INTRODUCTION

Ovarian cancer remains one of the most aggressive gynecologic malignancies with increasing incidence worldwide; in European women ovarian cancer represents up to 4% of all malignancies and is the sixth most common malignancy related death [1]. It is estimated that more than 75% of cases are diagnosed in advanced stages, respectively FIGO (International Federation of Gynecology and Obstetrics) stages III and IV when disseminated lesions are already present [2]. In all these cases even if a curative treatment consisting of radical surgery followed by adjuvant chemotherapy is performed only 20 up to 25% of patients will become long term survivors [3]. This aspect is especially related to the fact that ovarian cancer has a great capacity of recurrence even in cases in which a complete cytoreduction followed by adjuvant oncologic treatment is performed.
THE PRINCIPLES OF DEBULKING SURGERY

Proposed for the first time by Meigs in 1934 [4] and demonstrated by Griffiths in 1975 [5], the principles of debulking surgery are based on the observation that the long term outcomes of these patients are strongly influenced by the residual tumor. As Meigs himself declared, whenever a complete resection of the tumor is achieved, an improved response to adjuvant irradiation is expected [4]. The benefits of maximal cytoreductive effort were later demonstrated by Griffiths and co. in 1975 who included in their study 102 patients with FIGO stages III and IV ovarian cancers and demonstrated that a residual disease larger than 1,6 cm is associated with a poorer outcome [5]. Once both the surgical technique and the postoperative management of these patients improved, the surgeons worldwide tried to perform an even more radical surgical approach so the optimal residual disease decreased from 1.6 cm to 0.5 cm and even no residual disease [6,7]. This advantage was best suggested by Robert Bristow's metaanalysis published in 2002 and conducted on 6885 patients with advanced stage ovarian cancer; the authors demonstrated that each increase by 10% among patients submitted to maximal cytoreduction is associated with a concomitant increase of 5.5% of the median overall survival [8].

These results, in association with the improvement of the surgical techniques leaded to a wide introduction of various visceral resections as part of debulking surgery. This aggressive surgical approach was also sustained by the observation that in patients necessitating multiple visceral resections in order to achieve cytoreduction to no residual disease the rate of long term survival is similar to cases in which total hysterectomy with bilateral adnexectomy, omentectomy and peritonectomy are performed with curative intent.

DIGESTIVE TRACT RESECTIONS AS PART OF DEBULKING SURGERY

One of the most important characteristics which make ovarian cancer such an aggressive malignancy is the capacity of dissemination using multiple patterns of spread. Most often ovarian cancer cells spread via peritoneal route, leading to the apparition of peritoneal nodules of carcinomatosis, via hematogenous route leading to the apparition of parenchimatous metastases and via lymphatic route leading to the apparition of the lymph node metastases; in the meantime the lymphatic pattern of spread also leads to the apparition of an impaired lymphatic drainage due to the presence of enlarged, metatstatic adenopathies; this fact is responsible for the apparition of ascites. Once a free peritoneal fluid develops in the abdominal cavity, the exfoliated cells will migrate even faster and will lead to the apparition of disseminated lesions on the entire peritoneal surface. Due to all these mechanisms distant metastases with various locations occur and multiple resections are needed in order to achieve a complete cytoreduction. Digestive resections might be needed in order to reduce tumor burden to no macroscopic residual disease, or at least to provide palliation and impede the apparition of obstruction of the digestive tract [9,10,11]. Although initially it has been considered that association of digestive resections might associate
an increased risk of postoperative morbidity, studies have shown that digestive surgery can be safely associated as part of debulking surgery, with similar rates of postoperative complications and similar rates of long term survival [10].

