

The Intraoperative Correlation of The Sugarbaker's Peritoneal Cancer Index for the Surgical Resectability of Advanced Epithelial Ovarian Cancers

Praveen S Rathod¹, Pallavi VR¹, Rajatharangani T¹ and Vijay CR²

¹Department of Gynaecologic Oncology, Kidwai Memorial Institute of Oncology, Bengaluru, India

²Department of Biostatistics, Kidwai Memorial Institute of Oncology, Bengaluru, India

*Corresponding author: Praveen S Rathod, Department of Gynaecologic Oncology, Kidwai Memorial Institute of Oncology, Bangalore, India, Tel: +919632044072, E-mail: rathodps2003@yahoo.com

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Abstract

Aim: This study aimed to investigate Sugarbaker's peritoneal cancer index (PCI) as an objective indicator for the resectability of epithelial ovarian carcinoma (EOC), as depicted in the study using the completeness of cytoreduction score (CCS). Currently, the intraoperative assessment of operability in EOC surgery is primarily a subjective measurement that is dependent on the surgeon.

Methods: The prospective data from 51 patients with EOC FIGO stage III to IV who underwent surgery in a regional cancer institute between July 2015 and June 2017. The PCI and the CCS were recorded intraoperatively using sugarbaker's PCI chart. The details of cytoreductive procedures done were documented in the patient's file. A spearman's rank correlation applied to analyse the surgical predictability of CCS using the PCI.

Results: All the 51 cases underwent gynecological surgeries. More than 49% (25 of 51) patients required extensive surgeries in the upper abdomen. The mean PCI's in CCS 0, CCS 1, CCS 2, and CCS 3 were 8.1, 12.8, 18.6, and 18.5 respectively. There was a strong correlation found between PCI and CCS, and the lower PCI is significantly (P -value <0.0001 , $r=0.69$) associated with better optimal CCS. The 45 (88.2%) of 51 recovered uneventfully, four cases (7.8%) developed surgical site infections, and there were two deaths (3.9%).

Conclusion: The PCI more precisely defined the heterogeneous group of patients with EOC stage III. The PCI provided objectivity and reproducibility, and it seems to be a reliable indicator for EOC resectability. We propose a multi-centric study to define cut-off PCI for the optimal resectability of advanced EOC.

Keywords: Epithelial Ovarian cancer; Carcinomatosis; Peritoneal cancer index; Resectability; Cytoreductive surgery

Introduction

Epithelial ovarian cancer (EOC) is the gynecological malignancy with the highest mortality rate [1]. The treatment is challenging because EOCs are typically diagnosed in advanced stages after the development of peritoneal metastases. Due to this metastatic pattern, surgery for an EOC is often multivisceral and the surgeon must be highly skilled [2]. Primary debulking surgery (PDS) followed by platinum-based chemotherapy has long been considered the only standard treatment for advanced EOC [3]. The aim of primary surgical treatment of EOC was the complete resection of the tumor [4-6]. Of the established prognostic factors of EOC, the amount of tumor that remains postoperatively is the one of the prognostic factors that can be effectively influenced [2]. Complete tumor removal is not dependent only on the ability of the gynecological oncologist to perform a multivisceral operation. An excellent surgeon cannot always ensure complete removal of all tumors, and the ability to decide whether the findings are resectable or inoperable is also important.

The preoperative assessment of operability is primarily dependent on the surgeon and is thus subjective. This was currently shown in the CHORUS trial, where a rate of complete resection of only 15% at primary surgery was achieved [7]. Possibly operational options are often underestimated and neoadjuvant chemotherapy is preferred too early. There is not a quantitative and reproducible assessment. The predictive factors for the resectability of EOCs were analyzed in several studies. A well-researched predictor is the AGO score, which was designed for recurrent ovarian cancer only. On the basis of 3 factors (resection at first surgery, performance status, presence/absence of ascites) resectability can be estimated [8,9].

Among the general surgeons at many institutions, the peritoneal cancer index (PCI) is part of the surgical therapy for gastrointestinal carcinomas [10,11]. The PCI and the completeness of cytoreduction score (CCS) were developed for gastrointestinal carcinoma in 1996 by Jacquet and Sugarbaker. These scores were meant to standardize the management of patients experiencing peritoneal metastatic gastrointestinal carcinoma [12]. The new WHO classification 2014, it incorporates many major scientific advances in our understanding of epithelial cancers of the ovary, fallopian tubes, and peritoneum. It recognizes probable precursor events, lineages, and molecular characteristics, and the EOC is considered as one of the peritoneal surface malignancy [13].

