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The Utility of Diagnostic Laparoscopy in Patients Being Evaluated for Cytoreductive Surgery and Hyperthermic Peritoneal Chemotherapy

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Background: To assess the role of diagnostic laparoscopy (DL) to evaluate candidates for optimal cytoreduction surgery of peritoneal carcinomatosis (PC) combined with hyperthermic intraperitoneal chemotherapy in a consecutive series.

Methods: The characteristics of 31 patients undergoing DL between August 2012 and October 2016 for a diagnosis of PC secondary to digestive neoplasms were retrospectively reviewed.

Results: Laparoscopic evaluation was successful and well-tolerated in 100% patients (N = 31). In 17 patients (54.8%) the PC was deemed unresectable. A cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy was performed in 10 of 12 patients with PC considered resectable at laparoscopy wity a positive predictive value of 83.3%. One patient was diagnosed with more extensive disease than that as assessed by the DL at the time of laparotomy and 1 patient elected not to have further surgery. There were no port-site recurrences and morbidity at mean follow-up of 19.3 months.

Conclusions: Laparoscopic assessment of PC is a useful tool to assess the complete resectability of peritoneal surface disease in patients for whom there is inadequate information concerning disease extent. DL also helps selected patients to avoid an unnecessary laparotomy.

Key Words: diagnostic laparoscopy, peritoneal surface malignancy, carcinomatosis, hyperthermic intraperitoneal chemotherapy, cytoreductive surgery

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Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) has emerged as an attractive treatment option for selected patients with peritoneal carcinomatosis (PC).[1] The task of preoperative imaging is to determine accurate extension of peritoneal disease, stratifying patients who are good surgical candidates from those who may be candidates for systemic chemotherapy in an attempt to reduce tumor burden. Currently, noninvasive methods such as computerized tomography (CT), magnetic resonance imaging, and positron emission tomographic (PET) scans often fail to accurately assess the extent and potential resectability of the disease because they rely on tumor volume density and typically PC has a low volume density.[2,3]

The most reliable way of assessing tumor severity is to visualize it directly. Unfortunately, this necessitates an unnecessary exploratory laparotomy where the disease is found to be unresectable and the CRS-HIPEC procedure has to be abandoned. Laparoscopic exploration of the abdomen supplements the information provided by the imaging techniques and enables direct visual assessment of peritoneal involvement with an outpatient and low-risk procedure. It has been established that laparoscopy is associated with less pain, shorter hospitalization, and quicker time to recovery in comparison with laparotomy.[4] Despite these advantages, there are some limitations associated with laparoscopy. For example, is technically difficult to evaluate patients with extensive prior surgery and lymph node involvement in the retroperitoneal space. However, the Peritoneal Cancer Index (PCI),[5] which is considered the most accurate system for staging PC from different primary tumor types based on quantification and distribution of peritoneal implants, can be assessed with laparoscopy.[6,7] There is as yet no general agreement with regard to the routine use of diagnostic laparoscopy (DL) in patients with peritoneal surface disease.

In this study, we report our single institution experience with DL in the assessment of patients with peritoneal surface metastases being evaluated for possible CRS-HIPEC.

METHODS

A retrospective review of patients treated with explorative laparoscopy for PC at the University of California, Irvine Medical Center (Orange, CA) between August 2012 and October 2016 was performed. This study was approved by the Internal Review Board (IRB) of the University of California, Irvine.

The Sugarbaker PCI score was used as the frame of reference for the description of the extent of peritoneal dissemination at surgical exploration (surgical PCI score).[5] No standard scoring system exists for the evaluation of PC on CT.[8]

Chart review was performed on all patients urdergoing DL for PC. Patient demographic, preoperative imaging, diagnostic findings, and postoperative outcomes were reviewed.

Positive predictive value (PPV) was determined for DL. This was defined as the number of patients who achieved complete cytoreduction and HIPEC among the number of patients deemed to be eligible for complete cytoreduction by laparoscopy who underwent surgery.

Surgical Technique

We used the standard Veress needle on the left upper quadrant to establish a pneumoperitoneum of 15 mm Hg under general anesthesia. A 5-mm trocar was inserted through a vertical supraumbilical incision. The 30-degree laparoscope was introduced for the examination of the abdominal and pelvic cavities. One or 2 more trocars of 5 mm were placed, under direct vision, in the midline, 5 cm below and above the first port. The midline laparoscopy trocar-site wounds were resected at the time of the laparotomy.

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The authors declare no conflicts of interest.

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TABLE 1. Preoperative Characteristics

Variables	N (%)
Sex	
Male	21 (67.7)
Female	10 (3.3)
Age (median [range]) (y)	54.2 (13-74)
BMI (median [range]) (Kg/m²)	24.8 (16.5-34.1)
Primary site	
Appendix	16 (51.6)
Colorectal	8 (25.8)
Gastric	4 (12.9)
Unknown	2 (6.5)
Jejunal	1 (3.2)
Preoperative chemotherapy	
Yes	25 (80.6)
No	6 (19.4)
Evidence of disease by imaging	
Yes	26 (83.9)
No	5 (16.1)

BMI indicates body mass index.

