Staging Laparoscopy in Digestive Cancers

Valentin Muntean[1], Traian Oniu[1], Corneliu Lungoci[1], Ovidiu Fabian[1], Doru Munteanu[2], Geza Molnar[2], Vasile Bintintan[3]

1) CF Clinical Hospital; 2) Emergency Clinical Hospital "Octavian Fodor"; 3) Emergency Clinical County Hospital, University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Background. Laparoscopy and laparoscopic ultrasonography may assist in the more accurate staging of digestive cancers. We assessed the diagnostic value of staging laparoscopy in patients with cancers of lower esophagus, stomach, liver, biliary tract, pancreas and colon. **Material and method**. Extended staging laparoscopy, laparoscopic ultrasonography and peritoneal cytology were performed in 165 patients with primary digestive cancers, admitted between January 2006 and December 2008 at three tertiary referral hospitals participating in the study. Staging laparoscopy was immediately followed by open surgery in 63 patients without distant metastases or with uncertain primary tumor resectability, and in 20 colorectal cancer patients with resectable hepatic metastases. The sensibility, sensitivity and diagnostic accuracy of staging laparoscopy for distant metastases and tumor resectability were assessed against the findings on open surgery and the final pathological report. **Results.** An unnecessary laparotomy was avoided in 36 of the 99 patients (36.4%) without distant metastases on imaging pre-therapeutic staging. The staging laparoscopy sensitivity for distant metastases varied between 66% and 100% and the diagnostic accuracy between 87% for the lower esophageal cancer and 100% for the biliary tract tumors. The overall morbidity of staging laparoscopy was 2.5% and the mortality 0. **Conclusion.** Staging laparoscopy avoids unnecessary laparotomies and changes the therapeutic plan in a significant number of patients. It can be performed just before the planned surgery or as a separate diagnostic procedure. The laparoscopy indications in digestive cancers are changing fast, with ongoing new developments in cancer treatment and laparoscopic technology.

Received: 30.01.2009 Accepted: 07.07.2009
J Gastrointestin Liver Dis
December 2009 Vol.18 No 4, 461-467
Address for correspondence: Valentin Muntean,
CF Clinical Hospital
Republicii 18
400015, Cluj-Napoca, Romania
E-mail: valentin.muntean@gmail.com

Key words

Esophageal cancer – gastric cancer – pancreatic cancer – colon cancer – staging laparoscopy – laparoscopic ultrasonography – peritoneal cytology.

Introduction

Many patients with digestive cancers present with locally advanced or metastatic disease and therefore accurate staging assists in the appropriate treatment selection for cure or palliation. Moreover, research regarding neoadjuvant protocols for locally advanced cancers is ongoing, which makes accurate staging imperative. Even after modern preoperative imaging screening (trans-abdominal and endoscopic ultrasound, CT scan, MRI and PET scan), many patients are found to have unsuspected, unresectable disease at exploration.

Staging laparoscopy (SL) may aid in the more accurate staging of digestive cancers, offering guidelines for the most appropriate treatment and avoiding the morbidity associated with non-therapeutic laparotomy [1]. The procedure enables the direct inspection of intra-abdominal organs and facilitates obtaining biopsy specimens and aspiration cytology. Laparoscopic ultrasound (L-US) can be used to evaluate deep organ parts that are not amenable to inspection. In some patients, the therapeutic intervention can be performed through a laparoscopic approach [2].

We undertook a prospective study to assess the value of SL, L-US and peritoneal cytology in patients with digestive cancers.

Patients and methods

This is a prospective, cohort, observational study of patients with primary digestive cancers on imaging investigations, endoscopy and pathological examination, admitted between January 2006 and December 2008 at three tertiary referral hospitals which participated in the DIASTAL Consortium (Diagnosis and Staging Laparoscopy in Abdominal Cancers, CEEX Program). Six primary locations were studied: lower esophagus, stomach, liver,

biliary tract, pancreas and colon. After the exclusion of patients with complications related to cancer and patients with distant metastases at admission or medically unfit, 165 patients were prospectively enrolled in DIASTAL study. For colon cancer patients the inclusion criteria in the study was the presence of resectable liver metastases on imaging tests. A study protocol was developed for each of the six locations [3] and approved by the Ethics Committee of the University of Medicine and Pharmacy.

