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Laparoscopic surgery for cancer: A systematic review and a way forward

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Laparoscopic surgery; Open surgery; Cancer; Nodal harvest; Resection margin; Survival; Recurrence

Introduction

While laparoscopic approaches are used for many abdominal procedures and allow for faster recovery of bowel function, better immunologic response and overall accelerated recovery for the patient, the use of laparoscopy for cancer surgery is still a matter of debate. For patients with cancer, questions remain about the immunologic implications of laparoscopic surgery, the adequacy and standardization of laparoscopic techniques, the risk for disease recurrence, and the impact on survival. The safety and efficacy of laparoscopic surgery for colorectal cancer has certainly been established, but the same rigorous approach to other cancers has yet to be reported. In this article we review the current data and state of the art for laparoscopic approaches in abdominal cancer surgery.

Methods

Literature Review

An electronic search of the Medline database was performed using different key words that described abdominal cancer surgery. For each organ a search was conducted including as key words and phrases: cancer, laparoscopic versus open surgery, and the specific organ. The search terms were identified in the title, abstract, or medical subject heading. Abstracts of each identified publication were screened, and only publications that addressed the clinical questions of this analysis were further assessed. Each of these publications was independently and thoroughly reviewed by 2 authors (E.A. and O.J.H.).

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Analysis

Relevant data, including authors, title, study design, methodology, main results, and conclusions, were extracted and documented on a separate data sheet for each publication. For every organ, the grade of recommendation based on the available literature was determined as proposed by Sackett (Table 1).[1] Data for various malignancies are compared in Table 2.

Colon

Level of Evidence: I Grade of Recommendation: A

Laparoscopic surgery for the colon was first described in the 1990's.[2] In the initial reports of laparoscopic procedures for adenocarcinoma of the colon, a prohibitive port-site metastasis rate of 21% tempered the enthusiasm for this approach.[3] Subsequent animal studies helped to elucidate the mechanism of port-site recurrences. Direct manipulation of the tumor, extraction of the tumor through the small wound without adequate wound protection, contamination of the laparoscopic instruments with cancer cells and inexperience of the surgeon were identified as important risk factors.[4] As surgeons gained more experience with this approach, the rate of port-site metastasis declined to less than 1%, comparable to wound recurrences reported for open procedures.[5-8]

Several major randomized clinical trials were conducted to ultimately determine the efficacy of laparoscopic surgery for colon cancer, including COLOR (Colon Cancer Laparoscopic or Open Resection) in the Netherlands,[9] the Barcelona trial in Spain,[10] COSTSG (Clinical Outcomes of Surgical Therapy Study Group) in the United States,[8] and CLASICC (Conventional versus Laparoscopic-assisted Surgery in Colorectal Cancer) in the United Kingdom.[11] These studies demonstrated results comparable to open surgery with regard to number of lymph nodes resected, likelihood of a tumor free resection margin and size of specimen removed (Table 3).[8-11] In groups undergoing a laparoscopic resection, operative times were longer, use of narcotics and analgesics was significantly less,[8] and postoperative ileus was shorter combined with earlier resumption of oral intake[9-12] and a shorter hospital stay.[8-12]

The most important goal of cancer surgery is cancer-free survival. As most recurrences occur in the first three years after operation,[13] the primary endpoint for these prospective randomized controlled clinical trials was therefore the three-year survival. Cancer free survival was comparable or better in the laparoscopic groups. The Barcelona trial showed a survival advantage for the laparoscopic group after a median follow-up of 95 months.[14] This difference was identified only in stage III cancer patients and has not been reproduced by any other study. The COSTSG trial reported a median follow-up of 52.8 months with similar survival and recurrence rates.[8] Recently the three-year results of the CLASICC trial have been published and showed no difference in disease-free survival, local recurrence or quality of life.[15] The COLOR trial failed to exclude the possibility that the laparoscopic procedure was inferior, but the differences were very small.[16] Conversion rates varied between 11 and 30%. In the CLASICC trial, 143 (29.3%) of the 488 laparoscopic procedures were converted to open operations, with the risk factors for conversion including high BMI, male gender, ASA III grading and local tumor invasion.[17]

A recent meta-analysis of the published literature strengthens the justification for the use of laparoscopy for colon cancer surgery. In 10 randomized clinical trials including 2474 patients, there were no statistically significant differences in local cancer recurrence, port or wound site recurrence and distant metastases between laparoscopic and open surgery.[18]

Since the large randomized clinical trials excluded cancer located in the transverse colon, the corresponding data are not as strong as those for the left and right colon. Laparoscopic resection

of transverse colon cancer is technically feasible,[19] but the long-term outcome and results still need evaluation in prospective randomized trials.

