

The importance of lower gastrointestinal tract endoscopy regarding the preoperative evaluation of malignant adnexal masses

MALİGN ADNEKSİYAL KİTLELERİN PREOPERATİF DEĞERLENDİRMESİNDE ALT GASTROİNTESTİNAL SİSTEM ENDOSKOPİSİNİN ÖNEMİ

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ABSTRACT

Objective: Our aim in this study was to investigate the value of lower gastrointestinal system (GIS) endoscopy regarding the detection of colon invasion and its importance in recognizing primary and secondary ovarian cancers in cases clinically prediagnosed as advanced stage ovarian cancers.

Materials and Methods: Records of patients, who were operated due to adnexal mass suspicious for malignancy at our clinic between September 2012 and May 2017, were examined. One hundred thirteen cases of advanced stage (Stage III - IV) malignant adnexal masses were detected.

Results: Cases that underwent laparotomy because of a prediagnosis of malignant adnexal mass (mostly ovarian), and had stage III and IV disease, were compared regarding clinical characteristics and foreseeing bowel resection (51 patients had undergone lower GIS endoscopy, 62 had not). Six of the 51 patients, who underwent endoscopy, were diagnosed with colon involvement during endoscopy while 4 other patients were diagnosed intraoperatively. Among the 62 patients, without preoperative endoscopy, 10 patients underwent intraoperative bowel resection. The mean age of the patients with bowel resection was 57.35±13.53y; the mean age of the remaining patients was 55.8±12.54y. Rectosigmoid region was the most common area of resection (17/20). The positive predictive value of colonoscopy for predicting bowel resection was 100%, while the negative predictive value was 91%.

Conclusion: Bowel resection is a pivotal component of the surgical approach to advanced stage malignant adnexal masses. The detection of tumor spread in lower GIS endoscopy is very important while planning the surgery, dealing with postoperative stoma problems and emotional issues and during the differential diagnosis of metastatic tumors.

Keywords: bowel resection, colonoscopy, malignant adnexal mass

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ÖZ

Amaç: Bu çalışmada amacımız; klinik olarak ileri evre over kanseri (OK) düşünülen olgularda, alt gastrointestinal sistem (GİS) endoskopisinin; kolon invazyonunu saptamadaki değerini ve ayrıca primer sekonder OK ayrımındaki önemini araştırmaktır.

Gereç ve Yöntem: Eylül 2012 – Mayıs 2017 yıllarında, DEÜTF Hastanesinde opere edilen ve DSÖ ICD-10 2016 versiyonuna göre malign adneksiyal kitle tanısı kodlanan ve laparotomi uygulanan, ileri evre (evre III-IV) 113 olgunun dosya kayıtları alt GİS endoskopisi uygulananlar ve uygulanmayanlar olarak karşılaştırıldı.

Bulgular: Malign adneksiyal (en sık over) kitle ön tanısıyla laparotomi uygulanan, evre III- IV,113 olgu, klinik özellikler ve barsak rezeksiyonunu öngörme açısından (alt GİS endoskopik inceleme yapılanlar, 51 olgu, yapılmayanlar, 62 olgu) karşılaştırıldı. Kolonoskopi yapılan grupta 6 olguda kolon tutulumu gözlemlendi, 4 olguda tutulum intraoperatif saptandı. Kolonoskopi yapılmayan grupta 10 olguda intraoperatif rezeksiyon uygulandı. İki grupta da 10' ar olguya barsak rezeksiyonu gerekti. Rezeksiyon yapılan 20 olgunun ortalama yaşı, $57,35 \pm 13,53$, rezeksiyon yapılmayan 93 olgunun ortalama yaşı $55,81 \pm 12,54$ tür. En sık rezeksiyon rektosigmoid bölgede olup, (17 olgu) tüm olguların %85'ini oluşturmaktadır. Kolonoskopinin barsak rezeksiyonunu ön görmedeki pozitif prediktif değeri (PPV); %100, negatif prediktif değeri (NPV); %91 olarak bulundu.

Sonuç: İleri evre malign adneksiyal kitlelere cerrahi yaklaşımda alt GİS barsak rezeksiyonları tedavinin önemli bir komponentidir. Alt GİS endoskopisinde tümör tutulumunun saptanması cerrahi tedaviyi planlama, postoperatif dönemde stoma problemleri ve emosyonel sorunlarla baş etmede ve metastatik tümörlerin ayırıcı tanısında önemlidir.

