ORIGINAL RESEARCH ARTICLE

Preoperative PET/CT score can predict incomplete resection after debulking surgery for advanced serous ovarian cancer better than CT score, MTV, tumor markers and hematological markers

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Abstract

Introduction: Complete resection after debulking surgery is strongly associated with prolonged survival for advanced serous ovarian cancer (ASOC). Though positron emission tomography/computed tomography (PET/CT) is more advantageous than computed tomorgraphy (CT) for detecting metastases, studies on the PET/CT prediction model for incomplete resection for ovarian cancer are insufficient. We analyzed and compared the predictive value of preoperative PET/CT score, CT score, metabolic parameters, tumor markers and hematological markers for incomplete resection after debulking surgery for ASOC.

Material and methods: A total of 62 ASOC patients who underwent preoperative [18F]FDG PET/CT and debulking surgery were retrospectively analyzed. PET/CT and CT scores were based on the Suidan model. The predictive value of PET/CT score, CT score, the maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), human epididymis protein 4 (HE4), cancer antigen 125 (CA125), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) for incomplete resection were analyzed and compared.

Results: Preoperative PET/CT score had the highest predictive value for incomplete resection in primary debulking surgery group (sensitivity: 65.0%, specificity: 88.9%, area under the ROC curve (AUC): 0.847, $p < 0.001$), however, in secondary debulking surgery group, preoperative PET/CT score and CT score had the same and highest predictive value for incomplete resection (sensitivity: 80.0%, specificity: 94.7%, AUC: 0.853, $p = 0.017$), compared with preoperative metabolic parameters SUVmax and MTV, tumor markers HE4 and CA125, and hematological markers LMR, PLR and NLR. Preoperative PET/CT score ≥ 3 (Suidan model) and preoperative PET/CT score ≥ 2 predicted a high risk of incomplete resection after primary and secondary debulking

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Abbreviations: [18F]FDG, 2-deoxy-2-[18F]fluoro-D-glucose; ASOC, advanced serous ovarian cancer; CA125, cancer antigen 125; CT, computed tomography; EOC, epithelial ovarian cancer; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET/CT, positron emission tomography/computed tomography; PLR, platelet-to-lymphocyte ratio; SUVmax, the maximum standardized uptake value.

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surgeries, respectively. There was no statistical difference between primary and secondary debulking surgery groups in predictive value of PET/CT score for incomplete resection ($p = 0.971$). There were significant differences between PET/CT scores and CT scores in primary debulking surgery group and no significant differences in secondary debulking surgery group.

Conclusions: A high PET/CT score predicted a high risk of incomplete resection. The preoperative PET/CT score had an identical predictive value in primary and secondary debulking surgery groups. PET/CT score was more accurate in the detection of metastases than CT score was.

KEYWORDS
advanced serous ovarian cancer, incomplete resection, positron emission tomography/computed tomography score (PET/CT score), primary debulking surgery, secondary debulking surgery, Suidan model

1 | INTRODUCTION

Ovarian cancer is a common gynecological malignancy and has the highest mortality rate ofg all gynecological malignancies, with approximately 22000 newly diagnosed cases annually.[1] Epithelial ovarian cancer (EOC) is the most common pathological type of ovarian cancer, and serous ovarian cancer is the most common subtype of EOC. Most patients with ovarian cancer are diagnosed at an advanced stage due to a lack of specific clinical symptoms. About 80% of patients with ovarian cancer who received treatment, relapse within 5 years.[2]

The standard treatment for EOC is debulking surgery, with an acceptable morbidity, followed by taxane-platinum chemotherapy. Neoadjuvant chemotherapy may decrease the tumor burden for interval debulking surgery; however, it does not improve survival.[3] So, prediction for feasibility of debulking surgery is important to avoid futile surgery. Postoperative residual disease is a significant prognostic predictor for survival, and optimal debulking is generally defined as a maximum diameter of residual disease ≤1 cm. Complete resection without macroscopic residual disease has been confirmed to be more beneficial than optimal debulking with macroscopic residual disease ≤1 cm for patients with advanced ovarian cancer, and patients in whom complete resection is achieved after debulking surgery have the best survival outcome.[4] Therefore, it is necessary to identify patients with a high risk of incomplete resection before debulking surgery.

To date, some tumor markers, hematological markers, radiological imaging and diagnostic laparoscopy[5] have been used to predict optimal debulking for patients with ovarian cancer. Radiological imaging is non-invasive, convenient and economical. One of the most comprehensive and robust computed tomography (CT)-based models available to predict incomplete resection was proposed by Suidan et al.[6] The Suidan model consists of eight CT criteria and three clinical criteria to predict incomplete resection after debulking surgery for advanced ovarian cancer; the rate of incomplete resection was proportional to a predictive score.

Positron emission tomography/computed tomography (PET)/CT is a molecular imaging technology. Due to its unique characteristics related to glucose metabolism, 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]FDG) PET/

Key message

This study showed that the Suidan model-based PET/CT score can predict incomplete resection for advanced serous ovarian cancer better than CT score, metabolic parameters SUVmax and MTV, tumor markers HE4 and CA125, and hematological markers LMR, PLR and NLR.

CT has clinical value in the staging of EOC patients, recurrent lesion detection, treatment response monitoring and prognosis prediction.[7] PET/CT has clear advantages over conventional imaging in accurately staging and detecting lymph node metastases and extra-abdominal metastases and assessing equivocal manifestations in conventional imaging.[8] Although CT is the most routinely performed radiological imaging examination, PET/CT may be more valuable than CT for predicting incomplete resection. At present, studies on the PET/CT prediction model for incomplete resection for ovarian cancer are insufficient.

This study aims to analyze and compare the predictive value of preoperative Suidan model-based PET/CT score, Suidan model-based CT score, metabolic parameters, tumor markers and hematological markers for incomplete resection after debulking surgery for advanced serous ovarian cancer (ASOC). Furthermore, we aim to compare the predictive value of PET/CT score between primary and secondary debulking surgery groups.

2 | MATERIAL AND METHODS

2.1 | Patient selection and evaluation of clinical data

We retrospectively analyzed patients with ASOC at our hospital from July 1, 2015 to January 31, 2022 (stages III–IV according to the International Federation of Gynecology and Obstetrics [FIGO]

staging system). All clinical data were obtained from electronic medical records. Inclusion criteria were: (1) [¹⁸F]FDG PET/CT examination performed at our hospital within 2 months before debulking surgery; (2) no treatment between PET/CT examination and debulking surgery; (3) disease-free and treatment-free period of more than 6 months from the last treatment cycle if the patients had been treated; and (4) ASOC diagnosed by pathological and histological examination. Patients were excluded if they (1) were <18 years old; (2) had a history of other malignancies; (3) had a diagnosis of multiple primary malignancies before or during surgery; (4) had incomplete or uncertain data; or (5) had fertility-sparing surgery, bone marrow suppression, any medical condition which influences hematological markers, any medication that influences inflammatory condition such as corticosteroids, current infection, previous history of local or systemic infection and hematological malignancy.