The PCI scores are used for the intraoperative quantification of peritoneal carcinomatosis and applied at the beginning of the exploration of the abdomen and pelvis, before the start of operative measures. The CCS is applied after completion of the operative measures. Currently, the intraoperative assessment of operability in EOC surgery is primarily a subjective measurement that is dependent on the surgeon. Therefore, we aimed to conduct this study to find a parameter, which, at the beginning of the operation, allows for an objective and standardized assessment of the site and resectability of an ovarian tumor. As the PCI was efficacious in general surgery, our aim was to investigate whether this score could be applied to EOCs.

Methods

This is a prospective study of 51 patients with advanced epithelial ovarian cancers (EOC) International Federation of Gynecology and Obstetrics (FIGO) stage III to IV who underwent cytoreductive surgery in the department of Gynaecological Oncology at a regional cancer institute between July 2015 and June 2017 were analyzed. The departmental board approval was obtained. The departmental policy for selecting patients to primary debulking surgery is based on patient's good performance status Eastern Cooperative Oncology Group (ECOG) 0-1, optimal resectability on CT scan study, clinical examination and serum albumin >3g/dl, and the patients with poor performance status ECOG >2, serum albumin <3g/dl, malignant pleural effusion, optimally non-resectable disease on CT scan, age >80 years will receive 2-3 courses neoadjuvant chemotherapy (NACT) followed by interval cytoreduction (IDS). Patients with FIGO stage IVB as well as those assigned to receive neoadjuvant treatment were excluded from the study. The PCI and the CCS were recorded intraoperatively using sugarbaker's PCI chart (Figure 1). The details of cytoreductive procedures done were documented in the patient's file. A spearman's rank correlation test applied to analyse the surgical predictability of CCS using the PCI.

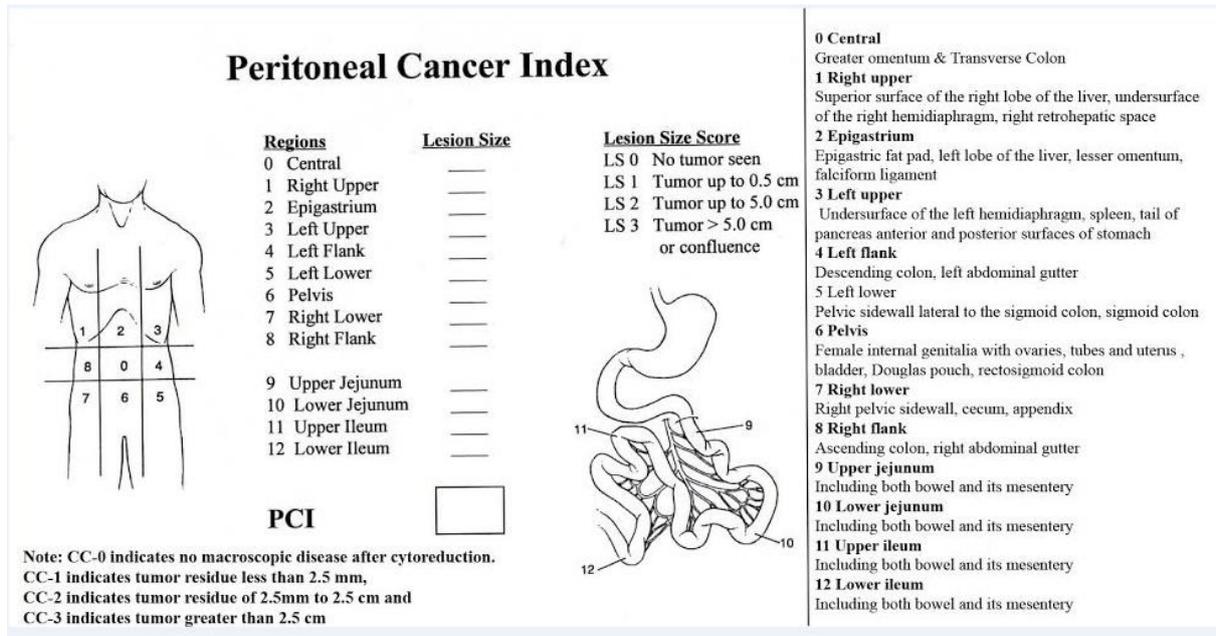


Figure 1: Sugarbaker's PCI chart

Results

A total of 51 cases with advanced EOC were recorded for the PCI at the beginning PDS and CCS was recorded at the end of PDS and the details of various cytoreductive procedures in each patients were recorded in patient's files (table 1). All the 51 cases underwent gynecological procedures, ovarian tumour debulking (TD) with total abdominal hysterectomy with bilateral salpingo-opherectomy (TAHBSO) with total omentectomy (TO) and one of the case which was a post- hysterectomy underwent ovarian tumour debulking with bilateral salpingo-opherectomy with total