An interesting observation regarding the results of optimal debulking surgery including bowel resections in patients with advanced ovarian cancer comes from Pawel Derlatkaet al. and was published in World Journal of Surgical Oncology in 2016 [12]. The authors demonstrated that the maximum diameter of the tumor involving the bowel is a predictor for the long term outcomes. The authors introduced in their study 33 patients with advanced stage ovarian cancer in whom bowel surgery was needed in order to achieve an optimal cytoreduction. In the present study optimal cytoreduction was defined as residual tumor smaller than 1 cm and was achieved in all cases: in 26 patients debulking surgery was performed to no macroscopic residual disease, in other four cases residual tumor lesser than 0.5 cm was achieved while in the other three cases residual tumor measured 0.5 to 1 cm. the most commonly performed digestive resection was rectosigmoidectomy (in 27 cases), followed by left colectomy (in three cases) and right colectomy in two cases; in one case rectosigmoidectomy was associated with right colectomy. There was no complication related to bowel surgery, a single patient requiring reoperation due to gastric ulcer perforation. After a median follow up of 656.9+/−332.2 days relapse was found in seven cases: five patients reported intraperitoneal spread while the other two cases reported pelvic recurrences. Four patients with recurrent disease died; the mean overall survival was 775.8+/−521.4 days. As for the most important prognostic factors predicting long term outcomes, the authors demonstrated that optimal debulking surgery (to less than 1 cm) and the dimension of the largest tumor infiltrating the bowel had a significant impact. The maximum diameter of the tumor invading the bowel was significantly higher among patients who developed recurrent disease. Other factors such as CA 125 level or time from surgery to chemotherapy onset did not influence the development of recurrent disease. The authors concluded that bowel surgery as part of debulking surgery for advanced stage ovarian cancer can be performed with acceptable rates of postoperative complications and might bring survival benefit; moreover, the maximal dimension of the tumor which invades the bowel seem to be a prognostic factor for recurrent disease [12].

COLIC RESECTION IN OVARIAN CANCER

It is estimated that colic resections are associated with debulking surgery in up to 50% of cases, most commonly encountered resections being rectosigmoidian resection followed by ileocolic resection due to the pelvic location of these viscera, in the close proximity to the genital viscera [13-17]. Other common involved colic segments include transverse colon and left colon, via omental spread. The presence of bulky omental masses usually associate transverse colon invasion necessitating a segmental resection of this segment [13-7]. Moreover, dissemination via omental route might lead to en bloc involvement of the left superior abdominal quadrant creating here the premises of an en bloc resection involving the great gastric curvature, the spleen, the
pancreatic tail and the left colon [18]. However, multiple sites of colic involvement might be seen in the same patient; in these cases multiple colic resections are performed. The most common situation consists of rectosigmoidian and ileocolic involvement; after resection the continuity of the digestive tract will be most probably re-established by creating two anastomoses. In other cases association of ileocolic and transverse colon invasion might impose a single, extended colic resection.

The role of transverse colectomy as part of cytoreductive surgery for ovarian cancer was demonstrated in the study conducted by Robert Bristow and published in 2008 [19]. In this study the author included 39 patients submitted to transverse colectomy as part of primary and secondary cytoreduction. However transverse colectomy was associated with resection of another segment of bowel in 30 patients (76.9%), while 25 of these cases were submitted to a non-contiguous bowel resection necessitating at least two anastomoses in order to re-establish the continuity of the digestive tract. In ten cases small bowel resections were also performed. The most common indication for transverse colectomy was the presence of omental disease infiltrating the transverse colon followed by the presence of bulky tumors into the lesser sac involving the transverse colon mesentery. In 24 cases transverse colectomy was associated with rectosigmoidectomy; among these cases three patients were submitted to an en-bloc resection of the transverse, left colon and rectosigmoidectomy and a single anastomosis while in the other 21 cases two separate resections were performed; in 19 cases two separate anastomoses were performed in order to reestablish the continuity of the remnant colic segments while in the other two patients a terminal left colostomy and one anastomosis were performed. Rectovaginal fistula developed in a case submitted to a contiguous resection of the transverse, left and rectosigmoid colon and in another case submitted to separate resections with two separate anastomosis. The median estimated blood loss was 500 cm³. Residual disease was: no gross in 33.3%, 0.1–1.0 cm in 59.0% of cases, and greater than 1 cm in 7.7% of patients. Post-operative morbidity occurred in 25.6% of patients, with a fistula rate of 5.1% and a mortality rate of 2.6%. a single patient died in the early postoperative outcome due to a pulmonary embolism. The median survival time after primary surgery was 68.3 months. The authors concluded that transverse colectomy can be safely associated to debulking surgery in advanced stage and relapsed ovarian cancer. Moreover, other bowel resections can be safely performed in order to maximise the debulking effort. In these cases the authors demonstrated that the placement of two separate anastomosis is not associated with a significantly higher rate of anastomotic leak [19].

