Differences in the clinical significance of CA125 for detecting progression among histological subtypes of epithelial ovarian carcinoma

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Abstract. Serum cancer antigen 125 (CA125) is the standard tool for surveillance of patients with epithelial ovarian carcinoma (OC). However, its utility may vary by histological subtype. The present study included patients with epithelial OC who completed primary therapy (surgery and chemotherapy) at the National Defense Medical College Hospital (Tokorozawa, Japan) between January 2006 and December 2022, achieved complete or partial response, and had a post-treatment CA125 level of <35 U/ml. Recurrence was defined using the Response Evaluation Criteria in Solid Tumors criteria via computed tomography (CT) imaging. Surveillance included quarterly CA125 testing for 5 years, and semiannual CT in year 1 followed by annual CT. All patients were classified into Group A, which included clear cell carcinoma and mucinous carcinoma, or Group B, which included high-grade serous carcinoma and other subtypes. Among 243 patients, there were 85 in Group A and 158 in Group B. First, the diagnostic performance of the standard CA125 cutoff (≥35 U/ml) for detecting recurrence was evaluated. The sensitivity was 28.6% in Group A and 81.8% in Group B; and the specificity was 98.4% in Group A and 98.8% in Group B. Second, because the sensitivity in Group A was very low, the CA125 ratio and a combined model (defined as CA125 ≥35 U/ml or CA125 ratio ≥1.5) were introduced. The CA125 ratio was defined as the maximum CA125 value measured at CT surveillance divided by the CA125 value measured just after the initial treatment for patients with CA125 <35 U/ml. The sensitivity was 66.7% in Group A and 93.5% in Group B; and the specificity was 84.1% in Group A and 86.4% in Group B. In conclusion, the utility of CA125 for the detection of recurrence differs substantially between histological subtypes, highlighting the need for histological subtype-specific surveillance strategies in epithelial OC.

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Abbreviations: OC, ovarian carcinoma; ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Cancer Network; FIGO, International Federation of Gynecology and Obstetrics; CA125, cancer antigen 125; CT, computed tomography; HGSC, high-grade serous carcinoma; CCC, clear cell carcinoma; MC, mucinous carcinoma; EC, endometrioid carcinoma; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic

Key words: OC, recurrence, histological subtypes, CA125, Response Evaluation Criteria in Solid Tumors

Introduction

Ovarian carcinoma (OC) ranks as the eighth leading cause of both cancer incidence and mortality among women globally (1). For epithelial OC, the standard primary consists of a combination of maximal debulking surgery and platinum-based chemotherapy (2). Both the European Society for Medical Oncology (ESMO) and National Comprehensive Cancer Network (NCCN) guidelines report that over 70% of patients with International Federation of Gynecology and Obstetrics (FIGO) stages III-IV disease experience recurrence within 3 years of initial treatment (3,4). Therefore, these guidelines recommend efficient and accurate follow-up observations after treatment (3,4).

The ESMO guidelines recommend cancer antigen 125 (CA125) level monitoring and physical examinations as primary surveillance methods, with computed tomography (CT) performed when CA125 levels rise or when clinical symptoms indicative of relapse occur (3). In comparison, the NCCN guidelines suggest physical examinations and CA125 assessments every 2-4 months for the first 2 years, every 3-6 months for the following 3 years, and annually for up to 5 years (4). Both guidelines recommend CT imaging when CA125 levels increased or when new symptoms suggestive of recurrence emerge. These standardized approaches underscore

the clinical importance of CA125 monitoring for detecting OC recurrence.

The tumor marker CA125, known as Mucin16, is widely used for monitoring initial presentation and recurrent disease. While approximately 85% of patients with OC demonstrate elevated CA125 levels at initial diagnosis (3), significant variation exists across histological subtypes (5). Notably, high-grade serous carcinoma (HGSC) typically presents with markedly elevated CA125 levels at initial diagnosis, whereas clear cell carcinoma (CCC) often shows comparatively lower levels (5,6). Consequently, although current ESMO and NCCN guidelines recommend CA125 for OC surveillance, its predictive value for recurrence detection potentially varies substantially among histological subtypes.

This study examined the utility of CA125 for recurrence detection across different histological subtypes of epithelial OC.

