

Diagnostic accuracy of ¹⁸F-FDG PET/CT scan for peritoneal metastases in advanced ovarian cancer

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Background: To assess the diagnostic accuracy of ¹⁸F-FDG PET/CT to determine the Eisenkop score and peritoneal cancer index (PCI) in correlation with surgical findings.

Methods: Forty-three patients underwent preoperative ¹⁸F-FDG PET/CT scan, followed by primary cytoreductive surgery for advanced ovarian cancer between September 2015 and February 2018. Clinical data were prospectively collected, including intraoperative assessment (with Eisenkop and PCI scores) and surgical results. The sensitivity, specificity, and accuracy were calculated at each anatomical site. The Eisenkop score, PCI score, and tumor volume of PET/CT scans were compared with surgical findings.

Results: A total of 32 (74.4%) patients were diagnosed with stage III, and 11 (25.6%) patients were stage IV. Among these individuals, 19 (44.2%) patients had no residual disease after primary surgery. The median [range] Eisenkop score on PET/CT scans and surgical findings were 5 [1–13] and 6 [2–13], respectively. PET/CT scans correctly predicted the Eisenkop score with high sensitivity (84.2%), specificity (87.0%), and accuracy (85.1%). The diagnostic accuracy of PET/CT scans for PCI scores was lower (78.5%), with 72.7% sensitivity and 84.9% specificity. Preoperative PET/CT scans might underestimate tumor volume compared with surgical findings.

Conclusions: ¹⁸F-FDG PET/CT scans accurately predicted peritoneal metastases in advanced ovarian cancer before surgery using Eisenkop score.

Keywords: Ovarian cancer; ¹⁸F-FDG PET/CT; Eisenkop score; peritoneal cancer index (PCI); peritoneal metastases

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Introduction

Ovarian cancer is one of the most common and lethal diseases among women around the world. At initial diagnosis, over two-thirds of patients are of advanced stage, with widespread intraabdominal disease (1,2). The standard treatment for ovarian cancer includes staging or debulking surgery and platinum-based adjuvant chemotherapy. Intraabdominal extent of ovarian cancer could influence treatment strategy and surgical outcomes.

Eisenkop score and peritoneal cancer index (PCI) are intraoperative ranking systems to quantify the tumor burden (3,4). These scores have been reported correlated with complete cytoreduction and patients' survival (5,6). Thus, an accurate preoperative tumor burden assessment would be useful for appropriate treatment strategy selection and prognosis prediction.

¹⁸F-FDG PET/CT has been an important molecular imaging modality for preoperative and therapeutic effect assessment in ovarian cancer for several decades. Previous studies have shown that these semi-quantitative parameters are associated with patient clinical characteristics and prognosis in ovarian cancer (7-14). However, there is limited data showing diagnostic accuracy of PET/CT scans for peritoneal metastases in advanced ovarian cancer.

The aim of the present study was to assess the diagnostic accuracy of PET/CT to determine the Eisenkop score and PCI in correlation with surgical findings.

Methods

Data collection

This study was conducted according to the Declaration of Helsinki and was approved by the Committee at Fudan University Shanghai Cancer Center (FUSCC). All individual participants consented to the use of their medical records for research purposes. Between September 1, 2015, and February 28, 2018, forty-three patients underwent preoperative PET/CT scans, followed by primary cytoreductive surgery for advanced ovarian cancer. The histological diagnoses were based on WHO criteria. No patients included in this group received any disease treatment prior to referral, and the clinical data were prospectively collected.

¹⁸F-FDG PET/CT scan

All patients had PET/CT scans within 2 weeks before treatment. ¹⁸F-FDG was produced automatically by cyclotron (Siemens CTI RDS Eclipse ST, Knoxville, TN, USA) using the Explora FDG4 module in our center. Radiochemical purity was over 95%. All patients were asked to fast at least 6 hours before the ¹⁸F-FDG PET/CT procedure. Each patient's blood glucose level was below 10 mmol/L at the time of radio-tracer injection. The standard dosage of intravenous ¹⁸F-FDG administration was 7.4 MBq/kg. Before and after injection, patients were kept lying comfortably in a quiet, dimly lit room. Examination was performed 60 minutes after ¹⁸F-FDG injection. A

Siemens Biograph 16HR PET/CT scanner (Knoxville, TN, USA) with 4 mm transaxial intrinsic spatial resolution (full width at half maximum) and 16.2 cm axial field width was used for image scanning. Whole-body PET/CT data acquisition began with low-dose CT from the inguinal region to the head, with 120 kV, a 130-370 mA automatic adjustment, a pitch of 3.6, and a 0.5 second rotation time, followed by PET emission scan in a three-dimensional mode, with 2-3 minutes per bed position. The PET data were reconstructed using the ordered-subset expectation maximization technique selecting 8 subsets and 4 iterations, a 168×168 matrix. The CT data were used for attenuation correction of the PET images, and coregistered images were displayed on a workstation. The reconstructed images were then converted to a semiguantitative image corrected by the injection dose and the subject's body weight [standardized uptake value (SUV)].

