Laparoscopy in the Management of Peritoneal Carcinomatosis

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Abstract: The use of videoultrasoundoscopy in the assessment of peritoneal carcinomatosis extent is now universally accepted. This procedure allows us to define with certainty the origin of the neoplasm, the peritoneal cancer index (PCI), the involvement of the small bowel and its mesentry, the feasibility of surgery and the index of attainable cytoreduction, the evaluation of an eventual multimodality resection, and finally results in no mortality and very low morbidity.

The indications for laparoscopy are as follows: staging of the carcinomatosis already diagnosed with imaging (CT scan and MRI), staging of carcinomatosis of dubious origin (biopsy), restaging after neoadjuvant chemotherapy, restaging during follow-up in the case of dubious imaging, and restaging after adjuvant chemotherapy.

Open (Hasson) technique has always been used in the introduction of the first trocar, and the changing position of the surgical bed allows for the evaluation of all the abdominal quadrants, limiting viscerolysis to the essential minimum to avoid iatrogenic lesions. Associating the intraoperative ultrasound allowed us to reduce understaging of lesions at the depth of the diaphragm, of hepatic metastases and neoplastic masses at the pancreatic tail, and of the omental retroevacuity.

In all the cases in which diagnostic laparoscopy was followed by peritoneotomy, we found a good correlation between open surgery data and the laparoscopic PCI. We excluded patients from peritoneotomy if the staging laparoscopy showed a significant involvement of the small bowel or mesentry.

We used videoultrasoundoscopy to stage 197 cases of peritoneal carcinomatosis and achieved full laparoscopic PCI assessment in 196 of 197 (99.49%) cases, whereas only 4 of 197 (2.03%) cases were understaged before the routine use of laparoscopic ultrasound. Four complications were observed: 2 cases (1.02%) involved an infection of the trocar insertion site, which was treated with antibiotic therapy, and 2 cases (1.02%) involved diaphragm perforation and intraoperative bleeding, respectively, both resolved with videoultrasoundoscopic technique. Two trocars were sufficient in 184 of 197 cases. There was no mortality and no port site metastasis.

More recently, we have used videoultrasoundoscopic surgery in the treatment of neoplastic ascites that did not respond to chemotherapy for palliative purposes, which resulted in the total disappearance of the ascites. It is now possible, in light of acquired experience, to evaluate with precision the indications, the technique, and the limits of the method both in the assessment of the carcinomatosis extent and in its palliation. In 28 cases of neoplastic ascites nonresponsive to chemotherapy, we were able to implement fully laparoscopic hyperthermic chemotherapy for the palliative treatment of the ascites, with total disappearance of it in all cases. The 1-hyperthermic intraperitoneal chemotherapy was carried out at 42°C for 90 minutes with 1.5% dextrose solution as a carrier. The chemotherapy solution was cisplatin and doxorubicin, or mitomycin, depending on the type of primary tumor. The drains were left in place and were removed when profuse drainage ceased.

Ascites were controlled in all treated cases. A computed tomography scan performed in follow-up showed a small, clinically undetectable, fluid accumulation in the pelvis of 1 patient. Neither mortality nor morbidity was observed in connection with the procedure.

Key Words: peritoneal carcinomatosis, staging, staging laparoscopy, refractory ascitis, intraperitoneal hyperthermic chemotherapy


The greatest problem in handling a patient affected with peritoneal carcinomatosis is carrying out a correct preoperative assessment of carcinomatosis extent before engaging in an extremely complicated surgical procedure that entails high rates of complications and mortality, even after a simple explorative laparotomy.

From the beginning of our experience, we found it necessary to integrate information deriving from diagnostics of videoultrasoundoscopic staging that resulted in a correct assessment of patients, the peritoneal cancer index (PCI) definition and, above all, the possibility of deciding the feasibility of a complete cytoreduction (CCO) procedure with the aim of bringing patients to a postoperative CCO stage. By using this methodology many patients were excluded from treatment [peritonectomy + hyperthermic intraperitoneal chemotherapy (HIPEC)] because more than 2/3 of the small intestine was affected or because of extremely high PCI: the patients excluded at the first VLS of stadiation underwent VLS restaging after an average of 6 to 8 cycles of systemic neoadjuvant chemotherapy. A small series of patients affected with neoplastic ascites who did not respond to chemotherapy, in very advanced stages of the disease, were treated with completely videoultrasoundoscopic palliative hyperthermic chemotherapy.

