European Review for Medical and Pharmacological Sciences 2016; 20: 4426-4434

Diagnostic accuracy of MDCT in the evaluation of patients with peritoneal carcinomatosis from ovarian cancer: is delayed enhanced phase really effective?

E. RODOLFINO[1], E. DEVICIENTI[1], M. MICCÒ[1], A. DEL CIELLO[1], S.E. DI GIOVANNI[1], M. GIULIANI[1], C. CONTE[2], B. GUI[1], A.L. VALENTINI[1], L. BONOMO[1]

[1]Department of Radiological Sciences, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, School of Medicine, Rome, Italy
[2]Department of Obstetrics and Gynecology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, School of Medicine, Rome, Italy

Abstract. – OBJECTIVE: To assess the diagnostic accuracy of delayed enhanced phase in addition to portal enhanced phase in MDCT imaging for depicting peritoneal carcinomatosis (PC) implants in patients with ovarian cancer.

PATIENTS AND METHODS: We retrospectively reviewed double-phase, portal enhanced phase (PEP) and delayed enhanced phase (DEP), MDCT-examinations of 40 patients with clinical suspicion of recurrent PC from histopathologically-proven ovarian cancer, previously treated with both cytoreductive surgery and adjuvant/ neoadjuvant chemotherapy. Image assessment was performed by three independent blinded readers (2 experienced and 1 less-experienced radiologists) in 3 different reading sessions: PEP (set A), DEP (set B), and PVP + DEP (set C). All CT-images were qualitatively assessed on the basis of the location of the lesion (based on Sugarbaker scheme), presence (indicating a confidence level for the diagnosis of PC), size and pattern. Reference standard both for detection and exclusion of PC was the evaluation of double-phase MDCT exams performed by two experienced readers in consensus, knowing clinical and laboratoristic parameters as well as previous and subsequent imaging (follow-up minimum of 12 months). Sensitivity, specificity, PPV, NPV and diagnostic accuracy of each reader for each reading session were calculated and compared. A subgroup analysis based on lesion pattern was also performed.

RESULTS: On a total of 507 abdominal-pelvic sites evaluated, PC was found in 182 regions (35.9%). When considering experienced radiologists, no statistically significant differences (p>0.05) were found between the different sets of images. The analysis by less-experienced radiologist showed lower statistical results, which significantly improved when both PEP and DEP were evaluated. In the subgroup analysis, DEP showed significantly higher statistical results in the case of micronodular patterns.

CONCLUSIONS: Our results indicate that the CT-acquisition protocol in patients with ovarian cancer for tumor staging should be based on portal phase alone, with a significant radiation dose reduction, whereas the addition of delayed phase images is useful for less-experienced readers.

Key Words
Peritoneal carcinomatosis, Ovarian cancer, Multidetector Computed Tomography (MDCT), Delayed enhanced phase.

Introduction

Peritoneal carcinomatosis (PC) represents the most common pathway for the spread of ovarian cancer and is found in 70% of patients at the time of diagnosis[1], characterizing an advanced stage of the disease. The introduction of more aggressive surgical treatments and intra-peritoneal chemotherapy appears to increase significantly the overall survival rate. In detail, advanced-stage disease is treated either with initial cytoreductive surgery (debulking) followed by adjuvant chemotherapy, or with initial neoadjuvant chemotherapy followed by debulking[2]. Accurate pre-operative imaging assessment of PC, in terms of disease's presence and extension, is mandatory to determine the most appropriate therapeutic strategy[3]. In detail,

Corresponding Author: Ersilia Devicienti, MD; e-mail: ersadev@yahoo.it

it plays a crucial role in identifying patients who may benefit from neoadjuvant chemotherapy before debulking[2].

The gold standard for detection and staging of PC is open surgery or laparoscopic approach; however, thanks to technological improvements, non-invasive imaging modalities could also be used to detect implants of PC and evaluate their extent and localization before surgery or treatment. In detail, Multidetector-row Computed Tomography (MDCT) is still considered the imaging technique of choice, performed routinely in staging of ovarian cancer, both for its wide availability and its ability to obtain thin-section images of the entire abdomen and pelvis with high resolution multiplanar reconstructions (MPR)[4-8]. Also, MDCT plays a crucial role in the evaluation of any persistence of disease after cytoreductive surgery and during follow-up period because the detection of any recurrent lesion of PC at imaging can obviate a diagnostic second-look laparotomy[4].

However, literature has demonstrated that MDCT sensibility in the detection of PC varies greatly, ranging from 25% to 90%, depending not only on the size of the carcinomatosis[9-13], but also on the CT protocol used and/or the peritoneal enhancement obtained[3]. In some early stage cases, an abnormal enhancement of the peritoneum may be the only finding suggestive of peritoneal infiltration. Based on this assumption, it is obvious that an appropriate CT acquisition protocol is mandatory for an adequate MDCT examination to obtain an accurate tumoral staging. It is well known that portal venous phase is considered the phase of choice in the detection of PC[2]. However, there is no consensus about the role of other acquisition phases, particularly the delayed phase, generally considered optional only in the case of pelvic implants or retroperitoneal metastases that involve ureters causing hydroureteronephrosis[4].

