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Utility of CA-125 in interval surgery

Abstract

Standard treatment for advanced-stage epithelial ovarian cancer (EOC) consists of debulking surgery and chemotherapy. Progression-free survival (PFS) and overall survival (OS) correlate with residual tumor burden after debulking surgery. There are situations in which it is not feasible to perform the aforementioned surgery, requiring neoadjuvant chemotherapy (NACT) with eventual interval surgery.

The objective of the study was to retrospectively evaluate patients who were not plausible for primary cytoreduction, analyzing the value of CA-125 pre and post neoadjuvant chemotherapy and its suitability between these values and the surgical result.

Keywords: interval surgery, chemotherapy, cytoreduction, ovarian cancer

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Abbreviations: EOC, epithelial ovarian cancer; PFS, progression-free survival; OS, overall survival; NACT, neoadjuvant chemotherapy; CC, complete cytoreduction

Introduction

CA-125 is a murine-type glycoprotein that associates with the cell membrane and is recognized by the murine monoclonal antibody OC125. CA-125 is not only manifested in the tubal, endometrial and endocervical epithelium, but also in the mesothelial cells of the pleura, pericardium and peritoneum. Therefore, CA-125 is not a specific biomarker for COE.[1]

CA-125 is a tumor marker that is elevated in 80-90% of patients with EOC. Patients with EOC will generally undergo a CA-125 blood test prior to treatment.[2] Preliminary studies have shown that a lower preoperative CA-125 level is associated with a greater probability of achieving optimal cytoreduction.[3–5] Over the last few years, the definition of "optimal cytoreduction" has changed in relation to the maximum residual tumor diameter from 3cm to less than 1cm.[6] Currently, when performing primary or interval cytoreduction surgery, our goal is to achieve complete cytoreduction (CC) without any macroscopic residual disease.

The predictive value of CA-125 level for CC is still inconclusive. Likewise, it is unknown if normalization of CA-125 is a predictor of CC or if a scarce blood sample can be used as a predictor of surgical outcome.

If a cut-off point of 35 U/mL is chosen according to the upper limit of standard parameters, an elevated level of CA-125 should be found in 1% of apparently normal blood donors. In 6% of patients who have a benign disease, 28% of individuals who present non-gynecological malignancies; and 82% of patients who have surgically demonstrable EOC. Taking into account that CA-125 levels are not diagnostic, their increase can raise the suspicion of ovarian cancer.[1]

Although maximal primary surgical effort appears to be the cornerstone of potential long-term survival, the timing of surgical effort remains a matter of debate. In patients with extensive effusions (particularly pleural or pericardial), and in patients with extensive, noncytoreducible abdominal disease, initiation of NACT should be seriously considered. After three to four cycles, an optimal clinical response to chemotherapy may provide the opportunity for complete surgical cytoreduction, with an acceptably low complication rate.[7,8] Before starting chemotherapy, the diagnosis of ovarian, tubal or peritoneal cancer must be confirmed, in our case through minimally invasive surgery.

Objective

The end point of this study is to assess whether the decrease in the tumor marker CA-125 after NACT is related to a greater probability of complete cytoreduction (CC) in interval surgery. Secondary objective: modification of the CA-125 cut-off point post neoadjuvant therapy.

Methods

Retrospective study based on a digitalized database of the Gynecology Oncology Section of the Hospital Aleman. During the period January 2015 to December 2022, 189 patients with ovarian cancer were diagnosed by exploratory laparoscopy and thoracoscopy (as appropriate), in 48 of them it was not feasible to perform primary cytoreduction surgery. Of these 48, two had incomplete digital medical records, one had mucinous carcinoma, and one died during NACT. Forty-four patients diagnosed with high-grade serous ovarian cancer were included. Likewise, NACT was performed between 3-4 cycles, due to presenting criteria of primary unresectability. Emphasis was placed on the value of CA-125 pre and postchemotherapy and its relationship with the resectability of the disease (Complete, Optimal, Unresectable).

Results

The age range is between 45 and 77 years, average 59 years. FIGO stages were IIIB (1), IIIC (31) and IV (12).