Anahtar Sözcükler: barsak rezeksiyonu, kolonoskopi, malign adneksiyal kitle

Primary ovarian cancers constitute the largest portion of malignant adnexal masses. Adnexal structures, especially malignant tumors of fallopian tubes and secondary tumors of other organs (primarily gastrointestinal system and breast) are important in differential diagnosis. After the importance of cytoreductive surgery was emphasized by Munnell in 1968 and by Griffiths in 1975, critical advancements were achieved in the treatment of patients with ovarian cancer (1). Cytoreductive surgery continues to be significant since the first day.

Ovarian cancers are encountered at advanced stage in 70% of cases (Fédération Internationale de Gynécologie et d'Obstétrique – FIGO stage III and IV) (2). The preoperative clinical evaluation and surgical treatment of these cases require multidisciplinary approach. Preoperatively unpredicted bowel resections and ostomies

cause physical and emotional fragilities among patients especially after cytoreductive surgery.

We have examined 351 cases that underwent laparotomy due to malignant adnexal masses. The advanced stage (FIGO III-IV) 113 of them were divided into two groups: The cases that were examined with preoperative lower GIS endoscopy and the cases that did not undergo the same procedure. The two groups were compared regarding the prediction of bowel involvement and bowel resection preoperatively. Our aim is to question the significance of colonoscopy or flexible rectosigmoidoscopy concerning the prediction of bowel resection in clinically advanced stage malignant adnexal masses (advanced stage ovarian cancers).

MATERIALS AND METHODS

The study was conducted in the department of gynecology and obstetrics at a tertiary medical center. After the required permissions were received from the hospital administrations and the local ethics board (4288 – GOA – Dokuz Eylul University School of Medicine Ethics Board for Non-Invasive Studies), with the Declaration of Helsinki. All patient files of cases of malignant adnexal masses that were operated between September 2012 and May 2017 were scanned. All cases had a dedicated ICD-10 (World Health Organization, International Classification of Diseases 10th Revision -2016) code for their diagnosis. 133 cases diagnosed with advanced stage (Stage III and IV) malignant adnexal mass were identified. Cases, which were examined, had malignancies of gynecological origin like ovarian, tubal and endometrial or the gynecological origin of the malignancy could not have been excluded. The inclusion criteria for this study were as follows: clinical diagnosis of malignant stage III-IV adnexal mass, confirmation of malignancy after laparotomy, presence of sufficient data in the case file. The exclusion criteria were: early stage disease (stage I and II), cases operated after neoadjuvant therapy, cases diagnosed with non-adnexal primary malignancy intraoperatively (such as gastric, intestinal or lymphatic), benign diagnosis (endometriosis, pelvic abscess, etc.), cases undergone operation in another center. After further examination, 113 of these cases were found to be meeting the inclusion criteria and included in the study.

These 113 cases were divided into two groups. The first group (study group) constituted of the cases that underwent colonoscopy or flexible rectosigmoidoscopy preoperatively (n=51) and the second group (control group) constituted of the cases that were not examined with endoscopy preoperatively (n=62). Groups were compared concerning clinical characteristics, detection of tumoral invasion in endoscopy findings (mucosal infiltration, ulceration, vegetation, complete or partial obstruction, erosion, hemorrhage, and edema). The data analysis was performed with SPSS 22.0 program (Statistical Package for the Social Sciences, Version 22, IBM Corporation and others, NY, USA). Chi-Square test was used for the analysis of numerical variables, while Mann-Whitney U test was

used for the measured variables. The cutoff for statistical significance was determined as $p < 0.05$.

RESULTS

The mean age of patients, who were operated due to the diagnosis of malignant adnexal mass, was 56.08 ± 12.67 . The mean age of the 51 patients in the study group was 59.02 ± 10.46 , while the mean age of the 62 patients in the control group was 53.66 ± 13.85 . The patients, who had undergone endoscopy evaluation, had a greater mean age. Since the both age groups were normally distributed, the age groups were compared with a parametric test: t-test. The mean age of patients that had undergone colonoscopy was significantly older than the others ($p = 0.023$).

Among the 113 patients that underwent laparotomy due to the diagnosis of malignant adnexal mass, ovary was the most common origin (78 cases, 69.03%). Fallopian tubes (15 cases, 13.27%) and uterus (14 cases, 12.38%) followed. (Table 1)

Table 1: The distribution of malignant adnexal masses according to originating primary organs after postoperative diagnosis.

