

## Resectability of Peritoneal Carcinomatosis: Learnings from a Prospective Cohort of 533 Consecutive Patients Selected for Cytoreductive Surgery

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### ABSTRACT

**Purpose.** The aim of this study was to identify the risk factors and causes of unresectability in a large cohort of patients with peritoneal carcinomatosis (PC) selected for cytoreductive surgery (CRS), and to assess the contribution of the different imaging modalities to the patient-selection process.

**Methods.** The pre- and intraoperative data of 533 consecutive patients with PC planned for CRS at a single institution were reviewed. All patients underwent computed tomography (CT) magnetic resonance imaging and/or positron emission tomography/CT within the 2 days prior to surgery.

**Results.** Among the 533 patients, 436 (82 %) underwent complete CRS, 86 (16 %) underwent exploratory laparotomy without CRS because of multiple small-bowel involvement ( $n = 31$ ), invasion of different digestive segments ( $n = 15$ ), an elevated PC index ( $n = 14$ ), invasion of the mesenteric root ( $n = 12$ ), or another cause ( $n = 14$ ), and 11 (2 %) did not undergo laparotomy because of disease progression on preoperative imaging findings. On univariate analysis, elevated levels of tumor markers and a short delay between the last cycle of chemotherapy and the scheduled surgery were identified as predictors of

unresectability for the colonic PC population, while a younger age was identified in patients with gastric PC. Multivariate analysis disclosed the use of neoadjuvant chemotherapy and a younger age as independent predictors of unresectability in the colonic PC population.

**Conclusions.** The current modalities for the assessment of PC resectability, including functional imaging examinations, have a low impact on patient selection for CRS. New tools are needed to decrease the rate of open-close procedures.

Peritoneal carcinomatosis (PC) is the natural evolution of up to one-third of intra-abdominal malignancies, and is usually considered as the terminal stage of the disease.<sup>1,2</sup> However, cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) could lead to long-term survival in highly selected patients.<sup>3–7</sup> Such procedures can prove to be aggressive and require considerable logistical and intensive care resources. Identifying preoperative predictors of unresectability could allow physicians to avoid unnecessary laparotomy for patients with unresectable PC, but currently there is no reliable tool to predict the resectability of PC. While staging laparoscopy is not routinely recommended, morphological findings strongly lack sensitivity in assessing PC resectability before surgery.<sup>8</sup> However, the combination of computed tomography (CT) with two functional imaging modalities, comprising magnetic resonance imaging (MRI), and 18-fluoro-desoxy-glucose positron emission tomography (FDG-PET) may improve the

preoperative detection of unresectable lesions. The aim of the present study was to (i) identify the risk factors and causes of unresectability in a large cohort of patients with PC selected for CRS, and (ii) assess the contribution of an imaging protocol combining CT, MRI, and FDG-PET/CT to the patient-selection process.

## METHODS

### *Patient Selection*

We retrospectively analyzed our prospectively maintained database of patients planned to undergo CRS with or without HIPEC with a curative intent for primary or secondary PC between January 2009 and June 2013. During this period, all patients whose files were discussed at our institutional multidisciplinary team meeting had previously undergone a CT, an MRI, and/or an FDG-PET/CT, depending on the etiology of PC. A staging laparoscopy was also indicated in patients with a high tumor load for whom the risk of unresectability was deemed high. Following this first step of selection, a large number of patients were excluded for CRS because of the evidence of unresectability, preoperative pathology, or progression under systemic chemotherapy. A total of 533 patients were finally selected for CRS after board approval, and were included in the present study. In addition to the radiological examinations performed before the multidisciplinary team meeting, all selected patients were scheduled to undergo an imaging protocol including CT, MRI examinations of the abdomen and pelvis, and FDG-PET/CT within the 2 days before surgery. Data were extracted from the prospective database, focusing on patient characteristics, clinical presentation, tumor marker levels, previous therapies, and imaging reports. The study was approved by our Institutional Review Board and reviewed in accordance with the precepts established by the Helsinki declaration.

