ABSTRACT  Minimal access approaches in the treatment of a variety of solid tumors of the stom-ach, large bowel, and genitourinary system are now being advocated in several surgical special-ty areas. The laparoscope has evolved from a diagnostic tool to a modality that allows for removal of tumors using small incisions and the application of pneumoperitoneum with carbon dioxide. Through studies using animal models and patient investigation, the immunologic benefits of laparoscopic cancer procedures appear to be beneficial when compared with conventional laparotomy. Overall benefits of analgesic reduction, more rapid postoperative recovery, and patient satisfaction are the byproducts of minimal access approaches. Patients with cancers of the stomach, colon, and kidney show similar long-term outcomes when compared with conventional open techniques. Caution, however, should be exercised in recommending laparoscopic approaches for routine management of primary tumors of the rectum and adrenal gland. (CA Cancer J Clin 2007;57:130–146.) © American Cancer Society, Inc., 2007

INTRODUCTION

“The cleaner and gentler the act of operation, the less pain the patient suffers, the smoother and quicker the convalescence, the more exquisite his healed wound, the happier his memory of the whole incident.” — Lord Moynihan, 1920

The treatment of cancer is a primary focus not only for the general surgeon, but also for surgeons in diverse specialty areas. Despite significant improvements in multimodality treatment over the last several decades, the extirpation of solid tumors continues to be the primary method of treating patients with cancer. Currently, neoadjuvant applications of chemotherapy and radiation are used to shrink tumor size or to “sterilize” the systemic circulation before removal of bulky tumors. These improvements in management of the cancer patient remain dependent on the ability to remove solid cancers, since the consequence of leaving residual tumor in place is incurability.

Before the operative treatment of any malignancy, information must be obtained to provide pathologic certainty of its histology and data relating to the stage of the cancer. The current edition of the Tumor–Node–Metastasis (TNM) Staging Manual provides staging strategies that relate to most solid tumors. Since the introduction of laparoscopic cholecystomy in the mid-1980s, the laparoscope has become a primary tool for surgeons in the application of minimal access procedures for both diagnostic and therapeutic maneuvers in the management of abdominal malignancy. Recent studies have highlighted the indications and techniques of diagnostic laparoscopy in the management of a number of tumors. The present review is limited to the laparoscopic management of a variety of gastrointestinal and genitourinary tumors once adequate diagnosis has been achieved.

BENEFITS OF MINIMAL ACCESS CANCER MANAGEMENT

In the early and mid-1990s, concern was raised in regard to the appropriateness of laparoscopic methods for the treatment of malignancy. These concerns were related to the possibility of performing adequate resections laparoscopically, as well as to the physiological consequences of applying pneumoperitoneum during the laparo-scopic procedures. Early reports concerning a rising incidence of port-site recurrence also created concerns as...
to the long-term outcome of laparoscopic abdominal cancer procedures. Over the last several years, it has been realized that the incidence of abdominal wall tumor recurrence has not been significant and, in fact, may be lower than recurrence rates occurring in conventional laparotomy wounds. Furthermore, long-term survival rates have proven that there are no significant differences between oncologic outcomes of laparoscopic and open operations for a variety of abdominal tumors.11,12

A significant body of information has also shown that, from an immunological standpoint,13 patients seem to benefit from a reduction of trauma to the abdominal wall as a consequence of laparoscopic approaches. The host’s ability to defend against tumor cell implantation may also be improved after laparoscopic resection. Most studies have suggested that laparotomy stimulates peritoneal macrophages when compared with CO2 pneumoperitoneum or anesthesia alone.14 This may be the only situation where there is a benefit for open laparotomy when compared with laparoscopic approaches. The effect on macrophages over the long term has not been elucidated, and it is believed that while immunologic consequences of open and minimal access techniques are important, these may, in fact, equalize in just a few weeks after a surgical procedure for cancer.

There is considerable evidence from animal studies that abdominal surgical procedures using full laparotomy incisions are associated with increased systemic tumor growth postoperatively.15,16 Laparoscopic procedures are associated with similar, but smaller, increases in tumor growth. It remains to be seen whether the surgical technique-related differences (open or closed methods) in tumor growth and improved immune function noted in animal and some human studies will translate into improvement in survival rates or a reduced incidence of distant metastases in patients treated with minimally invasive techniques.

GASTRIC CANCER

Since the first successful gastric resection by Billroth in 1881, surgeons have developed a number of approaches for the management of gastric cancer. Over the last 10 years, laparoscopic resection of gastric cancer has been used, especially by Japanese surgeons in their approaches to early gastric cancer. Both partial gastrectomy and total gastrectomy have been accomplished with laparoscopic techniques. The addition of hand-assisted methods has also allowed surgeons the dexterity of tactile mobilization of the stomach during resection. Appropriate numbers of lymph nodes have also been resected laparoscopically, when compared with open techniques.17

Shimizu and colleagues17 reported laparoscopic resection in 85 patients with gastric cancer. Most patients underwent distal gastrectomy, while a small number had wedge resection of their early gastric cancers. All lesions were located in the body or antrum in the distal gastrectomy group. For patients undergoing wedge resection, 55% of the lesions were in the cardia of the stomach. Conversion to open operations was necessary in 8% of the patients. Of the patients converted to laparotomy, 5 patients underwent open resection because of body habitus and the need to have a better lymph node resection. In this Japanese study, pathologic examination of the resected specimens of the patients undergoing resection for submucosal tumors showed that 9 gastrointestinal stromal tumors (GIST) were found. Several recent reports18,19 have suggested that GIST lesions are particularly amenable to the laparoscopic approach and that only a clear margin is necessary. This has led to wedge resection for many of these tumors.

