preoperative CA-125 >35 kU/L (n=191, 69.2%)	Unadjusted OR [95%CI]	P-value
Median AGE (IQR), years	68 (14)	67 (12)	1.00 [0.98-1.03]	0.884
Median BMI (IQR), kg/m ²	24.6 (5.8)	24.5 (6.0)	1.00 [0.95-1.06]	0.905
WHO performance, n (%)				
0 (ref)	48 (60.0)	93 (52.0)		
1	29 (36.3)	67 (37.4)	0.84 [0.48-1.466]	0.536
≥2	3 (3.8)	19 (10.6)	0.31 [0.09-1.09]	0.067
FIGO stage, n (%)				
IIIB/IIIC (ref)	56 (65.9)	124 (64.9)		
IV	29 (34.1)	67 (35.1)	0.96 [0.56-1.64]	0.877
Histology, n (%)				
Serous (ref)	84 (98.8)	183 (95.8)		
Non-serous	1 (1.2)	8 (4.2)	0.27 [0.03-2.21]	0.224
Presence of ascites/peritoneal carcinomatosis on CT, n (%)	57 (67.1)	140 (73.3)	0.74 [0.43-1.29]	0.291
Presence of ascites, n (%)	11 (12.9)	70 (36.6)	0.25 [0.13-0.50]	<0.001
Median ascites (IQR), ml	100 (185)	200 (300)	1.00 [0.99-1.00]	0.228
Presence of peritoneal carcinomatosis, n (%)	20 (23.5)	93 (48.7)	0.31 [0.18-0.55]	<0.001
Surgical outcome, n (%)				
Complete CRS	72 (84.7)	127 (66.5)	2.79 [1.44-5.41]	0.002
Non-complete CRS (ref)	13 (15.3)	64 (33.5)		

CA-125 = Cancer Antigen 125, CI = confidence interval, CRS = cytoreductive surgery, IQR = interquartile range, OR= odds ratio, REF = reference

Table S6. Univariable analysis of factors predicting >95% reduction in CA-125 after NAC

	>95% decrease in preoperative CA-125 (n=81, 29.6%)	≤95% decrease in preoperative CA- 125 (n=193, 70.4%)	Unadjusted OR [95%CI]	P-value
Median AGE (IQR), years	66 (15)	68 (12)	0.98 [0.96-1.01]	0.251
Median BMI (IQR), kg/m ²	24.5 (5.3)	24.6 (6.3)	0.97 [0.91-1.02]	0.228
WHO performance, n (%)				
0 (ref)	50 (61.7)	89 (46.1)		
1	23 (28.4)	73 (37.8)	0.56 [0.31-1.00]	0.052
≥2	4 (4.9)	18 (9.3)	0.40 [0.13-1.23]	0.110
FIGO stage, n (%)				
IIIB/IIIC (ref)	50 (61.7)	128 (66.3)		
IV	31 (38.3)	65 (33.7)	1.22 [0.71-2.09]	0.467
Histology, n (%)				
Serous (ref)	79 (97.5)	186 (96.4)		
Non-serous	2 (2.5)	7 (3.6)	0.67 [0.14-3.31]	0.626
Presence of peritoneal carcinomatosis on CT, n (%)	57 (70.4)	138 (71.5)	0.95 [0.54-1.67]	0.850
Presence of ascites, n (%)	15 (18.5)	66 (34.2)	0.44 [0.23-0.83]	0.011
Median ascites (IQR), ml	200 (200)	200 (300)	1.00 [1.00-1.001]	0.459
Presence of peritoneal carcinomatosis, n (%)	30 (37.0)	83 (43.0)	0.77 [0.45-1.32]	0.347
Surgical outcome, n (%)				
Complete CRS	61 (75.3)	136 (70.5)	1.28 [0.71-2.31]	0.416
Non-complete CRS (ref)	20 (24.7)	57 (29.5)		

CA-125 = Cancer Antigen 125, CI = confidence interval, CRS = cytoreductive surgery, IQR = interquartile range, OR= odds ratio, REF = reference