### *Imaging Protocol*

All 533 eligible patients underwent a CT. A total of 449 patients also underwent FDG-PET/CT, and 510 patients underwent an abdominal–pelvic MRI. All CT examinations were performed using contrast-enhanced CT and included explorations of the brain, chest, and abdominopelvic levels. All FDG-PET/CT studies were performed from the skull base to the mid-thigh, 60 min after intravenous injection of 3–3.5 MBq/kg FDG. Abdominopelvic MRI studies were performed using a 1.5-T unit. The protocol included morphologic axial T2- and T1-weighted sequences, axial diffusion-weighted sequences (*b*-value of 0 and 800), and axial and coronal fat-suppressed T1-weighted sequences

after the injection of gadobenate dimeglumine. All imaging examinations were performed at our institution.

### *Imaging Analysis*

Imaging examinations were analyzed by the onsite senior physicians. Patients were categorized as small [Peritoneal Cancer Index (PCI) 0–9], moderate (PCI 10–20), or large tumor volume (PCI > 20).<sup>9</sup> The following criteria were used as indicators of unresectability: massive infiltration of the mesenteric fat, more than three small-bowel strictures, infiltration of the hepatoduodenal ligament with main bile duct dilatation, and infiltration of the bladder neck when there was loss of tissue between the tumor and the wall of the bladder.<sup>10</sup>

On CT scans, tumor was reported if there was a mass effect on anatomical structures and/or if there was high attenuation peritoneal thickening, nodules or masses that could be distinguished from hypodense ascites, using windowing. The FDG-PET/CT was considered positive in cases of 18F-FDG uptake, and negative otherwise.<sup>11</sup> Calculation of standardized uptake value was not performed. On MRI, tumor was reported if there was peritoneal thickening, peritoneal tumor nodules, or masses showing enhancement on post-contrast images and/or high signal on the diffusion images.<sup>9</sup>

### *Operative Procedure*

All procedures started with a full abdominal exploration to assess the extent of the peritoneal spread and to confirm disease resectability. The following criteria were considered as indicators of unresectability: an elevated PCI with different cut-off values according to PC etiology (>15 for gastric cancer, >24 for ovarian and colorectal cancer),<sup>12</sup> diffuse small-bowel involvement with insufficient (<150 cm) estimated residual bowel length, hepatoduodenal ligament invasion, invasion with retraction of the mesenteric root, and bladder–neck invasion. Furthermore, in cases of concomitant involvement of the stomach and colon, patients with aggressive PC (i.e. of gastric or ovarian origin) were precluded from curative resection, whereas primary PC (pseudomyxoma peritonei, peritoneal mesothelioma) and PC of colorectal origin were still considered resectable, provided there were no other factors indicating poor prognosis. The quality of CRS was assessed according to the Completeness of Cancer Resection (CCR) score.<sup>13</sup>

### *Statistical Analysis*

We specifically compared the preoperative data of all unresectable patients, whether or not they underwent

exploratory laparotomy, with data of those who underwent complete CRS. Patients' baseline, morphological, and preoperative variables were analyzed to identify factors associated with unresectability. Categorical variables were analyzed using Chi-square analysis or Fisher's exact test appropriately, and continuous variables were analyzed using Student's *t* test or Wilcoxon's test for variables that did not satisfy the normality. Multivariate analyses were performed with multilogistic regression analyses. All statistical analyses were performed using SAS 9.3 Institute Inc., Cary, NC, USA. Statistical significance was defined as  $p < 0.05$ .

## RESULTS

Among the 533 consecutive patients included for analysis during the study period, 436 patients (82 %) underwent complete CRS, with ( $n = 353$ ) or without ( $n = 83$ ) HIPEC, achieving a CCR-0 score in 373 patients and a CCR-1 score in 63 patients. Meanwhile, 97 patients (18 %) were deemed unresectable, with 86 patients (16 %) having been explored by laparotomy without CRS, and 11 patients (2 %) without surgical exploration because of the findings of the preoperative imaging protocol. The rates of resectability per etiology of PC are reported in Table 1.