Another harder to manage situation consists of transverse colon and rectosigmoid invasion; in this specific situation preservation of the left colon might be proposed. However, the extent of resection and the number of anastomoses is strongly correlated with factors like location of the tumors, extent of resection, anatomic particularities of the blood supply and the general biological status of the patient [20]. Another particular situation consists of colic invasion at three levels imposing three separate resections and three anastomoses. However this particular condition is
less frequently seen, patient presenting multiple sites of colon invasion being rather candidates for subtotal colectomy with ileo-rectal anastomosis. When it comes to the functionality of ileo-rectal anastomosis, it is widely accepted that good functional outcomes are expected if the length of the rectal stump surpasses 12-14 cm. In all the other situations presenting a shorter rectal stump creation of an ileal pouch followed by ileo-rectal anastomosis seems to be the best therapeutic option [18,20].

In patients presenting colic obstruction due to the presence of bulky tumoral masses the standard therapeutic approach initially consisted of diverting colostomy followed by resection and re-establishing the continuity of the digestive tract in a three step procedure [21]. However, in the last decades this therapeutic sequence was definitively changed, per primam resection followed by anastomosis being performed [22,23].

RECTOSIGMOIDIAN RESECTION AS PART OF DEBULKING SURGERY IN ADVANCED OVARIAN CANCER

Due to its’ close proximity with the ovaries, the rectosigmoid is the most commonly involved segment of the digestive tract in patients with advanced stage ovarian cancer. In these cases the rectosigmoid becomes part of a tumoral mass, also comprising the genital organs and the pelvic peritoneum; in all these cases en block resections might be needed in order to achieve a good local control of the disease [20]. The infiltration of the pelvic peritoneum by the malignant cells is limited by the peritoneal lining of the cul de sac, the low extraperitoneal rectum mainly remaining free of tumoral involvement [24]. Depending on the extent of the pelvic disease, various surgical procedures have been proposed: while in cases presenting a surface involvement of the peritoneal surface of the rectosigmoid peritoneal stripping might be proposed, in cases presenting a more profound invasion en bloc resection of the rectosigmoid might be needed. Some authors consider that a complete tumor resection via peritonectomy is difficult and predisposes to significant complications such as rectal tear or incomplete resection [25]. The surgical technique of en bloc resection was first described in the 60’s and improved in the next decades (13,26); as a result, nowadays in most cases an anastomosis is performed with good acceptable rates of postoperative complications such as anastomotic leak [14-16].

It is estimated that rectosigmoidectomy is associated as part of radical pelvic surgery in up to 47% of patients diagnosed with advanced stage ovarian cancer [27]. Moreover, Brunschwig and Barber reported in 1965 a series of 22 patients submitted to posterior pelvic exenteration in order to achieve a good local control of the disease [26].

In order to evaluate the benefits and the postoperative complications after rectal resections as part of debulking surgery for advanced stage and relapsed ovarian cancer Jeong Yeol Park and co. conducted a study in which they introduced 46 patients with advanced stage ovarian cancer and 14 patients with relapsed ovarian cancer in whom rectosigmoidectomy was performed [28]. Neoadjuvant chemotherapy was performed in 22 cases in which it was estimated that resection
to no residual disease could not be achieved due to the extent of the local invasion. Optimal cytoreduction (defined as residual disease < 5 mm) was achieved in 89.2%. During the early postoperative period two patients developed complications related to rectosigmoid resection: an anastomotic leak and a rectovaginal fistula. The overall postoperative morbidity was strongly correlated with a lower level of serum albumin, with a lower than 20 kg/m2 body index and with the necessity of additional bowel resections. In both cases diverting ostomies were performed; reversal was performed after completing the adjuvant chemotherapeutic protocol. The median disease free survival time was 18 months for patients with advanced stage ovarian cancer while the three year survival rate was 70.3%. As expected, the most important prognostic factor predicting long term survival was cytoreduction to no residual disease. Among the 46 patients submitted to primary cytoreduction there were 33 cases with limited to subserosal invasion and 13 cases with muscularis or mucosal involvement. The depth of rectal wall invasion was strongly correlated with the positivity of para-colic lymph nodes \( (p = 0.014) \) and with a shorter disease free survival \( (p = 0.0176) \). The poor prognosis reported in cases with positivity of para-colic lymph nodes and bowel invasion was also reported by Scarabelliet al.; this fact was explained by Scarabelli by suggesting that in cases presenting ovarian cancer with bowel invasion a concurrent pattern of spread via peri-colic lymph nodes (similarly to patients with colic primaries) might be envisaged. This hypothesis is also sustained by the fact that these patients are more likely to develop distant metastases with hepatic localization [29]; this theory is also sustained by O’Hanlanet al.; their study came to demonstrate that performing a wedge resection in cases presenting limited bowel invasion predisposes to a higher rate of local recurrence [30]. Although muscularis or mucosal invasion were also correlated with a poorer outcome in terms of long term survival, this fact did not reach statistical significance \( (p = 0.0880) \). The presence of muscularis or mucosal invasion was associated with more aggressive tumor biology. The results were compared to the ones reported by a similar group of patients submitted to debulking surgery in the same period of time and by the same surgical teams; however the long term survival was similar between these two subgroups. When it came to the patients submitted to secondary cytoreduction, the median disease free survival was 17 months while the overall survival was 32 months [28]. The authors concluded that rectosigmoidian resections can be safely applied as part of debulking surgery for advanced stage and relapsed ovarian cancer, with acceptable rates of postoperative complications and may improve the overall survival [28].

