INTRODUCTION

Ovarian cancer remains one of the most aggressive gynecologic malignancies especially due to its’ high propensity to spread via multiple routes such as peritoneal, lymphatic and even hematogenous route. The multiple patterns of spread in association with the absence of specific symptoms are responsible for the fact that most patients are diagnosed in an advanced stage of the disease when multiple lesions are already present [1].

However, in the last four decades the principles announced by Meigs [2] in 1934 and demonstrated by Griffiths in 1975 [3] have been successfully applied and a significant number of cases were proposed for debulking surgery. When it comes to the most important factors related to an improved survival after debulking surgery, it seems that the completeness of resection remains the best predictor for an improved outcome. However, this fact is usually obtained only if multiple resections are performed. In these cases, initially a higher rate of postoperative
complications had been advocated, but, due to the improvement of the surgical techniques and of then postoperative management of these cases, these gestures became widely applied with acceptable rates of morbidity [4-6].

In order to establish which are the most important factors which might predict the possibility of obtaining a complete tumoral resection in cases with advanced stage ovarian cancer Fotopoulou et al. conducted a study on 360 patients submitted to debulking surgery at the Charité-Campus Virchow Clinic, Berlin between 09/2001 and 08/2009. The completeness of resection was classified according to the postoperative residual tumor mass (0, <0.5 cm, <1cm, <2cm and >2cm) while the location of tumoral dissemination was quantified according to a validated intra operative documentation tool – “Intra operative Mapping of Ovarian Cancer - IMO”. In multivariate analysis the authors demonstrated that the presence of extended lesions in more than four abdominal quadrants (according to IMO classification) was the strongest predictor factor for incomplete cytoreduction. Other factors such as age, FIGO stage, ascites, operative time, CA 125 levels or histology could not be identified as prognostic factors for complete resectability. Another significant prognostic factor which can predict the completeness of resection was the location of the tumor burden, cases presenting radix mesenterii, splenic (or left colic) flexure and portahepatis involvement being at risk to be submitted to an incomplete cytoreduction. As Fotopoulou study demonstrates, the presence of lower abdominal burden was not identified as a predictive factor for incomplete cytoreduction for advanced stage ovarian cancer [7].

EXTENDED PELVIC RESECTIONS AS PART OF DEBULKING SURGERY FOR ADVANCED STAGE AND RELAPSED OVARIAN CANCER

Once the malignant cells surpass the ovarian surface and exfoliate in the pelvic area, peritoneal nodules of carcinomatosis develop; in this way the other pelvic viscera will be invaded.

The concept of „debulking surgery” has become the standard of care in the last decades in order to achieve a good local control of the disease. When it comes to the applicability of this concept in locally advanced pelvic disease, multiple pelvic viscera might be needed, consisting of an „en bloc” resection of the pelvic tumor including the uterus, the ovaries, the pelvic peritoneum and the rectosigmoid. Depending on the depth of invasion, rectosigmoidectomy or peritonectomy should be performed in order to obtain a complete cytoreduction [8,9]. Due to the high frequency of this situation, the role of sigmoidectomy has been widely investigated in large studies. In this way the concept of “modified posterior pelvic exenteration” developed. The technique, proposed by Hudson is often needed in order to achieve a complete cytoreduction [10], although initially it has been advocated that performing a posterior exenteration and a colorectal anastomosis can become an unacceptable source of postoperative complications such as an anastomatic leaks which might impede the administration of adjuvant chemotherapy [11-13].
Although this surgical technique does not comprise any resection of the urinary tract, urinary bladder dysfunction has been described and has been associated with autonomic nerve injury [14]. While simple hysterectomy and simple rectosigmoidectomy would not theoretically harm the autonomic nerves in pelvis, in radical pelvic resections these structures might be blessed and various bladder dysfunctions might develop [15-20]. The autonomic pelvic nerves which provide a good functionality of the pelvic viscera can be divided in four components: the hypogastric nerves, the pelvic splanchnic nerves, the inferior hypogastric plexus and the peripheral branches of the previously described trunks. In cases presenting locally advanced ovarian cancer, nerve preservation might not be possible due to the tumoral invasion/extension; in these cases urinary dysfunctions such as voiding difficulties, weak urinary stream or stress incontinence might occur [14].