### *Causes of Unresectability in Patients Who Underwent Laparotomy*

The main cause of unresectability in the 86 unresectable patients who underwent laparotomy was linked to a digestive tract involvement: 31 patients (36 %) were

unresectable because of multiple involvements of the small bowel, 15 (17 %) because of an associated invasion of different digestive segments, such as a combined colic and gastric invasion, and 12 (14 %) due to the invasion of the mesenteric root. An elevated PCI value was identified in 14 unresected patients (16 %), diffuse micronodular PC was identified in 8 patients (9 %), while involvement of either the hepatoduodenal ligament (6 %,  $n = 5$ ) or the bladder neck (1 %,  $n = 1$ ) was seldom found intraoperatively.

### *Causes of Unresectability in Patients Who Did Not Undergo the Surgical Procedure*

In nine patients, the preoperative imaging protocol revealed extraperitoneal metastases, which were not present on imaging findings available at the time of the multidisciplinary team meeting. Additionally, two other patients were not operated on because of the progression of the PC lesions, consisting of an unequivocal involvement of the hepatoduodenal ligament in one patient and a bulky mesenteric infiltration in another. CT was sufficient to identify signs of unresectability in seven patients, including two patients with brain metastasis, two with radiological signs of unresectable PC lesions, one with lung metastases, one with pleural carcinomatosis, and one patient with pulmonary lymphangitic carcinomatosis. MRI alone detected signs of unresectability in two patients (one with liver metastases, and one with bone metastases), while both FDG-PET/CT and MRI detected the existence of liver metastases in the two remaining patients.

### *Imaging Features of Unresectability*

A small or moderate tumor volume was reported for all patients regardless of the imaging modality used, except for 25 patients with pseudomyxoma peritonei who had a large tumor volume reported on MRI only. Of these, eight patients were unresectable after laparotomy, either because of a high PCI ( $n = 3$ ) or multiple involvements of mesentery and/or small-bowel serosa ( $n = 5$ ).

No clear unresectable feature was identified in the imaging reports of the 522 operated patients. Sixteen patients with pseudomyxoma peritonei were described with a large mass of mucinous tumor surrounding the hepatoduodenal ligament on MRI, but without bile duct dilatation. Among these 16 patients, one had an unresectable infiltration of the hepatoduodenal ligament at surgical exploration.

### *Preoperative Risk Factors of Unresectability*

Etiology-specific univariate analysis did not identify any predictor of unresectability in patients with pseudomyxoma

**TABLE 1** Rate of resectability per etiology of peritoneal carcinomatosis

Etiology	Unresectable [N (%)]	Resectable [N (%)]	Total (N)
Overall study population	97 (18)	436 (82)	533
Colon cancer	31 (17)	148 (83)	179
Ovarian cancer	16 (13)	105 (87)	121
Pseudomyxoma peritonei	14 (16)	72 (84)	86
Gastric cancer	21 (43)	28 (57)	49
Malignant peritoneal mesothelioma	5 (13)	33 (87)	38
Serous primary carcinoma	0 (0)	13 (100)	13
Appendiceal cancer	4 (40)	6 (60)	10
Rectal cancer	0 (0)	8 (100)	8
Uterus cancer	2 (33)	4 (67)	6
Desmoplastic tumor	0 (0)	1 (100)	1
Other	4 (18)	18 (82)	22