In another similar study conducted by Obermairet al.regarding the effectiveness and safety of rectosigmoidian resections as part of debulking surgery 65 patients with advanced stage ovarian cancer were included. The authors reported a rate of anastomotic leak of only 3.1%; this low percentage (when compared to the data reported in literature, ranging between 1.25% and 20%) is explained by the authors through a particular technique: the blood supply is interrupted below the origin of the left colic artery [31]. However, this opinion is not unanimously accepted due to the fact that preserving the inferior mesenteric artery might expose to the apparition
of supplementary tension at the level of the anastomosis, impeding a facile mobilization of the superior partner of the anastomosis [28].

When it comes to the possibility of prediction of rectal invasion during the preoperative studies, the same study conducted by Park et al. reported that although flexible colonoscopy had been performed, rectal mucosa invasion was reported only in two cases and suggested that all patients presenting pelvic masses should be informed about the possibility of rectosigmoidian resection. However, the reverse situation can be also encountered; among the 46 patients submitted to rectosigmoidian resection as part of primary cytoreductive surgery, histopathological invasion was certified in 80% of cases. In patients submitted to rectosigmoidian resection as part of secondary cytoreduction the rectal wall invasion was confirmed in 93% of cases. In conclusion, the decision of performing a rectosigmoidian resection should be taken intraoperatively, after a close inspection of the lesion [28].

In order to maximize the effect of debulking surgery in patients presenting rectal invasion and to minimize the postoperative morbidity Kim et al. conducted a study on 61 patients with advanced stage and relapsed ovarian cancer submitted to rectosigmoidian resection with or without anastomosis [25]. Hartmann resection is usually performed in cases with poor prognosis, poor blood supply, residual tumor or with high risk of anastomotic leak due to the anastomotic tension. Among patients submitted to debulking surgery as part of primary cytoreductive surgery anastomosis was performed in 22 cases while Hartmann resection was performed in 15 cases. Among patients submitted to secondary cytoreduction anastomosis was performed in 10 cases while Hartmann resection was the procedure of choice in 14 cases. Postoperative complications and overall survival did not significantly varied either between the two subgroups submitted to primary or secondary cytoreduction. However, among patients submitted to cytoreduction and low rectal anastomosis anastomotic obstruction requiring re-operation and stoma creation developed in 9.1% of patients submitted to primary cytoreduction and 10% of patients submitted to secondary cytoreduction. However this percentage was found to be acceptable when compared to the psychological benefits offered in cases that an external digestive derivation wasn’t necessary. In conclusion, the study demonstrated that there is no significant difference between patients submitted to rectosigmoidian resection and anastomosis versus those submitted to Hartmann resection in terms of postoperative complications and survival outcome. The only significant difference was the one regarding the improved quality of life among cases who benefited from colorectal anastomosis; for this reason the authors expressed their support for anastomosis creation whenever this procedure is feasible [25].

Another important matter of debate regarding the effectiveness and safety of extended pelvic resections in advanced stage ovarian cancer is the one of rectosigmoidian resection versus peritoneal stripping. This controversy regards in special the optimally debulked patients (with residual tumor <1 cm) presenting remnant disease in Douglas pouch. In cases presenting limited,
non-infiltrative lesions peritoneal stripping might be a feasible alternative to the traditional rectosigmoidian resection.