All the patients received detailed information on diagnostic laparoscopy and only those who agreed to the study protocol were finally enrolled in the study. The pre-therapeutic imaging staging included conventional radiography of the thorax, abdominal ultrasonography, hydrosonography or endosonography and abdominal CT, MRI or PET-CT. The T1 patients (cTNM) and those with medical contraindications for pneumoperitoneum were referred for open surgery. Finally 119 patients were scheduled for SL, 99 with lower esophagus, stomach, liver, biliary tract and pancreas cancer and without distant metastases (M0 - cTNM) and 20 colorectal cancer patients with resectable synchronous hepatic metastases (M1-HEP – cTNM). Neodajuvant chemotherapy or irradiation was indicated in 5 patients with esophageal cancer, 2 with pancreatic and 4 with rectal cancer.

Extended SL, L-US and peritoneal cytology were performed under general anesthesia, with a single-dose antibiotic cover, immediately before scheduled laparotomy. The patient was positioned as for an open abdominal procedure and an angled 30^0 camera and 12 mm Hg insufflation pressures were used. The trocars (one 10 mm for camera, one 12 mm for ultrasonographic probe 7,5-MHz, Aloka Co.Ltd.,Tokyo, Japan, and one, two or three 5 mm trocars for retracting or dissecting organs) were positioned depending on the location of the tumor. Access to the abdomen was preferred using the open Hasson technique, with the first 10 mm trocar placed below or above the umbilicus, taking special precautions in patients with previous abdominal surgery.

A thorough evaluation of peritoneal surfaces was performed. Prior to any manipulation, ascites when present or irrigation fluid (100 ml in the upper abdomen and 100 ml in the pelvis) was suctioned and immediately sent for centrifugation and cytological examination using Giemsa and Papanicolaou staining methods. The suprahepatic and infrahepatic spaces, the surface of the bowel, the lesser sac, the root of the transverse mesocolon and small bowel, the ligament of Treitz, the paracolic gutters, and pelvis were inspected with frequent bed position changes as necessary. The lesser sac was opened when required. For the lower esophageal cancers, the exploration of the diaphragmatic hiatus was achieved through the incision of

Table I. Patients enrolled in the study, imaging staging and staging laparoscopy

LOCATION	Number of patients enrolled in the study	Imagistic staging: Number of patients / Number of patients enrolled in the study			Number of patients with neoadjuvant treatment	Number of patients with staging laparoscopy	Number of patients with SL technical failure	Staging laparoscopy: Number of patients / Patients with staging laparoscopy									
		Resectable tumor	N1-3	M1				Hepatic biopsy	Peritoneal biopsy	M1 (on frozen sections)	Lymph node biopsy	N1-3 (on frozen sections)	Positive peritoneal cytology	Primary tumor resectable	Resectable metastases (colorectal cancer)	Laparoscopic palliative surgery	Complications (%)
LOWER ESOPHAGUS	11	9/ 11	7/ 11	2/ 11	5	8	1	2/ 8	5/ 8	2/ 7	5/ 8	4/ 5	4/ 8	6/ 8	-	-/ 8	1/8 (12%)
STOMACH	57	52/ 57	32/ 57	8/ 57	-	45	1	6/ 45	18/ 45	17/ 24	33/ 45	25/ 33	19/ 45	39/ 45	-	4/ 45	1/45 (2.2%)
PRIMARY HEPATIC	15	12/ 15	3/ 15	2/ 15	-	9	-	4/ 9	2/ 9	2/ 9	4/ 9	2/ 4	1/ 9	8/ 9	-	-/ 9	-/9
BILIARY TRACT	7	5/ 7	3/ 7	2/ 7	-	4	-	2/ 4	3/ 4	2/ 4	3/ 4	1/ 3	1/ 4	3/ 4	-	-/ 4	-/4
PANCREAS	48	35/ 48	10/ 48	14/ 48	2	33	2	4/ 33	15/ 33	13/ 33	12/ 33	5/ 12	18/ 33	25/ 33	-	4/ 33	2/33 (6%)
COLON	27	24/ 27	7/ 27	27/ 27	4	20	1	20/ 20	5/ 20	18/ 20	9/ 20	5/ 9	3/ 20	18/ 20	14/ 18	-/ 20	-/20

the esophago-cardial peritoneal fold and blunt dissection, with the retraction of the stomach to the patient's right or left. Biopsies and frozen sections were examined for any suspicious abdominal lesions.