The clinical data collected in this study included age, FIGO stage, cancer antigen 125 (CA125) level, human epididymis protein 4 (HE4) level, lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) within 2 weeks before surgery.

2.2 | PET/CT protocol

PET/CT images were acquired on a Philips Gemini TF 64 PET/CT scanner. Each patient fasted for at least 6 hours to ensure a blood glucose level <8.0 mmol/L before undergoing [¹⁸F]FDG PET/CT imaging. [¹⁸F]FDG was intravenously injected at 0.14 mCi/kg body-weight 60 minutes before imaging ([¹⁸F]FDG with a radiochemical purity >95% was produced by Sumitomo Accelerator of Japan). Urination was required before PET/CT examination. The CT scan was performed from the thigh to the skull base (100 mA, 120 kV, slice thickness = 5 mm). Subsequently, PET images were captured at 7–9 beds (2.5 min/bed). After image acquisition was completed, the CT data were used to perform attenuation correction on the PET images, and Philips TOF PET software was used iteratively to reconstruct the images.

PET/CT images were independently assessed by two nuclear specialists with more than 10 years of experience who were blinded to the surgical outcome. Disagreements were resolved by consultation. Rectangular 3-dimensional volume of interest (VOI) was inserted on PET images to cover the entire tumor and adjusted to exclude surrounding non-tumor activity to measure standardized uptake value (SUV). SUV was calculated with the following formula: decay-corrected activity (kBq)/tissue volume (mL)/injected [¹⁸F]FDG activity (kBq)/body mass (g). SUVmax was the maximum SUV. Metabolic tumor volume (MTV, cm³) was defined as the volume where SUV was more than 42% of SUVmax, and MTV is the sum of all lesions. Both PET/CT scores and CT scores were based on the Suidan model.[6] Eight quantitative criteria and three clinical criteria based on the Suidan model were recorded, including lesions in the gastrohepatic ligament/porta hepatis (score = 1), splenic hilum/ligaments (score = 1) and retroperitoneal lymph nodes above

the renal hilum (including supradiaphragmatic) (score = 1), diffuse small bowel adhesions/thickening (score = 1), gallbladder fossa/liver intersegmental fissure lesions (score = 2), lesser sac lesions (score = 2), abdominal ascites (moderate–severe) (score = 2), root of the superior mesenteric artery lesions (score = 4), age ≥60 years (score = 1), CA125 ≥600 U/mL (score = 1) and American Society of Anesthesiologists (ASA) class ≥3 (score = 1). After surgery, the absence of macroscopic residual disease was defined as R0, residual disease with a maximum diameter ≤1 cm as R1, and residual disease with a maximum diameter >1 cm as R2. R0 was categorized as complete resection, and R1 and R2 as incomplete resection.

2.3 | Statistical analysis

The statistical software used was SPSS software (SPSS 22.0; IBM). Normally distributed measurement data are expressed as $\bar{x} \pm s$, independent sample t-test was used for comparison between groups. Non-normally distributed measurement data are expressed as the median (interquartile range), Mann–Whitney U-test was used for comparison between groups. Receiver operating characteristic (ROC) curves were used to analyze the predictive value of the indicators and determine the cutoff value. The Delong test was used to analyze and compare the predictive value of PET/CT score between primary and secondary debulking surgery groups. The Wilcoxon matched-pairs signed-ranks test was used to compare PET/CT scores and CT scores. Spearman correlation test was conducted among the indicators. A p-value <0.05 indicated that the difference was statistically significant.
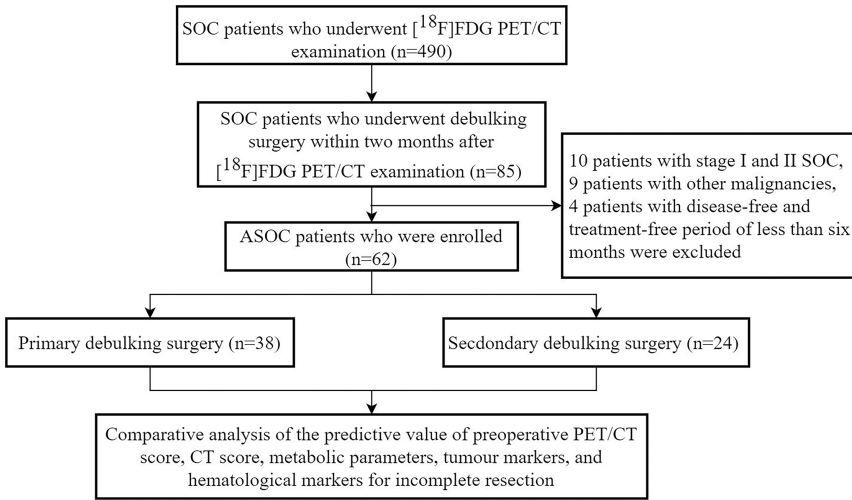
2.4 | Ethics statement

The study protocol was approved by the medical ethics committee of our institution (study number 2021–339) on July 27, 2021. Informed consent was waived due to the study's retrospective design.

3 | RESULTS

3.1 | Patient characteristics

A total of 490 serous ovarian cancer patients underwent [¹⁸F]FDG PET/CT examination at our hospital from July 1, 2015 to January 31, 2022; 62 ASOC patients were enrolled. The median (interquartile range) interval between PET/CT examination and debulking surgery was 6 (3–8) days. The flow chart of the study design is shown in Figure 1. The patient characteristics are shown in Table 1. The median age of the enrolled patients was 52 years (range, 31–76 years), 37/62 patients were at FIGO stage III, and 25/62 patients were at FIGO stage IV. Both PET/CT scores and CT scores were based on the Suidan model (Figure 2). The median (interquartile range) preoperative CA125 level, HE4 level, LMR, PLR, NLR, PET/CT score,

CT score, SUVmax and MTV are shown in Table 1. A total of 38/62 patients underwent primary debulking surgery; 24/62 patients suffered a recurrence and underwent secondary debulking surgery. All surgeries were performed by the gynecologists specialized in oncologic surgery, who had more than 10 years' working experience. The procedures included total hysterectomy and bilateral adnexectomy, omentectomy, peritonectomy, diaphragmatic stripping, hepatectomy, splenectomy, bowel resection, appendectomy, tumor removal from the urinary bladder flap, retroperitoneal lymph node resection in this cohort. In the complete resection group, 18 patients underwent primary debulking surgery, 19 patients underwent secondary debulking surgery, and 25 patients were in the incomplete resection group.

