

Importance of Surgical Treatment in Ovarian Neoplasm

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Ovarian neoplasm responds to primary surgical treatment, although the vast majority of patients are diagnosed in advanced stages of the disease, in which the rate of relapses is increased and the chance of survival at 5 years is below 45%. It represents the most lethal gynecological oncological condition.

Keywords: ovarian neoplasm, primary surgical treatment, increased relapse rate

- Predictive factors of maximum citoreduction

The paraclinical criteria for determining the inoperable stage of the disease may vary from one clinic to another, also taking into account the individual surgical aggressiveness of each surgeon individually [1].

In 2000, Bristow et al. proposed a predictive CT score based on a retrospective analysis of 41 patients by two radiologists without knowledge of operative plans. Following this study they concluded that the overall accuracy rate of CT scans was 92.7% and the diagnostic sensitivity of the patients chosen for optimal primitive cytoreductive surgery (RT <1 cm) was 100% [2].

In a study published at the beginning of 2019, in which the sensitivity of the detection of the disease stage following the ultrasound versus the computed tomography was monitored, it was found that the detection rate of the stage of the disease for the ultrasound was 71% compared to 75% for the tomography. [3].

The risk score for MRI malignancy may also be used. It is composed of the following parameters: the reproductive status of the woman, the imaging characteristics, the CA125 values. Such a score <25 correlates with a risk of <3% malignancy, while a score > 250 shows a 75% risk of malignancy. Objective imaging of neoplastic invasion at the V-level gates, liver, diaphragm, gastro-splenic ligament, extraperitoneal space correlates with advanced staging of the disease, most likely inoperable optimally [1].

A value of CA125 > 500 IU / mL is a strong predictor of suboptimal tumor cytoreduction, with a sensitivity of 69% and a specificity of 63% [4].

- Exploratory laparoscopy:

Exploratory laparoscopy is considered superior to the imaging investigations in the prediction of complete citoreduction.

A laparoscopic score was created based on 8 intraoperative criteria: the presence of single / bilateral ovarian tumor masses, the presence of massive omental tumor masses, of secondary determinations at the level of the diaphragm / peritoneum, mesentery retraction, infiltration of the small intestine / stomach. Thus a score greater than 8 has a prediction rate of incomplete cytoreduction of 100% and a negative predictive value of 70% [5].

It is also considered that in the face of a suspected advanced ovarian cancer, performing exploratory laparoscopy in order to correctly stage the disease reduced the number of unnecessary laparotomies. If after laparoscopy it is established that optimal tumor cytoreduction can be achieved then it is recommended to perform cytoreductive surgery per primam [6].

Even though it may be considered an additional surgery, it seems, however, that the total costs of the health system do not increase significantly, nor do they negatively affect the health status or frequency of patients' disease complications [7].

Besides the correct staging of the disease, laparoscopy can also bring a great advantage in the preoperative investigations, namely the diagnosis of the histo-pathological type, which can radically change the therapeutic behavior of the case, with its individualization [8].

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- Interval cytoreduction

In the situation where the intraoperative staging was advanced and the initial surgical intervention was limited to multiple biopsies or to suboptimal cytoreduction, there are two variants of management of the therapeutic management: neoadjuvant chemotherapy followed by interval surgery or direct surgical cytoreduction followed by non-chemotherapy. The question that arises is which of the two variants ensures a better survival of patients at a distance [9].

A study on this topic was carried out at Sp Clinic Fundeni between 2002-2014 (in which 99 patients were operated on suboptimally primed, of which 28 patients underwent direct surgery and the remaining 71 initially underwent neoadjuvant chemotherapy and later interval surgery) concluded that longer survival, as well as low frequency of postoperative complications, were among the patients who had preoperative adjuvant chemotherapy [10]. However, it is clearly proven that patients undergoing optimal surgical cytoreduction, followed by adjuvant chemotherapy, have a 5-year survival rate higher than patients who initially underwent adjuvant chemotherapy and then interval surgery [11]. Even if aggressive surgical treatment is performed, optimal primary debulking, preservation of sensitivity to chemotherapy cannot certify a favorable prognosis, but the bio-humoral characteristics of the tumor type can greatly influence the long-term postoperative evolution, so that favorable evolution can be justified following some advanced staging [12]. In a recently published study, it was found that the combination of Paclitaxel with hyperthermic chemotherapy following interval cytoreduction is a feasible therapeutic protocol for advanced ovarian cancer [13].

- Radical and ultraradical surgery in Ovarian Neoplasm

In 2010, the emergence of neoadjuvant chemotherapy led to the hypothesis that this may reduce the complexity of the radical surgery required to eradicate ovarian neoplasm (associated with an increased rate of postoperative morbidity), but at present it is reserved only for cases advanced by preoperative disease or in the case disease recurrence: single or in combination with interval surgery [14].

