The role of computed tomography in predicting peritoneal carcinomatosis and upfront surgery outcome in advanced ovarian cancer

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Abstract

Background Epithelial ovarian cancer is usually diagnosed at advanced stages. To choose the best therapeutic approach, an accurate assessment of the tumor spread is crucial. This study aimed to determine whether numeric scoring, the amount of ascites, and the presence of cardiophrenic nodes (CPLNs) visualized by computed tomography (CT), can predict the tumor extent and improve the outcome of AOC upfront surgery.

Methods This single center retrospective analysis of 194 patients diagnosed with AOC included 119 patients treated with upfront surgery at the Skåne University Hospital, Lund, Sweden, from January 2016 to December 2018.

CT based peritoneal cancer index (PCI) scores, enlarged cardiophrenic lymph nodes (CPLNs), and the amount of ascites were correlated to the surgical PCI (S-PCI) and the completeness of the cytoreductive surgery.

The patients were grouped according to the residual disease (RD) and the overall survival (OS) rates for the three groups were determined using Kaplan-Meier curves. Linear regression and the interclass correlation (ICC) analyses were used to determine the relationship between CT-PCI and S-PCI.

Results The survival rate was significantly higher in patients with no macroscopic residual disease compared those with residual disease <10 mm (p<0.03) or residual disease ≥10 mm (p<0.005).

S-PCI and large ascites volumes were correlated with the risk of suboptimal residual disease (for ascites > 1000 ml, OR 5.5626 (1.665-19.007) p<0.019; for S-PCI, OR 1.24 (1.141-1.348), p<0.001). CT-PCI, CA-125 level and CPLN were not predictive of the cytoreductive surgery results in the adjusted data to days from CT to operation and for ascites. CT-PCI correlated well to S-PCI ((95%) CI: 0.397 (0.252-0.541) p<0.001).

Conclusions CT is a reliable tool for assessing the extent of the disease in AOC, but it has limitations in predicting surgical outcome. This study was unable to show an association between the CT-PCI and surgical outcome when the data were adjusted and ascites, CA-125 level, days between the CT examination to surgery and CPLN. Ascites volumes exceeding 1000 ml increased the risk of residual disease and thereby worse outcome. That certain areas (e.g., small bowel region) are particularly critical when evaluating surgical outcome using preoperative CT-PCI warrants further investigation.

1. Background

Epithelial ovarian cancer is the gynecological malignancy with the highest mortality rate with five-years survival rate below 45% [41]. More than 70% of ovarian cancer cases are diagnosed at advanced stages after having spread throughout the abdominal cavity [37]. Advanced ovarian cancer (AOC) is generally found in the omentum, the peritoneal surfaces from the diaphragm to the pouch of Douglas, due to ascites formation and circulation in the abdominal cavity [8].

The standard treatment for AOC is primary debulking surgery (PDS) followed by platinum-based postoperative chemotherapy [29]. Since surgery is the only way to improve prognosis for patients with AOC, the abdominal tumor burden must be well characterized to effectively plan the surgery and achieve maximal radicality. Preoperative computed tomography (CT) examination of the patient to characterize the tumor spread is standard procedure. Another way to characterize the tumor burden is through visual quantification of the tumor in the peritoneal cavity (PCI), first described by Sugarbaker in 1998 for colorectal cancer[15, 38, 44]. A high peritoneal cancer index (PCI) indicates a worse surgical outcome and suggests considering other treatment options for the patient than primary surgery [10, 22]. PCI in AOC has not been used outside clinical of studies. Likewise, PCI estimation from a preoperative CT scan (CT-PCI) is not part of standard guidelines for ovarian cancer diagnostics, but previous studies on CT-PCI in ovarian cancer have shown a significant relationship between CT-PCI and suboptimal surgery,postoperative complications and OS[20, 35].

Investigators have tried to find the optimal benefit of preoperative CT scan to identify radiological predictors[21, 32]. Along with the development of the imagining technique, markers, like cardiophrenic lymph nodes (CPLNs) have been identified in patients with AOC[34].CPLN metastases are associated with impaired PFS and OS in patients with AOC [24, 30]. To our knowledge, there is no clear-cut evidence that removing the lymph node leads to better OS eller PFS in AOC [34].

CA-125 is a high molecular weight glycoprotein,expressed in a large number of diseases and by a large proportion of epithelial ovarian cancer cases, with poor specificity and sensibility [26]. Several studies have tried to predict surgical outcomes using CA-125 in AOC, with inconsistent results [7, 25, 27, 39].