Thus, based on this background, the aim of our study was to assess the diagnostic accuracy of delayed phase in addition to portal venous phase at MDCT imaging for depicting PC implants in patients with ovarian cancer, previously treated with cytoreductive surgery.

Patients and Methods

Study Population – Study Design

This study includes all patients suffering from ovarian cancer, with clinically suspected recurrent PC, referred to our Institute by the Gynecological Oncology Unit to undergo CT-staging/re-staging. A computer search was performed in our RIS-PACS system (Radiological Informatics System: Imagoweb-El.Co.S.r.l., Savona, Italy; Picture Archiving and Communication Systems: Carestream Health, Genova, Italy) using the following filters: interval time, 2011 - 2014; imaging technique: CT; UDC (cost diagnostic unit): Gynecology; ULD (hospital logistic unit): Gynecological Oncology Unit.

For a patient to be eligible, all the following inclusion criteria have to be present: first diagnosis of ovarian cancer proven by histopathology; previous treatment with both cytoreductive surgery and adjuvant/neoadjuvant chemotherapy; clinical/laboratory suspicion of recurrent ovarian cancer lesions in the peritoneum; double-phase (portal and delayed contrast-enhanced phases) CT-examination of abdomen performed at our Institute by using a multi-detector row helical scanner; additional follow-up for a minimum of 12 months obtained with a combination of CT/PET-CT and/or magnetic resonance (MR) imaging. Following the inclusion criteria, females submitted to biphasic CT in a 3-year period suspected of having recurrent PC could be identified and retrospectively enrolled in our study. Then, database research, medical history investigation as well as histopathology correlation were collected and reviewed.

All imaging performed in this research was part of the routine evaluation of patients at our Institute and was considered an acceptable part of patient care. The Institutional Review Board granted permission for this work; the requirement for informed consent was waived.

CT scanning

Double-phase acquisition (portal and delayed contrast-enhanced phases) was performed by using a multi-detector row helical scanner (Siemens – Somatom Definition Flash, Munich, Germany). CT images were obtained from the level of the diaphragm to the symphysis pubis with 128x0.6 mm-section collimation, 0.5-second gantry rotation, pitch of 6 and 1.00 mm slice thickness.

All patients were asked to drink 15 mL of oral water-soluble contrast medium (Gastrografin) dissolved in approximately 300 mL of water 20 minutes before CT examination; CT-enhanced images were acquired 70 seconds (portal phase) and 300 seconds (delayed phase) after bolus intravenous injection of iodinated non-ionic contrast medium (Iopromide 370 mgI/mL, Ultravist; Bayer Schering Pharma, Berlin, Germany), at a flow rate of 3 mL/s via an antecubital vein. To minimize variability in enhancement of the abdominal parenchyma related to differences in patient size, the volume of contrast material was calculated according to the body weight of the patient (2 mL of contrast material per kilogram of body weight). The ensuring average volume of contrast material was equal to 130 mL (range, 120-140 mL).

Image Analysis

Source of reference (SOR): Our reference standard for both detection and exclusion of PC was the evaluation of double-phase (portal and delayed contrast-enhanced phase) CT acquisition performed by two experienced readers (ALV and BG, with more than 15 years of experience in abdominal imaging), knowing clinical and laboratory parameters (CA-125 serum levels) as well as previous CT findings. Furthermore, proof of tumor burden and absence of disease were also confirmed during the additional follow-up with a combination of CT/PET-CT and/or magnetic resonance (MR) imaging for a minimum of 12 months.

For the best description of disease extension, the internationally recognized Sugarbaker's PCI was used in radiological analysis and SOR. In detail, it divides the entire abdominal and intestinal regions into 13 regions, of which 4 refer to small bowel, allowing the exact topography of tumor extension. Furthermore, in each of the 13 regions, the maximum visible lesion size was measured and assigned to a lesion size score between LS=0 and LS=3 (0: no tumor visible; 1: tumor lesion size <0.5 cm; 2: tumor lesion size between 0.5 and 5 cm; 3: tumor lesion size >5 cm)[14].

All CT-examinations or singular region evaluated in consensus by the two experienced readers as technically inadequate/non-diagnostic were excluded from the subsequent analysis.

Readers: Diagnostic Performance

CT-images were divided into different sets to be evaluated independently by three blinded readers: 2 experienced radiologists (respectively, with 10 and 7 years of experience in abdominal imaging) and 1 less-experienced radiologist (resident at fourth year of residency in radiology). These readers were unaware of previous imaging findings as well as surgical/pathological data. The different sets of images consisted of: set A = portal enhanced phase images (PEP), set B = delayed enhanced phase images (DEP), set C = portal plus delayed phase images (PEP + DEP).

During each reading session, the readers separately and independently assigned a confidence level for the diagnosis of PC, by using a five-point scale: score 1 for certainly-absent, score 2 for probably absent, score 3 for possibly present, score 4 for probably present and score 5 for certainly present. Before evaluating the images, the readers were informed that a confidence level of 3 or higher represented a positive diagnosis of PC.