Surgical treatment of ovarian cancer has evolved over time in favor of radical surgery. The surgical team should be highly motivated and experienced for these complex surgeries, as the ability to reach complete cytoreduction is the most important predictor of the survival of ovarian cancer patients [15].

In addition to the basic surgery, in front of an enlarged ovarian neoplasm at the level of the upper abdomen, radical surgical techniques (multiple digestive resections) or even ultraradical (exenterations) may be added. Even in the face of advanced staging, the classic recommendation remains valid, that of the maximum surgical effort.

Radical surgical techniques may include: appendectomy, total supracolic omentectomy, rectal sigmoidectomy, descending colon hemicolectomy, extended bowel resections of the transverse colon and / or right colonic angle, or pelvic and parietal peritonectomy. Ultraradical surgical procedures may include: hepatic, gastric, diaphragmatic, pancreatic (most commonly distal pancreatectomy) or splenectomy.

There is indeed controversy regarding the frequency of postoperative complications in radical / ultraradical surgery, but the latest scientific data, however, underline the improvement in the survival of these patients at 5 years, being about 48% [16].

In a recently published English study, they found that about 50% of patients with ovarian neoplasm underwent at least one ultra-radical surgery (including upper abdomen surgery) with at least one relapse of the disease later [17].

In the United States, an article published in 2017, highlights the increasing frequency of performing complex surgical interventions (radical or even ultra-radical), which even today demonstrates a late diagnosis of the disease in a country with an increased socio-economic status. [18].

A disadvantage of the increased postoperative morbidity of these types of interventions is the delay in initiating the adjuvant chemotherapy treatment, which can reach up to 6-8 weeks. Also, it has been found that the higher the number of surgical techniques for exertion during surgery, the higher the morbidity and risk of postoperative complications [19]. Also within the complex surgical procedures for advanced stages of the disease, the excision of the cardiophrenic lymph nodes is discussed, which seems to prevent the disease recurrence. Until now, this was only possible through thoracic surgery versus a massive open transdiaphragmatic or subxifoid surgery approach, but with the help of intraoperative ultrasound, guided excision of suspected lymph nodes is possible [20].

- Peritonectomy:

Starting from the hypothesis that the dissemination of the ovarian neoplasm is performed mainly by the peritoneal route, the peritonectomies represent an extremely important step in the surgical intervention. There are multiple surgical techniques to perform peritonectomies, but all have as main purpose the excision of the tumor tissue as wide as possible.

The association of peritonectomies with intraperitoneal chemotherapy based on Cisplatin and Paclitaxel has shown an prolonged survival both overall and without signs of disease in patients with advanced stages of the disease [21].

On the other hand, the association of ultraradical primary surgical cytoreduction (including peritonectomies and digestive resections) with intraperitoneal hyperthermic chemotherapy has shown overall survival as well as a duration of non-superior recurrence compared with postoperative chemotherapy-associated postoperative ultraradical surgery.

Hyperthermic intraperitoneal chemotherapy involves infusion with heated chemotherapeutic agents at temperatures of 44-46 Celsius degrees, maintaining an intraperitoneal temperature of about 41-43 Celsius degrees for 60-90 minutes. During the procedure, the most uniform distribution with the chemotherapeutic agents is essential through the easy mobilization of the viscera (this also contributes to reducing the risk of the onset of the adhesion syndrome). At the end of the intervention, the abdominal cavity is washed out of abundance with saline solution [23].

Pelvic peritonectomy involves: sectioning of the medial umbilical ligament, sectioning and ligation of the bilateral round ligaments at the entrance to the inguinal canal, identification of the ureters, continuation at the posterior peritoneum of the duodenum and the Treitz ligament and sectioning and ligation of the ovarian veins at the inferior renal pole [24].

In a recent study it was concluded that pelvic peritonectomy brings multiple advantages over recto-sigmoid resections (if not required): shorter postoperative hospitalization and the possibility of faster administration of adjuvant chemotherapy [25].

Radical peritonectomy, "in block" in the ovarian neoplasm, represents total peritonectomy and diaphragmatic stripping (tumor diaphragmatic invasion present in approximately 40% of advanced cases of the disease). It is true that the large tumor volume may prevent the achievement but achieving this objective contributes to the classification of the surgery as optimal [26].

The diaphragmatic surgical approach may consist of: diaphragmatic peritonectomy, total diaphragmatic excision or excision of the diaphragmatic tumor nodules. Following a study in Romania between 2014-2016 it was concluded that the diaphragmatic surgical approach is a key element in the surgical treatment of advanced ovarian neoplasm. Also, it was found that the postoperative evolution of the patients was approximately the same regardless of the technique performed, but the principle remains the same: maximal macroscopic tumor excision per primam [27].

