

GENERAL GYNECOLOGY

The role of appendectomy for mucinous ovarian neoplasms

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OBJECTIVE: To determine how frequently the appendix harbors pathology in women having surgery for mucinous neoplasms of the ovary and assess the associated morbidity.

STUDY DESIGN: A retrospective chart review of patients operated on at our institution with the diagnosis of a mucinous neoplasm of the ovary or appendix.

RESULTS: A total of 327 cases were identified. Of the 309 women with mucinous ovarian neoplasms, 197 (64%) were benign, 68 (22%) low malignancy potential, and 44 (14%) were invasive. Of 155 appendecto-

mies performed, only 1 metastatic low grade mucinous appendiceal tumor was found, but this appendix was grossly abnormal. There was no association between wound complications and appendectomy.

CONCLUSION: When a grossly normal appendix is removed during surgery for a mucinous ovarian neoplasm without evidence of pseudomyxoma peritonei, no primary or metastatic mucinous appendiceal tumors are found.

Key words: appendectomy, mucinous ovarian neoplasms

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Some experts recommend routine appendectomy during ovarian cancer staging. They propose that removing the appendix leads to upstaging of disease, prevention of acute appendicitis, more accurate diagnosis (including ruling out primary appendiceal disease), and decreased risk of future surgical complications from extensive adhesions. However, it remains controversial whether appendectomy should be performed as a routine part of the staging procedure for early ovarian cancer because the exact magnitude of these benefits is unknown.¹⁻⁴ Mucinous ovarian tumors account for 15-20% of all ovarian neoplasms, with the majority being benign.

For those that are invasive or of low malignant potential (LMP), appendectomies have been recommended to rule out the possibility of a primary appendiceal adenocarcinoma or metastasis from a gastrointestinal source.¹ This recommendation has often been extended in clinical practice to benign mucinous tumors as well.

These recommendations have stemmed from data looking at all ovarian histologies, as well as older experience with pseudomyxoma peritonei, or mucinous ascites and deposits within the peritoneal cavity. Pseudomyxoma peritonei was thought to originate in the ovary or peritoneal cavity; however, recent research has shown that this disease almost exclusively originates in the appendix.⁵

Although it has historically been reported that the appendix is the site of metastasis in 8% of mucinous ovarian cancers, none of these cases were isolated metastases that changed the final stage.⁶ Although it is known that appendiceal adenocarcinomas often metastasize to the ovary, the rate of positive appendiceal pathology in women having surgery for mucinous ovarian tumors without obvious metastatic disease is unknown.

Our primary objective was to determine how often the appendix is involved, or the primary source of cancer, in women undergoing appendectomy at the time of surgery for a mucinous ovarian tumor. Our secondary objective was to determine the frequency of complica-

tions arising from such appendectomies to better determine the risk/benefit ratio of the procedure.

MATERIALS AND METHODS

Approval of the University of Wisconsin Hospital and Clinics's Institutional Review Board for Health Sciences Research was obtained for this retrospective observational cross-sectional study. All patients operated on or seen in consultation at our institution from January 1994 to September 2009 with the final diagnosis of a mucinous neoplasm of the ovary or appendix were included. Cases were identified from pathology records of any mucinous ovarian tumors (benign, LMP, invasive) or mucinous appendiceal neoplasm from January 1994 to September 2009. Including all primary appendiceal cases was necessary to ensure that we did not miss any women operated on for an ovarian tumor that were found on final pathology to have a primary appendiceal tumor with ovarian metastasis. During this period, the practice of appendectomy for mucinous ovarian tumors was provider dependent.

Medical record numbers corresponding to pathology records were used to locate charts through the University of Wisconsin Hospital and Clinics electronic medical record. Paper charts were obtained if no or limited information was found electronically. Final pathol-