3.2 | Comparison between the complete resection group and the incomplete resection group

For the 38/62 (61.3%) patients who underwent primary debulking surgery, the median (interquartile range) preoperative PET/CT score (1 [0–2]) in the complete resection group was significantly lower than that in the incomplete resection group (3 [2–5.5]) ($p < 0.001$) (Table 2). Preoperative SUVmax, MTV, HE4 level, CA125 level, LMR, PLR and NLR were not statistically different between the complete resection group and the incomplete resection group ($p = 0.748$, $p = 0.219$, $p = 0.895$, $p = 0.483$, $p = 0.121$, $p = 0.306$, $p = 0.195$, respectively) (Table 2).

For the 24/62 (38.7%) patients who underwent secondary debulking surgery, the median (interquartile range) preoperative PET/CT score (0 [0–1]) in the complete resection group was significantly lower than that (2 [2–3]) in the incomplete resection group ($p = 0.009$) (Table 2). Preoperative HE4 and/or CA125 levels in the complete resection group were significantly lower than those in the incomplete resection group ($p = 0.033$ and $p = 0.036$, respectively) (Table 2). Preoperative SUVmax, MTV, LMR, PLR and NLR were not statistically different between the complete resection group and the incomplete resection group ($p = 0.722$, $p = 0.126$, $p = 0.469$, $p = 0.189$, $p = 0.826$, respectively) (Table 2).

3.3 | Predictive value of indicators for incomplete resection

For the primary debulking surgery group, ROC curves showed that preoperative PET/CT score and CT score had predictive value for incomplete resection after debulking surgery for ASOC (AUC: 0.847, 95% confidence interval [CI]: 0.73–0.97, $p < 0.001$; AUC: 0.821, 95% CI: 0.69–0.95, $p = 0.001$; respectively); preoperative SUVmax, MTV, HE4 level, CA125 level, LMR, PLR and NLR did not have predictive value for incomplete resection after primary debulking surgery for ASOC ($p = 0.748$, $p = 0.219$, $p = 0.895$, $p = 0.483$, $p = 0.121$, $p = 0.306$, $p = 0.279$, respectively) (Figure 3, Table 3). Among all the indicators, preoperative PET/CT score had the highest predictive value for incomplete resection (sensitivity: 65.0%, specificity: 88.9%, AUC: 0.847, $p < 0.001$) (Figure 3, Table 3). According to the principle of the maximum Youden index, the cutoff value of preoperative PET/CT score for incomplete resection fulfillment was 2.5, indicating that ASOC patients with a preoperative PET/CT score ≥3 were more likely to obtain incomplete resection after primary debulking surgery (Figure 3, Table 3).

For the secondary debulking surgery group, ROC curves showed that preoperative PET/CT score, CT score, HE4 level and CA125 level had predictive value for incomplete resection after debulking surgery for ASOC (AUC: 0.853, 95% CI: 0.60–1.00, $p = 0.017$; AUC: 0.853, 95% CI: 0.60–1.00, $p = 0.017$; AUC: 0.816, 95% CI: 0.55–1.00, $p = 0.033$; AUC: 0.811, 95% CI: 0.55–1.00, $p = 0.036$; respectively), but preoperative SUVmax, MTV, LMR, PLR and NLR did not ($p = 0.722$, $p = 0.126$, $p = 0.499$, $p = 0.189$, $p = 0.915$, respectively) (Figure 3, Table 3). Among all the indicators, preoperative PET/CT score and CT score had the same and highest predictive value for incomplete resection (sensitivity: 80.0%, specificity: 94.7%, AUC: 0.853, $p = 0.017$) (Figure 3, Table 3). According to the principle of the maximum Youden index, the cutoff value of preoperative PET/CT score for incomplete resection fulfillment was 1.5, indicating that ASOC patients with a preoperative PET/CT score ≥2 were more likely to obtain incomplete resection after secondary debulking surgery (Figure 3, Table 3).

TABLE 1 Patient characteristics ($n = 62$)

Characteristics	Value
Age (years)	
Median	52
Range	31–76
FIGO stage	
III	37/62 (59.7%)
IV	25/62 (40.3%)
Tumor markers	
Preoperative CA125 (U/mL)	359.15 (82.3–1200.9)
Preoperative HE4 (pmol/L)	157 (65–356.8)
Hematological markers	
Preoperative LMR	3.26 (2.5–5.13)
Preoperative PLR	168.16 (122.22–225)
Preoperative NLR	2.42 (1.77–3.75)
Preoperative PET/CT score	1 (0–3)
Preoperative CT score	1 (0–3)
Metabolic parameters	
Preoperative SUVmax	9.5 (6.9–13.1)
Preoperative MTV (cm^3)	47.61 (8.64–154.28)
Debulking surgery	
Primary debulking surgery	38/62 (61.3%)
Secondary debulking surgery	24/62 (38.7%)
Complete resection group (R0)	37/62 (59.7%)
Primary debulking surgery	18/38 (47.4%)
Secondary debulking surgery	19/24 (79.2%)
Incomplete resection group	25/62 (40.3%)
R1	15/62 (24.2%)
R2	10/62 (16.1%)

Note: Values are presented as median (interquartile range) or number (%). R0 was categorized as complete resection, and R1 and R2 were categorized as incomplete resection. R0, no macroscopic residual disease. R1, residual disease with the maximum diameter ≤1 cm. R2, residual disease with the maximum diameter >1 cm.

Abbreviations: CA125, cancer antigen 125; CT score, Suidan model-based CT score; FIGO, International Federation of Gynecology and Obstetrics; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET/CT score, Suidan model-based PET/CT score; PET/CT, positron emission tomography/computed tomography; PLR, platelet-to-lymphocyte ratio; SUVmax, maximal standard uptake value; TLG, the total lesion glycolysis.

3.4 | Comparison of predictive value of PET/CT score between primary and secondary debulking surgery groups

The Delong test showed that there was no statistical difference between primary debulking surgery group (AUC: 0.847, 95% CI: 0.73–0.97) and secondary debulking surgery group (AUC: 0.853, 95% CI: 0.60–1.00) in the predictive value of preoperative PET/CT score for incomplete resection for ASOC ($p = 0.971$).

