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Port site metastases after minimally invasive resection for colorectal cancer: A retrospective study of 13 patients

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ABSTRACT

Background: Minimally invasive surgeries are increasingly being performed for primary colon cancer resections since laparoscopic and robotic surgeries have less post-operative pain, shorter length of hospitalization, less morbidity, improved patient satisfaction and equivalent R0 resection rates compared to laparotomy.
Methods: To analyze characteristics of patients who developed port site metastases after minimally invasive colectomy, a retrospective case series of a single institution from 2004 to 2017 was performed. The study included patients who had a minimally invasive resection of the primary colon cancer and subsequent cytoreduction and heated intraperitoneal chemotherapy (CRS/HIPEC) for peritoneal metastases. Patient characteristics, histology, pathology, prior treatments, time between surgeries, carcinoembryonic antigen (CEA) levels and survival were reviewed.
Results: There were 123 patients who had CRS/HIPEC and 13 of them had a history of laparoscopic or robotic colectomy followed by the development of port site disease. Four were females, nine were males. Median age was 48 years (range, 19–64). Eleven of 13 primary colon cancers were T3 or T4. Ten of 13 patients had no clinical evidence of peritoneal metastases at the time of initial resection. All 13 patients had metastatic deposits at port sites that were confirmed histopathologically at the time of CRS/HIPEC.
Conclusions: Port site metastases were present concomitantly with peritoneal metastases in 13 patients. An advanced T-stage of disease occurred in 85% of patients. Port site metastases do occur after minimally invasive colon resection.

1. Introduction

Primary colon cancer can be surgically resected by open or minimally invasive techniques. Both open and minimally invasive techniques have been shown to have equivalent oncologic outcomes. The use of minimally invasive resection for primary colorectal cancers has increased since its advent in the 1990s. The University Health System Consortium which includes more than 300 academic hospitals in the United States estimated that 40–50% of colon resections are attempted laparoscopically and 16% are converted to open surgery [1].

When colorectal cancer has metastasized to the peritoneal cavity, the 2018 National Comprehensive Cancer Network Guidelines (NCCN) recommends evaluation of patients who may be candidates for cytoreduction surgery (CRS) and intraperitoneal chemotherapy [2]. Management strategies for peritoneal metastases are an important treatment modality because the peritoneum is the second most common site of recurrent disease [3]. Candidates for CRS and intraperitoneal chemotherapy should have good performance status and limited metastatic disease that can be completely resected. Only experienced centers should perform treatments for colorectal peritoneal metastases [2]. Patients may demonstrate microscopic or gross peritoneal disease at initial operation. At initial operation, 20% have positive peritoneal cytology [4] and 7% have synchronous peritoneal carcinomatosis [3].

The first laparoscopic surgery in the United States was performed in 1911. More specifically, laparoscopic appendectomy and cholecystectomy first occurred in Germany in 1981 and 1985 respectively [5]. A decade later, colectomy was first performed by a laparoscopic-assisted approach [6]. During the 1990s, laparoscopic surgery was still in its infancy and there was a concern for a 20% incidence of port-site metastases and consequently an avoidance of minimally invasive resections for malignancy [7]. There have been reports of port site metastases after laparoscopic and robotic resections for a variety of tumors

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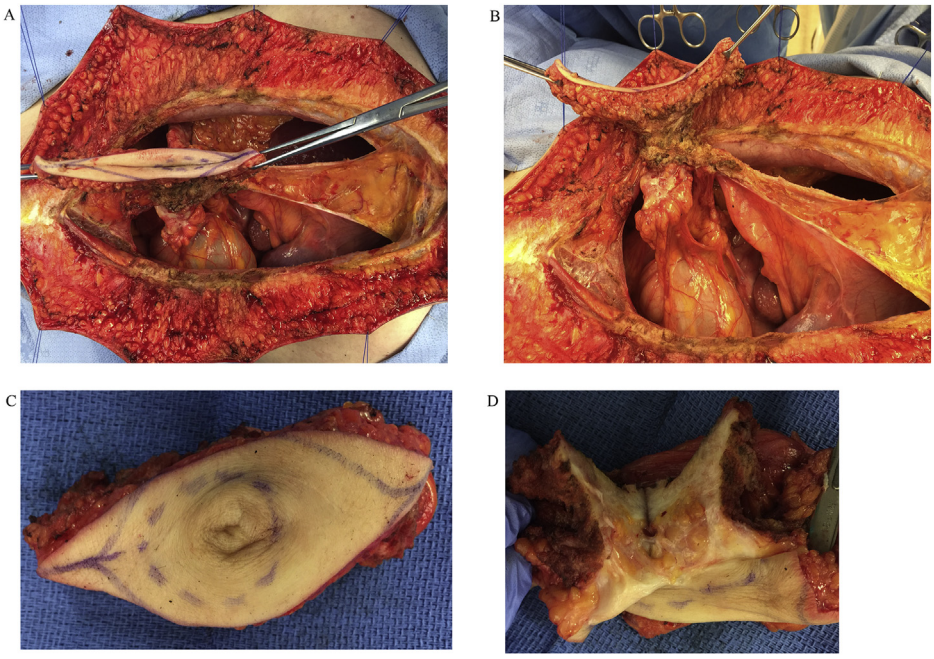