Tumor burden assessments and statistical analyses

Preoperative and intraoperative assessments of tumor burden [with Eisenkop (3) and PCI (4) score] were recorded by experienced radiologists and gynecological oncologists, respectively (Tables S1 and S2). Tumor volume was categorized according to Eisenkop score: 0-5 (small-volume tumor); 6-10 (moderate-volume tumor); and ≥ 11 (largevolume tumor).

SPSS statistical software (version 21.0, SPSS, IBM Inc., New York, USA) was used for the statistical analyses. Descriptive statistics were used for the demographic data and summarized as medians with ranges or frequencies with percentages. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy for identifying peritoneal metastasis were calculated for each anatomical site.

Results

Patient characteristics

The patient characteristics are summarized in *Table 1*. A total of 43 advanced ovarian cancer patients were included in the analysis. The median [range] age was 57 [38–76] years old. The median CA125 was 774.8 U/mL. Thirty-two (74.4%) patients were diagnosed with stage III, and 11 (25.6%) patients were stage IV. Among these individuals, 19 (44.2%) patients had no residual disease after primary debulking surgery.

Performance of ¹⁸F-FDG PET/CT scan for preoperative assessment

The median [range] Eisenkop score on PET/CT scan and surgical findings were 5 [1–13] and 6 [2–13], respectively. PET/CT scans correctly predicted the Eisenkop score with high sensitivity (84.2%), specificity (87.0%), and accuracy (85.1%) (*Table 2* and *Figure 1A*). The median (range) PCI score on PET/CT scans and surgical findings were 12 [2–31] and 12 [2–30], respectively. The diagnostic accuracy of PET/

Table 1 Patient characteristics

Variables	Number
Age, median [range]	57 [38–76]
FIGO stage, n (%)	
IIIA	3 (7.0)
IIIB	2 (4.7)
IIIC	27 (62.8)
IV	11 (25.6)
CA125, median [range]	774.8 [8.28 to >5,000]
Surgical Eisenkop score, median [range]	6 [2–13]
PET-CT Eisenkop score, median [range]	5 [1–13]
Surgical PCI score, median [range]	12 [2–30]
PET-CT PCI score, median [range]	12 [2–31]
Residual disease, n (%)	
RD	24 (55.8)
R0	19 (44.2)

PCI, peritoneal cancer index; FIGO, International Federation of Gynecology and Obstetrics.

Table 2 Eisenkop score on PET-CT scan compared with surgical findings

CT scans for PCI scores was lower (78.5%), with 72.7% sensitivity and 84.9% specificity (*Table 3* and *Figure 1B*).

Compared to PCI, Eisenkop score could also evaluate retroperitoneal metastases. The diagnostic accuracy of retroperitoneum was up to 93%, with 89.5% sensitivity and 95.8% specificity. The diagnostic accuracy was low for jejunum and ileum by PCI assessment. Also, the predictive values for left flank, left lower flank, right flank, and right lower flank were unsatisfactory (*Table 3*). However, the area of central abdomen for Eisenkop score, which included both intestine and lateral pericolic gutters, had considerable diagnostic accuracy (81.4%), with 89.7% sensitivity and 64.3% specificity (*Table 2*). Besides, the sensitivity of the right upper quadrant was a bit lower in both ranking systems.

As for tumor volume, 34 patients were correctly categorized; 6 patients with moderate volume tumor were misclassified as small volume on PET/CT scan, and 2 patients with large volume tumor were assessed as moderate volume. While only 1 patient with moderate volume was recognized as large volume. Thus, preoperative PET/CT scans might underestimate tumor volume compared with surgical findings (*Table 4*).

