Primary Cancers of the Small Bowel

Analysis of Prognostic Factors and Results of Surgical Management

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Hypothesis: This study was done to review the clinical presentation, surgical management, pathologic features, and prognostic factors for primary small-bowel cancers.

Design: Retrospective case series.

Setting: Tertiary care, university hospital.

Patients: One hundred twenty-nine patients were surgically treated between January 1, 1977, and December 31, 2000. There were 73 men and 56 women, with a median age of 55 years (age range, 19-82 years). Median follow-up was 36 months.

Main Outcome Measures: Presenting symptoms and signs, operations performed, and surgical pathologic features were analyzed and survival curves were generated.

Results: Clinical findings included abdominal pain (63%), vomiting (48%), weight loss (44%), and gastrointestinal tract bleeding (23%). The distribution of tumors by histological features was as follows: adenocarcinoma (33%), carcinoid tumor (29%), lymphoma (19%), and sarcoma (19%). Cumulative 5-year survival rate was 37% in the adenocarcinoma group, 64% in the carcinoid tumor group, 29% in the lymphoma group, and 22% in the sarcoma group. Significant prognostic predictors of overall survival for the entire cohort and for each tumor subtype included complete resection and American Joint Committee on Cancer tumor stage (P<.05). Patient age, tumor location, histological grade, and use of chemotherapy and radiation therapy did not significantly influence survival. Curative resections were accomplished in 83 patients (64%) with a median survival of 37 months compared with 46 patients undergoing incomplete or palliative resections with a median survival of 10 months (P<.05). Adjacent organ resection was required in 18 (22%) of the 83 patients undergoing potentially curative resections. The median time to recurrence was 16 months. Twenty-one patients (16%) developed associated primary cancers.

Conclusions: Aggressive surgical resection in an attempt to achieve complete tumor removal seems warranted. Despite complete resections, patients with high-stage tumors remain at risk for recurrence.

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Small-bowel cancers are uncommon tumors, accounting for 1% to 2% of all primary gastrointestinal (GI) tract malignancies. As a result of this relative infrequency, the accumulation of data regarding their natural history and the effect of surgical therapy has been difficult. The presence of several different histological subtypes of small-bowel cancers has complicated characterization of typical disease expression. Clinical presentations may also differ according to the location of the primary tumor. Because of the rarity and variety of small-bowel cancers, fundamental questions exist regarding appropriate treatment recommendations and the influence of surgical therapy on patient outcomes. The aims of this study were to characterize disease presentation, to define the optimal extent of surgical resection necessary for local tumor control, to examine the effect of surgical treatment on long-term survival, and to determine which clinical and pathologic features predict prognosis.
PATIENTS AND METHODS

The medical records of 172 patients who were diagnosed as having and were treated for primary small-bowel cancers at Northwestern Memorial Hospital, Chicago, Ill, were reviewed. We excluded all cases with an uncertain diagnosis, small-bowel cancers found in the GI tract but thought to have metastasized there from an extra-abdominal primary site, and patients operated on for periampullary tumors. The final study population was composed of 129 patients surgically treated between January 1, 1977, and December 31, 2000.

Information gathered from the medical records included standard demographic data, presenting signs and symptoms, and a review of medical histories and subsequent follow-up visits to document the occurrence of previous or subsequent associated primary cancers. Operative reports were reviewed for type of resection performed, completeness of resection, and necessity for en bloc resection. Patients who underwent exploratory procedures, but who had no disease resected and who underwent only biopsy were categorized separately.

A single surgical pathologist (S.R.) reviewed pathological specimens and histological features. Tumors were categorized into 1 of 4 histological subtypes (ie, adenocarcinoma, carcinoid tumor, lymphoma, and sarcoma), and staging of patients’ conditions was by the American Joint Committee on Cancer guidelines established in the fifth edition. 

Survival duration was measured from the time of diagnosis to last follow-up evaluation or death. The follow-up observations were obtained from patient medical records or direct contact with the patient, relatives, or primary care physician. Survival curves were constructed according to a modification of the Kaplan-Meier method, and the Lee-Desu tables for statistical analysis of survival were used to determine differences in survival. Statistical significance of categorical variables was determined by the log-rank test.

