Hypothesis: Clinical presentation of appendiceal mucocele is related to malignancy and can influence surgical approach.

Design: Retrospective study.

Setting: Tertiary referral center.

Patients: All cases of primary appendiceal mucoceles (simple mucocele, cystadenoma, cystadenocarcinoma) diagnosed between 1976 and 2000 were reviewed. There were 135 patients, 74 of whom were female. Mean age at diagnosis was 59 years. Mean follow-up was more than 6 years.

Interventions: A total of 129 patients underwent surgery, consisting of appendectomy (22 patients), right hemicolectomy (25 patients), or more extensive procedures (82 patients).

Main Outcome Measures: Clinical, diagnostic, and surgical variables were statistically compared with postoperative morbidity and mortality and the presence of malignancy. P<.05 was considered significant.

Results: The presence of symptoms was associated with malignancy (58% vs 15%, P<.001), particularly abdominal pain (56% vs 29%, P=.005) and weight loss (77% vs 31%, P=.002). Abdominal mass was also associated with malignancy (86% vs 25%, P<.001). Moreover, pseudomyxoma peritonei and mucocele extravasation were associated with malignancy (95% vs 13%, P<.001, and 83% vs 15%, P<.001, respectively). The lesion size was not associated with malignancy; however, cystadenomas were significantly larger than simple mucoceles (8.1 cm vs 4.1 cm, P<.001), and no cystadenoma was less than 2 cm in largest diameter.

Conclusions: A number of clinical, diagnostic, and intraoperative findings are associated with malignant mucoceles. All mucoceles greater than 2 cm should be excised to remove premalignant lesions.

Arch Surg. 2003;138:585-590

APPENDICEAL MUCOCELE is a well-recognized entity that can present in a variety of clinical syndromes or can occur as an incidental surgical finding.1-11 Although widely used, the term mucocele is inherently imprecise and inclusive of both benign and malignant lesions. The purpose of our study was to identify the clinical, diagnostic, and surgical factors that might be associated with malignancy and affect the surgical management of appendiceal mucocele.

METHODS

Institutional review board approval was obtained for this retrospective study. All patients with a diagnosis of primary appendiceal mucocele treated in our institution between January 1, 1976, and December 31, 2000, were included. Patients presenting with recurrent malignant mucoceles after primary surgical treatment elsewhere were excluded. We also excluded lesions, including cases of mucinous adenocarcinoma, that were not associated with the presence of a mucocele established at surgery and/or at pathological examination.

We subdivided the mucoceles histologically on the basis of the World Health Organization classification.12,13 In particular, we considered as a simple mucocele the appendiceal dilation with accumulation of mucus due to obstruction of the lumen. Cystadenoma was defined as the dilated, mucus-filled appendix containing adenomatous mucosa, and cystadenocarcinoma as the presence of adenocarcinoma associated with a dilated, mucus-filled appendix. However, the definition of mucinous tumor of uncertain malignant potential was not used in the pathology reports and, therefore, could not be considered as a separate category.

Collected demographic data included age, sex, and overall survival at the time of the last follow-up visit or letter. Specific symptoms col-
positive. Receiver operating characteristic analysis was used to examine the relationship between size of the mucocele and the presence of malignancy. Multivariate logistic regression was used to determine which variables were multivariately associated with the presence of malignancy. All statistical tests were 2-sided, and \( P < .05 \) was considered significant. The analysis was performed with SAS version 8.02 (SAS Institute Inc, Cary, NC) and S-Plus version 6.0.4 (Insightful Corporation, Seattle, Wash) software.

