Endolaparoscopic Approach vs Conventional Open Surgery in the Treatment of Obstructing Left-Sided Colon Cancer

A Randomized Controlled Trial

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Objective: To compare self-expanding metal stents with emergency open surgery in the treatment of obstructing left-sided colon cancer.

Design: A randomized controlled trial.

Setting: An acute care hospital.

Patients: Adult patients with an obstructing tumor between the splenic flexure and rectosigmoid junction.

Main Outcome Measures: Successful 1-stage operation, cumulative operative time, blood loss, hospital stay, pain score, and postoperative complications.

Results: Forty-eight patients were analyzed. Twenty-four underwent endoluminal stenting followed by laparoscopic resection and 24 underwent emergency open surgery. The 2 groups were matched for age, sex, body mass index, and disease staging. Patients in the endolaparoscopic group had significantly less cumulative blood loss and lower pain, incidence of anastomotic leak, and wound infection. Significantly more patients in the endolaparoscopic group had a successful 1-stage operation performed (16 vs 9, \( P = .04 \)). None of the patients in the endolaparoscopic group had a permanent stoma compared with 6 patients in the emergency open surgery group (\( P = .03 \)).

Conclusions: Self-expanding metal stents serve as a safe and effective bridge to subsequent laparoscopic surgery in patients with obstructing left-sided colon cancer. This endolaparoscopic approach makes a 1-stage operation more feasible, is associated with reduced incidence of stoma creation, and allows patients with malignant large-bowel obstruction to enjoy the full benefit of minimally invasive surgery.

Trial Registration: clinicaltrials.gov Identifier: NCT00654212

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First reported in 1991, laparoscopic-assisted colectomy is increasingly practiced worldwide.\(^1\)\(^2\) Abundant evidence exists in the literature that suggests that laparoscopic-assisted colectomy, compared with its open surgery counterpart, is associated with more favorable short-term outcomes, better cosmesis, and better patient satisfaction.\(^3\)\(^4\) Moreover, recent reports from large-scale randomized trials support the use of this minimally invasive technique in the treatment of colorectal cancer.\(^5\)\(^8\) a malignant condition common in many parts of the world. However, around 8% to 29% of patients with colorectal cancer present with acute large-bowel obstruction,\(^5\) a condition that used to be considered a contraindication to laparoscopic surgery owing to poor exposure and potential hazard of injury to the distended bowel. Thus, most cases of malignant large-bowel obstruction mandate an emergency open surgery to relieve the obstruction and resect the tumor, with many patients, especially those with obstructing left-sided colon cancer, ending up with temporary or permanent stomas, which can adversely affect their health-related quality of life.\(^10\)\(^11\)

See Invited Critique at end of article

In 1991, Dohmoto\(^12\) first described the self-expanding metal stent (SEMS) as an endoscopic palliative alternative for treating inoperable colon cancer. Three years later, Tejero et al\(^13\) published a preliminary report of using SEMS as a bridge to surgery in 2 patients with colonic obstruction. Since then, a number of studies and...
reviews have shown that endoluminal stenting is a relatively simple and safe alternative to standard surgical management of acute malignant obstruction of the left colon, thereby obviating the need for emergency surgery or colostomy. However, whether temporary endoscopic bowel decompression by SEMS could allow patients with malignant left colonic obstruction to undergo successful laparoscopic resection (endolaparoscopic approach) has never been studied in detail before. Specifically, as tumors that cause luminal obstruction are mostly bulky and locally advanced, the subsequent laparoscopic excision of these stented tumors might be associated with increased technical difficulty, leading to a possibly increased conversion rate and morbidity.

With this background in mind, we therefore conducted the current trial to study the endolaparoscopic approach in patients with obstructing left-sided colon cancer. Our hypothesis is that SEMSs could serve as a bridge to the subsequent 1-stage, laparoscopic colectomy, thus allowing these patients to enjoy the full benefits of minimally invasive surgery.

