# Interval cytoreduction in advanced ovarian cancer: Santa Casa São Paulo experience

## *Citorredução de intervalo no carcinoma avançado do ovário: experiência da Santa Casa de São Paulo*

Renato de Lima Rozenowicz, ACBC-SP[1]; Roberto Euzébio dos Santos[2]; Fabio Francisco Oliveira Rodrigues, TCBC-SP[1]; Ricardo da Fonseca Nadais[4]; Adriana Bitencourt Campaner[5]; Tsutomu Aoki[6]

A B S T R A C T

**Objective**: To analyze the interval cytoreduction in patients with advanced ovarian cancer. **Methods**: A prospective study was carried out with 25 patients with advanced ovarian cancer (stages IIIC or IV) who underwent interval cytoreduction. Non-resectability criteria were based on the ones from Gustave-Rousy Institute. After induction chemotherapy and rapprochement we evaluated the rates of optimal surgery and the morbidity and mortality of the procedure in addition to the overall survival at two years. **Results**: optimal cytoreduction was possible in 17 patients (68%) with morbidity and mortality from 8% to 4%. The overall survival at two years was 68%. **Conclusion**: The interval cytoreduction is an alternative therapy in advanced ovarian cancer, allowing optimal cytoreduction opportunity to patients suffering from unresectable disease, with acceptable morbidity and mortality.

**Key words**: Ovarian Neoplasms. Staging of cancer. Survival analysis. Female.

## INTRODUCTION

Ovarian cancer has the highest fatality rate among gynecological tumors; in Brazil about 3500 new cases/year, with 2000 deaths/year, are estimated[1].

So far there are no effective tracking methods for early detection of this neoplasia, only 25% being diagnosed in early stages. Despite optimal advances in chemotherapy and surgical treatment, the survival rate for ovarian carcinoma has remained steady in recent decades, with a 30% overall survival at five years[2].

Since the pioneering work of Griffiths in 1975 to the present day, numerous studies show that the optimal primary cytoreduction, i.e. the residual tumor less than 1 cm, implies survival gain[3-6]. However, this can only be reached in 50% of patients with advanced disease, not being exempt of morbidity and mortality, 30% and 10% respectively[7].

To improve surgery optimal rates, as well as decrease primary debulking's morbidity, comes the interval laparotomy, which consists of reapproach after neoadjuvant chemotherapy for patients with non-resectable disease or poor result from the first laparotomy[8].

In view of the evidence that present interval laparotomy as a therapeutic option to primary cytoreduction , showing similar survival but with lower morbidity and mortality, we felt motivated to study this approach in patients with advanced carcinoma of the ovary in our institution.

## METHODS

In the period from September 2004 to January 2007, after approval of the Committee of Ethics in Research of Santa Casa de Misericórdia de São Paulo (Protocol number 424/06), we carried out a prospective study of 25 patients with advanced carcinoma of the ovary (IIIC or IV) initially submitted to laparotomy during which non-resectable disease was diagnosed and a biopsy was performed. Irresectability criteria were based on the Institute *Gustave-Rousy*[9], which were the presence of at least one of these factors; resection of more than three segments of

Work conducted on the Oncology Sector, Department of Obstetrics and Gynecology of the Brotherhood of Santa Casa de São Paulo (DOGI-IMSCSP).

1. Assistant Physician, Pelvic Oncology Clinic, Department of Obstetrics and Gynecology, Brotherhood of Santa Casa de São Paulo (IMSCSP)-SP-BR; 2. Assistant Professor, Faculty of Medical Sciences of Santa Casa de São Paulo (FCMSCSP)-SP-BR; 3. Head, Pelvic Oncology Clinic of Department of Obstetrics And Gynecology, Brotherhood of Santa Casa de São Paulo (IMSCSP)-SP-BR; 5. Head, Lower Genital Tract Diseases Clinic, Brotherhood of Santa Casa de São Paulo (IMSCSP)-SP-BR; 6. Director, Department of Obstetrics and Gynecology of the Brotherhood of Santa Casa de São Paulo (IMSCSP)-SP-BR.

intestine, splenopancreatectomy, liver resection, presence of lymph nodes larger than 2 cm, "frozen pelvis", difuse carcinomatosis or invasion of the root of the mesentery.

We employed a neoadjuvant chemotherapy protocol with paclitaxel 175 mg/m$^2$ and carboplatin AUC 5 every 21 days in three cycles. In the sequence, patients were examined and evaluated by abdomen and pelvis CT and CA 125 dosage. In the absence of disease progression, patients were subjected to interval laparotomy with the goal of optimal cytoreduction.

After reapproach we evaluated the rate of optimal surgery, as well as the morbidity and mortality of the procedure and overall survival in two years.

## RESULTS

We were able to perform optimal cytoreduction in 17 patients (68%). The standard procedure, i.e., hysterectomy with bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and omentectomy, was performed in 13 patients, and there was need for extended resection in 12 (Table 1). The results of our initial experience with interval laparotomy are exposed in table 2.

