Preoperative colonoscopy in patients with a supposed primary ovarian cancer

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Abstract

The final diagnosis of ovarian cancer is based on surgery and pathological verification. Therefore patients who are presented to surgery may be described only as supposed ovarian cancer. According to the literature the diagnosis of ovarian cancer is confirmed only in 2/3 of them. The rest are that which mimic ovarian cancer. One of them is colorectal cancer. Colonoscopy is a gold standard in its diagnostics. On the other hand, ovarian cancer may disturb the bowel patency and makes the bowel resection or stoma necessary.

The main aim was to find out the distribution of bowel patency disturbances in ovarian cancer patients during preoperative colonoscopy and to assess their predictive value with respect to the bowel resection or stoma and the additional aim to identify the pathologies which mimic the ovarian cancer.

In a prospective study among 104 patients with supposed ovarian cancer, primary ovarian cancer was diagnosed in 68 patients. The rest of them suffered from colorectal cancer found at colonoscopy (N = 6), ovarian benign pathology (N = 8), ovarian borderline tumor (N = 5), and other nonandexal malignant diseases (N = 17). In ovarian cancer group dominated serous carcinoma and fedération international de gynécologie et d'obstétrique stage 3 (N = 33).

During preoperative colonoscopy in ovarian cancer patients, the complete obstruction was found in 27.9%, and relative risk of bowel resection or stoma was in them 4.29 and 4.38, respectively. Another colonoscopic finding was limited patency caused by extrinsic compression (29%) which is connected with relative risk of bowel resection or stoma 3.16 and 3.21 accordingly. The last colonoscopy finding was described as moderate limited patency of unknown origin (20.6%) and the relative risk of bowel resection or stoma was 5.14 and 4.17, respectively.

Colonoscopy enables the diagnoses of colorectal cancer one of the diseases which mimic ovarian cancer in patients supposed to have this diseases.

Bowel patency disturbances found at colonoscopy are a potential risk factor to intestine resection or ostomy.

Colonoscopy is not fully noninvasive procedure and its obligatory use in patients supposed to have ovarian cancer should be limited to the cases with specific symptoms, and tumor marker pattern. Preoperative computed tomography, dedicated to bowel examination, candidates as an alternative to colonoscopy, but not completely.

Abbreviations: Ca 125 = cancer antigen 125, Ca 19.9 = carbohydrate antigen 19-9, CEA = carcinoembryonic antigen, CT = computed tomography, FIGO = fedération international de gynécologie et d'obstétrique, NCCN = National Comprehensive Cancer Network, OV = ovarian cancer.

Keywords: colonoscopy, primary ovarian cancer

1. Introduction

Ovarian cancer (OC) is the seventh most commonly diagnosed cancer among women in the Word.[1] According to the National Comprehensive Cancer Network (NCCN), surgical treatment of OC is a very important element of therapy and has a decisive influence on survival.[2] The primary treatment of early stages of OC is based on staging surgeries, and cytoreductive surgery in advanced cases on. According to current data, the recommended cytoreduction is the complete removal of all cancer foci.[3–5] It was found that each 10% increase in rate of maximum or optimal cytoreduction (without macroscopic residual disease) rate prolonged median cohort survival by 5.5%.[6–8]

In advanced cases, optimal cytoreduction is often associated with operations on the gastrointestinal tract, such as bowel resection or stoma creation.[9] Necessity of bowel resection as a component of surgical intervention in advanced OC is estimated at 41.5% and stoma at 11%[10]; resection + stoma at 69.4%.[11] When this type of surgery is to be performed on the large

intestine, it seems important to know its condition. The gold standard for colon assessment is a colonoscopy.[12]

Colonoscopy, which is not part of obligatory examinations in patients with suspected OC, enables the identification of colon cancer, including synchronic cancer with OC and metastases of OC to the intestine and OC to intestine.[2,13,14] Colonoscopy enables also diagnosing non-neoplastic lesions, like bowel diverticula, and polyps.

The final diagnosis of OC is based on surgery and histopathological verification. Before the surgery are only as supposed to have primary OC.