This study aimed to investigate if preoperative imaging (CT-PCI, ascites, and CPLN) is associated with the surgical outcome, toward detecting cases that are not well suited for surgery. To optimize prognosis, surgery for AOC should reach macroscopic radicality [11]. Since there are no known preoperative markers specific to a negative surgical outcome, the purpose of this study was to identify factors that predict which cases are not suitable for extensive surgery. u

2. Methods

2.1 Patient's characteristics

A total of 194 patients with AOC (FIGO stage IIIB-IVB) were diagnosed and treated from January 2016 to December 2018 at Skåne University Hospital, a tertiary center for gynecologic cancer treatment for the 1.6 million inhabitants in Southern Sweden. Patient data were collected retrospectively from the patients' medical reports. Patients receiving neoadjuvant chemotherapy with interval debulking surgery (33 patients, 17%) or with palliative chemotherapy only (15 patients, 7.7%) were excluded. 27 patients were excluded due to insufficient data. 119 patients deemed suitable for upfront extensive surgery were included in the study.

Patient characteristics are shown in Table 1.

Table 1. Patient`s characteristics

Characteristics	No.	(%)
All cases	119	100
Age median (range) years	66.8 (28-89)	
ECOG		
0-1	94	79
≥2	25	21
Albumin		
≥ 30 g/L	100	84
<30g/L	19	16
FIGO		
IIIB	10	8.4
IIIC	80	67.2
IVA	13	10.92
IVB	16	13.4
Histology		
High-grade serous	100	85.47
Low-grade serous	9	7.7
Endometrioid	5	4.27
Mucinous	1	0.85
Carcinosarcoma	2	1.7
Squamous cell carcinoma	1	0.845
CA-125 median (range)	896 (15-10 000)	
S-PCI median (range)	16.5 (2-38)	

PCI 1-10	28	2352
PCI11-20	53	44.53
PCI≥ 21	38	31.93
CT-PCI median(range)	17 (0-36)	
PCI 1-10	30	25.21
PCI 11-20	40	33.61
PCI >21	49	41.18
S-Ascites (ml)		
<500	56	47.1
≥500- <1000	4	3.4
≥1000	32	16
Paracentesis	16	13.4
Missing	11	9.2
CT-Ascites		
<499	70	58
500-999	8	6.7
>1000	21	17.6
Paracentesis	16	13.4
Missing	4	3.4
Duration of surgery (range) min	335 (98-712)	
Residual tumor		
CCS	75	63
OCS	25	21
SCS	19	16
Days between CT and surgery	32(1-160)	

(range)		
CPLN		
Negative (<5mm)	59	49.6
Positive (≥5mm)	60	50.4
Diaphragm carcinomatosis		
No	27	22.7
Yes	84	70.6
Missing data	6	6.7

CT-PCI computer tomography peritoneal carcinomatosis index, S-PCI surgical peritoneal carcinomatosis index, CCS complete cytoreductive surgery, OCS optimal cytoreductive surgery, SCS suboptimal cytoreductive surgery, FIGO, Fédération Internationale de Gynécologie Obstétrique, CPLN cardiophrenic lymph node

2.2 Survival Analyses

The patients were divided into three groups according to residual postoperative disease (residual disease = 0, residual disease < 10 mm, and residual disease ≥ 10 mm). Kaplan-Meier curves were generated for each of the three groups and the OS from the groups with residual disease were compared with the group with no residual disease.

2.3 Assessment of operability, resectability, and the postoperative residual disease

Operability and resectability were evaluated for each patient according to age, medical history, symptoms, medication, social and nutritional status and feasibility of tumor debulking according to preoperative CT of the abdomen and thorax. This study was intended to evaluate the accuracy of CT using a quantitative assessment of the tumor burden performed by a radiologist (CT-PCI) and to compare this with the surgical PCI (S-PCI) determined by the surgeon at the beginning of the surgery. Only patients intended for upfront surgery were included since correlation between residual disease at the end of the surgery and survival, was shown primary in upfront situations [11]. The surgical outcome is indicated by the amount of residual disease after the surgery. The best outcome is complete cytoreductive surgery (CCS). Optimal cytoreductive surgery (OCS) indicates the residual disease under 10 mm, and suboptimal cytoreductive surgery (SCS) results in 10 mm or more of residual disease. The surgical PCI, the amount of ascites, surgery duration and the presence of residual disease were extracted from the surgical reports. The

volume of the ascites present at the surgery was categorized into groups (< 500 ml, 500 to 1000 ml, and ≥ 1000 ml). 23 of 119 patients underwent paracentesis because of abdominal swelling or tightness. Data from 10 patients were incomplete. The FIGO stage, tumor histology, and preoperative CA-125 levels were recorded.

2.4 Assessment Of Tumor Extent

To ensure the accuracy of the surgical documentation and S-PCI, both were performed by the same surgeon for a series of 25 patients of the cohort. The author calculated the PCI score for 25 surgical records and this was compared with the original PCI score calculated by the surgeon for each case. The mean and SD of the original S-PCI was 1.077 ± 9.406, and the newly calculated one was 16.231 ± 9.035, showing a very good correlation with the original measurement. Based on these findings, the remaining cases were assessed according to the PCI contained in the original surgical reports. The PCI score developed by Sugarbaker (1998) was used to quantify both CT-PCI and S-PCI[38]. The 13 abdominal regions were assessed for tumor content and scored from 0 to 3 depending on the tumor size, with a final sum ranging from 1 to 39 points. The results were categorized into three levels: 1−10, 11−20, ≥ 21 points.