### Table 1. Distribution of Symptoms and Signs by Tumor Type*

<table>
<thead>
<tr>
<th>Symptom or Sign</th>
<th>Type of Tumor</th>
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<tbody>
<tr>
<td></td>
<td>Adenocarcinoma</td>
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<tr>
<td>Abdominal pain</td>
<td>32</td>
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<tr>
<td>Vomiting</td>
<td>22</td>
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<tr>
<td>Weight loss</td>
<td>12</td>
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<tr>
<td>Gastrointestinal tract bleeding</td>
<td>10</td>
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<tr>
<td>Diarrhea</td>
<td>5</td>
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<tr>
<td>Mass</td>
<td>12</td>
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<tr>
<td>Occult fecal blood</td>
<td>16</td>
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<tr>
<td>Acute abdomen</td>
<td>8</td>
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<tr>
<td>Carcinoid syndrome</td>
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*Data are given as the number of patients unless otherwise indicated.

of the patients had stool specimens positive for occult blood. Emergent operations were done in 22% of the patients for obstruction, perforation, or bleeding (Table 1). Over 50% of the patients had more than 1 symptom or physical finding, though no combination of signs, symptoms, or acuity of presentation was thought to be unique to any particular histological subtype. The mean duration of symptoms before presentation was 10 months (range, 0-24 months).

HISTOPATHOLOGIC FEATURES

The distribution of tumors by histological features was as follows: adenocarcinoma (33%), carcinoid tumor (29%), lymphoma (19%), and sarcoma (19%). The distribution of each histological tumor subtype by location in the small intestine is listed in Table 2. Adenocarcinomas were located most frequently in the duodenum followed by the jejunum and ileum, respectively. The carcinoid tumors were distributed throughout the small intestines, but were located preponderantly in the ileum. Sarcomas were found most often in the jejunum; lymphomas occurred nearly equally in the jejunum and ileum. The relationship between histological feature and pathologic stage is given in Table 3. More than 50% of the patients in each tumor type presented with either stage III or IV disease. Twenty-nine (69%) of the 42 adenocarcinomas were poorly differentiated, 16 (38%) were positive for nodal metastases, and 16 (38%) had metastatic disease at presentation. Similarly, 14 patients (38%)...
with carcinoid tumors presented with nodal disease; 11 patients (30%) had synchronous liver metastases. Small-bowel sarcomas were classified as high grade in 72% and low grade in 28% of the patients. Twenty of the sarcomas (80%) measured 5 cm or larger. The median size of the sarcoma tumors was 16 cm (range, 10-55 cm).

Histological subtypes according to Rappaport's classification and the Working Formulation for GI lymphomas are summarized in Table 4. All lymphomas in this series represent B-cell tumors. The diffuse histiocytic type (Rappaport's classification) accounted for 68% of the tumors and was associated with a decreased average survival. This histiocytic subtype was the most common tumor at all sites and more frequently presented in a more advanced stage (stages III or IV).

**SURGICAL TREATMENT**

Complete resection of all gross disease with negative, final pathologic margins was accomplished in 83 patients (64%). Thirty patients (23%) had incomplete or palliative resections, 13 patients had gross residual disease, and 17 patients had margin-positive resections. Sixteen patients (13%) underwent exploratory procedures with biopsy only. Potentially curative resections were done in 26 patients (62%) with adenocarcinoma, 24 patients (65%) with carcinoid tumors, 21 patients (84%) with a GI sarcoma, and 12 patients (48%) with lymphoma. Most operations consisted of segmental small-bowel resection with wide proximal and distal margins and regional mesenteric lymphadenectomy. Adjacent organ resection was required in 18 (22%) of the 83 patients undergoing potentially curative resections. Four patients with GI sarcomas required a small-bowel resection and removal of a segment of adjacent colon, and 4 others underwent en bloc resection of the small bowel, colon, and partial clystectomy. One patient with a GI sarcoma required en bloc resection of the proximal jejunum, transverse colon, distal pancreas, and spleen. Three patients with locally advanced adenocarcinoma of the small intestine underwent combined small-bowel and colon resections, 2 others required resection of a significant portion of the anterior abdominal wall for complete removal, and 4 patients had en bloc resection of the small bowel and uterus. None of the patients with carcinoid tumors required extended local procedures, but 5 of these 24 patients did have combined hepatic resections for limited metastatic disease. Complete resections were done in only 7 of the 14 patients with carcinoid stage III disease because of bulky, unresectable, mesenteric adenopathy. The operative mortality rate for all groups was 2.3%.