3.5 | Comparison between PET/CT scores and CT scores

For patients who underwent primary debulking surgery, PET/CT scores and CT scores were the same in 33/38 (86.8%) patients and different in 5/38 (13.2%) patients. The difference was statistically significant between PET/CT scores and CT scores ($p = 0.041$). More lesions in the porta hepatis, splenic hilum, retroperitoneal lymph nodes above the renal hilum or lesser sac were detected by PET/CT scores than by CT scores (Figure 4).

For patients who underwent secondary debulking surgery, PET/CT scores and CT scores were the same in 23/24 (95.8%) patients and different in 1/24 (4.2%) patients. There was no statistical difference between PET/CT scores and CT scores ($p = 0.317$).

3.6 | Correlations between any of the indicators

For all patients who underwent debulking surgery, correlation analysis showed that preoperative PET/CT score was positively correlated with preoperative MTV, HE4 level, CA125 level, PLR and NLR ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.001$ and $p = 0.002$, respectively), negatively correlated with preoperative LMR ($p = 0.008$), and not correlated with preoperative SUVmax ($p = 0.627$) (Table 4). Preoperative LMR was negatively correlated with preoperative MTV, HE4, CA125, PLR and NLR ($p = 0.004$, $p = 0.004$, $p = 0.001$, $p < 0.001$ and $p < 0.001$, respectively) (Table 4).

4 | DISCUSSION

Our results showed that preoperative PET/CT score had the highest predictive value for incomplete resection in primary debulking surgery group, and preoperative PET/CT score and CT score had the same and highest predictive value for incomplete resection in secondary debulking surgery group, compared with preoperative metabolic parameters SUVmax and MTV, tumor markers HE4 and CA125, and hematological markers LMR, PLR and NLR. Preoperative PET/CT score ≥3 (Suidan model) and preoperative PET/CT score ≥2 predicted a high risk of incomplete resection after primary and secondary debulking surgeries, respectively. Preoperative PET/CT score had identical predictive value for incomplete resection in primary and secondary debulking surgery groups and more accurately detected metastases compared with the CT score. Finally, preoperative PET/CT score was positively correlated with preoperative MTV, HE4, CA125, PLR and NLR, and negatively correlated with preoperative LMR.

Our study used complete resection as the evaluation standard for the surgical effect rather than optimal debulking. In previous studies, complete resection has been confirmed to be more beneficial than optimal debulking, with macroscopic residual disease ≤1 cm for patients with advanced ovarian cancer.[4] Maximum resection of
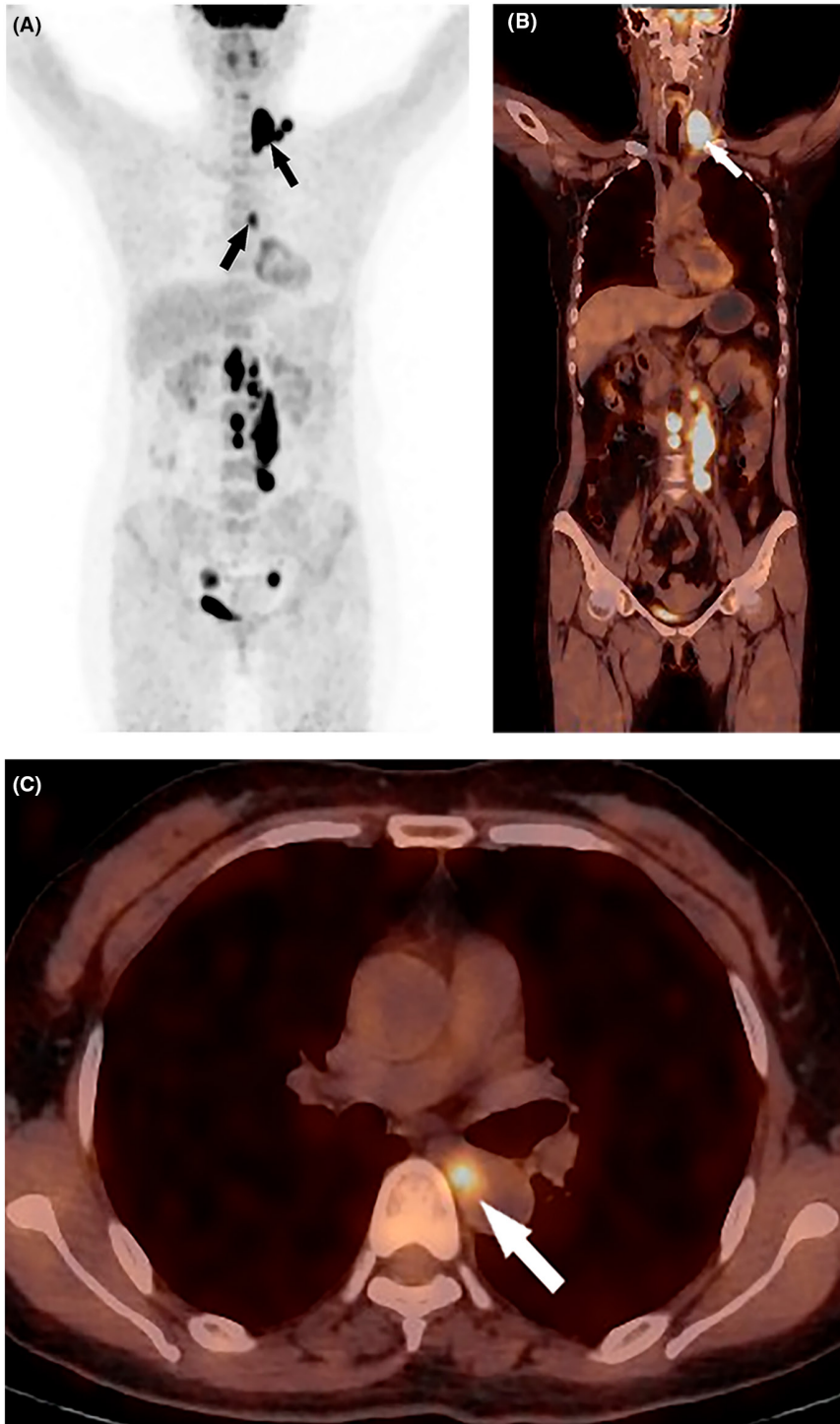
FIGURE 2 Preoperative [18F]FDG PET/CT images and PET/CT score in a 51-year-old woman with suspected ovarian cancer (A–C). Entire lesions are displayed in the maximum intensity projection image (A). Coronal PET/CT fused image (B) displays lesion (arrow) in supraclavicular lymph node, transaxial PET/CT fused image (C) displays lesion (arrow) in mediastinal lymph node. According to the Suidan model, the total PET/CT score was 1, corresponding to lesions (arrow) in the maximum intensity projection image (A). [18F]FDG, 2-deoxy-2-[18F]fluoro-D-glucose; PET/CT, positron emission tomography/computed tomography; PET/CT score, Suidan model-based PET/CT score

the tumor theoretically improves the sensitivity to chemotherapy because chemotherapy drugs may not be able to enter the inner parts of large tumors due to a lack of blood supply to those parts and thus cannot effectively kill tumor cells.[9]