## DISCUSSION

Van der Burg *et al.*[10], comparing interval laparotomy with chemotherapy in 278 patients with stages IIB and IV[11] ovarian carcinoma subjected to initial sub-optimal cytoreduction , observed a disease-free survival in two years of 56% for the group that underwent laparotomy versus 46% for the control group, submitted to chemotherapy alone ($p < 0.01$). They concluded that interval laparotomy presents a gain survival when compared to chemotherapy alone for patients subjected to initial sub-optimal cytoreduction[10]. However, these data has not been demonstrated in the study GOG152[11].

Morice *et al*[12] compared patients subjected to interval laparotomy with the one submitted to primary cytoreduction and obtained optimal cytoreduction rates of 94% in both groups. Nevertheless, morbidity in the interval laparotomy Group was lower than that of primary cytoreduction. After five years of follow-up, the rates of overall survival were 24% in both groups. The authors concluded that, although there is no gain in survival with interval laparotomy, it is an effective therapy option, with less morbidity, for the treatment of advanced ovarian cancer[12].

Chan *et al*[13]. used a EORTC (QLQ-C30) questionnaire to assess the quality of life of patients with stages III and IV submitted to interval laparotomy or primary cytoreduction. They demonstrated that the group submitted to interval laparotomy presented better scores in the questionnaire in relation to the group that received conventional treatment[13].

The purpose of this study was to evaluate the safety and efficacy of interval laparotomy in patients with advanced ovary carcinoma. Using this approach, we obtained cytoreduction in 88% of our patients, agreeing with the data from Onda *et al*[14]. As for the achievement of optimal surgery, our result of 77% (68%) was also consistent with the results found in the literature (50%-90%)[15].

Morbidity of cytoreduction in advanced carcinoma of the ovary is 12% and in our service it was 8%. Perioperative mortality in our series was 4%, similar to the literature data[16].

The need for an extended operation in interval laparotomy results from the more aggressive biological behavior of the tumor, with worse prognosis, and thus interval cytoreduction should only be performed with

**Table 1** - Procedures performed on 12 patients subjected to interval laparotomy with extended operation for carcinoma of ovary.

| Procedure | Number of procedures |
|---|---|
| Splenectomy | 2 |
| Enterectomy | 6 |
| Anterior Rectosigmoidectomy | 7 |
| Distal Pancreatectomy | 1 |
| Total of procedures | 15 |

**Tabela 2 -** Median time of operation, average transfusion units, length of stay (days), number of intraoperative deaths, morbidity, median follow-up (months) and overall survival (%) of patients with ovarian carcinoma subject to interval laparotomy.

| | | |
|---|---|---|
| Median operation time (minutes) | 240 | (200 - 420) |
| Average rate of transfusion (concentrated units of red blood cells) | 2 | (0 - 4) |
| Median time of hospitalization (days) | 7 | (6 - 9) |
| Perioperative Death | 1 | (4%) |
| Evisceration followed by resuturing (morbidity) | 2 | (8%) |
| Median Follow-up (months) | 24 | (6 - 36) |
| Overall survival (%) | 68 | |

standard procedures[17]. In this case extended resection was necessary in 48% of patients, and optimal cytoreduction occurred in 83%.

Our median of overall survival after 24 months was 68%, a result that corroborates with previous studies[18].

Our data suggest that the interval cytoreduction is an alternate therapy in advanced carcinoma of the ovary, enabling an opportunity of optimal surgery for patients with formerly non-resectable disease, with acceptable morbidity and mortality.

## R E S U M O

***Objetivo:*** *Analisar a citorredução de intervalo em pacientes com carcinoma avançado do ovário.* ***Métodos:*** *Estudo prospectivo com 25 pacientes portadoras de carcinoma avançado do ovário (IIIC ou IV) submetidas à citorredução de intervalo. Os critérios de irresecabilidade foram baseados nos do Instituto* Gustave-Rousy. *Após quimioterapia de indução e reabordagem avaliamos as taxas de cirurgia ótima e a morbi-mortalidade do procedimento além da sobrevida global em dois anos.* ***Resultados:*** *Foi possível citorreduçao ótima em 17 pacientes (68%) com morbidade de 8% e mortalidade de 4%. A sobrevida global em dois anos foi de 68%.* ***Conclusão:*** *A citorredução de intervalo constitui alternativa terapêutica no carcinoma avançado do ovário possibilitando oportunidade de citoredução ótima a pacientes outrora portadoras de doença irressecável, com morbi-mortalidade aceitável.*

***Descritores:*** *Neoplasias Ovarianas. Estadiamento de neoplasia. Análise de sobrevida. Feminino.*

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**Mailing address:**
Renato de Lima Rozenowicz
E-mail: rozenowicz.r@uol.com.br