

## Comparison of optimal cytoreduction rates in emergency versus non-emergency admissions for advanced ovarian cancer: A multi-institutional study

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### Abstract

**Aims:** to investigate whether first referral to the Emergency Department (ED) of a General Hospital is an independent risk-factor for sub-optimal debulking compared to a similar population electively admitted to cytoreductive surgery, in a cohort of 307 AOC patients.

**Methods:** this is a multicentre case–control study, analyzing a cohort of 307 AOC patients treated at San Raffaele Hospital of Milan (111 Center A) and Gemelli Hospital of Rome (196 Center B) between January 2006/2008 and December 2010. Women are classified as patients admitted to the Hospital from ED (Cases) and out-patients (Controls).

**Results:** At univariate analysis, Cases significantly differ from Controls in terms of worse ECOG PS, larger ascites, pleuric effusion and peritoneal carcinomatosis. The rate of optimal cytoreduction is statistically lower in the Cases than Controls. At multivariate analysis, significant independent predictors for suboptimal residual disease resulted ED admission, peritoneal carcinosis and mesenteral involvement, supra radical surgery.

**Conclusions:** Patients admitted from Emergency Department may have a lower likelihood of optimal cytoreduction, due to their poor clinical characteristics and large diffusion of the disease.

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**Keywords:** Ovarian cancer; Emergency admission; Cytoreduction; Performance status; Residual disease

### Introduction

Ovarian cancer is the most common cause of death among women with gynecologic cancer.<sup>1</sup> The majority of patients present with advanced stage disease and their standard treatment consists of primary cytoreductive surgery followed by platinum-based chemotherapy.<sup>2</sup>

Achieving resection of all macroscopic disease to lesions < 1 cm,<sup>3</sup> and preferably complete resection,<sup>4</sup> offers the best prognosis for women with advanced ovarian cancer (AOC) in terms of survival. In fact, the extent of residual

disease at the end of surgery has been recognized as the most powerful survival determinant in these patients.<sup>5,6</sup> The rate of complete cytoreduction in AOC has been reported to widely vary between 25% to more than 90% in different centers.<sup>7</sup> It has been shown to be surgeon/institution dependent,<sup>8</sup> but it also correlates with the dissemination of the tumor itself<sup>9</sup> and with patient's clinical condition to tolerate extensive surgical procedures.<sup>10</sup> Indeed, some patients seem to have disease that is too extensive to be completely removed, whereas others are too medically sick to initially undergo any type of abdominal surgery.<sup>11</sup> Recently, some factors, such as stage IV disease, age  $\geq 75$  years old, ASA score  $\geq 3$ , and pre-operative albumin serum levels  $\leq 3.0$  g/dl, have been related to poor surgical outcome in AOC patients.<sup>12–15</sup> Although a large proportion of advanced ovarian cancer patients, with poor performance status, distressing symptoms and extensive disease, first instance refer to the Emergency Department, the modality of admission to the Hospital has never been

*Abbreviations:* (AOC), advanced ovarian cancer; (ED), emergency admission; (ASA), American Society of Anesthesiologists; (ECOG), Eastern Cooperative Oncology Group; (PS), performance status.

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taken into consideration with respect to the chances of optimal cytoreduction.

We therefore undertook the current study with to investigate whether first referral to the Emergency Department (ED) of a General Hospital is an independent risk-factor for suboptimal debulking when compared to a similar population electively admitted to cytoreductive surgery.

### *Patients and methods*

The current study is a multicentric case–control study concerning AOC patients managed in two different Italian Scientific Institutes, specialized in gynecological cancers' care, both endowed with high-flow patients' Emergency Department.

A series of 111 and 196 AOC patients, treated at San Raffaele Hospital of Milan (Center A) and Gemelli Hospital of Rome (Center B) from January 2006/2008 to December 2010 was retrospectively analyzed. Two groups of women were identified: patients admitted to the Hospital from ED (Cases) and out-patients (Controls). Main causes of admission from ED were (sub)occlusion, NS-AID refractory abdominal pain, severe dyspnea. Controls were ovarian cancer patients recruited in the study period, after a gynecologic oncology consultation and planned for elective surgical treatment. The diagnosis of suspect AOC was made by preoperative examination (CA 125 levels, pelvic ultrasound, CT scan of pelvis and abdomen) and confirmed by histology. Women with non-epithelial histology of tumor, a history of prior or concomitant cancer were excluded.