RESULTS

Our analysis included 31 patients, 21 male individuals (67.7%) and 10 female individuals (32.3%), with a mean age of 54.2 ± 15.3 years (range, 13 to 74) and a mean body mass index of 24.8 ± 4.7 kg/m² (range, 16.5 to 34.1) Table 1. The most prevalent primary tumor type was appendiceal (51.6%), followed by colorectal (25.8%), gastric (12.9%), unknown (6.5%), and small intestine (3.2%). The presentation of PC was synchronous in 22 (71%) and metachronous in 9 (29%) patients. Primary tumor resection before CRS was performed in 19 patients (61.3%) overall. The median interval between primary tumor resection and the DL was 48.8 months (range, 5 to 204). Complete laparoscopic evaluation was possible in all 31 cases (Fig. 1). Seventeen (54.8%) patients were excluded from subsequent laparotomy for CRS-HIPEC because of extensive disease and/or significant small bowel involvement. Twelve patients (38.7%) were deemed good candidates to CRS-HIPEC. In 1 case the patient elected not to be resected and to be treated with intraperitoneal chemotherapy infusion. Laparotomy was performed in 11 patients. CRS-HIPEC achieving complete cytoreduction was completed in 10 cases. There was 1 patient diagnosed of unresectable disease at the time of laparotomy, therefore the case was aborted. The PPV of laparoscopy to predict the ability to achieve complete cytoreduction was 83.3%. Two patients with PCI > 20 were included for CRS-HIPEC. One of them had a peritoneal disease of gastric origin and died 10 months after surgery and the other one had a peritoneal disease of unknown origin and is disease free.

A CT was performed before DL in 22 patients, magnetic resonance imaging in 3 and PET/CT in 9 patients. Combined imaging modalities were performed in 3 patients. There was mismatch between imaging and laparoscopy in 5 patients (16.1%), 3 of them with a CT performed before DL and 2 of them with a PET/CT. DL revealed peritoneal disease in these patients despite negative findings on imaging (PCI > 20 in 4 patients and PCI 3 in 1 patient). There were no complications and mortality after DL and median length of hospital stay was 12 hours. There were no port-site recurrences at mean follow-up of 19.3 months.

DISCUSSION

Laparoscopy is increasingly being used as a diagnostic tool. It is a promising means in the workup of patients with peritoneal surface malignancies, providing direct access to the peritoneal cavity and therefore allowing better evaluation of disease. It is important to remark that exploratory laparotomy carries a significant risk of morbidity and mortality in this frail population and postpones the initiation of palliative chemotherapy. In this study, we found laparoscopy to be a safe procedure with no morbidity or mortality in a high-risk population. Laparoscopy was successfully completed in all 31 cases (100%), with 100% accuracy in identifying patients with peritoneal metastases. Among these, 12 patients (38.7%) were amenable to complete cytoreduction and 17 (54.8%) with peritoneal disease found at the time of laparoscopy were not deemed candidates for complete cytoreduction, thereby avoiding an unnecessary high rate of laparotomy. Different series showed that laparoscopic staging helped to exclude between a 7% and 41% patients with disease not amenable for CRS from an unnecessary laparotomy, increasing this rate to 54.8% in our series. It's true that this one is a small series but certainly there are no many works showing results about this matter. In addition, this series includes just patients diagnosed of PC with colorectal, appendicial, and gastric origin, excluding other peritoneal surface malignancies like ovarian, mesothelioma, or pseudomyxoma peritonei.

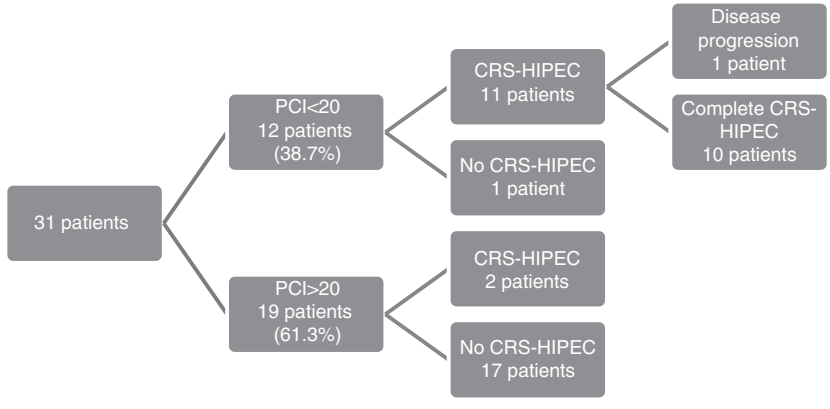

Figure 1. Patients distribution. CRS-HIPEC indicates cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy; PCI, Peritoneal Cancer Index.