When no metastatic disease was identified on inspection, a detailed L-US examination was employed during which the tumor, hepatic parenchyma, portal vein, mesenteric vessels, celiac trunk, hepatic artery and the pathologic lymph nodes were evaluated. The addition of color flow Doppler further assisted in the assessment of vascular relations and patency. Lymph node and liver biopsies were performed under direct vision and US-guidance and sent for frozen sections.

Open laparotomy was immediately performed in the 63 patients without distant metastases or with uncertain primary tumor respectability on SL, and in the 20 colorectal cancer patients with resectable hepatic metastases. The sensibility, sensitivity and diagnostic accuracy of SL for distant metastases was assessed against the final pathological report, on permanent sections (pTNM). The SL accuracy and positive and negative predictive value for resectability was assessed against the findings on open surgery.

Results

On preoperative imaging screening we found distant metastases in 37 of the 138 patients with lower esophagus, stomach, liver, biliary tract and pancreas cancers (Table I), and they were offered palliative therapy or supportive care. Seven patients refused SL and another two T1 gastric cancer patients underwent open laparotomy. The remaining 99 patients with lower esophagus, stomach, liver, biliary tract and pancreas cancer without distant metastases (M0 - cTNM) and 20 colorectal cancer patients with resectable synchronous liver metastases (M1-HEP- cTNM) were scheduled for SL, just before the planned open surgical procedure.

The SL in the 99 M0 - cTNM patients revealed 61 unsuspected peritoneal and liver lesions and the frozen sections were positive for adenocarcinoma in 36 patients (36.4%) (hepatic 4, peritoneal 24 and hepatic and peritoneal 8). The L-US and frozen sections confirmed the hepatic metastases in 18 of the 20 colorectal cancer patients (90%) (Table I). Of the 18 patients, 4 had unresectable disease on SL, 2 hepatic and 2 extrahepatic (one peritoneal and one peritoneal and extraregional lymph nodes).

In the 119 patients with SL the peritoneal cytology was positive in 46 patients (38.6%) and negative for malignant cells in 73 patients (61.3%).

On inspection and L-US examination the primary tumor was resectable in 99 of the 119 patients (83.2%), unresectable in 14 (11.8%), and the resectability remained uncertain in 6 patients (5%).

In 53 patients SL did not reveal suspicious lymph nodes. In the 66 patients with lymph node enlargement the biopsy and frozen sections evidenced carcinoma in 42 patients.

The mean operative time of the SL was 48 minutes (range 25-90 min). Dense adhesions impaired a thorough abdominal inspection in five patients, in whom only a limited examination was possible. The SL immediate morbidity was 2.5% (bleeding from short gastric vessels in two patients and from the gastro-hepatic omentum in one patient, all controlled during open surgery) and SL mortality 0. In 8 patients with M1 disease, SL was followed by palliative

Table II. Open surgery and pathological staging

LOCATION	Number of patients with staging laparoscopy	Number of patients with open surgery	Number of patients / Patients with open surgery							
			Primary tumor resectable	Liver metastases resectable (colorectal cancer)	RO+R1 resection	Palliation / R2 resection	Complications (%)	Deaths (%)	N1-3 (permanent sections)	M1 (permanent sections)
ESOPHAGUS	8	6	5/6	-	5/ 6	1/ 6	3/6 50%	1/6 16.6%	4/6	1/6
STOMACH	45	28	26/ 28	-	24/ 28	4/ 28	5/28 17.9%	1/28 3.5%	18/ 28	2/ 28
PRIMARY HEPATIC	9	7	5/ 7	-	5/ 7	-/ 7	3/7 42%	-/7	2/ 6	1/ 7
BILIARY TRACT	4	2	2/ 2	-	2/ 2	-/ 2	-/2	-/4	1/ 2	-/ 2
PANCREAS	33	20	16/ 20	-	13/ 20	7/ 20	9/20 45%	1/20 5%	9/ 20	4/ 20
COLON	20	20	18/ 20	14/ 20	7/ 20	13/ 20	2/20 10%	1/20 5%	13/ 20	19/ 20

