

Is appendectomy a must for borderline and invasive mucinous ovarian tumour ?

Tomoko Matsuzono¹, Li Wai Hon¹, Chan Yuk May May¹

¹Queen Elizabeth Hospital, Hong Kong (China)

Summary

Aim: The authors' objective is to review how often the appendix is involved in Chinese women undergoing appendectomy at the time of surgery for a mucinous borderline ovarian tumour (mBOT) or invasive mucinous ovarian tumour (IMOT), and to evaluate whether appendectomy is necessary. **Materials and Methods:** A retrospective study was performed in Queen Elizabeth Hospital in Hong Kong between 2010 and 2016. Women who underwent surgery and whose final diagnosis was mBOT, invasive mucinous ovarian tumour (IMOT) or mucinous appendiceal tumour were included. **Results:** A total of 78 cases of mucinous borderline or invasive ovarian tumour and appendiceal tumour were identified, of which 75 (96.2%) patients underwent an appendectomy at the time of primary surgery. Forty-six (58%) patients were finally diagnosed with borderline ovarian tumours and 32 (41%) with malignant mucinous tumours. Among the 46 borderline tumours, 4 (9.3%) appendices were grossly abnormal, but none of them were confirmed as malignant. As for those with malignant mucinous disease, 5 of the 32 (15.6%) appendices were visually abnormal, and three were confirmed to be primary mucinous appendiceal tumours. Based on these results, sensitivity, specificity, positive predictive value, and negative predictive value of the macroscopic appearance of the appendix were 100%, 91.7%, 33.3%, 100%, respectively. **Conclusion:** Primary or metastatic appendiceal neoplasm is not expected in case of the appendix is grossly normal during surgery for a mucinous ovarian tumour with borderline or malignant features. Appendectomy must be performed if the macroscopic appearance of the appendix is abnormal or when pseudomyxoma peritonei (PMP) is present.

Key words: Appendectomy; Appendiceal tumour; Invasive mucinous ovarian tumour; Mucinous borderline ovarian tumour; Pseudomyxoma peritonei.

Introduction

Mucinous tumours account for 10-15% of all primary ovarian tumours. Up to 30-50% are borderline ovarian tumours (BOT) and 6-10% of epithelial ovarian cancers are mucinous tumours [1]. Borderline tumours are distinguished from carcinoma by the absence of stromal invasion and high-grade atypia [2]. Mucinous borderline ovarian tumours (mBOTs) are subclassified into two clinicopathologic forms: the gastrointestinal-type and the endocervical-like tumours. Gastrointestinal type tumours account for 85-90% of mBOTs and they have similar histologic features as primary mucinous tumours of the appendix [3]. It is often difficult to distinguish a primary ovarian tumour from metastatic mucinous tumour of the appendix, therefore, most pathologists suggest that the diagnosis of primary mucinous ovarian tumour requires exclusion of metastases from the gastrointestinal tumours [4-6]. Historically, pseudomyxoma peritonei (PMP), which is a clinical term for widespread intraperitoneal deposits of extracellular mucin, was thought to be the result of spread of ruptured mucinous tumour of the ovary. However, it is now known that the origin of PMP is the appendix [7]. Based on this, some experts recommend routine appendectomy during surgery for mBOT and invasive mucinous ovarian tumour (IMOT), and propose that appendix removal leads to a more ac-

curate diagnosis [8]. Based on this, the clinical practice guidelines in oncology outlined by the National Comprehensive Cancer Network (NCCN) recommend that an appendectomy to be performed in all mucinous tumours involving the ovaries that are identified intraoperatively [9]. Nevertheless, the literature on the incidence of appendiceal pathology in patients with mBOT and IMOT remains limited. Therefore, this study was conducted to evaluate the appendiceal pathology in patients with a pelvic mass operated on by the gynecologic oncologists with a provisional intraoperative diagnosis of mBOT or IMOT.

Materials and Methods

A retrospective study was performed in the Queen Elizabeth Hospital in Hong Kong, which has a Gynecologic Oncology Department. The hospital database was searched for women who underwent surgery for adnexal mass and with a final diagnosis of mBOT, IMOT, and appendix carcinoma between 2010 and 2016. Cases were excluded from analysis if no information was available for pathology or operative reports either electronically or in the paper charts. Overall, 107 patients underwent surgery for mucinous ovarian tumour. Of these, 78 women with adequate medical data were identified.