Suspicion is based on physical examination, imaging and the level of tumor markers. According to Gornall, reasonable suspicion of OC is based on finding at least 2 of "either complexes of the pelvic mass on ultrasound," elevated cancer antigen 125 (Ca 125) or ascites.[15] Ravizza made initial diagnoses of OC on the basis of physical examination, computed tomography (CT) and the level of Ca 125, carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 (Ca 19.9) in blood.[16] The number of confirmed primary OCs was usually slightly above 60%; in Petru study – 64%,[17] in Gornall study – 66%.[15]

According to the literature, endoscopy of the colon was performed either on admission[15] or the day before the surgery.[16] The scope of endoscopy was limited to flexible sigmoidoscopy[15] or included the entire large intestine – colonoscopy.[16]

Two studies are devoted to the evaluation of preoperative colonoscopy in OC. One of them is based on a retrospective analysis of 144 patients.[16] In the second study, a concise group of 30 patients was prospectively examined.[15] In the first study, colonoscopy was used, whereas flexible sigmoidoscopy was used in the second one. The authors concluded that colonoscopy examination not only identifies patients requiring resection of the intestine and/or stoma, but also allows proper planning of surgical management. However, there are studies that negate the need for colonoscopy.[16,17] In addition, colonoscopy is not a standard procedure of preoperative workup in patients with a supposed OC.

2. Aim

Main aim of the study was to find out the distribution of bowel patency disturbances in OC patients during preoperative colonoscopy and to assess their predictive value with respect to the bowel resection or ostomy and the additional aim to identify the pathologies which mimic OC.

3. Material

After obtaining the approval of the Bioethics Committee No. 2/02/2016, a prospective study was conducted from October 2015 to March 2017. Initially, 143 patients qualified for surgery due to supposed OC were included. This suspicion was made, as in Gornall study, on the basis of "the existence of complex pelvic mass in ultrasound" and elevated Ca 125.[15]

The subjects excluded from the study were not subjected to colonoscopy: (N=39 patients, including 8 due to insufficient bowel preparation for the examination. The remaining 31 did not agree to the examination). Finally, 104 patients were analyzed which constituted the study group.

The mean age of the respondents was 62 years (30–87), body max index 28.13 (17.18–40.31), parity: 87 patients (83.7%) had vaginal deliveries, 7 patients (6.7%) had cesarean sections, 10 (9.6%) were nulliparous.

4. Methodology

According to the Bioethics Committee, in addition to the general patient's consent to the surgery and participation in the study, separate written consent for colonoscopy was obtained.

Colonoscopy was performed at the Gastroenterology Clinic of the Clinical Provincial Hospital No. 1 in Rzeszow, in most cases without sedation (N=92; 88.5%), in shallow sedation (N=9; 8.7%), and in deep sedation (N=3; 2.8%).

As preparation for the examination, bowel cleansing medication with macrogol, sodium sulfate, sodium chloride, potassium chloride, ascorbic acid, and sodium ascorbate was used (by Polyethylene Glycol-Ascorbic Acid).

The colonoscopies were performed using Olympus CF-H 190L, CF-Q 165L, PCF-H190L apparatuses. During the procedure, the degree of preparation for the examination was assessed in the Boston Bowel Preparation Scale. In most cases (N=74; 71.1%) bowel preparation was adequate (score above 6 points).

The whole colon was visualized up to the ileocecal valve and the initial section of the ileum. In 24 cases, the examination was discontinued due to the inability of the device to pass through limited patency or the risk of the intestine perforation (in the area close to the anus – 1 case, in most cases the obstacle occurred within 20–50 cm from the anal line, which mainly covers the sigmoid section of the large intestine).

During the colonoscopy limited patency, extrinsic compression or complete obstruction were assessed (Fig. 1). In the follow up in retrospective reassessment of CT scan we were able to identify scans which documented lesions corresponding to colorectal obturator disturbances (Fig. 1).

The lesions like ulcerations, polyps, and diverticulosis were notified and biopsied. The whole colonoscopy was recorded on CD and photographic documentation was prepared. In parallel to colonoscopy, all patients underwent gastroscopy.