The readers reviewed all sets of images in random order at a dedicated computer workstation (Advantage Workstation, GE Healthcare, Milwaukee, WI, USA), adjusting the image's level and window, and routinely using a 2D multiplanar reconstruction technique to evaluate better the peritoneal recesses. Names, ages, and identification numbers of patients, and imaging parameters were always hidden during the review to minimize learning bias. The specific image sets were randomly selected by another author (E.D.), who did not participate in the review. The interval between the reading sessions was at least 1 month.

Study Coordinator: Morphological Classification and Qualitative Assessment of Peritoneal Carcinomatosis

Study coordinator (E.R.) was asked to perform a CT qualitative assessment of true-positive abdominal-pelvic sites, proven by SOR. In detail, she was asked to classify them in terms of morphological aspects by using the following four different patterns: P1 micronodular (tiny 1-5 mm milky spots of peritoneal implants, diffusely involving the tunica serosa and subserosal fat); P2 nodular (nodular implants with a maximum diameter >5 mm); P3 plaque-like pattern (irregular soft-tissue thickenings of peritoneal walls and parenchyma and bowel surface); P4 linear (homogeneous and diffuse peritoneal thickening, with significant enhancement after contrast medium injection).

Furthermore, the study coordinator analyzed the morphological pattern of all misdiagnosed peritoneal lesions assessed by readers (false negative cases) in order to highlight a possible correlation between morphological pattern and misdiagnosis.

In the end, she was also asked to perform a subjective assessment of conspicuity of all lesions, based on peritoneal enhancement, by using a 4-point scale (1, barely perceptible with presence debatable; 2, subtle finding but likely a lesion; 3, definite lesion detected; and 4, strikingly evident and easily detected).

Statistical Analysis

Interobserver agreement for the evaluation of CT images was assessed with the K test. Degrees of agreement were categorized as follows: k values of 0.00-0.20 were considered to indicate poor agreement; k values of 0.21-0.40, fair agreement; k values of 0.41-0.60, moderate agreement; k values of 0.61-0.80, high agreement; and k values of 0.81-1.00, excellent agreement (15).

To evaluate the diagnostic accuracy of different CT-sets of images in detection and localization of PC, both patient-level and region-level analyses were performed. Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy to detect peritoneal carcinomatosis for all reading sessions were also calculated.

CT images evaluated with a score of 3 or higher and confirmed as positive for peritoneal carcinomatosis at SOR were considered as true-positive diagnoses, whereas CT images with a confidence level of 1 or 2 evaluated as negative for peritoneal carcinomatosis at SOR were considered as true negative diagnoses. False negative diagnoses were represented by CT images with a confidence of 1 or 2, evaluated as positive for peritoneal carcinomatosis at SOR, whereas false positive diagnoses were represented by CT images with a score of 3 or higher, evaluated as negative for peritoneal carcinomatosis at SOR.

Statistical analysis obtained for all reading sessions were compared by using the two-tailed Student's *t*-test for paired data. A two-tailed *p*-value of less than 0.05 was considered significant.

Results

Study Population

The computer search allowed to identify a total of 127 patients with previous history of ovarian cancer and clinically suspected recurrent PC, referred to our Institute by the Gynecological Oncology Unit to undergo CT-restaging. 87 patients were excluded for the following reasons: lack of acquisition of a delayed phase CT scan (n= 42), lack of additional follow-up CT for a minimum of 12 months (n= 33), lack of cytoreductive surgery (n=12).

Table I. Clinical and pathological characteristics of study population.

Patients Characteristics	N (%)
Age (years)	
Mean	48.5
Range	32-73
Pre-surgery FIGO Stage	
III	33/40 (83.5%)
IV	7/40 (17.5 %)
Histologic findings	
Serosus cystoadenocarcinoma	34 (85 %)
Mucinosus cystoadenocarcinoma	5 (12.5 %)
Endometrioid adenocarcinoma	1 (2.5 %)
Co-morbidities	15 (37.5 %)
Obesity / Overweight	11 (27.5 %)
Hypertension	8 (20 %)
Osteoporosis	6 (15 %)
Thyroid disfunction	4 (10 %)
Type 2 diabetes mellitus	3 (7.5 %)
Controlled asthma	2 (5 %)
Deep vein thrombosis	1 (2.5 %)
Sjogren syndrome	1 (2.5 %)
Multiple sclerosis	1 (2.5 %)

The remaining 40 patients (mean age: 48.5 years; age range: 32-73 years) formed the final study population. Study population characteristics are described in Table I.

SOR

In all patients, ovarian cancer was previously proven by histology, whereas concomitant PC was associated in 29 (29/40, 72.5%) of them, either stage III (n= 33) or stage IV (n= 7).