LAPAROSCOPY IN THE STAGING OF PERITONEAL CARCINOMATOSIS

Before submitting a peritoneal carcinomatosis to peritoneotomy with HIPEC, it is necessary to assess the prognosis and feasibility. It is therefore fundamental to pre-emptively know the following with accuracy:

- Origin of the tumor,
- PCI,
- Degree of involvement of the small bowel and its mesentry, and
- Number and extension of the organ resection to perform.

Computed tomography scans and magnetic resonance imaging are routinely used in image diagnostics, which allow for a good evaluation of omental cake and show the presence of tumor masses larger than 5mm, but they do not quantify the extension of the disease in the small bowel and its infiltration into the mesentry. Imaging diagnostics does consent us to exclude approximately 20% of patients with extraregional disease from the procedure. A recent study by Denzen et all demonstrates how a peritoneal carcinomatosis was found in 100% of patients who underwent VLS, whereas
an earlier CT showed that only 47.8% were apparently affected (P < 0.1) (Fig. 1).

Only recently have studies been performed with 18F-fluorodeoxyglucose-positron emission tomography/CT in the staging of peritoneal carcinomatosis that carry an actual real sensibility of 88%. 3-4

Peritoneotomy with HIPEC has a notable impact on survival only in cases where a complete CC0/1 cyoreduction is performed. 5-9 Morbidity varies from 20% to 30% and mortality from 4% to 8%. 10-14

This is often found even only with an explorative laparotomy, as is demonstrated by Esquivel et al15 in his study that reports morbidity from 12% to 23% and mortality from 20% to 36% in advanced neoplasms treated only with laparotomy.

It is thus fundamental to propose peritoneotomy with HIPEC only to patients in which a cyoreduction to CC0/1 can realistically be performed with a clear and safe preoperative program. Video-laparoscopic stadiation allows for an evaluation of PCI and of the cyoreduction index with no mortality and with very low morbidity.

Methods

Abdominal Cavity Exploration

Once the Hasson trocar was placed, the ascites was completely suctioned out of the peritoneal cavity through the trocar, taking care not to contaminate the wall with ascitic fluid. It was preferable not to position the trocar on the median line or on the umbilicus as there is a high incidence of adhesions both from previous surgery and from tumor masses that may have infiltrated the median line. We preferred to position the trocar in the right or left iliac fossa on the midaxillary line after a clinical evaluation and sonogram of the quadrants. Access to the iliac fossa also allowed for a better view in the presence of an omental cake in the small intestine and the mesentery below, with the possibility to raise the omental cake using the trocar (5 mm) placed in the contralateral iliac fossa (port II). A 30-degree scope was routinely used, and by rotating the scope once inserted, a discretion of adhesions could be performed, therefore reducing visceroscopy to a minimum.

Adhesiolysis was performed at a minimum before the stadiation procedure to avoid the risk of lesion to abdominal organs but nonetheless allowing for a complete evaluation of the cancer index. It was preferable, in the case of tenacious adhesions or neoplastic infiltrations of the median line, to explore the right and left sections separately to avoid visceroscopy and to carry out a second open access to view the contralateral quadrants.

Cytology samples should be taken under direct view. Highly mucinous carcinomatosis sometimes required a 10-mm trocar in port II, so that a larger suction cannula could be used. In peritoneal surface malignancies where the histopathologic findings were unknown or doubtful, it was important to harvest multiple biopsy specimens from the parietal, omental, and pelvic cavity lesions. Diaphragmatic biopsies that can cause perforation and provoke infiltration of the muscular wall should be avoided. In cases where the presence of liver metastases or the involvement of suprahepatic veins was suspected, or in diaphragmatic lesions of more than 2 cm, intraoperative ultrasound imaging through the laparoscope might be useful.

To accomplish the laparoscopic definition of PCI, which is determined on the basis of the distribution and size of the neoplastic nodules, the operating table was moved into at least 4 positions: steep anti-trendelenburg left tilt, steep anti-trendelenburg right tilt, steep Trendelenburg left tilt, and steep Trendelenburg right tilt. 16,17

Results

From August 2000 to September 2008, we performed 197 diagnostic VLS procedures in patients with peritoneal surface malignancies (Table 1). The mean time needed for a diagnostic and staging VLS procedure was 30 minutes (range: 15/45 minutes). In one patient with gastric cancer, access to the abdominal cavity was impossible because of thick cancerous adhesions between the small bowel loops and the abdominal wall.

The patient was subjected to midline laparotomy, but the disease was not resectable because of massive involvement of the small intestine loops tightly adherent to the abdominal wall.