Fig. 1. Intraoperative CRS/HIPEC photographs of a tumor at the umbilical port site from prior laparoscopic colectomy. (A–B) The midline abdominal incision is opened and tissue containing the umbilical port site is completely resected. (C–D) The skin and subcutaneous tissue at the umbilical port site is opened revealing full thickness penetration of the abdominal wall by adenocarcinoma.

including gastric, bladder, cervical, endometrial, ovarian, prostate, hepatocellular, and neuroblastoma [8–17].

In these early studies port site metastases were thought to be the result of the surgeon's learning curve in a new minimally invasive technology. Later studies have shown that port-site metastases occur in about 1% of patients after minimally invasive resection which is similar for open resections [18–21]. Since then, multiple prospective randomized controlled, multicenter trials, and meta-analyses have reported the non-inferiority of minimally invasive surgery compared to the open approach [22–32]. However, a meta-analysis of 2493 patients reports that laparoscopic converted to open resection has a higher risk of local recurrence [33] that may be a reflection of a larger tumor that is difficult to resect with minimal access surgery. Likewise, the long term outcomes of the CLASICC trial may favor open surgery in patients with stage III colon cancer [26]. However, there is overwhelming data of the benefits of laparoscopic surgery versus open with current utilization of laparoscopy surgery increasing and will likely continue to rise.

This report documents that port site metastases continue to occur. It is a retrospective review of a highly selected patient population and cannot give an accurate incidence of port site metastases. However, an analysis of the clinical and pathologic characteristics may suggest selection criteria that may identify patients who may be at increased risk of port site metastases.

2. Methods

This was a retrospective study of patients who had undergone CRS/HIPEC at MedStar Washington Hospital Center between 2004 and 2017. Institutional Review Board approval was obtained and there was no need to consent individual patients due to the retrospective nature of the study. These patients had been diagnosed with peritoneal metastases and referred to this institution. Patients were included if they had peritoneal metastases from colorectal cancer, had undergone a minimally invasive resection of their primary tumors and were shown to have port site metastases. This included laparoscopic and robotic resections. Patient characteristics, histology, pathology, prior treatments, and carcinoembryonic antigen (CEA) levels were reviewed from the medical record. The peritoneal cancer index score (PCI) was determined using the distribution and extent of peritoneal metastases at 13 abdominopelvic regions [34]. It varied between 0 and 39 and was determined at the time of the abdominal exploration. In some patients information regarding the distribution and extent of disease was added to the PCI assessment as the cytoreduction proceeded. The completeness of cytoreduction score (CC score) was determined at the completion of CRS. The CC score recorded no visible evidence of disease (CC-0), tumor nodules less than 2.5 mm (CC-1), between 2.5 and 5.0 cm (CC-2), and greater than 5 cm (CC-3) [34].

3. Results

There were 123 patients with a primary colorectal cancer who had CRS/HIPEC. All the patients were referred from an outside facility after being diagnosed with peritoneal metastases. There were no internally referred patients. These patients had undergone open resection (n = 109) or minimally invasive resection (n = 14) of the primary tumor. All but one patient with a minimally invasive resection had a port site metastasis (n = 13). The one patient with a minimally invasive resection without a port site metastasis had a laparoscopic converted to open resection for the primary tumor. The patients with port site metastases had laparoscopic (n = 12) or robotic (n = 1) resections. Fig. 1 shows intra-operative photographs of a patient with port site metastasis resected at the time of CRS/HIPEC.