Informed consent was obtained from the patients to collect and analyze their data retrospectively. San Raffaele Hospital and Gemelli Hospital's Institutional Review Board (IRB) approved the study.

Patient and tumor characteristics, intra-operative findings and surgical outcome were analyzed in each Group, in both Centers.

Data on the following preoperative variables were collected: patients' age, admission to the hospital (ED vs. elective admission), ASA (American Society of Anesthesiologists) score, performance status according to Eastern Cooperative Oncology Group (ECOG) performance status, patients' serum albumin levels.

Status of disease was obtained from surgical exploration notes. Patients having tumor nodules diffused on the majority of the bowel, parietal peritoneum of the abdomen and pelvis, diaphragm and mesentery were considered to have carcinosis. Women with large nodules retracting the root of the mesentery were classified as having mesentery involvement. Disease at the level of hepatic hilus and spleen was also described. Presence of ascites and pleuric effusion were recorded as well.

Patients admitted from ED underwent surgery after preoperative biochemical and imaging evaluation (CA 125, serum albumin levels, chest x-ray; abdomen CT scan, pelvic

ultrasound and possibly abdomen x-ray). During the days between admission and surgery, cases underwent preoperative evaluation and their clinical condition were stabilized (i.e. liquid infusion or liquid diet in (sub)occlusion cases, pain treatment and possibly drainage of massive pleural effusion and ascites based on specific clinical conditions. All patients underwent primary surgical exploration.

In the absence of standard criteria of unresectability,<sup>16,17</sup> an optimal debulking was attempted. Standard surgery included: peritoneal cytology, total abdominal hysterectomy and bilateral salpingo-oophorectomy, total omentectomy, pelvic and aortic lymphadenectomy and resection of all visible and palpable bulky tumors. Radical or supra-radical procedures,<sup>18</sup> such as bowel, pancreas or liver resection, splenectomy, diaphragmatic stripping or resection, were also performed in case of diffuse disease in the abdomen. At the end of surgery, residual tumor was registered. Optimal cytoreduction was defined as residual disease 1 cm or less.

Surgical staging and grading were defined according to the International Federation of Obstetricians and Gynecologists (FIGO system).<sup>19</sup>

### **Statistical analysis**

Statistical analysis was performed toward identifying risk-factors for suboptimal cytoreduction in AOC patients. We did not perform any survival evaluation in our patients, since it was outside of the aim of this study.

Univariate analysis was carried out to verify any clinical and surgical difference between Cases and Controls. To this purpose, variables regarding patients' characteristics were dichotomized in the following manner: age less or more than 65 years old; elective admission to hospital versus hospitalization for emergency, ASA status (American Society of Anesthesiology physical status grades) 1 and 2 versus 3 and 4; ECOG 0 and 1 versus ECOG  $\geq$  2; pre-operative CA 125 value less than 750 U/ml; amount of ascites less than 1000 ml; serous subtype versus other histological subtypes (i.e. mucinous, endometrioid, mixed); residual disease less than 1 cm; type of surgical procedures (standard vs. others).

The Student's *t*-test, Mann–Whitney test, Fisher's exact test, chi-square analysis were performed where occurred.

Multivariate analysis with a full/enter method was applied to identify parameters associated with the probability to achieve optimal resection. The following significant variable at univariate analysis were included: ECOG PS, ASA score, presence of ascites and pleural effusion, peritoneal carcinosis, mesenteric involvement, (supra)radical surgery. ED admission was also taken, whereas median albumin serum level was excluded due to the high number of missing values. Corresponding odds ratios are presented with their 95% confidence intervals. As post-hoc analysis, to check how closely the observed and predicted probabilities matching, we use the "Hosmer–Lemeshow Test". The null hypothesis is "the

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