The costs of laparoscopic surgery are higher than those of open procedures, but overall hospital stay appears to be one to two days shorter, allowing for an overall decrease in hospital costs.[20-22] The learning curve remains an important issue. A single center study including 900 patients found that the learning curve for laparoscopic colon cancer surgery was 55 cases for the right colon and 62 cases for the left colon.[23]

In experienced hands laparoscopic surgery for colon cancer has results similar to open surgery and it has certain short-term advantages. Surgeons experienced in laparoscopic colon surgery can therefore safely offer this option, but open approaches are also acceptable. Data for transverse colon cancers are accumulating, and further studies should be performed within the context of clinical trials.

Rectum

Level of Evidence: II Grade of Recommendation: B

Total mesorectal excision, advocated by Heald et al., is the accepted best practice for adenocarcinoma of the rectum.[24] As total mesorectal excision has been associated with lower recurrence rates and improved survival, alternative approaches for rectal cancer must be measured against total mesorectal excision. Several randomized controlled trials of laparoscopic rectal cancer surgery, among many retrospective studies, have shown the safety and feasibility of laparoscopic rectal cancer resection with short term benefits.[25-27] A retrospective study of 86 patients with a mean follow-up of 6.5 years found no difference in local recurrence rates and incidence of distant metastases.[28] A meta-analysis including 20 retrospective and prospective non-randomized studies identified short-term advantages for the laparoscopic group, including earlier stomal function, bowel movements and oral intake, and a shorter hospital stay. The procedures were found to have no differences in resection margin positivity or lymph node clearance.[29] A Cochrane Review including 48 studies (randomized controlled trials, controlled clinical trials, case series and case reports) representing 4224 patients found no differences in disease-free survival rate, local recurrence rate, morbidity, mortality, anastomotic leakage, resection margin positivity and number of recovered lymph nodes. Advantages of the laparoscopic procedure included lower blood loss, earlier return to oral intake, lower use of narcotics and less inflammation measured by lower levels of interleukin-1, interleukin-6 and C-reactive protein.[30,31] The disadvantages include longer operative time and higher procedural costs.[31] Lymph node clearance and distribution also analyzed by prospective randomized trials showed no difference between the techniques.[32-34] A prospective randomized trial comparing laparoscopic with open surgery for 171 patients with low or ultra-low rectal cancer demonstrated no statistical differences in operation time, analgesic use, oral intake or mortality for the two procedures. Moreover, the laparoscopy group had lower blood loss and shorter hospitalization.[35]

The CLASICC trial for colon cancer included rectal cancers and was followed by three other prospective randomized trials with long-term results.[15,32,34,36] The CLASICC trial showed more positive margins and port-site metastases in the 3-year follow-up for the laparoscopic group,[11] but the other three trials showed a similar local recurrence rate and disease free survival.[15,32,34,36] These findings in the CLASSIC trial may be due to a specific lack of expertise for laparoscopic rectal surgery during the trial as evidenced by a high conversion rate, a preponderance of procedures differing from total mesorectal excision, and the multicentric recruitment of the patients to the trial. Bladder function was similar for laparoscopic and open rectal operations, while overall sexual function and erectile function were insignificantly worse after laparoscopic rectal surgery.

Although the evidence remains weaker than for colon cancer, laparoscopic surgery for rectal cancer seems comparable to that of open surgery and has short-term advantages. Due to the learning curve involved in this operation, surgeons experienced in both total mesorectal excision and laparoscopic surgery can therefore safely offer this option, but open surgery is also acceptable.

Stomach

Level of Evidence: II Grade of Recommendation: B

Gastric adenocarcinoma is a highly lethal form of malignancy, with a high incidence in Pacific Asian countries. Most studies of laparoscopic surgery include patients in Japan and Korea with early gastric cancer limited to the gastric mucosa or submucosa, regardless of lymph node involvement. Several retrospective studies have shown that laparoscopic distal gastrectomy for early gastric cancer is feasible and safe and associated with less pain, quicker recovery of gastrointestinal function, shorter hospital stay but longer operative time, compared with open surgery.[37-42] However, the long-term quality of life after 5 years does not differ.[43] The rate of positive resection margin has been found to be equivalent; the numbers of retrieved lymph nodes have been less than for open procedures in most of the studies, but above the required standard of 15 nodes.[38,40,41] A meta-analysis of 4 randomized controlled trials and 12 retrospective studies of mainly early gastric cancer has confirmed a significantly lower number of lymph nodes in the laparoscopic group.[44] Survival has been analyzed in retrospective and small prospective randomized studies and found to be similar between laparoscopic or open procedures, but these smaller studies have limited power to detect differences.[45-47] A Korean study analyzing the learning curve for laparoscopic-assisted distal gastrectomy found that 50 cases are necessary for optimal operative performance.[48]

