
The role of appendectomy as part of the treatment of a mucinous borderline ovarian tumor

S. Cosyns, N.P. Polyzos, M. Carprireaux, H. Tournaye, P. De Sutter

UZBrussel University Hospital, Brussels (Belgium)

Summary

Guidelines in surgical treatment of mucinous ovarian neoplasms recommend the use of appendectomy as a measure to rule out a primary appendiceal origin of the ovarian tumor and proper staging. In extension this guideline is also applied for mucinous borderline ovarian tumors (mBOTs). As borderline ovarian tumors (BOTs) are often diagnosed postoperatively, most patients must undergo a second surgery to add appendectomy and staging to their surgical treatment. *Objective:* To assess the role of appendectomy as part of the surgical treatment of mucinous BOTs. *Materials and Methods:* A retrospective single institute based study was carried out. The authors evaluated the clinical charts of patients undergoing surgical treatment by a gynecologic oncologist in their institution for a mucinous BOT between January 1990 and January 2014. *Results:* Twenty-seven patients were included. Appendectomy was performed in 30% of patients during primary or secondary surgical treatment. No appendiceal carcinoma was identified in any of the cases. Five patients already had a previous appendectomy. In eight patients the appendix was described as normal during surgery and left in place. For six patients the authors did not retrieve any information on previous appendectomy neither on the intraoperative state of the appendix. In the present overall study population, 78% showed no appendiceal involvement. For the remaining patients this information was missing. *Conclusions:* Secondary appendectomy to rule out a primary appendiceal origin of the mucinous BOT should not be performed when the appendix is described as grossly normal during primary laparoscopic surgery.

Key Words: Mucinous borderline ovarian tumor; Low malignant potential; Appendectomy; Restaging; Laparoscopy.

Introduction

Epithelial ovarian cancer has five main histologic subtypes (serous, mucinous, endometrioid, clear cell, and Brenner-type). Almost 10% of ovarian epithelial tumors are of mucinous origin. Most of mucinous neoplasms are benign (75%), 15% are invasive carcinomas and 10% borderline tumors [1]. Although borderline ovarian tumors (BOTs) behave indolently in the vast majority of cases and the prognosis is usually favorable, national and international clinical practice guidelines often recommend the use of appendectomy as a key part of the surgical approach for all mucinous malignancies, including borderline tumors [2, 3]. Removal of the appendix in these cases mostly aims to either identify microscopic metastasis of the tumor on the serosal part of the appendix, which leads to upstaging of the tumor, or to rule out a primary carcinoma of appendiceal origin with metastasis in the ovary [4,5].

Appendectomy can be considered as a part of optimal cytoreduction surgery in all stages, especially in advanced stage ovarian cancer. With BOTs diagnosis cannot always be performed intraoperatively. Frozen section is not always available at the time of surgery, whereas in almost one out of three cases during primary surgery, it fails to reach adequate diagnosis [6, 7].

In this regard, in a significant number of patients with mucinous BOTs (mBOTs), the diagnosis is established postop-

eratively, after surgery for a presumed benign cystic ovarian tumor. In many of these cases appendectomy is not performed during primary surgery, especially when the appendix appears grossly normal. Based on the available guidelines, restaging surgery with appendectomy might be considered in these patients in order to exclude appendiceal involvement. However, the critical question to be answered is whether re-intervention after postoperative diagnosis of mBOT is essential in order to perform an appendectomy as suggested by the available guidelines. The clinical importance of this query appears to be of paramount importance since an intervention that could differentiate an appendiceal involvement of a primary ovarian malignancy from a metastatic tumor of appendiceal origin is crucial towards the optimal management of the disease. On the other hand prevention of a surgical intervention (appendectomy) with ambiguous value would preserve patients from general anesthesia, any possible complication of re-intervention, postoperative pain, medical costs, and productivity loss due to hospitalization.

Taking into account the above available evidence, the authors decided to evaluate whether appendectomy should be performed during primary or restaging surgery, in postoperatively diagnosed patients, whenever the diagnosis of mucinous histological type BOT is established.

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Table 1. — Patients' baseline characteristics.

