

Minimally invasive interval cytoreductive surgery: it's time for a randomized trial

Alexander Melamed,¹ Jose Alejandro Rauh-Hain^{2,3}

¹Department of Obstetrics and Gynecology and Herbert Irving Comprehensive Cancer Center, Columbia University, New York Presbyterian Hospital, New York City, New York, USA

²Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States

³Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States

Correspondence to

Dr Jose Alejandro Rauh-Hain, Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; jarauh@mdanderson.org

Received 26 September 2019
Accepted 27 September 2019



► <http://dx.doi.org/10.1136/ijgc-2019-000413>



© IGCS and ESGO 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Melamed A, Rauh-Hain JA. *Int J Gynecol Cancer* 2019;**29**:1339–1340.

The role of minimally invasive surgery in the management of epithelial ovarian cancer has expanded remarkably in the last two decades. From an era when experts cautioned against the use of laparoscopy in all cases of suspected ovarian cancer,¹ we have arrived at a period where National Comprehensive Cancer Network Guidelines acknowledge the utility of minimally invasive surgery for managing early-stage disease, assessing the feasibility of cytoreduction, and performing interval cytoreductive surgery for advanced-stage disease after neoadjuvant chemotherapy.² While the feasibility of minimally invasive surgery interval cytoreductive surgery, in well-selected patients, has been demonstrated in several non-randomized studies, this application of minimally invasive surgery remains most controversial among its uses in the management of ovarian cancer.

In this issue of the *International Journal of Gynecological Cancer*, Abitbol *et al* provide further evidence that minimally invasive surgery cytoreduction is feasible, and may be safe, in advanced-stage ovarian cancer patients treated with neoadjuvant chemotherapy.³ The authors described their institutional experience of 91 patients who were selected to undergo interval cytoreduction either via robotic surgery or laparotomy after clinical response to neoadjuvant chemotherapy. Consistent with prior studies, the median survival was not significantly different between patients who underwent minimally invasive surgery interval cytoreduction compared with patients who had a laparotomy. Furthermore, all patients selected to undergo interval robotic debulking surgery achieved optimal cytoreduction to less than 1 cm, of whom 82% had no gross residual disease.

These promising findings add to a growing literature suggesting that minimally invasive surgery interval cytoreduction may be a reasonable approach for some patients with advanced ovarian cancer. For example, in a prospective observational study of 30 women with clinical response to neoadjuvant chemotherapy, Gueli Alletti *et al* performed minimally invasive surgery cytoreduction, and achieved resection of all visible disease in 29 women.⁴ Melamed *et al*⁵ compared 450 women who underwent minimally invasive surgery interval cytoreduction with 2621 women who underwent laparotomy in the National

Cancer Database, and found no difference in overall survival between the groups. In a multi-center observational study of 127 patients who underwent minimally invasive surgery cytoreduction after neoadjuvant chemotherapy, Fagotti *et al* found a median progression-free survival of 23 months and a 5 year overall survival rate of 52%.⁶

It is important to consider the study by Abitbol *et al*,³ and other non-randomized studies evaluating minimally invasive surgery interval cytoreductive surgery, in light of their common limitations. First, patients selected to undergo minimally invasive surgery may have had a better response to neoadjuvant chemotherapy than those who receive open cytoreductive surgery. Second, patients who undergo minimally invasive surgery may belong to a more recent cohort than the patients treated with open surgery with whom they are compared, leading to bias due to advances in systemic and supportive care. Finally, small studies and those with limited follow-up may be underpowered to detect clinically meaningful differences in survival between minimally invasive surgery and open surgery.

Of further concern, studies that have investigated minimally invasive surgery in other anatomic sites have yielded contradictory results. Among women with early-stage endometrial cancer, minimally invasive surgery improves perioperative outcomes without impairing survival,⁷ whereas in early-stage cervical cancer, minimally invasive surgery radical hysterectomy, until recently the standard approach, is inferior to open radical hysterectomy.⁸ There are also concerns regarding technical aspects of minimally invasive surgery interval cytoreductive surgery, such as the inability to assess completely the abdominal cavity, which raises the question of whether the approach can yield the same rates of complete resection compared with an open approach. Despite these concerns the use of minimally invasive surgery for interval cytoreductive surgeries is on the rise, reaching 21% in 2016 (Figure 1).