Since the incidence of gastric cancer is significantly greater in Asia, surgeons practicing minimal access techniques have been at the forefront in these areas and have perfected minimal access techniques of gastric resection. In 1994, Ohgami and colleagues20 reported a technique using the laparoscopic wedge resection for intramucosal cancers less than 25 mm in diameter without evidence of lymph node metastases. Subsequently, intragastric surgical procedures were developed for the resection of early gastric cancer. This approach was unique in that trocars or instruments were placed into the gastric lumen through both the abdominal and gastric walls.
The technique of laparoscopic distal gastrectomy with lymph node dissection developed by Kitano and colleagues\textsuperscript{21} is the primary procedure used for patients with T1 and T2 carcinomas.\textsuperscript{2} When compared with conventional open gastrectomy, the less-invasive approach used by laparoscopy is associated with a faster postoperative recovery and a better quality of life. Goh and colleagues\textsuperscript{22} found that laparoscopic gastrectomy was superior to open gastrectomy because laparoscopic gastrectomy was associated with less pain, faster recovery, and better cosmesis. Similarly, earlier return to oral intake and a shorter duration of hospitalization have been cited as absolute benefits of laparoscopic gastrectomy when compared with open techniques. In view of the faster recovery and less need for analgesia, the overall cost of laparoscopic gastrectomy is favorable when compared with conventional approaches.\textsuperscript{23}

Curability of gastric cancer is, of course, the most significant of outcomes, and the extent of lymph node dissection is associated with the opportunity to cure these patients. Studies have shown that the use of hand-assisted techniques further assures that the lymph node dissection is equivalent to that seen with open surgical procedures.\textsuperscript{11,17} As in most operative procedures, the learning curve is important. An increase in the number of dissected lymph nodes is generally found as the surgeon’s experience with the technique increases.\textsuperscript{17}

Although laparoscopic distal gastrectomy has not been fully accepted worldwide, surgeons working in Japan and in other Asian countries have accepted this technique as being oncologically equivalent to open surgical techniques for gastric cancer. The minimal access approach for gastric cancer was officially approved by the Japanese Gastric Cancer Association in 2001 as a procedure for the treatment of early gastric cancer. For surgeons throughout the rest of the world, the laparoscopic management of gastric cancer should be performed in centers with a significant interest in the minimal access approaches to gastrointestinal cancer and in the institutions where patients can be entered into clinical trials and computerized databases.

### LAPAROSCOPIC MANAGEMENT OF GENITOURINARY TUMORS

During the past decade, laparoscopic nephrectomy and laparoscopic adrenalectomy have become important surgical approaches for most renal and adrenal tumors. When compared with the traditional open approach, laparoscopic solid organ surgery has been associated with substantial reductions in perioperative morbidity, length of stay, and convalescence.\textsuperscript{24–27} As experience with these techniques has evolved, more aggressive approaches have led to minimally invasive resection of larger tumors, bilateral pathology, and metastatic disease. From an oncologic perspective, data have been quite favorable with respect to long-term outcomes for the laparoscopic resection of renal cell cancer. Laparoscopic management of adrenal malignancies, however, remains controversial, particularly in the setting of primary adrenal cancers.

#### Renal Cell Carcinoma

The safety and efficacy of minimally invasive approaches to renal cell carcinoma (RCC) have been well-documented and widely accepted. As a result, laparoscopic radical nephrectomy (LRN) has rapidly become the standard approach to RCC in the majority of centers during the past decade.\textsuperscript{28} Although strong arguments have been made for the superiority of various operative approaches (transperitoneal versus retroperitoneal and laparoscopic versus hand-assisted), the benefits of laparoscopy in general have been relatively easy to agree on.

Whether performed for benign or malignant disease, standard laparoscopic nephrectomy has uniformly demonstrated less blood loss, a reduction in narcotic requirements, earlier oral intake, fewer hospital days, and a more rapid return to normal activities when compared with the open approach.\textsuperscript{29} When one considers the magnitude of the traditional radical nephrectomy incisions alone (flank, subcostal, or thoracoabdominal), the ability of the laparoscopic approach to reduce patient morbidity is not surprising. In the earliest report on radical nephrectomy outcomes in 1969 by Robson et al,\textsuperscript{30} 75% of patients were managed through a thoracoabdominal incision,
a fact that likely reflects both the size of tumors encountered, as well as the lack of less invasive surgical techniques available at that time. With recent improvements in diagnostic imaging, earlier diagnosis of smaller lesions, and advances in surgical technology, the ability to cure RCC through minimally invasive means has been accelerated drastically. Not only can we now perform radical nephrectomies through three or four laparoscopic ports, but we can also perform nephron-sparing surgery in the form of laparoscopic partial nephrectomy, and percutaneous techniques for tumor ablation are being used on a regular basis in many centers. These techniques are associated with dramatic reductions in short-term morbidity. More importantly, the oncologic efficacy and safety of the minimally invasive management of RCC have now been substantiated by longer-term data.

In one of the earliest published series, Gill and colleagues reported that LRN decreases morbidity and expedites recovery without sacrificing oncologic efficacy. Thirty-four patients with early stage RCC undergoing laparoscopic retroperitoneal radical nephrectomy were compared with a contemporary group of 34 patients undergoing open surgery. Patients treated laparoscopically had fewer complications, less blood loss, lower analgesic requirements, fewer hospital days, and a more rapid convalescence. At a mean follow up of 13 months, there were no differences in cancer-free survival or overall survival between the laparoscopic and open groups, and there were no local recurrences or port-site tumor implants following laparoscopy.

Ono and coworkers subsequently reported their 5-year data in 60 patients who underwent transperitoneal LRN and compared them with 40 patients treated with open surgery for small (T1) renal cell cancers. Operative time was significantly longer for laparoscopy (5.2 versus 3.3 hours), while blood loss (255 mL versus 512 mL) and convalescence (23 versus 57 days) were less. The conversion rate was 1.6%. Five-year disease-free survival rates were equivalent for the 2 groups at greater than 95%.