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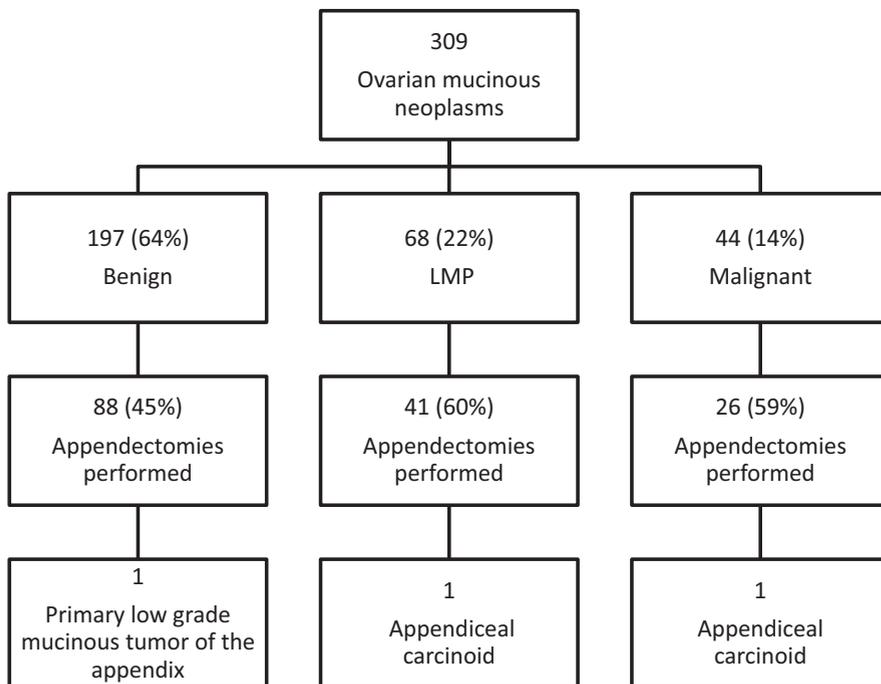
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FIGURE 1
Primary ovarian tumors



When appendectomy was performed for a mucinous ovarian neoplasm, 1 primary low grade mucinous appendiceal tumor was found that was grossly abnormal in appearance.

LMP, low malignant potential.

Lin. Appendectomy and mucinous ovarian neoplasms. *Am J Obstet Gynecol* 2013.

ogy reports were reviewed for information pertaining to final ovarian and appendiceal diagnoses, tumor diameter, and cytology. Operative reports were reviewed for information pertaining to date of surgery, type of surgery, tumor laterality, presence of ascites, and gross appearance of appendix. We assumed a grossly normal appendix when there was no mention of appendiceal abnormality on the operative note. Other information collected included diagnosis (stage, grade, and histology), age, history of appendectomy, postoperative admissions, and wound complications, including abscess formation, relating to appendectomy. Complications occurring within 30 days of surgery were considered related to the surgical procedure.

Cases were excluded if no other information besides pathology record was available either electronically or in the paper chart and if the primary source of mucinous carcinoma was from neither ovary nor appendix.

Statistical analysis was performed using SAS version 9.2 software (SAS Institute Inc, Cary, NC). Fisher exact test was used to examine the significance of associations between categorical variables.

RESULTS

A total of 327 cases meeting criteria were identified, including 308 primary ovarian mucinous neoplasms and 19 primary appendiceal neoplasms. Only 1 of the 19 primary appendiceal neoplasms presented preoperatively as an isolated ovarian mass. The others presented preoperatively with either obvious metastatic disease, found intraoperatively to be pseudomyxoma peritonei, or a known appendiceal mass preoperatively. Therefore, we included the 1 patient with an isolated ovarian mass preoperatively in our analysis for a total of 309 patients who went to the operating room with the preoperative diagnosis of an ovarian mass only. Median patient age was 49 years.

The procedures performed included 147 (45%) total abdominal hysterectomies with bilateral salpingo-oophorectomy, 84 (26%) unilateral salpingo-oophorectomies, 64 (20%) bilateral salpingo-oophorectomies, 17 (5%) ovarian cystectomies, 11 (3%) total abdominal hysterectomies with unilateral salpingo-oophorectomy, and 4 (1%) other procedures. Other procedures included staging procedures after hysterectomy, removal of ovarian remnant, and right hemicolectomy.

Of these 309 patients operated on for ovarian neoplasms, 197 (64%) had benign, 68 (22%) LMP, and 44 (14%) invasive mucinous pathology (Figure 1). Fifty-six (18%) women had previously undergone appendectomy. Of 253 appendices present during procedures for mucinous ovarian neoplasms, 155 (61%) appendectomies were performed.

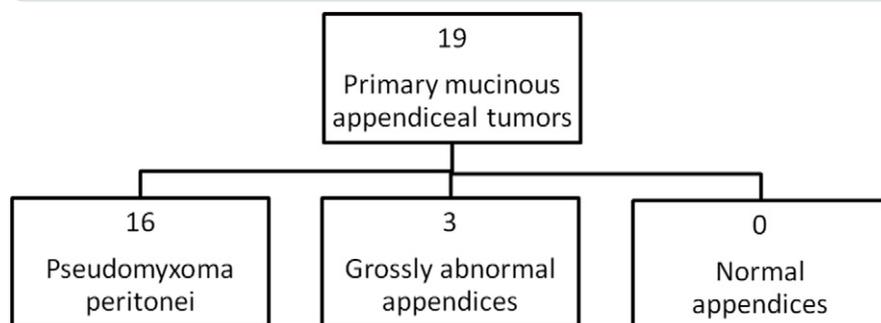
Of the 197 women with benign mucinous neoplasms, 88 (45%) had appendectomies, of which, 1 grossly abnormal appendix revealed a primary low-grade mucinous tumor of the appendix. Thirty-two (16%) had prior appendectomies and 77 (39%) had no appendectomy performed during the surgery for a benign mucinous ovarian neoplasm.