### RESULTS

There were 135 patients, 74 (55\%) of whom were female. A total of 129 patients underwent surgery and had a histologic diagnosis of appendiceal mucocele among 537 abdominal surgical procedures performed at our institution during the same study period (0.02\%). The remaining 6 patients (4\%) of the 135 did not undergo surgery, and their diagnosis was based solely on imaging studies. Data regarding symptoms could be collected for all except 1 patient. Of 134 patients, 69 (51\%) were asymptomatic or had symptoms that could not be reasonably attributed to appendiceal mucocele. These patients harbored either a synchronous malignancy (see the third paragraph following) or a variety of benign conditions for which surgery was indicated. Among these, the most frequent were nonneoplastic ovarian or uterine conditions (17 cases), chronic ulcerative colitis (9 cases), and cholelithiasis (5 cases). The mean follow-up was 6.7 years, while the median follow-up was 4.8 years (range, 3 days to 25 years). The most common symptoms in the remaining 65 patients are reported in Table 1.

The largest diameter of the mucocele was reported in 108 patients (80\% of cases). No case of cystadenoma had a diameter of less than 2 cm. There was no statistical difference in size between benign and malignant lesions. However, there was a significant difference in size between simple mucocele (mean, 4.1 cm) and cystadenomas (8.1 cm; \( P < .001 \)).

All patients except those who did not undergo surgery had histology reports, which showed simple mucocele in 62 cases (48\%; 95\% confidence interval [CI], 39.2\%-57.0\%), cystadenoma in 20 (16\%; 95\% CI, 9.7\%-22.9\%), and cystadenocarcinoma in 47 (36\%; 95\% CI, 28.1\%-45.4\%). A synchronous tumor for which surgery was considered present in 39 patients (29\%; 95\% CI, 21.4\%-37.3\%). The most frequent associated neoplasm was a colon or rectal tumor (15 patients [11\%]). Ten patients (7\%) had ovarian cancer, 3 (2\%) endometrial, 3 (2\%) bladder, 2 (1\%) prostate, 2 (1\%) other gastrointestinal tract, and 4 (3\%) other. Only 5 patients with synchronous neoplasms had symptoms that could be attributed to appendiceal mucocele. These included 2 patients with prostate cancer, 2 with gastrointestinal carcinoids (to the terminal ileum and appendix, respectively), and 1 with cecal adenocarcinoma. Several modalities were used for the preoperative assessment of patients who ultimately had a diagnosis of appendiceal mucocele, and none of them was used in more than 30\% of cases, as shown in Table 2. Only 24 patients (19\%; 95\% CI, 12.3\%-26.4\%) had an accurate preoperative diagnosis of appendiceal mucocele. While CT scan was the most

### Table 1. Presenting Symptoms in 65 Patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>37 (27)</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>22 (16)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>13 (10)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>12 (9)</td>
</tr>
<tr>
<td>Acute appendicitis</td>
<td>11 (8)</td>
</tr>
<tr>
<td>Change in bowel habits</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Unexplained anemia</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Obstipation</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Lower gastrointestinal bleeding</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Others (vaginal bleeding, etc)</td>
<td>8 (6)</td>
</tr>
</tbody>
</table>

### Table 2. Preoperative Diagnostic Modalities

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Not Performed</th>
<th>TP</th>
<th>FN</th>
<th>Indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium enema</td>
<td>94 (70)</td>
<td>4 (3)</td>
<td>21 (16)</td>
<td>16 (12)</td>
</tr>
<tr>
<td>CT scan</td>
<td>85 (63)</td>
<td>13 (10)</td>
<td>19 (14)</td>
<td>18 (13)</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>102 (76)</td>
<td>5 (4)</td>
<td>21 (16)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>103 (76)</td>
<td>6 (4)</td>
<td>19 (14)</td>
<td>7 (5)</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; FN, false negative; TP, true positive.
monly used test to establish the diagnosis (9 patients), colonoscopy and barium enema also provided fundamental information in 6 and 3 cases, respectively. Ultrasound, laparoscopy, and open biopsy were diagnostic in 2 patients each. A total of 3 patients with synchronous neoplasms underwent surgery with a preoperative diagnosis of appendiceal mucocele. They included a patient with cystadenocarcinoma of both the appendix and the right ovary who was referred after open biopsy with diagnosis of pseudomyxoma peritonei elsewhere; a patient with prostate cancer and ascites undergoing preoperative laparoscopy and biopsy; and a patient with rectal cancer whose appendiceal mucocele was diagnosed at preoperative abdominopelvic CT scan.