**URINARY TRACT RESECTIONS AS PART OF DEBULKING SURGERY FOR ADVANCED STAGE/RELAPSED OVARIAN CANCER**

When it comes to the role of urinary tract resections as part of debulking surgery, data are scarcer due to the low incidence of this situation. Most often urinary resections for locally advanced or relapsed ovarian cancer are described as collateral surgical procedures for locally advanced tumors with rectosigmoidian resections.

In Plotti’s study conducted at the Department of Gynecology of “La Sapienza” University of Rome data of 154 patients with advanced stage ovarian cancer were analyzed. The patients were separated in two groups according to the type of colorectal surgery performed to approach rectosigmoidian involvement: group A consisted of 82 patients who were submitted to total rectosigmoidian resection while group B consisted of 72 patients submitted to partial rectosigmoidian resection. Among these cases urinary tract resections followed by urinary diversions were also performed in order to maximize the debulking effort. The only complication related to the urinary tract was urinary tract infection which was reported in a single case submitted to partial rectosigmoidectomy [21].

Another study which included segmental urinary tract resections as part of debulking surgery for advanced stage ovarian cancer was the one conducted by Fotopoulou et al. and published in 2010. Among the 360 consecutive patients submitted to cytoreductive surgery for advanced stage ovarian cancer in University Hospital, Berlin, partial resection of the urinary bladder was performed in five cases. At the end of the procedure four of the five cases were debulked to no residual disease while in the fifth case residual tumoral tissue was reported. When it came to the postoperative complication, no urinary tract resection related complication was reported [7].

In order to determine whether extended pelvic resections are justified in patients with advanced stage or recurrent ovarian cancer Jeong Yeol Park et al. introduced in their study 60 patients submitted to multiple visceral resections; 46 cases were submitted to primary cytoreduction for advanced stage ovarian cancer while the other 14 cases were submitted to secondary cytoreduction for recurrent ovarian cancer. Among these cases urinary tract resections...
were performed in three cases at the time of primary cytoreduction (6.5%) and in six cases at the time of secondary cytoreduction (42.9%). The main surgical procedures performed as part of primary cytoreduction consisted of an ureteral mass excision and ureteroneocystostomy in one patient and a ureteral in-dwelling stent in two patients; in the meantime, at the time of secondary cytoreduction the performed urinary tract resections consisted of ureteral mass excision and ureteroureterostomy, a partial cystectomy and ureteroureterostomy, a ureteral in-dwelling stent and a partial pubic bone ostectomy each in 1 patient. When it comes to the early postoperative complications, there was no complications directly related to the urinary tract resections; however a febrile syndrome of unknown origin was reported in 8.7% of cases submitted to primary cytoreduction and 14.6% of cases submitted to secondary cytoreduction [22].

In a similar study conducted by David Silver and Nadim Zgheib the authors included 19 patients submitted to extended colic resections as part of complete cytoreduction for ovarian cancer. Among these cases urinary tract resections were performed in three cases (one patient underwent distal ureterectomy while the other two patients were submitted to partial cystectomy). Although extended colic resections and urinary tract resections were associated there was no case of digestive or urinary tract fistula was reported [23].

In the study conducted by Hoffman et al. conducted on 144 patients diagnosed with advanced stage ovarian cancer partial cystectomies were performed in four cases while partial ureterectomies were performed in three cases. Other associated visceral resections included rectosigmoidectomies, right/ left/transverse colectomies, splenectomies and even partial pancreatectomies. As for the major complications related to these extended surgical procedures, digestive leaks were reported in two cases while ureteral injuries were reported in other two cases. Overall, both the rate of reoperation within the first 30 days postoperatively and the mortality rate were null. The study came to demonstrate the safety and the effectiveness of extended pelvic resections as part of debulking surgery for advanced stage ovarian cancer [24].