**PROGNOSTIC FACTORS**

The cumulative 5-year survival rate was 37% in the adenocarcinoma group, 64% in the carcinoid group, 29% in the lymphoma group, and 22% in the sarcoma group (Figure 1). Prognostic factors analyzed for effect on overall survival included age, sex, signs and symptoms, tumor location, stage of disease, resection status, and use of postoperative chemotherapy and radiation therapy. Significant prognostic predictors of overall survival for the
entire cohort and for each tumor subtype included complete resection and American Joint Committee on Cancer tumor stage (P<.05) (Table 5). Patient age, tumor location, histological grade, and use of chemotherapy and radiation therapy did not significantly influence survival. Complete resections were done in 83 patients (64%) with a median survival of 37 months compared with 46 patients undergoing incomplete resections or biopsy only with a median survival of 10 months (P<.05).

For completely resected adenocarcinoma, the median survival was 40 months and the estimated 5-year survival rate was 42%. Those without lymph node metastases had a median survival of 62 months and an estimated 5-year survival of 48% compared with patients with positive lymph node metastases, who had a median survival of 24 months and an estimated 5-year survival rate of 28% (P<.05) (Figure 2). Complete resections were done in 24 patients with carcinoid tumors and included 5 patients with simultaneous hepatic resections for limited hepatic metastases. Estimated 5-year survival in this group was 75% compared with 46% in the 13 patients with incomplete resections (P<.05). Patients undergoing complete resection of primary GI sarcomas had a median survival of 54 months and an estimated 5-year survival of 37% compared with an 18-month median survival and no 5-year survivors for incompletely resected patients (P<.05) (Figure 3).

Although there are apparent differences in survival between the different histological types of lymphoma (Table 4), owing to the small numbers of patients in each group, these did not reach statistical significance. Survival curves were, therefore, generated in relation to the Ann Arbor classification for disease localized to one side of the diaphragm (stages I and II) vs disease on both sides of the diaphragm or with diffuse involvement of viscera or bone marrow (stages III and IV) and demonstrated a significant survival difference between the 2 groups (Figure 4).

The median time to recurrence for all patient groups was 16 months. Twenty-one patients (16%) developed associated primary cancers.

Primary malignancies of the small-bowel present unique challenges in terms of preoperative diagnosis, operative treatment decisions, and postoperative prognostication. The infrequency of these tumors relative to cancers of the colon, pancreas, stomach, and hepatobiliary tract accounts for part of this ambiguity. It is estimated that fewer than 2500 new cases of primary small-bowel cancers are
The incidence and distribution of cancers in the current series are similar to other reports.\textsuperscript{1,3,15-18} Adenocarcinoma was the most frequent small-bowel cancer (33\%) followed by carcinoid tumors (29\%), GI lymphomas (19\%), and GI sarcomas (19\%). In collected series, adenocarcinoma represents 32\% to 63\% of small-bowel cancers; carcinoid lesions are found 6\% to 35\% of the time followed by lymphomas in 7\% to 18\%, and GI sarcomas in 10\% to 20\%.\textsuperscript{1,3,15-18} The most common location of a small-bowel cancer in our group was the ileum (43\%) followed by the jejunum (35\%) and duodenum (22\%).