Characteristics of these 13 patients were analyzed. The mean age was 45 years (range, 19–64). There were 4 females and 9 males. The locations of the primary tumors were in the right colon (n = 9), transverse colon (n = 1), and left colon (n = 3). These 13 colon tumors were adenocarcinoma with mucinous (n = 8) or signet ring (n = 5) histology. Mean (and median) time between initial resection of the primary tumor and CRS/HIPEC was 24 (22) months (range, 10–52).

Our patients had a mean PCI of 22 (range, 9–29). The patients had CCR 0–1 (n = 9) or CCR 2–3 (n = 4). Patient characteristics are summarized in Table 1.

Tumor staging was available in 12 and nodal staging available in 11 patients. Patients had T2 (n = 1), T3 (n = 6), and T4 (n = 5) disease. Nodal staging consisted of N0 (n = 2), N1 (n = 5), and N2 (n = 4) disease. At the initial colectomy, there were 3 patients with peritoneal spread and 10 patients without known carcinomatosis. The stages at initial resection were Stage II (n = 2), Stage III (n = 7), and Stage IV (n = 2).

CEA level may be elevated in colorectal cancer and can be used as a

Table 1
Clinical and pathologic characteristics.

Sex	(n)	%
Male	9	69.2
Female	4	30.8
Age	**years**	
Range	19–64	
Mean	45	
Median	48	
Initial Resection	**(n)**	**%**
Laparoscopic colectomy	12	92.3
Robotic colectomy	1	7.7
Time between initial resection and CRS + HIPEC	**months**	
Range	10–52	
Mean	24	
Median	22	
Primary tumor location	**(n)**	**%**
Right colon	9	69.2
Transverse colon	1	7.7
Left colon	3	23.1
T stage	**(n)**	**%**
T4	5	30.8
T3	6	46.2
T2	1	7.7
Unknown	1	7.7
N stage	**(n)**	**%**
N2	4	30.8
N1	5	38.5
N0	2	15.4
Unknown	2	15.4
M stage	**(n)**	**%**
M1	3	23.1
M0	10	76.9
Overall stage	**(n)**	**%**
IV	2	15.4
III	7	53.8
II	2	15.4
Unknown	2	15.4
Tumor differentiation	**(n)**	**%**
Well-differentiated	2	15.4
Moderately-differentiated	4	30.8
Poorly-differentiated	2	15.4
Unknown	5	38.5
Histology	**(n)**	**%**
Adenocarcinoma	13	100.0
Mucinous	8	61.5
Signet ring	5	38.4
Peritoneal carcinomatosis index (PCI)	**(n)**	**%**
0–17	4	30.8
> 17	9	69.2
Completeness of cytoreduction (CC)	**(n)**	**%**
0–1	9	69.2
2–3	4	30.7

marker for response to treatment and recurrence. Fig. 2 demonstrates CEA level (when available) for patients 1–7 days prior to CRS/HIPEC and post-operatively. The CEA levels decreased post-operatively after CRS/HIPEC in 11 of 13 patients (see Fig. 3).

The median survival of these 13 patients from the time of colon cancer resection was 42 months and from CRS/HIPEC was 19 months. Currently, 1 patient is free of disease 172 months from CRS/HIPEC and another alive with disease at 16 months.

4. Discussion

All patients who have a resection of a colon cancer by laparotomy or by minimally invasive technology are at risk for peritoneal metastases. This group of 13 patients shows that patients who have undergone minimally invasive resection for colon cancer can develop peritoneal metastases at port sites. The limitations of these findings are several. This study was retrospective and includes a highly selected patient population at one institution. Patient selection was biased since patients were referred from outside institutions. Due to the patient referral pattern and retrospective nature, the incidence of port site metastases after minimally invasive colectomy could not be determined. The population size studied was also small and statistically significant associations would not be possible to calculate.

These data cannot definitively determine the cause and effect relationship between the primary tumor and the port site metastases. There may be an association with port site metastases and greater T stage in that all but 1 patient had T3 or T4 tumors. Carcinomatosis at the time of primary cancer resection (3 patients) was not a requirement for subsequent port site metastases (13 patients). There may be occult carcinomatosis or positive peritoneal cytology that was not identified at the time of initial surgery that causes the port site metastasis. Previously published literature was concerned that port site metastases were related to minimally invasive operative technique, tumor manipulation, or carbon dioxide insufflation. The role of the surgical technology as a cause of peritoneal metastases versus an aggressive tumor biology causing an unavoidable peritoneal dissemination cannot be determined from these data. There are several ongoing randomized controlled trials examining the use of HIPEC for T3 and T4 colorectal tumors to reduce peritoneal metastases. Also, a comparison of surgical outcomes of higher T-stage resections by open versus laparoscopic resections [35].