In the Western countries without mass population screening, only 10 - 20 % of the detected tumors are early gastric cancers.[49] For advanced gastric cancer, the few published studies show the feasibility of laparoscopic gastrectomy with adequate oncological clearance.[38,50] Only one small prospective randomized trial has demonstrated similar 5-year survival for laparoscopic compared to open gastric resection.[47] This single study raises the evidence to level II.

At present, evidence is insufficient to justify laparoscopic procedure for gastric cancer outside the context of a clinical trial. In addition, a large experience with this approach is needed for adequate outcomes and requires advanced laparoscopic training.

Staging laparoscopy for gastric cancer—Laparoscopic staging of gastric cancer, especially with the addition of laparoscopic ultrasonography, has been shown to be more reliable than other imaging techniques. A staging laparoscopy is useful in cases of questionable stage or resectability and spares the patient an unnecessary laparotomy.[51] It has been shown that staging laparoscopy can be performed safely and is not associated with port-site metastases.[52]

Esophagus

Level of evidence: III Grade of Recommendation: C

Both adenocarcinoma and squamous esophageal cancers have a poor prognosis, and the morbidity of surgical management approaches 50 %.[53] One problem is the extent of the surgery, with abdominal and thoracic components. While it seems intuitive that laparoscopic approaches could mitigate the effects of this extensive operation and diminish perioperative morbidity, several trials have been conducted to demonstrate the feasibility of laparoscopic esophageal resection, and none has shown a major advantage with regard to morbidity and mortality.[54] Two small non-randomized comparative studies have shown comparable

operative times, shorter hospital stay, no difference in morbidity and mortality and comparable lymph node yield.[55,56] Staging with laparoscopic or thoracoscopic ultrasonography and biopsy is feasible and prevents the need for explorations in patients with metastatic disease.[57]

Prospective randomized trials with large patient numbers to compare laparoscopic to open surgery are lacking; therefore, the open approach remains the standard for this disease. Laparoscopic procedures can be attempted, but should be performed in prospective randomized trials at this time.

Pancreas

Level of evidence: III Grade of Recommendation: C

Adenocarcinoma of the pancreas has an overall 5-year survival below 5%.[58] Several studies have reported the feasibility of laparoscopic pancreatic resection, especially for left or distal pancreatectomy.[59] A large retrospective multicenter comparison for left pancreatectomy yielded a similar rate of positive margin and pancreatic leak.[60] Most of these studies have included benign neoplasms, while some reports included malignant cases. The long-term outcome and the oncologic results cannot be assessed at this time. The short term benefits include a shorter hospital stay and faster return to normal activity.[61-63]

The feasibility of laparoscopic pancreaticoduodenectomy has been demonstrated by several studies, among them an impressive series of 42 laparoscopic pancreaticoduodenectomies for several diseases with a mean follow-up of 36 months and an actuarial 5-year survival of 19.1% for the subgroup of the adenocarcinomas.[64,65] The value of laparoscopy for pancreatic malignancy lies in its diagnostic and staging capabilities. The accuracy of assessment of resectability can be increased by laparoscopy and laparoscopic ultrasonography. The lesser sac can be assessed by laparoscopy but local involvement of the superior mesenteric vein cannot reliably be assessed independent of an open exploration.[66] In contrast liver and peritoneal metastases can be found in most cases and this avoids a non-therapeutic laparotomy.[66,67]

Laparoscopic resection of pancreatic cancer should only be performed in the setting of prospective randomized trial with long-term survival and oncologic clearance as endpoints.

Palliation for pancreatic cancer

Level of Evidence: III Grade of Recommendation: C—Palliative gastric and biliary bypass both may be performed laparoscopically. However, a study examining 155 patients with unresectable pancreatic cancer diagnosed by laparoscopy found that jaundice was relieved by endoscopic or transhepatic decompression in all patients, and only 3% of the patients needed an operative decompression before death.[68] The advantage of laparoscopic over open gastrojejunostomy was reported in a case-matched study showing reduced blood loss and shorter hospital stay in the laparoscopic group.[69]

Although prospective randomized trials are not available, laparoscopy can be used as an instrument to avoid non-therapeutic laparotomies in patients with pancreatic cancer.