In the study conducted by Alettiet al. published in 2006 the authors included 209 patients with advanced stage ovarian cancer submitted to surgery at the Mayo Clinic between January 1, 1994 and December 31, 1998 [14]. Among these patients rectosigmoidian resection in order to achieve an R0 resection was performed in 57 cases, peritoneal stripping was performed in 71 cases while in other 81 cases pelvic resection was limited to either adnexectomy, hysterectomy or both. Among patients submitted to rectosigmoidectomy anastomotic leak necessitating re-operation developed in a single case. When it comes to the completeness of the resection, in the group of patients submitted to rectosigmoidectomy or peritoneal stripping no residual disease was achieved in 25 patients (19.5%), residual disease less than 1 cm was achieved in 72 cases (56.5%), residual disease between 1 and 2 cm was reported in 18 cases (14%) and residual disease more than 2 cm was reported in 13 cases (10%). Among patients in whom neither rectosigmoidectomy nor peritoneectomy were performed the percent of suboptimally reduced patients was considerably higher: 24 patients (30%) had residual disease between 0 and 1 cm, 14 patients (17%) had a residual disease between 1 and 2 cm, and 43 patients (53%) reported residual disease greater than 2 cm(p<0.001). When analyzing the outcomes of patients cytoreduced to no residual disease submitted to peritoneal stripping or rectosigmoidectomy, the outcomes of patients submitted to rectosigmoidectomy reported an improved overall survival when compared to those submitted to peritoneal stripping (5-year overall survival of 89% versus 50%; p< 0.04). The authors concluded that the poorer outcome of patients’ submitted to peritoneal resection can be explained through the possible underestimation of the local extent of the disease: extensive microscopic disease on the peritoneal surface or partially removed tumor that involved the inner layers of the rectosigmoid [14].

In Galotta’s study 187 patients with advanced stage ovarian cancer submitted to cytoreductive surgery at the Division of Gynaecological Oncology of the Catholic University of Rome and Campobasso between January 2004 and December 2009 were included [32]. Among these patients rectosigmoidian resection was performed in 71 cases while peritoneal resections were performed in the remnant 116 cases. Optimal debulking surgery was defined as residual tumor lesser than 1 cm and was achieved in all cases. After a median follow up of 24 months recurrences were reported in 100 patients: 34 cases (47.9%) in the rectosigmoidian resection group and 66 (56.9%) in the peritoneectomy group (p value= 0.29). when analyzing the main patterns of recurrence, the peritoneal route proved to be the most commonly seen. When it comes to long term outcomes, there was no significant difference in terms of survival for patients submitted to peritonectomy versus patients submitted to rectosigmoidian resections. The authors concluded that the only prognostic factor which significantly influenced survival was the dimension of residual disease (no residual disease versus residual disease <1 cm). However, the rate of pelvic recurrence was significantly higher among patients submitted to pelvic peritoneectomy versus those submitted...
to rectosigmoidectomy (27.3% versus 2.9%, \( p = 0.003 \)). This fact did not significantly influenced survival due to the fact that once the pelvic recurrence was diagnosed; secondary cytoreduction to no residual disease was performed [32].

Another important aspect regarding the colorectal resections as part of debulking surgery in advanced stage or relapsed ovarian cancer is the one regarding the whether to perform an anastomosis or not. It is well known that anastomotic leak after colorectal resection in ovarian cancer is a devastating and even life-threatening complication, with an estimated incidence of 0.8%-3.2% and a mortality rate ranging between 7.3% and 16% [31,33-35]. Traditionally it has been considered that patients submitted to neoadjuvant radiation therapy, long operative times and low distance between the anastomosis and the anal verge are most likely to develop an anastomotic leak. However, other factors such as the preoperative albumin levels and the presence of a diverting stomy have been also incriminated.

In Richardson’s study regarding the risk factors for anastomotic leak after rectosigmoidian resection for ovarian cancer the author included 177 patients [36]. Among these cases the anastomotic leak rate was 6.8% and seemed to be significantly influenced by the serum albumin level. In patients presenting serum albumin levels higher than 3 g/dl the anastomotic leak rate was 0 while in cases presenting lower levels the anastomotic leak rate was 22%. In the meantime, other prognostic factors such as the presence of peritoneal carcinomatosis, addition of other bowel resections, obesity or the moment when rectosigmoidian resection is performed (primary versus secondary cytoreduction) did not significantly influenced the anastomotic leak rate [36].