Our analysis did not show the location of the tumor to be a significant prognostic variable, suggesting that the natural history of small-bowel cancers is more dependent on certain biological factors and disease stage than the site of origin. Similarly, the experience of Zollinger,\textsuperscript{1} Cunningham et al,\textsuperscript{16} and Ojha et al\textsuperscript{17} found that the site of the primary lesion did not influence survival. Other reports by Ashley and Wells,\textsuperscript{2} Bauer et al,\textsuperscript{18} and Frost et al\textsuperscript{19} have focused on adenocarcinoma of the intestine; in these series, tumors of the duodenum tended to present somewhat earlier than those occurring in the more distal intestine and, thus, had a slightly more favorable prognosis.

The next 2 aims of this study were to determine the effect of surgical therapy on survival and to determine which clinical and pathologic features predict prognosis. Using log rank analysis and the Kaplan-Meier method for statistical analysis of survival, significant prognostic predictors of overall survival for the entire cohort and for each tumor subtype included complete resection and American Joint Committee on Cancer tumor stage (P<.05). The relation between resection status and tumor stage varied subtly between the different tumor types but essentially, patients with advanced tumors that were able to be completely resected had a more favorable prognosis than incompletely resected cases, yet these patients remained at the greatest risk for early recurrence.

In the current series, patients with adenocarcinoma had a median survival of 30 months and an estimated 5-year survival rate of 37\%. Previous series demonstrate a generally poor survival in these patients, with most reporting only 20\% to 30\% of patients alive at 5 years. Prognostic factors shown to be of variable significance include depth of tumor penetration, nodal and systemic metastases, and histological grade. Series with improved differences in survival often contain periampullary malignancies and we specifically excluded those patients in this analysis. Potentially curative resections were accomplished in 26 (62\%) of 42 patients and of these, 9 patients (35\%) required extended resections. In patients with completely resected tumors, the presence of lymph node metastases was an ominous finding; however, these patients fared better than patients with local, advanced unresectable disease or metastatic cancer. It is our policy to perform aggressive resections with the qualification that all gross tumor and lymph node metastases can be removed. This policy of aggressive resection may have resulted in improved disease control and long-term survival. It has been our general practice to reserve chemotherapy and radiation treatments for patients with stage III or IV disease, and similar to other series, meaningful responses have been difficult to demonstrate.

Carcinoid tumors were the next most frequent cancers and were associated with the best 5-year survival rate (64\%). Most lesions (78\%) were located in the ileum, and 24\% developed some manifestation of the carcinoid syn-

![Figure 4. Actuarial survival based on Ann Arbor classification for gastrointestinal lymphoma stages I and II (12 cases) compared with stages III and IV (13 cases).](image-url)
drome during the course of their disease. This is slightly higher than reported in previous series and may reflect our role as a tertiary referral center for advanced neuroendocrine malignancies. Complete resections were done in 65%. None required extended local procedures, but 5 of these 24 patients had combined hepatic resections for limited metastatic disease. We have previously demonstrated improved overall survival for metastatic neuroendocrine tumors when complete resection of primary and hepatic metastases is accomplished, with an actuarial 5-year survival rate of 70%. Chen et al20 from Johns Hopkins University evaluated 38 patients with liver-only metastases including 21 carcinoid, 13 islet cell, and 4 atypical neuroendocrine neoplasms. This report compared 15 patients who underwent potentially curative hepatic resection with 23 patients with comparable liver disease who did not undergo hepatic resection. The actuarial 5-year survival rate was 73% in the surgical group vs 29% patients not operated on. Chamberlain et al21 reviewed 85 patients with hepatic neuroendocrine metastases treated at Memorial Sloan-Kettering Cancer Center. Among 34 patients undergoing hepatic resection, 15 had potentially curative resections and 19 were palliative. The median survival in the surgical patients had not been reached and the estimated 5-year survival in patients having complete resections was 85%. Previous series have demonstrated that, in the absence of metastatic disease, complete resection of localized carcinoid tumors results in 75% to 94% 5-year survival rates. In the current series, the 5-year survival for patients with completely resected stage I and II disease was 75%. Only 50% of our patients with stage III disease had complete resections owing to the presence of bulky mesenteric adenopathy and their 5-year survival was reduced to 53%.