Liver

Level of Evidence: III Grade of Recommendation: C

The theoretical concerns regarding laparoscopic surgery for liver cancer may be greater then for other organs because of the risks of bleeding and air embolism and the difficulties of exposure. As laparoscopic instrumentation and surgical skills have advanced, the staging of liver cancer by laparoscopy and laparoscopic ultrasonography has become a very useful tool. Resections of benign liver tumors including cysts in peripheral liver segments are technically

simple and associated with earlier recovery when compared with open approaches.[70] Diagnostic laparoscopy helps to avoid unnecessary exploratory laparotomies and does not appear to have an adverse effect on tumor recurrence in patients with ruptured hepatocellular carcinoma.[71] Nevertheless, the resection of malignant liver tumors is much more challenging since these are often located close to the central vessels and bile ducts. While hemorrhage and bile leaks are therefore more likely than for peripheral resections, the feasibility of laparoscopic tumor resections has been demonstrated in pair-matched controlled trials for primary (hepatocellular carcinoma, cholangiocarcinoma) and secondary liver tumors located in segments II-VII.[72-74] The follow-up of these patients showed outcomes similar to open surgery.

While these studies demonstrated the feasibility of left hepatic lobectomy and the more challenging segmental resections, concerns remain whether larger resections are justified if can be done laparoscopically. As these resections are performed for malignancy, mincing of the liver for extraction, as it is performed for splenic rescction, would impede pathological assessment. The large excision thus required for extraction, may undo the benefit of laparoscopy. As randomized clinical trials with prospective evaluation of survival have yet to be reported, laparoscopic surgery for malignant liver tumors should be undertaken within the confines of well designed trials.

Gastric gastrointestinal stromal tumor (GIST)

Level of evidence: IV Grade of Recommendation: none

GISTs are stromal tumors characterized by mutations in the tyrosine-kinase gene and they stain positive for CD117. They are often located in the stomach, but can occur in any portion of the alimentary tract. The goals of operation include a segmental resection with an intact pseudo-capsule and a thorough exploration of the abdomen for metastasis. Resection margins of 2 cm are sufficient.[75] Lymphadenectomy is unnecessary, as nodal metastases are rare. Risk factors for tumor recurrence include high mitotic index >10 / 50 high power fields (HPF), larger tumor size (>5 cm), tumor rupture, ulceration and necrosis.[76]

Many retrospective and some prospective studies have shown the feasibility of laparoscopic resection of gastric GIST's with reasonable survival.[77-80] Earlier studies included small tumors up to 2 cm. Later reports included larger tumors, but these are less easy to handle intraoperatively, and rupture of the tumor is a devastating complication. Comparative studies have demonstrated a shorter hospital stay for the laparoscopic group.[81] A higher level of evidence is missing in the literature as these tumors are rare.

Given the simple surgical procedure required for resection of GISTs, we believe that laparoscopic surgery is justified for these tumors although prospective randomized trials comparing laparoscopic to open surgery are missing. Depending on the surgeon's experience, smaller tumors can be resected laparoscopically. For bulky tumors or surgeons with less experience in laparoscopic surgery, an open operation is technically simpler and less likely to result in rupture of the tumor during the procedure.

Appendix

Level of Evidence: IV Grade of Recommendation: none

Tumors of the appendix are rare and often discovered during or following appendectomy for appendicitis. Tumors are found in about 0.4-1% of appendectomy specimens, and synchronous colon cancers are present in 10 – 30% of these cases.[82,83] Because of the rarity of this condition, the available literature is scarce. One retrospective study analyzed 43 appendiceal tumors (carcinoid and adenocarcinoma) treated by open or laparoscopic resection, with a higher rate

of tumor positive resection margins in the laparoscopic group but comparable long-term survival.[84]

There is no evidence to support laparoscopic resection of appendiceal tumors by appendectomy. If these tumors are suspected preoperatively, a colonoscopy should be performed to exclude a synchronous colon cancer, and a formal right hemicolectomy should be planned, which may be performed laparoscopically.[83]

Adrenal Gland

Level of Evidence: IV Grade of Recommendation: none

Laparoscopic adrenalectomy was first described in 1992 by Gagner[85] and since has been widely applied to different adrenal lesions. For benign conditions laparoscopic adrenalectomy has become the standard of care. Although large prospective studies are lacking, many retrospective reports and case-controlled studies as well as a small prospective study have shown excellent results for benign disease.[86-93] Walz et al. reported an impressive prospective series of 560 adrenalectomies including tumors up to 7 cm. It is technically challenging but possible to remove tumors over 6-7 cm by the laparoscopic route, but tumors larger than 5 cm are more often malignant.[92,94]

Adrenocortical cancer and malignant pheochromocytomas are rare tumors with a poor prognosis, likely not well suited to laparoscopic approaches. Only a few small retrospective studies including malignant adrenal disease are available, and these studies agree with expert opinion that primary adrenal malignancy should be treated by an open approach, especially when invasion of adjacent organs is present. Laparoscopic procedures that identify adrenal tumors with local infiltration should be converted to an open technique.[95-97]

At this time there are no prospective randomized series to guide or endorse the use of laparoscopic resection for adrenocortical carcinoma or malignant pheochromocytoma.