Primary Organ	Number (n)	Percentage (%)
Ovary	78	69,03
Fallopian Tubes	15	13,27
Uterus	14	12,38
Uterus-Ovary Synchronous	3	2,65
Peritoneum	1	0,88
Gastrointestinal System	2	1,76
Total	113	100

Bowel involvement was detected and the findings (ulceration, vegetative lesion, partial obstruction, infiltration) were confirmed with biopsy in six of 51 patients that underwent preoperative lower GIS endoscopy. These patients received counseling about bowel resection before surgery. Four other patients, whose colonoscopic evaluation did not detect any findings indicating bowel involvement but underwent bowel resection due to intraoperative observation, were also in this group. The final pathological records of these cases showed that tumoral invasion had developed infiltratively

from the serosa to the mucosa and the intestinal segment involved with the tumor had formed a gatto. If we evaluated the performance of lower GIS endoscopy as a test, the positive predictive value (PPV) was 100%; since there are no false positive cases. The negative predictive value was calculated 91% (41 true negative cases among 45 negatives according to the test). The sensitivity was 60% (Endoscopy detected 6 out of 10 colon involvements.) and the specificity was 100%, again due to the lack of false positive cases. In the group of patients without preoperative endoscopic assessment, 10 of 62 patients had bowel resection due to intraoperative findings of bowel involvement. Thus, the number of bowel resections reached to 10 in each group. 10 of 51 patients (19.23 %) that had preoperative lower GIS endoscopy had bowel resection, while 10 of 62 (16.12 %) patients that did not have preoperative endoscopic assessment had bowel resection. (Figure 1) In 113 cases, bowel resection due to tumoral invasion was required in 17.69 % (20 cases) of cases while it was not required in 82.30% of them (93 cases).

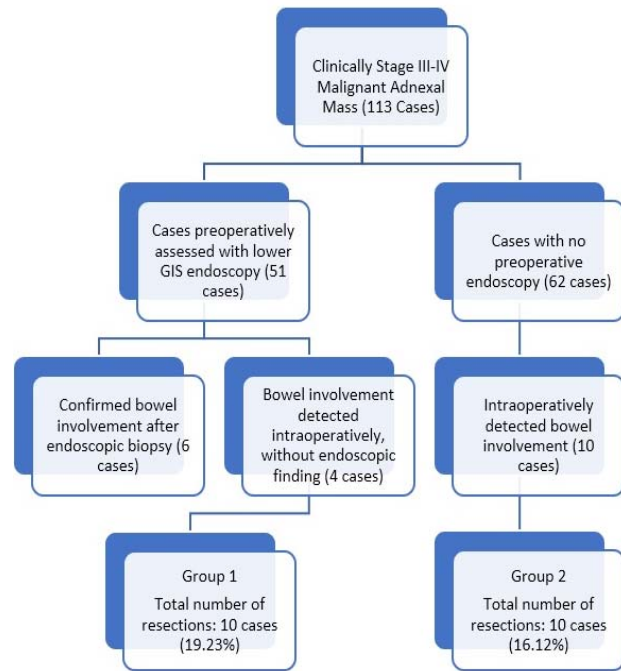


Figure 1: The comparison of groups according to bowel involvement

Table 2: The comparison of groups according to bowel resection

	Cases with Preoperative Endoscopy (n)	Cases without Preoperative Endoscopy (n)	Total (n)	
Number of cases (n)	51	62	113	
Preoperatively Diagnosed Bowel Involvement (n)	6	-	6	
Intraoperative Bowel Resection (n)	10	10	20	p=0.63

When the groups were compared regarding the number of bowel resections, no statistically significant difference was found (p=0.63, Chi-Square test) (Table 2). The mean age of the 20 patients, who had bowel resection, was 57.35±13.53 while the mean age of the remaining patients were 55.81±12.54. The difference of age between the groups was not statistically significant (p=0.988, Mann-Whitney U test). End to end anastomosis was performed to eight of the cases of bowel resection, while ostomies were created for the remaining 12 patients. The most common area of resection was rectosigmoidal region in both groups

(17 cases, 85% of all cases) and the following involved region was the ileocecal region (3 cases, 15%). The histological tumor type was serous carcinoma in half of the cases with bowel resection.

Table 3: Histopathological tumor type in the cases of bowel resection

Histological Type	Number (n)	Percentage (%)
Serous carcinoma	10	50
Endometrioid carcinoma	4	20
Clear-cell carcinoma	2	10
Sarcoma	2	10
Adenocarcinoma	2	10
Total	20	100

DISCUSSION

Cytoreductive surgery is the fundamental approach to the staging and primary treatment of patients with ovarian cancer. Ovarian cancer is intraoperatively widespread disease at the moment of diagnosis, and optimal debulking is critical regarding survival (2, 3). It is demonstrated that, a 10% increase in cytoreduction is associated with a 5.5% increase in median survival among exposed patients (3).