Date	Age	TNM	BIL	UNIL	Type of surgery	LSC	LT	RS	FS	neg FS	APX	former APX	INT	ECx
1	24-04-90	56	1A	*	H+BA		x		x		no	?	x	
2	21-01-92	60	1A	*	H+BA		x				no	?	x	
3	3-03-92	53	1A	*	H+BA		x		x		no	?		x
4	2-04-92	28	1A	*	UA+UC+O		x		x		no	?	x	
5	21-03-95	47	1A	*	H+BA+O		x		x		no	?	x	
6	22-03-96	61	1C	*	H+BA+O		x				no	?	x	
7	4-02-99	62	1B	*	BA		x					yes	x	
8	21-03-01	53	1A	*	BA (previous H)	x						no	x	
9	26-12-03	23	1A	*	UA+O+APX+BCLO		x		x		yes		x	
10	24-03-04	53	1A	*	UA+APX (appendicitis)	x					yes		x	
11	17-08-04	78	1A	*	H+BA+O		x					no	x	
12	21-09-04	60	1A	*	UA	x						no	x	
13	23-02-05	57	1A	*	H+BA		x		x	x		no	x	
14	28-02-05	71	1A	*	H+BA		x		x	x		no	x	
15	14-12-06	27	1A	*	UC (RS: UA+APX+BCLO+O)	x/x			x		yes		x	
16	14-12-06	32	1A	*	UA+O		x		x			yes	x	
17	26-11-08	28	1A	*	UA (RS: O+APX)		x (2)		x		yes		x	
18	9-11-09	20	1A	*	UA (RS: O+APX)	x (2)	x (1)		x		yes		x	
19	20-04-10	35	1A	*	BA+O		x		x	x		yes	x	
20	8-09-10	35	1A	*	UA+O+APX		x		x		yes		x	
21	15-04-11	57	1C	*	BA	x						yes	x	
22	14-02-12	40	1C	*	UA+O		x		x	x		yes	x	
23	1-06-12	41	1A	*	UA	x					no	no		x
24	14-08-12	63	1A	*	H+BA+O		x		x	x	no	no	x	
25	29-08-12	49	1A	*	H+BA+O		x				no	no	x	
26	6-12-12	21	1A	*	UA (RS: APX+O)	x (2)	x (1)		x		yes		x	
27	7-01-14	69	1A	*	H+BA+O+APX		x		x	x	yes		x	

Legend: H: hysterectomy; BA: bilateral adnexectomy; UA: unilateral adnexectomy; UC: unilateral cystectomy; O: omentectomy; APX: appendectomy; RS: restaging surgery; BCLO: biopsy of the contralesional ovary; LSC: laparoscopy; LT: laparotomy; (1): primary surgery (2) restaging surgery; FS: frozen section; FS neg: negative FS; INT: intestinal mucinous subtype; ECx: endocervical mucinous subtype.

Materials and Methods

After approval by the present Institutional Review Board, the authors scrutinized the electronic medical file for pathology reports, between January 1990 and January 2014, containing the search terms 'borderline', 'mucinous', and/or the international 'ICD-9 code' for 'benign' and 'malignant' ovarian neoplasia. A total of 27 patients were included in this study. Upon identification of the cases, the authors retrospectively reviewed charts of patients diagnosed with mBOT that underwent primary or restaging surgery by a gynecologic oncologist at the Department of Gynecology of the University Hospital UZBrussel, Brussels, Belgium. The following variables were recorded from patient files, operation, and pathology records: surgery through laparoscopy or laparotomy, type of surgery performed, whether or not the appendix was removed during primary or restaging surgery, history of appendectomy, was the appendix described in the operation protocol, was a frozen section carried out with or without a correct diagnosis, and histologic subtype of the mBOT. In selected cases slides were reviewed when subclassification between intestinal and endocervical mBOT was not clearly mentioned in the original protocol.

Results

Twenty-seven patients were included. Patients' baseline characteristics are presented in Table 1. Overall, 96% of the patients presented with a unilateral ovarian mass. Twenty-

one patients underwent laparotomy and six had a laparoscopic intervention. Restaging surgery was performed in only four patients and all of them underwent appendectomy during their second operation.