Secondary adrenal tumors—Adrenal metastases occur in patients with melanoma and cancers of the lung, kidney, gastrointestinal tract, and breast.[98] In a large series of abdominal CT scans, more than half of adrenal masses were secondary and often represented metastatic disease.[99] Some authors have reported the laparoscopic resection of metastatic lesions in the adrenal gland and consider it safe.[96,97,100,101] Paul et al. compared the outcome of laparoscopic resections in the literature to an unresected series and concluded that resection could result in prolonged survival in cases of favorable tumor biology.[98] However, there are no data of quality to support this approach.

Gall Bladder

Level of Evidence: V Grade of Recommendation: none

Laparoscopic cholecystectomy has replaced conventional open approaches for benign gallbladder disease, because it has been shown to be safe and cost effective.[102,103] In large series of laparoscopic cholecystectomies, adenocarcinoma of the gallbladder is reported at rates around 0.5%.[104] Early reports claimed that laparoscopic cholecystectomy worsens the prognosis for patients with unsuspected gallbladder cancer because of intraabdominal spread and port-site metastasis. Retrospective studies have shown contradictory results,[105-108] with little prospective data to resolve the question.[109] To minimize the risk of intraabdominal dissemination and port-site metastasis, the surgeon should avoid bile spillage, which occurs in 20 - 44% of the laparoscopic cholecystectomies and has been correlated with poor survival and increased recurrences.[110-112] Because of these concerns the surgeon should consider retrieving

the specimen in a bag and opening the gallbladder for examination before the abdomen is closed.[113]

If gallbladder cancer is identified following laparoscopic cholecystectomy, additional treatment depends on the tumor stage.[114] For patients with Tis and T1a tumors with negative resection margins, the laparoscopic approach is adequate.[113] For these tumors the 5-year-survival after simple cholecystectomy is 95-100%.[112,113] Other tumor stages may require a re-exploration with liver resection and lymphadenectomy. Current opinion states that en-bloc resection and portal node dissection are the best options for patients with more advanced gallbladder cancers.

There are no data to support the use of laparoscopic resection for advanced stages of gallbladder cancer. The importance of the excision of port-sites is debated. In the largest series, the occurrence of port-site metastasis is not higher than the wound recurrence after open operations with a rate of 5 – 6 %, but excision is advised by prominent reviews based on early studies.[105,109,115]

Although there are no current indications for laparoscopic resection in advanced stages, laparoscopy is an excellent staging method for gallbladder cancer with low morbidity.[115] Laparoscopic cholecystectomy should not be utilized if the diagnosis of cancer is known preoperatively for the risk of bile spilling.

Bile duct

Level of Evidence: V Grade of Recommendation: none

The location of an adenocarcinoma of the bile duct dictates the operative approach, including local resection, liver resection or pancreaticoduodenectomy. For the distal bile duct, the feasibility of laparoscopic pancreaticoduodenectomy has been demonstrated.[64] In a series of 56 cases of hilar bile duct cancers, diagnostic laparoscopy detected peritoneal or liver metastases for the majority of patients who had metastatic disease, but failed to identify unresectability in locally advanced tumors.[116]

As for other organs, diagnostic laparoscopy is a valuable tool to avoid non-therapeutic laparotomies in patients with metastatic disease. Evidence is insufficient to recommend laparoscopic resection of bile duct cancers at this time.

Small Intestine

Level of Evidence: V Grade of Recommendation: none

Malignancies involving the small intestine are rare, with an estimated 6230 new cases and 1110 patient deaths in the US in 2009, thus accounting for fewer than 0.5 percent of all cancers.[58] While laparoscopic surgery might seem advantageous for intestinal surgery, reports comparing outcome for intestinal malignancies are lacking. Studies are scarce even for benign disease and do not always show an advantage of laparoscopic over open procedures. We believe that laparoscopy is a useful tool for localization, resection of benign tumors, and exclusion of carcinomatosis, malignant ascites, and liver metastasis.

