

## Original Investigation

# Increased Risk of Mucinous Neoplasm of the Appendix in Adults Undergoing Interval Appendectomy

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**IMPORTANCE** The role of interval appendectomy after conservative management of perforated appendicitis remains controversial. Determining the etiology of perforated appendicitis is one reason to perform interval appendectomies.

**OBJECTIVE** To determine whether adult patients undergoing interval appendectomy experience an increased rate of neoplasms.

**DESIGN** Retrospective study.

**SETTING** A single tertiary care institution.

**PARTICIPANTS** All patients 18 years or older who underwent appendectomy for presumed appendicitis from January 1, 2006, through December 31, 2010.

**EXPOSURES** Appendectomy for presumed appendicitis.

**MAIN OUTCOMES AND MEASURES** Underlying neoplasm as the cause of presentation for presumed appendicitis. Demographic data, clinicopathologic characteristics, interval resection rate, and complication data were collected and analyzed.

**RESULTS** During the study period, 376 patients underwent appendectomies. Interval appendectomy was performed in 17 patients (4.5%). Neoplasms were identified in 14 patients (3.7%); 5 of those tumors occurred in patients who had undergone interval appendectomy (29.4%). Nine neoplasms were mucinous tumors (64.3%), including all neoplasms associated with interval appendectomies. The mean age of all patients with appendiceal tumors was 49 years (range, 35-74 years).

**CONCLUSIONS AND RELEVANCE** Mucinous neoplasms of the appendix were found in 5 of 17 patients (29.4%) undergoing interval appendectomy. Interval appendectomies should be considered in all adult patients, especially those 40 years or older, to determine the underlying cause of appendicitis. A multi-institutional study to determine the generalizability of these findings is warranted.

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Appendicitis is one of the most common problems seen by general surgeons, with an incidence of more than 500 000 cases per year in the United States alone.<sup>1-3</sup> For patients with simple appendicitis (nonperforated, no phlegmon), the usual treatment is an immediate appendectomy. For patients with complicated appendicitis (abscess, perforation, phlegmon), many surgeons delay appendectomy and initially treat the patient with antimicrobial therapy and drainage as indicated. The rationale for this approach is to avoid the potential increased morbidity of surgery in the acute setting, as well as the possibility of a more extensive operation.<sup>4</sup>

Following successful nonsurgical management of complicated appendicitis, the surgeon must decide whether to perform an interval appendectomy. The most common reason cited for an interval appendectomy is the prevention of recurrent appendicitis. Counterarguments are the relatively high cure rate with nonoperative management (75%-93%) and avoidance of the cost and risk of surgery.<sup>4,5</sup> Another less frequently considered indication for interval appendectomy is the potential to identify whether the appendicitis has a malignant origin.

Tumors are a relatively rare cause of acute appendicitis, with an estimated incidence of 0.7% to 1.7% of all appendectomies.<sup>6-11</sup> However, the unique anatomy of the appendix (long, thin-walled, and tubular) makes it easy for tumors to infiltrate through the wall or obstruct the appendiceal lumen, leading to dilatation and perforation. The most common presentation of appendiceal neoplasms is a history of right-lower-quadrant pain and/or appendicitis. Furthermore, studies have suggested an increased incidence of appendiceal tumors in adult patients undergoing interval appendectomy compared with patients undergoing immediate appendectomy for simple appendicitis.<sup>12</sup> To determine the incidence of appendiceal neoplasms in complicated appendicitis, this study reviewed the pathology data in all adult patients undergoing immediate and interval appendectomies for acute appendicitis during a 5-year period at a single tertiary care center.

## Methods

This was a retrospective study of all patients 18 years or older who underwent appendectomy for presumed acute appendicitis during a 5-year period (January 1, 2006, to December 31, 2010) at a single tertiary care center. Patient demographics, including age at the time of the appendectomy and sex, were collected in addition to the timing of the appendectomy (immediate [ $\leq 48$  hours after admission] vs interval appendectomy), surgical technique (laparoscopic vs open), surgical pathology data, complications, and length of hospitalization. Pathology reports were reviewed individually to determine the etiology of appendicitis for each patient. Statistical analysis was performed using SAS statistical software (version 9.2; SAS Institute, Inc). Groups were compared using the  $\chi^2$  test or paired *t* test as indicated. *P* < .05 was considered statistically significant in all analyses.