**TABLE 2** Factors of unresectability among patients with peritoneal carcinomatosis originating from colon cancer

Variable	Overall ( <i>N</i> = 179)	Resectable ( <i>N</i> = 148)	Unresectable ( <i>N</i> = 31)	<i>p</i> value
<b>Age</b>				
<i>n</i>	179	148	31	0.2218
Median (range)	59.15 (23.87–85.04)	59.47 (23.87–85.04)	58.59 (36.16–69.97)	
Mean (SD)	57.89 (9.62)	58.24 (9.75)	56.24 (8.92)	
<b>Sex</b>				
Female	80 (44.7)	69 (46.6)	11 (35.5)	0.2567
Male	99 (55.3)	79 (53.4)	20 (64.5)	
<b>ASA score</b>				
<i>n</i>	132	107	25	0.5829
1 or 2	127 (96.2)	102 (95.3)	25 (100)	
3	5 (3.8)	5 (4.7)		
<b>BMI</b>				
<i>n</i>	167	140	27	0.6552
Median (range)	24.3 (16–35.1)	24.3 (16–35.1)	24.3 (19.1–32.8)	
Mean (SD)	24.7 (3.91)	24.76 (3.97)	24.39 (3.67)	
<b>CEA</b>				
<i>n</i>	161	133	28	0.0005
Median (range)	3 (0.3–420.8)	2.8 (0.3–381.5)	6.15 (1.4–420.8)	
Mean (SD)	15.33 (53.11)	10.84 (41.75)	36.68 (87.31)	
<b>CA 19-9</b>				
<i>n</i>	162	134	28	0.0100
Median (range)	21 (2.9–3339)	20.5 (2.9–356)	29 (5–3339)	
Mean (SD)	59.45 (266.44)	32.77 (47.94)	187.14 (625.74)	
<b>CA 125</b>				
<i>n</i>	136	109	27	0.0001
Median (range)	16.5 (1–525)	15 (1–262)	30 (8–525)	
Mean (SD)	33.88 (60.52)	23.22 (33)	76.93 (109.97)	
<b>Acute bowel occlusion</b>				
No	160 (89.4)	131 (88.5)	29 (93.5)	0.5351
Yes	19 (10.6)	17 (11.5)	2 (6.5)	
<b>Medical history of abdominal surgery</b>				
No	117 (65.4)	93 (62.8)	24 (77.4)	0.1208
Yes	62 (34.6)	55 (37.2)	7 (22.6)	
<b>Medical history of staging laparoscopy</b>				
No	122 (68.2)	104 (70.3)	18 (58.1)	0.1847
Yes	57 (31.8)	44 (29.7)	13 (41.9)	
<b>Presence of ascites or increase in abdominal volume without any occlusion</b>				
No	177 (98.9)	147 (99.3)	30 (96.8)	0.3172
Yes	2 (1.1)	1 (0.7)	1 (3.2)	
<b>Number of lines of chemotherapy</b>				
0	21 (11.7)	19 (12.8)	2 (6.5)	0.5952
1 line	85 (47.5)	69 (46.6)	16 (51.6)	
2 lines or more	73 (40.8)	60 (40.5)	13 (41.9)	
<b>Delay between last day of chemotherapy and surgery</b>				
<i>n</i>	147	118	29	0.0255
Median (range)	36 (6–89)	37 (6–89)	30 (16–73)	
Mean (SD)	38.14 (12.86)	39.03 (13.06)	34.52 (11.53)	

TABLE 2 continued

Variable	Overall (N = 179)	Resectable (N = 148)	Unresectable (N = 31)	p value
Context of peritoneal carcinomatosis				
n	173	142	31	0.3797
Metachronous	77 (44.5)	61 (43)	16 (51.6)	
Synchronous	96 (55.5)	81 (57)	15 (48.4)	

ASA American Society of Anesthesiology, BMI body mass index, CEA carcinoembryonic antigen, n number of patients with available data, SD standard deviation

peritonei or malignant mesothelioma. In patients with secondary PC (Tables 2, 3, 4), predictors of unresectability were an elevated level of tumor markers and a short delay between the last cycle of chemotherapy and the surgery for colonic PC, an elevated level of CA 125 for ovarian PC, and a younger age for gastric PC.