Twenty-three patients (85%) did not undergo appendectomy during primary surgery. This was done either because five patients already had a previous appendectomy (19%) or due to the discretion of the operating surgeon, owing to the normal appearance of the appendix during surgery. Only four patients underwent a restaging surgery of which an appendectomy was a part. In six of the patients included, no data could be retrieved regarding history of previous appendectomy or state of the appendix during primary surgery and thus no information could be provided for these women. Nevertheless the records of these patients did not reveal any later diagnosis of appendiceal tumor during follow up.

Overall eight patients (30%) were subjected to an appendectomy, two in the laparoscopy group and six in the laparotomy group. However, in none of these patients appendiceal involvement or primary appendiceal tumor was identified in the pathology report. The only pathological feature described was the acute appendicitis in one of the specimens retrieved.

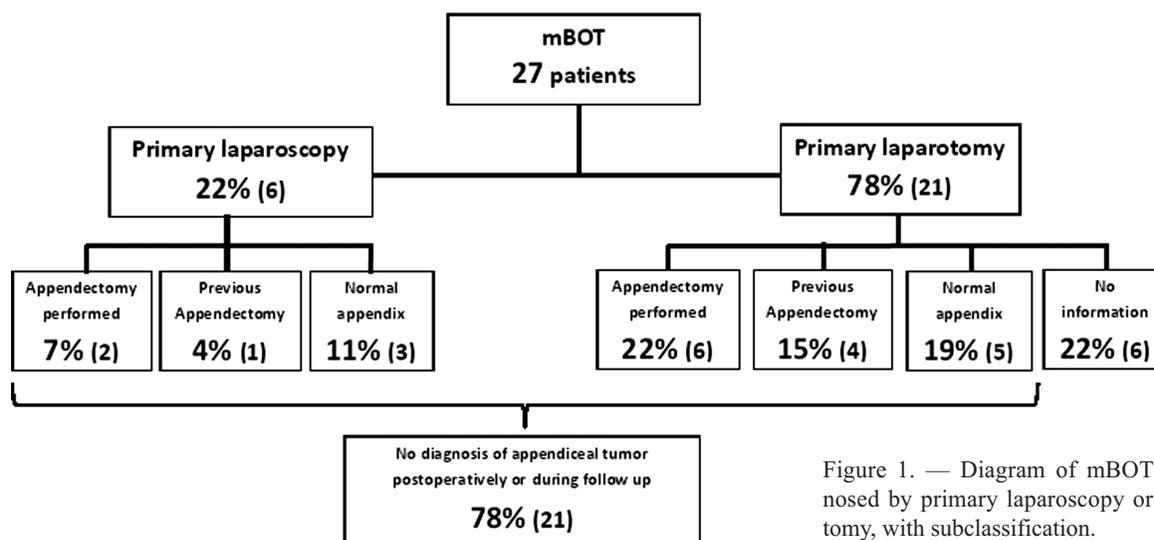


Figure 1. — Diagram of mBOT's diagnosed by primary laparoscopy or laparotomy, with subclassification.

Within the present series 13 intraoperative frozen sections were carried out. Of them 54% showed a correct diagnosis of mBOT. The other 46% were diagnosed as benign mucinous ovarian cysts, but definitive pathologic analysis demonstrated mucinous borderline origin. On frozen section no suspicion of invasive mucinous ovarian tumor was advanced.

Out of the sixteen (59%) patients in the present series with documented presence of the appendix, all except one with an acute appendicitis, were described as grossly normal during primary surgery. No primary appendiceal origin of a mucinous ovarian borderline tumor could be diagnosed within the present series of 27 patients, taking into account the absence of later registration of appendiceal involvement during follow up in the patients for whom perioperative data were missing (Figure 1).

Discussion

The present study aimed to evaluate whether appendectomy during primary or restaging surgery is essential for women with mBOT. According to the present results, none of the appendectomies performed in the context of mBOTs demonstrated appendiceal involvement, whereas no appendiceal malignancy was identified in the grossly normal appearing appendices during follow up.