**METHODS**

This study is a randomized controlled trial designed to evaluate the outcomes of the endolaparoscopic approach for patients with obstructing left-sided colon cancer, using patients undergoing emergency open surgery as controls. The primary outcome is a complication rate and morbidity.

**PATIENT SELECTION**

Consecutive adult patients (aged $\geq 18$ years) presenting with clinical features of left colonic obstruction were potential candidates. In the absence of peritonitis, right lower quadrant tenderness, or a grossly distended cecum ($\geq 10$ cm in maximal dimension) on plain abdominal radiography, an urgent water-soluble single-contrast enema was performed to determine the level of obstruction within 24 hours of admission. Patients were recruited if the lower border of an obstructing tumor was found between the splenic flexure and rectosigmoid junction. Informed consent was obtained from every patient recruited in the trial. The following patients were excluded from the study: (1) patients who were considered unfit for operative treatment; (2) patients with a previous laparotomy; and (3) patients with a clinically palpable tumor on abdominal examination. Patients in the last 2 categories were excluded from randomization because, in case they were randomized to undergo the endolaparoscopic approach, conversion to open surgery was more likely owing to the presence of adhesions or a bulky tumor.

**RANDOMIZATION**

Once recruited, patients were randomly allocated by computer to receive either endoluminal stenting followed by laparoscopic resection (the endolaparoscopic group, the study group) or emergency open surgery (the open surgery group, the control group).

**Endolaparoscopic Group**

Patients with SEMSs were placed under endoscopic and fluoroscopic guidance by a dedicated endoscopist (W.W.C.T. or M.K.W.L.) within 6 hours of the contrast study. The Wallstent Entral Endoprosthesis With Unistep Plus Delivery System (Boston Scientific Ireland Ltd, Galway, Ireland) was used in all cases. Stents were chosen so that the funnel-shaped ends were at least 2 cm beyond the limits of the tumor; more than 1 stent was placed if required. Abdominal radiography was performed the next day following stenting. Successful decompression was defined as clinical and radiological evidence of resolution of the obstruction within 24 hours of placement of the SEMS. After this, an oral diet was introduced, and patients were discharged from the hospital once they had a bowel movement. Preoperative workup for cancer staging was carried out, and patients were readmitted for elective laparoscopic-assisted colectomy within 2 weeks after placement of the SEMS. The operation was performed in a standardized manner. The resected specimen with the stent in situ was delivered by means of a linear analog pain scale (Visual Analog Scale), with scores ranging from 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable. The maximal pain score obtained in the first postoperative week was used for analyses. For patients who received multiple operations, only 1 score, the maximal pain score of all the postoperative periods, was used for analysis.

**Open Surgery Group**

All patients received self-controlled analgesia in the form of intravenous bolus morphine in the immediate postoperative period. The dosage and regimen were reviewed by the anesthetist in charge, who would discontinue the patient-controlled analgesia according to usual practice. Thereafter, 1 mg of meperidine per kilogram of body weight was given intramuscularly every 4 hours on demand. In addition, 2 tablets of acetaminophen/proxyphene napsylate were prescribed to be taken orally every 4 hours on demand. A pain score was obtained daily in the first postoperative week by a designated independent assessor (H.Y.S.C.) who was unaware of the randomization and technique used at operation. The patient was instructed to score pain by means of a linear analog pain scale (Visual Analog Scale), with scores ranging from 0 to 10, 0 being no pain at all and 10 being the worst pain imaginable. The maximal pain score obtained in the first postoperative week was used for analyses. For patients who received multiple operations, only 1 score, the maximal pain score of all the postoperative periods, was used for analysis.

Patients were allowed clear fluids on the first postoperative day. An oral diet was introduced gradually once flatus was passed or the stoma started to function. Patients were discharged once they were ambulatory and free from any complications that required inpatient management, did not require parenteral an-
algesia, and were capable of independent stoma care (if applicable). They were reviewed by clinical oncologists as outpatients, and chemotherapy was selectively offered based on the final histopathological staging of the disease.

Patients with end colostomy received reversal operations at 6 to 12 months after initial surgery. For patients with covering loop stoma, a water-soluble contrast enema was performed to prove the integrity of the anastomosis before closure.