Primary small-bowel sarcomas occurred throughout the intestines but were most frequent in the jejunum. These tended to be large, high-grade malignancies with local invasion seen in 9 of the 21 patients undergoing complete resections. The number of patients in the current series with complete resections was high (84%) compared with earlier reports.24-26 This may be partially explainable by our aggressive attempts to remove all gross disease and by the fact that most series also include primary sarcomas arising from the stomach. Our previous review of gastric and intestinal sarcomas demonstrated a complete resection rate of 64%.25 En bloc resection of contiguous organs did not adversely affect survival, and in patients with complete resection tumor grade was the most important prognostic factor. Univariate analysis of 191 patients with GI sarcoma treated at the M. D. Anderson Cancer Center identified tumor size of less than 5 cm, low histological grade, presence of localized disease, and complete surgical resection without tumor spillage as favorable prognostic factors. Using multivariate analysis, only complete resection was found to be a significant favorable prognostic factor. Median survival for patients undergoing complete resection was 46 months, compared with 21 months for incompletely resected patients.23 DeMatteo et al26 have reported a recent experience with GI stromal tumors from the Memorial Sloan-Kettering Cancer Center. Including all patients with a diagnosis of gut stromal tumor, 200 total patients were identified, 80 of whom had primary disease and subsequently underwent complete resection of all gross disease. Of the 80 resections, 65 (81%) had negative microscopic margins. Because this study included all stromal tumors of any malignant potential, tumor grade was not addressed as a prognostic factor. Patients with primary disease who underwent complete resection had a median survival of 66 months, compared with 22 months for those who had incomplete resections or whose tumor was unresectable. Adjuvant chemotherapy or radiation therapy after complete resection has not been shown to diminish the risk for subsequent recurrence.

By definition, patients with advanced lymphoma (stages III and IV) are not candidates for complete surgical resections. The role of surgical therapy for these patients is limited to diagnosis and palliation. Because of more sophisticated treatment options and better patient management by medical oncologists, the need for surgical intervention in these patients has diminished. Controversy still exists regarding the role of primary surgical therapy in patients with localized lymphoma (stages I and II). Much of the information on the effectiveness of surgery for early GI lymphoma is based on limited, retrospective reviews that do not specifically compare primary surgical therapy with primary medical management, be it chemotherapy, radiotherapy, or radiochemotherapy. The current series has these same inherent limitations. Perhaps the most significant investigative question posed by this and other series is whether there is a need for postoperative therapies after complete surgical resection of localized lymphoma.

Surgical therapy offers the only real hope for patients with cancers of the small bowel. Our patients with incomplete resections usually received chemotherapy or radiochemotherapy. All of these patients experienced the development of progressive disease. Despite optimal surgical procedures, even patients with complete resections had only a 52% 5-year survival rate and this figure is probably skewed by the relatively indolent nature of the small-bowel carcinoid tumors. Because most are at great risk for recurrence, they would be ideal candidates for novel, multimodality adjuvant therapies. The difficulty in answering these questions is accentuated by the low frequency and diversity of these biologically aggressive malignancies. These questions should be addressed through multicenter, cooperative clinical trials.

This study was presented at the 109th Scientific Session of the Western Surgical Association, San Antonio, Tex, November 13, 2001.

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REFERENCES

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This is a good review of the management of patients with primary small-bowel tumors. The authors’ conclusions are fairly straightforward and, unfortunately for me, fairly noncontroversial. I will, however, comment on a few questions raised by their data. The authors state the well-recognized nonspecificity of patient symptoms leading to delay in diagnosis and 22% urgent operations, presumably once again related to the late presentation of these patients. Did the authors break down the periods during the 23 years of this study to see if this lag is decreasing? My suspicion would be that with the increasing use of computed tomographic scans to investigate every symptom with which mankind is afflicted, these tumors are probably being diagnosed earlier today than previously.