The role of appendectomy in relation to upstaging early-stage invasive ovarian cancer has been examined by several groups. Some studies concluded that routine appendectomy is indicated in all patients with epithelial ovarian cancer as part of the initial surgical staging, owing to isolated microscopically appendiceal involvement in patients with early-stage disease [8, 9]. Due to this data, appendectomy is often recommended, in patients with mucinous tumors of the ovary, given that these tumors could be metastatic from the gastrointestinal tract and the appendix could eventually harbor the primary tumor [10]. Within the largest study published to date

by Ayhan *et al.*, routine appendectomy was clearly suggested for women with epithelial ovarian carcinoma, owing to the considerable rate of upstaging in early-stage disease and optimal cytoreduction in advanced stages [11].

Nonetheless, others failed to identify tumor upstaging in women with epithelial ovarian cancer with tumors grossly confined to the pelvis [10, 12, 13]. Lin *et al.* demonstrated that no primary or metastatic mucinous appendiceal tumor was present when the appendectomy was performed on a grossly normal appendix, when evaluating a cohort of 68 borderline and 44 invasive mucinous ovarian neoplasms [14], while no appendiceal involvement was identified in another study after appendectomy in 36 patients with apparent early-stage invasive mucinous tumor was performed [15].

Results appear to be even more robust in women with BOT, in whom the role of appendectomy appears to be considerably limited. Based on the extremely low prevalence of appendiceal involvement, performing an appendectomy in these cases might be considered superfluous. Indeed, none of the published studies up to date manage to diagnose any primary appendiceal carcinoma in appendectomies in women with mBOT. In two retrospective studies published in 2011 and 2013, no primary appendiceal carcinoma was identified in appendectomies from mBOT [15, 16], whereas no appendiceal involvement was found in the most recent analysis of 13 patients with mucinous borderline tumors recruited in two university hospitals in The Netherlands over a timeframe of 21 years [17].

The present study appears to be in accordance with the available evidence suggesting that appendectomy should not be considered in the primary surgical approach of mBOT nor as a secondary treatment measure in women with a confirmed histological diagnosis of mBOT following primary surgery.

It is of interest to underline that in the present series correct diagnosis through frozen section rate was accomplished only in 54% of cases. Frozen section on mucinous tumors is

known to be very difficult, even for trained pathologists, mainly owing to the fact that mucinous tumors are often very large and can comprise normal, borderline, and even invasive parts. In this regard, the larger the tumor, the lower the probability of a correct frozen section diagnosis [18-20]. Due to this high false negative rate, it may be postulated that several patients with a false negative frozen section or after postoperative diagnosis, may require restaging surgery, especially in case of appendiceal involvement. However, the present series and series from others clearly demonstrate that none of the patients had an appendiceal involvement when appearing grossly normal and thus no re-staging surgery was required.

One of the strengths of this study lies on the fact all patients were treated in the same institution and the operations were performed by the same experienced gynecologic oncologist. Their postoperative management took place in the same institution. In this regard treatment practices remained fairly consistent among different patients. However, this is a retrospective study with a limited sample size, similarly to previous reports [15-17]. Although this limitation should be acknowledged, the present authors need to underscore that the incidence of mucinous borderline tumors is extremely low and it would have been impossible to design such a study in a prospective manner in order to be completed in reasonable timeframe. Thus, they are obliged to rely on this evidence from small case series by their group and others in order to provide guidance for clinical practice.

Conclusion

In conclusion, allowing for the limitations described above, the authors suggest no benefit of a secondary appendectomy to rule out a primary appendiceal origin of the mBOT, when the appendix is described as grossly normal during primary laparoscopic surgery. In this setting a restaging surgery with known intraoperative risks, postoperative pain, medical costs, and productivity loss due to hospitalization can be withheld in patients with a mBOT. As mucinous ovarian tumors can be very large, a laparotomy is often needed to perform a surgery without spill of the ovarian content. In those cases, adding an appendectomy is simple and known without major complication risk. When a BOT is suspected or even every time adnexal surgery is performed, a careful inspection of the appendix and peritoneum should be performed and clearly described in the operation record. By carefully inspecting the omentum, appendix, pelvis, diaphragm, and other intra-abdominal organs, a restaging surgery will not provide any benefit in overall survival after postoperative diagnosis of a mBOT.

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Address reprint requests to:

S. COSYNS, M.D.

UZBrussel, Gynaecology-Oncology Department

Laarbeeklaan 101

1090 Jette (Belgium)

e-mail: SCosyns@uzbrussel.be