In the group of patients with colonic PC, multivariate analysis identified both a younger age and the use of neoadjuvant systematic chemotherapy as independent predictors of unresectability, with an odds ratio of 0.84 (95 % CI 0.71–0.95;  $p = 0.04$ ) for age, 18.98 (95 % CI 0.04 to >1000) for patients who underwent first-line chemotherapy, and >1000 (95 % CI 0.71 to >1000) for patients who underwent second-line chemotherapy. No other independent predictors were deduced by multivariate analysis in the other subgroups of patients.

## DISCUSSION

One of the crucial prerequisites for an optimal assessment of PC resectability is to identify the different causes of unresectability during surgical exploration, in a population of patients selected for CRS. All patients included in the present cohort had previously cleared a first step of selection based on the multidisciplinary team meeting decision and taking into consideration several factors, such as PC etiology, preoperative pathology, response to systemic chemotherapy, previous surgical explorations by laparotomy or laparoscopy, and evidence of unresectability on imaging examinations. The present study demonstrated that the main cause of unresectability in surgically explored patients was related to digestive tract involvement (66 %), including multiple small-bowel invasions (35 %), the combined involvement of different digestive segments (17 %), or the invasion of the mesenteric root (14 %). These findings are relevant, especially in patients with secondary PC of poor prognosis who tend to suffer from altered quality of life evaluations after major digestive resections, while survival is dismal, even in cases of complete CRS. In contrast, patients with pseudomyxoma peritonei or peritoneal mesothelioma with multiple digestive segment invasion tend to benefit from extensive CRS in terms of survival.<sup>14</sup> Therefore,

preoperative evaluation of resectability must also take into consideration the origin of PC.

The PCI is one of the main quantitative prognostic tools used intraoperatively. It is characterized by a high inter-surgeon concordance<sup>15</sup> and a good correlation with the prognosis of PC from digestive tract<sup>16</sup> or ovarian cancers.<sup>17</sup> However, in the present study, an elevated PCI value was the cause of unresectability in only 16 % of cases, which suggests that it does not necessarily imply unresectability. Indeed, some patients with a high PCI value may benefit from a complete CRS, depending on PC origin, with long-term survival.<sup>8</sup> A much more efficient prognostic factor is the ability to obtain a CCR score of 0, which is more related to the distribution of the disease and to the invasion of crucial anatomic sites, rather than to the PCI value.<sup>3</sup> Thus, it may be impossible to obtain a CCR score of 0 in some patients with low PCI because of vital organ invasion. Among peritoneal lesions that could lead to unresectability, Esquivel et al. identified multiple small-bowel strictures, massive invasion of the lesser omentum, and invasion of both ureters.<sup>18</sup> In line with previous studies, our results showed that mesenteric retraction, hepatoduodenal ligament invasion, and bladder neck invasion could be added to those criteria.<sup>8,19</sup>

Despite our imaging protocol, imaging reports failed to alert the surgeon to the presence of unresectable peritoneal lesions in 16 % of patients. Among the different imaging modalities for assessing PC resectability, contrast-enhanced multislice CT has been defined as the fundamental imaging modality.<sup>20</sup> Its sensitivity in detecting PC varies among studies and is better in ovarian PC (85–93 %) than in colorectal PC (41–79 %).<sup>21</sup> Despite its high spatial resolution, CT fails to detect small nodules due to its limited contrast resolution, with reported sensitivity of 24 and 11 % in detecting nodules smaller than 10 mm<sup>22</sup> and 5 mm,<sup>23</sup> respectively, resulting in a consistent underestimation of the PCI.<sup>23</sup> To improve the preoperative assessment of PC resectability, two functional imaging techniques comprising MRI with diffusion-weighted sequence and FDG-PET/CT were performed in addition to CT in most patients of our cohort. The rationale for the use of functional imaging techniques in addition to CT has

