


# Hyperthermic intraperitoneal chemotherapy in ovarian cancer: first, do no harm

Luis Chiva ,<sup>1</sup> Ignace Vergote<sup>2</sup>

<sup>1</sup>Clinica Universidad de Navarra  
Departamento de Ginecología y  
Obstetricia, Madrid, Spain  
<sup>2</sup>Department of Gynecology  
and Obstetrics, Gynecologic  
Oncology, Leuven Cancer  
Institute, Catholic University  
Leuven, Leuven, Belgium

## Correspondence to

Dr Luis Chiva, Clínica  
Universidad de Navarra  
Departamento de Ginecología  
y Obstetricia, Madrid, Spain;  
[lchiva@unav.es](mailto:lchiva@unav.es)

Received 15 November 2023

Accepted 22 November 2023

Published Online First

12 December 2023

The article published by Navarro-Santana et al, titled ‘Complications of HIPEC for ovarian cancer surgery: evaluation over two time periods’,<sup>1</sup> provides a detailed meta-analysis of the complications reported in the literature over two distinct time periods between 2004 and 2022. The authors conducted a thorough search of publications according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, on patients with ovarian cancer undergoing surgical cytoreduction with hyperthermic intraperitoneal chemotherapy (HIPEC) at the time of first-line treatment or recurrence. The time frame is divided into two periods, from 2004 to 2013, and from 2014 to 2022, allowing for a comparison over time of the different types of complications. We wish to congratulate the authors on their comprehensive work, which is likely the most substantial contribution to the literature that addresses complications following HIPEC in ovarian cancer. Furthermore, the article includes a very comprehensive supplementary document with relevant information, showcasing the quality of research.

As part of their assessment, the authors analyzed in almost 5000 patients from 69 studies the most frequent complications. The study’s most notable finding is that there have been no significant changes in the rate of complications associated with HIPEC at cytoreductive surgery over the past 18 years. In other words, the rate of complications has not decreased.

The use of hyperthermic chemotherapy in ovarian cancer has been a topic of discussion in recent years due to various factors. On the one hand, it is difficult to comprehend how a single chemotherapy treatment can have a significant impact on the disease within an hour. On the other, the scientific evidence has been inconclusive, with even a prospective randomized study<sup>2</sup> that yielded positive survival outcomes being criticized for its methodology and group imbalances.<sup>3</sup> Additionally, many researchers question whether the observed results in some studies are due to the heat or the cleansing effect of the hyperthermic solution, and whether chemotherapy truly has an impact on these patients. Lastly, there is the question of complications, and whether the increased morbidity counterweighs the unsure positive impact on survival.<sup>4</sup>

In recent studies, it has been observed that complications have decreased due to a more refined and cautious practice. The meta-analysis of Navarro-Santana et al is very meticulously performed and shows that complications have remained unchanged over the past 18 years. In fact, complications may even appear to be higher in some aspects, but the authors demonstrate that there are no significant differences between the two time periods.

The paper of Navarro-Santana and colleagues also has some weaknesses: (1) the inclusion of patients treated with HIPEC at the time of primary debulking, but also at the time of secondary debulking for recurrence; (2) reporting on all grades of complications; (3) not using a surgical morbidity scoring system, such as the Clavien-Dindo<sup>5</sup>; (4) failure to analyze the subgroup with low risk for bias according to the Newcastle-Ottawa scoring system<sup>6</sup>; and (5) comparing two periods over a long course of time (19 years) with changing operative and post-operative standards of care. Despite these shortcomings the study is also important because the authors observed overall complication rates with HIPEC that are high compared with cytoreductive surgery without HIPEC, such as a frequency in anastomotic leak of 4%, renal failure of 8%, ostomy of 22%, intensive care unit admission of 49%, re-operation of 7%, and a post-operative death rate of 3%.

In summary, the complication rate has not decreased over the years in patients undergoing surgery with HIPEC, and the complication rate of cytoreductive surgery with HIPEC remains high compared with cytoreductive surgery without HIPEC. Therefore, we concur with the authors in emphasizing the need to share these data with patients and continue to underscore the necessity of conducting HIPEC in the context of clinical trials.<sup>7</sup>

**Contributors** Both authors have equally contributed.

**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.



► <http://dx.doi.org/10.1136/ijgc-2023-004658>



© IGCS and ESGO 2024. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Chiva L, Vergote I.  
*Int J Gynecol Cancer*  
2024;**34**:10–11.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Commissioned; internally peer reviewed.

#### ORCID iD

Luis Chiva <http://orcid.org/0000-0002-1908-3251>

#### REFERENCES

- 1 Navarro Santana B, Garcia-Torralba E, Viveros-Carreño D, *et al*. Complications of HIPEC for ovarian cancer surgery: evaluation over two time periods. *Int J Gynecol Cancer* 2024;34:1–9.
- 2 van Driel WJ, Koole SN, Sonke GS. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. *N Engl J Med* 2018;378:230–40.
- 3 Vergote I, Chiva L, du Bois A. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. *N Engl J Med* 2018;378:1362–3.
- 4 Fotopoulou C, Sehouli J, Mahner S, *et al*. HIPEC: HOPE or HYPE in the fight against advanced ovarian cancer? *Ann Oncol* 2018;29:1610–3.
- 5 Clavien PA, Barkun J, de Oliveira ML, *et al*. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187–96.
- 6 Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- 7 Vergote I, Gonzalez-Martin A, Lorusso D, *et al*. Clinical research in ovarian cancer: consensus recommendations from the Gynecologic Cancer Intergrup. *Lancet Oncol* 2022;23:e374–84.