Patients and methods

Patient selection and data collection. This retrospective study analyzed patients with OC treated at the National Defense Medical College Hospital (Tokorozawa, Japan) between January 2006 and December 2022. Inclusion criteria required that patients underwent complete primary surgery and adjuvant chemotherapy, achieved either complete or partial response after initial treatment, and had CA125 levels <35 U/ml following initial treatment. Recurrence was defined as disease progression based on the Response Evaluation Criteria in Solid Tumors version 1.1 criteria using CT imaging (7). Patients diagnosed with recurrence through non-CT were excluded.

Surveillance protocol and recurrence definition. The follow-up schedule consisted of CA125 tests every 3 months and CT scans every 6 months for the 1st year after initial treatment and, then annually. Additional CT imaging was performed when any symptoms developed, when CA125 values reached ≥35 U/ml without symptoms, or when CA125 values showed a twofold increase from previous measurements. If CT imaging performed due to CA125 elevation failed to confirm recurrence, monthly CA125 testing was initiated followed by additional CT imaging as clinically indicated. Histological subtypes were divided into two groups: Group A comprised CCC and mucinous carcinoma (MC), while Group B included HGSC, endometrioid carcinoma (EC), mixed carcinoma, and carcinosarcoma. Staging followed FIGO classification (8), while pathological diagnosis adhered to 2020 World Health Organization criteria (9). For recurrent cases requiring repeated CT scans due to initial non-detection of recurrence when CA125 values ≥35 U/ml, we calculated the CA125-CT detection interval, defined as the time between the first instance of CA125 values ≥35 U/ml without CT-detected recurrence and the subsequent CT confirmation of recurrence.

Statistical methods. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. We evaluated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CA125 for detecting recurrence, both overall and by histological groups with 95% confidence intervals. P<0.05 was considered to indicate a statistically significant difference, and analyses were conducted using JMP software (version 17.0; SAS Institute Inc.).

Evaluation of the CA125 ratio. Among patients with CA125 <35U/ml during surveillance, we analyzed the CA125 ratio, defined as the maximum CA125 value at CT surveillance divided by CA125 value at post initial treatment. The formula was shown as follows.

The CA125 ratio=(The maximum CA125 value at time of CT surveillance)/(The CA125 value at post initial treatment).

The optimal CA125 ratio cutoff was determined using receiver operating characteristic (ROC) curve analysis for recurrence detection in these patients. We calculated sensitivity, specificity, PPV, and NPV using both CA125 ≥35 U/ml or the CA125 ratio, wither separately or in combination.

Results

Patient characteristics. A total of 333 patients with epithelial ovarian cancer received initial treatment at our institution. Of these, 243 patients treated between January 2006 and December 2022 were included in the analysis (Fig. 1). The cohort comprised 98 patients with recurrence and 145 without recurrence. As a supplemental analysis, we compared the clinical backgrounds of these two groups. Patients with recurrence exhibited significantly higher rates of advanced FIGO stages (P<0.01, χ^2 test), residual tumors (P<0.01, Fisher's exact test), elevated CA125 levels (P<0.01, χ^2 test), and neoadjuvant chemotherapy administration (P<0.01, Fisher's exact test).

Diagnostic performance of CA125 alone in Group A and Group B. The study population was stratified into Groups A (n=85) and Group B (n=158) (Table I). Group A consisted of 63 (74.1%) patients with CCC and 22 (25.9%) with MC, while Group B comprised 94 (59.5%) with HGSC, 47 (29.7%) with EC, 14 (8.9%) with mixed carcinoma, and 3 (1.9%) with carcinosarcoma. Compared to Group B, Group A had significantly more patients at early FIGO stages (P<0.01), with no residual tumors (P<0.01), normal CA125 levels (P<0.01), and no neoadjuvant chemotherapy (P<0.01). Among 24 patients with recurrence, CT failed to detect recurrence when initially raising CA125 values ≥35 U/ml required repeated testing. This occurred in two Group A patients and 22 Group B patients (P=0.09). The median CA125-CT detection interval was 3 months (range: 1-7) overall; 1 month (range: 1-1) in Group A vs. 3 months (range: 1-7) in Group B. No significant difference was observed in median CA125-CT detection intervals between groups A and B (P=0.12). Using CA125 ≥35 U/ml as the sole criterion, sensitivity were 70.4% in all patients, 28.6% in Group A, and 81.8% in Group B, and specificity were 98.6% in all patients, 98.4% in Group A, and 98.8% in Group B (Table II).