omentectomy (table 1,2), and the additional surgical procedures done to achieve optimal CCS were 29 (56.9%) cases required pelvic peritonectomies, 11(21.6%) cases abdominal peritonectomies, 12 (23.5%) cases diaphragm stripping with or without diaphragm resection / and or liver surface deposit excision (Figure 2), nine cases (17.6%) underwent appendicectomy, six cases (11.8%) with mesenteric deposits excision with or without fulguration, three cases (5.9%) large bowel resection and anastomosis, two cases (3.9%) small bowel resection and anastomosis, one case required cholecystectomy and porta hepatis tumour debulking and one case needed splenectomy (Table 1, 2) (Figure 3).

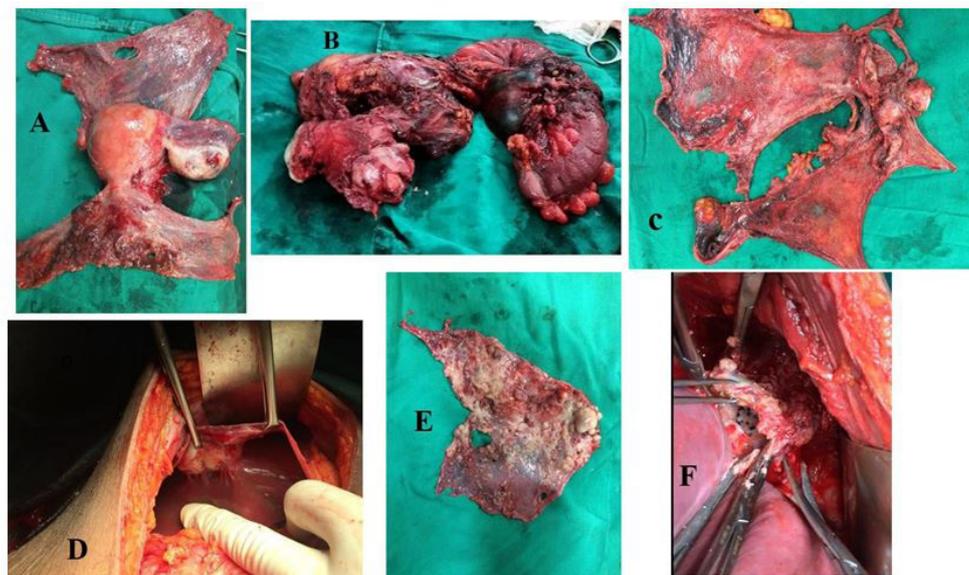


Figure 2: A= en bloc pelvic peritonectomy specimen with uterus and ovaries, B= En bloc resection of uterus with ovarian tumor and recto-sigmoid in an ovarian cancer infiltrating recto-sigmoid mesentery, C= en bloc pelvic and abdominal peritonectomy, D= perihepatic deposit excision with diaphragm peritonectomy, E= diaphragm peritoneum stripped with tumor deposits, F= diaphragm central tendon excision with a deposit

