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Peritoneal Cancer Indexes in Ovarian Carcinomatosis: Correlation Between CT and Intraoperative Results and Survival

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Abstract: The aim of this study is to value the performance of computed tomography (CT) for the detection of ovarian peritoneal carcinomatosis (PC). We review retrospectively abdominopelvic CT and compare them with surgical reports to value the correlation between surgical and radiological PC indexes and survey. We compare the peritoneal tumor implants detected on CT performed before surgery with pathology results obtained after surgery. 47 patients with an average age of 58 years are investigated. Tumor localization and size are documented applying Sugarbaker´s Peritoneal Carcinomatosis Index (PCI) in both, radiological and surgical investigations, which divide the entire abdominal and intestinal regions into 13 spaces. In each one, the bigger visible lesion is measured and scored between 0 and 3. In our study, the correlation of Pearson shows there is a moderate correlation between the findings of the PCI obtained in the TC and surgical findings, appreciating a general low correlation in all regions, although the better results belong to regions 1, 2, 0 and 10. Also we observed a lower survival to greater PCI regarding carcinomatosis index in both TC and surgery. All patients received systemic chemotherapy before surgery, so its effect on the size of the peritoneal implants could explain the low correlation. In conclusion, we can consider that TC is a useful tool for the planning of the surgery and the preoperative treatments. The peritoneal cancer index is a significant index of survival in ovarian cancer patients and by using PCI a detailed evaluation of the peritoneal spread is possible being useful as a prognostic factor.

Keywords: Ovary, Carcinoma, Peritoneal Cavity, Computed Tomography, Surgery

1. Introduction

Ovarian cancer is the sixth most common cancer in the world if we consider the impact in developed countries. It is also the most lethal of all gynecologic malignancies and the fifth cause of the global dead from cancer in women [1-4].

The cause of this late diagnosis is the result of the low symptomatology that produces and also that there are no effective screening methods that have been adequately validated [5]. The 90% of neoplasm affect the surface of the ovary and this is the reason that the most frequent pattern of dissemination is peritoneal carcinomatosis (PC) [6].

Some years ago PC was considered as a final stage of unresectable cancer, but now with the best combination of treatment techniques (association of hypertermic intraoperative intraperitoneal chemotherapy, surgical peritonectomy procedures and intravenous systemic chemotherapy) it can be managed with curative intention [7].

When PC is diagnosed, disseminated metastatic disease by other organs such as the liver or the lung is not usually found and it is still possible to get a curative surgical resection, [8]

it is important to get a correct as soon as possible diagnosis of PC.

The extent of carcinomatosis represents one of the most important prognostic factors for the patients. Tumor implants of different sizes can occur anywhere from the diaphragm until the pelvis [9]. Several methods of classifications for the PC have been used throughout the history. For all methods to classify the degree of the carcinomatosis extension we commonly use the Peritoneal Cancer Index (PCI), described by Jacquet and Sugarbaker [10]. PCI has been cataloged as a useful quantitative prognostic tool [11].

Nowadays, we have several therapeutic procedures for the PC. These treatments should be selected depending on the PC´s location and the extension. Some of these therapies are surgery, systemic chemotherapy, cytoreductive surger. The peritonectomy procedure related with a previous hyperthermic intraperitoneal chemotherapy (HIPEC) has demonstrated to significantly improve survival in patients with peritoneal metastases from abdominal primary cancers [12-14].

2. Objective

The aim of this study is to compare the findings obtained in the surgery and its correlation with the preoperative CT in patients with malignant ovarian peritoneal carcinomatosis and to determine the overall survival and the disease-free survival in patients with malignant ovarian peritoneal carcinomatosis treated by surgery and HIPEC in our center according to the SugarBaker Score detected on CT and with findings obtained in surgery.

3. Methods

This is an observational and analytical study of prospective cohorts. It is a Unicentric study carried out in the Interventional Radiology with the collaboration of the Service of General Surgery.