The demographic and clinical characteristics of the patients included in the final cohort including age, par-

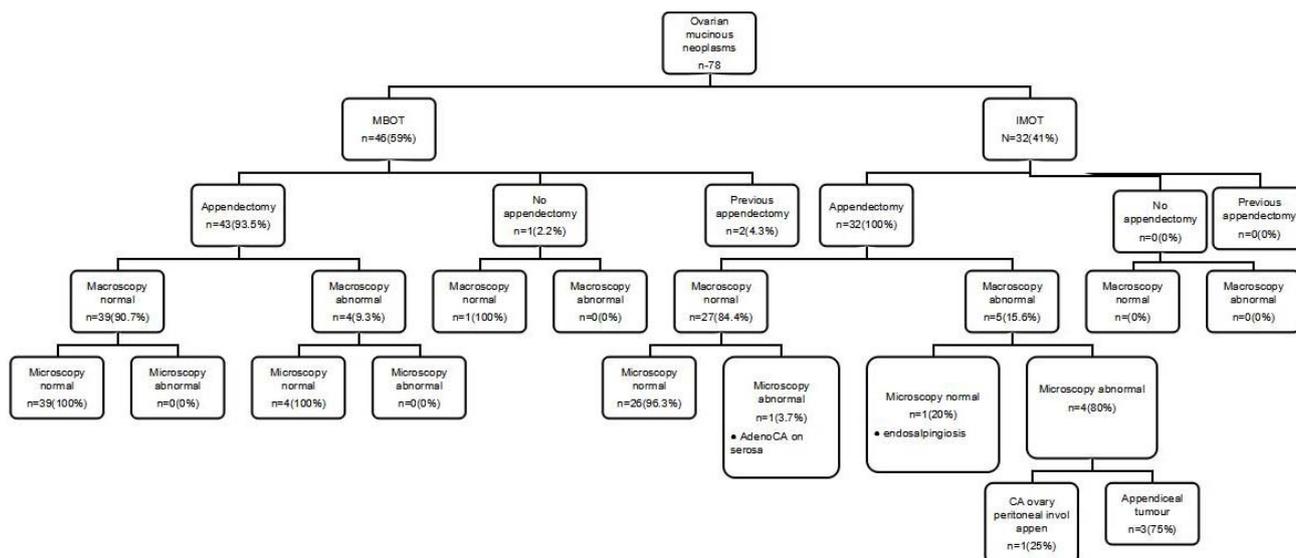


Figure 1. — Study design and results. MBOT = mucinous borderline ovarian tumour; IMOT = invasive mucinous ovarian tumour

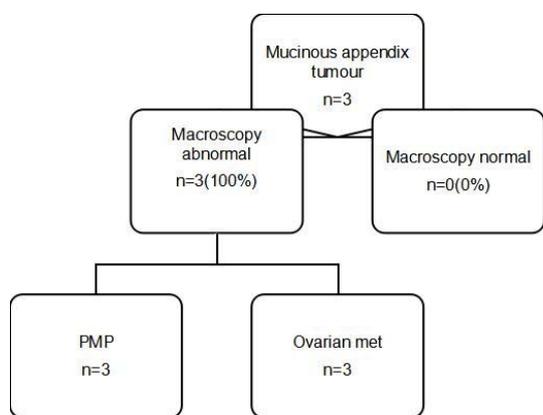


Figure 2. — Primary mucinous appendix tumours

ity, previous appendectomy, preoperative tumour markers (CA125), postoperative complications and follow up were retrieved for analysis. Operative records were reviewed for information pertaining to the type of surgery, clinical staging of disease, presence of PMP, and gross appearance of the appendix. If there was no information about the gross appearance of the appendix in the operative records, then it was regarded as normal. Final pathology reports were reviewed to ascertain the mean tumour diameter, the final histopathology of the ovarian and appendiceal specimens, as well as the final staging.

Data were analyzed using Statistical Package for the Social Science version 18.0. Sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio for macroscopic appearance of the appendix were calculated. Descriptive analyses were performed for the study variables, *T*-tests was used for intergroup comparisons. *p*-values of less than 0.05 were considered to indicate a significant difference.

Table 1. — Demographics and clinical characteristics of the patients.

