



Appendicular Pathologies in Ovarian Mucinous Adenocarcinoma and Borderline Tumor: A Retrospective Analysis

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Abstract

Background: The role of appendectomy in the control of mucinous adenocarcinoma of the ovary has become a controversial issue, and its effectiveness in increasing the 5-year survival rate of patients is not well known. Mucinous carcinoma account for 3-4% of primary ovarian cancer. Nearly all mucinous carcinoma of the ovary presents with early-stage disease stage 1. Therefore, in this study, the aim was to examine simultaneous appendectomy in ovarian mucinous adenocarcinoma surgery and its reported pathologies.

Methods: This review is a retrospective study. The participants in this study included patients with mucinous ovarian mass with borderline mucinous pathology (n=101) or mucinous adenocarcinoma (n=69). These patients were selected from among the patients referred to Mahdia and Imam Hossein (AS) Hospitals who underwent surgery for mucinous adenocarcinoma of the ovary between 2017 and 2022.

Results: In terms of the pathology of the appendix, the results showed that the percentage of ACA was higher in the borderline mucinous group compared to the other group, however, there was no significant relationship between the two groups ($p=0.60$). In terms of the appearance of the appendix, the results showed that the nodular, thickened and normal state was more in the borderline mucinous group compared to the other group, which was statistically significant ($p=0.04$). In terms of disease stage, it was also found that there was no statistically significant relationship between the two groups ($p=0.65$).

Conclusion: It can be said that the appearance of the appendix can play an important role in distinguishing the two groups.

Keywords: Appendectomy, Mucinous tumor, Ovarian adenocarcinoma, Pathology

Introduction

Ovarian tumors are among malignancies that are of particular importance due to their high mortality. This malignancy is the second most common cancer of the reproductive system and is the most common cause of death of malignancies related to the reproductive system (1). This malignancy is very diverse due to the structure of the identified tissue. Therefore, there are different types of ovarian cancers according to histological characteristics (2,3). Ovarian mucinous adenocarcinoma is a group of malignant and aggressive epithelial neoplasms that are usually asymptomatic until they metastasize to other organs. Therefore, in most cases, they can be recognized when they have metastasized to other parts of the body. Common sites that metastasize from mucinous adenocarcinoma of the ovary are: diaphragm, pelvis, and appendix. This type of malignancy accounts for 12 to 15% of ovarian tumors in America (4). In addition, studies have shown that the overall incidence of mucinous adenocarcinoma worldwide is between 2-7% (5).

According to what was said, the metastasis of mucinous adenocarcinoma of the ovary to the appendix has non-specific symptoms, and in many cases, the symptoms may appear long after the diagnosis of these tumors in the ovary, and after surgery to remove ovarian tumors, it may require re-examination (6,7). On the other hand, failure to diagnose and remove them will cause recurrence and many problems and complications for the patient. For this reason, the role of appendectomy in the control of mucinous adenocarcinoma of the ovary has become a controversial issue, and its effectiveness in increasing the 5-year survival rate of patients is not known properly (8,9). Therefore, in this study, the aim was to examine simultaneous appendectomy in ovarian mucinous adenocarcinoma surgery and its reported pathologies.

Materials and Methods

Design study

This study is a retrospective study. The participants in this study included patients with mucinous ovarian mass with borderline mucinous pathology (n=101) or mucinous adenocarcinoma (n=69). These patients were selected from among the patients referred to Mahdیه and Imam Hossein (AS) Hospitals who

underwent surgery for mucinous adenocarcinoma of the ovary between 2017 and 2022. All patients underwent appendectomy.

After obtaining the necessary permits, the records of all participants were reviewed and the patients who underwent appendectomy in mucinous adenocarcinoma surgery were identified.

Later the demographic information of the patients as well as the description of the procedure and their pathology report were extracted from their files and analyzed. Finally, the information collected from the registered patients was analyzed using SPSS statistical software and the necessary statistical tests.

Inclusion and exclusion criteria

Inclusion criteria included all surgically treated ovarian masses, known borderline mucinous pathology and adenocarcinoma, and appendiceal carcinomas of known ovarian origin. Exclusion criteria included unspecified ovarian mass pathologies, non-mucinous pathology, appendectomy patients, ovarian masses undergoing medical treatment, and non-malignant appendiceal pathologies.

Statistical analysis

All analyzes were done using SPSS version 26 software. Data were shown as mean±standard deviation and number (%). Non-parametric Mann-Whitney test, Chi-2 Pearson and Fisher exact tests were used to analyze the data. The significance level in this study was $p<0.05$.