Second, could the authors provide us with their guidelines for resecting small-bowel lymphomas? There are some who, by extrapolating from the gastric lymphoma literature in which chemotherapy alone may be effective, advise chemotherapy for these patients. My own experiences with this treatment modality have usually been accomplished during the wrong phase of the solar cycle when I have opened a number of abdomens emanating the aroma of a summertime latrine; so I would appreciate the authors’ comments on lymphoma treatment.

Last, this review, like others, shows that small-bowel adenocarcinomas are more likely to be present in the duodenum. In our published series of these patients, we advised a Whipple procedure as the preferable treatment. Do the authors agree or do they believe there still may be a role for segmental resection?

In closing, this paper is as good as anything yet published in the surgical literature on this subject, and I commend it to you.

Steven A. De Jong, MD, Mayo: I wonder if they could share with us some specific data on those patients who underwent complete resection for the jejunal and the ileal tumors. Specifically, do they have data on exactly the width of margin that was obtained on those particular specimens, and did the magnitude of those margins influence at all their long-term survival? Finally, on the basis of their data, have they changed the recommendations on patients who intraoperatively are felt to be complete resection candidates in terms of the optimal margins that should be obtained for those patients?

Merrill T. Dayton, MD, Salt Lake City, Utah: In the authors’ presentation they describe a 16% incidence of antecedent or subsequent cancers at other sites in this patient population. It is a well-known observation that carcinoid tumors are associated with another GI tract malignancy about 23% of the time. Were most of the tumors of your patients in this series who had cancers at other sites carcinoid tumors or is there a similar association with sarcomas, lymphomas, and adenocarcinomas?

James A. Madura, MD, Indianapolis, Ind: I, too, have enjoyed this paper very much and have struggled with many of the same problems the authors have described. I am unclear about one thing. I can understand leaving residual tumor because you cannot totally and safely remove it, but positive margins I do not understand. Did you manage your resections with frozen section? How could you leave positive margins in this time. Were most of the tumors of your patients in this series who had cancers at other sites carcinoid tumors or is there a similar association with sarcomas, lymphomas, and adenocarcinomas?

I shall attempt to redress that this year. As I get closer to the evening he reminded me that at that time my comments fell even more short of my standard levels of Christian charity. So I shall attempt to redress that this year. As I get closer to the barn, I have to clean up my behavior.

Dr Pickleman: I made my palms sweat

Dr Talamonti: I share with us some specific data on those patients who underwent complete resection for the jejunal and the ileal tumors. Specifically, do they have data on exactly the width of margin that was obtained on those particular specimens, and did the magnitude of those margins influence at all their long-term survival? Finally, on the basis of their data, have they changed the recommendations on patients who intraoperatively are felt to be complete resection candidates in terms of the optimal margins that should be obtained for those patients?


DISCUSSIONS

Jack Pickleman, MD, Maywood, Ill: Thirteen years ago Dr Talamonti presented the Northwestern University data on GI lymphomas before the Western Surgical Association, and I was the discussant of that paper. At the reception Sunday evening he reminded me that at that time my comments fell somewhat short of my standard levels of Christian charity. So I shall attempt to redress that this year. As I get closer to the barn, I have to clean up my behavior.
ments, though. Dr Pickleman’s first observation is very perceptive. That is regarding the diagnosis of these patients in the more recent period compared with the earlier time frame in this study. This study spans 23 years, and there is no question that these patients’ conditions are being diagnosed, I do not know if I would say at an earlier stage, but there is no question that these patients’ conditions are being diagnosed using computed tomographic scans more frequently than they were in the past. The incidence of patients who presented with an acute abdomen has declined. Many of the patients who presented with an acute abdomen were in the first 5 or 10 years of this report, and in the latter 10 or 15 years of the report, most of these have been picked up by computed tomographic scanning or magnetic resonance imaging for patients who have persistent or chronic symptoms. So that is an accurate perception and I would concur with it.