To evaluate the possible effect of time on the relationship between CT and surgery, CT-PCI was assessed within 20 days as a reference, which was related to 21−40 days and more than 40 days. The 20 day interval was chosen as a reference regarding the actual standardized cancer care pathway in Sweden, which requires a maximum of 24 days until the start of treatment [18]. The median time between the CT and the surgery was 31.76 days (1-160). In this study, patients with prolonged time intervals were not excluded, rather, the data were categorized in three intervals.

2.5 Image Analysis

All eligible patients underwent CT in the supine position with intravenous and oral contrast. Digital CT-images were by convention reformatted in the coronal and sagittal planes. Since the images spanned several years, there was a variety of radiology systems; this has, however, been showed not to affect the detection of peritoneal carcinomatosis[6]. CT-PCI was retrospectively scored using the Sugarbaker classification [12, 15] by one of two radiology specialists (HS or JB). The CT-PCI was calculated as the sum of the numerical lesion scores assigned to the 13 abdominopelvic regions, and the lesion score to the largest visible implant. Ascites (three groups) were qualitatively estimated by one of two radiologists (HS or JB) concurrent with the CT-PCI evaluation. CPLN was retrospectively assessed by one of two radiology specialists (SP or NOW). CPLN was defined as a pathological enlargement measuring ≥ 5 mm the short axis in the axial plane [30] and was scored as negative (i.e., normal) or positive (i.e., enlarged).

2.6 Statistical Analyses

For descriptive data including means, medians and percentages, standard analyses were used. The Stata SE (version 16.0. College Station, Texas: StataCorp), and R studio were used for all statistical analyses.

Kaplan Meyer analyses were used for survival analyses by dividing the patients into three groups according to their surgical outcome (SCS, OCS and CCS).

Linear and logistic regression analyses were used to determine the relationships between S-PCI, CT-PCI, and surgical outcome. We adjusted the data for different variables (ascites, CPLN, CA-125). Some data were log transformed due to asymmetric distribution.

Linear and logistic regression analyses were used to determine the impact of positive radiological CPLN on the surgical outcome (regarding the residual disease at the end of the surgery). We compared the presence or absence of CPLN, dichotomized and continuous. The results are presented as odds ratios (OR) with 95% confidence interval (CI).

Linear regression and interclass correlation (ICC) analyses were used to characterize the agreement between CT-PCI (continuous) and S-PCI (continuous). We adjusted the data for CA-125 level (continuous), ascites (grouped into three categories : < 500 ml, 500 to 1000 ml, and ≥ 1000 ml) and the number of days between the CT examination and surgery (grouped into three categories : <20 days, 20–39 days, and ≥ 40 days). An ICC analyses was used to compare S-ascites and CT-ascites (nominal) and weighted kappa and percent agreement were calculated. Kappa value was used to compare the agreement between those two groups (S-ascites and CT-ascites, both divided in three intervals :< 500 ml, 500–1000 ml and ≥ 1000 ml). A kappa values of = 1.00 is reflective of perfect agreement, 0 indicates no agreement, 0.81-1.00 shows very good agreement, and 0.61–0.80 good agreement.

3. Results

3.1 Survival analysis

Kaplan-Meier curve estimates the probability of OS for patients with CCS (residual disease RD = 0 mm) (n = 71), OCS (RD < 10 mm) (n = 23) and SCS (RD ≥ 10 mm) (n = 17) (Fig. 1).

The survival of patients with complete resection was significantly increased compared with the OCS (p < 0.03) and SCS groups (p < 0.005).

3.2 Effects of S-PCI, CT-PCI, ascites, CA-125, and CPLN on surgical outcome

Results from linear the regression models showed a significant association between S-PCI and surgical outcome (OR 1.240 (1.141–1.348), p < 001).

In the unadjusted analyses, there was a significant association between preoperative assessment of CT-PCI and the surgical outcome (OR 1.008 (1.037–1.141), p < 0.001). When the results were adjusted for CA-125 level, CPLN, and ascites, the association was no longer significant (OR 046 (0.987–1.108), p < 0.128) (Table 2).

Table 2. Preoperative evaluation of the surgical outcome (residual disease ≥ 10 mm)

| | A | | B | |
VARIABLES	OR (95% CI)	p-val	β (95% CI)	p-val
CT-PCI	1.088 (1.037 - 1.141)	<0.001	1.046 (0.987 - 1.108)	0.128
log2(CA-125)	1.279 (1.017 - 1.608)	0.036	0.981 (0.695 - 1.386)	0.914
CPLN	1.742 (0.820 - 3.701)	0.149	1.202 (0.446 - 3.239)	0.716
CT-ascites (ml)		0.001		0.019
<500	Ref.		Ref.	
500-1000	4.000 (0.888 - 18.009)		2.990 (0.578 - 15.468)	
≥1000	8.000 (2.717 - 23.555)		5.626 (1.665 - 19.007)	

A: Unadjusted analysis of each variable alone.

