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Oncological and surgical characteristics of patients with ovarian cancer diagnosed in the main multidisciplinary hospital in Romania

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ABSTRACT

Malignant ovarian neoplasms represent a public health issue, being one of the most frequent cancers among women, exhibiting the highest mortality rate. The general purpose of this study lays in the analysis of the metastasizing potential of malignant ovarian neoplasms, the correlation between the histological subtype and the genesis of the metastasis. We present an observational retrospective study spanning over 2 years, between 2018-2019, on 30 admitted patients who were treated for malignant ovarian neoplasms in the department of Obstetrics and Gynecology of Bucharest Emergency University Hospital. The most frequent histopathological subtype encountered in our study has been the high grade serous ovarian carcinoma 46,67%, with 30% presenting poorly differentiated neoplasms (G3), therefore having poor prognosis. A considerable number of patients 56,67% presented ascites (among which 43,33% of patients also exhibited peritoneal carcinomatosis, direct dissemination representing the main metastasizing pathway of malignant ovarian neoplasms in the patients included in our study.From our study we can conclude that patients with ovarian malignant neoplasms are diagnosed in an advanced stage of the disease, when metastasis are already present, with a poor prognosis. This is mainly due to the lack of regular gynecological check-ups in menopausal womenand because it is considered that once past the fertile age the gynecological examination no longer represents a necessity.

Keywords: ovarian cancer, metastasis, histological subtype

INTRODUCTION

Malignant ovarian neoplasms represent a public health issue, with a complex pathogenesis and heterogeneity, them being the seventh most frequent malignancy in women in first-world countries and occupying fourth place regarding the frequency of gynecological cancers (1,2). Despite the physicians' efforts to early detect a malignant ovarian neoplasm, only 15% of patients are diagnosed in the first stage of the disease, when the 5-year survival rate amounts to 92%. The relative 5-year survival rate is 30-40% globally, recording slight increases of 2-4% since 1995 (3).

According to Global Cancer Observatory (IARC) in Romania, in 2020 there were 1909 new cases and 1121 cancer-related deaths, with a high incidence (16 per 100.000 women) and a 5-year prevalence that amounts to 5302 women with ovarian cancer (4).This is owed mainly to the non-specific symptoms that occur in a moment when the stage of the cancer is already advanced and to a lack of efficient screening strategies which could detect it in an early stage of the disease.

Although progress has been made in the last decades regarding surgical techniques and intensive combined chemotherapy regimens, the survival rate drops significantly once the cancer metastasiz-

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es in the pelvic organs or further, in the abdominal viscera or other parenchymatous organs. Malignant ovarian neoplasm dissemination is most likely to occur through transcoelomic (the most frequent), lymphatic and hematogenous pathways, the latter one being thought to occur only in the late stages of ovarian cancer (5). Transcoelomic dissemination represents the main pathway through which malignant ovarian neoplasms spread, this process being owed to the lack of an anatomical barrier and also to the peritoneal fluid (which facilitates the spread of malignant cells throughout the peritoneal cavity with the appearance of ascites and peritoneal carcinomatosis) (6).

During the genesis of the primary tumor, the ovarian carcinoma malignant cells go through a process of transition from an epithelial to a mesenchymal phenotype, process that encompasses changes in the expression of cadherin and integrin andthe up-regulation of certain proteolytic pathways. These malignant cells become spheroid, overcome anoikis and migrate by way of the peritoneal fluid, attaching themselves on the abdominal peritoneum or omentum. There, the malignant cells return to their original epithelial phenotype (7). Recent data reveal that the metastatic pathways of ovarian cancer depend on the histologic type, the four major histologic types including serous, mucinous, endometroid and clear cell types. On the contrary, transitional cell and squamous cell cancers appear less frequently (3,8-10). Studies in literature incriminate certain risk factors as taking part in the occurrence of ovarian cancer, such as: infertility, nulliparity, late menarche, early menarche, family history of malignant ovarian neoplasms, BRCA1/2 mutations, pelvic inflammatory disease, endometriosis, polycystic ovary syndrome, substitution hormonal therapy, obesity, asbestos exposure, smoking (11).

MATERIAL AND METHODS

We conducted an observational, retrospective and single-center study spanning over 2 years, between 2018 and 2019, on 30 admitted patients who were treated for malignant ovarian neoplasms in the Obstetrics and Gynecology Department of the Bucharest Emergency University Hospital.