Leiomyoma—A few case reports show the feasibility of the laparoscopic or laparoscopic assisted procedure for bleeding and non-bleeding leiomyomas.[117-121] Tumors with a mitotic index < 2 / 50 HPF may be locally excised.[122] There is no evidence to sustain laparoscopic treatment for these tumors at this time.

GIST—GISTs are commonly found in the jejunum, followed by the ileum, duodenum, colon or rectum, and surgical resection is the best therapeutic option. Only a few reports of laparoscopic cases appear in the literature.[123] Predictors for poor survival include high tumor cellularity, mitotic index > 5 / 50 HPF, and KI-67 index >=10%.[124] Aggressive or advanced stages are treated with imatinib.[123] Oncologic resection includes the inspection of the bowel and resection of the entire tumor with 2 cm margins, with efforts to avoid tumor rupture.[125]

As small tumors < 2 cm are unlikely to behave aggressively, we believe these may be resected laparoscopically, but there is no evidence to support use of the laparoscopic approach for larger tumors.

Carcinoid—Carcinoids account for up to 40 % of malignant tumors of the ileum, with synchronous tumors identified in 30% of the patients. Tumors < 1 cm rarely metastasize, but it appears that carcinoids of the small intestine metastasize earlier than similar tumors in the appendix. Treatment should include wide en-bloc resection including adjacent mesentery and lymph nodes. Virtually no data exist that support the laparoscopic resection of intestinal carcinoids.

Adenocarcinoma—No data exist for the use of a laparoscopic approach to resect adenocarcinoma of the small intestine. Wide surgical resection should include the tumor, mesentery and surrounding tissue at risk for contiguous spread. Right hemicolectomy is recommended for tumors of the distal ileum. Laparoscopic exploration followed by conversion to open resection was described in a single case report.[126] The evidence to support laparoscopic resection is lacking.

Lymphoma—Risk factors for lymphoma of the small intestine include AIDS, permanent immunosuppression in transplant recipients, autoimmune disease and Crohn's disease. In the literature there are only a few case reports of laparoscopic diagnosis or resection.[127-129] There are no data to support laparoscopic resection.

Palliative resection for metastasis—Metastases to the small intestine can arise from melanoma, cancers of the breast, lung and kidney, while direct invasion may occur with cervical, ovarian, gastric and colon cancer. Resection or bypass are mostly palliative except for melanoma where resection can possibly prolong survival.[130] Laparoscopic or laparoscopic assisted resection/internal bypass may be considered to ameliorate obstruction and improve quality of life.[131]In the palliative situation we believe a laparoscopic therapy may be attempted, although there is no evidence to substantiate this.

Discussion

Appropriate trials for colorectal cancer have demonstrated that the laparoscopic approach is safe and at least equivalent to open techniques with regard to survival and recurrence rates.[8-11] This allows the surgeon to offer the laparoscopic option to patients without restriction. To date the same cannot be assumed for other organs. In contrast to Pacific Asian countries early gastric cancers only makes up for a small percentage of all gastric cancers. Therefore the evidence to perform a laparoscopic procedure for our patients with gastric cancer is less strong (level II).[49] Analogous prospective randomized clinical trials are necessary for all organs, comparing resection margin positivity, nodal harvests where appropriate, recurrence rates, survival, quality of life, and cost.

Innovation and the development of new techniques are critical to the advancement of surgery. But strictly speaking laparoscopic surgery for most gastrointestinal cancers must still be regarded as experimental. The learning curves for laparoscopic cancer surgery are

considerable.[11,23,48,94] These were mostly determined by indirect measures of surgical experience like conversion rates and operating time.[11,94] Studies specifically designed to analyze the learning curve determined a vast panel of outcome measures including operative time, transfusion requirement, conversion rate, readmission and postoperative complication rates.[23,48] For distal gastrectomy only operative time improved with the surgeons experience.[48] For colon resection there was an additional benefit regarding the conversion rate which was also dependent on body mass index, ASA grade, type of resection and the presence of abscess or fistula.[23] For the US colon cancer trials, cadre of surgeons across the country were evaluated for their skills and in some cases trained under the guidance of experts to ensure uniform operative technique and enough case expertise.[8] The surgical community insisted on the completion of these randomized trials for colon and rectal cancer before it was determined that laparoscopic resection could be recommended.