Antithrombotic prophylaxis-*enoxaparin* and prophylactic antibiotic *cefuroxime* and *metronidazole* were used in the preparation for the operation.

All surgeries were performed under general endotracheal anesthesia. The incision of the abdominal wall was carried on the midline above the navel to the pubic symphysis. During the procedure, OC stage was assessed according to fedération international de gynécologie et d'obstétrique (FIGO) (version 2014), and the location of lesions on the external surface of the intestines was additionally assessed. Guided by the results of colonoscopy and intestinal lesions, intestinal resection was performed intraoperatively, supplying them with staplers or stitches. When necessary ostomy was performed.

To assess the significance of differences in the frequency of resection or ileostomy depending on the results of the colonoscopy, the Chi-square independence test was used. The typical statistical measures: relative risk, sensitivity, specificity, positive predictive value (PPV) and negative predictive value were used to predict the performance of resection or ileostomy against the outcome of the colonoscopy. The values of all these measures were given together with a 95% confidence interval. All data regarding the preoperative, operative, and postoperative course were entered into the Excel form, and Statistica 10 was used for statistical analysis.
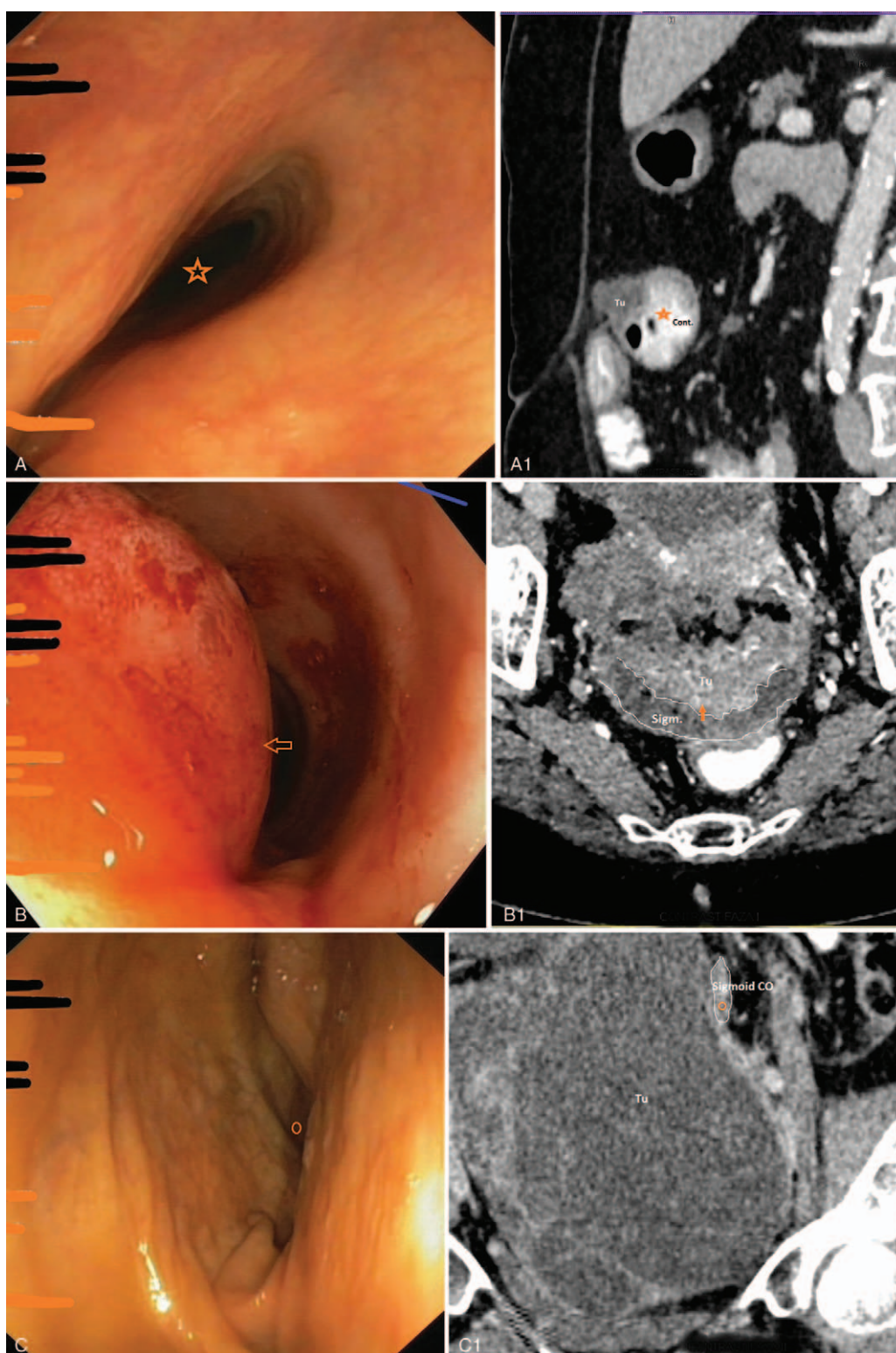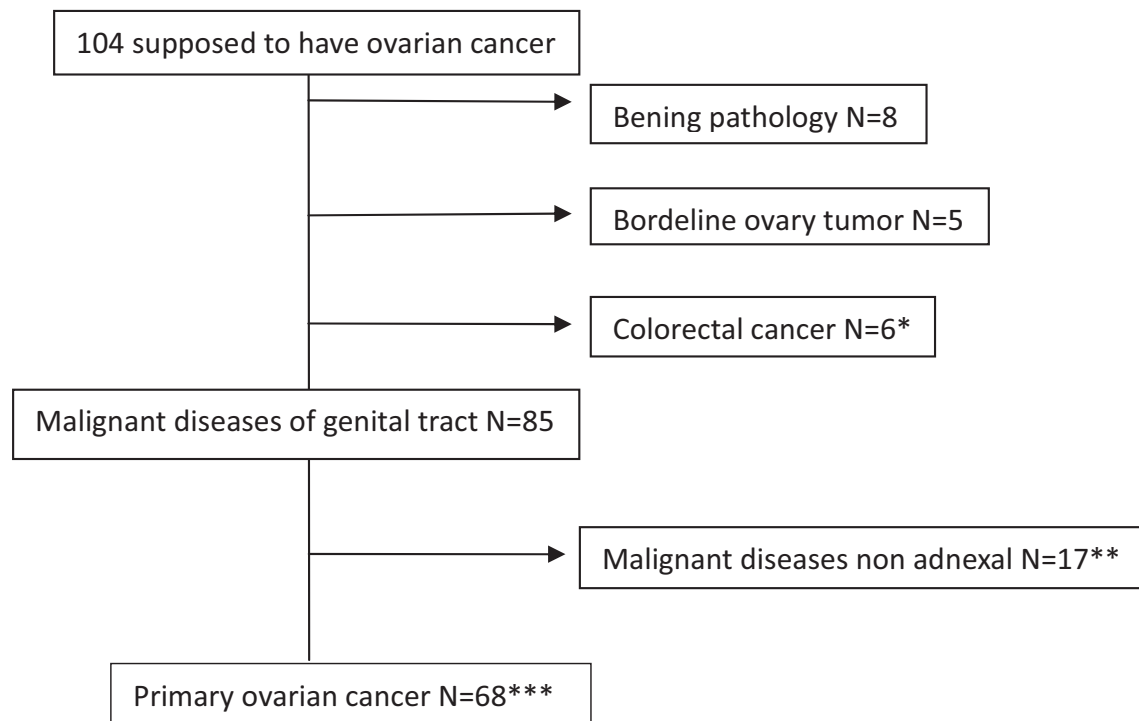
Figure 1. The examples of colonoscopic (A, B, C) and CT (A1, B1, C1) views of bowel patency disturbances in study group. A, A1 – moderate limited patency unknown origin, (marked by ☆); B, B1 – limited patency caused by extrinsic compression (marked by ⇧); C, C1– complete obstruction (marked by ◯). Cont = contrast inside constricted transverse colon, Sigm. = sigmoid colon compressed from outside, Sigmoid CO = completely obstructed sigmoid colon, Tu = tumor.