	MBOT N = 46	IMOT N = 32
Median age	51	60 (<i>p</i> < 0.01)
CA125 (IU/ml)	72	224 (<i>p</i> < 0.10)
Stage		
I	43 (93.5%)	19 (59.3%)
II	1 (2.2%)	2 (6.3%)
III	1 (2.2%)	9 (28.1%)
IV	1 (2.2%)	2 (6.3%)
Mean tumour diameter (cm)	12	12 (<i>p</i> < 0.92)
Presence of PMP (%)	0	3 (9.4%)
Primary appendiceal tumour (%)	0	3 (9.4%)
Appendectomy complication (%)	0	0

MBOT = mucinous borderline ovarian tumour; IMOT = invasive mucinous ovarian tumour; PMP = pseudomyxoma peritonei

Results

A total of 78 cases of mBOT, IMOT, and appendiceal tumours with adequate medical data were identified, of which 75 (96.2%) patients underwent an appendectomy at the times of primary surgery. Of these 78 patients, 46 (59%) were finally diagnosed with mBOT and 32 (41%) with malignant mucinous tumours. At the time of surgery, 62 (80%) of patients were Stage I, 3 (3.8%) Stage II, 10 (12.8%) Stage III, and 3 (3.8%) Stage IV. Detailed demographic and clinical characteristics of patients are presented in Table 1. Among the 46 mBOT patients, 4 (8.7%) appendices were grossly abnormal, and none of them were confirmed as having appendiceal metastasis of mBOT, while all the normal-looking appendices were histologically benign.

As for those with malignant mucinous disease, 5 of the 32 (15.6%) appendices were visually abnormal. One case

Table 2. — Literature overview.

Reference	mBOT	IMOT	Appendectomy performed	Mucinous malignancy in appendix		Advice to perform standard appendectomy
	n	n	n	(%)	n (%)	
Feigenberg et al. 2013 [13]	30	36	66	(100)	11 (17)	No
Lin et al. 2013 [12]	68	44	67	(60)	1 (2)	No
Timofeev et al. 2010 [11]	26	14	40	(100)	3 (8)	Yes
Ramirez et al. 2007 [14]	15	35	50	(100)	0 (0)	No
Ozcan et al. 2015 [15]	69	51	88	(73)	4 (4.5)	No
Cheng et al. 2017 [16]	98	66	71	(43)	6 (8.4)	No
Current study	46	32	75	(96)	3 (4)	No
Total	352	278	341	(54)	28 (8.2)	

MBOT = mucinous borderline ovarian tumour; IMOT = invasive mucinous ovarian tumour. Literature overview: mucinous borderline ovarian tumour and invasive mucinous ovarian tumour, appendectomy, frequency, and incidence of primary malignancy of the appendix.

had endosalpingiosis commented by pathologist, another one had serosal involvement by IMOT, and the remaining three cases were confirmed primary mucinous appendiceal carcinomas. One patient with a normal looking appendix was diagnosed with microscopic peritoneal involvement by IMOT. The details are shown in Figure 1.

No patient was upstaged solely based on isolated appendiceal involvement, as intraoperative exploration revealed other metastatic tumour implants. All appendices were reported as being grossly abnormal in the operative records of all three patients with primary mucinous appendix carcinoma (Figure 2). All these three women were operated with an initial diagnosis of adnexal mass and all of these had ovarian metastasis and PMP. In the whole study group of 75 patients who underwent appendectomy, no complications were reported. According to these results sensitivity, specificity, positive predictive value, and negative predictive value of the macroscopic appearance of the appendix were 100%, 91.7%, 33.3%, 100%, respectively.

Discussion

The NCCN guideline suggested appendectomy to be recommended with suspected or confirmed mucinous ovarian tumors. Their belief is that metastases to the ovaries are more common, and primary mucinous tumors of the ovaries are uncommon, and it is difficult to distinguish between metastatic adenocarcinomas to the ovaries and primary mucinous carcinomas [9].

Ayhan *et al.* [8] evaluated 285 patients with epithelial ovarian cancer who underwent appendectomy at the time of primary cytoreductive surgery. The authors found that 37% of patients had appendiceal metastasis. Furthermore, 5% of the patients with apparent Stage I to II disease had their disease upstaged because of isolated appendiceal metastasis [10]. The authors then concluded that appendectomy is indicated in all patients with epithelial ovarian carcinoma as part of the initial surgical staging because of the considerable chance of upstaging in patients with early stage disease

and the need for optimal cytoreduction in patients with advanced stage disease.

Another study by Timofeev *et al.* [11] investigated 191 patients with oophorectomy and appendectomy performed during the same surgical procedure. They observed a significant rate of appendiceal metastases associated with ovarian carcinomas (65.9%) with all cases occurring in patients with other evidence of Stage III or IV disease. They also concluded that appendectomy is recommended when frozen diagnosis is mucinous ovarian carcinoma, borderline tumor or metastatic carcinoma of suspected gastrointestinal origin.