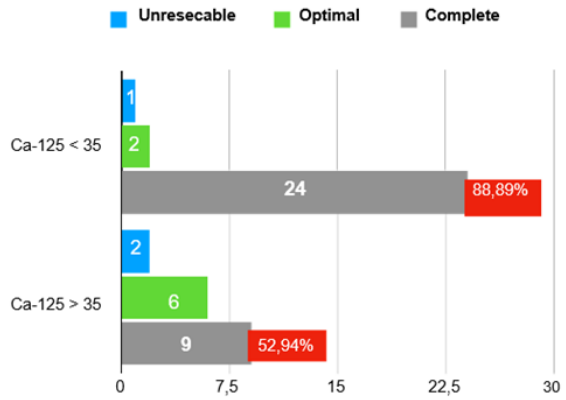
Average CA-125 value prior to NACT 2065.08 kU/L (94.1-10996 kU/L)

The NACT regimen used was Carboplatin (C) + Paclitaxel (P) in 100% of the patients.

After NACT, a total of n=27 (62.36%) patients reduced their CA-125 value to <35 kU/L, while n=17 (38.63%) patients reduced their CA-125 value, remaining is above 35 kU/L.

Of the 44 patients, 3 (6.81%) continued to present unresectability criteria, in 8 (18.18%) cytoreduction was optimal and in 33 (75%) CC.

Patients who underwent interval surgery with preoperative CA-125 levels ≤35 kU/L were more likely to achieve CC compared to patients with a CA- 125 level >35 kU/L (88.89% vs 52. 94%, p: 0.02) Graph 1.



Graph 1 Patients undergoing interval surgery, grouped according to cytoreduction result and postneoadjuvant ca-125 value.The percentage of CC with respect to each group is highlighted in red.

We were able to observe that 6 patients had decreased their CA-125 value between 35 and 45 kU/L, 5 of them had CC and 1 had optimal.

When we divided the patients into those who decreased to <45 and >45kU/L, the percentage of CC was 87. 88 and 36. 36% p: 0. 002 respectively.

Discussion

The use of baseline CA-125 value to assess a response to therapy, and increasing or decreasing levels of CA-125 have been correlated with disease progression or regression in more than 90% of patients. Rapid decline in CA-125 to normal values shortly after initiation of chemotherapy has been shown to be associated with a more favorable outcome. In contrast, consistently elevated levels of CA-125 have been associated with disease persistence or decreased response to treatment.[9–11]

Various authors have shown that patients in whom the CA-125 value drops to the normal range in the third cycle of adjuvant chemotherapy have greater survival, compared to patients who remain with high CA-125 values before the fourth cycle. Adjuvant chemotherapy cycle.[9–11]

Five studies reported a significant relationship between lower preoperative CA-125 levels and an interval CC rate at surgery, consistent with our study.[12–16] Matsuhashi et al reported a significant relationship between lower preoperative CA-125 levels and complete/optimal cytoreduction (p = 0.003).[17]

Gupta et al demonstrated higher CC rates in patients with preoperative CA-125 values <100 kU/L (p = 0.001),[18] while Zeng et al reported the cut-off value of CA-125 ≤200 kU/L (p = 0.012) 6. According to our results, we can report the cut-off value of CA-125 for CC <45 kU/L, (p = 0.002). In two studies, preoperative CA-125 was not a significant predictor of surgical outcome in multivariate analysis.[19,20] Likewise, patients in the studies received NACT, ranging from 1 to 14 cycles. Only one study reported 3 cycles before interval surgery for all patients. These studies overestimate the concept of neoadjuvant given the large number of cycles,[12] The patients included in our study had between 3-4 neoadjuvant cycles.