The same caution seems prudent for other cancers as well. The fundamental question is whether there is anything truly different about a laparoscopic approach or is it really just a different surgical instrument but the same operation? Do we really need to answer the question in randomized trials for each organ or can we extrapolate from open surgery? Approaching these operations requires immense laparoscopic skills, therefore the surgeon might short cut on the procedure making the operation different from an open procedure. The techniques for laparoscopic gastric and pancreatic resections currently are not uniform. While it is correct that a laparoscopic distal pancreatectomy can yield a nodal harvest similar to an open procedure, the laparoscopic approach currently used by many surgeons across the country often results in a skeletonization of the gland with few nodes retrieved. A randomized trial would address this deficiency. Randomized trials also stimulate technical innovation and provide a large bank of tumors for basic science research. As randomized trials for any of these conditions require financial resources, patient accrual, and surgical skill, a national organization will be needed to organize and complete this task. A way forward may be for the American College of Surgeons Surgical Oncology Group (ACOSOG) to engage specific surgical specialty organizations with the backing of the National Institutes of Health (NIH) for funding. As an example, both the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the Society for Surgery of the Alimentary Tract (SSAT) have members with expertise in both the laparoscopic and open treatment of intestinal tumors. Utilizing the resources and expertise of ACOSOG, the membership of these and other surgical organizations could work with ACOSOG to initiate and complete the trial. This process would allow adequate involvement of surgeons, patient accrual, assure sufficient medical and technical expertise, and reliably determine the utility of laparoscopic surgery for malignant disease that involves these organs (Figure 1).

For the present, the surgeon is left to counsel the cancer patient regarding plans for operative treatment. Other than colon and rectal cancer, there are no data to support anything short of an open procedure for a known cancer, and the patient should be informed of this. As long as the patient understands the potential implications of this data void, the patient and surgeon may well come to the conclusion that a laparoscopic approach seems feasible. In selected cases a laparoscopic approach is reasonable, provided the surgeon has significant laparoscopic skill and experience. A better solution, though, would be a commitment to randomized trials so that we can be armed with reliable data that help to guide our surgical community and assure the best of patient care.

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Abbreviations

AAES	American Association of Endocrine Surgeons
ACOSOG	American College of Surgeons Surgical Oncology Group
ACSEI	American College of Surgeons Education Institutes
AHPBA	American Hepato-Pancreato-Biliary Association
APA	American Pancreatic Association
ASTS	American Society of Transplant Surgery
CLASICC	Conventional versus Laparoscopic-assisted Surgery in Colorectal Cancer
COLOR	Colon Cancer Laparoscopic or Open Resection
COSTSG	Clinical Outcomes of Surgical Therapy Study Group
GIST	Gastrointestinal stromal tumor
HPF	High power field
NIH	National Institute of Health
SAGES	Society of American Gastrointestinal and Endoscopic Surgeons
SSAT	Society for Surgery of the Alimentary Tract
SSO	Society of Surgical Oncology
STS	Society of Thoracic Surgeons

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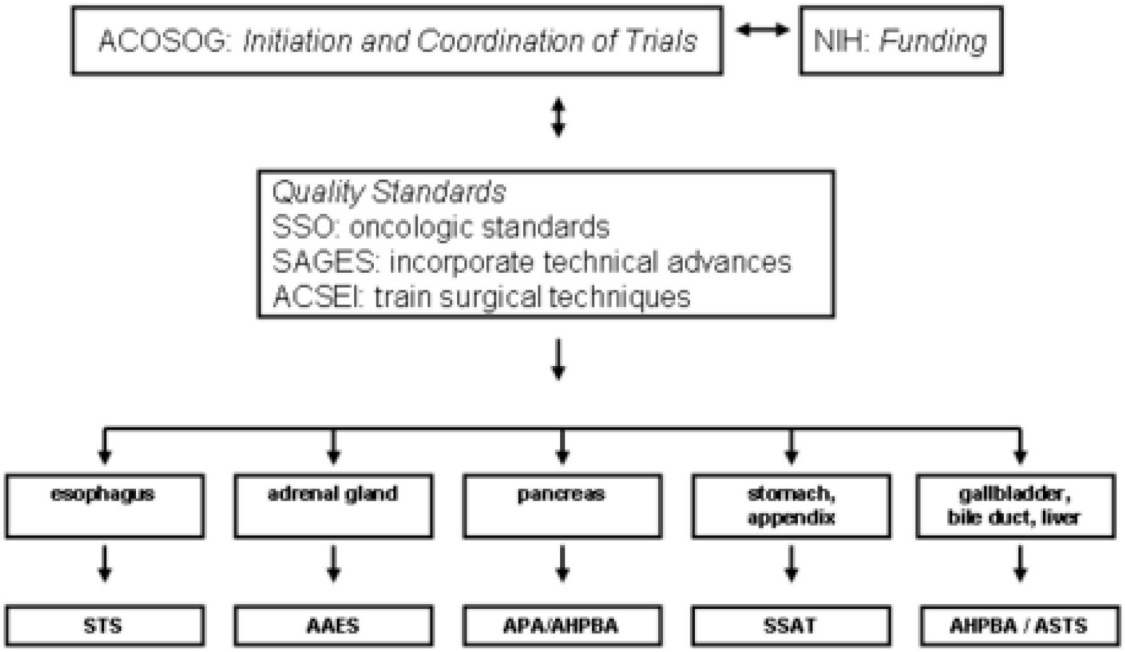