MAIN OUTCOME MEASURES

Besides successful 1-stage operation, other outcomes measured included cumulative operative time; cumulative blood loss; conversion rate; postoperative pain score and analgesic requirement; cumulative length of hospital stay; operative mortality; postoperative complications, including anastomotic leak; and rates of permanent stoma creation (permanent stoma rates). A designated pathologist (Wai Lun Tand, FRCPA) was specifically requested to evaluate and record the total number of lymph nodes harvested in the colectomy specimen. Cumulative operative time is defined as the sum of the time of all the operations required for a patient, in case some patients had more than 1 operation performed. Similarly, cumulative blood loss is the sum of the blood loss of all operations performed for each patient, while cumulative hospital stay is defined as the total number of days spent in the hospital. Operative mortality is defined as deaths that occurred within 30 days postoperatively. Anastomotic leak is defined as clinical or radiological evidence of leakage from the anastomosis. All data were collected prospectively using a structured pro forma form.

STATISTICAL ANALYSIS

Using a successful 1-stage operation for estimation of sample size and through power calculations with a 2-sided t test, we estimated that approximately 22 patients in each arm were necessary to detect a 40% difference in the 2 groups with 80% power at a 5% significance level. Assuming 15% of the patients initially randomized to the endolaparoscopic group did not proceed to definitive surgery after placement of a SEMS owing to widely disseminated disease, a minimum of 25 patients total should be recruited in each group. Patients were analyzed according to the intention-to-treat principle, and analysis was performed using SPSS software (version 15.0; SPSS Inc, Chicago, Illinois). Analysis was performed with the χ² test, Fisher exact test, t test, or Mann-Whitney U test where appropriate. P ≤ .05 was considered significant.

RESULTS

During a 40-month period (January 2002-May 2005), 50 patients with obstructing left-sided colonic tumors who met the inclusion criteria were identified and randomly assigned. One patient in the open surgery group withdrew consent after operation. One patient in the endolaparoscopic group was found to have extensive liver metastases as well as malignant ascites after placement of the SEMS and was excluded from further surgical intervention. These 2 patients were counted as postrandomization dropouts and were excluded from subsequent analysis.

Forty-eight patients (24 in the open surgery group; 24 in the endolaparoscopic group) were analyzed. Characteristics of these patients and the tumors are listed in Table 1. The 2 groups were matched for age, sex, body mass index, as well as final histopathological staging. A total of 12 patients (25%) were found to have disseminated disease (stage IV) on subsequent cancer workup.

The final operations performed in both groups are shown in the Figure. In the open surgery group, 11 patients had Hartmann operations performed initially, and 11 others had primary anastomosis without covering stoma. Overall, 9 patients (38%) in the open surgery group had successful 1-stage operations performed; 6 patients (25%) were left with a permanent colostomy. For the endolaparoscopic group, no stent-related complications occurred. Four patients had failed endoluminal stenting owing to failed cannulation. Self-expanding metal stents were successfully implanted in the remaining 20 patients and all showed successful decompression, giving the technical as well as clinical success rates of 83%. Laparoscopic-assisted colectomy was performed in these patients after a median of 10 days (range, 2-16 days). Conversion was required in 1 patient (5%) owing to bulky tumor. Overall, 16 patients (67%) in the endolaparoscopic group had successful 1-stage operations performed, none of whom were left with a permanent stoma.