Evaluation of the CA125 ratio for recurrence detection. Among 162 patients with CA125 <35 U/ml, 78 patients were in Group A, 94 patients were in Group B. ROC analysis of the CA125 ratio yielded an AUC of 0.75 (Fig. 2). At a cutoff ratio of 1.5, sensitivity were 58.6% in all patients, 53.3% in Group A, and 64.3% in Group B, and specificity were 86.7% in all patients, 85.7% in Group A, and 87.5% in Group B (Table III).

Table I. Characteristics of each group.

Variable	Group A[a] (n=85)	Group B[b] (n=158)	P-value
Age (%)			0.17
≥61 years	29 (34.1)	68 (43.0)	
<60 years	56 (65.9)	90 (57.0)	
FIGO[c] stage (%)			<0.01
I, II	76 (89.4)	65 (41.1)	
III, IV	9 (10.6)	93 (58.9)	
Presence of residual tumor (%)			<0.01
Yes	4 (4.7)	32 (20.3)	
No	81 (95.3)	126 (79.7)	
Neoadjuvant chemotherapy			<0.01
Yes	1 (1.2)	68 (43.0)	
No	84 (98.8)	90 (57.0)	
Recurrence (%)			<0.01
Yes	21 (24.7)	77 (48.7)	
No	64 (75.3)	81 (51.3)	
Number of recurrent or non-recurrent patients with CA125 ≥35 U/ml (%)			
Recurrence	6 (85.7)	63 (98.4)	0.19
Non-recurrence	1 (14.3)	1 (1.6)	
Number of recurrent or non-recurrent patients with CA125 <35 U/ml (%)			
Recurrence	15 (19.2)	14 (14.9)	0.45
Non-recurrence	63 (80.8)	80 (75.1)	

[a]Group A included clear cell carcinoma and mucinous carcinoma. [b]Group B included serous carcinoma, endometrioid carcinoma and mixed carcinoma and carcinosarcoma. [c]FIGO, International Federation of Gynecology and Obstetrics. P-values were calculated using the χ^2 test or Fisher's exact test, as appropriate.

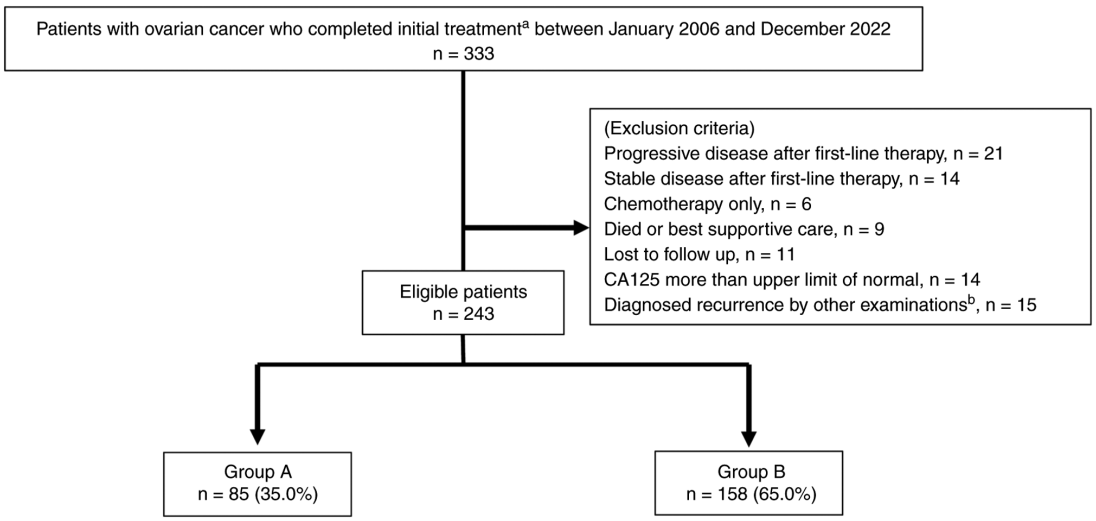

Figure 1. Flow chart of the patient selection process. This study includes patients with ovarian carcinoma treated at our institution between January 2006 and December 2022. Inclusion criteria included patients who completed initial treatment, achieved either a complete or partial response following treatment, and had CA125 levels below 35 U/ml following treatment. Patients diagnosed with recurrence using methods other than CT are excluded. [a]The initial treatment consists of primary debulking surgery following adjuvant chemotherapy and neoadjuvant chemotherapy following interval debulking surgery and adjuvant chemotherapy. [b]Other examinations included biopsy, magnetic resonance imaging, and positron emission tomography-CT. CA125, cancer antigen 125; CT, computed tomography.