The inclusion criteria are women with malignant peritoneal disease from ovarian cancer, diagnosed by clinical, radiological and pathological characteristics between November 2008 to January 2012 with a prospective follow-up until August 2015 who were treated with cytoreductive or radical peritonectomy associated with intraoperative chemotherapy (HIPEC). No patients were excluded.

We collected dates including demographics, epidemiological, tomography findings and other related to surgical treatment and follow-up of patients. Informed consent was obtained from all individual participants included in the study.

All patients received systemic chemotherapy before surgery, so its effect on the size of the peritoneal implants could influence the findings in preoperative CT regarding to the histopathological, so we assume that systemic chemotherapy could be a confounding variable.

All the CT scan of the abdomen and pelvis were performed after the administration of ionated intravenous and oral barium contrast, in a 16-row CT multidetector CT (different machines).

Peritonectomy surgery with intraoperative chemotherapy (HIPEC) was performed by the same team of expert surgeons.

For clinical use, the CT was read by a staff radiologist. For the current clinical research study, every CT images were read by a single expert abdominal radiologist who knew that all patients included in the study had clinical evidence of PC but without knowledge of the operative findings.

Once obtained radiological and surgical PCI-dates, a second radiologist is responsible for entering the data in Excel format.

Tumor localization and size were documented applying Sugarbaker´s PCI in both, radiological and surgical investigations, which divide the entire abdominal and intestinal regions into 13 spaces. Two transverse planes and two sagittal planes divide the abdomen into 9 regions. The upper transverse plane is located at the lowest aspect of the costal margin and the lower transverse plane is placed at the anterior superior iliac spine. The sagittal planes divide the abdomen into three equal sectors. The lines define the nine regions which are number in a clockwise direction with 0 at the umbilicus. Regions 1, 2 and 3 are subdiaphragmatic from the right to the left of the patient. Region 4 is left flank, region 5 is left iliac fosse, 6 is pelvis, 7 is right iliac fosse, 8 is right flank and 0 is umbilicus. Regions 9-12 divide the small bowel considering regions 9 and 10 from jejunum proximal and distal respectively, and regions 11 and 12 from ileum proximal and distal. (Figure 1).

ABDOMINOPELVIC REGIONS 0-12

Figure 1. *Sugarbaker´s PCI in CT.*

In each of the 13 regions the maximum visible lesion size is measured and assigned to a lesion size score between LS = 0 and LS = 3. LS = 0 means no tumor visible, LS = 1 means a tumor lesion size below 0.5 cm, LS = 2 means a tumor lesion size between 0.5 cm and 5 cm, and LS = 3 means a tumor lesion size larger than 5 cm or describes a confluent tumor. LS scores in the individual regions are summed up to the PCI score which can assume a minimum score of 0 and maximum score of 39.

CT scans were analyzed before explorative laparotomy being the CT results compared with intra-operative findings.

The explorative laparotomy and intra-operative data evaluations were conducted by a surgical team of surgeon following a standard procedure and protocol. Intra-operative results regarding PC existence, lesion size and localization are considered the Gold Standard.

Prior to analyze the results regarding survival, we have artificially grouped patients into groups according to PCI values obtained in both CT and surgery:

a. Mild PCI (TC and surgery): it includes patients with a PCI score obtained in TC between 0 and 12 points.
b. Moderated PCI (TC and surgery): it includes patients with a PCI score obtained in TC between 13 and 26 points.
c. Histologic type: nine groups are defined for the histological descriptive statistical study. To performe the overall survival and disease-free survival, we grouped these histologic types into three groups with the most frequent types: Undifferentiated/differentiated serous and the anaplastic tumors.

For the statistical study we use Windows 7 as operating system, Microsoft® Word 2010, Microsoft® Excel 2010 and SPSS® 22.0 Armonk, NY: IBM Corp.