Residual disease after debulking surgery is related to tumor spread. Some models have been studied for the evaluation of tumor spread and tumor burden, including the Fagotti model,[10] Bristow model,[11] Suidan model, and peritoneal carcinosis index (PCI) score.[12]

Routine laparoscopy cannot increase the sensitivity and causes more unnecessarily exploration with a lower specificity for predicting resectability in women suspected of advanced ovarian cancer.[5] Compared with laparoscopic exploration-based models, imaging-based prediction models are less invasive, more convenient and more economical. However, studies on the PET/CT prediction model for incomplete resection are insufficient, and no consensus on accurate prediction has been reached.

TABLE 2 Comparison between the complete resection group and the incomplete resection group

	Complete resection	Incomplete resection	z/t	p
Primary debulking surgery group				
PET/CT score	1 (0–2)	3 (2–5.5)	−3.728	<0.001
SUVmax	11.17 (9.4–14.6)	11.89 (7.77–14.44)	−0.322	0.748
MTV	108.85 (44.2–168.3)	153.85 (85.25–250.22)	−1.228	0.219
HE4	293.6 (154–597.8)	322.75 (158–429)	−0.132	0.895
CA125	725.5 (262.3–1700.6)	857 (375.8–2442.65)	−0.702	0.483
LMR	3.34 (2.19–5.25)	2.78 (1.86–3.26)	−1.550	0.121
PLR	174.93 (128.7–228)	193.06 (165.08–264.28)	−1.023	0.306
NLR	3.20 ± 1.30	3.92 ± 1.98	−1.322	0.195
Secondary debulking surgery group				
PET/CT score	0 (0–1)	2 (2–3)	−2.622	0.009
SUVmax	7.6 (6.1–9.4)	7.3 (3.3–11.7)	−0.356	0.722
MTV	6.27 (4.29–10.95)	29.76 (9.47–51.01)	−1.528	0.126
HE4	61 (50–70)	119 (96–194)	−2.133	0.033
CA125	45.2 (20.6–95.7)	157.7 (105.5–442.9)	−2.097	0.036
LMR	4.69 ± 1.79	4.06 ± 1.26	0.736	0.469
PLR	122.22 (78.38–151.58)	161.9 (151.85–168.84)	−1.315	0.189
NLR	1.91 ± 0.61	1.97 ± 0.39	−0.222	0.826

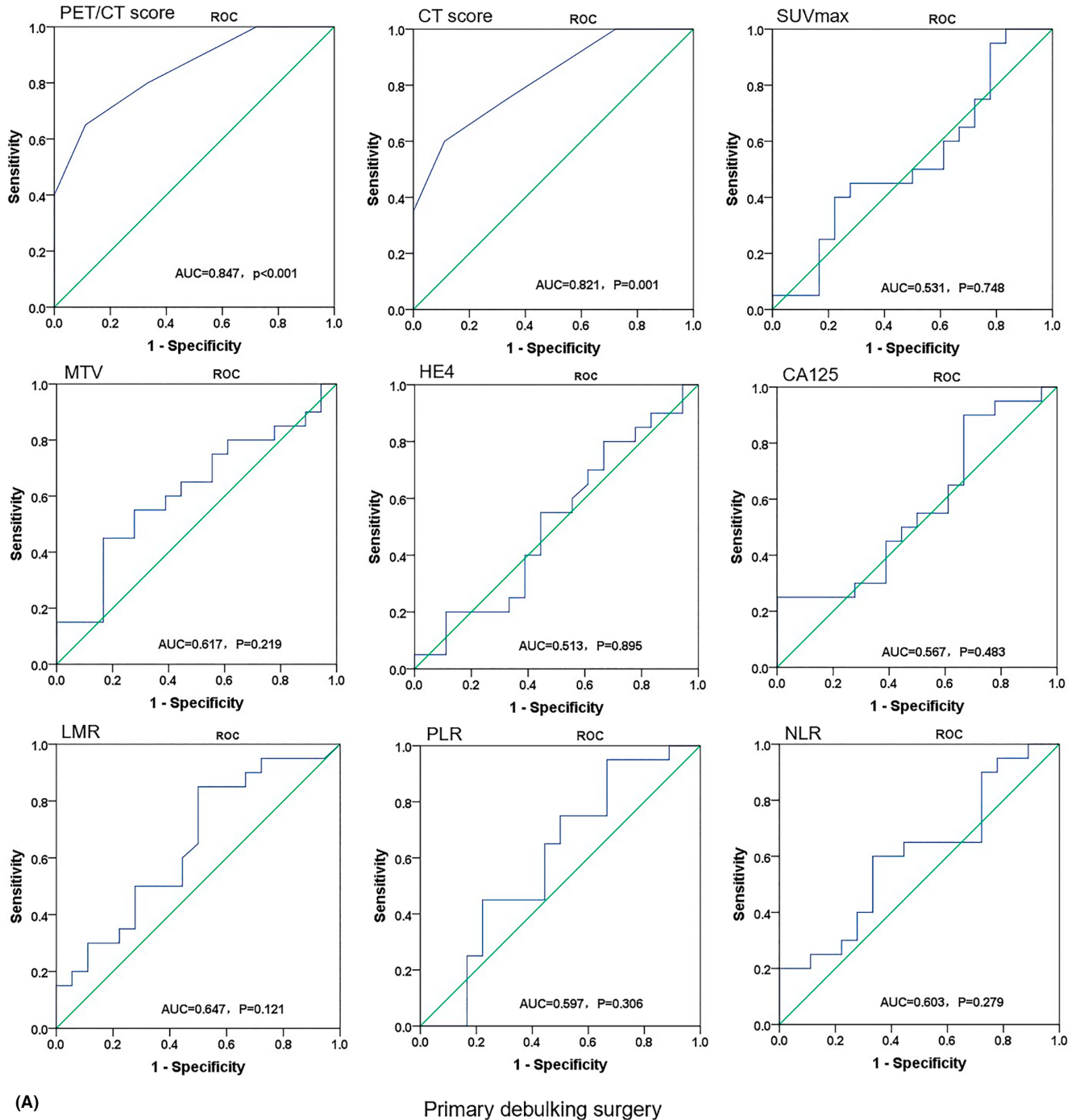*Note*: Values are presented as x̄ ± s or median (interquartile range).