Figure 1.
Schematic for proposed studies to establish laparoscopic surgery in abdominal cancer.

TABLE 1

Modified Level of Evidence and Grade of Recommendation According to Sackett[1]

Level of Evidence	Type of Trial	Grade of Recommendation
I	Large randomized trials with clear-cut results (and low risk of error)	A
II	Small randomized trials with uncertain results (and moderate to high risk of error)	B
III	Nonrandomized contemporaneous controls	C
IV	Nonrandomized, historical controls	none
V	No controls, case-series only, opinion of experts	none

TABLE 2

Evidence and Recommendations in the literature

Organ	Level of Evidence	Grade of Recommendation	Literature
Colon	I	A	Veldkamp et al.[9] Lacy et al.[10,14] COSTSG[8] Guillou et al.[11] Hewett et al.[12] Jayne et al.[15] Buunen et al.[16] Liang et al.[18]
Rectum	II	B	Lujan et al.[31] Pechlivadines et al.[32] Zhou et al.[34] Ng et al.[35] Jayne et al.[15] Guillou et al.[11] Braga et al. [33]
Stomach	II	B	Hayashi et al.[45] Huscher et al.[46]
Esophagus	III	C	Bresadola et al.[54] Benzoni et al.[55]
Pancreas	III	C	Rotellar et al.[58] Kooby et al.[59] Palanivelu et al.[63]
Liver	III	C	Cai et al.[71] Lee et al.[72] Topol et al.[73]
Gastric GIST	IV	none	Hindmarsh et al.[80]
Appendix	IV	none	Bucher et al.[83]
Adrenal Gland	IV	none	Toniato et al.[91] Walz et al.[93]
Gall Bladder	V	none	Paoluccci et al.[108]
Bile Duct	V	none	Weber et al.[115]
Small Intestine	V	none	Tricarico et al.[120] Eccher et al.[122] Soeda et al.[125] Kim et al.[128]

TABLE 3

Prospective Randomized Trials on Laparoscopic versus Open Surgery for Colon Cancer

Reference	Study	Resection Type	Exclusion	n	Technique	Operating time (min)	Morbidity	Mortality	Lymph nodes (n)	Median Follow-up (months)	Recurrence	Overall 3-Year Survival
Veldkamp et al[9] Buunen et al[16]	COLOR	Right Side Left Side Sigmoid Other	BMI > 30 kg/m^2 Transverse Splenic Flexure Metastasis Intestinal Obstrruction Multiple Primary Tumors Synchronous Abdominal Surgery Organ Invasion Previous Colon Surgery Previous Malignancy	551	open	115 *	20.0%	2%	10	53	17.0%	84.2%
				544	laparoscopy assisted	145 *	21.0%	1%	10		19.7%	81.8%
Lacy et al[10,14]	Barcelona Trial	Right Side Left Side Sigmoid Anterior Resection Subtotal Colectomy Hartmann Procedure	Transverse Metastasis Organ Invasion Intestinal Obstruction Previous Colon Surgery	102	open	118 *	28.7% *	2.9%	11.1	95	28.0%	~82%
				106	laparoscopy assisted	142 *	10.8% *	<1%	11.1		18.0%	~86%
Clinical Outcomes of Surgical Therapy Study Group[8]	COSTSG	Right Side Left Side Sigmoid	Transverse Rectal Metastasis Emergency	428	open	95 *	20.0%	1%	12	53	19.6%	~85%
				435	laparoscopy assisted	150 *	21.0%	<1%	12		17.5%	~85%
Guillou et al[11] Jayne et al[15]	CLASICC	Right Side Left Side Sigmoid Anterior Resection Abdominoperineal Resection	Transverse Intestinal Obstruction Previous Malignancy Multiple Primary Tumors Pregnancy Other GI Disease	253	open	–	42.0%	5%	13.5	36.8	22.2%	66.7%
				484	laparoscopy assisted	–	47.0%	4%	12		23.8%	68.4%

* significant in original publication