When considering the region-level evaluation, based on Sugarbaker classification, a total of 507 abdominal-pelvic sites were evaluated for PC, with the last 13 sites not evaluated as considered technically inadequate, due to beam hardening artifacts or patients movements compromising the diagnosis. In detail, PC was found in 182 regions (182/507, 35.9%), among them 38 (38/182, 20.9%) classified as LS1, 81 (81/182, 48.8%) as LS2, and the last 63 (63/182, 34.6%) as LS3.

Reading sessions

When considering experienced readers, the K analysis showed excellent interobserver agreement (K analysis value ≥0.88) in all reading sessions for PC detection, so the data were pooled.

Experienced Readers

When considering a patient-level analysis, set A was able to correctly correlate with SOR

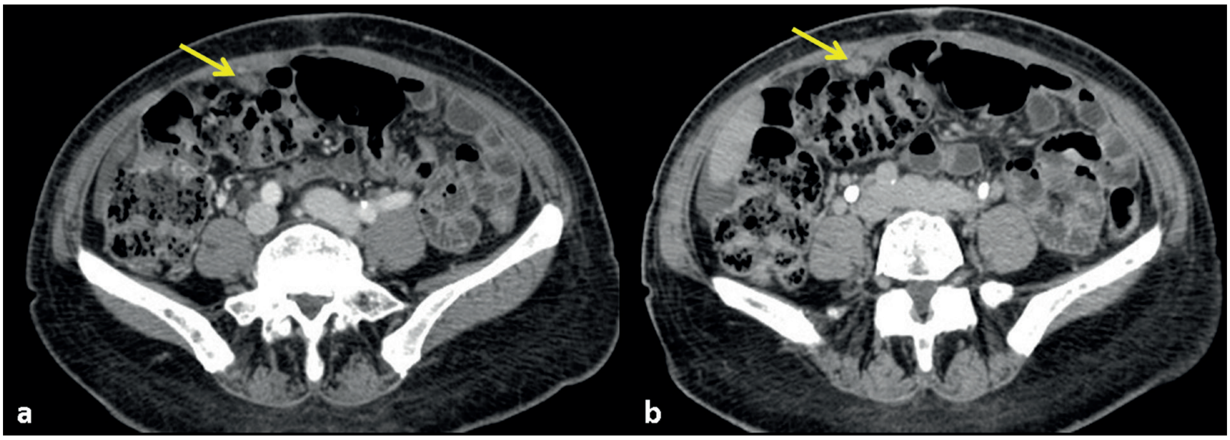

Figure 1. ***a-b***, Axial CT images obtained in portal (***a***) and delayed (***b***) phases. Experienced readers assigned a score of 5 (certainly present) in all reading sessions *(arrow in a and b)*, as confirmed by SOR (nodular pattern of carcinomatosis involving the omentum) = True positive case.

in 26/29 (89.6%) patients with PC (true positive) and in 7/11 patients without PC (true negative), set B in 26/29 (89.6%) patients with PC (true positive) and in 6/11 patients without PC (true negative), and set C in 27/29 (93.1%) patients with PC (true positive) and in 8/11 patients without PC (true negative), with a consequent diagnostic accuracy of 82.5%, 80%, and 87.5%, respectively (Figure 1).

When dealing with region-level analysis, the reading session A (PEP) allowed to correctly correlate with SOR in 169 pathological regions (169/182, 92.9%) and in 298 negative regions (298/325, 91.7%), session B in 164 pathological regions (164/182, 90.1%) and in 285 negative regions (285/325, 87.7%), whereas session C in 171 pathological regions (171/182, 94%) and in 304 negative regions (304/325, 93.5%), with a consequent diagnostic accuracy of 92.1%, 88.6%, and 93.7%, respectively.

No statistically significant differences (p>0.05) were found between the different sets of images for both patient-level and region-level analyses, even if set B obtained lower results when compared with set A and C. Sensitivity, specificity, negative and positive predictive values, as well as diagnostic accuracy for PC detection in all different CT image sets are showed in Table II.

Less-Experienced Reader

When considering a patient-level analysis, set A was able to correctly correlate with Standard of Reference (SOR) in 22/29 (75.9%) patients with PC (true positive) and in 6/11

Table II. Statistical comparison between results obtained by the experienced and less-experienced readers for patient- and region-level analysis.

	Experienced Readers						Less - Experienced Reader					
	Patient-level analysis			Region-level analysis			Patient-level analysis			Region-level analysis		
	Set A	Set B	Set C	Set A	Set B	Set C	Set A	Set B	Set C	Set A	Set B	Set C
Sens	89.6	89.6	93.1	92.9°	90.1°	94.0	75.9	79.3	89.7*	84.6	81.3	91.8*
Spec	63.6	54.5	72.7	91.7°	87.7°	93.5	54.5	54.5	63.6	82.2	76.3	91.4*
PPV	86.7	83.9	90.0	86.2°	80.4°	89.1	81.5	82.1	86.7	72.6	65.8	85.6*
NPV	70.0	66.7	80.0	95.8	94.1	96.5	46.2	50.0	70.0*	90.5	87.9	95.2
Acc	82.5	80.0	87.5	92.1°	88.6°	93.7	70.0	72.5	82.5*	83.0	78.1	91.5*

*For less-experienced reader: Significantly higher values in comparison with set A (p<0.001). °Significantly higher values in comparison with that obtained for the same set of images evaluated by less-Experienced reader (p<0.05). Data were described as percentages. Set A = portal enhanced phase images (PEP), set B = delayed enhanced phase images (DEP), set C = portal plus delayed phase images (PEP + DEP).