Table III. Avoided unnecessary laparotomies and diagnostic accuracy of SL for resectability and distant metastases

LOCATION	Number of patients with staging laparoscopy	Number of patients with open surgery	Number of unnecessary laparotomies avoided (%)	Patients with adjuvant therapy	Staging laparoscopy					
					Resectability of primary tumor			Diagnosis of distant metastases		
					Positive predictive value	Negative predictive value	Accuracy	Sensibility	Specificity	Accuracy
ESOPHAGUS	8	6	2(25%)	5	0.83	-	0.83	0.66	1	0.87
STOMACH	45	28	17(37.8%)	10	0.96	0.50	0.93	0.89	1	0.95
PRIMARY HEPATIC	9	7	2(22%)	3	0.71	-	0.71	0.66	1	0.89
BILIARY TRACT	4	2	2(50%)	3	1	-	1	1	1	1
PANCREAS	33	20	13(40%)	22	0.94	0.75	0.90	0.80	1	0.88
COLON	20	20	-	18	0.94	0.50	0.90	0.94	1	0.95

laparoscopic gastroenterostomy in 3 patients and feeding jejunostomy in 5 cases. In one patient a gastroenterostomy anastomotic fistula healed on conservative management (Table I).

The SL was followed by open surgery in 83 patients (Table II). In the 63 patients without distant metastases on SL, 49 underwent R0-R1 resections, 12 R2 resections or palliative procedures and 2 exploratory laparotomies. In the 20 colorectal cancer patients 7 R0-R1 resections and 13 R2 or palliative resections were performed. Five of the 14 patients with resectable secondaries underwent R0 resections (tumor and synchronous metastases), and in 9 patients only the primary tumor was removed and a hepatectomy postponed. We recorded major complications in 22 patients (26.5%) and 4 (4.8%) patients die.

An unnecessary laparotomy was avoided in 36 (36.4%) of the 99 M0 patients by imagistic pre-therapeutic staging (Table III).

The positive and negative predictive value and the diagnostic accuracy of SL and L-US for primary tumor resectability are depicted in Table III. In patients with colorectal cancer, SL and L-US correctly predicted resectability of distant metastases in 13 out of 14 patients and unresectability in 3 out of 4 patients: positive predictive value 92.8%; negative predictive value 75%; diagnostic accuracy 88.9%.

The SL sensitivity for distant metastases varied between 66% and 100%. Because of the small number of cases these data are difficult to interpret. Distant metastases were systematically confirmed by frozen sections, and this explains the 100% specificity of SL for all localizations. The diagnostic accuracy of SL for distant metastases varied between 87% for lower esophageal cancer and 100% for biliary tumors (one gallbladder and three Klatskin tumors) (Table III).

Discussion

Indications

As other invasive diagnostic procedures, SL should be only performed when there are no available non-invasive staging methods with similar or equivalent information and diagnostic yield and the information provided by SL is necessary and capable of changing the treatment plan [4-6]. The therapeutic decisions shoud be taken by oncologic multidisciplinary commissions and the management alternatives, depending on SL findings, should be clearly stated. And, finally, the hospital should have the prerequsite conditions for an efficient and safe SL, i.e. a surgical team experienced in cancer therapy and laparoscopic surgery, who can recognize and treat common complications and can perform additional therapeutic procedures, when indicated; the necessary surgical and laparoscopic equipment, including L-US; available laboratory facilities, experience and support for intra-operative cytology and frozen sections.