The statistical analysis includes:

-For quantitative variables: calculation of the average (m) as a measure of central tendency and the standard deviation or standard (DS) as a measure of dispersion. For qualitative variables calculation of percentages or proportions. The magnitude of association between quantitative variables using the Pearson-correlation-coefficient. The survival analysis was conducted using the estimation method of Kaplan Meyer curves. The method for the comparison of proportions of survival was performed using the Mantel test-cox (Long rank test). In all the statistical tests are considered "significant" with level of confidence was 95% ($p < 0.05$).

4. Results

The patients analyzed were 47 women with an average age of 58 years. The most frequent histological types were (55.3%) of serous and undifferentiated (14.9%). In 76% of cases, radical peritonectomia was carried out and in 23.4 patients a cytoreductive surgery was performed.

After calculate the Sugarbaker´s PCI in both radiological and surgical investigations, we obtain respectively for TC and surgery the following values according to localizations and size: space 1 (30 points on CT and 67 points on surgical procedure), space 2 (19, 28), space 3 (48, 22), space 8 (22, 53), space 0 (22, 53), space 4 (11, 40), space 7 (27, 86), space 6 (67, 126), space 5 (13, 76), space 9 (25, 15), space 10 (37, 17), space 11 (31, 30) and space 12 (46, 34).

The score PCI obtained in both CT and surgery according to the size of the lesions (LS0-LS3), and abdominopelvic regions where localized (0-12), is shown in table 1, being the average score in CT 8.64 (0.34) and in surgery 14.66 (4-27).

Table 1. *The score PCI obtained in both CT and surgery according to the size of the lesions (LS0-LS3), and areas abdominopélvicas where localized (0-12).*

		Abdominopelvic region												
	Lesion size	**1**	**2**	**3**	**8**	**0**	**4**	**7**	**6**	**5**	**9**	**10**	**11**	**12**
CT	LS 0	35	38	24	36	34	40	35	23	42	36	33	35	31
	LS 1	1	1	3	3	2	3	3	1	0	3	1	1	0
	LS 2	4	6	15	5	1	4	3	3	2	2	3	3	2
	LS 3	7	2	5	3	10	0	6	20	3	6	10	8	14
Surgery	LS0	16	26	24	13	5	17	2	2	3	35	31	22	18
	LS1	8	15	13	17	18	21	16	2	20	9	15	20	24
	LS 2	10	5	5	15	11	8	17	5	16	3	1	5	5
	LS 3	13	1	5	2	13	1	12	38	8	0	0	0	0

Distribution of lesión size in the various abdominoplevic regions

The correlation of Pearson shows there is a moderate correlation between the findings of the PCI obtained in the CT and surgical findings (0.379), being this correlation statistically significant ($P < 0.01$). Then we analyze the correlation between the PCI by CT and surgery in each abdominal region following the score of Sugar Baker, using the statistician Pearson and Spearman bivariante correlation (figure 2).

We can observe marked in yellow the significant correlations ($p < 0.05$), appreciating a general low correlation in all regions, although the better results belong to regions 1, 2, 0 and 10. (Table 2).

Table 2. *Correlation between the findings of the PCI obtained in the CT and surgical findings in each abdominal region following the score of SugarBaker, using the statistician Pearson and Spearman bivariante correlation.*

PEARSOAN	**PEARSON**	**BILATERAL SIGNIFICANCE**	**SPEARMAN**	**BILATERAL SIGNIFICANCE**
1	0.403	0.05	0.379	0.009
2	0.315	0.03	0.297	0.053
3	0.269	0.068	0.223	0.132
8	0.272	0.064	0.262	0.075
0	0.636	0.012	0.343	0.018
4	-0.204	0.170	-0.246	0.095
7	-0.009	0.950	-0.029	0.849
6	0.285	0.053	0.308	0.035
5	-0.125	0.404	-0.102	0.496

PEARSOAN	PEARSON	BILATERAL SIGNIFICANCE	SPEARMAN	BILATERAL SIGNIFICANCE
9	0.243	0.101	0.253	0-086
10	0.312	0.033	0.267	0.070
11	0.115	0.442	0.62	0.678
12	0.234	0.113	0.025	0.128