The main and mandatory inclusion criteria was the histopathological result of a form of primary ovarian cancer. Patients that had only a presumptive diagnosis were not included in our analysis.

In order to elaborate this study, the patients' data were collected from the observational charts abiding by the ethical rules of medical research. We focused on the main symptomatology which alerts the patient, significant medical history, obstetrical antecedents, cancer related conditions and histopathological results.

The data were processed using IBM SPSS Statistics 22 program, resulting graphics and tables by codifying certain parameters and variables.

RESULTS

Regarding the age of the patients included in this study, the maximum recorded age was 75 and the minimum age was 32, while the mean age of the 30 patients was 56 years.

In this study a majority of patients have had at least one pregnancy, 40% of them being second parousand only 13.33% nulliparous patients.

Regarding the diagnosis of certainty, this is established following the histopathological examination. Among the 30 patients, 29 developed epithelial malignant ovarian neoplasms (46.67% of patients high grade serous ovarian carcinoma, 13.33% of patients endometrioid ovarian carcinoma, 10% of patients clear cell ovarian carcinoma, 10% of patients mucinous ovarian carcinoma, 6.67% of patients low grade serous ovarian carcinoma, 3.33% of patients undifferentiated ovarian carcinoma, 3.33% of patients sero-mucinous carcinoma, 3.33% of patients borderline mucinous ovarian tumor) and one patient exhibited non-epithelial ovarian neoplasm (one ovarian metastasis from a gastrointestinal malignancy).

Regarding the histopathologic aspect, in our study group, 30% of patients presented G3 differentiation grade, followed by G2 differentiation grade.

Patients presented with various symptoms on admission to the hospital: 34% of patients accused abdominal and pelvic pain, in second place, 16% of patients accused vaginal bleeding (menorrhagia, metrorrhagia, menometrorrhagia) and digestive symptoms: meteorism, eructation, nausea, changes in bowel movement with diarrhea, constipation, early satiety sensation. In the third place, 10% of patients presented for a palpable mass and urinary symptoms: pollakiuria, dysuria, imperious need to urinate, urinary tract infections.

Particularly, almost 60% of patients presented ascites in different quantities upon diagnosis, which was evacuated by paracentesis and cytologically evaluated (Figure 1). The most frequent histological subtype associated with the presence of ascites in our study group being the serous ovarian carcinoma present in nearly 40% of patients (Table 1).

43.33% of patients presented peritoneal carcinomatosis at diagnosis (Figure 2). Moreover, from a histopathological point of view, 30% of them were diagnosed with high grade serous ovarian carcinoma subtype (see Table 2).

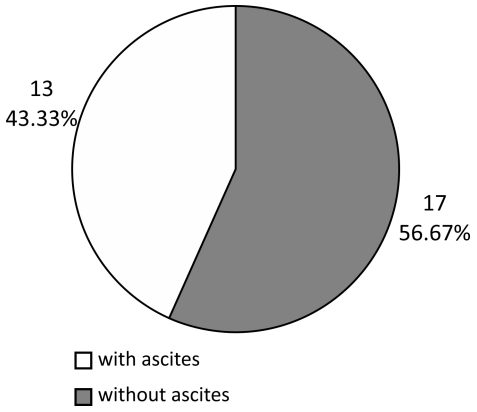

FIGURE 1. Distribution of ascites at diagnosis

TABLE 1. The correlation between histological subtype and ascites

	Ascites		
Histological subtype	**Without ascites**	**With ascites**	**Total**
High grade serous ovarian carcinoma	10%	36,66%	46,66%
Low grade serous ovarian carcinoma	3,33%	3,33%	6,66%
Clear cell ovarian carcinoma	10%	0%	10%
Endometrioid ovarian carcinoma	10%	3,33%	13,33%
Borderline mucinous ovarian tumor	3,33%	0%	3,33%
Undifferentiatedovarian carcinoma	0%	3,33%	3,33%
Mucinous ovarian carcinoma	3,33%	6,66%	10%
Sero-mucinous carcinoma	3,33%	0%	3,33%
Ovarian metastasis	0%	3,33%	3,33%
Total	43,33%	56,67%	100%