The perioperative data and short-term outcomes are shown in Table 2. While the cumulative operative time and hospital stay in the 2 groups remained similar, patients in the endolaparoscopic group had significantly less cumulative blood loss, less wound infection, and reduced incidence of anastomotic leak and other morbidities compared with the open surgery group. Moreover, patients in the endolaparoscopic group experienced significantly less pain than those in the open surgery group (median maximal pain score, 4 vs 5) and required significantly less parenteral (morphine) and enteral (acetaminophen/propoxyphene) analgesia in the early postoperative period. Overall, significantly more patients in the endolaparoscopic group had successful 1-stage operations performed (16 vs 9 patients). None of the pa-

Table 1. Patient Demographics and Characteristics of Tumor

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Open</th>
<th>Endolaparoscopic</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, M/F, No.</td>
<td>12/12</td>
<td>14/10</td>
<td>.6a</td>
</tr>
<tr>
<td>Body mass index, median (range)b</td>
<td>24 (17.4-30.3)</td>
<td>23.8 (17.5-27.2)</td>
<td>.8b</td>
</tr>
<tr>
<td>Age, y, median (range)</td>
<td>68.5 (27-96)</td>
<td>64.5 (39-68)</td>
<td>.7c</td>
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<tr>
<td>Pathological staging, VII/II/IV, No.</td>
<td>0/7/8/9</td>
<td>1/7/13/3</td>
<td>.1d</td>
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</tbody>
</table>

aχ² Test.
bCalculated as weight in kilograms divided by height in meters squared.
cMann-Whitney U test.
dt Test.
Patients in the endolaparoscopic group had a permanent stoma, contrasting with 6 patients in the open surgery group.

**COMMENT**

While current opinion favors right or extended right hemicolectomy with primary anastomosis for most obstructing tumors proximal to the splenic flexure, the optimal treatment for left colonic cancers with acute obstruction remains unclear. The Hartmann procedure allows tumor removal and avoids a risky anastomosis; however, the patients are left with the physical and psychological morbidities of a colostomy, and only 40% to 50% of these patients have their colostomies subsequently closed. Additionally, the cumulative mortality of the Hartmann procedure and subsequent reversal is as high as 10%.9,10 The other alternative is primary anastomosis after subtotal or total colectomy or after segmental colectomy with on-table lavage. The reported mortality rate of this 1-stage approach is nearly 10% with a leakage rate of 4% to 6%; moreover, cases are often highly selected.9,10 Initially reported as a palliative measure for nonresectable malignant colonic tumors, a SEMS has recently been reported as a means of initial bowel decompression for delayed elective resection in malignant left colonic obstruction13-15,17; this approach avoids a stoma and converts an emergency operation to a safer, planned operation after mechanical bowel preparation. Two studies have compared the outcomes of SEMS followed by elective open surgery with those of emergency surgery without prior stenting and showed an increase in the proportion of patients who underwent successful primary anastomosis in the stented group, with a reduction in stoma formation.18,19 Additionally, a study by Saida et al20 indicated that the 3- and 5-year survival rates of patients who underwent SEMS insertion followed by elective resection were similar to those who underwent emergency surgery, suggesting that the SEMS did not compromise oncologic clearance and long-term prognosis, an issue of concern because of the potential risk of tumor seeding at the time of stent deployment. However, all these reports are nonrandomized comparative studies that focus on open surgery. Whether SEMS could

<table>
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<tr>
<th>Characteristic</th>
<th>Surgery Group, Median (Range)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative operative time, min</td>
<td>Open (95-320)</td>
<td>170 (73-349)</td>
</tr>
<tr>
<td>Cumulative blood loss, mL</td>
<td>200 (20-750)</td>
<td>50 (10-330)</td>
</tr>
<tr>
<td>Cumulative hospital stay, d</td>
<td>14 (7-55)</td>
<td>13.5 (7-29)</td>
</tr>
<tr>
<td>Lymph node harvest, No.</td>
<td>11 (3-38)</td>
<td>23 (5-40)</td>
</tr>
<tr>
<td>Maximal pain score</td>
<td>5 (1-10)</td>
<td>4 (1-7)</td>
</tr>
<tr>
<td>Morphine, mg</td>
<td>60 (17-192)</td>
<td>40 (0-156)</td>
</tr>
<tr>
<td>Meperidine, mg</td>
<td>100 (0-500)</td>
<td>0 (0-300)</td>
</tr>
<tr>
<td>Acetaminophen/proxypoxyhene napsylate, No. of tablets</td>
<td>16 (0-98)</td>
<td>8 (0-46)</td>
</tr>
<tr>
<td>Anastomotic leakage, No. of patients</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Wound infection, No. of patients</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Chest infection, No. of patients</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Intra-abdominal sepsis, No. of patients</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other morbidities, No. of patients</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Successful 1-stage operation, No. of patients</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Permanent stoma, No. of patients</td>
<td>6</td>
<td>0</td>
</tr>
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* Mann-Whitney U test.
* Fisher exact test.
allow patients with these obstructing, mostly bulky tumors to undergo subsequent laparoscopic surgery safely in the same way as with open surgery remains unclear. There is still a complete lack of good quality clinical data evaluating the use of SEMS as a bridge to elective laparoscopic surgery.