Abbreviations: CA125, cancer antigen 125; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET/CT score, Suidan model-based PET/CT score; PET/CT, positron emission tomography/computed tomography; PLR, platelet-to-lymphocyte ratio; SUVmax, maximal standard uptake value.

Thus, we defined PET/CT score based on the Suidan model, which is one of the most comprehensive and robust quantitative prediction models for incomplete resection proposed thus far. In 2017, based on a prospective, nonrandomized, and multicenter trial of 350 patients who underwent primary debulking for AEOC, Suidan et al.[6] developed a predictive model in which the rate of any residual disease was proportional to a predictive score.

In our study, preoperative PET/CT score had the highest predictive value for incomplete resection among the indicators included. The results were encouraging, as preoperative PET/CT score may be a feasible and quantitative model for predicting incomplete resection after debulking surgery for ASOC. MTV, a volume-based metabolic parameter, is better than SUVmax at reflecting glucose metabolism in the entire tumor and intratumoral heterogeneity[13] PET/CT scores that reflect tumor sites may be more valuable than MTV in predicting surgical outcomes. Tsoi et al.[14] demonstrated that the number of metabolic active peritoneal sites was the only significant risk factor for incomplete tumor debulking (odds ratio, 2.983; 95% CI, 1.10–8.06; p = 0.031),

unlike presence of peritoneal carcinomatosis, SUVmax, MTV and TLG in ovarian and peritoneal cancers. Chong et al.[15] found that presence of hypermetabolic lesions in the central, left upper and right upper regions had predictive value for suboptimal debulking, which also confirmed the importance of tumor sites.

We found that a high preoperative PET/CT score indicated a high risk of incomplete resection, which was consistent with the literature. In 2020, Bingxin et al.[16] first proposed the PET/CT score based on the Suidan model to predict complete resection for advanced EOC (AEOC) and eight radiological criteria based on the Suidan model were recorded. The results showed that among the 11 patients who achieved complete resection, 10/11 (90.9%) patients had a preoperative PET/CT score ≤2, suggesting that a low preoperative PET/CT score is useful for predicting complete resection in patients with AEOC. Compared with the study by Bingxin et al.,[16] we increased the sample size, and analyzed the predictive value of PET/CT score in primary and secondary debulking surgery groups, respectively; only ASOC patients were included in our study, and our study included more three additional clinical criteria based on the

FIGURE 3 Predictive value of the indicators for incomplete resection after debulking surgery for advanced serous ovarian cancer analyzed using ROC curves. (A) ROC curves for primary debulking surgery. (B) ROC curves for secondary debulking surgery. CA125, cancer antigen 125; CT, computed tomography; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET, positron emission tomography; PET/CT score, Suidan model-based PET/CT score; PLR, platelet-to-lymphocyte ratio; ROC, receiver operating characteristic curve; SUVmax, maximal standard uptake value

Suidan model. According to the study by Suidan et al.,[6] these three clinical criteria (age ≥60 years, CA125 ≥600 U/mL, and ASA class ≥3) were significantly associated with residual disease ($p = 0.003$, $p < 0.001$, $p < 0.001$, respectively) and were included in the Suidan model. Therefore, the inclusion of these three clinical criteria in our study will increase the accuracy and comprehensiveness.

We found that preoperative PET/CT score had identical predictive value for incomplete resection in primary and secondary debulking surgery groups ($p = 0.971$). Previous studies have shown that complete resection after both primary and secondary debulking surgeries is strongly associated with prolonged survival[4,17] Therefore, predicting incomplete resection is important for both primary and secondary debulking surgeries.
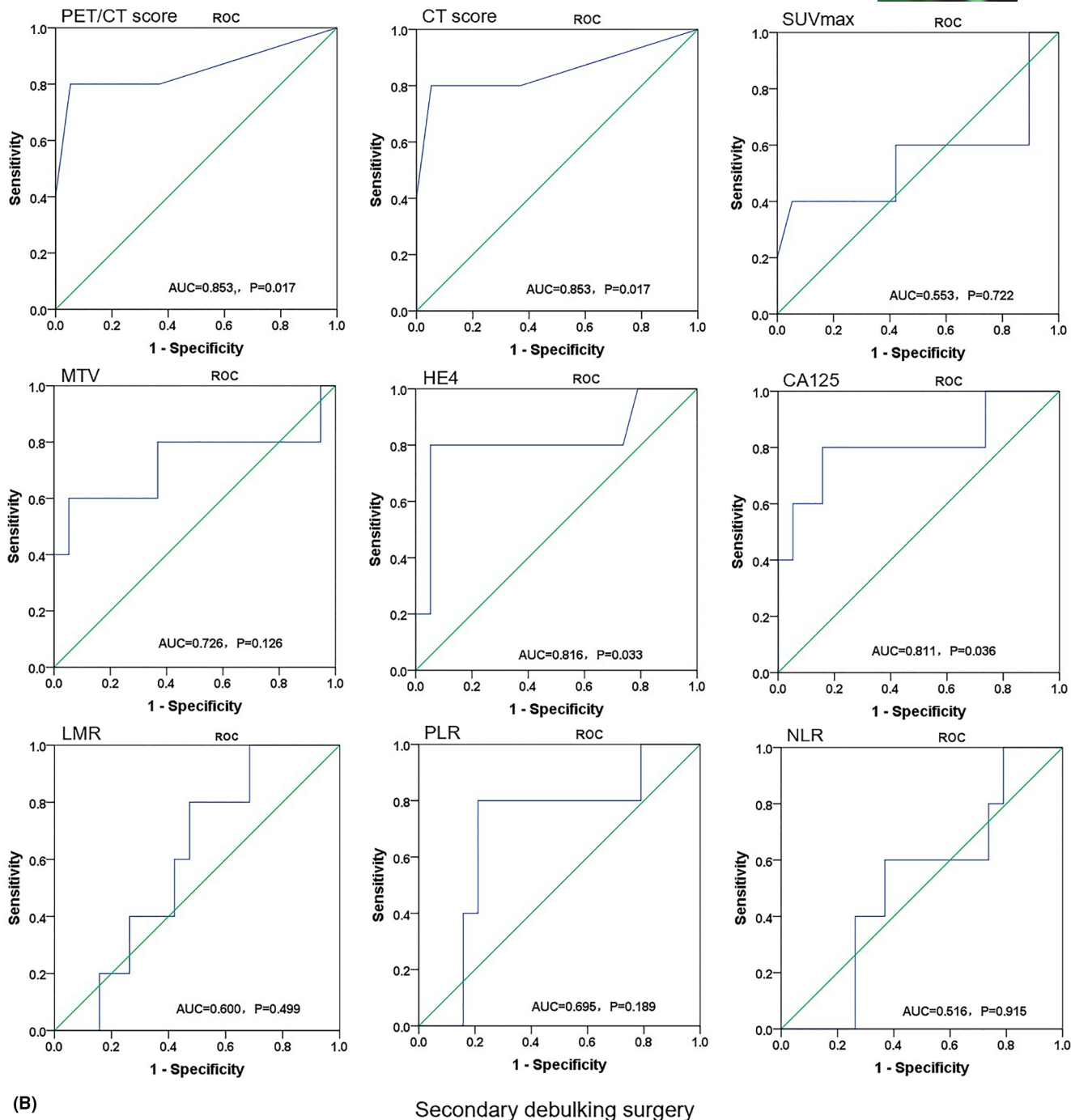
(B)

