



FREQUENCY OF APPENDICEAL METASTASES OF OVARIAN NEOPLASMS – EXPERIENCE FROM A TERTIARY REFERRAL CENTER

Gynecology

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ABSTRACT

Introduction: The importance of routine appendectomy in patients with ovarian cancers remains under debate.

Objective: Study aimed at assessing the frequency of appendiceal metastases in patients with ovarian neoplasms.

Methods: Study included all patients operated due to ovarian neoplasms during past two years. Postoperatively, removed tumor masses were examined histopathologically to determine the tumor type, grade and stage and describe in detail appendiceal involvement.

Results: Out of 86 patients with ovarian malignancies 57 had appendectomy during staging/debulking surgery. Appendiceal metastases were registered in 61.4% of assessed cases. Only clear cell tumors did not give appendiceal metastases. Significantly more tumors of stage III and IV gave metastases in the appendix than those that were in stages I and II ($p=0.001$).

Conclusion: Ovarian cancer appendiceal metastases were confirmed to be quite often especially in advanced stage disease implying on the need for appendectomy at the time of surgery.

KEYWORDS

ovarian neoplasms, appendix, metastases, risk factors

INTRODUCTION

Currently recommended standard procedure for optimal primary debulking surgery for ovarian carcinomas encompasses extrafascial hysterectomy with bilateral adnexectomy, pelvic and paraaortic lymph node dissection, ascites sampling or peritoneal washing, multiple peritoneal biopsies, and omentectomy (1, 2). The importance of appendectomy in patients with ovarian cancers remains under debate. Most clinicians do not routinely recommend appendectomy for early stages of ovarian cancers (I and II). However, appendix should be removed in all cases of mucinous ovarian carcinomas, that consist of gastrointestinal-type cells, in order to exclude Krukenberg tumors or appendiceal carcinomas (3, 4). Moreover, routine appendectomy provides complete staging and cytoreduction (5). Some studies found that appendectomy increases the final stage of ovarian cancers in significant percent (6).

OBJECTIVE

The study aim was to assess the frequency of appendiceal metastases in patients with ovarian neoplasms in order to determine the need for appendectomy at the time of surgery.

METHODS

Study included all women operated due to ovarian neoplasms in the Clinic for Gynecology and Obstetrics Clinical Center of Serbia during past two years (2016. and 2017.). Women with previous appendectomies were excluded from the study. Written informed consent for all diagnostic and therapeutic procedures of our study was signed by all participants.

Upon admission to the Clinic basic epidemiological data (age, Body Mass Index – BMI, etc.), detailed history (general medical and gynecological) and with laboratory analyses (tumor markers) were taken from every patient. After clinical gynecological examination transvaginal ultrasound (US) with Doppler scan of pelvic organs was performed. The obligatory part of preoperative diagnostics was also magnetic resonance (MR) and/or computerized tomography (CT) scan of the abdomen and pelvis to assess the tumor localization, presentation, diameter, local spreading to surrounding structures, ascites presence and distant metastases (intestines, appendix, omentum, peritoneum, etc.).

All patients had surgery, mostly debulking, but in some cases only for staging (laparotomy; total abdominal hysterectomy with bilateral adnexectomy, omentectomy, lymphadenectomy and extirpation of all available secondary deposits). Appendectomy was performed based

on macroscopically suspected malignant spreading beyond ovaries (metastases in lymph nodes or abdominoplevic cavity visualized on imaging and/or during surgery). After surgery extracted timorous tissue was examined histopathologically (HP) in order to make the final diagnosis. On HP analysis tumor diameters, histopathological type and grade as well as tumor stage were determined according to FIGO classification (International Federation of Gynecology and Obstetrics). Extracted appendices were specially analyzed and their involvement in the malignant process was described in detail.

Preoperatively and postoperatively obtained data were compared and statistically analyzed by methods of descriptive (number, percentage) and analytical statistics applying the SPSS 20 software. Hi square test and Kruskal Wallis nonparametric ANOVA were used to investigate the significance of differences between categories of assessed parameters.