Based on these data, there is no debate regarding the applicability of LRN to organ-confined, clinical stage T1 and T2 lesions. The feasibility of LRN for larger lesions (stage T3, including those with renal vein tumor thrombus) has been more slowly established, primarily due to the technical challenges associated with the laparoscopic resection of these tumors. While various authors have argued the pros and cons of transperitoneal versus retroperitoneal and pure laparoscopic versus hand-assisted LRN, there have been no significant differences in short-term or long-term outcomes based on approach. The exact technique chosen should be based on the training, comfort level, and skill of the individual surgeon. While using all three approaches described, we have favored the hand-assisted approach.

In our experience (K.W.K., C.M.T., unpublished data, 2006), the transition from a purely laparoscopic approach to a hand-assisted approach resulted in a 56-minute reduction in mean operative time. This was achieved with no differences in blood loss, length of stay, total charges, or rate of return to normal activity. From a technical standpoint, we have found that the extraction/morcellation dilemma is eliminated by allowing for kidney removal through the same abdominal incision used for insertion of the hand-assist device. Consistent with the literature, we have been able to successfully perform hand-assisted LRN in 212 patients with tumors as large as 20 cm, including patients with tumor thrombus extending into the renal vein and/or vena cava (stage T3b). Of these, 19 presented with metastatic disease and were treated with cytoreductive LRN before the initiation of immunotherapy. For patients undergoing LRN, mean tumor size was 6.8 cm (range, 1.5 to 20 cm), mean blood loss was 112 mL, and mean operative time was 189 minutes. Three cases (1.4%) were converted to open due to...
invasion of adjacent organs and/or inferior vena cava tumor thrombus. Average length of stay was 4.6 days. There have been no perioperative mortalities. To date, we have observed no local or port-site metastases, which is consistent with the very low rates of local recurrence (2.2%) and port-site metastases (only 4 cases to date reported in the literature) in other series.35

Five patients in our series (1 right and 4 left-side tumors) presented with tumor thrombus extending into the renal vein and/or vena cava below the diaphragm. Mean blood loss for these cases was 215 mL, with a mean operative time of 265 minutes. There were no positive margins and no instances of venous tumor embolism. One right nephrectomy was converted to open due to local invasion of the liver. Other authors have reported their experience with the laparoscopic management of tumor thrombus, although follow up has averaged less than 18 months.36,37 While these procedures are technically feasible, longer-term clinical outcomes data will be required to establish equivalency with the traditional open approach.

Cytoreductive nephrectomy (whether performed laparoscopically or open) for patients with metastatic disease has the potential palliative benefit of improvement in quality of life. Nephrectomy in these patients, while not curative, has also been shown to improve survival with or without the addition of postoperative immunotherapy.38 In this subset of patients with overall poor survival and often compromised performance status, the advantages of a minimally invasive approach may be even more important with respect to perioperative morbidity and functional recovery. In addition to a more rapid convalescence, patients treated with LRN have a shorter interval to the initiation of Interleukin-2 therapy compared with patients treated with an open procedure.38 Despite these potential advantages, LRN is technically much more difficult in these patients due to larger tumor size, increased vascularity, and local desmoplastic response with adherence to adjacent structures (particularly the colonic mesentery). As a result, we believe that the development of a high level of comfort with LRN or hand-assisted LRN for organ-confined disease should be obtained before attempting these cases laparoscopically.

The potential technical challenges of laparoscopic nephrectomy are even more exaggerated for partial nephrectomy, which requires vascular dissection and control, excision of the lesion, and repair of the kidney. Recent developments in technique, instrumentation, and increasing surgeon comfort with laparoscopic nephrectomy have generated a technically feasible and reproducible procedure that is comparable to the open approach with respect to perioperative parameters (operative time, blood loss, complications) and short-term oncologic outcomes. Gill et al39 reported 50 patients undergoing laparoscopic partial nephrectomy for tumors with a mean size of 3 cm (range, 1.4 to 7 cm), a mean operative time of 3 hours, and an average blood loss of 270 mL. Average warm ischemia time was 23 minutes (range, 9.8 to 40 minutes), all of which compares very favorably with the authors’ experience and accepted standards for open partial nephrectomy. More importantly, all excisions were achieved laparoscopically with negative margins and no local recurrences at 7.2 months follow up. In a recent series with longer-term follow up, Allaf and colleagues40 found a positive surgical margin in 1 patient (2%) and no local recurrence in 46 of 48 (95.8%) patients at 3 years. When compared with open partial nephrectomy (with a local recurrence rate of 1% and a 97% 3-year disease-specific survival), the applicability of laparoscopy to favorably located T1 lesions appears to be well supported and is rapidly becoming the standard approach, even in patients with a normal contralateral kidney. We have adopted a similar strategy and have obtained similar results for laparoscopic partial nephrectomy in patients with small (less than 4 cm) tumors that do not involve the renal hilum. In the past 2 years, 29 patients have undergone laparoscopic partial nephrectomy, with a mean operative time of 158 minutes, average warm ischemia time of 31 minutes, and mean blood loss of 168 mL. The overall minor complication rate was 10%, with no conversions, no renal losses, and no local recurrences during short-term follow up. These results compare favorably with our previous experience with open partial nephrectomy, with a trend toward shorter operative times, less blood loss,
and fewer complications for patients managed laparoscopically. With larger numbers of cases analyzed, we anticipate that these differences will become statistically significant.