Surgical procedures performed are reported in Table 3. Appendectomy only was performed in 22 patients (17%; 95% CI, 11.0%-24.7%) and right hemicolectomy was performed in 25 patients (19%; 95% CI, 13.0%-27.3%). The remaining 82 patients underwent more complex procedures in addition to the excision of the mucocele, including various types of debulking procedures for pseudomyxoma peritonei, total abdominal hysterectomy and salpingo-oophorectomy, segmental colonic resections, and cholecystectomy for concurrent conditions.

The main indications for surgery were treatment of symptoms in 25 patients (19%; 95% CI, 13.0%-27.3%) and establishing a diagnosis in 26 (20%; 95% CI, 13.6%-28.1%). The remaining 78 patients (60%; 95% CI, 51.5%-69.0%) who underwent surgery had incidental removal of their appendiceal mucocele during an operation performed for concurrent conditions.

A total of 37 patients (29%; 95% CI, 21.1%-37.3%) had pseudomyxoma peritonei and 41 (32%; 95% CI, 23.9%-40.6%) had either spontaneous rupture of the appendix or extravasation of mucus in the immediate vicinity of an intact appendix evident at the time of surgery.

A total of 14 patients (comorbidity rate, 11%; 95% CI, 6.0%-17.4%) had at least 1 concurrent condition subjectively defined as severe at the time of preoperative evaluation or patient assessment. Of these, 10 patients had cardiac comorbidity, while 4 had a neurologic condition and 1 had chronic renal failure. Among patients operated on, 14 were categorized as having an ASA score of 1, 78 an ASA score of 3, and 2 an ASA score of 4. There was 1 postoperative death (0.8%; 95% CI, 0.0%-4.2%), in a patient who underwent sigmoid resection complicated by anastomotic leak. This caused sepsis that eventually progressed to multiple organ failure. Twenty-one patients developed 1 or more postoperative complications, corresponding to a total postoperative morbidity of 16% (95% CI, 10.4%-23.8%). The postoperative complications were wound infection in 7 patients (5%), urinary tract infection in 6 (5%), and anastomotic leak, pneumonia, cerebrovascular accident, and cardiac arrhythmia in 2 (2%) each.

Symptomatic patients were more likely to have a malignant appendiceal mucocele when compared with those presenting with no mucocele-related symptoms. Some specific symptoms were significantly correlated with malignancy (Table 4). Patients with a known preoperative diagnosis of appendiceal mucocele were significantly more likely to harbor a malignancy than those without a preoperative diagnosis (58% [95% CI, 36.6%-77.9%] vs 31% [95% CI, 22.7%-41.2%]; P = .01).

Pseudomyxoma peritonei at the time of surgery was highly significantly associated with malignancy. A malignant appendiceal mucocele was present in 95% (95% CI, 81.8%-99.3%) of patients with pseudomyxoma peritonei, but only in 13% (95% CI, 6.9%-21.7%) of patients without pseudomyxoma peritonei (P < .001). Similarly, 83% (95% CI, 67.9%-92.9%) of patients having a spontaneous rupture of the appendix or a localized periappendiceal mucus collection had a malignant mucocele vs 15% (95% CI, 8.1%-23.9%) of those without these findings (P < .001). A multivariate model evaluating factors associated with increased risks of malignant mucocele confirmed that pseudomyxoma peritonei and mucus extravasation from the appendix were independently associated with increased risk of malignancy (corrected odds ratios, 7.2 [P < .001] and 5.0 [P < .001], respectively).