RESULTS

Study included 86 women operated due to ovarian malignant tumors, out of which 57 had appendectomy during staging/debulking surgery. Postoperatively, it was found that most tumors were histopathologically serous adenocarcinomas, while the most common stage at the time of surgery was FIGO 3c. On histopathological analysis we registered appendiceal metastases in 61.4% of assessed cases (Table 1).

Preoperatively metastatic disease was visualized in 80.7% of women, while intestinal metastases were noted for 64.9% of investigated patients (Table 1). Our results showed that significantly more appendiceal metastases had patients with intestinal and other metastases that were seen preoperatively (Table 2). This confirmed reliability of imaging methods for preoperative determination to perform the appendectomy in ovarian cancer patients.

According to our results only clear cell tumors did not give appendiceal metastases, while all other tumor types mostly involved appendix. Still, mucinous adenocarcinomas involved appendix more than serous tumor type (Table 2).

Significantly more tumors of stage III and IV gave metastases in the appendix than those that were in stages I and II. We registered no cases of appendiceal involvement in patients with FIGO stage I ovarian cancers. However, postoperatively on histopathological analysis there were two cases of appendiceal metastases in patients preoperatively regarded to have FIGO stage II disease. Significantly less women with

FIGO stage IIIB cancers had metastases in the appendix, but if the disease was in stage IIIC significantly more patients had malignantly changed appendices. Appendix was malignantly involved in all patients with FIGO stage IV ovarian cancers.

DISCUSSION

The main target in the treatment for epithelial ovarian carcinoma is accurate surgical staging and maximal cytoreduction (1, 7). According to literature appendix seems to be a one of the common sites of ovarian carcinoma metastases due to the well-known fact that initial spreading of ovarian carcinoma typically goes through abdominopelvic cavity (8). Therefore, determining the real extent of carcinoma metastatic spreading is the only way to remove as much of the tumor as possible at the time of surgery for staging and debulking (9). Consequently, appendectomy is frequently required to achieve optimal cytoreduction as part of ovarian cancer surgery (8, 10).

Removing the appendix was proven to lead to more accurate diagnosis (potentially upstaging ovarian carcinoma and ruling out primary appendiceal disease), while also preventing acute appendicitis and surgical complications such as adhesions (4, 5). Some authors therefore claimed that adequate cytoreductive surgery with appendectomy positively affects optimal survival of ovarian carcinoma patients (9, 11).

Evaluation of appendix is also considered necessary during surgery because finding malignant deposits in the appendix demands adjuvant therapy (1,2). Moreover, in patients with ovarian mucinous cystadenocarcinoma appendectomy should always be in integral part surgery even if it is only for staging due to the fact that histological appearance of gastrointestinal tumor metastases to ovaries may be indistinguishable from a primary ovarian mucinous borderline tumor or the cases with primary malignancy of the appendix (3, 4, 7). Therefore, in some studies it was concluded that routine appendectomy should be performed in all epithelial ovarian carcinoma patients during the initial surgical staging as it enables upstaging in patients with early disease and optimal cytoreduction in patients with advanced disease (8, 9).

Nevertheless, role of routine prophylactic appendectomy during surgery of early stage ovarian cancers is still controversial (8, 10). The most authors who do not consider appendectomy necessary base their belief on the fact that appendiceal metastasis are generally infrequent and the risk is low if there are no other pelvic metastases (9, 12).

A consistent finding in majority of available studies is the significant association between appendiceal metastases and advanced stage (III and IV) of ovarian cancers. Most literature data indicate that appendiceal metastasis in advanced stage ovarian carcinomas can be quite frequent (as high as 80 to even 90%) (8, 11). Furthermore, in such cases appendiceal involvement is usually not the only site of secondary deposits (omentum and peritoneum are also involved) (1, 3). Moreover, it seem that serous carcinomas are the predominant tumor type that gave metastases into the appendix as in some investigations more than 91% of patients had serous histology (1, 5). Appendiceal involvement was found to be less frequent for mucinous and poorly differentiated carcinomas (6, 8). In our sample appendiceal metastases were present in around 61% of patients with ovarian cancers that had appendectomy performed during surgical treatment based on preoperative and/or intraoperative findings of potential disease spreading.