Secondary debulking surgery

FIGURE 3 (Continued)

One of the interesting things was that the cutoff values of preoperative PET/CT scores for incomplete resection fulfillment in primary and secondary debulking surgery groups were different (2.5 vs 1.5) in our study. Primary debulking surgery is used to remove malignant lesions in patients who are newly diagnosed with ovarian cancer,[18] whereas secondary debulking surgery is performed in patients with recurrent platinum-sensitive ovarian cancer if complete resection appears to be feasible,[17] especially in those with isolated or limited-volume recurrent disease. Therefore, PET/CT score before secondary debulking surgery is generally lower than that before

primary debulking surgery, which may have resulted in the difference in cutoff values.

In our study, there was a statistical difference between PET/CT scores and CT scores in the primary debulking surgery group ($p = 0.041$), with more metastases shown by PET/CT scores than by CT scores. There was no statistical difference in the secondary debulking surgery group ($p = 0.317$). The advantage of PET/CT scores over CT scores was greater in primary debulking surgery group than in secondary debulking surgery group; this may be related to the complexity of the lesions in the former. Advantages

	AUC	95% CI	p	Sensitivity (%)	Specificity (%)	Cutoff value
Primary debulking surgery group						
PET/CT score	0.847	0.73–0.97	<0.001	65.0	88.9	2.5
CT score	0.821	0.69–0.95	0.001	60.0	88.9	2.5
SUVmax	0.531	0.34–0.72	0.748	40.0	77.8	9.165
MTV	0.617	0.44–0.80	0.219	45.0	83.3	189.05
HE4	0.513	0.32–0.70	0.895	80.0	33.3	157
CA125	0.567	0.38–0.75	0.483	25.0	100.0	3364.55
LMR	0.647	0.47–0.83	0.121	85.0	50.0	3.51
PLR	0.597	0.41–0.79	0.306	95.0	33.3	134.585
NLR	0.603	0.42–0.79	0.279	60.0	66.7	3.255
Secondary debulking surgery group						
PET/CT score	0.853	0.60–1.00	0.017	80.0	94.7	1.5
CT score	0.853	0.60–1.00	0.017	80.0	94.7	1.5
SUVmax	0.553	0.19–0.91	0.722	40.0	94.7	3.45
MTV	0.726	0.40–1.00	0.126	60.0	94.7	21.63
HE4	0.816	0.55–1.00	0.033	80.0	94.7	94.5
CA125	0.811	0.55–1.00	0.036	80.0	84.2	104.95
LMR	0.600	0.36–0.84	0.499	80.0	52.6	5.055
PLR	0.695	0.43–0.96	0.189	80.0	78.9	151.715
NLR	0.516	0.25–0.78	0.915	60.0	63.2	2.015

TABLE 3 Predictive value and cutoff value of the indicators for incomplete resection after debulking surgery for advanced serous ovarian cancer analyzed using ROC curves

Abbreviations: AUC, Area under ROC curve; CA125, cancer antigen 125; CI, confidence interval; CT score, Suidan model-based CT score; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET/CT score, Suidan model-based PET/CT score; PET/CT, positron emission tomography/computed tomography; PLR, platelet-to-lymphocyte ratio; ROC, receiver operating characteristic curve; SUVmax, maximal standard uptake value.

of PET/CT are consistent with the literature (Table S1). A meta-analysis[19] demonstrated that preoperative PET/CT had a very high diagnostic accuracy, especially for specificity (0.96, 95% CI 0.91–0.99), to detect metastases of pelvic and para-aortic lymph nodes in EOC, and should be evaluated systematically in the preoperative staging of AEOC. Hynninen et al.[20] found supradiaphragmatic lymph node metastases in 67% of AEOC patients through preoperative PET/CT examination, which was twice the detection rate of CT alone. The study of Schmidt et al.[21] showed that [18F]FDG PET/CT had the highest specificity for the detection of peritoneal carcinomatosis in ovarian cancer compared with multidetector CT and MRI, and whole-body FDG PET/CT may be more accurate for the detection of supradiaphragmatic metastases. Mallet et al.[22] indicated that [18F]FDG PET/CT metabolic parameters were highly accurate in predicting peritoneal metastases, and [18F]FDG PET/CT improved the detection of extra-abdominal lesions, leading to treatment modification in a significant proportion of patients compared with CT. Van 't Sant et al.[23] found that PET/CT and (DW)MRI had a comparable overall diagnostic value in detecting peritoneal metastases. Rubini et al.[24] reported that the sensitivity, specificity and accuracy of [18F]FDG PET/CT in the identification of peritoneal carcinomatosis in patients with

ovarian cancer were 78.6%, 91.3% and 84.3%, respectively; for CT with contrast enhancement (CECT), they were 53.6%, 60.9% and 56.9%, respectively.

Correlation analysis showed that preoperative PET/CT score was positively correlated with preoperative MTV, HE4 level, CA125 level, PLR and NLR, and negatively correlated with preoperative LMR. The results were consistent with previous studies. Gong et al.[25] found that a low LMR before treatment was correlated with high CA125 level (OR: 2.18; 95% CI: 1.71–2.77; p < 0.001). The study of Kwon et al.[26] revealed that a high NLR (>2.3) and a low LMR were significantly correlated with low 5-year progression-free survival (PFS) and overall survival (OS) rates in patients with ovarian clear cell cancer. Glickman et al.[27] found that both preoperative HE4 and CA125 were correlated with MTV.

This study also had some limitations. First, compared with conventional imaging, PET/CT has not been widely used in gynecological tumors, and many patients were excluded because the treatment did not meet the criteria for inclusion, thus the sample was limited. Secondly, this study was retrospective and there might be bias in the data collection. To reduce this bias, incomplete or uncertain data were excluded from this study.