LRN provides the perioperative advantages of minimally invasive surgery when compared with the traditional approach. More importantly, recent intermediate and long-term data confirm that the technique offers equivalent oncologic outcomes for RCC. Early data regarding the applicability of the laparoscopic approach to locally advanced disease, as well as cytoreductive nephrectomy for metastatic patients, is encouraging; however, long-term outcomes will need to be evaluated. For favorably located lesions less than 4 cm, laparoscopic partial nephrectomy is safe and effective, though technically challenging. While varying laparoscopic operative approaches have been advocated, all are effective, and all maintain the benefits of minimally invasive surgery, while providing long-term outcomes that are comparable to the traditional open approach. Ultimately, the individual surgeon should use the approach with which he or she has the most comfort and experience.

Laparoscopic Adrenalectomy

Since the procedure was initially described in 1992, laparoscopic adrenalectomy has become the preferred approach for the surgical treatment of benign functional and nonfunctional adrenal tumors because multiple studies have shown significant reductions in short-term perioperative morbidity compared with the traditional open approach. As a result, many surgeons have broadened the indications for the procedure at both ends of the spectrum, including the adoption of more liberal size criteria for the resection of smaller, indeterminate lesions (“incidentalomas”), as well as more aggressive approaches to the laparoscopic resection of increasingly larger adrenal neoplasms. Despite arguments in favor of applying minimally invasive approaches to the majority of adrenal lesions, the laparoscopic resection of metastatic and primary adrenal malignancies remains controversial.

Adrenal Metastasis

Although the adrenal glands are relatively common sites for metastatic disease in a number of primary cancers, isolated (and potentially curable) metastasis to the adrenal is rare. In most cases, the finding of an adrenal metastasis is a manifestation of a more systemic process and does not lend itself to surgical resection for cure or even long-term disease control. Yet, there is growing evidence that the resection of isolated (adrenal-only) spread of melanoma, lung, kidney, colon, and breast cancer may improve survival in select patients. In series of open adrenalectomy for metastatic lesions, median survival rates of up to 30 months have been reported, compared with historical survival ranges of 6 to 8 months without resection. The Memorial Sloan-Kettering experience supports adrenalectomy for metastases in patients with isolated disease in which complete resection is feasible, particularly in patients with disease-free intervals of greater than 6 months.

Adrenalectomy for metastases from RCC has been associated with some of the most favorable results. In a review of the literature by Heniford and Pratt, 35 patients with contralateral adrenal metastasis underwent curative resection. Over an average follow-up period of 26 months, 62% of patients had no evidence of residual or recurrent RCC. Our group has had a similarly favorable experience with the management of renal cell metastases to the adrenal gland. In the past 4 years, 5 patients with a mean tumor size of 10.4 cm (range, 4 to 19 cm) have undergone adrenalectomy (2 laparoscopic, 2 hand-assisted laparoscopic, 1 open) for RCC metastatic to the contralateral adrenal gland. Four are disease-free at an average of 15 months (range, 4 to 40 months) post adrenalectomy. One patient with preoperative bony and pulmonary metastases has experienced stabilization of metastatic disease with Interleukin-2 therapy and is alive 18 months after laparoscopic contralateral adrenalectomy for an 11-cm locally expansive adrenal implant.

Long-term disease-free survival after resection of isolated adrenal metastases from nonsmall cell lung cancer has also been reported. In Luketich and Burt’s retrospective series of 14 patients, chemotherapy followed by surgical resection
was superior to chemotherapy alone in select patients. All patients subject to medical management alone were dead by 21 months. In the surgically resected group, the 3-year actuarial survival was 38%. Other authors have reported similarly favorable outcomes, with 5-year survival rates of 25% to 40% in selected patients undergoing adrenal metastasectomy for lung cancer. Regardless of tumor pathology or origin, all authors point to careful patient selection for successful outcomes. These outcomes include complete control of the primary tumor, a metastatic survey that confirms isolated adrenal disease, and complete surgical resection of the involved adrenal gland.

Several factors support the minimally invasive resection of adrenal metastases. One is the dramatic increase in surgeon experience with advanced laparoscopic techniques. With the growth of laparoscopic solid organ surgery, surgeon comfort levels with organ dissection, atraumatic retraction, vascular control, and specimen retrieval have increased dramatically. As a result, laparoscopy has become the preferred approach for many surgeons who manage both benign and malignant lesions of the kidney, adrenal, spleen, and pancreas. Minimally invasive techniques offer excellent visualization, early vascular control, and the ability to effectively screen for conditions such as peritoneal spread of disease that might preclude resection. These features, along with the general consensus that laparoscopy can be safely applied to cancer, have made the transition from open to laparoscopic adrenal metastasectomy a natural progression.

One feature that provides substantial support for the laparoscopic approach is the recognition that most malignancies metastasize to the medullary portion (center) of the gland, rather than to the adrenal cortex. Adrenal metastases rarely penetrate through the capsule of the gland, making laparoscopic surgical resection much less likely to result in tumor fracture, which could potentially predispose to increased rates of local recurrence or intraperitoneal dissemination. To date, 8 series totaling 98 patients have reported the use of laparoscopic adrenalectomy for metastasis with no port-site recurrences and only 1 patient (1%) developing peritoneal dissemination of disease. Disease-free survival rates have ranged from 42% to 91% over a mean follow-up interval of 8 to 26 months.

Moinzedah and Gill recently described 31 patients who underwent laparoscopic adrenalectomy for malignancy; 26 had isolated adrenal metastasis, 6 had primary (incidentally discovered) adrenal cortical carcinoma (ACC), and one had malignant pheochromocytoma. In this series, the overall local recurrence rate was 23%, including 5 of 26 (19%) patients with adrenal metastases and 2 of 6 (33%) with ACC. There were no port-site recurrences, and there were no positive margins in patients with adrenal metastasis. One patient with metastatic RCC developed carcinomatosis. The remainder of patients with local recurrence also recurred at other (systemic) sites. Notably, patients with local recurrence had a lower likelihood of survival at 3 years than patients without local recurrence (17% versus 66%, \( P = 0.016 \)). Overall 5-year actuarial survival was 40% at a median follow up of 26 months. These data compare favorably with a similar series of 37 patients who underwent open resection of adrenal metastases with a 5-year actuarial survival of 24% and a median survival of 21 months. Other authors have published similar results in small series of patients, with no differences in the incidence of positive resection margins or survival compared with similar groups undergoing open resection of adrenal metastases and no reports of port-site recurrences.