B: Adjusted model including all variables in the table.

When the value of 20 was used as a cut-off for S-PCI, 14 of 17 patients with suboptimal surgeries (RD ≥ 10 mm) were identified. This gives a sensitivity of 82.35% and a specificity of 74%. When the same cut-off point was used for CT-PCI, 11 of 17 patients with suboptimal surgeries were identified giving a sensitivity of 64, 4% and a specificity of 61%.

To identify the reason for the unresectability, the group of 19 patients with residual disease ≥ 10 mm was analyzed according to the site of this residual disease and the other reasons for terminating the surgery. 12 cases involved small intestine carcinomatosis and, in 9 of these, the intestinal carcinomatosis was referred to abdominal regions 9 to 12 (i.e., the small intestine) on the CT scan.

The preoperative amount of ascites, measured by CT, was significantly associated with a negative surgical outcome, defined as suboptimal cytoreductive surgery (for ascites ≥ 1000 ml (OR 5.626 (1.665–19.007), p < 0.019) (Table 2).

CA-125 level was related to the surgical outcome by increasing the risk of suboptimal surgery by 28% (OR 1.278 (1.017–1.608), (p < 0.036), when the CA-125 value was doubled. However, this result was no longer statistically significant when adjusted for CT-PCI, CPLN, and ascites (OR 0.981 (0.695–1.386) (p < 0.914). The presence of CPLN was not correlated with the amount of residual disease at the end of the surgery in both the unadjusted and adjusted analyses (Table 2).

3.3 Preoperative assessment of tumor spread using preoperative CT-scan (CT-PCI and CT-ascites) and CA-125

Linear regression analysis revealed a significant association between increasing CT-PCI and the S-PCI (95%) CI: 0.511 (0.387−0.639), p < 0.001 (Fig. 2) representing a positive relationship between CT-PCI and S-PCI (both continuous data). Statistical significance was maintained when the data were adjusted for CA-125 level, ascites and time between the CT scan and surgery (95%) CI: 0.397 (0.252−0.541) p < 0.001) (Table 3).

Table 3. PCI surgery relative to CT-PCI, CA-125, ascites, and the time interval between the CT examination and the surgery.

VARIABLES	A β (95% CI)	p-value	B β (95% CI)	p-value
CT-PCI	0.511 (0.387 - 0.636)	<0.001	0.397 (0.252 - 0.541)	<0.001
log2(CA-125)	1.439 (0.665 - 2.212)	<0.001	-0.040 (-0.840 - 0.760)	0.921
Days from CT to operation		0.001		0.021
<20	Ref.		Ref.	
20-39	6.019 (2.630 - 9.408)		3.163 (0.230 - 6.097)	
≥40	7.179 (3.277 - 11.080)		4.678 (1.260 - 8.097)	
Ascites CT (ml)		<0.001		0.038
<500	Ref.		Ref.	
500-1000	6.121 (0.807 - 11.436)		2.542 (-2.147 - 7.231)	
≥1000	7.842 (4.288 - 11.395)		4.390 (1.027 - 7.753)	

A: Unadjusted analysis of each variable alone.

B: Adjusted model including all variables in the table.

Using ICC to compare CT-PCI and S-PCI divided into three groups (< 11, 11−20, ≥ 21) also showed good agreement (95%) CI: 0.580 (0.442−0.691), 79% agreement (Table 4).

Table 4. The relationship between CT-PCI and S-PCI.

| | S-PCI | | |
CT-PCI	<11	11-20	≥21
<11	18	9	1
11-20	11	22	19
≥21	1	8	30

Intra class correlation (ICC) (95%): 0.580(0.442-0.691)

Weighted kappa: 0.491

Percent agreement: 79%

The amount of ascites was positively correlated with S-PCI in both the unadjusted and adjusted data (for ascites volume > 1000 ml: (95%) CI: 4.390 (1.027−7.753) p < 0.038) (Table 3). When S-ascites and CT-ascites were compared, the weighted kappa value was 0.678, indicating good conformity (86% agreement) (Table 5).

Table 5. The agreement between CT-ascites and S-ascites.

| | Ascites surgery | | |
Ascites CT	<500 ml	500-1000 ml	≥1000 ml
<500 ml	51	2	4
500-1000 ml	0	1	7
≥1000 ml	3	1	17

Weighted kappa: 0.678

Percent agreement: 86%

CA-125 level was related to tumor burden in the non-adjusted data (1.439 (0.665−2.212), p < 0.001) but when the data were adjusted for CT-PCI, ascites, and days between CT examination and surgery, no significant association was found (95%) CI: -0.040 (-0.840-0.760) p < 0.921) (Table 3).