5. Results

Final diagnosis in the group of patients subjected to operation due to OC suspicion (N = 104) is presented in Figure 2.

Figure 2 enumerated the variety of diagnosis in the study group.

It is noteworthy that there were 2 cases of synchronous tumors in the study group, including 2 colorectal cancer synchronous with small intestine (N = 1), and OC (N = 1).

Figure 2. Flow chart of patients recruited to the study.

It is noteworthy that in the considered 6 cases with intestine involvement, 4 had high CEA, 2 cases had normal level of CEA. The last 2 cases were metastases of OC to intestines.

In final diagnosis, there are 68 patients with primary OC. The distribution of FIGO stages and histology in them is presented in Table 1.

The bowel patency disturbances were found in colonoscopy in the group with primary OC were presented in Table 2.

Complete bowel obstruction during colonoscopy was found in 27.9% of the patients with primary OC, limited patency caused by extrinsic compression in 29.0% and moderate limited patency of unknown origin in 20.6%.

All cases of bowel resection and stoma formation concerned OC, the only exception was the case of uterine carcinosarcoma where resection and stoma were performed.

In our OC group we performed 16 bowel resection and 8 ostoma (Table 3).

Relative risk of bowel resection and stoma in case of colonoscopic findings of bowel patency disturbances were assessed in the group of primary OC (N=68). The data presented in Table 3 and graphically in Figure 3.

During the colonoscopy, we additionally removed the lesions that have the character of polyps. The histopathology of them is presented in Table 4.

6. Discussion

The papers on colonoscopy in patients with OC are scarce,[15–18] and the conclusions drawn from them are contradictory. Our paper attempts to answer the question what is the role of

Table 1

The distribution of FIGO stages and histology in patients with ovarian cancer.

FIGO	Serous carcinoma	Endometrioid carcinoma	Mucinous carcinoma	Clear cell carcinoma	Non epithelial types	All group (N=68)
1	2	1	2	2	3	10
2	1	1	0	0	0	2
3	33	1	2	2	2	40
4	6	0	3	2	5	16
All group (N=68)	42	3	7	6	10	68

FIGO = fedération international de gynécologie et d'obstétrique.

Table 2

The bowel patency disturbances in colonoscopy in the group (N = 68).

The bowel patency disturbances	Ovarian cancer (N = 68)
Complete obstruction	19 (27.9%)
Limited patency caused by extrinsic compression	20 (29.0%)
Moderate limited patency unknown origin	14 (20.6%)

colonoscopy in patients with OC. In the assessment of this role, the reference point is the preoperative separation of patients who will require bowel surgery during ovarian surgery: resection and/or stoma. The other works on this subject are similarly constructed.[15–17] However, colonoscopy findings are differently divided. None of them has a clearly distinguished degree and nature of constriction. Ravizza divided endoscopic bowel involvement into: infiltration, no infiltration, and uncertain infiltration.[16] Whereas Petru divided lesions into malignant infiltration or normal findings and the separate group of extrinsic compression.[17]

In the present study, the constrictions not infiltrations were assessed, they were divided into total obturations, that is,

those in which it was impossible to overcome constrictions without the risk of perforation and moderate, in which the colonoscope could move further. The causes of complete obstruction may be due to infiltration and also inflammations, diverticulosis, and acute bend. Separately distinguished was a group with the stenosis resulting from external compression. This division exhausted all possible types of stenosis, but of course, it was still based on the subjective assessment by an endoscopist.

In this report, we introduced a term of "disturbance in bowel patency" at colonoscopy. Meanwhile, in other report[16,17] the authors used term infiltration. But they realized that colonoscopy diagnosis of infiltration is not certain and added in some cases word "uncertain."[16] According to us the term "disturbances in patency" is wider and more objective.

Table 3

Probability of bowel intestines resection and stoma according to colonoscopic findings.