Future investigations will study the predictive value of PET/CT score for progression-free survival and overall survival.
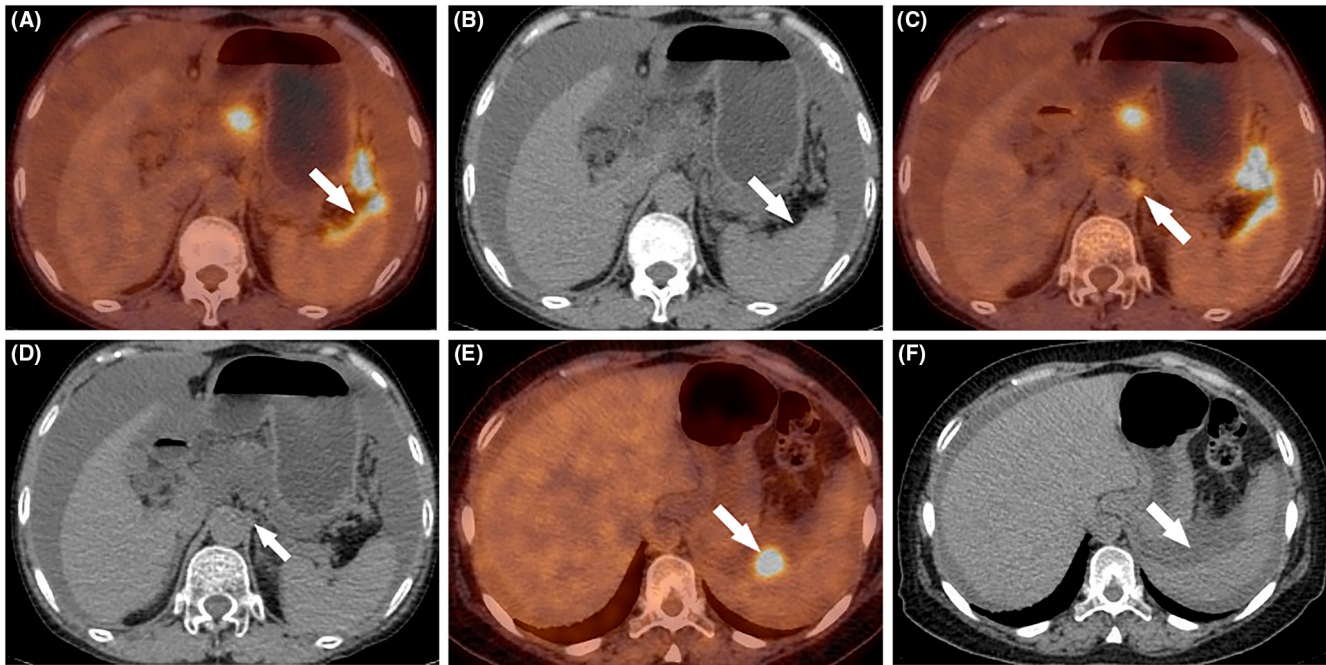
FIGURE 4 Metastases identified by [18F]FDG PET/CT scores but not by CT scores. (A–D) Transaxial images of preoperative [18F]FDG PET/CT in a 54-year-old woman with suspected ovarian cancer. PET/CT fused image (A) displays lesion (arrow) in splenic hilum (score = 1) that CT scan (B) could not identify. PET/CT fused image (C) displays lesion (arrow) in retroperitoneal lymph node above the renal hilum (score = 1), CT scan (D) displays a lymph node approximately 10×4mm in size with uniform density and a regular border, which was not identified as a lesion. (E,F) Transaxial images of preoperative [18F]FDG PET/CT in a 64-year-old woman with suspected ovarian cancer. PET/CT fused image (E) displays lesion (arrow) in splenic hilum (score = 1) that CT scan (F) could not identify. [18F]FDG 2-deoxy-2-[18F]fluoro-D-glucose; CT, computed tomography; PET, positron emission tomography; PET/CT score, Suidan model-based PET/CT score

TABLE 4 Correlations between any of PET/CT score, SUVmax, MTV, HE4 level, CA125 level, LMR, PLR and NLR

		PET/CT score	SUVmax	MTV	HE4	CA125	LMR	PLR	NLR
PET/CT score	r	1.000							
	p								
SUVmax	r	0.063	1.000						
	p	0.627							
MTV	r	0.512	0.447	1.000					
	p	<0.001	<0.001						
HE4	r	0.435	0.394	0.684	1.000				
	p	<0.001	0.002	<0.001					
CA125	r	0.585	0.292	0.588	0.708	1.000			
	p	<0.001	0.021	<0.001	<0.001				
LMR	r	−0.335	−0.027	−0.359	−0.359	−0.404	1.000		
	p	0.008	0.835	0.004	0.004	0.001			
PLR	r	0.424	0.187	0.55	0.532	0.524	−0.561	1.000	
	p	0.001	0.145	<0.001	<0.001	<0.001	<0.001		
NLR	r	0.389	0.107	0.383	0.453	0.459	−0.739	0.586	1.000
	p	0.002	0.409	0.002	<0.001	<0.001	<0.001	<0.001	

Abbreviations: CA125, cancer antigen 125; HE4, human epididymis protein 4; LMR, lymphocyte-to-monocyte ratio; MTV, metabolic tumor volume; NLR, neutrophil-to-lymphocyte ratio; PET/CT score, Suidan model-based PET/CT score; PET/CT, positron emission tomography/computed tomography; PLR, platelet-to-lymphocyte ratio; SUVmax, maximal standard uptake value.

5 | CONCLUSION

Among preoperative PET/CT score, CT score, SUVmax, MTV, HE4, CA125, PLR, NLR and LMR, preoperative PET/CT score had the highest predictive value for incomplete resection after primary debulking surgery and preoperative PET/CT score and CT score had the same and highest predictive value for incomplete resection after secondary debulking surgery. ASOC patients with a high preoperative PET/CT score were more likely to obtain incomplete resection. Preoperative PET/CT score showed the same predictive value in primary and secondary debulking surgery groups and was more accurate in the detection of metastases compared with CT score. Therefore, preoperative PET/CT score may be a feasible and quantitative model for predicting incomplete resection after debulking surgery for ASOC.

AUTHOR CONTRIBUTIONS

JW contributed to data collection and analysis and was a major contributor in writing the manuscript. LiL assisted with data collection. HP contributed to the image analysis. LiliL assisted with the data analysis. XJ contributed to the image analysis. YL contributed to the conception of the study and revision of the article. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

None.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.