Table 2 shows the results of review of the literature on the incidence of appendectomy and associated histopathological results in patients with mBOTs and IMOT, including data from the present study [11-16]. Lin *et al.* [12] identified 327 cases of ovarian mucinous tumours including 68 patients with mBOT and 19 primary mucinous appendiceal tumours. Appendectomy was performed in 41 of the 68 patients with mBOT, and only one appendiceal carcinoid and no report of mucinous tumour of appendix was found. In the 19 cases with primary mucinous appendiceal tumours, all the appendices were described to be macroscopically abnormal. The investigators therefore suggest that appendectomy should only be performed in the cases of mucinous ovarian tumours when the appendix is grossly abnormal.

The incidence of primary appendiceal tumour is approximately 0.5% among all gastrointestinal tumours, and preoperative diagnosis is difficult. These tumours are usually metastatic to the ovary, and therefore, they are often diagnosed as an adnexal mass preoperatively, but the appendix is almost always grossly abnormal at the time of surgery [7].

Feigenberg *et al.* [13] identified 121 cases of mucinous ovarian tumours whose surgeries were performed by a gynecologic oncologist that included an appendectomy as part of their surgical procedure. Eleven (14%) patients were diagnosed as metastatic appendiceal carcinoma involving the ovary. Evidence of metastatic disease, an abnormal-

looking appendix, or PMP was identified at the time of surgery for all 11 cases diagnosed with metastatic appendiceal cancer. Although they had a 17% positive yield in the appendix, the authors still believed that adding an appendectomy carries a questionable benefit in cases of early-staged mucinous borderline or malignant ovarian tumour. However, the presence of an abnormal-looking appendix and evidence of metastatic disease or PMP necessitates an appendectomy owing to the high prevalence of primary appendiceal cancer mimicking an ovarian tumor.

Among the 630 MBOTs and IMOTs reported in the present review, appendectomy was performed in 341 (54%) cases and appendiceal malignancies were reported in 25 (7%) cases in the literature. Because of the low yield of appendiceal malignancy on routine appendectomy, and because almost all diseased appendixes are grossly abnormal intraoperatively, five out of six studies did not recommend performing appendectomy in all patients with mucinous ovarian tumour with borderline or malignant features [11-16].

Routine appendectomy is still controversial due to its potential complications, such as haemorrhage, infection, abscess, peritonitis, bowel perforation, and intestinal obstruction. Other factors such as cost of operation and prolonged operation time must also be considered [17]. One can argue that, although the incidence of identifying a primary mucinous appendix tumour is very low, performing an appendectomy has no major negative consequence. However, according to a systematic review by Davis *et al.* [18], they reported possible complications following such seemingly simple surgical procedure.

According to the present study, no appendiceal pathology was identified in the patients with mBOT. As for the patients with IMOT, three out of five of the grossly abnormal appendix were involved by primary appendiceal malignancy in the final histology. Furthermore, no patients with apparent early-stage tumours had evidence of isolated metastatic disease to the appendix, hence, none of the patients evaluated had their disease upstaged because of histopathologic findings in appendix.

The present retrospective study compared with the results of the present literature review indicates that careful inspection of the appendix should be performed in patients with a mucinous ovarian tumour with borderline or malignant features. Appendectomy should be performed in cases in which the appendix is macroscopically abnormal, or in the presence of PMP. The risk of having a pathological appendix in patients with MBOT is incredibly low.

The major limitation of this study is the retrospective nature of the clinical data. Furthermore, information on the macroscopic appearance of the appendix during surgery could not be obtained for all of the patients, they could only be assumed to be normal if not documented in the operative records. After all, the literature review and the study suggest that the evidence to justify a routine appendectomy is insufficient.

Conclusion

Primary or metastatic appendiceal neoplasm is not expected if the appendix is grossly normal during surgery for a mucinous ovarian neoplasm with borderline or malignant features, without evidence of PMP. Appendectomy should be performed if the macroscopic appearance of the appendix is abnormal or PMP is present. However, further studies with a larger sample size should be carried out to confirm the present findings.

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Conflict of interest

There are no conflicts of interest to declare for any of the authors.

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Corresponding Author:

T. MATSUZONO, M.D.

2/F, Block F, Queen Elizabeth Hospital 30 Gascoigne Road Hong Kong (China)

e-mail: tomoko821@gmail.com