Bowel surgery Colonoscopic findings in the bowel	Resection	Ileostomy
Complete obstruction	RR 4.29 (2.17–8.48) Se 52.63% (31.71–72.67) Sp 91.84% (80.81–96.78) PPV 71.43% (45.35–88.28) NPV 83.33% (71.26–90.98) P = .0001	RR 4.38 (2.48–7.74) Se 36.84% (19.15–58.96) Sp 97.96% (89.31–99.64) PPV 87.5% (52.91–97.76) NPV 80% (68.22–88.17) P = .0001
Limited patency caused by extrinsic compression outside	RR 3.16 (1.64–6.08) Se 45% (25.82–65.79) Sp 89.58% (77.83–95.47) PPV 64.29% (38.76–83.66) NPV 79.63% (67.1–88.23) P = .0013	RR 3.21 (1.75–5.91) Se 30% (14.55–51.9) Sp 95.83% (86.02–98.85) PPV 75% (40.93–92.85) NPV 76.67% (64.56–85.56) P = .0026
Moderate limited patency unknown origin	RR 5.14 (2.13–12.40) Se 57.14% (32.59–78.62) Sp 88.89% (77.81–94.81) PPV 57.14% (32.59–78.62) NPV 88.89% (77.81–94.81) P = .0002	RR 4.17 (1.86–9.34) Se 35.71% (16.34–61.24) Sp 94.44% (84.89–98.09) PPV 62.5% (30.57–86.32) NPV 85% (73.89–91.9) P = .0018

NPV = negative predictive value, PPV = positive predictive value, RR = relative risk, Se = sensitivity, Sp = specificity.
P-value- chi-square test independence result.

As in above-mentioned papers, predictive values of our authorial division of constrictions in relation to the resection and stoma were calculated. It turned out that the highest PPV was found in complete obstruction and moderate limited patency.

All 3 degrees of constrictions were associated with statistically significant increased risk of resection and/or stoma. This gives grounds for stating that even small constrictions give rise to the risk of having to be operated on the intestine.
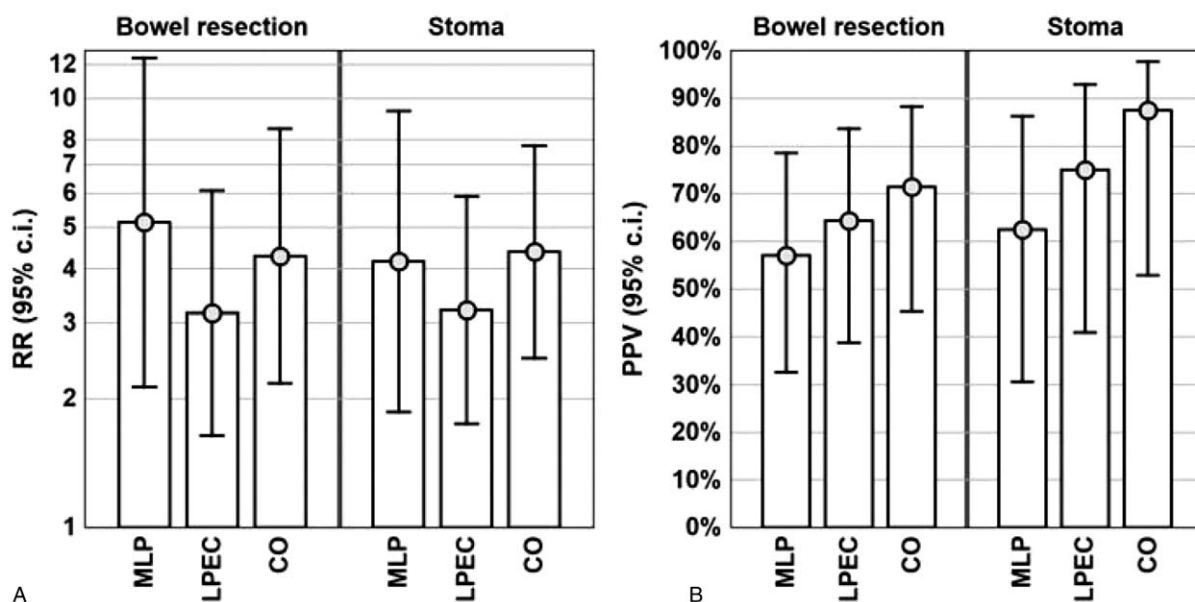