Staging laparoscopy and L-US are mainly indicated for diagnosis of peritoneal and hepatic metastases in advanced digestive cancers. In many patients with distant metastasis neoadjuvant therapy improves survival and the quality of life. Palliative chemotherapy or chemoradiation and/or supportive

care are indicated in other patients with advanced disease. As SL is less invasive than exploratory laparotomy and patients have a more rapid postoperative recovery, the time interval to adjuvant therapy may be shorter. In addition, other surgical procedures can be performed laparoscopically, such as tumor bypass or feeding jejunostomy, when neoadjuvant therapy is anticipated.

Patients with liver metastases from a primary colorectal cancer may be candidates for curative resection when there is no extrahepatic disease and when the liver disease is resectable. Staging laparoscopy for these patients can provide identification of some hepatic lesions non-visualized on preoperative non-invasive imaging. In patients who are candidates for neoadjuvant treatment, SL and L-US improve pre-therapeutic staging and enable minimally invasive stoma formation [7].

For early digestive cancers the diagnostic yield of SL is low [2] and patients should undergo curative resection, open or laparoscopic. A possible indication for SL in early digestive cancers might be the sentinel lymph node detection with isosulfan blue or gamma camera [8; 9]. In a recent study, the SL blue dye sentinel lymph node mapping accuracy for early gastric cancer was 100% [10].

The main risks of SL are complications related to the surgery and anesthesia, the false negative results that lead to unnecessary laparotomies and the potential adverse oncologic effects. Other possible inconveniences are the delay in definitive treatment when the SL is planned as a separate surgical procedure and the unnecessary cost when the procedure has a very low yield [6].

Staging laparoscopy is contraindicated in cancer patients with complications which should be treated with open surgery. Patients with general contraindications for laparosopy and pneumoperitoneum should be spared the risks of SL, even if they are low. Dense intra-abdominal adhesions from prior surgery are considered a relative contraindication for SL.

We have systematically introduced SL in our cancer staging protocols for about four years, and since then the inclusion and exclusion criteria have been changed based on the best available evidence [3]. The SL indications change rapidly according to the evolution in cancer treatment protocols and new developments in laparoscopic technology.

Technique

Staging laparoscopy can be performed in an inpatient or outpatient setting under general or occasionally local anesthesia with IV sedation in carefully selected patients [6].

The extent of SL is a matter of controversy. A short duration procedure, based only on inspection of abdominal organ surfaces, does not require significant expertise, and can be performed with a minimal risk through one port with a good diagnostic accuracy [11, 12]. On the other hand, a more extensive procedure that includes opening the lesser sac, assessment of the vessels and L-US examination improves the diagnostic accuracy of the procedure and can be performed safely within a reasonable time, without a significant increase in morbidity [13-15]. For lower esophageal cancer, combined thoracoscopic and laparoscopic staging has been described as improving staging by increasing the number of positive lymph nodes [16]. We have performed extended SL in all our patients apart from five, in whom only a limited examination was possible because of dense adhesions. The mean operative time of SL was 48 minutes and the immediate morbidity 2.5%.

There is also controversy regarding the SL timing. Most authors perform SL immediately before the planned open, surgical procedure. The arguments supporting this comprise the efficient surgical treatment, shorter hospitalization and lower costs, avoiding the patient inconveniences related to a second surgical procedure and the delay of adjuvant therapy, when necessary. It should be mentioned that the previous arguments are fragile. As has been mentioned, SL can be performed as a short inpatient or even outpatient procedure, with minimal inconvenience and is perceived by the patient as a pretherapeutic test.

If performed before the laparotomy, SL should be well planned. The surgical team should be prepared to integrate the new intraoperative findings and pathological report (cytology and frozen sections) with previous data and to change the initial therapeutic plan accordingly. The operating room time should be well scheduled, taking into account the operative time for SL plus the waiting time for cytological examination and frozen sections. In addition, there is the possibility of a short surgical procedure, when distant metastases or unresectable tumor are found on SL. Moreover, the length of time in the operating theatre equipped for laparoscopy with open surgical procedures can be a problem for most of our hospitals, with a limited number of operating rooms dedicated to laparoscopic procedures.