Rather than providing a rationale for widespread adoption, the study by Abitbol *et al* provides additional justification for proceeding with a prospective randomized trial evaluating the oncologic efficacy of minimally invasive surgery cytoreductive surgery.

Editorial

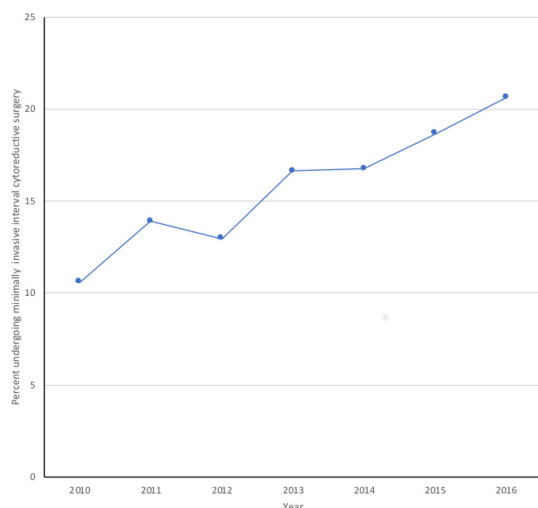


Figure 1 Trends in the use of minimally invasive surgery among women with stage IIIC and IV epithelial ovarian cancer undergoing cytoreductive surgery after neoadjuvant chemotherapy. Source: National Cancer Database, public use file 2016.

Within the next 6 months, the Laparoscopic Cytoreduction After Neoadjuvant Chemotherapy (LANCE) trial will begin enrollment. This is a multi-center, international, non-inferiority trial comparing disease-free survival between minimally invasive surgery and open surgery in patients with advanced-stage epithelial ovarian cancer who have a complete or partial response to neoadjuvant chemotherapy. Rather than accepting the promise of minimally invasive surgery cytotoreductive surgery based on equivocal and limited evidence, we hope that centers that are enthusiastic about this approach will consider participating in the LANCE trial. Until, we

have prospective randomized data, patients should be informed about the limitations of the available literature on this subject and physicians should proceed with caution in offering this option to patients after neoadjuvant chemotherapy.

Contributors All authors contributed to this editorial.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

REFERENCES

- 1 Canis M, Rabischong B, Botchorishvili R, *et al*. Risk of spread of ovarian cancer after laparoscopic surgery. *Curr Opin Obstet Gynecol* 2001;13:9–14.
- 2 Armstrong DK, Alvarez RD, Bakkum-Gamez JN, *et al*. NCCN clinical practice guideline in oncology: ovarian cancer including fallopian tube cancer and primary peritoneal cancer. version 2.2019. Available: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf
- 3 Abitbol J, Gottlieb W, Zeng Z, *et al*. Incorporating robotic surgery into the management of ovarian cancer after neoadjuvant chemotherapy. *International Journal of Gynecologic Cancer* 2019;29:1341–7.
- 4 Gueli Alletti S, Bottoni C, Fanfani F, *et al*. Minimally invasive interval debulking surgery in ovarian neoplasm (mission trial–NCT02324595): a feasibility study. *Am J Obstet Gynecol* 2016;214:503.e1–6.
- 5 Fagotti A, Gueli Alletti S, Corrado G, *et al*. The INTERNATIONAL MISSION study: minimally invasive surgery in ovarian neoplasms after neoadjuvant chemotherapy. *Int J Gynecol Cancer* 2019;29:5–9.
- 6 Melamed A, Nitecki R, Boruta DM, *et al*. Laparoscopy compared with laparotomy for debulking ovarian cancer after neoadjuvant chemotherapy. *Obstet Gynecol* 2017;129:861–9.
- 7 Walker JL, Piedmonte MR, Spirtos NM, *et al*. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *J Clin Oncol* 2012;30:695–700.
- 8 Ramirez PT, Frumovitz M, Pareja R, *et al*. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med* 2018;379:1895–904.