Results

Description information of patients

The following table shows the demographic data of the patients. Based on the results, it has been shown that only the gravid variable was statistically significant between the two groups ($p=0.0$), while no significant relationship was observed between the two groups for other variables ($p>0.05$)

The results showed that the most common tumor marker in both groups was CA125. On the other hand, in the borderline mucinous group, 2 patients had CEA marker. The number of patients with infertility was 4 (5.8%) in the mucinous adenocarcinoma group and 5 (5%) in the other group ($p=0.80$). In terms of smoking, 1 (1.4%) in the mucinous adenocarcinoma

group and 3 (3%) in the other group had a history of smoking ($p=0.52$) (Table 1).

Evaluation of appearance, pathology of appendix and disease stage in two groups

In terms of the pathology of the appendix, the results showed that the percentage of ACA was higher in the borderline mucinous group compared to the other group, however, there was no significant relationship between the two groups ($p=0.60$). In terms of the appearance of the appendix, the results showed that the nodular, thickened and normal state was more in the borderline mucinous group compared to the other group, which was statistically significant ($p=0.040$). Regarding the stage of the disease, it was also found that there was no statistically significant relationship between the two groups ($p=0.65$) (Table 2).

Evaluation of the correlation of variables in two groups

In table 3, using linear regression, the relationship between the mucinous adenocarcinoma, mucinous borderline groups and independent variables such as infertility, smoking, gravid, age, pathology, and markers have been measured, as seen between gravid

and two A significant relationship can be seen in the mentioned group (Table 3).

Discussion

In recent years, gynecological surgeons have thought about improving oncology surgeries. These ideas have been obtained by examining the pathology of organs. Currently, patients who are candidates for surgery with an ovarian mass suspected to be cancer are first staged with tumor markers and ultrasound, and then surgically staged, and depending on the results of the frozen section, the surgery is completed. In this study, the aim was to limit appendectomy during mucinous tumor surgery by examining the risk factors and the appearance of the appendix and comparing the pathology.

NCCN and FIGO guidelines recently recommended that borderline and malignant mucinous patients must undergo appendectomy during primary surgery. This idea was strengthened by three reasons. As mucinous tumors with intestinal pathology may have a primary origin from the appendix or ovary, therefore, by removing the appendix, both the possible primary origin and hidden metastases are removed, and cell removal surgery is performed at the optimal level

Table 1. Evaluation of demographic data of patients

Variable	Mucinous adenocarcinoma (n=69)	Borderline mucinous (n=101)	p-value
Age [year (median (IQR))]	57.6(8.5)	58(9.2)	0.77 *
Gravid (N)	1	2(2.9%)	<0.001 **
	2	5(7.2%)	
	3	61(88.4%)	
	4	1(1.4%)	
Smoking	Yes	1(1.4%)	0.52 **
	No	68(98.6%)	
Infertility	Yes	4(5.8%)	0.80 **
	No	65(94.2%)	
Tumor markers	CA125	8(11.6%)	0.13 **
	CEA	0(0%)	

* Man Witney, ** Chi square.

Table 2. Assessment of the appearance, pathology of the appendix and the stage of the disease in two groups

Variable		Mucinous adenocarcinoma (n=69)	Borderline mucinous (n=101)	p-value
Ovarian tumor pathology	ACA	26(37.7%)	43(42.6%)	0.60*
	AFP (tumor pathology)	0(0%)	3(2%)	
	Borderline	43(62.3%)	55(54.5%)	
The appearance of appendix	Normal	66(95.7%)	92(91.1%)	0.04*
	Congested	3(4.3%)	7(6.9%)	
	Nodular	0(0%)	2(2%)	
Stage	1A	19(27.5%)	22(21.8%)	0.65*
	1B	3(4.3%)	2(2%)	
	2A	0(0%)	1(1%)	
	2B	23(33.3%)	35(34.7%)	
	3A	1(1.4%)	0(0%)	
	3B	11(15.9%)	18(17.8%)	
	3C	12(17.4%)	23(22.8%)	

*Chi square, AFP= Alpha phyto protein.

Table 3. Linear regression model to evaluate variables in two groups

Model	Unstandardized coefficients		Standardized coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	2.586	0.232		11.15	0 *
Infertility	-0.14	0.103	-0.064	-1.356	0.177 *
Smoking	-0.23	0.154	-0.071	-1.495	0.137 *
Gravid	-0.507	0.028	-0.828	-18.26	0 *
age	-0.002	0.004	-0.028	-0.61	0.542 *
Pathology	0.007	0.06	0.007	0.121	0.904 *
Marker	0.02	0.013	0.07	1.497	0.136 *
Appearance of appendix	0.13	0.074	0.084	1.749	0.082 *
Stage	0.013	0.016	0.047	0.785	0.433 *

* Linear regression.

(10,11).