**TABLE 3** Factors of unresectability among patients with peritoneal carcinomatosis originating from gastric cancer

Variable	Overall ( <i>N</i> = 49)	Resectable ( <i>N</i> = 28)	Unresectable ( <i>N</i> = 21)	<i>p</i> value
<b>Age</b>				
<i>n</i>	49	28	21	0.0324
Median (range)	53.01 (26.67–75.49)	57.48 (33.83–75.49)	46.64 (26.67–70.93)	
Mean (SD)	52.74 (11.93)	55.87 (10.89)	48.57 (12.22)	
<b>Sex</b>				
Female	26 (53.1)	13 (46.4)	13 (61.9)	0.2827
Male	23 (46.9)	15 (53.6)	8 (38.1)	
<b>ASA score</b>				
<i>n</i>	38	22	16	0.3741
1 or 2	33 (86.8)	18 (81.8)	15 (93.8)	
3	5 (13.2)	4 (18.2)	1 (6.3)	
<b>BMI</b>				
<i>n</i>	46	28	18	0.4713
Median (range)	20.75 (14.8–33.4)	20.65 (16.8–33.4)	20.9 (14.8–27.8)	
Mean (SD)	21.45 (4.07)	22.01 (4.35)	20.57 (3.53)	
<b>CEA</b>				
<i>n</i>	42	24	18	0.3089
Median (range)	1.9 (0.3–150.9)	1.7 (0.3–4.6)	2.1 (0.5–150.9)	
Mean (SD)	5.62 (23)	1.89 (1.1)	10.6 (35.05)	
<b>CA 19-9</b>				
<i>n</i>	43	24	19	0.8066
Median (range)	15 (3–9572)	15.5 (4–691)	15 (3–9572)	
Mean (SD)	490.21 (1944.26)	64.04 (161.18)	1028.53 (2870.38)	
<b>CA 125</b>				
<i>n</i>	40	22	18	0.0622
Median (range)	20 (4–206)	13 (4–113)	24 (9–206)	
Mean (SD)	35.5 (44.98)	26.5 (29.96)	46.5 (57.44)	
<b>Acute bowel occlusion</b>				
No	48 (98)	28 (100)	20 (95.2)	0.4286
Yes	1 (2)		1 (4.8)	
<b>Medical history of abdominal surgery</b>				
No	45 (91.8)	26 (92.9)	19 (90.5)	1.0000
Yes	4 (8.2)	2 (7.1)	2 (9.5)	
<b>Medical history of staging laparoscopy</b>				
No	15 (30.6)	10 (35.7)	5 (23.8)	0.3709
Yes	34 (69.4)	18 (64.3)	16 (76.2)	
<b>Presence of ascites or increase in abdominal volume without any occlusion</b>				
No	47 (95.9)	28 (100)	19 (90.5)	0.1786
Yes	2 (4.1)		2 (9.5)	
<b>Number of lines of chemotherapy</b>				
0	7 (14.3)	4 (14.3)	3 (14.3)	0.4363
1 line	28 (57.1)	18 (64.3)	10 (47.6)	
2 lines or more	14 (28.6)	6 (21.4)	8 (38.1)	
<b>Delay between last day of chemotherapy and surgery</b>				
<i>n</i>	36	20	16	0.9491
Median (range)	35 (18–86)	35 (18–86)	36 (18–85)	
Mean (SD)	39.25 (16.32)	39.75 (16)	38.63 (17.23)	



TABLE 3 continued

Variable	Overall (N = 49)	Resectable (N = 28)	Unresectable (N = 21)	p value
Context of peritoneal carcinomatosis				
n	47	26	21	0.5050
Metachronous	11 (23.4)	5 (19.2)	6 (28.6)	
Synchronous	36 (76.6)	21 (80.8)	15 (71.4)	