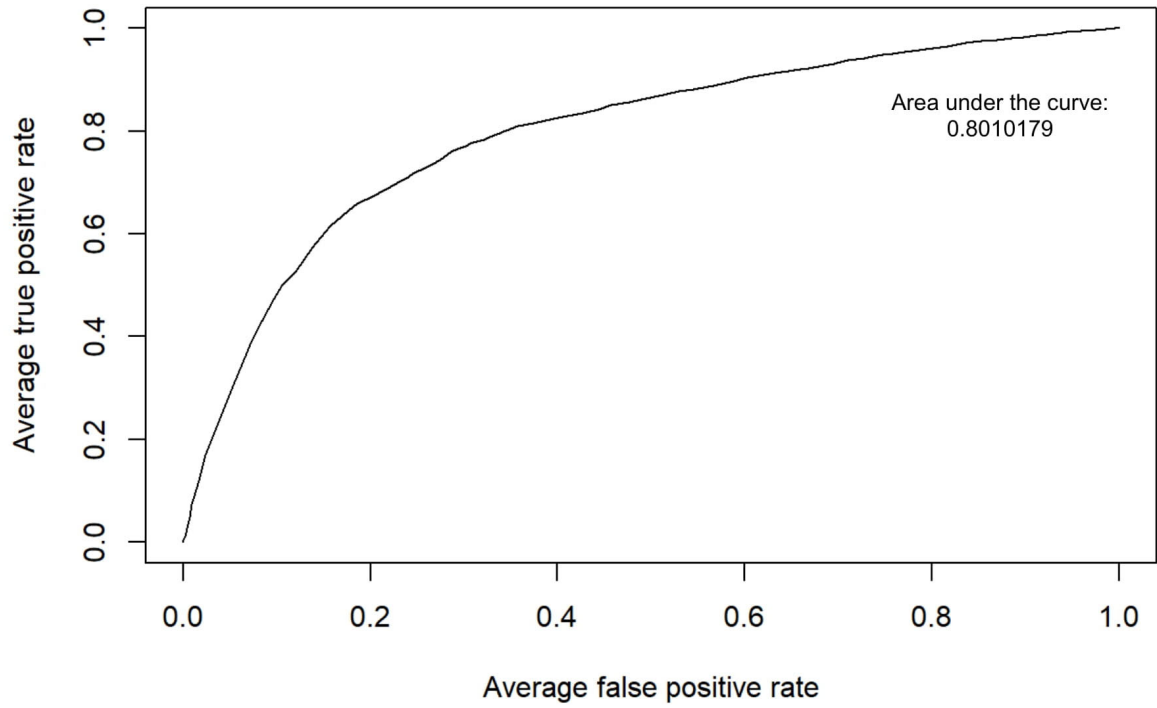


Figure S1. cross-validated ROC-curve for primary CRS.

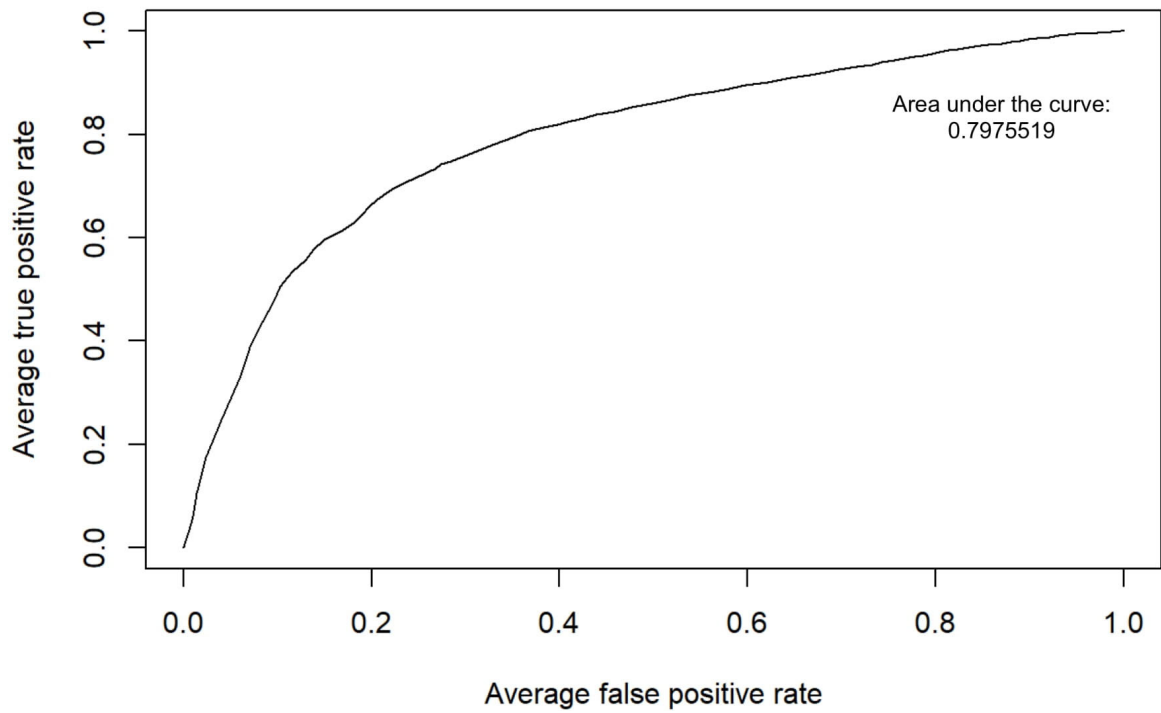


Figure S2: cross-validated ROC-curve for interval CRS.