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TABLE 2. Literature Review of Diagnostic Laparoscopy Before Cytoreduction Plus Hyperthermic Intraperitoneal Chemotherapy

References	N	Predictive Positive Value (%)	Avoid Unnecessary Laparotomy (%)
Pomel et al[11]	11	87.5	27.3
Garofalo and Valle[12]	197	96.5	34
Iversen et al[13]	45	63	40
Jayakrishnan et al[14]	73	85.4	24.7
Marmor et al[15]	145	82.8	49.6
Present study	31	83.3	54.8

Although there are no reported negative consequences of laparoscopy when histologic confirmation is needed, some controversy exists about its routine use for staging purposes, especially with regard to the possibility of providing more information about actual disease extent compared with noninvasive diagnostics. A study by Denzer et al[9] reported that DL detected PC in 100% of the treated cases, whereas only 47.8% had been revealed by a CT scan previously performed on the same patients. Our study confirms this finding, but in our series diagnostic imaging is more accurate: DL detected PC in 100% of the treated cases while only 83.8% had been revealed by a previous imaging.

In 2006, the results of a survey reported at the Fifth International Workshop on Peritoneal Surface Malignancy with regard to consensus on preoperative investigations[10] showed that laparoscopy was fundamental in 9.4%, useful in 78.1%, and useless in 12.5% of cases by a worldwide expertise panel. Nevertheless, some recent reports emphasize the efficacy of DL to predict resectability and optimal CRS, achieving a PPV for resectability ranging from 63% to 96% of cases (Table 2). Pomel et al[11] achieved complete cytoreduction in 7 of 8 patients who were considered resectable by laparoscopy. In the remaining patients, there was an underestimation of the extent of the disease. Garofalo and Valle[12] used videolaparoscopy to stage 197 cases of peritoneal carcinomatosis and achieved full laparoscopic PCI assessment in 196 of 197 (99.49%) cases, and only 4 of 197 (2.03%) cases were understaged before the routine use of laparoscopic ultrasound. Ninety-eight patients underwent CRS-HIPEC, and laparoscopic evaluation excluded 67 patients from further surgery. Iversen et al[13] concluded that DL was valuable in preoperative evaluation of the extent of peritoneal carcinomatosis and improved patient selection for CRS-HIPEC with a PPV value rising from 56% to 63% comparing laparotomy versus laparoscopy. This was confirmed by Jayakrishnan et al[14] who reported CRS-HIPEC was performed in 85.4% with previous DL versus 74.2% with exploratory laparotomy. They concluded that laparoscopy is a feasible technique for selecting patients with PC for CRS-HIPEC. Finally, Marmor et al[15] had the same conclusion with a PPV 82.8%.

Despite the poor clinical conditions of patients with PC, complication grade and rates are low in literature reports after laparoscopy.[16] Trocar-site metastasis after a laparoscopic approach for removing various intra-abdominal tumors has been reported at about 1.18%.[17] However, no clear data are available with regard to trocar-site metastases after a diagnostic or staging laparoscopy in patients with PC for whom a higher incidence would be expected due to the presence of malignant ascites in 60% of cases, which is considered a predisposing factor for their development.[18–20] Among the 31 patients in our series who underwent a diagnostic or staging laparoscopy, no one developed trocar-site metastases. As excision of port-site metastases is difficult, it is therefore being recommended to use the least possible number of trocars and, if possible, place them all in the midline.[13]

The use of laparoscopy seems to be growing and is routinely used in many centers, even if no clear data or prospective randomized trials are available to support its use in patients with peritoneal metastases from different tumor types. Laparoscopy seems, instead, to play a relevant role in predicting resectability in PC and to evaluate the efficacy of the increasing use of aggressive neoadjuvant intraperitoneal and systemic chemotherapy.[21]

This study has several limitations due to its retrospective design at a single institution. In addition, patients with disease judged not resectable at laparoscopy did not have an exploratory laparotomy. This approach carried the potential risk that possible candidates for CRS-HIPEC whose disease was overstaged by laparoscopy might have been denied treatment. However, we think this risk is minimal as PC is more likely to be understaged by laparoscopy. Anyway, when we perform a laparoscopy and the patient is deemed not to be candidate for debulking, usually this patient start a chemotherapy treatment, we reevaluate the chemotherapy response with imaging and if there is a goos response we can perform a DL again to check if actually this patient could have been debulked after chemotherapy.

The main indications for DL surgery are to confirm the presence of peritoneal metastases when other imaging techniques give uncertain results and to obtain tissue samples for histopathologic study for diagnosing the primary tumor if it is unknown. In addition, laparoscopy permits us to evaluate intra-abdominal tumor spread, assess resectability, to predict optimal CRS in primary and recurrent PC and to assess response to neoadjuvant/adjuvant chemotherapy. Laparoscopy may obviate the need for unnecessary laparotomy in many cases and may, therefore, contribute to a better quality of life for patients found to have unresectable disease. For preoperative staging, further prospective controlled studies are needed to confirm the potential indications and efficacy of laparoscopy compared with other noninvasive diagnostic tools while considering its risks and possible complications.

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