ASA American Society of Anesthesiology, BMI body mass index, CEA carcinoembryonic antigen, n number of patients with available data, SD standard deviation

been supported by several studies.<sup>9,11,24,25</sup> For instance, MRI with delayed gadolinium-enhanced and diffusion-weighted sequences may provide a better contrast resolution and a more accurate preoperative PCI compared with CT,<sup>9,24</sup> while FDG-PET/CT has been proven more accurate in exploring PC,<sup>11</sup> predicting the pathology grade and informing on the probability of complete CRS in patients with pseudomyxoma peritonei.<sup>25</sup> Nevertheless, one of the main weaknesses of MRI is the need for an adequate learning curve, which makes its contribution in patient selection uncertain,<sup>26</sup> while the contribution of FDG-PET/CT on patient management is far from being established.<sup>27,28</sup> Therefore, several authors have claimed that the current imaging modalities are of limited help in the preoperative assessment of the peritoneal spread.<sup>18,23,27,29–31</sup> One way to improve the accuracy of the radiological PCI and the identification of unresectable lesions may be the performance of a combined reading of all three imaging techniques, taking into account their spatial and contrast resolutions, rather than reading each imaging modality separately. Further studies are thus needed to evaluate the potential complementarities of these imaging modalities in a common analysis.

Although the purpose of our imaging protocol was not to contraindicate patients for CRS the day before the procedure, but rather to allow accurate correlations with surgery, our study showed that 11 (2 %) of the 533 patients showed either peritoneal disease progression (n = 2) or extraperitoneal metastases (n = 9) during the period of time between the multidisciplinary staff and the scheduled procedure. This very low rate reflects the careful patient-selection process performed before determining patient eligibility for CRS.

Another preoperative tool utilized to select potential surgical candidates is staging laparoscopy. While its sensitivity in detecting PC is approximately 100 %, <sup>32</sup> its accuracy in estimating PC resectability is lower. In a study by Pomel et al., eight patients who were initially considered resectable after staging laparoscopy underwent exploratory laparotomy and, in the end, one patient appeared to be unresectable during surgical exploration.<sup>33</sup> In the present study, approximately half of the patients in both the resectable and unresectable groups had undergone

staging laparoscopy, showing its insufficiency to improve patient selection, as it may not precisely assess diffuse bowel involvement, mesentery retraction, and the extent of the disease in some anatomical areas, such as the cardiophrenic angle or the bladder neck. The accuracy of staging laparoscopy may be even lower in patients with adhesions caused by prior surgery. One way to improve the contribution of laparoscopy may be the use of hand-assisted laparoscopy, which detects PC of gynecological origin more accurately than standard laparoscopy.<sup>34</sup>

In line with the recent study by van Oudheusden et al. on colorectal PC,<sup>35</sup> the predictors of unresectability that were identified in the present study, such as elevated levels of tumor markers or a short delay between the last cycle of chemotherapy and the scheduled procedure, may only have a small contribution in the patient-selection process. The analysis even led to the identification of some surprising predictors of unresectability. A younger age was identified in patients with gastric or colonic PC, which suggests that PC in younger patients might be more aggressive. Moreover, CRS is sometimes attempted for younger patients with morphological evidence of advanced PC, while older patients with the same morphological findings would be naturally excluded for surgical exploration. Another surprising predictor of unresectability found in this study was the use of neoadjuvant chemotherapy for patients with colonic PC. According to previous studies, the use of neoadjuvant chemotherapy is associated with prolonged survival in patients with colonic PC, but its efficacy on the peritoneal disease remains controversial.<sup>36</sup> Therefore, neoadjuvant chemotherapy may be sometimes avoided in highly selected patients with a very limited disease, which could at least partly explain why patients without neoadjuvant chemotherapy may have a higher probability of being resectable.