Figure 3. Relative risk (A) and positive predictive value (B) of the colonoscopy findings: MLP, LPEC, and CO in respect a bowel resection and stoma /graphically based on data from Table 3. CO = complete obstruction, LPEC = limited patency caused by extrinsic compression, MLP = moderate limited patency.

Table 4

The histopathology of polyps removed during colonoscopy in group ovarian cancer patients (N=68).

Pathology type
   – adenoma (N=13)
     including tubulo-villosum (N=12)
      seratum (N=1)
   – hyperplastic (N=4)
   – inflammatory (N=1)
Polyp coexisting with dysplasia/cancer
   – with low-grade dysplasia (N=13)
   – with high-grade dysplasia (N=13)
   – bowel cancer (N=1)

The need of mechanical bowel cleansing before gynecological surgery is argued.[19,20] But it is also obligatory before colonoscopy.[21] In our study, all patients had performed colonoscopy a day before surgery so bowel was cleansed automatically.

The whole current report is based on a prospective study of 104 patients supposed to have OC. In Gornall study as in our prospective study, 30 patients with suspected OC were included and, similarly to our retrospective analysis, a group was identified with the definitive diagnosis of OC, which amounted to 20 patients.[15] In our study from the group of 104 patients, we finally selected a group of 68 with OC and for this group the above-described calculation of the predictive values of colonoscopy results was carried out. The remaining group of that mimicked OC was analyzed for the type of these diseases. It turned out that, as in other studies,[16,17] this group was 1/3 of patients supposed to have OC. The results of this analysis coincide with Ravizza results.[16]

In the present study and Ravizza study,[16] the percentage of colorectal cancer found in the colonoscopy was about 6%, which means that every 15 patient supposed to have OC has colorectal cancer. It should be emphasized that among these cases there were synchronous ovarian and colon cancer, as well as cases of colorectal cancer metastasis to the ovary. Our material confirmed 1 metastasis of OC to the large intestine as well as 2 cases of synchronous cancer.

O'Hanlan assessed the fragments of excised intestine during surgeries of OC patients and found that OC metastases affecting the entire thickness of the intestine occurs only during OC secondary surgery.[21]

Hence her conclusion about the legitimacy of performing a colonoscopy before second look operations was drawn.

Colonoscopy is not a completely noninvasive examination. Colonoscopy performed in the screening of colorectal cancer showed an improvement in the quality of life of the subjects, but it is associated with the risk of complications.[22] According to Taupin, adverse events appeared in 30/231 patients and serious adverse events in 2/231 (<1%).[22]

In addition, colonoscopy may worsen the quality of life of patients with OC, which at the time of diagnosis and initial treatment already have a reduced quality of life. As shown by the analyzes of Grzankowski, Chase, and Ahmed-Lecheb, the quality of life of patients with OC improves along with the duration of the disease.[23–25]

It is worth noting that in the present paper as many as 31 patients, that is, about 19%, did not consent to colonoscopy. We can explain this phenomenon like Yamada by personal reasons such as mental health and physical function.[26] Hsueh

demonstrated that education before the colonoscopy effectively reduced the examination-related anxiety and pain of patients.[27]

Therefore, a reflection arises on the one hand about the necessity of providing the patient with complete information on the validity of the colonoscopy, as well as carrying out other than colonoscopy diagnostic tests combined with the analysis of the accompanying symptoms.

It may be necessary to consider the use of CT oriented to bowel or even virtual colonoscopy which is not complete alternative for traditional colonoscopy because it lacks pathological confirmation.

According to us, nowadays colonoscopy belongs to the wider current trend for preoperative staging in OC, including staging laparoscopy. Fagotti et al and Feng et al concluded that preoperative laparoscopic staging is useful in making decisions about primary debulking surgery.[28,29]

Preoperative colonoscopy in patients with OC, which is the subject of present study, can also be classified as suo generis preoperative staging.