Table 1: The details of PCI, CCS and cytoreductive surgeries done

Case, S. No	PCI	CCS	Cytoreductive procedures done							Morbidity mortality
			TAH+BS O+ RPLND +TD+TO	Pelvic peritonec tomy	Diaphragm peritonec tomy	Bowel resection anastomosis (RA)	Mesenteric deposits excision	Splene ctomy	Abdominal peritonec tomy	
1	13	2	Yes	Yes						Died on POD5, PTE
2	19	0	yes	Yes	Yes	Appendicectomy	Yes		Yes	
3	14	1	yes	Yes					Yes	Died on POD3, MI
4	10	0	yes	Yes						
5	34	2	yes	Yes	Yes		Yes		Yes	
6	21	1	yes	Yes	Yes		Yes			
7	18	3	yes			Ileal- RA				SSI
8	21	2	yes			Appendicectomy				
9	21	2	yes	Yes		Appendicectomy				
10	15	1	Yes	Yes	Yes	Appendicectomy				SSI
11	15	1	Yes	Yes		Appendicectomy			Yes	
12	17	0	Yes	Yes	Yes			Yes	Yes	
13	5	0	Yes	Yes						
14	12	0	Yes	Yes	Yes					
15	6	0	Yes	Yes						
16	13	0	Yes	Yes	Yes	Appendicectomy				
17	17	1	Yes	Yes	Yes	Trans. colon -RA				
18	18	1	Yes	Yes	Yes	Appendicectomy			Yes	SSI
19	9	1	Yes	Yes					Yes	
20	7	0	Yes							
21	14	2	Yes							
22	8	0	Yes							
23	13	1	Yes							
24	7	0	Yes							
25	11	1	Yes	Yes						
26	4	0	Yes	Yes						
27	5	0	Yes							
28	9	0	Yes	Yes					Yes	
29	9	1	Yes	Yes						
30	10	1	Yes							
31	7	0	TD+BSO+							
32	13	1	Yes	Yes						
33	6	0	Yes							
34	11	1	Yes	Yes					Yes	
35	16	2	Yes			Cholecystectomy	Yes			
36	10	1	Yes	Yes						
37	11	1	Yes		Yes					
38	9	1	Yes	Yes						
39	7	0	Yes	Yes						
40	4	0	Yes							
41	18	2	Yes				Yes			
42	11	1	Yes			Rectosigmoid-RA				
43	12	1	Yes			Ileal -RA				
44	5	0	Yes			Appendicectomy				
45	13	1	Yes			Rectosigmoid-RA				SSI
46	11	1	Yes	Yes						

47	14	1	Yes		Yes			Yes	
48	19	3	Yes			Yes			
49	12	2	Yes	Yes	Yes				
50	3	0	Yes						
51	15	1	Yes	Yes				Yes	

Table 2: The types of cytoreductive procedures done

Surgical procedures	Number
Gynaecological procedures: Tumour debulking with TAHBSO with RPLND and total omentectomy	51
Pelvic peritonectomy (bladder and pouch of Douglas)	29
Abdominal (para colic) peritonectomy	11
Diaphragm stripping/resection with or without liver surface tumor excision	12
Appendicectomy	09
Mesenteric deposit excision/fulguration	06
Large Bowel resection anastomosis	03
Small bowel resection anastomosis	02
Cholecystectomy with porta hepatis tumor debulking	01
Splenectomy	01

PCI= peritoneal cancer index, CCS= cytoreductive completeness score, TAH=Total abdominal hysterectomy, BSO=bilateral salpingo-ophorectomy, TD= tumor debulking, TO=total omentectomy, RPLND=retroperitoneal lymphadenectomy, RA= resection anastomosis, PTE= pulmonary thromboembolism, MI= myocardial infarction, SSI= surgical site infection, POD=post-operative day