Table 1. Characteristics and Demographic Data of Patient Population

Characteristic	No. (%)
No. of appendectomies	376 (100.0)
Sex	
Male	182 (48.4)
Female	194 (51.6)
Age, mean (range), y	41 (18-94)
Technique	
Open	191 (50.8)
Laparoscopic	170 (45.2)
Conversion, laparoscopic→open (n = 361)	15 (4.2)
Interval appendectomy	17 (4.5)
Morbidity	25 (6.6)
Length of stay, mean, d	
Immediate appendectomy	1.9
Interval appendectomy	1.4
Negative appendectomy <sup>a</sup>	10 (2.7)
Neoplasms	
Overall	14 (3.7)
Immediate appendectomy (n = 359)	9 (2.5)
Interval appendectomy (n = 17)	5 (29.4) <sup>b</sup>

<sup>a</sup> Indicates no pathologic evidence of appendicitis.

<sup>b</sup> *P* < .001 compared with immediate appendectomy.

## Results

In all, 376 patients underwent appendectomy during the study period (Table 1). Twenty-six surgeons were involved in the management of appendectomy for these patients. The mean patient age was 41 years (range, 18 to 94 years), and 182 (48.4%) were men. Open appendectomies were performed in 191 patients (50.8%), 170 (45.2%) were performed laparoscopically, and 15 (4.0%) were initiated laparoscopically and converted to an open procedure. The negative appendicitis rate (no pathologic evidence of appendicitis) was 2.7% (n = 10). Seventeen patients (4.5%) underwent interval appendectomy. The mean time to interval appendectomy was 9 weeks (range, 3-20 weeks). Six of the 17 appendectomies (35.3%) were performed as open procedures, and 11 (64.7%) were performed laparoscopically. The most common indication for interval management was right-lower-quadrant pain with an associated phlegmon or abscess seen on computed tomography (n = 15).

Complications were categorized according to the Clavien-Dindo classification.<sup>13</sup> The overall complication rate was 6.1% (n = 23). Of these, there were 18 (78.3%) grade I, 4 (17.4%) grade II, and 1 (4.3%) grade III complications. No grade IV or V complications were identified. The most common complications were wound infections (8 patients [34.7%]), small-bowel obstructions (5 [21.7%]), and intra-abdominal abscess (3 [13.1%]). The only complication in the interval appendectomy subgroup (5.9%) was an intra-abdominal abscess. The mean length of stay for all patients undergoing appendectomy was 1.8 days (range, 1-38 days); the mean length of stay for patients under-

Table 2. Incidence and Type of Appendiceal Neoplasm by Age

Age Range, y	No. of Patients	No. (%) of Patients		
		Mucinous Neoplasms	Carcinoid Tumors	Other Tumors <sup>a</sup>
35-39	39	2 (5.1)	0	0
40-44	41	1 (2.4) <sup>b</sup>	1 (2.4)	1 (2.4)
45-49	27	2 (7.4) <sup>c</sup>	0	1 (3.7)
50-54	25	2 (8.0) <sup>d</sup>	1 (4.0)	0
55-59	20	0	0	1 (5.0)
60-64	23	0	0	0
65-69	14	1 (7.1)	0	0
70-74	10	1 (10.0) <sup>b</sup>	0	0

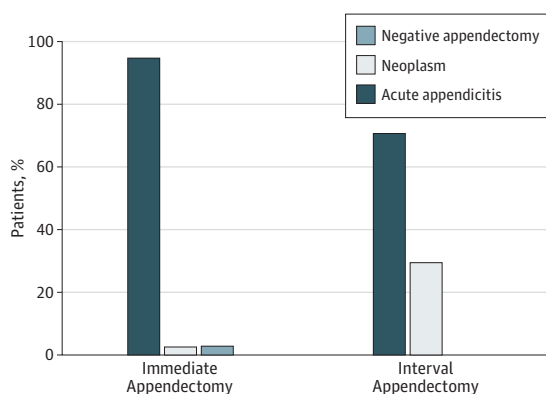
<sup>a</sup> Includes metastatic cancer and lymphoma.

<sup>b</sup> This patient underwent interval appendectomy.

<sup>c</sup> Of these, 1 patient underwent interval appendectomy.

<sup>d</sup> Two patients who underwent interval appendectomy had 1 neoplasm each.

Figure. Pathologic Findings in Patients Who Underwent Immediate (n=359) vs Interval (n=17) Appendectomy



going immediate appendectomy was 1.9 days (range, 1-38 days) and for interval appendectomy, 1.4 days (range, 1-3 days) ( $P = .11$ ).

