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Editorial

Turning up the heat does not affect quality of life

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The prognosis of women with ovarian carcinoma remains poor despite recent therapeutic developments. Most patients are diagnosed with an advanced stage with extensive peritoneal metastases. Although cytoreductive surgery (CRS) frequently results in a complete cytoreduction and ovarian cancer cells are typically sensitive to platinum-containing (neo-) adjuvant chemotherapy, disease recurrence occurs in more than 80% of patients, and frequently affects the peritoneum. Recent developments in medical treatment include the addition of bevacizumab and poly(ADP-ribose)polymerase inhibitors (PARPi). While long-term benefits of bevacizumab are limited, PARP inhibition has the potential to provide important reduction in recurrence rate, especially in the BRCA*mutated* patients. Regarding surgical developments, combining CRS with intraperitoneal administration of chemotherapy under hyperthermic conditions (HIPEC) has evolved in the last decades. In recent years, reports of randomized controlled trials (RCT) have been published providing guidance on the potential benefit of combining HIPEC with CRS.

Lim et al. [1] recently presented the results on efficacy of the KOV-HIPEC-01 trial elsewhere. A total of 184 patients with stage III-IV ovarian carcinoma received either primary or interval CRS with or without the addition of cisplatin-based HIPEC (75 mg/m^2, 90 minutes). In the overall trial population, HIPEC did not improve progression-free survival (PFS) and overall survival (OS). In the subgroup of patients receiving interval CRS, a significant difference in PFS (hazard ratio [HR]=0.60; 95% confidence interval [CI]=0.37–0.99; p=0.04) and OS (HR=0.53; 95% CI=0.29–0.96; p=0.04) was observed in favor of the HIPEC-arm. These results confirm the earlier results of the randomized OVHIPEC-1 trial in which the addition of cisplatin-based HIPEC resulted in a significant recurrence-free survival (RFS) and OS benefit in patients who received interval CRS [2]. Lim et al. [1] did not find any benefit of HIPEC in patients undergoing primary CRS. The international OVHIPEC-2 trial (NCT03772028) and French CHIPPI trial (NCT03842982) investigate this question in large randomized trials.

One of the concerns raised when evaluating treatment with HIPEC for ovarian carcinoma is a potential increase in postoperative morbidity and compromised health-related quality of life (HRQoL). Kim et al. [3] performed a HRQoL analysis in 165 out of 184 participating patients in the KOV-HIPEC-01 study; 89.1% of the control group and 90.2% of the HIPEC group.

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Author Contributions

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QLQ-C30, QLQ-OV28, and MDASI were used to assess HRQoL. Baseline questionnaires were completed before randomization, i.e. either before primary CRS or before interval CRS following 3 cycles of neo-adjuvant chemotherapy. During seven additional time points, HRQoL was assessed: postoperative day 7, after 3 and 6 cycles of adjuvant chemotherapy (presumably, the latter only for patients following primary CRS) and at 3, 6, 9 and 12 months after treatment. Questionnaires completed after disease recurrence were excluded from the analyses. The results show no significant difference in overall HRQoL between the HIPEC- and the control-arm. The strength of this analysis is the high percentage of available baseline questionnaires of almost 90% in both arms. Further compliance with the planned schedule of questionnaires was high, and balanced between arms. At time of analysis, 897 out of 1,038 questionnaires were available.

The results of this trial are consistent with other studies reporting HRQoL after treatment with HIPEC, such as HRQoL analysis of the OVHIPEC-1 participants [4]. This growing evidence indicates that concerns regarding impact on HRQoL should not be a limiting factor to perform HIPEC. Together with the previously reported improvement in survival outcomes, the application of HIPEC is supported in patients undergoing interval CRS. However, the benefit of HIPEC in patients treated with primary CRS and in the recurrent setting has yet to be determined. Therefore, further clinical trials which are currently undertaken should be awaited, irrespective of the fact that quality of life seems not to be affected by adding HIPEC to the surgical treatment.

REFERENCES

1. Lim MC, Chang SJ, Park B, Yoo HJ, Yoo CW, Nam BH, et al. Survival after hyperthermic intraperitoneal chemotherapy and primary or interval cytoreductive surgery in ovarian cancer: a randomized clinical trial. JAMA Surg 2022;157:374-83.
PUBMED | CROSSREF
2. van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HW, Hermans RH, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med 2018;378:230-40.
PUBMED | CROSSREF
3. Kim JH, Lee D, Lee Y, Ha HI, Chang YJ, Chang SJ, et al. Quality of life outcomes from the randomized trial of hyperthermic intraperitoneal chemotherapy following cytoreductive surgery for primary ovarian cancer (KOV-HIPEC-01). J Gynecol Oncol 2022;33:e54.
CROSSREF
4. Koole SN, Kieffer JM, K Sikorska , Schagen van Leeuwen JH, Schreuder HW, Hermans RH, et al. Health-related quality of life after interval cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with stage III ovarian cancer. Eur J Surg Oncol 2021;47:101-7.
PUBMED | CROSSREF