Eight studies demonstrated the favorable effect of NACT with respect to the decrease in CA-125 values and how it positively influenced the surgical outcome.[6,12,13,16–20] After adjusting for potential confounders, Gupta et al detected a significant correlation between the >95% decrease rate of preoperative CA-125 and CC18. Pelissier et al.[19] also reported a significant relationship between a CA-125 level after three cycles of NACT and CC in multivariate analysis.[19] Furthermore, Merlo et al reported an association >96.4% of CA-125 reduction after QTNA and CC.[16]

However, other studies found no relationship in the decrease in CA-125 values after NACT as an independent predictor of CC.[6,12,13,17,20] Preoperative CA-125 cut-off values ranged from ≤20 kU/L to ≤500 kU/L to predict CC in interval surgery in ten studies.[6,12,13,15–21]

Results from a systematic review by Brons et al indicated a significant relationship between lower preoperative CA-125 values and CC in patients who underwent interval surgery.[22] However, the definitions of normal CA-125 value and optimal CA-125 reduction cut-off values varied between studies, denoting that the effect of CA-125 reduction rate after NACT could not be directly compared in the surgical outcome. The studies included in that systematic review did not report the effect of ascites or peritoneal carcinomatosis and lacked multivariable analysis. Our analysis is univariate because these two data were not complete in the medical records of all patients.

Brons et al, in their prospective cohort study of 326 patients, found that normal CA-125 values who received interval surgery showed a significant relationship with CC in the univariate analysis. CC was achieved in 84.7% (n = 72) of patients with CA-125 values ≤ 35 kU/L, and in 66.5% (n = 127) of patients with CA-125 values ≤ 35 kU/L. 125 > 35 kU/L. This work coincides with the interval cytoreduction percentages according to our case series.[22]

However, only the absence of ascites and peritoneal carcinomatosis during surgery, FIGO stage IIIB/IIIC and high-grade serous histology were significant independent predictors of CC in interval surgery, demonstrated in multivariate analysis. This analysis coincides with our review of cases where 100% of the histology was high-grade serous, which could explain the high response rate to NACT and CC.

It should be noted that we proposed this study retrospectively, and with a small number of patients, with all patients managed under the same diagnostic and therapeutic protocol, by the same multidisciplinary treatment team in a center of high surgical complexity in gynecological oncology. As well as the decisions regarding resectability or not, they were carried out by the same surgical team that has a case mix of more than 25 cytoreductions per year.

Conclusion

The results of our review suggest that the decrease in CA-125 below the cut-off point of 35kU/L is an important variable to take into account when planning interval surgery. Within our population, it was of greater statistical significance when 45kU/L was taken as the cut-off point, so it could be considered as an eventual value when determining cytoreduction in interval surgery. We propose further studies to evaluate tumor resectability and the decrease in CA-125, as well as a new cut-off point, in patients with ovarian cancer who undergo NACT.

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Conflicts of interest

There is no competing interests between the authors.