The data shown in Table 1 may be interpreted to suggest that the presence of a port site metastasis should be considered a manifestation of peritoneal metastases. The presences of port site nodules should be aggressively investigated since there is a high likelihood of concomitant peritoneal metastases. In our study population of colorectal cancer patients with peritoneal metastases who had a minimally invasive resection (n = 14), most had concomitant histopathologic confirmation of port site and peritoneal metastatic disease (n = 13) at the time of CRS/HIPEC. These data would suggest that if a patient is found to have a port site metastases from colorectal cancer, there should be a high index of suspicion that the patient also has peritoneal metastases at some site within the abdomen and pelvis until proven otherwise.

Our study confirms that port site metastases do occur and are seen concomitantly with peritoneal metastatic disease. Port site metastases should be regarded as a life endangering condition and not as a mass on

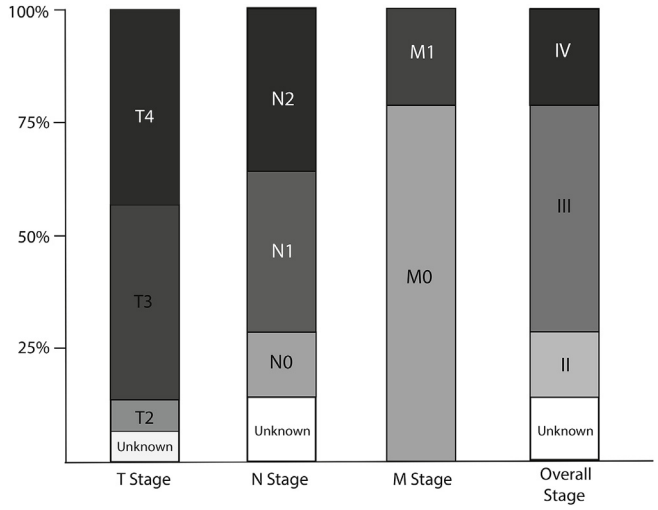

Fig. 2. TNM stage of primary cancer in 12 patients with port site metastases from colon cancer.

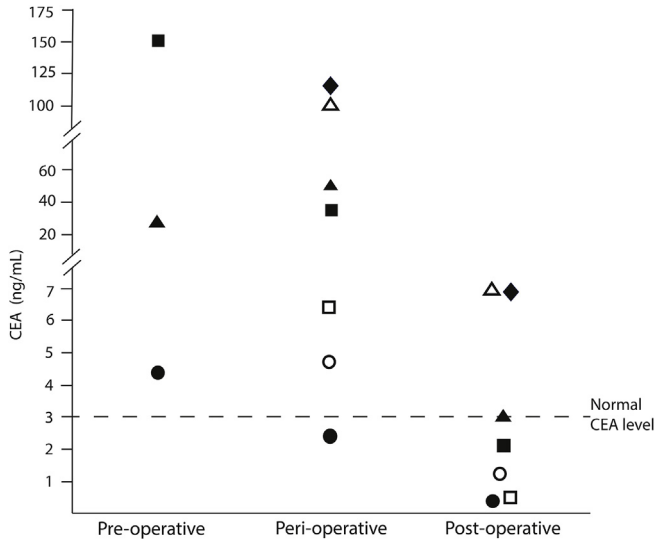

Fig. 3. Carcinoembryonic antigen (CEA) levels decreased after cytoreduction and heated intraperitoneal chemotherapy (CRS/HIPEC). CEA was measured pre-operatively (within 8 months prior to CRS/HIPEC), peri-operatively (within 24 h of CRS/HIPEC) and post-operatively (within 60 days post CRS/HIPEC). Each shape represents an individual patient.

the abdominal wall to be observed. The implications of this study of port site metastases might become clearer as more data becomes available. This may occur in the context of increased use of CRS/HIPEC for peritoneal metastases of colorectal cancer. Additionally, due to the referral pattern of CRS/HIPEC, the original minimally invasive surgeon may be unaware of the port site recurrence since they can occur years after primary resection. In an era of computerized medical records and global mobility, the occurrence and prevalence of port site metastases that occur with minimally invasive colon cancer resection can be further scrutinized.

Conflicts of interest

None declared.

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Author Contribution

All authors contributed equally to the manuscript including (a) conception/design, acquisition of data or analysis/interpretation of data, (b) drafting/revising article, (c) final approval of manuscript

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2019.02.008.

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