Unfortunately, diaphragmatic surgery does not seem to have the same value if performed after adjuvant chemotherapy, during interval surgery. An important marker, which may evaluate any indication of diaphragmatic peritonectomy, however, may be the dosage of CA125 [28,29].

- omentectomy

Omentectomy, especially in advanced cases of the disease, is part of the staging and complete surgical cytoreductive treatment of ovarian neoplasm. A thorough inspection and eccentric exposure (with the help of the Thompson autostatic department) are required to achieve it [30]. However, it appears that in the face of an incipient ovarian neoplasm, with the large normal macroscopic epiploon, omentectomy does not significantly improve survival [31].

Assuming that the large epiploon represents a barrier to the spread of peritoneal carcinomatous cells, the subject of omentectomy in the absence of macroscopic invasion is highly controversial, which is why after some authors a reconsideration of performing routine omentectomy is recommended, especially in early stages. [32].

Even if, following omentectomy and routine multiple peritoneal biopsies in front of normal macroscopic tissues, there is the possibility of ovarian epithelial cancer overestimation by diagnosing HP of microscopic metastases, the management of the adjunct chemotherapeutic post-operative will, in most cases, not be influenced by their presence [33].

Very rarely, there may be an association of early intraoperative staging with isolated macroscopic lesions in the large epiploon. In the face of such a situation it can be considered that it is not absolutely obligatory to perform omentectomy but multiple biopsies may be sufficient [34].

- splenectomy

Only 1-1,3% of the patients operated on ovarian neoplasm undergo splenectomy during the primary surgery, but especially during the interval surgery. The main indication of splenectomy is macroscopic invasion, much less accidental intraoperative trauma. Splenectomy improves overall survival, so it is recommended to be performed in all patients with local invasion, both in primary and secondary surgical cytoreduction [35].

In contrast, in a recently published study, in which 121 patients with ovarian neoplasm (in stages > II of the disease) were followed, it was found that in 47% of cases a rectosigmoidectomy was performed, 23% of small bowel resections and 21% splenectomy [36]. Unfortunately, there is the possibility of recurrence of the disease by splenic metastasis. Following the complete performed paraclinic balance and careful selection of cases, if single metastasis with splenic localization has been found, laparoscopic splenectomy can be attempted, performing secondary surgical cytoreduction [37].

Splenic invasion may associate invasion of the pancreas tail, thus imposing itself alongside splenectomy and distal pancreatectomy [38].

However, it appears that there is significant morbidity of postoperative patients, but it was found that the vast majority of complications could be treated conservatively, with no need for surgical reintervention [39].

- the front sigmoidectomy

Since most patients with ovarian cancer are diagnosed in advanced stages of the disease, the incidence of colonic invasions is approximately 50%, of which the vast majority are located at the rectum-sigmoid level [40].

After recto-sigmoid, a-2 of the most frequent intestinal localization of the ovarian neoplasm is the ileum and the cecum. In the face of advanced intraoperative staging, invasion of both the recto-sigmoid colon and the cecum, and even of the transverse colon can be noted. Although multiple bowel resections can be performed, with or without stoma, the decision of the surgical act depends primarily on the real chance of primary debulking, the length of the remaining colon and the possible postoperative complications with significant morbidity [41]. The intestinal invasion can be summarized at the level of the serosa or it can penetrate in depth, in the lumen and the intestinal mesenter, a situation that requires the intestinal resection. Thus, it is assumed that there is an inverse proportional relationship between the depth of invasion and the chance of survival at 5 years postoperatively [42].

In the face of a macroscopic recto-sigmoid invasion or invasion of the Douglas-sack Fund, block excision of the tumor formation together with recto-sigmoidectomy, as primary debulking is associated with a favorable prognosis [43].

If ovarian mucinous carcinoma is suspected then appendectomy is recommended in order to differentiate between a primary appendicular or ovarian neoplasm [44].

- lymphadenectomy

The lymphatic system carries excess extracellular fluid that can be recirculated or excreted. The lymphatic pathway from the ovaries can be initially through the pelvic stations and subsequently para-aortic or directly para-aortic [45].

The pelvic ganglion stations are divided into anterior and posterior stations by the bifurcation of the common iliac artery (the posterior ones: common iliac, promontory, pararectal and parasacral ganglia: they do not have major importance in surgical excision because they are unapproachable). The anterior pelvic stations are divided into external iliac ganglia (with their lateral, middle and internal chains), internal iliac (hypogastric), common iliac and those in the obturator fossa.