(54.5%) patients without PC (true negative), set B in 23/29 (79.3%) patients with PC (true positive) and in 6/11 (54.5%) patients without PC (true negative), and set C in 26/29 (89.7%) patients with PC (true positive) and in 7/11 (63.6%) patients without PC (true negative), with a consequent diagnostic accuracy of 70%, 72.5%, and 82.5%, respectively.

When dealing with region-level analysis, the reading session A (PEP) allowed to correctly correlate with SOR in 154 pathological regions (154/182, 84.6%) and in 267 negative regions (267/325, 82.2%), session B in 148 pathological regions (148/182, 81.3%) and in 248 negative regions (248/325, 76.3%), whereas session C in 167 pathological regions (167/182, 91.8%) and in 297 negative regions (297/325, 91.4%), with a consequent diagnostic accuracy of 83%, 78.1%, and 91.5%, respectively (Figure 2).

No statistically significant differences (p>0.05) were found between set A and B of images for both patient-level and region-level analyses. On the other hand, the addition of delayed phase to portal one (set C vs set A) allowed to obtain statistically significant higher values (p<0.001) in terms of sensitivity, negative predictive value as well as diagnostic accuracy, for patient-level analysis and sensitivity, specificity, positive predictive value as well as diagnostic accuracy for region-level analysis (Figure 3).

Sensitivity, specificity, negative and positive predictive values, as well as diagnostic accuracy for PC detection in all different CT image sets are showed in Table II.

Experienced versus Less-Experienced Readers

The values of sensitivity, specificity, VPP and diagnostic accuracy in reading sessions A and B were significantly higher for experienced than for less-experienced reader.

No significant differences were found between the differently experienced readers when considering set C (Table II).

Morphological Classification and Qualitative Assessment of Peritoneal Carcinomatosis

Study coordinator classified 41 lesions as P1 (micronodular) (41/182, 22.5%), 64 as P2 (nodular) (64/182, 35.1%), 46 as P3 (plaque-like) (46/182, 25.2%), and 31 as P4 (linear) (31/182, 17%).

Based on the morphological classification, a distribution of false negative cases assessed by readers was performed, as shown in Table III.

For the less-experienced reader, delayed phase significantly reduced the number of false negative cases for pattern P1 (p=0.04); similar results were also obtained for P4 (p=0.056), when added to the portal phase.

Results of the subjective assessment of conspicuity of lesions, based on peritoneal enhancement, distributed on the basis of morphological pattern are reported in Table IV.

Discussion

Epithelial ovarian cancer (EOC) is the sixth most common cancer and the seventh cause of

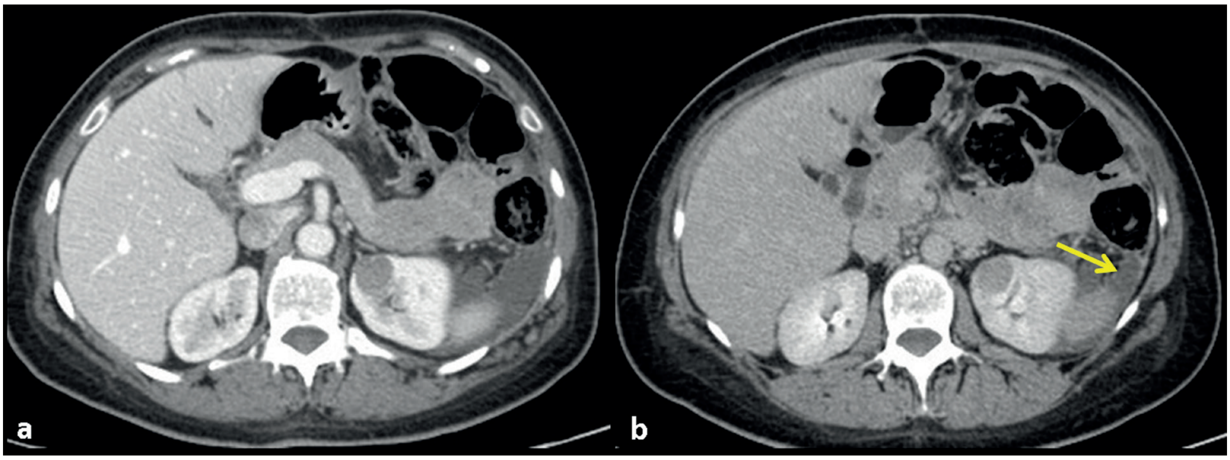

Figure 2. ***a-b***, Axial CT images obtained in portal (***a***) and delayed (**b**) phases. A micronodular lesion was correctly detected by less-experienced reader only at reading session **b** and **c**, based on higher enhancement of lesion obtained in delayed phase image *(arrow in* **b***)*, as confirmed by SOR (micronodular pattern of carcinomatosis involving the left paracolic gutter). False negative case for SET A – True positive case for SET B and C.