When it comes to the issue of urinary tract resection as part of secondary cytoreduction for relapsed ovarian cancer, only few cases have been reported. Most often urinary tract resections are presented as associated visceral resections which can provide a complete cytoreduction to no residual disease. In Robert Bristow’s study conducted in two centers (Kelly Gynecologic Oncology Service at the JHMI in Baltimore, Maryland and the Division of Gynecologic Oncology at the European Institute of Oncology in Milan, Italy) 56 patients were included. Segmental urinary tract resections such as distal ureterectomy or partial cystectomy were performed in eight cases (14.3%). In all cases the continuity of the urinary tract was reestablished by ureteroneocystostomy and psoas hitch, with or without Boari flap. No urinary fistula was reported. As for the completeness of resection, complete cytoreduction to no gross residual disease was achieved in 85.7% of cases, leading in terms of survival to a median overall survival period after secondary cytoreduction of 38.4 months. The authors concluded that extended pelvic resections can be safely performed as part of secondary cytoreduction, with comparable morbidity rates to those reported after primary cytoreduction; in the meantime a similar benefit in terms of survival is to be expected [25].
ASSOCIATION BETWEEN URINARY TRACT RESECTIONS AND INTRAPERITONEAL HYPERThERMIA AS PART OF CYTOREDUCTIVE SURGERY FOR ADVANCED STAGE AND RELAPSED OVARIAN CANCER

The fact that segmental resections of the urinary tract can be associated as part of debulking surgery for advanced stage and relapsed ovarian cancer was also demonstrated by the study conducted by Cascales Campos and published in 2014. The authors introduced in their study 91 cases diagnosed with ovarian peritoneal carcinomatosis and submitted to surgery between January 2008 and July 2011 at Carretera Madrid-Cartagena, Spain. In the meantime in all cases intraperitoneal Hyper Thermic Chemotherapy (HIPEC) with paclitaxel was associated. Among the 91 cases, primary cytoreduction and HIPEC was performed in 22 cases, cytoreductive surgery and HIPEC after neoadjuvant systemic chemotherapy was performed in 38 cases while in the remnant 31 cases secondary cytoreduction and HIPEC were performed. Ureteral resections were performed in three cases while other segmental urinary tract resections were performed in other four cases. HIPEC was associated in all patients. When it comes to the appearance of adverse postoperative events after debulking surgery and HIPEC, urinary tract fistula was encountered in a single patient. However, it seems that urinary tract resections were not associated with a significantly increased risk of postoperative complications. In univariate analysis the impact of an urinary fistula (considered as grade III complication) on the postoperative outcome was associated with a p value of 0.413 for all type complications and 0.549 for grade III-IV complications respectively. The same study demonstrated that while urinary tract resection does not associate a significant risk of postoperative complications, other resections such as colon resections or diaphragmatic resections can significantly impact on the rate of postoperative complications. Other factors such as performing a digestive anastomosis, a higher rate of intraoperative blood transfusion or an increased surgical time were also associated with a poorer outcome at univariate analysis. However, at multivariate analysis none of these factors had prognostic value for postoperative morbidity. These results are particularly important due to the association of HIPEC to these extended procedures; it has been considered that whenever HIPEC is associated other complications related to systemic toxicity of the chemotherapeutic agent are to be expected. The study concluded that the use of HIPEC after aggressive surgical procedures consisting of multiple visceral resections and anastomosis is associated with acceptable rates of postoperative complications [26]. Other authors went even further and tried to demonstrate if urinary tract reconstructions can be safely performed in cases submitted to debulking surgery and HIPEC for peritoneal carcinomatosis originating from various primaries. In the study conducted by Michael Leapman et al. the authors included all patients submitted to debulking surgery and HIPEC for peritoneal carcinomatosis with various origins; the authors identified 34 cases that underwent concomitant urologic reconstructions and were matched by disease burden and extent of surgery with a group of 38 cases without genitourinary involvement. Ovarian primaries were reported...
in 5.9% of cases among patients submitted to genitourinary reconstructions and 13.2% of cases who did not needed urologic resections. The most commonly performed urinary tract resections were partial cystectomies followed by segmental ureteral resections and uretero-ureterostomies. The authors demonstrated that urinary tract resections and reconstructions at the time of cytoreductive surgery and HIPEC are not associated with increased morbidity rates or worsened outcomes. Moreover, the presence of urinary tract involvement did not influence the time to disease recurrence or overall survival [27].