In 184 cases, 2 trocars (10 and 5 mm, respectively) were sufficient to carry out the procedure, whereas in 13 cases, it was necessary to add a third 10-mm trocar to gain full view of the abdominal cavity because of neoplastic adhesions located along the midline.

In 70 cases, the peritoneal surface malignancy was due to ovarian tumor, in 40 due to gastric tumor, in 35 due to a recurrent colorectal neoplasm, in 14 due to a pseudomyxoma peritonei, in 14 due to mesothelioma, in 6 due to neoplasm of the uterine cervix, in 6 due to abdominal sarcomatosis, in 5 due to recurrent pancreas neoplasm, in 1 due to peritoneal carcinomatosis to prostate neoplasm, in 1 due to intra-abdominal desmoplastic small round cell tumor, and in 9 due to the carcinomatosis was secondary to a primary breast tumor.

In 4 cases (2%), VLS understaged the carcinomatosis (mesothelioma, gastric cancer, pseudomyxoma, and ovarian cancer) and on laparotomy, massive infiltration of the pancreas was detected in gastric cancer and mesothelioma, which resulted in a CC2 peritoneomy. In the pseudomyxoma and ovarian cancer, the VLS cancer index was less than that confirmed by the PCI determined at surgical exploration, but it was nonetheless possible to carry out a peritoneomy with CC0 cyoreduction.

In 162 (82.2%) cases, advanced carcinomatosis was found with PCI >17. In fact, in 35 cases, PCI was range 0 to 13, in 13 cases 14 to 16, in 48 cases 17 to 23, in 53 cases, 24 to 33, and in 48 cases 34 to 39. Sixty-seven patients were excluded from surgical exploration because of massive infiltration of the small bowel or of its root seen by the VLS.

One hundred forty-one of 197 patients (71.5%) on whom we performed diagnostic VLS procedure had undergone at least 1 prior

<table>
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<th>VLS Unfeasible</th>
<th>Understaging</th>
<th>Trocar Infection</th>
<th>Diaphragm Perforation</th>
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Total                           | 197            | 196           | 1            | 4                | 2                     | 1                      | 184     | 13      | 6.60    |

Laparotomy. Ninety-eight (50.7%) patients were treated with a peritoneotomy and HIPEC. Four (2%) patients who were not eligible for a peritoneotomy because of massive infiltration of the small bowel and occlusion underwent a videolaparoscopic decompressive ileostomy.

As far as morbidity is concerned in videolaparoscopic surgical exploration, we observed 4 (2.08%) complications, of which 2 (1.04%) were intraoperative: one was a perforation of the diaphragm during biopsy, sutured with laparoscopic technique, one early postoperative bleeding treated with a blood transfusion, and 2 (1.04%) were delayed postoperative: infections of the trocar site, which were treated with topical antibiotic therapy. No neoplastic seeding was detected at the trocar sites, and all patients who underwent peritoneotomy procedures resulted negative to port site metastasis 10 to 40 days from the procedure. We observed no mortality.

LAPAROSCOPY IN THE TREATMENT OF REFRACTORY ASCITES

The use of laparoscopic assessment of carcinomatosis extent in the restaging of peritoneal carcinomatosis subject to adjuvant and neoadjuvant chemotherapy has allowed for, on the one hand, the use of a peritoneotomy procedure in patients with peritoneal carcinomatosis responding to neoadjuvant chemotherapy and, on the other hand, a re-evaluation of patients with carcinomatosis that do not respond to systemic chemotherapy. In the nonresponsive group, we observed a group of patients with debilitating ascites who not only failed to respond to systemic chemotherapy but also to any other therapy attempted to diminish the ascites (albumin infusions, diuretics at high dosages repeated paracentesis), which resulted in an extremely negative impact on quality of life. Twenty-eight (14.21%) patients underwent intraperitoneal hyperthermic chemotherapy for the palliation of ascites with a videolaparoscopic technique (Fig. 2).18–20

Methods

A Hasson trocar was placed in the right or left pararectal area through a 1-cm incision taking care not to contaminate the wall with the ascitic fluid. The ascites was completely suctioned out of the peritoneal cavity through the trocar before insufflating with CO2. After placing the 30-degree 5-mm scope under direct vision, a second 5-mm trocar was placed in the iliac fossa contralateral to the scope. If necessary, viscerolysis was performed to free the abdominal cavity of cancerous adhesions. If extended viscerolysis was considered dangerous, it was only pursued to ensure communication between all abdominal quadrants, so that the hyperthermic chemotherapy agent could flow through the inflow tubes and drains to reach all the peritoneal surfaces. Then, 3 additional 5-mm trocars were sequentially placed on the right and left side into the free iliac fossa.