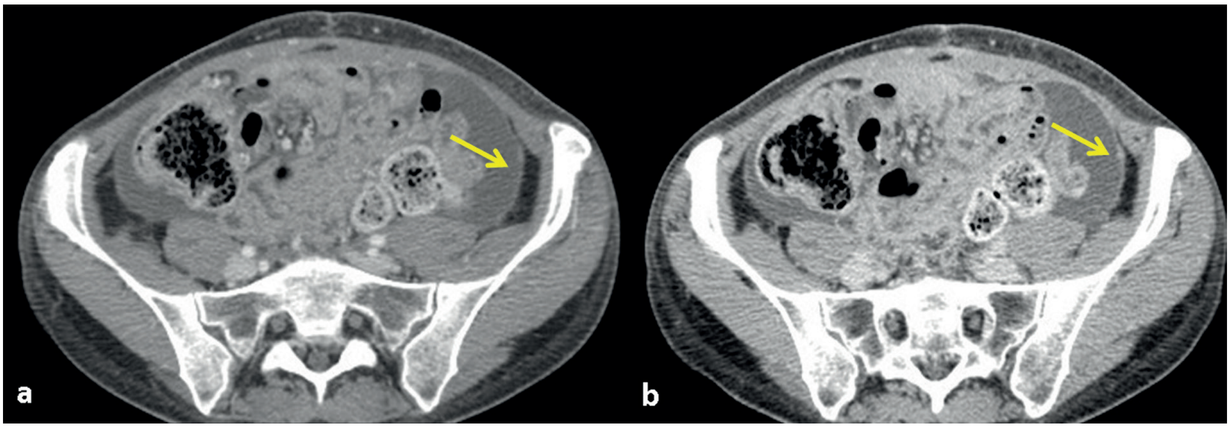

Figure 3. ***a-b***, Axial CT images obtained in portal (***a***) and delayed (**b**) phases. Linear thickening of parietal peritoneum was correctly detected by less-experienced reader only at reading session C, based on the evaluation of both portal and delayed phase images (*arrow in* ***a*** *and* **b**), as confirmed by SOR (linear thickening of parietal peritoneum diffusely involving the left paracolic gutter). False negative case for SET A and B – True positive case for SET C.

death from cancer in women (4.0% of cases and 4.2% of deaths)[16]. EOC usually spreads to the abdomen via the trans coelomic route and, less commonly, to other distant sites via lymphatic and haematogenous routes[17]. One of the important prognostic factors in EOC is the degree of peritoneal disease. The gold standard for staging ovarian cancer remains the surgical approach, which serves the dual purpose of both staging and obtaining disease cytoreduction. The goal of debulking surgery is to obtain a complete cytoreduction of all tumoral implants leaving no evidence of residual disease (NED). This is because it is well proven that patients with no residual disease have a better prognosis when treated with platinum-based agents[18,19].

CT remains one of the main imaging modalities used to detect peritoneal seeding; the ease of access, fast image acquisition time, thin section scanning and multiplanar reformations make MDCT the ideal imaging modality[4]. However, there is no consensus about the acquisition protocol to be used for depicting PC during CT staging; in particular, it is not well defined the appropriate role of the acquisition phases beyond the portal one. Some scholars highlighted the potential crucial role of delayed phase on MRI in increasing the sensitivity for detecting PC[20-23]. They concluded that it should be related to a better visualization of thickened enhanced peritoneum in the delayed phase reflecting the slow accumulation of contrast material in the peritoneal tissues. Nothing similar seems to be defined for CT examinations. Even if this conclusion could lead to a routine use of this phase also in CT, it is well known that the acquisition of images at an additional phase leads to increased patient exposure to ionizing radiation and an increase in the time of CT examination. As a matter of fact, it became crucial to clarify the real advantages of delayed phase in CT imaging to warrant their routine use. Based on this assumption, we performed our retrospective evaluation to assess the diagnostic accuracy of delayed enhanced phase in addition to portal enhanced phase MDCT imaging for depicting PC implants in patients with clinically

Table III. Distribution of false negative cases assessed by readers performed on the basis of morphological classification.

	SET A					SET B					SET C				
	Tot	P1	P2	P3	P4	Tot	P1	P2	P3	P4	Tot	P1	P2	P3	P4
Expert readers	13	5	2	3	3	18	3	5	8	2	11	3	2	3	3
Unexpert Reader	28	11*	4	4	9	34	4	14	10	6	15	4	3	4	4

P1 = micronodular pattern; P2 = nodular pattern; P3 = plaque-like pattern; P4 = linear pattern. Set A = portal enhanced phase images (PEP), Set B = delayed enhanced phase images (DEP), Set C = portal plus delayed phase images (PEP + DEP). *Significantly higher values in comparison with set B and C.

Table IV. Subjective assessment of conspicuity of lesions.