On the other hand, frequency of appendiceal involvement is not that high in early stage ovarian carcinoma patients. In some investigations no appendiceal involvement was observed in patients with I and II stages of ovarian carcinoma (1, 12). Usually no occult metastases are noted if the appendix is macroscopically intact and if no other deposits are visualized on preoperative diagnostic (6, 8). Still, microscopic appendiceal metastases were reported in patients with apparent early stage epithelial ovarian carcinomas, leading to disease upstaging, mostly not more often than in 5% of cases (1, 10). In our study, there were no appendiceal metastases registered in patients with FIGO stage I ovarian carcinomas. Contrary, if the disease was in stage IIIC and IV, appendix was malignantly involved in almost all cases. Still, it should be noted that the limitation of our study was the fact that appendectomy

was not performed in patients that had no visible (on preoperative imaging and during surgery) disease spreading beyond ovaries. Therefore, some appendiceal involvement in stage I patients might have been missed. Nevertheless, we had only 12.3% of stage I cancers cases, and as in some of those patients appendectomy was performed, we could have misdiagnosed very few patients.

CONCLUSION

In this study we registered appendiceal metastases in around 61% of patients with ovarian cancers that had appendectomy as a part of their staging/debulking surgery. Significantly more tumors of stage III and IV gave metastases in the appendix, while there was no registered appendiceal involvement in patients with stage I disease. Almost all mucinous and numerous serous adenocarcinomas involved appendix. Therefore, appendectomy at the time of ovarian cancer surgery should be reconsidered every time. If the disease is spread anywhere beyond ovaries it is highly likely that appendix will be involved.

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Table 1. Findings of preoperative imaging and postoperative histopathological analysis

Parameters		Number	Percent	χ^2	p
Intestinal metastases on US/CT/MR	no	20	35,1	2.965	0.085
	yes	37	64,9		
Other abdominopelvic metastases on US/CT/MR	no	11	19,3	15.686	0.001
	yes	46	80,7		
Histopathological findings	serous adenoCa	45	78,9	101.286	0.001
	mucinous adenoCa	5	8,8		
	endometrioid Ca	2	3,5		
	clear cell tumor	2	3,5		
	mixed Muller tumor	3	5,3		
Tumor FIGO stage	1b	2	3,5	77.200	0.001
	1c	5	8,8		
	2a	3	5,3		
	3b	5	8,8		
	3c	39	68,4		
	4a	1	1,8		
Metastases of the appendix on histopatology	no	22	38,6	5.071	0.024
	yes	35	61,4		

Legend: FIGO – International Federation of Gynecology and Obstetrics; CT – computerized tomography; MR – magnetic resonance; US – ultrasound; Ca – carcinoma

Table 2. Differences in investigated parameters regarding appendiceal involvement

Parameters		Metastases of the appendix on HP		χ^2	p
		no	yes		
Intestinal metastases on US/CT/MR	no	13	9	9.063	0.003
	yes	7	28		
Other abdominopelvic metastases on US/CT/MR	no	11	0	25.216	0.001
	yes	9	37		
Histopathological findings	serous adenoCa	15	30	13.095	0.023
	mucinous adenoCa	1	4		
	endometrioid Ca	0	2		
	clear cell tumor	2	0		
	mixed Muller tumor	0	3		

Tumor FIGO stage	1b	2	0	31.783	0.001
	1c	5	0		
	2a	1	2		
	3b	4	1		
	3c	6	33		
	4a	0	1		
	4b	0	2		

Legend: FIGO – International Federation of Gynecology and Obstetrics; CT – computerized tomography; MR – magnetic resonance; US – ultrasound; Ca carcinoma; HP - histopathology

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