When planned as a separate surgical intervention, SL becomes a preliminary diagnostic procedure, with dedicated operating room time and is important in its own right not only as a preliminary examination which can be completed during laparotomy. The information offered by SL and L-US and the final pathological report on permanent sections can be judged by the multidisciplinary commission and the patient can be informed about the possible therapeutic alternatives. This is of paramount importance when neoadjuvant therapeutic protocols are available or when alternative therapeutic procedures, other than surgery, can be applied.

Complications and cost-effectiveness

Reported complications are rare and include bleeding, infection, visceral injury, bile leak, particularly if liver biopsy is performed, and anesthesia-related complications. Procedure-related morbidity has been reported between 0 and 4% [2, 17-19]. In a retrospective study of 747 patients with SL, there were 11 severe complications (1.5%), of which 5 were converted to open surgery and one death (0.13%) [20]. In our 119 patients with SL we observed three complications (2.5%) and no deaths.

The average length of hospital stay after SL is 1-3 days, which compares favourably with open exploration [17, 21-

23]. In patients with locally advanced pancreatic cancer, SL increases the number of patients who receive chemotherapy and shortens the time to treatment initiation [24].

With regard to oncological safety, initial concerns for more port-site recurrences after laparoscopic procedures in cancer patients have not been substantiated. Multiple studies report an 0-2% incidence of port-site recurrences after SL, which is similar to the incidence after open explorations of cancer patients [24, 25]. Staging laparoscopy has not been associated with peritoneal disease progression [24].

Staging laparoscopy is more cost-effective than open exploration when it is the only procedure required, with a 55-60% reduction in total hospital charges [21, 23]. On the other hand, when used in all cancer patients, the cost-effectiveness of SL appears to be linked to the yield of the procedure in identifying occult disease on imagistic staging [26].

The laparoscopy indications in digestive cancers are changing fast, with ongoing new developments in cancer treatment and laparoscopic technology. As the experience of the surgical team increases and together with the advances in laparoscopic technology, many curative and palliative surgical procedures for cancer might be performed laparoscopically.

Conclusions

Staging laparoscopy may spare cancer patients unnecessary laparotomies and have an associated decreased morbidity and pain, faster recovery and earlier time to adjuvant treatment.

A short SL, through a single port, can be performed just before the planned surgical procedure to certify the operability of the early stages digestive cancers. A good example is the SL to exclude peritoneal carcinomatosis in early stages of gastric or pancreatic cancer. Open surgery should be always postponed when the information offered by SL and frozen sections is insufficient, in contradiction to other available data or when there is not a patient consent for the surgery indicated by the new findings. In advanced stages and when neoadjuvant therapy is available, SL is better planned as a separate surgical procedure from the very beginning.

Acknowledgement

Research support from the CEEX Program of Romanian Ministry of Education and Research, Grant No.54/2005 “Diagnosis and Staging Laparoscopy in Abdominal Cancers”.

Conflicts of interest

Nothing to declare.