### Adrenal Cortical Carcinoma

While the laparoscopic resection of adrenal metastases has been generally accepted as oncologically sound, the same has not been true for primary ACC. ACC is universally recognized as an extraordinarily aggressive malignancy with an overall poor prognosis. Radical surgical resection provides the only means for cure. Despite aggressive surgical therapy, the actuarial 5-year survival for patients who undergo complete resection ranges from 23% to 48%. Failure to achieve complete resection (including removal of adjacent, involved organs) is associated with a median survival of less than 1 year. As a result, the applicability of laparoscopic techniques, with the possibility of tumor
fracture or inadequate resection of adjacent organs, has been questioned.

Controversy stems from several case reports in the late 1990s that described peritoneal carcinomatosis following the laparoscopic resection of primary ACC. These concerns have been fueled by more recent comparisons of local recurrence rates and long-term survival after laparoscopic and open resection of ACC. In the initial case reports, early postoperative development of carcinomatosis was the outcome in all 5 patients with an incidentally discovered primary ACC who had undergone laparoscopic adrenalectomy for a presumed benign, functional adrenal mass (Conn’s [2]; Cushing’s [2]; virilizing tumor [1]). Three of 5 also suffered from local recurrence, and 1 experienced a port-site recurrence, all occurring between 4 and 14 months after laparoscopic adrenalectomy.

A more contemporary review of the literature between 1998 to 2004 reveals 25 cases of primary adrenal carcinoma resected laparoscopically. Local recurrence and/or intraperitoneal dissemination occurred in 10 of 25 (40%) patients. The disease-free interval averaged 34.1 months. In the most recent report from the group at the MD Anderson Cancer Center, the authors compared recurrence rates for laparoscopic and open resection of ACC. In the open group, 86% of patients (115 of 133) had recurred at a median follow up of 28 months, with 62% dying of metastatic disease and 24% alive with disease. Of these, 35% developed a local recurrence, 8% had peritoneal carcinomatosis, and the remainder recurred with distant disease. Among the 6 patients resected laparoscopically, all recurred, with a significantly higher percentage (83%) developing carcinomatosis. At a mean follow up of 15 months, 66% of laparoscopically managed patients died from metastatic disease, and 33% were alive with disease. Importantly, of the 6 patients with tumors less than or equal to 6 cm who underwent open adrenalectomy, 4 of 6 were disease-free at 21 months. In contrast, 5 of 6 patients in the laparoscopic group presented with tumors less than or equal to 6 cm that were confined to the gland, all of whom developed locally recurrent, distant, and/or peritoneal metastases. The authors concluded that any adrenal lesion suspected of harboring adrenal cortical cancer should be treated in an open fashion.

All of the patients who underwent laparoscopic resection had surgery at outside hospitals and were referred to MD Anderson for further care after recurrence. The training, skill, and expertise of the various surgeons who performed the initial laparoscopic resections is unclear. Given the aggressive nature of ACC, it has been clearly established that the care taken during dissection and tumor handling is of utmost importance. In at least 2 of the 6 cases, tumor fracture, rupture, or uncontrolled hemorrhage was reported to have occurred at the time of the initial operation. We and others have demonstrated that the laparoscopic removal of large adrenal tumors (greater than 10 cm) is feasible and that the operation can be performed in a “radical” fashion, with resection of the adjacent adipose tissue (including adjacent organs if necessary) and without violation of the tumor. To minimize the chances of tumor dissemination, however, these cases must be performed with caution to avoid tumor fracture, and standard oncologic principles absolutely must be maintained.

Since there are no absolute radiographic characteristics, biochemical studies, or size criteria that can reliably predict malignancy, the preoperative diagnosis of ACC is difficult. Of the information available preoperatively, lesion size provides the best objective data for predicting the malignant potential of a given adrenal lesion. In 2002, the National Institutes of Health Consensus Conference Statement on the management of nonfunctioning adrenal incidentalomas recommended resection of all tumors greater than 6 cm. This was based on an estimated risk of ACC between 35% and 98% for these lesions. For tumors between 4 and 6 cm (with an estimated 6% risk of harboring ACC), the consensus recommended resection in patients with low operative risk. For tumors less than 4 cm (with an estimated 2% risk of ACC), recommendations are for serial imaging at 6-month intervals for 18 months to document stability. Although few would argue that all lesions greater than 6 cm should be removed, due to the increasing likelihood of malignancy, the removal of nonfunctional lesions as small as
3 cm has been adopted in some institutions. Since complete surgical resection remains the only potentially curative treatment for ACC, the removal of smaller (early stage) adrenal masses may increase the probability of curative resection. Given the limited morbidity of laparoscopic adrenalectomy, we agree with this philosophy and have, therefore, advocated more aggressive surgical guidelines to include the resection of smaller (3 to 4 cm) nonfunctioning masses.

Long-term disease-free survival after adrenal metastasectomy for isolated metastases from renal, colorectal, lung, and melanoma primaries shows promise in select patients. By reducing the trauma of surgical access, minimally invasive adrenalectomy has clear advantages over an open approach. Yet, improvements in patient satisfaction and early postoperative outcomes should not overshadow the primary goals of patient safety and the performance of an accepted and established oncologic resection. While existing data are encouraging, only through careful staging and appropriate patient selection can the long-term efficacy of the laparoscopic approach be assessed in these patients.