Extrapelvic ganglion stations are divided into para-aortic, lumbar-aortic and pericarp glands. Paraortic lymphadenectomy consists of excision of the lymph nodes between the Aorta and the left ureter from the origin of the inferior mesenteric artery to the middle of the left common iliac artery, as well as of the superior lymph nodes from the inferior vena cava, to the origin of the inferior mesenteric artery to the middle of the artery [46].

In 1988, the International Federation of Obstetrics-Gynecology published a surgical staging of ovarian neoplasm that included pelvic and paraaortic lymph node stations [47].

There are recent studies with controversial conclusions regarding the relapse-free survival following lymphadenectomy in the early stages of the disease: some believe that lymphadenectomy provides a favorable prognosis and others believe that lymphadenectomy can overestimate the cases of disease with unnecessary imposition of " of the postoperative chemotherapy, so only biopsy of the enlarged paraAortic lymph nodes is recommended. Due to the fact that paraAortic systemic lymphadenectomy is associated with significant intra- and postoperative complications at present, international guidelines propose for the early stages of the disease only macroscopically enlarged lymph node biopsy.

However, in the prospective study by Maggioni et al, it was concluded that para-aortic lymphadenectomy performed improved overall survival, but not significantly in order to claim that it is a positive prognostic factor for survival [48].

However, in the situation of the pelvic and para-aortic lymph nodes excised invaders (histopathologically proven) a much improved prognosis was observed both in the short and long term [49].

There are also two methods of approaching the lymph nodes intraoperatively: excision or sampling. The difference between the two methods is the number of lymph nodes approached: more or less than 20 lymph nodes. It appears that patients in stage IIIC / IV disease who had pelvic and aortic lymph node excision had progression-free recurrence and overall survival rate better than those who had only lymph node sampling [50].

- Palliative surgical treatment in ovarian neoplasm

35% of patients with advanced ovarian cancer develop into intestinal occlusion. As a time interval, it was found that this complication most commonly occurs about 2 years after the initial diagnosis and then about 1.5 years after the first relapse of the disease. In most cases, these patients cannot undergo radical surgery, thus opting for palliative surgery - ileostomies / colostomies. Considering that the bio-humoral status of these patients is significantly altered, the frequency of postoperative complications is important: localized abscesses, fistulas and even peritonitis with subsequent septic shock. Another palliative method is the installation of intestinal stents, but in the case of major obstructions this cannot be done [51].

The causes of intestinal occlusion can be multiple: direct tumor invasion of the colon (intrinsic invasion), enlargement of the intra-abdominal tumor (extrinsic invasion), intestinal dysfunction associated with extended peritoneal carcinomatosis, omental tumor development or mesenteric tumor infiltration of the secondary musculoskeletal disorder. In 1983, an index was tried to help select patients to undergo palliative surgery. It is made up of several prognostic criteria: the age of the patient, its nutritional status, the degree of tumor invasion, the presence / absence of ascites and the previous therapeutic management. In principle, surgery is indicated in patients who have a life expectancy longer than 8 weeks, otherwise drug treatment is indicated: example: Haloperidol, Morphine, etc. [52].

Necessary ileostomies or colostomies can be performed classically or laparoscopically. As a rule, if the clinical-paraclinical status of the patient is appropriate, minimally invasive surgery is preferred.

This reduces morbidity and accelerates postoperative recovery. In addition, mobilization of the affected intestinal tract is often difficult, and by laparoscopic approach, this is easier. It is preferable to mount the colostomy on the handle at the expense of the Hartman procedure. The main complications regarding laparoscopic interventions are intestinal injury at the introduction of the trocar (due to postoperative complex adhesion syndrome), postoperative bleeding, stricture-intestinal stenosis, hernia or prolapse of the colostoma and not least its retraction (due to defective colonic mobilization) [53].

Subsequently, a more complex index was tried, having as prognostic factors several criteria: the age of the patient, the time interval between the time of diagnosis of the neoplasia and that of the intestinal occlusion, the type of surgery, radio-chemotherapy protocols to which the patients were subjected, current bio-humoral status (Ht, PSK lymphocytes, albumin), presence / absence of ascites, anatomical location of obstruction, palpation of tumor masses, presence or absence of pain, vomiting. Following the study performed on a batch of 64 cases with intestinal occlusion, of which 70% were treated conservatively and the rest underwent surgery. In conclusion, it was found that although postoperative morbidity was about 10%, these patients had a survival rate (about 2 months) higher than those who underwent conservative treatment (about 8 weeks) [54].

Of all the predictive and prognostic factors listed above, it is considered to be the most important presence / absence of ascites. An important negative predictive factor is the presence of palpation of an abdominal-pelvic formation.

Of all patients with intestinal occlusion, about 20% of the cases were found to be inoperable. However, the vast majority of patients had a survival rate of less than 1 year [55-57].

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