But later studies showed that mucinous carcinoma in apparently healthy appendix has a very low prevalence (about 1.4%). In the present study, the prevalence was 1.6%. Therefore, performing routine appendectomy for mucinous patients has become challenging. For example, in the study of Cosyns *et al*, a systematic review was conducted on 12 articles and a total of 667 borderline mucinous patients. In this

study, a total of 232 people underwent appendectomy and their pathology was examined retrogradely. The results showed that only two cases (0.86%) of carcinoma were discovered in the appendices, both of which were suspicious and abnormal in the gross view. In another study, out of 30 borderline mucinous tumor cases, there were 11 appendices (30%) with suspicious appearance, and out of these 11 cases, only 2 (18.1%) had microscopic appendiceal involvement

(12).

In the present study, which was conducted on 101 borderline mucinous patients, no cases of appendiceal involvement were reported. This of course could be because all the patients were in stages 1 and 2 of the disease, and therefore it seems that the surgeon's vision during surgery and the stage of the disease may be useful in diagnosing the microscopic involvement or non-involvement of the appendix.

In another study, 71 patients underwent appendectomy for mucinous tumor, of which 41% (n=29) had mucinous borderline and 59% (n=42) had mucinous adenocarcinoma. Also, in this study, among the borderline mucinous patients, 4 of them (14%) had an abnormal appearance of the appendix, and there was microscopic involvement of the appendix in half of these people (2 people), and no microscopic involvement was seen in all the people with normal appendix. In patients with malignant mucinous pathology, 5 people (12%) had gross appendicitis, the pathology of 2 people (40%) was appendicitis, 2 people (40%) had primary mucinous carcinoma of the appendix, and 1 person (20%) had metastatic carcinoma of origin. It was the ovary. Only one of the apparently normal appendices (2.7%) had microscopic involvement (13).

In this study, a total of 170 people with mucinous tumor were examined, 100% of whom had undergone appendectomy. Of these patients, 101 (59.5%) had mucinous borderline and 69 (40.5%) had mucinous adenocarcinoma. Out of 101 borderline mucinous cases, 96 cases (95.1%) had normal appearance and 5 cases (4.9%) had abnormal appearance. None of these 5 cases had microscopic involvement, and all the people whose appendix had a normal appearance, did not have microscopic involvement. In 69 patients with mucinous adenocarcinoma, 59 people (85.5%) had a normal appearance of the appendix [and the pathology of one of these people (1.6%) had tumor involvement], and 10 cases (14.5%) had an abnormal appearance of the appendix, and the pathology of 2 of them (20%) people with abnormal appearance), mucinous adenocarcinoma of the appendix. In general, out of 170 mucinous tumors, 1.7% of appendix pathology showed involvement. The prevalence of malignancy was 0.6% in appendices with gross normal appearance and 13.3% in abnormal

appendices.

Albavishi *et al* examined the files of 460 patients with mucinous ovarian tumor pathology. In the meantime, 246 people had mucinous tissue in the frozen sample, and 214 people had mucinous tissue in the final pathology sample, and 82 people had undergone appendectomy. In 30 cases of these appendices, 3 conditions were met: the appendix had a normal gross appearance, there was no intraperitoneal or intra-abdominal lesion at the same time, and the involvement of the ovary was unilateral. Out of these 30 appendices, only one of them was reported as a 4 mm carcinoid as a random finding, and the others were normal. Of the other 52 appendices that aroused the surgeon's suspicion, 12 cases (23%) had neoplastic involvement. Finally, the authors of this study advised surgeons to perform appendectomy if any of the above 3 features are present, and otherwise, not to perform routine appendectomy (14).

In comparison with the present study, 170 cases of mucinous tumor were examined, all of which were mucinous, and all of them underwent appendectomy. Out of 170 appendectomy cases, 155 cases that appeared normal during surgery, only in one case there was simultaneous intra-abdominal pathology in the form of adhesion and colon involvement, and in all cases, the ovarian lesion was unilateral. Out of 155 cases of appendix with normal appearance, only one case (0.64%) had involvement limited to appendiceal serosis. Out of the other 15 cases of appendicitis, whose appearance aroused the surgeon's suspicion (12 cases of congested appearance and 2 cases with nodular lesion on the surface of the appendix and one case of adhesion to the appendix), only two cases (13.3%) had microscopic involvement on the serosal level of the appendix.

Several suggestions are made for future studies: examining influential factors such as age, macroscopic appearance, tumor markers, and examining symptoms of concomitant gastrointestinal diseases can be effective in deciding to reduce surgery at the same time as appendectomy in patients.

Conclusion

The results showed that the appearance of the appendix, which includes normal, congested, and nodular, can play an important role in differentiating

mucinous adenocarcinoma from borderline mucinous. This was while ovarian pathology and stage had no significant effect.

Ethical approval

All the procedures performed on human participants followed the ethical standards of the local ethics committee of Shahid Beheshti University of Medical Science (IR.SBMU.MSP.REC.1400.396), as well as the 1964 Helsinki Declaration.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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