References

1. Torab FC, Bokobza B, Branicki F. Laparoscopy in gastrointestinal malignancies. Ann N Y Acad Sci 2008; 1138: 155-161.
2. Chang L, Stefanidis D, Richardson WS, Earle DB, Fanelli RD. The role of staging laparoscopy for intraabdominal cancers: an evidence-based review. Surg Endosc 2009; 23: 231-241.
3. Clinical Practice Guidelines in Oncology. The National Comprehensive Cancer Network, 2008.
4. Greene FL. Indications and General Oncologic Principles. In: Greene FL, Heniford BT, eds. *Minimally Invasive Cancer Management*. New York, Berlin, Heidelberg: Springer, 2001.
5. Easter DW, Michaelson B. Biopsy and Staging-Technical Issues. In: Greene FL, Heniford BT, eds. *Minimally Invasive Cancer Management*. New York, Berlin, Heidelberg, Springer, 2001.
6. Guidelines for Diagnostic Laparoscopy. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). 2007. Ref Type: Electronic Citation.
7. Koea JB, Guillem JG, Conlon KC, Minsky B, Saltz L, Cohen A. Role of laparoscopy in the initial multimodality management of patients with near-obstructing rectal cancer. J Gastrointest Surg 2000; 4: 105-108.
8. Gretschel S, Schlag PM. Limited surgery in early gastric cancer. Onkologie 2005; 28: 243-244.
9. Bembenek AE, Rosenberg R, Wagler E, et al. Sentinel lymph node biopsy in colon cancer: a prospective multicenter trial. Ann Surg 2007; 245: 858-863.
10. Orsenigo E, Tomajer V, Di Palo S, et al. Sentinel node mapping during laparoscopic distal gastrectomy for gastric cancer. Surg Endosc 2008; 22: 118-121.
11. Luque-de Leon E, Tsiotos GG, Balsiger B, Barnwell J, Burgart LJ, Sarr MG. Staging laparoscopy for pancreatic cancer should be used to select the best means of palliation and not only to maximize the resectability rate. J Gastrointest Surg 1999; 3: 111-117.
12. Jimenez RE, Warshaw AL, Rattner DW, Willett CG, McGrath D, Fernandez-Del Castillo C. Impact of laparoscopic staging in the treatment of pancreatic cancer. Arch Surg 2000; 135: 409-414.
13. Hunerbein M, Rau B, Hohenberger P, Schlag PM. Value of laparoscopic ultrasound for staging of gastrointestinal tumors. Chirurg 2001; 72: 914-919.
14. Schachter PP, Avni Y, Shimonov M, Gvirtz G, Rosen A, Czerniak A. The impact of laparoscopy and laparoscopic ultrasonography on the management of pancreatic cancer. Arch Surg 2000; 135: 1303-1307.
15. Rau B, Hunerbein M. Diagnostic laparoscopy: indications and benefits. Langenbecks Arch Surg 2005; 390: 187-196.
16. Krasna MJ, Reed CE, Nedzwiecki D, Hollis DR, Luketich JD, DeCamp MM, Mayer RJ, Sugarbaker DJ. CALGB 9380: a prospective trial of the feasibility of thoracoscopy/laparoscopy in staging esophageal cancer. Ann Thorac Surg 2001; 71: 1073-1079.
17. Stefanidis D, Grove KD, Schwesinger WH, Thomas CR Jr. The current role of staging laparoscopy for adenocarcinoma of the pancreas: a review. Ann Oncol 2006; 17: 189-199.
18. Nieveen van Dijkum EJ, de Wit LT, van Delden OM, et al. Staging laparoscopy and laparoscopic ultrasonography in more than 400 patients with upper gastrointestinal carcinoma. J Am Coll Surg 1999; 189: 459-465.
19. Bemelman WA, Nieveen van Dijkum EJ, de Wit LT, Gouma DJ. Staging laparoscopy for gastrointestinal malignancies: current indications. Z Gastroenterol 2001; 39: 25-28.
20. Adamek HE, Maier M, Benz C, Huber T, Schilling D, Riemann JF. Severe complications in diagnostic laparoscopy. 9 years experience in 747 examinations. Med Klin (Munich) 1996; 91: 694-697.
21. Jarnagin WR, Bodniewicz J, Dougherty E, Conlon K, Blumgart LH, Fong Y. A prospective analysis of staging laparoscopy in patients with primary and secondary hepatobiliary malignancies. J Gastrointest Surg 2000; 4: 34-43.

22. Tilleman EH, de Castro SM, Busch OR, et al. Diagnostic laparoscopy and laparoscopic ultrasound for staging of patients with malignant proximal bile duct obstruction. J Gastrointest Surg 2002; 6: 426-430.
23. Jarnagin WR, Conlon K, Bodniewicz J, et al. A clinical scoring system predicts the yield of diagnostic laparoscopy in patients with potentially resectable hepatic colorectal metastases. Cancer 2001; 91: 1121-1128.
24. Velanovich V. The effects of staging laparoscopy on trocar site and peritoneal recurrence of pancreatic cancer. Surg Endosc 2004; 18: 310-313.
25. Deogracias ML, Rodriguez-Sanjuan JC, de la Torre F, et al. Absence of port-site metastases following staging laparoscopy for gastric carcinoma. Rev Esp Enferm Dig 2006; 98: 755-759.
26. Obertop H, Gouma DJ. Essentials in biliopancreatic staging: a decision analysis. Ann Oncol 1999; 10 Suppl 4: 150-152.