The suitability of the laparoscopic approach to primary ACC remains an area of intense debate. The aggressive nature of this tumor and the lack of effective chemotherapy demand complete surgical resection as the only means for obtaining long-term survival. An aggressive approach to the removal of smaller, nonfunctional adrenal tumors may allow for the curative resection of some patients at earlier stages of disease. Based on the available data, a cautious operative approach is warranted for all adrenal tumors that have characteristics suspicious for primary ACC, regardless of size. If the likelihood of ACC is believed to be low based on size, functional status, and/or radiographic imaging, then a minimally invasive approach is reasonable as long as oncologic principles are maintained. These oncologic principles include wide local resection, avoidance of tumor fracture or spillage, and the use of an impermeable extraction bag. Until further data become available, open radical resection remains the most judicious approach for lesions with a high likelihood of harboring a primary adrenal cortical malignancy.

### TABLE 1 Trials Comparing Laparoscopic with Open Colectomy

| Trial            | Laparoscopic | Open   | Conversion |
|------------------|--------------|--------|------------|
| Barcelona        | 111          | 108    | 12 (11%)*  |
| COSTSG†          | 435          | 437    | 90 (21%)   |
| COLOR‡           | 627          | 621    | 91 (17%)   |
| CLASICC§         | 526          | 268    | 143 (29%)  |

*Indicates "tumor-related" for the Barcelona trial.
†COSTSG = Clinical Outcomes of Surgical Therapy Study Group.
‡COLOR = Colon Carcinoma Laparoscopic or Open Resection.
§CLASICC = Conventional Versus Laparoscopic-assisted Surgery in Colorectal Cancer.

Laparoscopic resection of the colon was first described in 1992. Although techniques and equipment were at first cumbersome, laparoscopic colectomy for benign and malignant conditions of the colon soon became a reality. It was not until the mid-1990s that concerns regarding port-site recurrences generated alarm, and a virtual moratorium was placed on laparoscopic colectomy for curable colon cancer. Port-site implant rates as high as 21% stimulated a more cautious and controlled introduction of laparoscopic colectomy. Results from randomized clinical trials (RCTs) are now available to support the benefits and refute the harm of laparoscopic colectomy for curable colon cancer.

Operative and postoperative results have been reported from at least four prospective RCTs comparing laparoscopic with open colectomy (Table 1). As expected, these RCTs showed similar demographics, ie, the distribution of patients according to age, gender, prior abdominal surgery, health status, and body mass index were balanced between the two treatment arms. Not surprisingly, all four trials demonstrated consistent differences between patients treated with laparoscopic colectomy compared with open colectomy. The duration of laparoscopic resection always exceeded open surgery by 24 to 55 minutes. For the 2 trials reporting length of incision, patients treated with laparoscopic surgery had shorter incisions by 60 to 120 mm. Rates of conversion to open surgery...
ranged from 11% to 29%. Finally, it is reassuring that rates of morbidity and mortality after surgery differed more between the studies than they did between the two arms of the trials.

Patient-related benefits were consistently reported for laparoscopic colectomy in the Barcelona, Clinical Outcomes of Surgical Therapy Study Group (COSTSG), Conventional Versus Laparoscopic-assisted Surgery in Colorectal Cancer (CLASICC), and Colon Carcinoma Laparoscopic or Open Resection (COLOR) trials. Length of ileus, measured as time to first bowel movement, was significantly less, by 1 day, in both the CLASICC and COLOR trials (Table 2). Laparoscopic colectomy patients resumed fluid intake significantly sooner (COLOR trial) and discontinued narcotics and oral analgesics sooner than their counterparts treated with open colectomy (COSTSG trial). Taken together, these recovery advantages added up to significant reductions of approximately 2 days in length of hospital stay for laparoscopic patients. Another approach to measuring patient-related benefits is to directly query patients on quality of life. At least one RCT measured short-term quality-of-life outcomes using a number of validated quality-of-life instruments (Figure 1).
only minimal short-term quality-of-life benefits were found for laparoscopic colectomy. However, there was a statistically significant difference observed between groups based on the 2-week postoperative assessment of global rating score. Quality-of-life benefits alone, since modest, would not compel the acceptance of laparoscopic colectomy for cancer in the absence of solid evidence confirming its oncologic equivalence. Fortunately, oncologic data are now mature and available from the Barcelona and COSTSG trials.

As mentioned previously, the grave concern stimulating international prospective trials was the consistent and concerning reports of wound tumor implants. Several case series, and even some registries, reported rates of trocar-site recurrences in excess of what was historically reported for open surgery. This generated great interest in animal model investigations including mechanisms of tumor cell dissemination and immunologic studies. Clinical evidence was required to refute or confirm the association between the wound tumor implants and laparoscopic colectomy for cancer.

The Barcelona trial was the first to describe long-term cancer data for laparoscopic colectomy, with 106 patients assigned to laparoscopic and 102 assigned to open surgery. No differences in overall survival or disease-free survival were reported for all stages of disease. A provocative difference in cancer-related survival favoring laparoscopy was described for a subset of Stage III patients. Similar differences were not observed for Stage I or II disease, and the subset of Stage III disease was small at 37 patients.

Conclusive long-term cancer data from the COSTSG trial were reported in 2004 (Figures 2 and 3). It was reassuring that wound tumor implants were rare occurrences in both groups of patients and occurred no more often for patients treated with laparoscopic colectomy (2 patients; 0.5%) than with open colectomy (1 patient; 0.2%). The conversion rate in the COSTSG trial was 21%. Although the data were analyzed as intent-to-treat, they were also considered as treatment received, and in no circumstance were survival or recurrence rates compromised by the laparoscopic treatment. Although definitive long-term oncologic outcomes from the other trials should be forthcoming, there appears to be no oncologic harm from this approach. Three caveats from the COSTSG trial regard the credentialing, conversion, and patient selection details of the trial.
Within the COSTSG trial, patient safety was maximized through protocol-specific eligibility and protocol-mandated conversion for tumor findings, as well as through surgeon credentialing for participation. The wide application of laparoscopic colectomy for colon cancer requires compliance with these clinical trial specifications.