Studies report that, the resection of rectosigmoid colon is needed in 16-58 % of FIGO stage III-IV ovarian cancer cases (4–6). Colon resection is performed in averagely 26% of advanced stage (FIGO III-IV) ovarian cancer cases as a component of primary cytoreduction (6). Due to the localization in the pelvis, rectosigmoid colon is the most commonly involved bowel segment concerning ovarian cancer (7). The necessity of bowel resection among all of the cases that constitute the study population of 113 was 17.69% and the most common site of resection is the rectosigmoid region (17 out of 20 cases, 85%).

The rate of ovarian metastasis of colorectal cancers is reported between 4% and 30.8% (8, 9). Due to this high incidence, ovarian cancer with colonic involvement or colon cancer with ovarian metastasis may be diagnostically challenging during clinical assessment. We encountered 2 cases of GIS-originated ovarian metastasis in our series (1.76%).

58.8 % of metastatic ovarian malignancies can be correctly diagnosed with intraoperative frozen section pathological examination. However, the distinction is more difficult for the cases of poorly differentiated serous

carcinoma (10, 11). Poorly differentiated serous carcinomas constitute half of the cases that had undergone bowel resection. Particularly regarding cases like these, preoperative endoscopic examination may help distinguishing the intestinal infiltration of ovarian cancer from the adnexal metastasis of advanced stage colon cancer and therefore provide guidance for the treatment (12). It is also valuable for preoperative bowel preparation and counseling the patient about the necessity of intraoperative bowel resection and potential postoperative morbidities before the surgery.

We have found the positive predictive value (PPV) and the negative predictive value (NPV) of lower GIS endoscopy for predicting bowel resection as 100% and 91% respectively. Lower GIS endoscopy has high specificity for predicting bowel resection but a lower sensitivity (100% specificity and 60% sensitivity was calculated in our study). These results are consistent with studies of other researchers (8–10, 12)

Recent scientific findings suggest that when mechanical bowel preparation (MBP) (with or without antibiotics) is performed before the resection of left colon and rectum, there is a reduction in the rate of surgical site infection, anastomosis leakage and necessity for a diverting stoma and therefore MBP is recommended (13–15).

There are several data about the sensitivity and specificity of colonoscopy (9, 16, 17). The primary reasons for this variety of data are: the incomplete evaluation of serosal and muscular layers although external protruding masses can be noticed, total obstruction by the tumor and suboptimal assessment of patients with advanced age or poor clinical condition (12, 16–18). According to the guidelines published by the National Comprehensive Cancer Network (NCCN Guideline for Ovarian Cancer, Version 1.2019), the clinician should determine the diagnostic method after evaluating the clinical findings and indications (19). Colonoscopy is not a completely non-invasive method – may not be a favorable method concerning patients in poor clinical condition - and given its technical limitations, imaging techniques may be an alternative tool for evaluation. Computed tomographic (CT) colonography, magnetic resonance (MR) colonography and finally positron emission tomography/computed tomography (PET/CT)

colonography are latest non-invasive techniques, which provide information about both functional and structural anatomy (19–22).

Despite the fact that different imaging methods have different limitations, sensitivities and specificities, they offer important information concerning primary originating site and relationship with neighboring organs. These factors are important regarding the surgical treatment plan.

The same team has provided the standard treatment approach and used their experiences and all treatments were performed in a single-center, tertiary medical institution. We see these features as strength of our study. On the other hand the most important limitations of our study are the retrospective construction of the study and the lack of information about the difference between the cases that had undergone lower GIS endoscopy and the ones that had not concerning the long term tumor recurrence and overall survival. In addition the patient files unfortunately lacked information about the method of endoscopic evaluation: flexible sigmoidoscopy or colonoscopy.

Lower GIS endoscopy is important concerning the treatment plan of malignant adnexal masses for a few aspects. First of all, being able to know bowel involvement as a part of tumor spread and preoperative bowel preparation, helps the surgical team regarding performing optimal cytoreduction, reducing postoperative complications and informing the patient about the possible need for a stoma. Bowel preparation increases the chance of end-to-end anastomosis. Second of all knowing the primary origin (colon, ovary or another origin) before surgery for poorly differentiated tumors is critical for better treatment plan and the success of the treatment. In cases of limitations regarding colonoscopy, diagnosis and the following treatment should be supported by imaging techniques.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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