**COMMENT**

Our study shows that appendiceal mucocele in general is most frequently an incidental finding at the time of surgery and is occasionally discovered only at pathological examination. Despite the specific endoscopic, ultrasonographic, and radiologic features described for appendiceal mucocele, preoperative diagnosis was rare. Computed tomographic scanning was not available at the time when several patients in the earlier period of this series underwent surgery, and it is reasonable to presume that preoperative diagnosis will be easier with contemporary imaging modalities. Most cases were asymptomatic and,

---

Table 3. Surgical Procedures Performed

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendectomy only</td>
<td>22</td>
</tr>
<tr>
<td>Right hemicolectomy only</td>
<td>25</td>
</tr>
<tr>
<td>TAH/BSO, appendectomy</td>
<td>13</td>
</tr>
<tr>
<td>TAH/BSO + omentectomy, appendectomy</td>
<td>10</td>
</tr>
<tr>
<td>Other intestinal resections*</td>
<td>33</td>
</tr>
<tr>
<td>Other gynecologic surgical procedures*</td>
<td>15</td>
</tr>
<tr>
<td>Debulking procedures*</td>
<td>14</td>
</tr>
<tr>
<td>Cholecystectomy*</td>
<td>8</td>
</tr>
<tr>
<td>Others (radical prostatectomy, staging laparotomy, etc)*</td>
<td>7</td>
</tr>
</tbody>
</table>

Abbreviations: BSO, bilateral salpingo-oophorectomy; TAH, total abdominal hysterectomy.

*Possible combinations with other surgical procedures.

Table 4. Symptoms and Malignancy

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Malignancy, No./Total No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall symptoms</td>
<td>36/62 (58)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No symptoms</td>
<td>10/66 (15)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>19/34 (56)</td>
<td></td>
</tr>
<tr>
<td>No abdominal pain</td>
<td>27/94 (29)</td>
<td>.005</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>19/22 (86)</td>
<td></td>
</tr>
<tr>
<td>No abdominal mass</td>
<td>27/106 (25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Weight loss</td>
<td>10/13 (77)</td>
<td>.002</td>
</tr>
<tr>
<td>No weight loss</td>
<td>36/115 (31)</td>
<td></td>
</tr>
</tbody>
</table>
in particular, clinical presentation as acute appendicitis was rare, at variance with what has been reported by others.\textsuperscript{1,2,5,26} However, when symptoms were present, a cystadenocarcinoma was more likely to be encountered. These findings are probably influenced by 2 factors. First, routine incidental appendectomy is generally performed in our institution at the time of gynecologic surgical procedures, which arguably increases the rate of incidental benign appendiceal mucocles, as they would not be detected otherwise. Second, there might be a referral bias in favor of tertiary referral centers for symptoms patients with abdominal mass and weight loss, who are more likely to harbor appendiceal cystadenocarcinoma.

Also of note was the elevated incidence of associated neoplasms, which occurred in almost one third of our patients. If the incidence of ovarian and uterine neoplasms might be, in part, explained by the high number of gynecologic procedures in our series, the association between appendiceal mucocle and colonic neoplasm is more clear and confirms reports by others.\textsuperscript{1,2} It would therefore seem logical to recommend surveillance colonoscopy in patients with a diagnosis of appendiceal mucocle, at least in those with appendiceal cystadenoma. In fact, while there are no conclusive data demonstrating a progression from appendiceal cystadenoma to cystadenocarcinoma, it is accepted by most investigators that the adenoma-adenocarcinoma sequence is comparable with the colonic polypladenocarcinoma sequence.\textsuperscript{28} All mucocles should probably be removed to eliminate the chance of progression to malignancy, in particular for those measuring at least 2 cm, which is the minimum size of cystadenomas encountered in our series. Conversely, our data do not support the contention that it is safe to leave a mucocle of less than 2 cm, especially considering that the removal of the appendix containing a small lesion is unlikely to increase the magnitude and morbidity of a surgical procedure. However, we do not have data on small mucocles left in situ and observed.

All of the operations performed in this current series were open. Laparoscopic appendectomy for mucocle removal has been described,\textsuperscript{29} but caution has also been suggested because of risk of port-site recurrences.\textsuperscript{30} As laparoscopic colectomy gains acceptance for treatment of colon cancer, it might in the future become an acceptable procedure also for this indication.