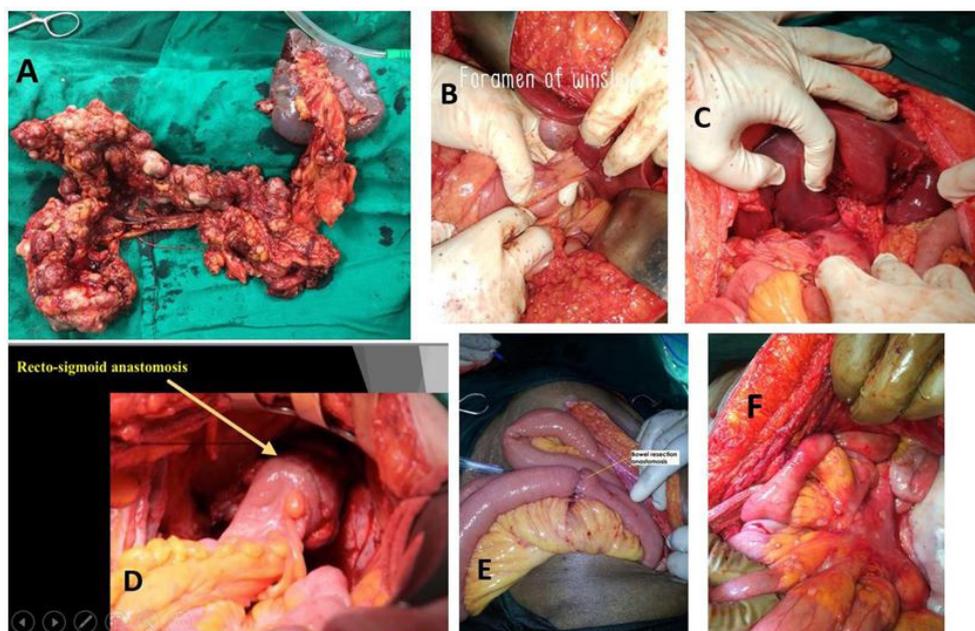


Figure 3: A= omental cake and splenectomy en bloc excision, B= foramen of Winslow and porta hepatis, C= porta hepatis deposit excision following cholecystectomy, D= Recto-sigmoid resection anastomosis, E= Small Bowel resection anastomosis, F= multiple bowel mesenteric tumor deposits

The table 3 reveals the mean PCI's in CCS 0, CCS 1, CCS 2, CCS 3 were 8.1, 12.8, 18.6, 18.5 respectively, and the PCI range in CCS 0 was 03-19, CCS 1 was 09-21, CCS 2 was 12 -34 and CCS 3 it was 18-19. A spearman's rank correlation test reveals a strong correlation found between PCI and CCS, and the lower PCI is significantly (P -value <0.0001 , $r =0.69$) associated with better optimal CCS (Table 3).

The post-operative period events in our study, the 45 (88.2%) of 51 recovered uneventfully, four cases (7.8%) developed surgical site infections were managed with sensitive antibiotics and sterile dressings. There were two deaths (3.9%) one case developed acute pulmonary thromboembolism on 5th post-operative day, and the other case had a myocardial infarction on 3rd post-operative day (Table 1).

Table 3: PCI and CCS distribution

	CCS 0	CCS 1	CCS 2	CCS 3
	19	14	13	18
	10	21	34	19
	17	15	21	
	05	15	21	
	12	17	14	
	06	18	16	
	13	09	18	
	07	13	12	
	08	11		
	07	09		
	04	10		
	05	13		
	09	11		
	07	10		
	06	11		
	07	09		
	05	11		
	04	12		
	03	13		
		11		
		14		
		15		
*Mean PCI	8.1	12.8	18.6	18.5
Total cases	19	22	08	02
PCI= peritoneal cancer index, CCS= completeness cytoreduction score. * A spearman's rank correlation test P-value <0.0001, r=0.69				

Table 4: Overview of peritoneal carcinomatosis scores

Score	Principle	Progressiveness/Aim	Advantages	Disadvantages
Eisenkop score [15]	Score from 0 to 15; 5 anatomical regions; ranks from 0 to 3 per region	Ovary; prediction survival	Includes pelvic and para-aortic lymph nodes	Less precise than the PCI
Fagotti score [16]	Score from 0 to 14; 7 anatomical structures; 0/2 points per region	Ovary; prediction resectability	Concise	Based on laparoscopy
Fagotti-modified score [17]	Score from 0 to 8; 4 anatomical structures; 0/2 points per region	Ovary; prediction resectability	Concise	Based on laparoscopy
Gilly classification [18]	G0-G4; information regarding location of carcinomatosis (locally, disseminated)	Colorectal tumors	Concise	Imprecise localization of the lesions
P-Score of the Japanese Research Society of Gastric Cancer [19]	P0-P3; information about the location of the metastases	Gastric carcinoma	Specially for gastric carcinoma	Imprecise localization and sizing of the lesions only for gastric carcinoma
PCI [12]	Score from 0 to 39; 13 abdominal and pelvic regions, per region LS 0-3	Gastrointestinal tumors; management standardized	Very precise description of the peritoneal carcinomatosis, can be universally used	Lymph nodes not included
Simplified PCI [20]	Score from 0 to 21; 7 abdominal and pelvic regions, per region LS 0-3	Colorectal and appendix tumors; staging	Concise	Less precise than the PCI