## CONCLUSIONS

The present findings suggest that the current modalities for the evaluation of PC resectability still have a low influence on the decision to perform exploratory laparotomy for patients with PC. Despite our imaging protocol combining CT, MRI, and FDG-PET/CT, one of six patients

**TABLE 4** Factors of unresectability among patients with peritoneal carcinomatosis originating from ovarian cancer

Variable	Overall ( <i>N</i> = 121)	Resectable ( <i>N</i> = 105)	Unresectable ( <i>N</i> = 16)	<i>p</i> value
<b>Age</b>				
<i>n</i>	121	105	16	0.8333
Median (range)	60.06 (24.3–74.84)	59.44 (24.3–74.84)	61.03 (43.96–69.67)	
Mean (SD)	58.04 (9.02)	58.07 (9.24)	57.86 (7.66)	
<b>ASA score</b>				
<i>n</i>	94	86	8	1.0000
1 or 2	91 (96.8)	83 (96.5)	8 (100)	
3	3 (3.2)	3 (3.5)		
<b>BMI</b>				
<i>n</i>	116	101	15	0.4106
Median (range)	23.25 (16–40.1)	23 (16–40.1)	24.7 (19–30.3)	
Mean (SD)	24.14 (4.39)	24.08 (4.55)	24.57 (3.28)	
<b>CEA</b>				
<i>n</i>	96	82	14	0.9876
Median (range)	1.3 (0.2–33.6)	1.3 (0.2–12)	1.3 (0.5–33.6)	
Mean (SD)	2.19 (4.63)	1.61 (1.59)	5.59 (11.24)	
<b>CA 19-9</b>				
<i>n</i>	99	84	15	0.7176
Median (range)	15 (3–116)	14.5 (4–101)	16 (3–116)	
Mean (SD)	19.16 (16.91)	18.07 (14)	25.27 (28.16)	
<b>CA 125</b>				
<i>n</i>	97	83	14	0.0032
Median (range)	16 (0–9939)	15 (2–9939)	38 (0–374)	
Mean (SD)	136.54 (1007.32)	144.36 (1088.61)	90.14 (124.07)	
<b>Acute bowel occlusion</b>				
<i>n</i>	120	104	16	1.0000
No	119 (99.2)	103 (99)	16 (100)	
Yes	1 (0.8)	1 (1)		
Mean (SD)	10.11 (8.33)	8.5 (6.57)	23.75 (9.43)	
<b>Medical history of abdominal surgery</b>				
<i>n</i>	120	104	16	0.9413
No	46 (38.3)	40 (38.5)	6 (37.5)	
Yes	74 (61.7)	64 (61.5)	10 (62.5)	
<b>Medical history of staging laparoscopy</b>				
<i>n</i>	120	104	16	0.2637
No	67 (55.8)	56 (53.8)	11 (68.8)	
Yes	53 (44.2)	48 (46.2)	5 (31.3)	
<b>Presence of ascites or increase in abdominal volume without any occlusion</b>				
<i>n</i>	120	104	16	0.6985
No	103 (85.8)	90 (86.5)	13 (81.3)	
Yes	17 (14.2)	14 (13.5)	3 (18.8)	
<b>Number of lines of chemotherapy</b>				
<i>n</i>	120	104	16	0.2774
0	11 (9.2)	11 (10.6)		
1 line	44 (36.7)	39 (37.5)	5 (31.3)	
2 lines or more	65 (54.2)	54 (51.9)	11 (68.8)	
<b>Delay between last day of chemotherapy and surgery</b>				
<i>n</i>	101	86	15	0.0770



TABLE 4 continued

Variable	Overall (N = 121)	Resectable (N = 105)	Unresectable (N = 16)	p value
Median (range)	40 (2–90)	42 (2–90)	34 (24–52)	
Mean (SD)	43.36 (17.83)	44.64 (18.75)	36 (8.21)	

ASA American Society of Anesthesiology, BMI body mass index, CEA carcinoembryonic antigen, n number of patients with available data, SD standard deviation

underwent exploratory laparotomy without achieving complete CRS. Surgical exploration remains and should be considered the standard of care for resectability assessment. However, being invasive, by definition, it appears urgent to find new preoperative exploratory modalities, including imaging technique combinations or scores to improve the assessment of PC resectability and the selection for CRS.

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