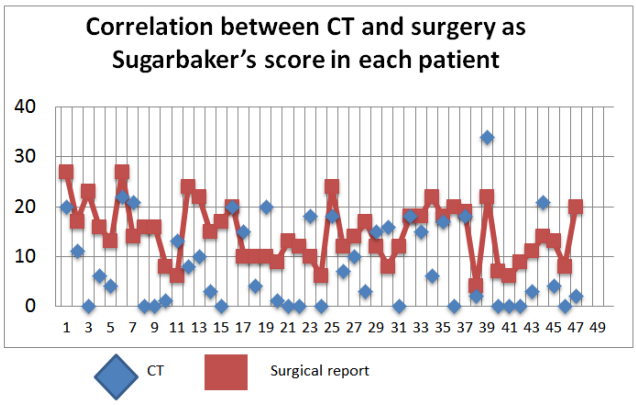

Figure 2. *Correlation between the findings of the PCI obtained in the CT and surgical findings in each abdominal region following the score of SugarBaker, using the statistician Pearson.*

Once classified the percentages according to:

a. The Score (mild PCI 0-12 vs moderate 13-26) both in CT as in surgery

b. Type of peritonectomía (cytoreductive vs radical)

c. Histopathology, performing three groups on the basis of its frequency: serous carcinoma, Undifferentiated and differentiated

The following results were obtained:

(1). Survival according to PCI in CT: median survival of 64 for mild and an average of 41 months to the moderate, being observed a lower survival to greater PCI, being statistically significant ($p < 0.05$). (figure 3).

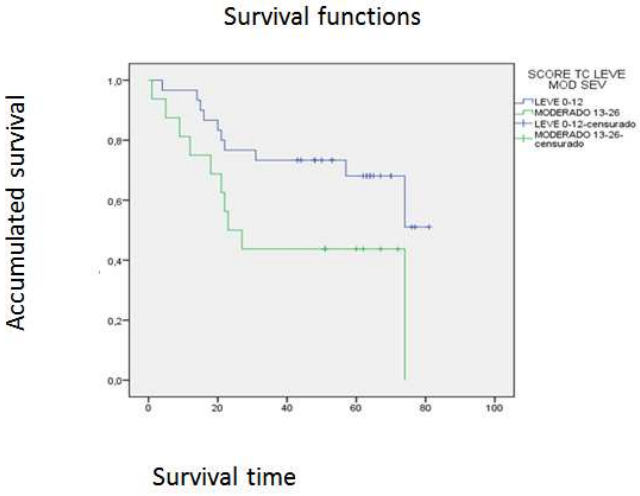

Figure 3. *Survival according to PCI obtained in CT.*

(2). Disease-free survival according to PCI in CT: average of disease-free survival of 63 and 68 months respectively for mild and moderate, showing a lower survival to greater PCI, not being statistically significant ($p < 0.05$). (figure 4).

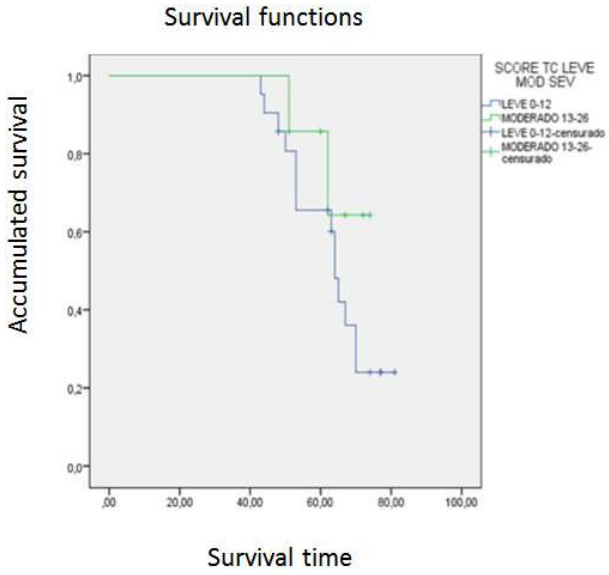

Figure 4. *Disease-free survival according to PCI obtained in CT.*

(3). Survival according to PCI in surgery: average of disease-free survival of 68 and 45 months respectively for mild and moderate, showing a lower survival to greater PCI, being statistically significant ($p < 0.05$). (figure 5).