A 5-mm grasper was passed from the peritoneal cavity out through the 5-mm trocar to place closed-suction drains into the pelvic cavity and into the right and left subdiaphragmatic space. These 3 suctioning drains are connected together to provide a single outflow. The 5-mm trocars were removed, and an infusion trocar was placed directly through the 10-mm trocar site where the camera had been inserted. To make the peritoneal space watertight, all drains were secured with a purse-string suture to the skin and connected to the perfusion machine, which should be set at an inflow temperature of 43°C to 44°C. An average temperature of 42°C in the whole peritoneal cavity was sought.

The temperature was measured by means of 2 probes. One was at the inflow site and the other at the junction between the 3 outflow drains. The patient's body temperature was monitored by means of 3 probes: at the skin, in the external ear canal, and in the rectum or bladder. The mean duration of laparoscopic preparation

FIGURE 2. Videolaparoscopic HIPEC procedure.
was 45 minutes, with a range of 30 to 120 minutes depending on the extent of visceralysis.

To allow the chemotherapy solution to distribute itself throughout the whole peritoneal surface, the operating table tilt was changed at 15-minute intervals during perfusion as follows: (1) level, (2) Trendelenburg + left tilt, (3) Trendelenburg + right tilt, (4) level, (5) reverse Trendelenburg + left tilt, and (6) reverse Trendelenburg + right tilt.

Perfusion lasted 90 minutes after which the chemotherapy agent was recovered and a lavage of 2000 mL of 1.5% dextrose was performed to remove residual chemotherapy. The drains were connected to gravity bags and were removed postoperatively after copious drainage ceased. After removing all drains, the patient was discharged from the hospital.

chez the hyperthermic intraperitoneal chemotherapy was performed using cisplatin 50 mg/m² and doxorubicin 15 mg/m² for ascites from ovarian cancer, peritoneal mesothelioma, or breast cancer. In ascites from rectal cancer, peritoneal metastases, or breast cancer, doxorubicin 15 mg/m² was used. The volume of perfusate used was 2000 mL; it consisted of a peritoneal dialysis solution containing 1.5% dextrose. Fresh frozen plasma (1200 mL) was infused during perfusion. Furosemide was administered along with intravenous fluids to maintain a 400-mL/h diuresis.20

Results
Of the 28 patients treated, at the origin of malignant ascites there were 10 cases of gastric cancer, 7 colon cancer, 5 breast lobular cancer, 5 ovarian cancer, and 1 peritoneal mesothelioma. In all cases, we observed a complete disappearance of the ascites within 9 days of laparoscopic perfusion. The average increment on the Karmofsky index postoperatively was 20 points. Even though the treatment is of a palliative nature, the disappearance of the refractory ascites did have an impact on average survival rate, of 152 days (range 21–796). The longest survival times were observed in 3 of 5 cases of breast lobular cancer (807, 736, and 216 days), whereas the shortest survival times were observed in the cases of ascites from gastric cancer. Follow-up ultrasound or CT 1 month after the laparoscopic HIPEC revealed complete resolution of ascites in 26 of the 28 patients, one patient died in the 21st postoperative day free from ascites. In one case, a CT scan 1 year later showed a small, clinically undetectable, ascitic accumulation in the pelvis. In 2 cases of concomitant neoplastic intestinal occlusion, a laparoscopic ileostomy was performed before beginning the hyperthermic intraperitoneal chemotherapy.

In the video-laparoscopic perfusion, for refractory ascites, no intraoperative or postoperative complications and no mortality due to the procedure were observed.20,21

**DISCUSSION**

**Staging**
We began using laparoscopy in the assessment of peritoneal carcinomatosis extent and in the treatment of refractory ascites in 2000, publishing in 2003 the first 48 cases of stadiation and the first 9 cases of closed perfusion.17

Objections regarding feasibility tied to the difficulty of trocar positioning in the presence of abdominal wall tumor masses or because of adhesions from previous surgeries, skepticism on the reliability and efficacy of the method in the stadiation phase, fear of neoplastic contamination at the trocar entry sites, and the absence of a curative objective tied to the laparoscopic procedure have been overcome in our experience.

Eight years from our first proposal to use laparoscopy in the staging of peritoneal carcinomatosis, the role of laparoscopic procedure has now become clear, well defined in its indications, technique, and possible applications.