At the time of surgery, a spontaneous appendiceal perforation or any mucus extravasation that emanates from the appendiceal lumen is strongly suggestive of malignancy and should prompt an oncologically sound procedure. If the lesion is limited to the appendix, the ideal operation should be right hemicolectomy.\textsuperscript{31} In our series, a right hemicolectomy or different segmental colonic resections were often performed for concurrent conditions and not purposely for the treatment of appendiceal mucocle, which hampers the assessment of different surgical procedures for appendiceal mucocle as a specific indication. However, a right hemicolectomy was always performed when the lesion was suggestive of malignancy and an operation with curative intent was possible.

Accepted for publication February 12, 2003.

This study was funded by the Mayo Clinic Foundation, Rochester, Minn.

This study was presented at the 110th Scientific Session of the Western Surgical Association, Vancouver, British Columbia, November 18, 2002, and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

Corresponding author and reprints: Bruce G. Wolff, MD, Division of Colon and Rectal Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55903 (e-mail: wolff.bruc@mayo.edu).

REFERENCES

25. Landen S, Bertrand C, Maddern GJ, et al. Appendiceal mucocles and...
DISCUSSION

Merrill T. Dayton, MD, Salt Lake City, Utah: Dr Stocchi and his colleagues have conducted a retrospective chart review to evaluate the clinical behavior of a fairly uncommon lesion, primary appendiceal mucocele. A literature review reveals how truly uncommon this lesion is. Most of the papers in the author’s bibliography are case reports and anecdotal experience. In fact, even at the Mayo Clinic, with its legacy of large series of rare lesions, it took 24 years to compile this group of 135 patients: a little quick math will show you that that is about 5 of these cases per year.

The authors reach 5 conclusions based on their chart review: (1) a majority of these patients are not diagnosed preoperatively, and in fact 60% of them were diagnosed during an operation for some other disease; (2) only a third of these mucoceles are malignant; (3) the majority of patients with preoperative symptoms end up being diagnosed with a carcinoma; (4) pseudomyxoma peritonei and mucocele extravasation are predictors of malignancy; and (5) all lesions greater than 2 cm in size should be removed.

They conclude that there are a number of clinical, intraoperative, and diagnostic findings that suggest malignancy, ergo, the need for a more aggressive operation. While this series has the vagaries of any retrospective study, it has been carefully conducted. I believe appropriate statistical methods have been used. This is an important paper because of its sheer size. There is not another recent paper in the literature that matches its size.

In conclusion, the authors should be commended for compiling this impressive series. I believe that it will be a reference series that surgeons will use for years to come because of its size. There are a few things that they can do to strengthen the manuscript, such as the survival data.

Susan Galandiuk, MD, Louisville, Ky: Dr Stocchi has done an excellent job with his presentation, and I have several questions. The authors discuss appendiceal mucocele, but are really referring to 4 different entities: simple mucocele, cystadenoma, and then cystadenocarcinoma, both with and without pseudomyxoma peritonei. Although the authors stated that there is a logical progression from cystadenoma to cystadenocarcinoma, do the authors think that the presence of a simple mucocele is perhaps the precursor to cystadenoma; in other words, are they all related?

Regarding the “intraluminal testing,” ie, colonoscopy and barium enema, were these ever positive in the presence of benign mucocele, without adencarcinoma?

The third question refers to those patients who had associated colorectal cancers. Were those colorectal cancers or lesions blocking the appendiceal orifice and therefore causing the mucocele from direct obstruction, or was there an association with colon cancers located at sites other than in the vicinity of the appendiceal orifice?

The authors mentioned pseudomyxoma and treatment of that entity, and specifically mentioned debulking procedures. There is a lot written in the literature about treating pseudomyxoma patients with intraoperative hyperthermia and intraperitoneal chemotherapy. Has that been part of their treatment for these entities?

The important question that is going to affect us all is, nowadays with decreasing reimbursement and the very negative attitude regarding incidental appendectomies, since in this series the bulk of these lesions were discovered after incidental appendectomies during GYN procedures, if we are not doing these, are we going to be seeing more cystadenocarcinomas in the future?

