I would like to compliment the authors on their comprehensive review of cytoreductive surgery for ovarian cancer. However, some of their interpretation of the literature warrants amplification, and some conclusions merit presentation of an alternative perspective.

**Presurgical Tumor Burden**
Understandably, "optimal" cytoreduction is more easily accomplished for small tumor burdens than large ones. However, as indicated in the review, ovarian cancer with extensive intra-abdominal disease is suggested to have a natural history that is unalterable due to "tumor biology," even if "optimal" cytoreduction is achieved.[1-4] Unfortunately, the literature correlating the extent of intra-abdominal disease present before cytoreduction with subsequent survival has flaws that Drs. McCreath and Chi have not addressed. As noted in the review, Hoskins et al reported a better median survival for patients cytoreduced to ≤ 1 cm of residual disease if the extrapelvic disease was ≤ 1 cm in largest dimension before cytoreduction than for patients with extrapelvic disease > 1 cm in largest dimension before cytoreduction, and concluded that innate biologic properties of the disease, as manifested by the extent of intra-abdominal tumor burden, may play a greater role in determining prognosis than treatment.[2] However, the percentage of patients in each group with excision of all visible disease was not reported. All visible disease was probably excised in a higher percentage of those with small-volume disease before surgery than of those with extensive disease to resect. Because excision of all visible disease has a more significant influence on survival than an "optimal" outcome of ≤ 1 cm residual disease, as reported by numerous investigators, then stratification by any parameter producing subgroups with dissimilar cytoreductive outcomes cannot produce equivalent survival.[5-8] Hence, the superior survival noted for patients with small-volume disease before surgery probably reflects more complete cytoreduction within that group rather than differences in tumor biology. Our group recently reported a prospective investigation in 408 patients with stage IIIC epithelial ovarian cancer for whom a ranking system was developed to quantify the extent of intra-abdominal disease at multiple locations before cytoreduction.[7] Cytoreduction to a visibly diseasefree outcome had a more significant influence on survival (P = .001) than the extent of metastatic disease present before surgery (P = .05). Although "aggressive" or unfavorable tumor biology, as defined by a diminished possibility of significantly altering the natural history of the disease by treatment, may play a more significant role in determining survival than the operative outcome for some patients, the extent of intra-abdominal disease before surgery does not correlate with tumor biology predictably enough to influence treatment strategies.[7]

**Optimal Cytoreduction**
The authors acknowledge a range of criteria to define optimal cytoreduction in the literature and indicate that the Gynecologic Oncology Group defines this parameter as ≤ 1 cm of residual disease. However, little insight is given as to why specific thresholds are used to define optimal cytoreduction by different individuals. In all probability, these different criteria are used as a result of personal beliefs about the feasibility of achieving specific operative outcomes and traditional training, rather than correlation of operative outcomes with survival.[9] Clearly, a visibly disease-free operative outcome is associated with the highest probability of long-term survival or cure, has been shown to be achievable for the majority of patients with advanced-stage disease, and should probably be used to define optimal cytoreduction in the future.[5-8,10] Efforts should be made to acquire and use all available techniques to achieve complete cytoreduction primarily, as it is feasible.[7,10]

**Neoadjuvant Chemotherapy**
The authors note the purpose of neoadjuvant chemotherapy to be reduction of the extent of intraabdominal disease before interval cytoreductive surgery, thus diminishing morbidity and facilitating "optimal" cytoreduction by reducing the extent of surgery required. They acknowledge that overall median survival following neoadjuvant chemotherapy and interval surgery does not approach the median survival achieved with primary surgery and adjunctive chemotherapy. Indeed,
throughout the cytoreductive literature, patients with advanced epithelial ovarian cancer whose macroscopic disease is completely resected before chemotherapy, as well as those with ≤ 1 cm of residual disease, are reported to have better median and 5-year survivals than patients with equivalent operative outcomes after interval cytoreduction following neoadjuvant chemotherapy.[5-8,11-13] A theoretical disadvantage associated with neoadjuvant chemotherapy is the possibility of metastatic disease developing drug resistance during exposure to cytotoxic agents. Hence, residual disease after interval cytoreductive surgery may have an increased probability of resistance to chemotherapy compared to residual disease after primary cytoreductive surgery. Although available data may justify neoadjuvant chemotherapy in patients with absolute contraindications to surgery and findings that conclusively preclude complete or optimal cytoreduction, correlation of specific radiographic and/or laparoscopic observations with primary cytoreductive outcomes has undergone minimal investigation. Given the significant variation in both the ability to perform specific procedures described to facilitate cytoreduction and opinion concerning applicability of the procedures among gynecologic oncologists, it is possible that the probability of complete or optimal primary cytoreduction is more significantly influenced by the operating physician than by any specific radiographic or laparoscopic finding.[9] In light of the fact that reports of neoadjuvant chemotherapy and interval cytoreduction have not duplicated the more favorable outcomes of primary cytoreductive surgery and adjunctive chemotherapy, the appropriateness of undertaking a phase III trial comparing the outcomes of neoadjuvant chemotherapy/interval cytoreduction to those achieved with primary cytoreductive surgery/adjunctive chemotherapy remains questionable. Finally, because patients who undergo both complete primary and interval cytoreduction achieve a better survival than corresponding patients with small-volume (≤ 1-2 cm) visible residual disease following either strategy, any prospective investigation without a visibly disease-free surgical objective may not determine the most efficacious treatment strategy with acceptable morbidity.[5-8,11-13]

**Surgery at Expert Centers**

McCreath and Chi summarize the status of cytoreductive surgery admirably but indicate that the extent of surgery necessary during cytoreductive operations justifies performing the procedures at "expert centers." Although such an idealistic recommendation may be politically correct, suggestions such as this one distract attention from the fundamental issue of the importance of involving a gynecologic oncologist in the care of all women with genital cancers, and ovarian cancer in particular. Available data indicate that the treating physician is more important to the outcome than the institution.[5-7,9,10,14] "Private practitioners" and "academicians" should cooperate as a team to facilitate the treatment of all women with ovarian cancer by gynecologic oncologists.

**Disclosures:** The author has no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

**References:**


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