Gynecologic Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

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☆,☆☆,☆☆☆

Ramez N. Eskander [a,*], James Kauderer [b], Krishnansu S. Tewari [c], Robert S. Mannel [d], Robert E. Bristow [c], David M. O'Malley [e], Stephen C. Rubin [f,m], Gretchen E. Glaser [g], Chad A. Hamilton [h], Keiichi Fujiwara [i], Warner K. Huh [j], Frederick Ueland [k], Jean-Marie Stephan [l], Robert A. Burger [f]

[a] University of California, San Diego Medical Center, La Jolla, CA, United States
[b] NRG Statistics and Data Management Center, Roswell Park Cancer Institute, Buffalo, NY, United States
[c] University of California, Irvine Medical Center, Orange, CA, United States
[d] University of Oklahoma, Oklahoma City, OK, United States
[e] Ohio State University and Wexner Medical Center, Columbus, OH, United States
[f] University of Pennsylvania, Philadelphia, PA, United States
[g] Mayo Clinic, Rochester, MN, United States
[h] Gynecologic Cancer Center of Excellence, John P. Murtha Cancer Center, Walter Reed National Military Medical Center and Uniformed Services University of the Health Sciences, Bethesda, MD, United States
[i] Saitama Medical University International Medical Center, Saitama, Japan
[j] University of Alabama Medical Center, Birmingham, AL, United States
[k] University of Kentucky Medical Center, Lexington, KY, United States
[l] University of Iowa Hospital; Iowa City, IA, United States
[m] Chief of Gynecologic Oncology at Fox Chase Cancer Center, Philadelphia, PA

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.

ARTICLE INFO

Article history:
Received 19 January 2018
Received in revised form 7 March 2018
Accepted 9 March 2018
Available online xxxx

Keywords:
Surgeon's assessment
Radiographic evaluation

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.

☆ This study was supported by National Cancer Institute grants NRG Oncology SDMC grant U10 CA180822 and the NRG Oncology Operations grant U10 CA180868. The clinical trial upon which this manuscript is based was sponsored by the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI), under the Collaborative Research and Development Agreement (CRADA) for bevacizumab between NCI and Genentech, Inc.

☆☆ NCT00262847

☆☆☆ Abstract was presented on March 28, 2015 at the 46th Annual SGO Meeting on Women's Cancer held in Chicago, IL.

* Corresponding author at: Division of Gynecologic Oncology, Department of Obstetrics, Gynecology & Reproductive Sciences, University of California San Diego, 3855 Health Sciences Drive, La Jolla, CA 92093, United States.

E-mail addresses: Reskander@ucsd.edu (R.N. Eskander), kaudererJ@NRGOncology.org (J. Kauderer), ktewari@uci.edu (K.S. Tewari), Robert_Mannel@ouhsc.edu (R.S. Mannel), rbristow@uci.edu (R.E. Bristow), omalley.46@osu.edu (D.M. O'Malley), Stephen.rubin@fccc.edu (S.C. Rubin), Glaser.Gretchen@mayo.edu (G.E. Glaser), chad.a.hamilton2.mil@mail.mil (C.A. Hamilton), whuh@uabmc.edu (W.K. Huh), fuela0@uky.edu (F. Ueland), jean-marie-stephan@uiowa.edu (J.-M. Stephan), burgerr@uphs.upenn.edu (R.A. Burger).

https://doi.org/10.1016/j.ygyno.2018.03.043
0090-8258/

Ovarian cancer
Surgical cytoreduction
NRG
GOG

Results. Of 1873 enrolled patients, surgical outcome was described as optimal (RD ≤ 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 pretreatment CT scan were abstracted from the surgical reporting form (form C version 2), the surgical status form (SRGSTAT), and pretreatment 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

Please cite this article as: R.N. Eskander, et al., Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian canc..., Gynecol Oncol (2018), https://doi.org/10.1016/j.ygyno.2018.03.043