Discussion

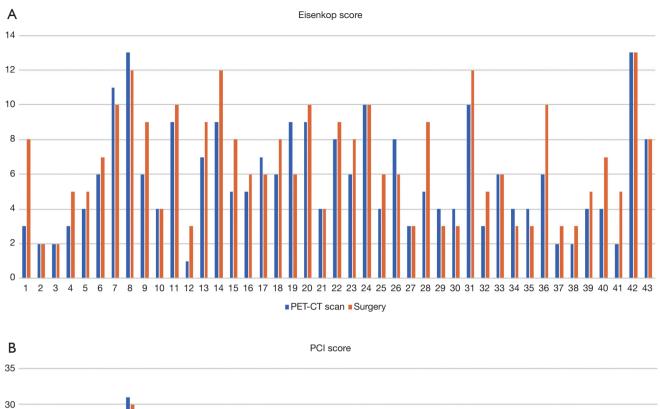
The present study validated two ranking systems for tumor burden on preoperative PET/CT scans and surgical findings in a prospective patient cohort. ¹⁸F-FDG PET/CT scans were not effective for preoperative PCI assessment in advanced ovarian cancer. That being said, it could accurately predict peritoneal metastases using Eisenkop score.

Advanced ovarian cancer is characterized by peritoneal dissemination, and the volume of residual disease is

Region	True positive	False negative	True negative	False positive	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Right upper quadrant	22	9	11	1	71.0	91.7	95.7	55.0	76.7
Left upper quadrant	22	6	15	0	78.6	100.0	100.0	71.4	86.0
Pelvis	36	3	2	2	92.3	50.0	94.7	40.0	88.4
Retroperitoneum	17	2	23	1	89.5	95.8	94.4	92.0	93.0
Central abdomen	26	3	9	5	89.7	64.3	83.9	75.0	81.4
Total	123	23	60	9	84.2	87.0	93.2	72.3	85.1

PPV, positive predictive value; NPV, negative predictive value.

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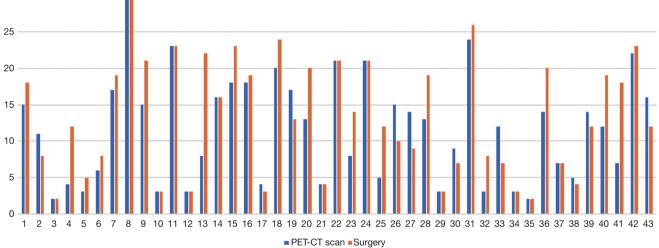


Figure 1 Comparison of Eisenkop score (A) and PCI score (B) on preoperative PET-CT scan and surgical findings. PCI, peritoneal cancer index.

inversely correlated with the prognosis (15-17). Two ranking systems, Eisenkop score and PCI, have been reported to be correlated with patients' surgical and survival outcomes (3-6). For patients with tumors too extensive to be adequately cytoreduced, appropriate preoperative imaging helps prevent unnecessary surgeries. Our study aimed to contribute to careful patient selection and preoperative treatment prediction.

CT used to be the most common preoperative method for ovarian cancer patients, with good specificity but poor sensitivity for identifying peritoneal metastases (18-21). Compared to conventional CT scan, ¹⁸F-FDG PET/CT

Region	True positive	False negative	True negative	False positive	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
0 central	24	5	12	2	82.8	85.7	92.3	70.6	83.7
1 right upper	24	7	11	1	77.4	91.7	96.0	61.1	81.4
2 epigastrium	7	4	29	3	63.6	90.6	70.0	87.9	83.7
3 left upper	15	1	22	5	93.8	81.5	75.0	95.7	86.0
4 left flank	13	6	20	4	68.4	83.3	76.5	76.9	76.7
5 left lower	21	11	9	2	65.6	81.8	91.3	45.0	69.8
6 pelvis	43	0	0	0	100.0	-	100.0	-	100.0
7 right lower	18	11	13	1	62.1	92.9	94.7	54.2	72.1
8 right flank	14	7	19	3	66.7	86.4	82.4	73.1	76.7
9 upper jejunum	7	3	24	9	70.0	72.7	43.8	88.9	72.1
10 lower jejunum	6	4	27	6	60.0	81.8	50.0	87.1	76.7
11 upper ileum	7	11	24	1	38.9	96.0	87.5	68.6	72.1
12 lower ileum	9	8	21	4	52.9	84.0	69.2	72.4	69.8
Total	208	78	231	41	72.7	84.9	83.5	74.8	78.5

Table 3 PCI score on PET-CT scan compared with surgical findings

PCI, peritoneal cancer index; PPV, positive predictive value; NPV, negative predictive value.