To date, this is the first randomized controlled trial comparing the outcomes of the endolaparoscopic approach with those of open surgery in the management of obstructing cancers of the left colon. As analysis is performed using an intent-to-treat principle, the efficacy of this combined, staged endolaparoscopic approach as a whole is dependent on a number of variables, including the success and complication rates of placement of SEMSs, as well as conversion rate and morbidities of laparoscopic surgery in these obstructing tumors. It is important to remember that while many patients with acute obstruction might benefit from endoluminal stenting, failure or stent-related perforation can occur in others resulting in emergency laparotomy. Open surgery was performed in the control arm, as this is still widely practiced for intestinal obstruction and remains a standard against which other techniques should be compared.

In an attempt to minimize bias due to surgeon factors, a single surgical team performed all operations throughout the study, and an independent assessor was designated to obtain all postoperative pain scores. In the open surgery group, 38% of patients had successful 1-stage operations; this was comparable with the reported figures of 28% to 41% in other studies. In the endolaparoscopic group, no stent-related complications occurred and the success rate of decompression was 83%, a value in keeping with the reported rates of 64% to 94% for obstructed colon during an emergency setting, where surgeons might spend most of the effort on the relief of obstruction rather than cancer cure.

In conclusion, our data showed that placement of SEMS is safe and carries a high success rate for patients with obstructing left colon cancer. A SEMS allows patients to recover from acute obstruction and buys time for proper preoperative investigations. The stent serves as a palliative measure for high-risk patients or those with nonresectable tumor on subsequent workup. For low-risk patients with resectable disease, SEMS serves as a safe and effective bridge to subsequent laparoscopic surgery. This endolaparoscopic approach makes a 1-stage operation more feasible, is associated with reduced risk of stoma creation, and allows these patients to enjoy the full benefits of minimally invasive surgery. Further large-scale studies to investigate the long-term oncologic outcomes of this approach are warranted.
Does Every Question Deserve a Randomized Controlled Trial?

Despite the fact that the quality of the available evidence on use of colonic stents as a bridge to surgery for patients with obstructing left colon tumors might be considered relatively poor, systematic review shows that the median technical success rate (appropriate placement of the stent) and the median clinical success rate (resolution of obstruction) are both greater than 90%, with a median short-term perforation rate of less than 5%. Decompression provides time for staging, resuscitation, bowel preparation, and safe, elective resection. The rate of primary anastomosis is twice that following emergent surgery and the stoma rate is significantly reduced. Morbidity and mortality rates for emergent operation in this setting range from 4% to 50% and 15% to 20%, respectively. In addition, in about half the cases, when emergent surgery is done, the stoma rate is significantly reduced.

What we know with some certainty is that malignant left colon obstruction is a bad problem and the standard emergent surgical approaches are problematic. We also know that conducting a randomized clinical trial requires clinical equipoise, a genuine uncertainty regarding the benefit of one treatment over another. In recruiting for a randomized clinical trial, patients must be counseled about what is known regarding both treatments. In this context, conducting this trial in the United States would be difficult. Patients would have to consent to immediate operation or attempted stent placement while being informed about what we think we already know about these approaches, as detailed above. The average patient may not feel much clinical equipoise with stent placement serving as a means to reduce morbidity, mortality, and colostomy rates in the setting of an acute, malignant left colon obstruction and as a bridge to surgery. We are not sure that we do either.

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