Patients were eligible for the COSTSG trial if they had curable, Stage I-III colon cancer and had no contraindications to laparoscopic surgery. To ensure long-term data on a high percentage of patients, those with Stage IV cancer or life-limiting comorbidities were not included. To protect patients from undue risk, the presence of bowel obstruction, perforation, or locally advanced bulky disease rendered patients ineligible for the trial. Patients with transverse colon cancers were excluded for technical reasons related to the complexity of mobilizing 2 flexures with 1994 techniques and equipment.

For contemporary clinical practice purposes, patients can be offered the laparoscopic approach to treat all stages of colon cancer. From a cancer treatment standpoint, we would discourage the use of laparoscopic colectomy in a patient with a large, bulky, or adherent (T4) tumor or in tumors associated with bowel obstruction or perforation. As with any laparoscopic case, we would not offer laparoscopy to patients with prohibitive adhesions from prior surgical procedures or to patients with severe cardiac or pulmonary comorbidities or other contraindications to pneumoperitoneum. Once patients are selected for surgery, there are a few intraoperative tumor-specific reasons for converting to open surgery, including the identification of resectable hepatic metastases or bulky T4 lesions.

Credentialing of surgeons in the performance of laparoscopic colectomy for cancer is of paramount importance. The high-quality results from the COSTSG trial (including the 0.2% to 0.5% incidence of trocar recurrence) support the credentialing criteria used to enlist surgeons. Surgeons had to submit operative and pathology notes on 20 laparoscopic colon cases to show a minimal experience with laparoscopic colorectal surgery. They also had to submit a video of a laparoscopic colectomy to demonstrate critical features, including handling of tissues, exploration for metastatic disease, and vascular pedicle ligation. To ensure adequate recruitment, we examined tumor registry data on annual colon cancer cases at their institutions. The lack of evidence in this trial of
a “learning curve” effect speaks favorably of this credentialing process. The practical implications of these credentialing guidelines are that surgeons should seriously consider fulfilling the same guidelines before embarking on a laparoscopic colectomy for cancer.

Before surgery, colon cancer patients should undergo sufficient imaging to evaluate the liver for metastases and the primary tumor for bulky size or local adherence to other structures. Both conditions would encourage an open approach. It is also imperative that preoperative tests provide a high degree of confidence regarding the location of the primary tumor. As screening increases, tumor sizes decrease, rendering the relative contribution of endoscopic tattooing more useful. Intraoperative tips specific to cancer include the rapid assessment of feasibility based on presence of prohibitive adhesions, T4 lesions, resectable metastatic lesions, or altered anatomy. Bowel and tumor handling should be kept to a minimum. The abdomen should be thoroughly explored for spread of disease to the liver, peritoneal surfaces, omentum, and/or ovaries. We encourage wound protection and irrigation, as well as standard oncologic approaches such as proximal vascular ligation.

Developing a systematic or standardized surgical plan and sharing this with the house staff and operating team helps coordinate the surgical efforts. We have described a simple 5-step procedure for laparoscopic colectomy; this can be reversed and applied for the left colon as well. We also have written and illustrated the 6-step procedure for laparoscopic sigmoid colectomy. Both approaches can be adopted to use with the hand port.

There are numerous issues unique to rectal cancer and its resection, which have contributed to its exclusion from recent prospective clinical trials. Surgical resection of rectal cancer remains the most important method to achieve cure, to accurately stage, and to give valuable prognostic information to be used in treatment decisions. Additionally, the quality of the surgery and the accuracy of pathologic staging are the most important prognostic factors in predicting recurrent rectal cancer. Laparotomy and meticulous total mesorectal excision, as advocated by Heald et al, is currently the accepted standard of care for middle and low rectal cancers. This technique has consistently been associated with low recurrence rates and optimal survival statistics in the literature. Laparoscopic resection of rectal cancer must duplicate these oncologic results and prove equivalent to open surgery with solid Level 1 evidence before becoming an accepted surgical modality for rectal cancer.

Although most studies of laparoscopic-assisted colon resection exclude rectal cancer, there are several single institution studies that demonstrate the feasibility of laparoscopic-assisted resection of rectal cancer (LARR). Feliciotti et al prospectively studied LARR and open resections and found both methods respected surgical oncologic principles, with similar long-term outcomes. Additional studies have mimicked these results.

A number of single-center case series have evaluated the morbidity and mortality in LARR. Prospective studies revealed that LARR did not worsen survival or disease control for patients with rectosigmoid cancer when compared with open surgery. Barlehner et al studied and reviewed the literature, demonstrating that laparoscopic resection for rectal carcinoma is not associated with a high morbidity or mortality.

Two recent meta-analyses have reviewed the current literature on LARR. Gao and coworkers analyzed 11 studies in the literature from 1995 to 2005, which included 285 patients who had undergone LARR. The study found laparoscopic surgery to be associated with lower morbidity rates but longer operative times. Rates of wound infection, anastomotic leakage, and mortality rates were similar between open and laparoscopic procedures. Aziz et al analyzed 20 studies...
from 1993 to 2004, reporting on 909 patients who underwent a laparoscopic resection and 1,162 who underwent an open resection for their rectal cancer. This analysis revealed a decrease in the length of hospital stay, time to first bowel movement, and time to stomal function in patients who underwent laparoscopic surgery. Specifically, in the set of patients requiring an abdominal perineal resection, laparoscopic patients required less parenteral analgesics and had a reduced rate of postoperative wound infections. Oncologic outcomes in both meta-analyses did not reveal a difference between the open or laparoscopic surgery groups.