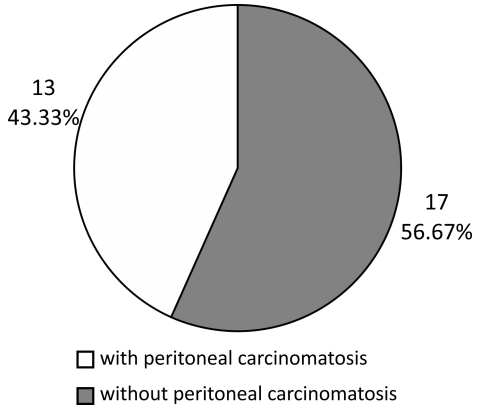

FIGURE 2. Distribution of peritoneal carcinomatosis

Upon diagnosis, only 13,33% of our patients exhibited pleural effusion (Figure 3).

Metastasis in parenchymatous organs identified in our study group are as follows: 13.33% of patients exhibited secondary hepatic tumors, 10% patients secondary pulmonary tumors and 3.33% of patients developed renal metastasis (Figure 4).

TABLE 2. The corelation between histological subtype and peritoneal carcinomatosis

Histological subtype	**Peritoneal carcinomatosis**		**Total**
	Without	**With**	
High grade serous ovarian carcinoma	16,66%	30%	43,33%
Low grade serous ovarian carcinoma	3,33%	3,33%	6,66%
Clear cell ovarian carcinoma	10%	0%	10%
Endometrioid ovarian carcinoma	13,33%	0%	13,33%
Borderline mucinous ovarian tumor	3,33%	0%	3,33%
Undifferentiatedovarian carcinoma	3,33%	0%	3,33%
Mucinous ovarian carcinoma	3,33%	6,66%	10%
Sero-mucinous carcinoma	3,33%	0%	3,33%
Ovarian metastasis	0%	3,33%	3,33%
Total	56,65%	43,33%	100%

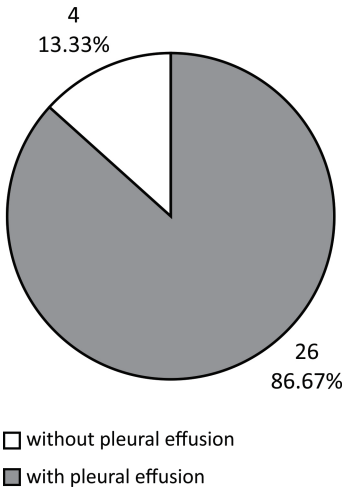

FIGURE 3. Distribution of pleural effusion

From a staging point of view, 43,44% of patients have been diagnosed in the third (III) stage and the second most frequent is stage IV with a percentage of 23.33% patients.

DISCUSSIONS

Regarding the age of the patients included in this study group, the mean age recorded correlates with results from literature, the diagnostic rate of malignant ovarian neoplasms being the highest among patients 55-64 years of age (12,13).

The literature encompasses studies that analyzed the correlation between ovarian cancer and pregnancy, with parity being a protective factor, multiparous women presenting a 30-60% lower risk to develop ovarian cancer than nulliparous women (14). In this study, a majority of patients have had at

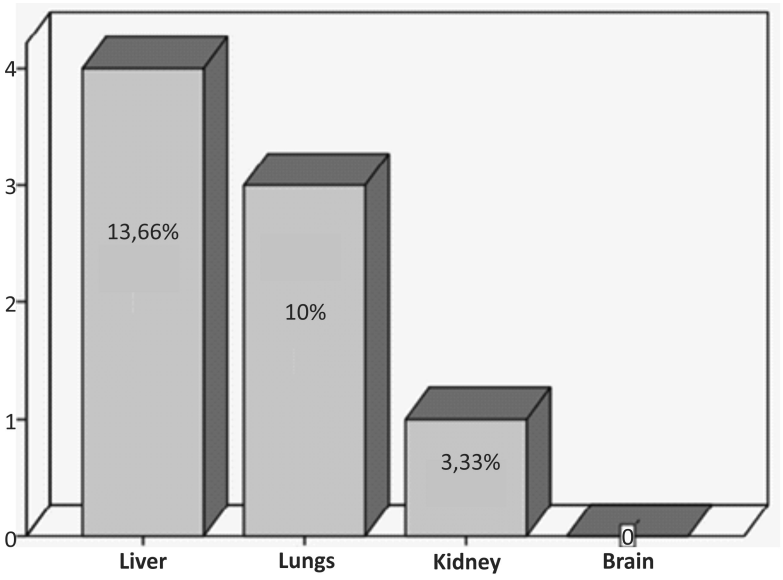

FIGURE 4. Distribution of metastasis in parenchymatous organs

least one pregnancy. These patients had developed ovarian cancer despite the parity and, therefore, this study does not corelate with pre-existing studies, the data being different due to the small number of patients included.