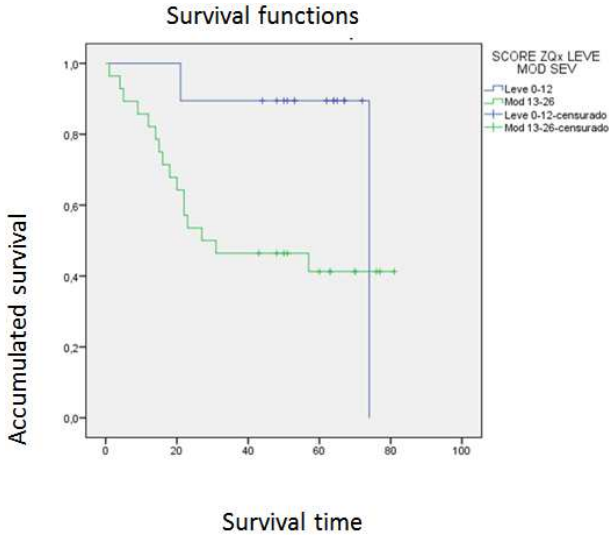

Figure 5. *Survival according to PCI obtained in surgery.*

(4). Survival according to histological type: we analyzed the probability of survival of patients with peritoneal carcinomatosis malignant according to the histological type grouping in serous, differentiated and undifferentiated anaplastic, with an average of disease-free survival of 49, 69 and 69 months respectively, not being these differences were statistically significant ($p < 0.05$).

5. Discussion

In our study, the correlation of Pearson showed there is a moderate correlation between the findings of the PCI obtained in the CT and surgical findings, appreciating a general low correlation in all regions, although the better results belong to regions 1, 2, 0 and 10. Also we observed a lower survival to greater PCI regarding carcinomatosis index in both CT and surgery. All patients received systemic chemotherapy before surgery, so its effect on the size of the peritoneal implants could explain the low correlation.

There are very few published studies about the correlation between surgical and radiological results in ovarian PC. This may be due to the extent of the peritoneal carcinomatosis has always been considered difficult to evaluate preoperatively by CT and especially before technological development of the image methods. Some years ago, precise evaluation was necessary during the surgery because there were not enough reliable imaging studies.

Nowadays, with multidetector CT, we can obtain images to assess for subcentimeter implants and to create three-dimensional images. Multiplanar images can be used as a problem-solving tool to confirm the presence of implants and to assess areas that can be difficult to evaluate on axial images [9].

That is the reason because although there are other techniques that can also be used for the evaluation of peritoneal carcinomatosis, as MR or PET-CT, the technique usually employed is CT [15].

Our study results indicate better correlation between surgical and radiological peritoneal carcinomatosis indexes in the higher regions (especially on the right side and not so good on the left). The lower values were obtained in both iliac fosses maybe because in those spaces are difficult to distinguish from bowel loops. The same findings have been demonstrated in the articles reviewed.

Duhr et al [16] conclude that there is higher correlation in the upper and middle abdominopelvic regions compared to the lower region and the smaller bowel. In the smaller bowel they have obtained lower levels of correlation (less than 0.6) and sensitivity below 70%. The best evaluated regions were left flank (4) with 100% sensitivity, right lower (7) and right flank (8) with 96% and left lower (5) with 93%. The lowest sensitivity in this study is for smaller bowel (50%).