3.4 CPLN

50.4% (n = 60) of the patients exhibited CPLNs ≥ 5 mm in the short axis of the CT scan. In 46% (n = 56), the dominant lymph node was located on the anterior side of the cardiophrenic space, whereas in 22% (n = 27) of the patients, it was located on the posterior side. 23 patients had enlarged lymph nodes on both the anterior and posterior sides. A median of 1.17 (range 0−6) enlarged CPLNs was detected.

The surgical outcome was not affected by enlarged CPLNs present on the CT images (OR 1.742, (95%) CI: 0.820−3.701), p < 0.149), nor by the number of enlarged CPLNs (OR 1.139, (95%) CI: 0.896−1.447) (Table 6).

Table 6.

The relationship between the surgical outcome and CPLN

Variables	OR	CI	95%	p-value
Number of CPLN	1.139	1.447	0.896-	0.289
Presence of CPLN/yes	1.742	3.701	0.820-	0.149

4. Discussion

The preoperative estimation of tumor spread and its resectability are both of great importance to surgical outcome in AOC. In this study, poor surgical outcome, defined as residual disease ≥ 10 mm, was strongly connected with S-PCI (one unit on the S-PCI increased unresectability risk by 24%), which is in accordance with studies on colorectal and ovarian cancer [10, 19, 28]. Llueca et al tried to establish a predictive model for unresectability using CT, laparoscopy, and laparotomy. The authors concluded that the best cut-off for predicting SCS with PCI > 20 for the three diagnostic techniques, with a 91% specificity and 27% sensitivity for the CT scan [23]. In this study, a cut-off value of 20 on the S-PCI, identified 82% patients with SCS with a specificity of 74%. The same cut-off value for CT-PCI, detected 64% of the cases. The sensitivity was slightly lower for CT-PCI, however, the number of patients with macroscopic residual disease above 10 mm was considerably lower than the number of patients with CCS. Jönsdottir et al. studied the correlation between S-PCI and surgical outcome and found a PCI cut-off of 24. In their study 62% of patients with PCI above 24 had an unsatisfactory surgical outcome defined as SCS. The authors conclude that neoadjuvant chemotherapy could be considered if the PCI is higher than 24 .Theis study just emphasizes the reasons underlying SCS but has no predictive value for SCS or open-close surgery [16].

If preoperative CT-PCI could mimic the operative S-PCI, it would be an excellent tool for assessing the resectability of a tumor, since S-PCI is a good indicator of OS, [4, 19]. In the present study, CCS resulted in a significantly longer OS compared with patients with residual disease < 10 mm and those with suboptimal debulking (residual disease ≥ 10 mm), in line with previous studies [5, 11]. This study intended to elucidate whether patients with residual disease over 10 mm could be identified preoperatively, since CT-PCI correlated with intraoperative PCI (S-PCI). When the CT-PCI value was high PCI, S-PCI was high PCI as well. In the non-adjusted data, CT-PCI correlated well with surgical outcome, which is in agreement with other studies, but when we adjusted to CA-125 level, ascites, and CPLN, the

association between CT-PCI and the surgical outcome became non-significant. It could be that the groups of patients with macroscopic residual disease left were small relative to the group of patients with complete resection. Avesani et al. (2020) found a strong correlation between the CT-PCI and residual disease of any size at the end of the surgery. This was probably due to a different patient population with a substantial amount (24%) of patients included from early FIGO stages (I and II) and different data analyses.

Nevertheless, our study failed to demonstrate a statistically significant relationship between surgical outcome and CT-PCI, enlarged CPLN (measured by CT scan), or CA-125 level. On the other hand, CT-PCI still correlate to S-PCI, when the results were adjusted to CA-125 level, ascites, and the time interval between CT and the surgery.

Some studies have analyzed PCI regions separately and found that certain areas are more related to unresectability. Regions 9–12, corresponding to the small intestine, were significantly more predictive of residual disease than the entire PCI [31]. The same trend was found in the present study in the SCS group, 12 patients exhibited small intestine carcinomatosis. Nine (75%) of them had small intestinal carcinomatosis, correctly predicted from the CT scan.

The quantitation of ascites has, to our knowledge, never been evaluated in preoperative CT scans in patients with AOC. In this study, the CT based evaluation of ascites volume correlated with the ascites volume determined intraoperatively. Others have found that, in the intraoperative quantification of ascites, a large volume correlate with unresectability and worse PFS and OS [2, 40]. In the recurrent situation too, ascites is a negative predictor of surgical success [14]. Massive ascites evaluated by CT scan also correlated with increased SCS risk in the present study. A three-fold increased risk for unresectability in CT-quantified ascites over 500 ml was found; furthermore, in ascites over 1000 ml, 5.6-fold more patients had residual disease exceeding ≥ 10 mm.

