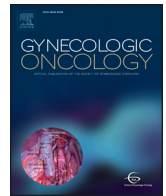




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Review Article

Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian cancer reported to have undergone optimal surgical cytoreduction: An NRG Oncology/Gynecologic Oncology Group study☆☆☆☆☆☆

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HIGHLIGHTS

- A 40% discordance was identified between surgeon and CT imaging with respect to residual disease.
- The most frequently identified areas of discordance include the retroperitoneum and upper abdomen.
- Objective measures of residual disease volume should be explored.

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ABSTRACT

Purpose. We sought to determine the level of concordance among surgeons' assessment of residual disease (RD) and pre-treatment computed tomography (CT) findings among women who underwent optimal surgical cytoreduction for advanced stage ovarian cancer.

Methods. This is a post-trial ad hoc analysis of a phase 3 randomized clinical trial evaluating the impact of bevacizumab in primary and maintenance therapy for patients with advanced stage ovarian cancer following surgical cytoreduction. All subjects underwent imaging of the chest/abdomen/pelvis to establish a post-surgical baseline prior to the initiation of chemotherapy. Information collected on trial was utilized to compare surgeon's operative assessment of RD, to pre-treatment imaging.

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Results. Of 1873 enrolled patients, surgical outcome was described as optimal ($RD \leq 1$ cm) in 639 subjects. Twelve patients were excluded as they did not have a baseline, pretreatment imaging, leaving 627 participants for analysis. The average interval from surgery to baseline scan was 26 days (range: 1–109). In 251 cases (40%), the post-operative scan was discordant with surgeon assessment, demonstrating $RD > 1$ cm in size. $RD > 1$ cm was most commonly identified in the right upper quadrant (28.4%), retroperitoneal para-aortic lymph nodes ($RD > 1.5$ cm; 28.2%) and the left upper quadrant (10.7%). Patients with $RD > 1$ cm on pre-treatment CT (discordant) exhibited a significantly greater risk of disease progression (HR 1.30; 95% CI 1.08–1.56; $p = 0.0059$).

Conclusions. Among patients reported to have undergone optimal cytoreduction, 40% were found to have lesions > 1 cm on postoperative, pretreatment imaging. Although inflammatory changes and/or rapid tumor regrowth could account for the discordance, the impact on PFS and distribution of RD may suggest underestimation by the operating surgeon.

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1. Introduction

Epithelial ovarian cancer (EOC) remains the most lethal gynecologic malignancy. In 2017, there will be an estimated 22,440 new ovarian cancer cases in the United States with 14,080 deaths [1]. Advanced stage disease is traditionally managed with surgery, followed by platinum and taxane-based combination chemotherapy [2]. Several factors have been identified as prognostic for clinical outcome in patients with EOC, with extent of residual disease being investigated in numerous studies [3]. The prognostic implication of optimal cytoreduction has been extensively reported in the literature, with a survival benefit described in both retrospective and non-randomized prospective studies beginning with Griffith's landmark publication in 1975 [3–6]. Most recently, Landrum et al. detailed the survival outcomes of patients with no visible residual disease treated with intraperitoneal chemotherapy, reporting a median overall survival of 110 months [7]. Several other authors have also validated these findings [8,9].

Although various cutoff values have been used to define “optimal” cytoreduction, NRG Oncology currently defines optimal residual disease as 1 cm or less in largest diameter after completion of cytoreductive surgery [10]. In addition to the prognostic implications discussed above, extent of residual disease may impact decisions regarding adjuvant therapy, eligibility for enrollment in clinical trials as well as the interpretation of clinical trial results [11].

Currently, the extent of disease remaining at the completion of primary surgery is determined in a subjective manner, and not confirmed by objective means. The operating surgeon relies on visual inspection and palpation, which are limited by patient body habitus, incision size, and location of disease. Furthermore, significant interobserver variability in tumor measurements has been previously reported [12]. To date, two single institution exploratory studies have been conducted examining the relationship between surgeon and imaging based assessment of residual disease. There was a consistently reported 40% discordance between surgeon assessment and baseline, pre-treatment computed tomography scan [13,14].

Given the potential prognostic and therapeutic implications of residual disease volume, exploring the ability of the operating surgeon to accurately describe the extent of residual disease is warranted. The aim of

this study was to explore the correlation between post-operative computed tomography scan and operating surgeon assessment of residual disease in patients with EOC who underwent primary surgical cytoreduction to ≤ 1 cm of residual disease on GOG protocol 218.

2. Materials and methods

2.1. Background on GOG protocol 218

Gynecologic Oncology Group (GOG) protocol 218, was a randomized phase 3, double blind, placebo-controlled study developed to evaluate the impact of bevacizumab in primary and maintenance therapy for patients with newly diagnosed International Federation of Gynecology and Obstetrics (FIGO) stage III and IV ovarian, fallopian tube or primary peritoneal cancer who underwent maximal effort cytoreductive surgery [15]. Patients with stage III disease and residual lesions less than 1 cm in maximal diameter (as reported by operating physician) were initially excluded, but following protocol modification in July 2007, were permitted to enroll on study.

Patients were required to enroll between 1 and 12 weeks following surgery. All subjects underwent imaging (magnetic resonance imaging or computed tomography scan) of at least the abdomen and pelvis to establish a post-surgical baseline prior to the initiation of chemotherapy, and within 4 weeks of registration. Measurable lesions on radiographic imaging were defined as ≥ 10 mm in at least one dimension. CT scans were performed with contiguous cuts of 5 mm or less in slice thickness, with a contiguous reconstruction algorithm. Disease was assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) [16].

2.2. Ancillary data statistical analysis

Data regarding residual disease volume (as assessed by operating surgeon), disease location, and radiographic findings on baseline pre-treatment CT scan were abstracted from the surgical reporting form (form C version 2), the surgical status form (SRGSTAT), and pre-treatment summary form (form DR version 5). Patients with FIGO stage III EOC who were reported to have undergone surgical cytoreduction to ≤ 1 cm residual disease ($n = 639$) subsequently

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