Dr Wolff: It is a great honor for us to be able to present our data on this intriguing and rare condition in an attempt to make some sense out of it. This work actually grew out of a previous paper published in the Annals of Surgery in 1994 from our institution on primary appendiceal carcinoma.

Dr Dayton, I appreciate your comments. They are most helpful. The 6-year follow-up and survival, although not the focus of this study, in the previous paper that I just referenced, the overall 5-year survival in that group of 94 patients with appendiceal carcinoma of various types was 53%. This was stage dependent: with stage A there was 100% survival; with stage B, 67% survival; stage C, 50%; and stage D, 6%. In that particular study, patients with mucinous carcinomas fared better in survival than colonic-type adenocarcinoma or adenocarcinoid-type tumors. Why that is, we don’t know specifically. Mucinous adenocarcinomas don’t tend to metastasize to the lymph nodes or hematogenously. Having said that, if you look at this group of patients with cystadenocarcinoma, they range from patients with a small amount of mucous, a small quantity of intraperitoneal neoplastic cellular elements, sometimes implanted, sometimes not, sometimes just a large amount of mucin associated with an adenocarcinoma of the appendix. And so it is very hard to say with that sort of information as a background how a specific patient is going to do. Pseudomyxoma peritonei is a very nonspecific term, and you know there are all sorts of variations of presentation in that category.

We, too, are somewhat dumfounded by the lack of accurate diagnostic capability of any of the studies that were done, particularly CT scan, and I don’t have any explanation for that. I wonder if in the future, with the advent of CT colonography, diagnosis of mucocele might become more accurate, and we might be seeing a more definitive preoperative diagnosis of mucocele and related disorders.

As with any abdominal surgery, it's a matter of judgment as to how extensive a procedure you would perform. As we have said, any mucocele over 2 cm deserves excision. Anything with firmness at the base certainly deserves excision. If you have frozen section capability, and there is mucus within the abdomen, you could send that off and look for neoplastic epithelial elements. But in general I do not see a significant downside to doing a right hemicolectomy. It's one of the safest operations we do, if there is the slightest suspicion that there might be an appendiceal carcinoma. In the previous study that I referenced, the patients with appendiceal carcinoma clearly did dramatically better if they had right hemicolectomy even as a secondary procedure, than if a simple appendectomy was done. And that goes for both mucinous and nonmucinous adenocarcinomas.

Dr Galandiuk, thank you for your comments. I can't say that a simple mucocele is a precursor to carcinoma, but it is hard to tell whether the mass is a simple mucocele or whether it is a cystadenoma. I do believe that a cystadenoma, if you follow the adenoma-carcinoma sequence, is a precursor to carcinoma, and it's hard to tell which is which unless you remove it. We did not look at the false-positive rate of diagnostic studies in this review because there just simply wasn't enough data for us to really say anything intelligent about it.

We carefully excluded from this study cecal carcinomas that obstructed the lumen of the appendix. These were all true appendiceal carcinomas. Granted, some of those have origin at the base of the appendix. There seems to be something of a field effect in these patients because of the high risk of associated malignancies, and this is the same information we found in the previous study with appendiceal adenocarcinoma—a very high rate of synchronous and metachronous carcinomas, not only of the GI tract, but of other organs.

Finally, treatment: this again is sort of a quagmire. We treated some patients with P32 after debridement, and intraperitoneal injection of 5-FU and so forth. How effective that is I do not know. We have done a few procedures, like Dr Sugarbaker is well known for doing, with pseudomyxoma peritonei, and I really can't comment on outcomes because we just don't have the extensive experience that he has had. On the other hand, I don't see anything wrong with putting a catheter in the abdominal cavity if you find this as an incidental finding. If you don't use it you can always take it out later.

As to incidental surgery, we need to keep the patient's interest foremost. If there is any abnormality of the appendix, we should remove it. Hopefully, we will not see an increase in the incidence of cystadenocarcinoma.