Discussion

The majority of EOCs are diagnosed at an advanced stage. The FIGO classification reflects tumor spread relatively imprecisely, particularly in disease stages III and IV. In FIGO stage III is a heterogeneous group, patients with peritoneal metastases outside the pelvis are grouped with patients without peritoneal metastases whose lymph nodes are affected [14]. Various scores have been developed to describe tumor spread more precisely. Among others, the Eisenkop-, Fagotti-, and the Fagotti-modified scores have been developed to describe EOCs. For gastrointestinal carcinomas, the classification scores include the Simplified PCI, the P-Score of the Japanese Research Society for Gastric Cancer, and the Gilly classification. An overview of those scores is shown in Table 4. Of these scores, the PCI is the most precise for describing peritoneal carcinomas. Because the PCI creates 13 abdominopelvic regions, the description of the affected zones is markedly precise. The lesion size component allows for a description of the size of the tumor mass in the score. The PCI is the most precise score for describing the location of a carcinomatosis. The other scores create only 2 to 7 abdominopelvic regions. Only the PCI score and the Gilly classification refer to the size of the tumor mass. Other scores can be applied to EOCs to a certain extent. The Fagotti- and the Fagotti-modified scores are laparoscopy based. The P-score is particularly adapted for stomach cancer. The PCI can be applied, in principle, to any type of peritoneal cancer from any source. This score describes the distribution of tumors in the abdomen and pelvis, without particularly weighing a certain region. For the prognosis of resectability, the PCI and Fagotti- modified score were the most suitable. In 2012, Koppitsch and Sebek analyzed various preoperative and intraoperative classification systems. They emphasized that the PCI can be used universally and with much more precision than the P-score and the Gilly classification [21]. Our results have shown that the PCI can be used for EOCs. It precisely mirrors the extent of the tumor and can be used for the assessment of resectability. Our statistical analysis resulted in to a strong correlation of the PCI to the surgical outcome, shown in the study by the CCS.

The current practices by most Gynaecological oncological surgeons is the intraoperative assessment of resectability in EOC surgery is primarily a subjective measurement that is dependent on the surgeon. It was the aim of this study to identify the PCI as a parameter that would standardize and objectify the management of EOCs. The entire site must be explored using a predefined scheme to determine the PCI. The assignment of a lesion size to each region is simple and clear, and it automatically

leads to a precise exploration. There is little room for subjective interpretation in the given scheme.

In 1998, Sugarbaker reported that the PCI has 2 weak points. In cases in which more critical areas are affected, that is, the root of the mesentery, a possibly lower score does not properly reflect that it cannot be resected. In the case of a non-invasive pseudomyxoma peritonei, it is possible that even with a high PCI, surgery can result in a tumor-free outcome. In these cases, the PCI does not reflect the resectability [22]. In our study two cases had PCI with PCI 18 and 19 had CCC 3 due involvement of tumour deposits at the root of mesentery at multiple places. One case with PCI 19 achieved CCS 0 as the carcinomatosis was confined mainly over the parietal peritoneum.

The root of the mesentery was significantly affected in more than 11.8 % (6/51) of the cases. More than 49% of the patients required extensive intervention in the upper abdomen such as diaphragm stripping/resection with few cases underwent liver surface tumour excision, splenectomy, resection of the lesser omentum, and cholecystectomy with porta hepatis tumour debulking. The grading of peritoneal carcinomatosis, according to Sugarbaker, requires the precise exploration of 13 regions. Frequently, if problematic regions such as the celiac trunk or portal vein are affected, it is impossible to achieve a macroscopic tumor-free outcome. The apparently low rate of macroscopically tumor-free outcomes possibly reflects the precise exploration of these problem regions in which we could not achieve freedom from tumors despite advanced surgical techniques.

In this study, the PCI and CCS scores were determined prospectively, based on intraoperative findings, and a possible criticism of the study is, it's a single centre small number prospective determination of the scores. For this analysis, consistency in the determination of the scores was efficacious and was assured by having the determination performed by the same person.

A study to investigate whether there is a cut-off that would be useful for determining resectability would be useful. May be PCI could then be of help deciding on operability. Of course, the surgeon will always use several parameters to decide on operability, other than only the PCI. The patient's general status and the location of the tumor play a role, too. In case of inoperability, the authors would always remove the omentum as this simple procedure leads to an enormous relief of symptoms with improvement in quality of life. It is possible that the PCI could be used to measure the quality of the surgeon and thus create an opportunity for comparison. The objective documentation is preferred over the currently practised subjective assessment.

The PCI score, which is already established in general surgery, seems applicable to other peritoneal metastasizing tumors. It is markedly precise and all abdominal and pelvic regions are weighted equally in the description. It is a useful extension of the existing classification systems for the treatment of EOCs and could be used as a parameter for the assessment of resectability (table 4).

Conclusion

The PCI more precisely defined the heterogeneous group of patients with EOC stage III. The PCI provided objectivity and reproducibility, and it seems to be a reliable indicator for EOC resectability. We propose a multi-centric study to define cut-off PCI for the optimal resectability of advanced EOC.

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