VLS in stadiation allows the following:
- Evaluation of the mesentery (superficial lesions and retractions; Fig. 3).
- Evaluation of lesions on the antimesenteric margin.
- Evaluation of the omental bursa, pelvic cavity, diaphragm, and abdominal wall.
- Evaluation of sectors according to the cancer index, with PCI similar to VLS.
- The possibility of peritoneal washing and biopsies for the typing of the primitive tumor, and
- The predictive evaluation of the cyoreduction index after peritoneectomy.

The above-mentioned points give us a certain indication regarding the “feasibility” and “cost/benefit” of a peritoneectomy procedure with HIPEC.

Some weak points regarding the use of VLS in stadiation could be tied to the following:
- Evaluation of the thickness of lesions of the diaphragm,
- Evaluation of pancreatic involvement, and
- Necessity of a skilled laparoscopic surgeon, expert in advanced laparoscopy and carcinomatosis.

The weak points of the procedure can become points of strength if VLS is coupled with a video-assisted laparoscopic sonogram, which will in turn permit:
- A good evaluation of the thickness of lesions of the diaphragm,
- The qualitative and quantitative evaluation of pancreatic involvement, as well as that of the retrocavity, and
- The evaluation of hepatic metastasis and of their resectability.

The indications for VLS stadiation are as follows:
- Staging of a carcinomatosis already diagnosed via imaging technology (Te-Rm),
- Staging of a carcinomatosis of dubious origin (biopsy),
- Restaging after neoadjuvant chemotherapy (Figs. 4 and 5),
- Restaging during follow-up in the case of dubious imaging,
- Restaging after adjuvant chemotherapy.

**FIGURE 3.** Peritoneal seeding from gastric cancer: involvement of the small bowel and its mesentery PCI: 39. Patient excluded from peritoneectomy.
The use of VLS stadiation is not advisable for patients who have already undergone a peritoneectomy with the objective of a second look, as the presence of adhesions will not allow for a comprehensive evaluation of the eventual relapse or a good evaluation of all abdominal quadrants. We believe that in the case of dubious relapses in CT scan, the 18F-fluorodeoxyglucose-positron emission tomography/CT can offer further information on the origin and entity of the relapse and of its possible treatment.

**Treatment of Refractory Ascites**

Laparoscopic HIPEC may result in deeper penetration of the cancer chemotherapy drug in the peritoneal layers and tumor nodules. In the absence of cytoreductive surgery during these palliative laparoscopic HIPEC procedures, one can assume that the direct cytotoxic effect of this single chemotherapy instillation will be limited. The heated chemotherapy may eradicate viable cancer several cell layers deep on all the peritoneal surfaces. Then, a thin layer of fibrosis may develop on the exposed surfaces. The fibrous layer may direct the cancerous fluid into the capillary bed and thereby into the systemic circulation, causing a resolution of the problematic reaccumulation of ascites.\textsuperscript{16,19}

Abdominal sclerosis and induction of dense adhesions are probably the major factor of efficacy of this technique. Ozols et al\textsuperscript{19} in their phase I study reported sclerozing peritonitis and subsequent pain at the dose-limiting factor of 18 uM when performing intra-cavitary chemotherapy with doxorubicin in patients with advanced ovarian cancer. The absence of major complications and treatment-related mortality in our patients suggests that laparoscopic HIPEC is a safe technique.

The treatment is to be considered palliative for ascites that do not respond to therapy and must be performed exclusively on patients that, after VLS stadiation, present a peritoneal carcinomatosis noneligible for peritonectomy with HIPEC according to the PCI, or for extensive evolution of the disease.

The objective of the treatment is to improve on the Kornowsky index, ultimately impacting the patient’s quality of life. In patients with PCI <13 affected by peritoneal carcinomatosis from lobular breast cancer, the treatment can be performed even though the carcinomatosis in these cases is the expression of a systemic disease and thus not eligible for peritonectomy surgery with HIPEC.

**CONCLUSIONS**

Videolaparoscopy is placed, within a strategy of treatment of peritoneal carcinomatosis, at the beginning of a critical path analysis to classify the patient and provide a correct indication for integrated treatment and, in the end, associated with HIPEC, is an effective palliative instrument for neoplastic refractory ascites.

VLS is safe and reliable, absent of major complications, and mortality. VLS in peritoneal carcinomatosis foresees that the surgeon have experience in advanced videolaparoscopy and in the surgical treatment of carcinomatosis to prevent downstaging and greater complications.

**REFERENCES**