In addition to CT, recent imaging studies also include FDG-PET/CT and MRI. A systematic review of five studies (544 participants) addresses the ability of FDG-PET/CT and MRI to predict SCS. Both FDG-PET/CT and MRI showed high specificity with moderate sensitivity [32]. Due to the small sample size of the studies and the lack of sensitivity, the quality of the evidence was fairly low. A study by Schmidt et al. establish CT, MRI, and PET-CT as reliable instrument for the evaluation of intraoperative PCI[36]. Some evidence supports the use of ultrasonography in the preoperative staging of AOC; for example, as shown by Weinberger et al. for the detection of pelvic carcinomatosis [42, 45]. Preoperative tumor staging in AOC by laparoscopy is standard procedure in some centers but carries some disadvantages including invasiveness and lack of full visualization [13]. The patients were exposed to a large scale surgery with risks of complications and a FIGO stage migration due to tumor infiltration into the abdominal wall [3, 43]. Incomplete visualization of the abdominal cavity might result in an incorrect assessment of the tumor burden due to difficulties in inspecting certain abdominal regions [1]. Rutten et al. concluded that diagnostic laparoscopy should not be considered standard procedure in clinical practice [33].

CPLNs in AOC are associated with carcinomatosis in the upper abdomen, diaphragmatic carcinomatosis, and a worse prognosis regardless of the surgical removal during the cytoreductive surgery. Prader et al. analyzed 350 patients, of which almost 40% had negative CPLNs while the rest had radiologically positive CPLNs. In patients with macroscopically completely resected tumors, CPLN metastases were associated with reduced PFS and OS. Still, the role of the CPLN resection remains unclear [30]. In this study, the CT-PCI for patients with radiologically enlarged CPLN was more than doubled for SCS group (nevertheless, not statistically significant), and no correlation was found between the presence of CPLNs on CT images and the surgical outcome.

A relationship between CA-125 level and surgical outcome is controversial. Many studies have found a correlation between CA-125 > 500 U/mL and suboptimal cytoreduction [7, 9, 17, 25, 39]. The data analyzed in the present study indicated study a positive relationship between high CA-125 level the amount of residual, for every duplication of CA-125, the OR for the remaining tumor tissue increased by 28% (unadjusted data). When the data were adjusted for CT-PCI, ascites, and CPLN, no significant association between CA-125 level and the surgical outcome was found.

5. Conclusions

Numerical estimation of the tumor spread by CT is feasible but requires a technically skilled radiologist who has mastered the evaluation of the different abdominal areas in the abdomen. Based on the findings of the present study, CT-PCI alone does not predict the surgical outcome in this study, but correlated well with increasing surgical PCI, which is a marker of worse surgical outcome. That certain abdominal areas, (e.g., small bowel region) strongly associated with unresectability, should be investigated in further studies. Together with a high volume of ascites, as shown in this study, the CT-PCI count in essential areas of the abdomen might be a better indicator of surgical outcome than the total sum of CT-PCI in the abdominal cavity.

Abbreviations

OC: Ovarian cancer

AOC: Advanced ovarian cancer

PCI: Peritoneal cancer Index

CT: Computerized tomography

CT-PCI: PCI evaluated by CT

S-PCI: PCI evaluated during surgery

CCS: Complete cytoreductive surgery

OCS: Suboptimal cytoreductive surgery

SCS: Suboptimal cytoreductive surgery

RT: rest tumor/residual disease

CPLN: Cardiophrenic lymph nodes

ECOG: Eastern Cooperation Oncology Group

OS: Overall survival

PFS: Progression-free survival

FIGO: International Federation of Obstetrics and Gynecology

Declarations

Ethical declaration

All patient data were handled according to the Word Medical Association´s Declaration' 2008 Declaration of Helsinki and in compliance with national law. This study was approved by the Swedish Ethical Review Authority with apl.no.2019/00450.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed in the present study are available from the corresponding author upon reasonable request.

Competing interests

The authors have no competing interest.

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Author Contribution

Mihaela Asp is the main contributor to the study design, data collection, data interpretation, and manuscript writing. Hanna Sartor is the main contributor to the CT data collection and participated in designing the study, data interpretation and manuscript revision. Päivi Kannisto coordinated and

contributed to the study design and manuscript revision. Susanne Malander provided oncological expertise and manuscript revision. NilsOlof Wallengren, Sonja Pudaric and Johan Bengtsson collected and interpreted the CT data. All of the authors read and approved the final manuscript.