While these results from multiple case series and case-matched studies seem optimistic, there is a paucity of high-quality evidence to support the practice of LARR. Only a single, large, prospectively RCT of laparoscopic surgery has reported on both colon analgesics and rectal cancer.74 This study specifically raised concerns regarding LARR. The conversion rate was 29% (n = 143 conversions, 61 colon and 82 rectal cases) for the entire cohort, and the conversion rate was 34% (82/242) for the rectal cases. In the rectal surgery subgroup, the circumferential radial margin positivity was greater in the laparoscopic group when compared with open surgery. This difference was not appreciated in the abdominal perineal laparoscopic procedure group, but was specific to the laparoscopic low anterior resection procedure. While this difference did not reach statistical significance, there was a trend toward a higher margin positivity with laparoscopic low anterior resection, compared with the open arm. Findings from the CLASICC trial led Guillou and colleagues74 to conclude that “impaired short-term outcomes and pathological features after laparoscopic anterior resection do not yet justify routine use of the approach in cancers of the rectum.” These findings raise concerns as to the level of precision that is achievable in laparoscopic surgery and pose the question of whether LARR is a safe, effective oncologic approach to rectal cancer. These concerns must be addressed with a prospective RCT of LARR.

To address the need for Level 1 evidence in the debate surrounding LARR, members of the American College of Surgeons Oncology Group (ACOSOG) have developed a prospective, randomized, Phase II trial to test the hypothesis that laparoscopic surgery is a technically and oncologically safe and feasible approach to the resection of rectal cancer. The primary endpoint is a composite of oncologic and technical factors that are indicative of a safe and feasible operation. Oncologic parameters include the adequacy of the lymph node harvest and circumferential and distal margin status. Technical factors include anastomotic leak rate and the incidence of iatrogenic rectal perforation. These parameters are based on the surgical guidelines for rectal cancer.95 Disease-free survival and local pelvic recurrence rates will be evaluated at 2 years as secondary endpoints. Quality-of-life measures, sexual function outcomes, length of stay, and recovery data will be assessed preoperatively, immediately postoperatively, and at established follow-up intervals in the trial. Until clinical equipoise is resolved regarding this technique, it is paramount for all surgeons and investigators to contribute to the clinical research that addresses laparoscopic rectal surgery.

Through prospective RCTs, the question will ultimately be answered regarding the appropriate place of laparoscopic surgery in the field of rectal cancer. To establish the equivalency of the laparoscopic approach, all laparoscopic rectal resections should be completed in an environment where the outcomes can be meaningfully evaluated and the clinical relevance of laparoscopic resection can be established.

The following statement, produced and supported by the surgeons of two prominent organizations, reflects the current professional opinion of participating surgeons interested in LARR:

“The American Society of Colon and Rectal Surgeons (ASCRS) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) recognize that laparoscopic proctectomy may be an alternative approach to traditional resection of benign disease involving the rectum. The absence of 5-year survival data makes it premature to endorse laparoscopic proctectomy for curable cancer. Laparoscopic proctectomy must follow traditional surgical principles and standards including adequate mesorectal excision and the achievement of appropriate clear margins. It is only appropriate to perform laparoscopic proctectomy for curable cancer in
an environment where the outcomes can be meaningfully evaluated and until laparoscopic approaches have been shown to be as efficacious as open approaches. The ASCRS and SAGES encourage the development of properly designed studies to evaluate the safety, efficacy and benefits of this approach. The ASCRS and SAGES consider laparoscopic proctectomy to be within the expertise of trained surgeons who focus on the treatment of rectal cancer. Development of this expertise should include observation of procedures, laboratory experience, and graduated clinical responsibility.”

**FUTURE PERSPECTIVE**

During the first decade of the 21st century, we have continued to see the introduction of many innovative techniques for the diagnosis and treatment of cancer. These technical advances have been based on the application of laparoscopic and minimal access approaches, which have led to newer methods of cancer resection and tumor ablation. Current approaches to metastatic and primary disease in the liver, kidney, and other organs include radiofrequency ablation performed with small probes placed directly into the organ under ultrasound guidance. These and other ablative therapies, such as high-intensity focused ultrasound, will become an even greater force in the future when combined with advanced imaging technologies. The obvious problem with these destructive therapies is lack of accurate pathologic staging, which will continue to be important despite the application of new prognostic factors in the computation of patient survival.

One of the most exciting areas for the future of minimal access cancer techniques will be in the extirpation of small cancers that are identified by appropriate surveillance using new imaging modalities. Potentially, the combination of advanced helical computed tomography (CT) scanning and positron emission tomography (PET) will allow for the identification of small colonic lesions, which may be resected using a combination of flexible and laparoscopic techniques. The era is rapidly approaching when flexible endoscopy alone may be used through “natural orifices” to remove malignant lesions without transgressing the abdominal cavity. It is important to continue to apply good science to these future applications in the form of RCTs and guideline development to avoid the pitfalls associated with application of inappropriate oncologic principals. Continued randomized prospective trials developed by recognized trial groups are mandatory to answer the appropriate questions posed by newer and more aggressive minimal access approaches. The benefactor of these studies must always be the patient.

As we have realized through the application of laparoscopic techniques in the treatment of benign disease, the reduced need for hospital stay and the overall reduction of pain and suffering may be the most important outcomes in assessing minimal access cancer management. Realizing that these technical advances are dependent on the skill and appropriate application by physicians, we must constantly be reminded that technology moves faster than knowledge, which, in turn, moves faster than wisdom.

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