Of the 68 women with mucinous ovarian LMP tumors, 41 (60%) had appendectomies, 15 (22%) had prior appendectomies, and 12 (18%) had no appendectomy. One incidental appendiceal carcinoid tumor was found of the 41 appendectomies performed for LMP tumors. No mucinous tumors of the appendix were identified in the LMP group.

For the 44 women with invasive mucinous ovarian tumors, 26 (59%) had appendectomies, 9 (20.5%) had prior appendectomies, and 9 (20.5%) had no appendectomy performed. One incidental appendiceal carcinoid tumor was found of the 26 appendectomies performed for invasive mucinous ovarian tumors. No mucinous tumors of the appendix were identified in the invasive group.

Nineteen primary mucinous appendiceal cancers were identified. Sixteen (84%) of these were associated with pseudomyxoma peritonei. The appendix was noted to be grossly abnormal at the time of surgery in the remaining 3, with pathology

FIGURE 2
No normally appearing appendices harbored appendiceal pathology



Lin. Appendectomy and mucinous ovarian neoplasms. Am J Obstet Gynecol 2013.

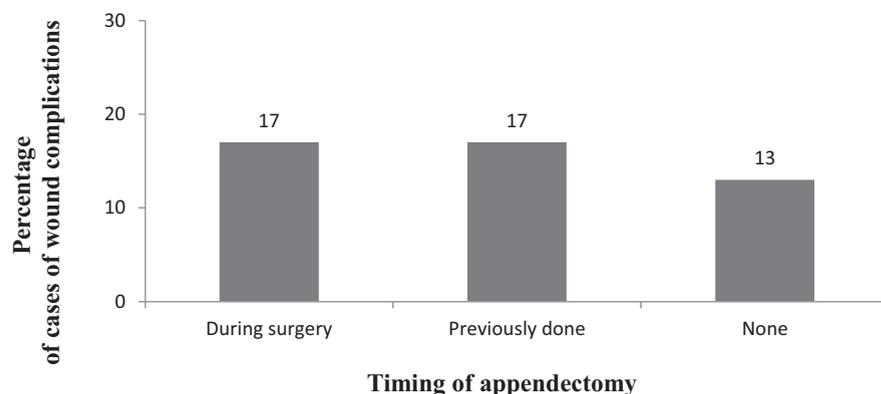
showing mucinous cystadenocarcinoma for 2 appendices and 1 appendix harboring a primary appendiceal mucinous low-grade tumor detailed earlier and included in the benign mucinous ovary group (Figure 2). Gross appendiceal abnormalities included nodules, thickening of the wall, adhesions, and tumor implants.

We performed subgroup analyses where data was available for complications ($n = 304$). The only complications noted were wound complications. Of 163 cases where the appendix was removed during the procedure, 27 patients (17%) had wound complications. Fifty-four women had prior appendectomies and 9 (17%) of these had wound complications. Of 87 cases where the appendix was not removed, 11 (13%) had wound complications (Figure 3). Statistical significance was not found in the association between wound complication and appendectomy ($P = .72$).

COMMENT

Our findings show that no primary or metastatic appendiceal tumors of mucinous histology were identified when appendectomy was performed for a mucinous ovarian neoplasm when the appendix is grossly normal and no evidence of pseudomyxoma peritonei was encountered. We found only 1 case of a primary low-grade mucinous neoplasm of the appendix when the preoperative diagnosis was for an ovarian neoplasm only. However, this appendix was noted to be grossly enlarged and fluid filled at the time of surgery. Furthermore, we found that all 19 primary appendiceal tumors of mucinous histology were associated with either grossly abnormal appendices or pseudomyxoma peritonei. We found no increase in postoperative complications because of appendectomy at the time of surgery.

FIGURE 3
There was no association between wound complications and timing of appendectomy



Lin. Appendectomy and mucinous ovarian neoplasms. Am J Obstet Gynecol 2013.

These findings support those of Timofeev and colleagues,⁷ in which 76 mucinous ovarian tumors were evaluated with similar breakdown of benign (47%), LMP (34%), and malignant (19%) mucinous types. They found 1 of 36 benign mucinous cases had an associated carcinoid appendiceal tumor, 1 of 26 LMP cases with a carcinoid appendiceal tumor, and 1 of 14 malignant mucinous cases with metastasis to a grossly abnormal appearing appendix.⁷ Similarly, Fontanelli and colleagues² found that 20% of ovarian tumor types were mucinous, with only 1 of 31 (3%) mucinous cases having appendiceal involvement. However, this involvement did not change the final ovarian cancer stage.² Incidentally, 3 carcinoid tumors were also identified in their study.