PET-CT scan	Surgical findings					
FEI-OT SCAIL	Small volume	Moderate volume	Large volume			
Small volume	17	6	0			
Moderate volume	0	15	2			
Large volume	0	1	2			

can also provide functional or metabolic characteristics, and it has been used increasingly during ovarian cancer treatment (7-13). Hynninen *et al.* (22) demonstrated that PET/CT was superior to conventional CT for the detection of carcinomatosis in subdiaphragmatic peritoneal surfaces and bowel mesentery for advanced ovarian cancer. However, the sensitivity of both PET/CT and CT scans was poor in certain areas (64% *vs.* 27% in the small bowel mesentery and 65% *vs.* 55% in the right upper abdomen). Unlike previous studies, our study evaluated, for the first time, the diagnostic accuracy of PET/CT scans using two intraoperative ranking systems. Our data showed considerable sensitivity of PET/CT scans for peritoneal metastases in advanced ovarian cancer, with 84.2% for Eisenkop score and 72.7% for PCI. We demonstrated that Eisenkop score performed better than PCI by preoperative PET/CT scan. The diagnostic accuracy of PET/CT by Eisenkop score was higher than that acquired using PCI score, with simple anatomical classification. For PCI assessment, it was hard to distinguish jejunum from ileum, especially to divide the intestines into four anatomical areas. Thus, the diagnostic accuracy was low for these parts. When considered as a whole, the diagnostic accuracy rose for the central abdomen by Eisenkop score. In addition, Eisenkop score could also correctly evaluate retroperitoneal metastases, although this was not included in the PCI assessment. However, the sensitivity of the right upper quadrant was a bit lower in both ranking systems because small-volume metastases on diaphragm and subcapsular liver metastases could be affected by physiological FDG distribution of liver. This may also lead to the result that tumor volume is underestimated by PET/CT scan.

The limitation of our study was the small number of enrolled patients. However, our systematic prospective data collection by the multidisciplinary team could compensate for that, making our results more reliable and applicable.

Our study suggested that ¹⁸F-FDG PET/CT scan accurately predicted peritoneal metastases in advanced ovarian cancer before surgery using Eisenkop score. PET/ CT scans should be regarded as a helpful preoperative assessment method.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/qims-20-784). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Committee at Fudan University Shanghai Cancer Center (FUSCC). All individual participants consented to the use of their medical records for research purposes.

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Table S1 Eisenkop score

Anatomic regions		Score
Right upper quadrant (diaphragm, right hepatic surface, crural area, portal area, peritoneum adjacent to right kidney, and duodenum)	No visible disease	0
	Metastatic implants and/or confluent disease involving <50% of the surface area of the diaphragm	1
	Metastatic implants and/or confluent disease involving >50% of the surface area of the diaphragm	2
	Any confluent diaphragm disease with invasion into muscle or contiguous involvement of the bare area and/or surface of the liver, peritoneum adjacent to the right kidney and duodenum, or portal region	3
Left upper quadrant (omentum,	No visible disease	0
gastrocolic ligament, spleen, stomach, transverse colon,	Involvement of the infracolic omentum	1
splenic flexure of colon, left	Involvement of the infracolic omentum and gastrocolic ligament	2
hepatic surface, and left diaphragm)	Involvement of the infracolic omentum and/or gastrocolic ligament and contiguous involvement of spleen, stomach, transverse colon, splenic flexure of colon, left diaphragm, or liver surface	3
Pelvis (reproductive organs,	Adnexal disease only	0
pelvic peritoneum, cul-de- sac, bladder peritoneum, rectosigmoid	Individual metastatic implants on the pelvic peritoneum, and/or adnexa adherent to pelvic sidewall	1
	Extensive confluent disease involving pelvic peritoneal surfaces, including the cul-de-sac, bladder peritoneum, and/or rectosigmoid serosa	2
	Bulky disease encasing much of the pelvis, including the cul-de-sac and rectosigmoid colon	3
Retroperitoneum (retroperitoneal nodes distal to crura)	No positive nodes and/or microscopic positive	0
	Grossly positive nodes, largest <1 cm	1
	Grossly positive nodes >1 cm	2
	Confluent bulky positive retroperitoneal nodal disease	3
Central abdomen (small intestines, ascending and descending colon, intestinal	No visible disease	0
	<50 metastatic implants	1
mesentery, lateral pericolic	>50 metastatic implants	2
gutters, anterior abdomen)	Metastatic implants contiguous with bulky disease involving bowel and/or mesentery	3

Table S2 Peritoneal cancer index (PCI)

Regions	Lesion size score (LS)
0 central	
1 right upper	
2 epigastrium	
3 left upper	
4 left flank	
5 left lower	
6 pelvis	
7 right lower	
8 right flank	
9 upper jejunum	
10 lower jejunum	
11 upper ileum	
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LS: 0 no tumor, 1 tumor up to 5 mm, 2 tumor up to 5 cm, 3 tumor ${>}5$ cm or confluence.