Optimization of recurrence detection using the combined model. The combined approach (CA125 ≥35 U/ml or the CA125 ratio ≥1.5) demonstrated a sensitivity of 87.7% in all patients, 66.7% in Group A, and 93.5% in Group B, and

Table II. Diagnostic performance of CA125 alone (≥35 U/ml) for predicting recurrence.

Patients	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All patients (n=243)	70.4 (60.3-79.1)	98.6 (95.2-99.8)	97.2 (90.3-99.7)	83.1 (76.8-88.3)
Group A[a] (n=85)	28.6 (11.3-52.2)	98.4 (91.7-99.9)	85.7 (42.1-99.6)	80.8 (70.3-88.8)
Group B[b] (n=158)	81.8 (71.3-89.8)	98.8 (93.5-100)	98.4 (91.6-100)	85.1 (76.5-91.6)

[a]Group A included clear cell carcinoma and mucinous carcinoma. [b]Group B included serous carcinoma, endometrioid carcinoma and mixed carcinoma and carcinosarcoma. PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Table III. Diagnostic performance of the CA125 ratio (≥1.5)[a] for predicting recurrence in patients with CA125 <35 U/ml.

Patients	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All patients with CA125 <35 U/ml (n=162)	58.6 (38.9-76.5)	86.7 (80.0-91.8)	47.2 (30.4-64.5)	91.2 (85.1-95.4)
Group A[b] (n=78)	53.3 (26.6-78.7)	85.7 (74.6-93.3)	47.1 (23.0-72.2)	88.5 (77.8-95.3)
Group B[c] (n=94)	64.3 (35.1-87.2)	87.5 (78.2-93.8)	47.4 (24.4-71.1)	93.3 (85.1-97.8)

[a]CA125 ratio was defined as the ratio of the maximum CA125 value measured at the same time as CT and CA125 immediately after the initial treatment for patients with CA125 <35 U/ml. [b]Group A included clear cell carcinoma and mucinous carcinoma. [c]Group B included serous carcinoma, endometrioid carcinoma and mixed carcinoma and carcinosarcoma. PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Table IV. Diagnostic performance of the combined model (CA125 ≥35 U/ml or CA125 ratio[a] ≥1.5) for predicting recurrence.

Patients	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All patients (n=243)	87.8 (79.6-93.5)	85.5 (78.7-90.8)	80.4 (71.6-87.4)	91.2 (85.1-95.4)
Group A[b] (n=85)	66.7 (43.0-85.4)	84.1 (72.7-92.1)	58.3 (36.6-77.9)	88.3 (77.4-95.2)
Group B[c] (n=158)	93.5 (85.5-97.9)	86.4 (77.0-93.0)	86.7 (77.5-93.2)	93.3 (85.1-97.8)

[a]CA125 ratio was defined as the ratio of the maximum CA125 value measured at the same time as CT and CA125 immediately after the initial treatment for patients with CA125 <35 U/ml. [b]Group A included clear cell carcinoma and mucinous carcinoma. [c]Group B included serous carcinoma, endometrioid carcinoma and mixed carcinoma and carcinosarcoma. PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

a specificity of 85.5% in all patients, 84.1% in Group A, and 86.4% in Group B (Table IV).

Discussion

This study evaluated the clinical utility of CA125 in detecting epithelial OC recurrence by histological subtype. While the CA125 test was inadequate for CCC and MC, it demonstrated higher utility for the group mainly comprising HGSC and EC. Furthermore, combining the CA125 test with CA125 ratio improved sensitivity for CCC and MC, though this approach remained limited. However, this combined analysis was more effective for the HGSC and EC groups.

Among OC, CCC and MC subtypes, CCC and MC represented minor subtypes worldwide; however, CCC is a relatively more prevalent in Asia, accounting for 30% of cases (10,11). Therefore, HGSC is widely recognized as the major histological subtype (2). Compared to HGSC, CCC and MC exhibited greater chemoresistance, are diagnosed at a younger age and earlier stage, and are associated with a higher potential for complete resection (no residual tumor) and a lower rate of Neoadjuvant chemotherapy (12-14). Since our results align with previous studies, the study groups included in our study reflect common clinical presentations. Previous studies reported a median CA125-CT detection interval of 3-5 months in HGSC (15). Consistent with this, our study found a median interval of 3 months in both groups, with no significant difference across histological subtypes.