Interestingly, our findings are not dissimilar from the study most classically cited as the reason to remove the appendix when an ovarian mucinous cystadenocarcinoma is found.¹ In Malfetano's review of 94 patients with appendectomy at the time of ovarian cancer surgery, only 2 patients had microscopic involvement of the appendix, and this involvement did not change the stage. Malfetano did not specify the histologic types of ovarian cancer in his review, but made the recommendation to remove the appendix for mucinous cystadenocarcinomas of the ovary to rule out a primary appendiceal mucinous adenocarcinoma.

Our study deviates from the results of Ayhan and colleagues⁸ who showed 28% appendiceal involvement with mucinous ovarian cancers and no significant relationship between appendiceal metastases and histopathology. However, these findings are different from multiple studies that reveal smaller numbers of metastasis from mucinous tumors and show that serous ovarian malignancies were more likely to have appendiceal involvement.^{2,4,6,9} An earlier study by Ayhan's group also identified 4 primary appendiceal mucinous adenocarcinomas on final pathology after removal for preoperatively suspected ovarian carcinoma.¹⁰ However, there is no mention of the gross appearance of these 4 appendices in the manuscript. In fact, there is limited data on the gross appearance of the appendix at the time of removal in

many earlier studies, which could account for the higher rates of appendiceal involvement reported.^{1,8,9,11}

A strength of our study is the large number of patients with mucinous ovarian neoplasms that we evaluated as well as evaluating all of the primary appendiceal tumors. However, there are several limitations to address besides the inherent limitations of a retrospective review. Selection bias could have confounded our study, as cases were obtained based on final pathology results and not intraoperative frozen section. A further limiting factor is that not all cases had appendectomies performed, potentially resulting in an underestimation of appendiceal pathology. We were unable to assess provider preference in removing the appendix at the time of surgery for mucinous ovarian neoplasms, thus leaving the decision to remove or not elusive. It is possible that these decisions were made based on findings not mentioned in the operative note, thus influencing our results. In addition, gross evaluation of the appendix was not always mentioned in the operative report. Although we assumed a grossly normal appendix if there was no mention of abnormality in the operative note, we could have underestimated the number of grossly abnormal appendices with this analysis.

We found 2 (0.7%) occult carcinoid tumors of the appendix, 1 associated with LMP and 1 with malignant mucinous ovarian tumors. Incidentally, Timofeev and colleagues⁷ also noted 2 carcinoid appendiceal tumors in a smaller study size of 76 mucinous ovarian cases (2.6%). Carcinoid tumors are rare, with a reported incidence of 2-4/100,000, but are the most common neoplasms found in the appendix, generally diagnosed after appendectomy.¹² Most patients with undiagnosed carcinoid tumors of the appendix take on average 9 years to become symptomatic and these symptoms are similar to acute appendicitis.¹² When appendectomy is performed for acute appendicitis, the incidence of carcinoid tumors ranges from 0.5–1.1%.^{12,13} The prognosis for appendiceal carcinoid tumors is predicted by size, with <2 cm

(95%) unlikely to metastasize and cured with simple appendectomy. In general, the prognosis is good with little need for further follow up.

The potential risks of performing an appendectomy for a grossly normal appendix include hemorrhage, peritonitis, intraabdominal abscess, bowel perforation, intestinal obstruction, cost, and increased time in the operating room. However, many studies have shown no increase in complications from appendectomies at the time of benign and malignant gynecological surgeries.^{2-4,6,11,14} The American Congress of Obstetrics and Gynecology, in its Committee Opinion, suggests that it is still unclear whether the benefits of elective coincidental appendectomy outweigh the risks and that this should be an individualized decision.¹⁵ Snyder and colleagues¹⁶ support appendectomy in those patients younger than 35 years of age as the risk of acute appendicitis is greater in this age group, as opposed to those over age 50, where routine appendectomy might not be justified. Although our results do not justify routine appendectomy of a grossly normal appendix for mucinous ovarian neoplasms, one could argue that the complication rate is so low, that routine appendectomy does not add appreciable harm. However, in light of our findings, our group has abandoned routine appendectomy for mucinous ovarian tumors in women over the age of 35 with a grossly normal appendix.

In conclusion, when a grossly normal appendix is removed during surgery for an ovarian mucinous neoplasm without evidence of pseudomyxoma peritonei, there was no primary or metastatic appendiceal tumor of mucinous histology noted. All primary mucinous appendiceal tumors were associated with either grossly abnormal appearing appendices or pseudomyxoma peritonei. There was no significant increase in complications postoperatively in association with appendectomy. We recommend that appendectomy be performed only for those appendices that are grossly abnormal or associated with pseudomyxoma peritonei at the time of surgery for mucinous ovarian neoplasms. ■

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