Classic CT is to some extent able to diagnose colorectal cancer. The interesting study was performed by Mangat.[30] In this study, the authors reviewed retrospectively CT scans of patients in whom the colorectal cancer was diagnosed an operated. In 59% patients colorectal cancer was visualized in previously undiagnosed group.

Using a similar methodology in our material during the retrospective re-evaluation of CT scans, we found images of constrictions in CT corresponding with our colonoscopic classification (Fig. 1A and B).

In our study, 6 cases of colorectal cancer were confirmed. In this group, the nonspecific symptoms for intestinal cancer, such as abdominal distension, abdominal pain, were found in 49%, and specific symptoms such as nausea, vomiting, constipation, diarrhea – 33% of studied patients.

In the group of 68 women with OC who required an ostomy, 71% of the subjects had specific symptoms, 28% nonspecific symptoms. In the group with intestinal resection, 42% of specific symptoms were recorded, in 58% nonspecific symptoms. The above distribution confirms the thesis that the scope of bowel surgery cannot be predicted based on symptoms. This is in line with Rassmussen report.[31] In this study, there are cases of intestine cancer with scarce symptoms.

A noninvasive test indicating the possibility of bowel cancer is the assessment of biomarkers, for example, fecal hemoglobin, Ca 19.9 and CEA.[32] In our group of 6 cases with colorectal cancer, 4 subjects had elevated CEA marker. This may support the fact that if this marker is increased, this may be an indication for a colonoscopy.

It is worth mentioning that in the preoperative differential diagnosis between primary OC and metastatic OC, a parallel assessment of ratio Ca 125 and CEA antigen is useful.[18,33]

CT in case of OC is used for preoperative staging of this cancer. However, in cases of patients not consenting to a colonoscopy, when there is a low total constrictions in the colonoscopy as well as in advanced cases of OC, preoperative CT dedicated for intestinal assessment may be useful. Such an examination may be carried out with the use of contrasting medium and have the character of a virtual colonoscopy.

Retrospective bowel assessment in preoperative CT may enhance the experience of preoperative assessment in the future. This sentence is in line with the conclusion of Mangat that the retrospective assessment of preoperative CT gives hope for the usefulness of prospective CT in the diagnosis of colorectal cancer.[30]

Additionally, during the colonoscopy in our group we removed polyps. In 1 paper among the findings in the colonoscopy were polyps that were histologically divided into adenoma (65%) and hyperplastic polyps (35%). According to the NCCN, polyps in the colonoscopy can be divided histologically into Adenoma/Adenomatous Polyps, Flat Adenoma, Sessile Serrated Polyps, and Hyperplastic Polyps.[12] In our material, the majority were tubular adenomas with low-grade LG dysplasia, 2 cases with high-grade HG dysplasia, 3 cases with adenoma tubulovillosum, and 3 cases of hyperplastic polyps.

In our group, we evaluated the upper gastrointestinal tract with gastroscopy in parallel to the colonoscopy to rule out the presence of metastasis of gastric cancer into the ovary. We found only 1 case of endoscopic suspicion of stomach cancer, which; however, was not confirmed in the HP examination.

There are some limitations of our report. One of them is use of subjective descriptions of bowel patency. Another one is calculations of resection or stoma on the base of colonoscopy only. We realize that there are some other risk factors which may be taken into account like clinical intestines related symptoms, FIGO stage of OC, ascites, patient age, and serum tumors markers.

7. Conclusions

Colonoscopy enables the diagnoses of colorectal cancer one of the diseases which mimic OC in patients supposed to have this diseases.

Bowel patency disturbances found at colonoscopy are a potential risk factor to intestine resection or stoma.

Colonoscopy is not fully noninvasive procedure and its obligatory use in patients supposed to have OC should be limited to the cases with specific symptoms, and tumor marker pattern. Preoperative CT, dedicated to bowel examination, candidates as an alternative to colonoscopy, but not completely.

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