In our study, the CA125 test demonstrated low sensitivity for detecting recurrence in patients with CCC and MC, whereas HGSC it showed high sensitivity and specificity for HGSC, consistent with ESMO and NCCN guidelines (3,4). This discrepancy arises because CA125 levels are potentially reflect HGSC disease burden at recurrence or initial diagnosis (16), while CCC and MC typically exhibit lower CA125

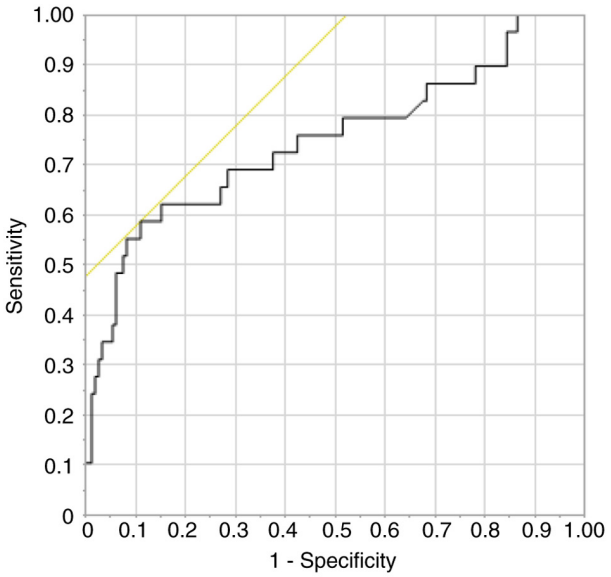

Figure 2. Receiver operating characteristic curve analysis of recurrence and the CA125 ratio among patients with CA125 <35 U/ml. The area under the curve of the combination was 0.75. The CA125 ratio was defined as the ratio of the maximum CA125 value measured at the same time as CT and CA125 immediately after the initial treatment for patients with CA125 <35 U/ml.

responsiveness (5). Therefore, alternative methods may be required to detect recurrence in patients with CCC and MC.

Detecting recurrence in patients with CA125 levels of <35 U/ml remains challenging (17,18). Therefore, we evaluated the CA125 ratio, the rate of CA125 increase. Although the CA125 ratio was only moderately efficient for all patients, the combined CA125 ≥35 U/ml or the CA125 ratio model had a higher sensitivity, particularly for patients with the group including HGSC as the major types. Therefore, this method might be useful in reducing the number of CT scans required for patients with HGSC and EC as the major types. However, its utility was limited to patients with CCC and MC, highlighting that CT scans cannot be omitted during surveillance in patients with CCC and MC.

The difference of the utility of CA125 between two Groups in our study might be affected with the imbalance of FIGO stage. In fact, most cases were discovered at early-staged diseases in Group A, while most cases in Group B were found at advanced-staged diseases. Generally, several reports showed CCC and MC are diagnosed at an early stage and HGSC is often found at an advanced stage because of these biological characteristics itself (10-13). Therefore, this distribution reflected the actual clinical situation in daily practice. Because our study analyzed the utility of CA125 on the perspective of histology, we considered this imbalance as not confounding factor but histological characteristics. Thus, our study emphasized the specific follow-up strategies using CA125 for different histological subtypes.

This study had several limitations. First, our findings are based on a single-institution retrospective design with a relatively small sample size. Second, we did not perform the analysis with factors effected with CA125 such as tumor size or sites of recurrence. Finally, this real-world, non-standardized imaging protocol could influence the calculated sensitivity and specificity compared to a theoretical study where all patients received imaging at fixed intervals regardless of CA125. Further large-scale studies are needed to evaluate the biological influence of histology and to optimize follow-up protocols for these subtypes.

Our findings would be useful for the follow-up methods at clinical setting. Because the sensitivity of the follow-up methods by the CA125 value and the CA125 ratio of patients with CCC and MC was not satisfactory, CT scan was often performed in order to miss the recurrence. Hence, because the sensitivity of this follow-up method for patients with HGSC was sufficient, we could reduce the times of CT scan to discover recurrence. Thus, our results might minimize medical costs and medical radiation exposure.