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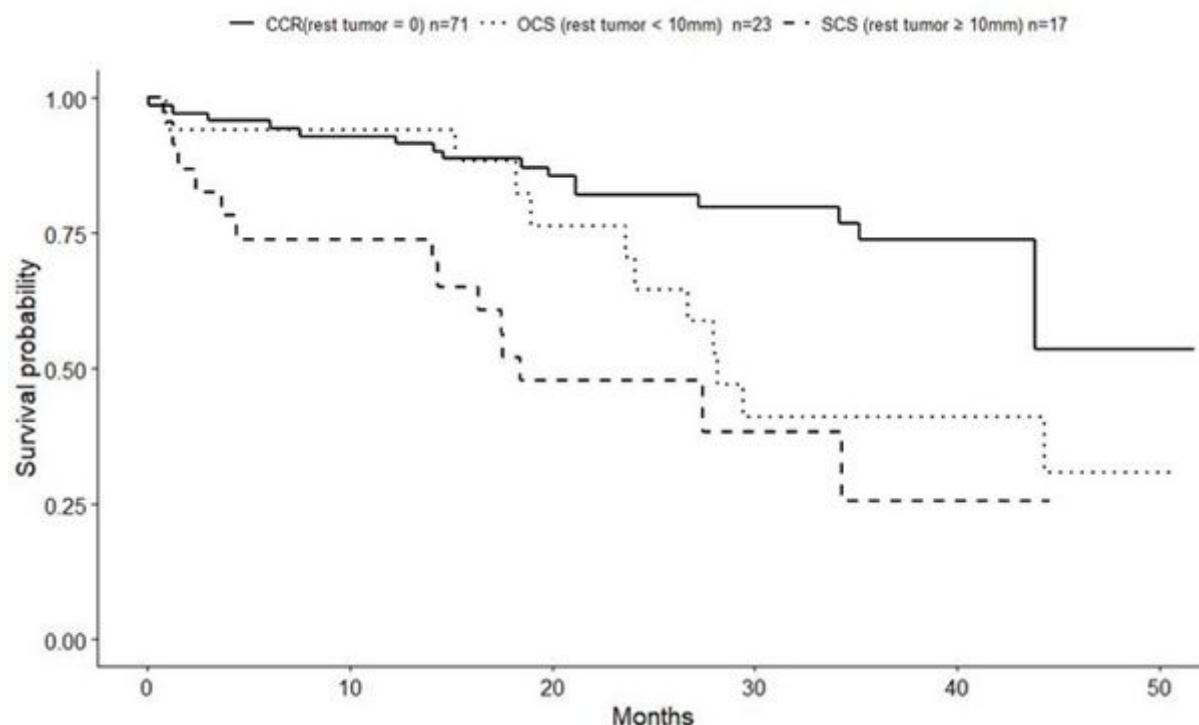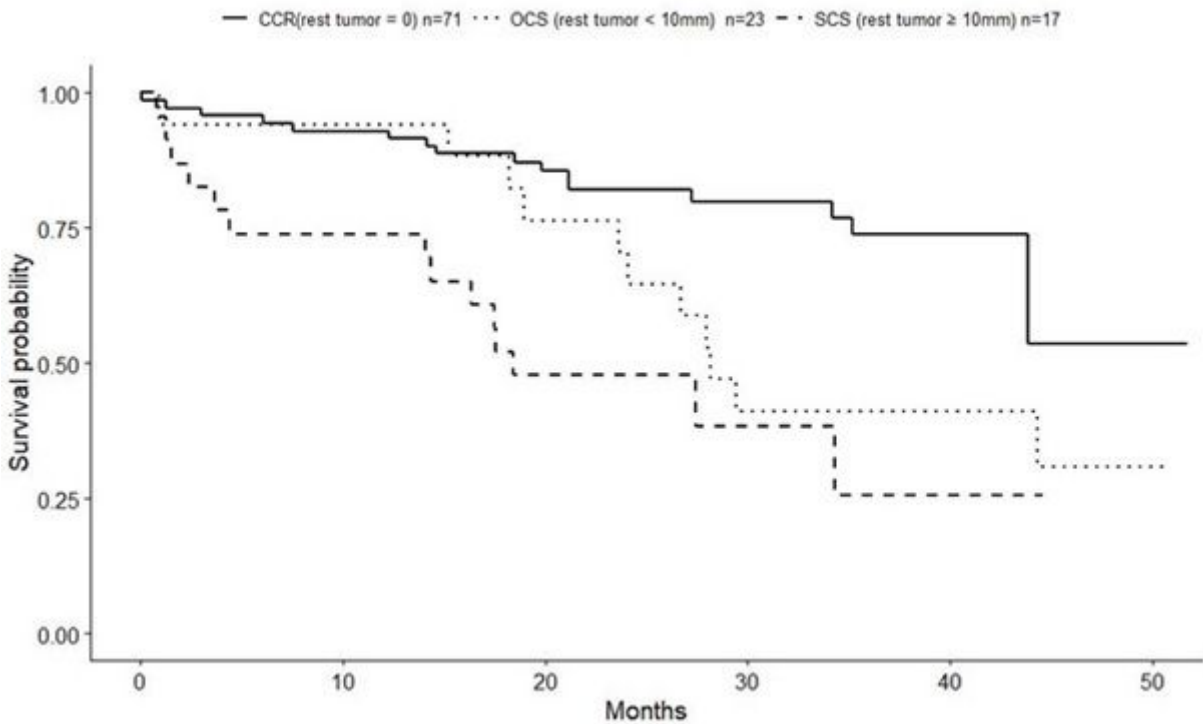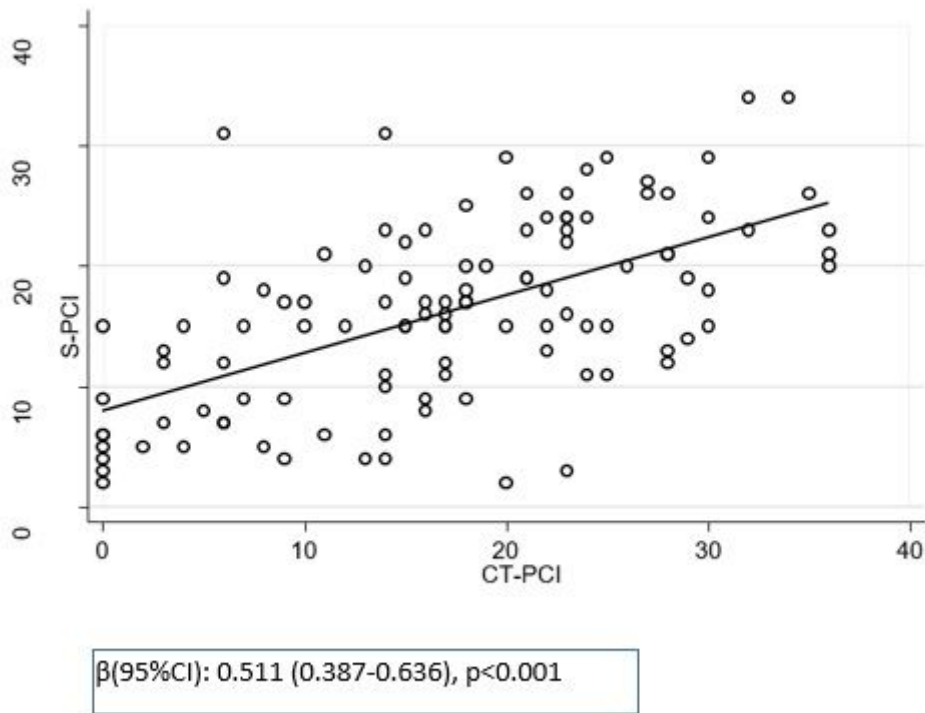
Figures