Dr Pickleman also raised the question about the management of patients with GI lymphomas who present with an acute abdomen, and in the middle of the night you are asked to operate on a patient with a perforated small intestine or peritonitis or a severe bowel obstruction and you go in and find that you are dealing with a massive small-bowel lymphoma. In those patients I would not recommend trying to attempt a complete surgical resection. Remember, those are patients who are presenting in an acute episode. They have not undergone staging, and the vast majority of those patients that we found in this review who presented with that combination, an acute abdomen and lymphoma, on subsequent staging studies were found to have stage III or IV disease, so I do not think that patients who present with a small-bowel lymphoma in an acute abdomen in the middle of the night are really going to be patients that are amenable to complete surgical resection and, indeed, when subsequent staging studies are done, you will find that most of those patients are of an advanced stage.

We particularly left out the patients with periampullary carcinomas. I am familiar with Dr Pickleman’s paper and it is an important paper in the management of duodenal cancers because it suggests that patients with node positive duodenal cancers who undergo Whipple procedures are still potentially curable with surgery alone. We would certainly concur with that. We specifically left out the periampullary malignancies just not to deal with that question of whether a Whipple procedure should be done. So in this study the patients with adenocarcinomas of the duodenum, by definition, or by inclusion parameters that we set up for this study did not include the patients with periampullary malignancies who underwent a Whipple procedure. We would do a Whipple procedure. I think it is a sound operation, but these are patients with duodenal cancers near the ligament of Treitz near the third and fourth portion of the duodenum in which we felt comfortable doing sleeve resections or segmental resections.

Dr DeJong asked some pertinent questions about margins, and part of this paper was prompted by questions in the middle of the night by my residents asking me that very same question. What kind of margins should we take? I did not have a good answer for them in the middle of the night and I am not sure I have a good answer for you, Steve, in the middle of the day. Suffice it to say that what we defined in this retrospective review as a clear margin was the absence of any gross tumor transection and the absence of any microscopic disease on the pathology specimens that were reviewed. It is a retrospective study. In trying to get the difference between a 5-cm margin and a 10-cm margin vs a 15-cm margin in retrospective reviews of operative reviews was very difficult.

Having said that though, I think that this study and an earlier study published from our institution that looked at gastric and small-bowel sarcomas would suggest that every attempt should be made to get at least a 5-cm margin and an attempt even using frozen sections in the operating room to clear microscopic margins is worthwhile.

I would like to address Dr Madura’s question. Some of these patients who had incomplete resections or margin positive resections were patients with bulky mesenteric adenopathy from the carcinoid tumors in which we had to take the disease right down to the mesenteric artery and perhaps some of those lymph nodes were transected at the root of the small bowel. Other patients had sarcoma and they underwent combined hysterectomies, bladder resections, small-bowel resections, and may have had a positive margin say on the pubic symphysis or on the iliac crest. So there were times where just the extent of the disease, usually vascular involvement, mesenteric vessels, or bony involvement precluded a margin-negative resection. In those situations you just do the best you can and you accept the fact that you are getting out all gross disease and whether that has any positive implications, it is unpredictable.

There were 2 questions, 2 very relevant questions about the incidence of other cancers that we found in our series. In other reports on small-bowel cancers, the incidence of either preceding or subsequent nonrelated primary cancers is very high. Ours was 16%. In some of the reports it is as high as 25%. I think it was Dr Dayton who asked me if most of these were found in the patients with carcinoid tumors, and they were not. Surprisingly, in our group we found patients with either subsequent or previous antecedent cancers in the carcinoma group, the patients with carcinoid tumors, and the patients with lymphomas. We did not see any cancers in the sarcoma group, but we found them in other patients besides the patients with carcinoid tumors.

Dr Michelassi asked me about the incidence of stricturoplasty cancers, and we did not see that. We did not find any cancers in the stricturoplasties, but it did seem to me a relevant finding that 5% of the patients did have chronic inflammatory bowel disease, and that too has been identified as a potential risk factor.

The final question was about cholecystectomy, and it is a very good question. We did not address it in this review.