Fourteen neoplasms (3.7%) were found on pathologic analysis after the 376 appendectomies: 6 (42.9%) mucinous adenocarcinomas, 3 (21.4%) mucinous cystadenomas, 2 (14.3%) carcinoid tumors, 2 (14.3%) metastatic endocervical and lung lesions, and 1 lymphoma (7.1%) (Table 2). Five tumors occurred among the 17 patients who underwent interval appendectomies (29.4%), and 9 occurred among the 359 patients who underwent immediate appendectomy (2.5%) ( $P < .001$ ) (Figure). Six of the tumors occurred in men (42.9%). The mean age of all patients with appendiceal tumors was 49 years (range, 35-74 years). There was no significant difference in the mean age for patients with appendiceal tumors in the immediate vs interval appendectomy groups ( $P = .36$ ). None of the tumors in the immediate appendectomy group were associated with perforation or abscess. All 5 tumors that occurred in patients who underwent interval appendectomy were mucinous adenocarcinomas or mucinous cystadenomas.

## Discussion

Although appendicitis is one of the most common presenting signs of an appendiceal tumor, appendiceal tumors are a relatively rare cause of appendicitis. This study demonstrates a

3.7% incidence of appendiceal tumors in all patients undergoing appendectomy for presumed appendicitis at a single tertiary care institution. In patients who underwent interval appendectomy for complicated appendicitis, the incidence of appendiceal tumors was 29.4% compared with 2.5% in patients with simple appendicitis. Although these incidences are high relative to those reported in larger studies, they are almost identical to those found by Carpenter et al,<sup>12</sup> suggesting that these results are not unique to one institution. Consequently, these results should encourage surgeons to carefully consider performing interval appendectomy in adult patients, especially those 40 years or older.

The role of interval appendectomy after successful nonoperative management of complicated appendicitis is still debated. A systematic review and meta-analysis by Andersson and Petzold<sup>4</sup> showed a 7.4% incidence of recurrent appendicitis and a 1.2% incidence of malignant neoplasm in patients with successful nonoperative management of complicated appendicitis. Based on these findings, the authors concluded that interval appendectomy is not necessary. Lien et al<sup>14</sup> reviewed the medical records of 128 adult patients who received nonoperative treatment for acute appendicitis. Twenty (15.6%) of the patients experienced recurrent appendicitis, and the authors identified male sex as a significant risk factor for recurrence. They did not identify any appendiceal malignant neoplasms and concluded that routine interval appendectomy is not indicated. Similarly, Tekin et al<sup>15</sup> evaluated the data for 94 patients with a mass in the right lower quadrant. Only 6 patients (6.7%) experienced recurrent appendicitis, and no malignant tumors were identified. As in the other studies, Tekin and colleagues concluded that routine interval appendectomy is not necessary. We agree that interval appendectomy may not be indicated for the prevention of a less than 10% risk of recurrent appendicitis, especially when appendicitis has been shown to be treated with less morbidity at the time of recurrence than by planned interval appendectomy.<sup>16</sup> However, we are concerned that the incidence of malignant neoplasm may be underestimated in most studies given the inclusion of pediatric patients, the lack of surgical pathology data, and the time and follow-up required to identify an appendiceal malignant neoplasm.

As in our study, the study by Carpenter et al<sup>12</sup> demonstrates a remarkably high incidence of appendiceal tumors (overall, 2.5%) in both the immediate appendectomy group (1.0%) and the interval appendectomy group (27.7%). In addi-

tion, they found a similar association between increased age and the incidence of noncarcinoid malignant neoplasms. Currently, there are no known environmental risk factors for appendiceal cancer. In addition, no hereditary components or genetic pathways have been identified. One study<sup>17</sup> has suggested a relationship between the presence of *Helicobacter pylori* bacteria and the development of pseudomyxoma peritonei of appendiceal origin; however, a causal effect of *H pylori* has yet to be demonstrated. The 2 institutions at which these studies were performed are in geographically distinct regions of the United States (the desert Southwest and New England), suggesting that these are not isolated, region-specific findings. A multi-institutional study incorporating patients from different geographic regions and environmental settings could provide valuable information about the necessity of interval ap-

pendectomy, as well as potentially identify risk factors for appendiceal tumors.

We recognize that our study has limitations. First, it was a retrospective study. Second, the study population was relatively small, with only 17 interval appendectomies. Third, we did not identify patients for whom appendicitis was managed nonoperatively and who also did not undergo interval appendectomy. However, we are aware of at least 2 adult patients at our institution with complex appendicitis who did not undergo interval appendectomies and who later presented for stage IV appendiceal cancer within the study period. Consequently, like Carpenter et al,<sup>12</sup> we believe that the findings of these 2 studies should prompt surgeons to regularly perform interval appendectomies, especially in patients 40 years or older.

#### ARTICLE INFORMATION

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