References

1. Selim Afsar. Biomarkers in gynecologic tumors. Pınar Atukeren, Hafize Uzun, Biomarkers in Medicine, Bentham Science Publishers 2022:16–36.
2. Duffy MJ, Bonfrer JM, Kulpa J, et al. CA125 in ovarian cancer: European Group on Tumor Markers guidelines for clinical use. *Int J Gynecol Cancer*. 2005;15(5):679–691.
3. Kang S, Kim TJ, Nam BH, et al. Preoperative serum CA-125 levels and risk of suboptimal cytoreduction in ovarian cancer: A meta-analysis. *J Surg Oncol.* 2010;101(1):13–17.
4. Zhang D, Jiang YX, Luo SJ, et al. Serum CA125 levels predict outcome of interval debulking surgery after neoadjuvant chemotherapy in patients with advanced ovarian cancer. *Clin Chim Acta.* 2018;484:32–35.
5. Chi DS, Venkatraman ES, Masson V, et al. The ability of preoperative serum CA-125 to predict optimal primary tumor cytoreduction in stage III epithelial ovarian carcinoma. *Gynecol Oncol.* 2000;77(2):227–231.
6. Zeng J, Yin J, Song X, et al. Reduction of CA125 levels during neoadjuvant chemotherapy can predict cytoreduction to no visible residual disease in patients with advanced epithelial ovarian cancer, primary carcinoma of fallopian tube and peritoneal carcinoma. *J Cancer*. 2016;7(15):2327–2332.
7. Quentin DT, Amal B, Classe JM, et al. Optimal timing of interval debulking surgery for advanced epithelial ovarian cancer: A retrospective study from the ESME national cohort. *Gynecol Oncol*. 2022;167(1):11–21.
8. Pinelli C, Guerrisi R, Brusadelli C, et al. Interval debulking surgery for advanced ovarian cancer: when, how and why?. *Gynecology And Pelvic Medicine.* 2021;4.
9. Charkhchi P, Cybulski C, Gronwald J, et al. CA125 and ovarian cancer: a comprehensive review. *Cancers*. 2020;12(12):3730.
10. Cummings M, Nicolais O, Shahin M. Surgery in advanced ovary cancer: primary versus interval cytoreduction. *Diagnostics* 2022;12:988.
11. Wang D, Zhang G, Peng C, et al. Choosing the right timing for interval debulking surgery and perioperative chemotherapy may improve the prognosis of advanced epithelial ovarian cancer: a retrospective study. *J Ovarian Res.* 2021;14:49.
12. Furukawa N, Sasaki Y, Shigemitsu A, et al. CA-125 cut-off value as a predictor for complete interval debulking surgery after neoadjuvant chemotherapy in patients with advanced ovarian cancer. *J Gynecol Oncol.* 2013;24(2):141–145.
13. Rodriguez N, Rauh-Hain JA, Shoni M, et al. Changes in serum CA-125 can predict optimal cytoreduction to no gross residual dis- ease in patients with advanced stage ovarian cancer treated with neoadjuvant chemotherapy. *Gynecol Oncol.* 2012;125(2):362–366.
14. Nakamura K, Kitahara Y, Nishimura T, et al. Nadir CA-125 serum levels during neoadjuvant chemotherapy and no residual tumor at interval debulking surgery predict prognosis in advanced stage ovarian cancer. *World J Surg Oncol.* 2020;18(1):200.
15. Morimoto A, Nagao S, Kogiku A, et al. A preoperative low cancer antigen 125 level (≤25.8 mg/dL) is a useful criterion to determine the optimal timing of interval debulking surgery following neoadjuvant chemotherapy in epithelial ovarian cancer. *Jpn J Clin Oncol.* 2016;46(6):517–521.
16. Merlo S, Besic N, Drmota E, et al. Preoperative serum CA-125 level as a predictor for the extent of cytoreduction in patients with advanced stage epithelial ovarian cancer. *Radiol Oncol.* 2021;55(3):341– 346.
17. Matsuhashi T, Takeshita T, Yamamoto A, et al. Serum ca 125 level after neoadjuvant chemotherapy is predictive of prognosis and debulking surgery outcomes in advanced epithelial ovarian cancer. *J Nippon Med Sch.* 2017;84(4):170–176.
18. Gupta M, Patel S, Arora R, et al. Does preoperative CA-125 cutoff value and percent reduction in CA-125 levels correlate with surgical and survival outcome after neoadjuvant chemotherapy in patients with advanced-stage ovarian cancer?—Our experience from a tertiary cancer institute. *South Asian J Cancer.* 2020;9(1):30–33.
19. Pelissier A, Bonneau C, Chéreau E, et al. CA125 kinetic parameters predict optimal cytoreduction in patients with advanced epithelial ovarian cancer treated with neoadjuvant chemotherapy. *Gynecol Oncol.* 2014;135(3):542–546.
20. Ghisoni E, Katsaros D, Maggiorotto F, et al. A predictive score for optimal cytoreduction at interval debulking surgery in epithelial ovarian cancer: A two- centers experience. *J Ovarian Res.* 2018;11(1):42.
21. Eltabbakh GH, Mount SL, Beatty B, et al. Factors associated with cytoreducibility among women with ovarian carcinoma. *Gynecol Oncol.* 2004;95(2):377–383.
22. Brons PE, Nieuwenhuyzen-de Boer GM, Ramakers C, et al. Preoperative cancer antigen 125 level as predictor for complete cytoreduction in ovarian cancer: a prospective cohort study and systematic review. *Cancers (Basel)*. 2022;14(23):5734.