	PEP	DEP	
All lesions	3.4±0.6	3.3±0.5	NS
P1	3.1±0.3	3.7±0.4	$p = 0.04$
P2	3.8±0.4	3.1±0.5	$p = 0.016$
P3	3.6±0.3	2.9±0.6	$p = 0.002$
P4	3.2±0.4	3.6±0.3	$p = 0.06$

P1 = micronodular pattern; P2 = nodular pattern; P3 = plaque-like pattern; P4 = linear pattern. PEP = portal enhanced phase images, DEP = delayed enhanced phase images (p-value statistically significant <0.05).

suspected recurrence of PC from ovarian cancer, with previous cytoreductive surgery and adjuvant chemotherapy.

In our series, no statistically significant differences were found comparing set A (portal phase images) with set B (delayed phase images) and set C (portal + delayed phase images), respectively, for experienced readers. In detail, for experienced readers, the delayed enhanced phase reported lower results than the portal phase alone, even if not significant, whereas in addition to the portal phase didn't increase the diagnostic accuracy of MDCT imaging for depicting PC implants.

As a matter of fact, set A (portal phase images) allowed a correct diagnosis in 87.4% of cases, with only 13 false negative diagnosis; in detail, when dealing with morphological pattern analysis, the combination with delayed phase images allowed only the additional diagnosis of two small micronodular (P1, <5 mm) implants, without significant differences.

When considering less-experienced reader, no statistically significant differences were found between set A and B of images for both patient-level and region-level analyses. However, the addition of the delayed phase to the portal one allowed to obtain values of sensitivity, PPV and diagnostic accuracy significantly higher. With the addition of the delayed phase to the portal one, increase of PC detection rate (set A: 154/182, 82,4%; set C: 167/182, 89.3%) and more confident exclusion of PC (set A: 267/325, 67.4%; set C: 297/325, 75%) were observed. The real benefit of adding the delayed phase to the portal phase images is evident comparing experienced and less-experienced readers. In detail, experienced readers obtained significantly higher values when considering reading sessions A and B, whereas no significant differences were found between the differently experienced readers when considering set C, composed by the combination of portal and delayed phases.

An accurate evaluation of morphological pattern analysis showed that the combination of portal and delayed phase images decreased significantly the false negative rate from 28 to 15, with additional diagnosis of a total of 7 small micronodular (P1, <5 mm), 1 nodular (P2, 5-50 mm), and 5 linear (P4) implants. According to the experience performed in MRI, our study seems to confirm that delayed phase could be useful in the evaluation of small micronodular or linear peritoneal lesions, due to a better delineation of enhanced peritoneal layers, with a reduction of false negative cases. In fact, the qualitative evaluation of subjective assessment of conspicuity of lesions showed a significantly higher enhancement for micronodular (P1) implants in the delayed phase rather than in the portal one (3.7±0.4 *vs.* 3.1±0.3, p=0.04), with higher results, even if not significant, obtained for linear (P4) implants (3.6±0.3 *vs.* 3.2±0.4, p=0.06).

The main limits of our work are the retrospective design and the relatively small number of patients enrolled; further prospective investigations with a large sample of patients are needed to confirm our findings. A further limit is the lack of a surgical/histological confirmation. Our cohort was composed of advanced patients with clinically suspected recurrence of PC from ovarian cancer, with previous cytoreductive surgery and adjuvant chemotherapy, not requiring another surgical approach but only a systemic medical treatment. On the other hand, a surgical histological gold-standard would be mandatory to evaluate the real role of CT in detecting PC but this purpose is beyond our scope. The aim of our research was only to compare the diagnostic accuracy of different CT acquisition phases in order to understand if the addition of a delayed phase to the portal one, with the consequent increment of radiation dose, would be clinically justified. Therefore, the double-phase CT study evaluated by two experienced readers who knew the clinical, laboratory as well as previous CT findings, with the confirmation of imaging follow-up, seems to be adequate for the scope of our investigation.

The last limit of the study could be the fact that we performed our analysis on a site-by-site rather than per nodule basis; this decision was determined by the impracticality of accurate radiologic-pathologic correlation for small nodules, particularly in patient with disseminated disease.

Conclusions

Our findings suggest that the portal venous phase alone is effective and sufficient to detect PC from ovarian cancer when CT images are analyzed by experienced readers. The combination of portal venous and delayed enhanced phase may help less-experienced radiologist to significantly improve diagnostic accuracy allowing a better qualitative assessment of enhancement, particularly for micronodular and linear implants.

Our results indicate that the CT-acquisition protocol in patients with ovarian cancer for tumor staging should be based on portal phase alone, whereas the addition of delayed phase images is useful for less-experienced readers.

Conflict of Interests:

The Authors declare that they have no conflict of interests.