In conclusion, our findings demonstrate that CA125 is clinically useful for detecting recurrence in patients with HGSC but shows limited utility in CCC and MC. These results highlight the need for subtype-specific recurrence detection strategies, particularly for CCC and MC, warranting further investigation into surveillance methods.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KK, MM and MT conceptualized the study. KK and MM were involved in data curation. KK, SN, RT, TI, NK, JS, YO, TH, HS, KO and YH performed the formal analysis. KK wrote the original draft. MM and MT reviewed and edited the manuscript. KK and MM confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Institutional Review Board of National Defense Medical College (approval no. 4925; Tokorozawa, Japan). All patient records and information were anonymized and de-identified before analysis. The present study was exempt from obtaining informed consent from all participants.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A: Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.CA Cancer J Clin 74: 229-263, 2024.
2. Kuroki L and Guntupalli SR: Treatment of epithelial ovarian cancer. BMJ 371: m3773, 2020.
3. González-Martín A, Harter P, Leary A, Lorusso D, Miller RE, Pothuri B, Ray-Coquard I, Tan DSP, Bellet E, Oaknin A, *et al*: Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 34: 833-848, 2023.
4. NCCN Guidelines: Version 4.2026: Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf
5. Liu H, Xu Y, Ji J, Dong R, Qiu H and Dai X: Prognosis of ovarian clear cell cancer compared with other epithelial cancer types: A population-based analysis. Oncol Lett 19: 1947-1957, 2020.
6. Charkhchi P, Cybulski C, Gronwald J, Wong FO, Narod SA and Akbari MR: CA125 and ovarian cancer: A comprehensive review. Cancers (Basel) 12: 3730, 2020.
7. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, *et al*: New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). Eur J Cancer 45: 228-247, 2009.
8. Prat J; FIGO Committee on Gynecologic Oncology: FIGO's staging classification for cancer of the ovary, fallopian tube, and peritoneum: Abridged republication. J Gynecol Oncol 26: 87-89, 2017.
9. World Health Organization Classification of Tumours Editorial Board, Female Genital Tumours: WHO Classification of Tumours. Vol 4, 5th edition. International Agency for Research on Cancer, Lyon, 2020.
10. Kim SI, Lim MC, Lim J, Won YJ, Seo SS, Kang S and Park SY: Incidence of epithelial ovarian cancer according to histologic subtypes in Korea, 1999 to 2012. J Gynecol Oncol 27: e5, 2016.
11. Okamoto A, Glasspool RM, Mabuchi S, Matsumura N, Nomura H, Itamochi H, Takano M, Takano T, Susumu N, Aoki D, *et al*: Gynecologic Cancer InterGroup (GCIG) consensus review for clear cell carcinoma of the ovary. Int J Gynecol Cancer 24 (9 Suppl 3): S20-S25, 2014.
12. Oliver KE, Brady WE, Birrer M, Gershenson DM, Fleming G, Copeland LJ, Tewari K, Argenta PA, Mannel RS, Secord AA, *et al*: An evaluation of progression free survival and overall survival of ovarian cancer patients with clear cell carcinoma versus serous carcinoma treated with platinum therapy: An NRG Oncology/Gynecologic Oncology Group experience. Gynecol Oncol 147: 243-249, 2017.
13. Takano M, Kikuchi Y, Yaegashi N, Kuzuya K, Ueki M, Tsuda H, Suzuki M, Kigawa J, Takeuchi S, Tsuda H, *et al*: Clear cell carcinoma of the ovary: A retrospective multicentre experience of 254 patients with complete surgical staging. Br J Cancer 94: 1369-1374, 2006.
14. Borella F, Mitidieri M, Cosma S, Benedetto C, Bertero L, Fucina S, Ray-Coquard I, Carapezzi A and Ferraioli D: Update on prognostic and predictive markers in mucinous ovarian cancer. Cancers (Basel) 15: 1172, 2023.
15. Rustin GJ, van der Burg ME, Griffin CL, Guthrie D, Lamont A, Jayson GC, Kristensen G, Mediola C, Coens C, Qian W, *et al*: Early versus delayed treatment of relapsed ovarian cancer (MRC OV05/EORTC 55955): A randomised trial. Lancet 376: 1155-1163, 2010.
16. Rustin GJ, Nelstrop AE, Tuxen MK and Lambert HE: Defining progression of ovarian carcinoma during follow-up according to CA 125: A North Thames Ovary Group Study. Ann Oncol 7: 361-364, 1996.
17. Gupta D and Lis CG: Role of CA125 in predicting ovarian cancer survival-a review of the epidemiological literature. J Ovarian Res 2: 13, 2009.
18. Plotti F, Guzzo F, Schirò T, Terranova C, De Cicco Nardone C, Montera R, Luvero D, Scaletta G, Lopez S, Capriglione S, *et al*: Role of human epididymis protein 4 (HE4) in detecting recurrence in CA125 negative ovarian cancer patients. Int J Gynecol Cancer 29: 768-771, 2019.