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

Pelvic exenteration as part of the therapeutic strategy in treating advanced pelvic malignancies was first introduced by Brunschwig in 1948 in order to treat advanced stage and relapsed cervical and anal cancer and was purely palliative [28]. However few long term survivors were identified so attention was focused on identifying the patients who could benefit most from this aggressive surgical procedure. In the meantime improvement of the surgical technique and of the postoperative management leaded to a significant decrease of the postoperative morbidity and mortality rate associated with a higher number of patients reporting long term survival [29,30].

Nowadays the most common indications for pelvic exenteration are locally advanced or relapsed cervical cancer, rectal cancer, uterine cancer, vaginal cancer, vulvar cancer, and, less frequent, ovarian cancer.

In Maggioni’s study conducted at the Division of Gynecologic Oncology, European Institute of Oncology in Milan, the authors included 106 patients submitted to pelvic exenteration for persistent or recurrent pelvic malignant tumors. Among these cases pelvic exenteration for advanced stage or relapsed ovarian cancer was performed only in four cases. When it comes to the urinary tract resection as part of pelvic exenteration, it was found in 101 cases and required performing a total pelvic exenteration in 48 cases and anterior pelvic exenteration in 53 cases. As for the main urinary tract reconstructive procedures, continent urinary diversions were performed in 53 cases and consisted of Indiana pouch reconstructions (in 37 cases following total pelvic exenteration and 16 cases following anterior pelvic exenteration) while non-continent urinary diversions were performed in 48 cases and consisted of Wallace II reconstruction in 30 cases, Bricker reconstructions in eight cases, Wallace I reconstructions in four cases, colon conduit in four cases and ureteroneocutaneostomy in two cases. When it comes to the postoperative complications, specific surgical complications related to anterior pelvic exenteration were described in 58.4% of cases while specific complications related to total pelvic exenteration were seen in 66.6% of cases. However there was no postoperative death within the first 30 days from surgery. Although Maggioni’s study was not focused on the special issue of pelvic exenteration for ovarian cancer, these results come to sustain the idea that ultraradical surgical procedures involving the pelvic viscera are perfectly justified in order to achieve a good control of the disease.
in cases presenting locally advanced malignancies. The reduced number of cases necessitating pelvic exenteration for locally advanced or relapsed ovarian cancer remains the main reason why these cases are not treated separately, usually being incorporated in larger studies focused on the idea of extended pelvic resections for locally invasive gynecologic malignancies. In the meantime reported results of these studies can be successfully applied in isolated cases necessitating pelvic exenterations for advanced stage or relapsed ovarian cancer [31].

CONCLUSIONS

Although urinary tract invasion is not a common finding in patients with advanced stage and relapsed ovarian cancer, urinary resections seem to be perfectly justified in order to maximize the debulking effort. In the meantime it has been demonstrated that these surgical procedures can be safely performed with acceptable rates of postoperative complications. Moreover, a significant benefit in terms of survival is expected whenever debulking to no residual disease is achieved.

References

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