References

1) Choi HJ, Lim MC, Bae J, Cho KS, Jung DC, Kang S, Yoo CW, Seo SS, Park SY. Region-based diagnostic performance of multidetector CT for detecting peritoneal seeding in ovarian cancer patients. Arch Gynecol Obstet 2011; 283: 353-360.
2) Nougaret S, Addley HC, Colombo PE, Fujii S, Al Sharif SS, Tirumani SH, Jardon K, Sala E, Reinhold C. Ovarian carcinomatosis: how the radiologist can help plan the surgical approach. Radiographics 2012; 32: 1775-1800.
3) Mazzei MA, Khader L, Cirigliano A, Cioffi Squitieri N, Guerrini S, Forzoni B, Marrelli D, Roviello F, Mazzei FG, Volterrani L. Accuracy of MDCT in the preoperative definition of Peritoneal Cancer Index (PCI) in patients with advanced ovarian cancer who underwent peritonectomy and hypertermic intraperitoneal chemotherapy (HIPEC). Abdom Imaging 2013; 88: 1422-1430.
4) Pannu HK, Bristow RE, Montz FJ, Fishman EK. Multidetector of peritoneal carcinomatosis from ovarian cancer. Radiographics 2003; 23: 687-701.
5) Iafrate F, Ciolina M, Sammartino P, Baldassari P, Rengo M, Lucchesi P, Sibio S, Accarpio F, Di Giorgio A, Laghi A. Peritoneal carcinomatosis: imaging with 64-MDCT and 3T MRI diffusion-weighted imaging. Abdom Imaging 2012; 37: 616-627.
6) Klumpp BD, Aschoff P, Schwenzer N, Fenchel M, Koenigsrainer I, Falch C, Bruecher B, Claussen CD, Koenigsrainer A, Pfannenberg C, Kramer U, Miller S. Peritoneal carcinomatosis: comparison of dynamic contrast-enhanced magnetic resonance imaging with surgical and histopathologic findings. Abdom Imaging 2012; 37: 834-842.
7) Funicelli L, Travaini LL, Landoni F, Trifirò G, Bonello L, Bellomi M. Peritoneal carcinomatosis from ovarian cancer: the role of CT and FDG-PET/CT. Abdominal Imaging 2010; 35: 701-707.
8) Kim HW, Won KS, Zeon SK, Ahn BC, Gayed IW. Peritoneal carcinomatosis in patients with varian cancer: enhanced CT versus 18F-FDG PET/CT. Clin Nucl Med 2013; 38: 93-97.
9) Chandrashekhara SH, Thulkar S, Srivastava DN, Kumar L, Hariprasad R, Kumar S, Sharma MC. Pre-operative evaluation of peritoneal deposits using multidetector computed tomography in ovarian cancer. Br J Radiol 2011; 84: 38-43.
10) Coakley FV, Choi PH, Gougoutas CA, Pothuri B, Venkatraman E, Chi D, Bergman A, Hricak H. Peritoneal metastases: detection with spiral CT in patients with ovarian cancer. Radiology 2002; 223: 495-499.
11) de Bree E, Koops W, Kroger R, van Ruth S, Witkamp AJ, Zoetmulder FA. Peritoneal carcinomatosis from colorectal cancer or appendiceal origin: correlation of preoperative CT with intraoperative findings and evaluation of interobserver agreement. J Surg Oncol 2004; 86: 64-73.
12) Pannu HK, Horton KM, Fishman EK. Thin section dual phase multidetector row computed tomography detection of peritoneal metastases in gynecological cancers. J Comput Assist Tomogr 2003; 27: 333-340.
13) Marin D, Catalano C, Baski M, Di Martino M, Geiger D, Di Giorgio A, Sibio S, Passariello R. 64-section multi detector row CT in the preoperative diagnosis of peritoneal carcinomatosis: correlation with histopatological findings. Abdom Imaging 2010; 35: 694-700.
14) Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res 1996; 82: 359-374.
15) Rosner B. Fundamentals of biostatistics New York, NY: Duxbury, 1995; 420-426.
16) Parkin DM, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. CA Cancer J Clin 2005; 55: 74-108.
17) Meyers MA. Distribution of intra-abdominal malignant seeding: dependency on dynamics of flow of ascetic fluid. Am J Roentgenol Radium Ther Nucl Med 1973; 119: 198-206.
18) Schwartz PE. Cytoreductive surgery in the management of ovarian cancer. Oncology (Williston Park) 2008; 22: 1025-1033.
19) Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effects of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta analysis. J Clin Oncol 2002; 20: 1248-1259.
20) Low RN, Sigeti JS. MR imaging of peritoneal disease: comparison of contrast enhanced fast multiplanar spoiled gradient recalled and spin echo imaging. AJR Am J Roentgenol 1994; 163: 1131-1140.
21) Low RN, Barone RM, Lacey C, Sigeti JS, Alzate GD, Sebrechts CP. Peritoneal tumor: MR imaging with dilute oral barium and intravenous gadolinium-containing contrast agents compared with unenhanced MR imaging and CT. Radiology 1997; 204: 513-520.
22) Low RN. Gadolinium-enhanced MR imaging of liver capsule and peritoneum. Magn Reson Imaging Clin N Am 2001; 9: 803-819.
23) Low RN. MR Imaging of the peritoneal spread of malignancy. Abdom Imaging 2007; 2: 267-283.