Referring to histological subtype, data from this study resemble the data in literature, malignant epithelial neoplasia registering the largest percentage (approximately 90%) of all malignant ovarian neoplasms (15).

The patients included in this study group accused similar symptoms with the ones described in literature.Symptomatology of ovarian cancer is non-specific, vague and overlaps, being known as "silent killer" with the symptomatology of more frequent afflictions, such as digestive pathology ("borrowed symptomatology"), menstruation and menopause (16). Patients usually complain of pain, pelvic or abdominal discomfort, digestive symptoms: meteorism, eructation, nausea, diarrhea, constipation, early satiety, rectal or anormal vaginal bleeding (metrorrhagia, post-menopause), weight loss, anemia associated with pale skin, fatigue, vertigo and urinary symptoms: dysuria, pollakiuria, urinary tract infections, imperious need to urinate and even hydronephrosis in advanced stages, which imposes the need for percutaneous nephrostomy (17,18).

Pertaining to the presence of ascites, which was evacuated by paracentesis and cytologically evaluated, and the advanced stage of the disease (stages III or IV) upon diagnosis, our results corelate with data in literature (19,20). Ascites plays a key role in the genesis of ovarian tumors, facilitating metastasizing in peritoneal organs, but also at distance (19). The most frequent histological subtype associated with the presence of ascites in our study group is the serous ovarian carcinoma, this data coincides with results from literature, 70% of patients with ascites presenting serous carcinoma (20).

Peritoneal carcinomatosis appears by direct dissemination of the malignant cells through the peritoneal fluid at a mesothelial level, microenvironment level (omentum, abdominal organs). There normally is a small quantity of peritoneal fluid, thus the dispersion of malignant cells is restricted to vicinity organs of the ovarian tumor. Therefore, the ascites fluid facilitates the spread of the exfoliated malignant cells in the entire peritoneal cavity (5,10). From a histopathological point of view, a majority of them were diagnosed with high grade serous ovarian carcinoma, this data resemble the ones in literature, metastasis in the peritoneal cavity with the appearance of carcinomatosis being relatively more frequent than distant metastasis and appears especially in the case of advanced serous carcinomas (7,10).

Metastasis in the pleura occur through a hematogenous pathway, representing one of the most frequent sites of metastasis following this pathway (10). The percentage in our study does not correlate with the literature because of the small number of patients, thus the importance of this value is limited.Moreover, through the hematogenous and lymphatic pathway, malignant ovarian neoplasms can metastasize in distant organs, more frequently at a hepatic (26%) and pulmonary level (15%), and rarely in the osseous system, nervous system, breast, eye, pericardium, placenta, cutaneous (10).

This is an observational, retrospective, single-center study, which has its limits, such as the small number of patients, the lack of access to certain data about the survival rate of the patients, the

absence of information regarding the oncologic treatment of the patients, the lack of patients' treatment follow-up and the lack of access to certain paraclinical test results. An important advantage of the study was the data offered by the intraoperative staging, surgical management, the direct extension of the tumor in the pelvic and intraabdominal region. One of the disadvantages of the study was that it can't be extrapolated because of the small number of patients included in our study and because of the fact that the patients were selected from only one hospital.

CONCLUSIONS

From our study we can conclude that patients with ovarian malignant neoplasms are diagnosed in an advanced stage of the disease, when metastasis are already present, with a poor prognosis. This is mainly due to the lack of regular gynecological check-ups in menopausal women (the diagnostic rate of malignant ovarian neoplasms being the highest among patients 55-64 years of age), and because it is considered that once past the fertile age the gynecological examination no longer represents a necessity and symptoms such as anormal vaginal bleeding or digestive symptoms are ignored. Also, in our study, we can incriminatedirect dissemination (transcelomic, by way of the peritoneal fluid) as the main metastasizing pathway of malignant ovarian neoplasms Unfortunately, we couldn't evaluate the impact nulliparity has on the malignant ovarian neoplasms genesis and their subsequent metastatic potential given the small number of patients included and their multiparous status.

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