Figure 1

Survival probability estimated by Kaplan-Meier curves for the entire cohort based on residual disease. Survival probability was significantly reduced for patients with SCS p< 0.005 and OCS p <0.03 (log-rank test) relative to their CCS counterparts. Observation time indicated in month.
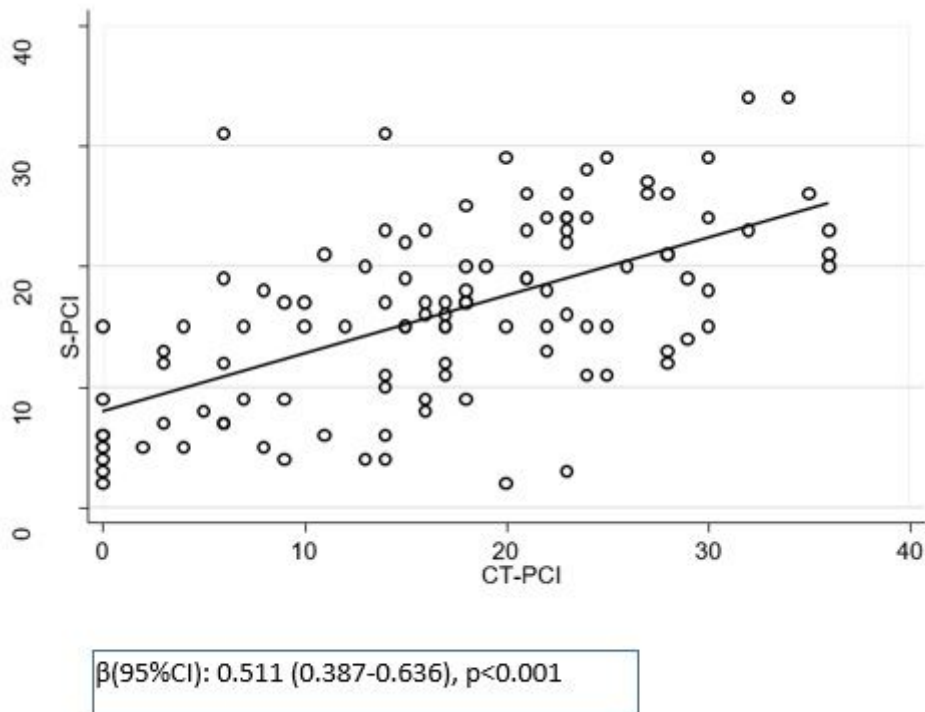

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β(95%CI): 0.511 (0.387-0.636), p<0.001

Figure 2

Linear regression analysis showing an association between increasing CT-PCI and S-PCI.

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