The detection of implants is also influenced by the frequency of implants in each of the spaces. In our study, spaces with most demonstrated lesions were pelvis and subdiaphragmatic space. In Chandrashekhara et al. [17] the most common sites of abdominal deposits were the right subdiaphragmatic space, greater omentum and the pouch of Douglas. The same results were obtained in the Buy et al study [18].

As it is described in literature we have also noticed that the use of reformatted coronal and sagittal images can be so helpful to detect lesions in certain regions as liver dome, right and left hemi diaphragms, mesentery and the pelvis because here it could be difficult to define lesions looking only at transverse images [19]. For example, sagittal images allow assessment of the vaginal cuff, cul-de-sac, peritoneal surface of the bladder and rectosigmoid. Axial oblique and coronal images can be used to evaluate the region of the uterosacral ligaments and pelvic side wall. The paracolic can also be evaluated on coronal images for small implants near the bowel surface.

Returning to the subject of the importance of lesion size for detection, some the majority of investigators agree that CT is not so useful for detecting a low-volume tumor. The sensitivity of CT in detecting peritoneal metastases for tumoral implants of 1 cm in diameter or greater is not significantly different from surgery results. For lesions less than 1 cm the sensitivity of CT is significantly worse [20].

It has further been shown that the usefulness of CT in the detection of peritoneal carcinomatosis depends on the primary type of tumor. It has been demonstrated better correlation in ovarian and colorectal carcinoma but worse in mesenterium and small bowel among others.

The PCI is the most commonly used staging system for PC, and also an independent prognostic indicator for long-term outcomes. The French multiinstitutional study confirmed the importance of PCI in the prognosis of colorectal peritoneal metastases, being a 50% survival with a PCi 1-6, 25% survival with a PCI of 7-12 and 13-19 and only 10% survival at 5 years with a PCI greater than 19 [21].

In the study of Tentes et al, patients with a peritoneal cancer index lower than 10 had a significantly better survival than those with a PCI greater than 10 [22].

In peritoneal carcinomatosis from gastrointestinal cancer, Harmon and Sugarbaker observed some cases of low PCI score is recorded in the presence of invasive cancer at a crucial anatomic site. Even thought the PCI is low, a complete cytoreduction may not be possible. In these cases, invasive cancer at a crucial anatomic site places the patient into the same category as would systemic metastases [23]. We must be careful in assessing the CT in case of low PCI in ovarian peritoneal carcinomatosis to performed a correct staging of the invasive cancer.

Related to histopathology, numerous studies show that tumor-grades of more importance. It is believed that mucious or endometrioid tumors have more favorable prognosis than serous tumors that are more aggressive [24, 25].

We can find some limitations of our study that we must discuss. In the first place, the type of study is retrospective, although all studies of CT were re-evaluated prospectively. The fundamental limitation to assess the existing corrrelacion between pre- and postsurgical PCI is the systemic chemotherapy treatment given to the patients after the study of image that influence the intraoperative findings.

6. Conclusions

The peritoneal metastases are the most common form of manifestation of ovarian cancer. It has always been considered difficult to assess findings by surgically pre image; however, the development of the CT has improved

detection of these injuries. At present we can consider that it is a useful tool for the planning of the surgery and the preoperative treatments.

Our findings indicate that there is a good correlation between the findings obtained in CT and surgery in a global way, although when we look at regions of PCI, the findings are not significant in the most regions. If is found abdominal regions in which the correlation is low, corresponding with the regions adjacent to the small intestine, probably due to the difficulty in differentiating between adjacent implant or located in the wall of the handle. On the other hand the score obtained in both CT as in surgery, is a good predictor of the overall survival and disease-free survival, both being lower than the highest score.

In the future we will have to increase the sample of our study for best results of statistical significance. We should also consider the need to perform a second CT to the patients between the administration of systemic chemotherapy and surgery, provided by valuing the cost-benefit in terms of radiation dose, to improve the correlation between PCI CT and surgery.

The peritoneal cancer index is a significant index of survival in ovarian cancer patients and by using PCI a detailed evaluation of the peritoneal spread is possible being useful as a prognostic factor.

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