When it comes to the impact of the distance between the anastomosis and the anal verge, colorectal surgeons consider that low anastomoses (performed at 7 cm or less from the anal verge) constitute an important risk factor for leaks’ apparition. In the meantime in patients submitted to ovarian cancer the level of rectal involvement is usually situated just below the peritoneal reflection, so, in result, most anastomoses will be situated at 7 cm or more from the anal verge. In conclusion, this fact might be responsible for the lower rate of anastomotic leaks after ovarian cancer surgery when compared to colorectal surgery [36].

As for the benefits of diverting stomies, it has been demonstrated that they can decrease the adverse sequelae of leaks without preventing them to occur. In the meantime they can be associated with other complications such as electrolyte disturbance, small bowel obstruction, incisional hernias or wound infections; therefore they are not routinely indicated after rectosigmoidian resections for advanced stage ovarian cancer [37-40].

**POSTERIOR PELVIC EXENTERATION AS PART OF DEBULKING SURGERY FOR ADVANCED STAGE OR RELAPSED OVARIAN CANCER**

Reported for the first time in 1948 by Alexander Brunschwig, pelvic exenteration became the archetype of ultraradical surgery for locally invasive pelvic malignancies [41]. Although initially
it was considered extremely aggressive, its’ benefits were reported by the first patients who had been submitted to this procedure. These patients declared that they do not regret the decision to undergo this operation due to the fact that it provided a significant palliation of the symptoms. In the meantime among the first cases submitted to pelvic exenteration with palliative intent long survivors appeared, so attention was focused on identifying which cases are most suitable for this surgical procedure [41]. When it comes to the role of pelvic exenteration for advanced stage and relapsed ovarian cancer it has been demonstrated that most often a posterior pelvic exenteration might be needed in order to achieve a good local control of the disease. The technique of modified posterior exenteration was described by Hudson and was successfully associated as part of debulking surgery whenever there is no cleavage plane between the posterior surface of the uterus and the anterior surface of the rectum [42].

In order to determine the role of posterior pelvic exenteration for advanced stage ovarian cancer, Herve Tixier et al. conducted a multicentric, retrospective study on 41 patients submitted to posterior pelvic exenteration for advanced stage ovarian cancer from July 1989 to July 2007 [43]. Among these cases the continuity of the digestive tract was reestablished by creating an anastomosis in 34 cases while in the other seven cases a stoma was created. As for the completeness of resection, a macroscopic complete resection was achieved in 19 cases; in other 19 cases residual tumor<2 cm was achieved while in the other three cases residual tumor was larger than 2cm. during the postoperative follow up complication occurred in 14 cases, seven of them needing reoperation. The median overall survival was 33 months (range 20-46 months). During the postoperative follow up 33 of the 41 cases presented evolutive recurrence (31 died, two are alive with evolutive tumors) while the other eight patients were alive without relapse. Disease free survival was significantly lower in cases that required extensive bowel resections and in cases with positive lumbo-aortic lymph nodes. In the meantime the overall survival was significantly influenced by the achievement of optimal surgical resections and by the accomplishment of colorectal continuity during initial surgery. The authors demonstrated that pelvic exenteration for advanced stage ovarian cancer can be safely performed; in the meantime it seems that it does not delay the implementation of adjuvant chemotherapy. As for the performance of rectal anastomosis after resection, it was strongly correlated with the extent of the disease in the sub-peritoneal rectum and with the possibility of creation of an anastomosis in healthy tissue [43].

CONCLUSIONS

Digestive tract resections can be safely associated as part of debulking surgery for advanced stage ovarian cancer, with acceptable rates of postoperative complications. Although the absence of residual disease remains the strongest predictor for long term survival, other prognostic factors such as the diameter of the largest lesion invading the bowel seem to have a significant influence on the long term outcomes.
References


27. Eisenkop SM and Spirios NM: Procedures required to accomplish complete cytoreduction of ovarian cancer: is there a correlation with “biological aggressiveness” and survival? Gynecol Oncol 2001; 82: 435-444.


41. BRUNSCHWIG A. Complete excision of pelvic viscera for advanced carcinoma; a one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into the colon above the colostomy. Cancer. 1948; 1: 177-183.
