Variable CT Findings of Epithelial Origin Ovarian Carcinoma According to the Degree of Histologic Differentiation

Yun-Jin Jang, MD
Jeong Kon Kim, MD
Sung Bin Park, MD
Kyoung-Sik Cho, MD

Objective: We wanted to evaluate the CT findings of epithelial origin ovarian carcinoma according to the degree of histologic differentiation.

Materials and Methods: This study enrolled 124 patients with 31 well differentiated, 44 moderately differentiated and 95 poorly differentiated carcinomas with epithelial origin. The CT images were retrospectively evaluated with regard to bilateral ovarian involvement, the tumor's nature, lymphadenopathy, adjacent organ invasion, peritoneal tumor seeding, a large amount of ascites and distant metastasis. In cystic, predominantly cystic and mixed tumors, the tumor wall, septa, papillary projection and necrosis in the solid portion were assessed.

Results: Bilateral ovarian involvement was more common in the poorly (48%) and moderately (42%) differentiated carcinomas than in the well differentiated carcinomas (7%) ($p < 0.05$). The frequency of a predominantly solid or solid nature was greater in the moderately and poorly differentiated carcinomas than in the well differentiated carcinomas ($p < 0.0001$). In the 87 tumors with a cystic, predominantly cystic or mixed nature, septa greater than 3 mm, papillary projection and necrosis in the solid portion were more common in the poorly differentiated carcinoma (91%, 91% and 77%, respectively) than in the moderately (64%, 68% and 34%, respectively) and well differentiated carcinomas (63%, 47% and 27%, respectively) ($p < 0.05$). Lymphadenopathy, organ invasion, tumor seeding and a large amount of ascites were more common in the poorly differentiated carcinomas (38%, 27%, 73% and 69%, respectively) than in the moderately (13%, 10%, 48% and 45%, respectively) and well differentiated carcinomas (3%, 0%, 10% and 17%, respectively) ($p < 0.05$).

Conclusion: Epithelial origin ovarian carcinoma shows different CT findings according to the degree of histologic differentiation.

Index terms:
Ovarian cancer, differentiation
Computed tomography (CT)

Korean J Radiol 2007;8:120-126
Received October 19, 2005; accepted after revision February 9, 2006.

Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul 138-736, Korea

Address reprint requests to:
Jeong Kon Kim, MD, Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul 138-736, South Korea, 388-1 Poongnap-dong, Songpa-gu, Seoul 138-736, Korea.
Tel. (822) 3010-4355
Fax. (822) 476-0090
e-mail: rialto@ amc.seoul.kr

Ovarian cancer is the second most common gynecologic malignancy, and it is one of the leading causes of death from cancer in women (1). Physicians play important roles for both early detection and making an accurate diagnosis of malignant tumors, based on proper tissue characterization, for optimally managing these patients. Many previous studies have investigated the imaging findings for differentiating malignant ovarian tumors from benign tumors. According to those reports, irregular wall thickening, large size, irregular septa, papillary projections and necrosis in the solid portion favor the diagnosis of ovarian malignancy (2–9). In the early 2000s, Hricak et al. (9) postulated that necrosis in a solid lesion and vegetations in a cystic lesion are the most predictive MR imaging findings of ovarian malignancy. However, most previous studies had classified ovarian tumor simply as benign or malignancy, but the studies had not considered the degree of histologic differentiation

in malignant tumors. The degree of differentiation of ovarian carcinoma is thought to be related to the gross morphology. Therefore, it can be hypothesized that the imaging findings of ovarian carcinoma may vary according to their degree of differentiation.

Epithelial origin ovarian tumors consist of the largest portion of ovarian tumor.

Despite the inferiority of CT compared to MR for characterizing ovarian tumor, CT is still widely used for making the diagnosis of ovarian carcinoma. The purpose of this study is to investigate the variable CT findings of epithelial origin ovarian cancer according to the histologic degree of differentiation.

MATERIALS AND METHODS

Our institutional review board approved this study; however, informed consents from the subjects were not required for this retrospective study.

Patient Population

A computerized search of the medical records between January 1997 and March 2003 at our institution revealed 164 patients who had undergone surgery for epithelial origin ovarian carcinoma. From those patients, we collected the records of 124 patients (mean age: 52 years) who had available abdomen and pelvic CT images obtained before surgery (1–30 days), and who had no past history of other malignant disease before the diagnosis of ovarian carcinoma. None of these patients had undergone chemotherapy for ovarian cancer prior to the CT examination. All the tumors included in this study arose from epithelial cells, and the histologic diagnoses are summarized in Table 1.

Based on the pathologic reports of these patients that were written by various staff pathologists at our institution, each epithelial origin ovarian carcinoma was classified as well, moderately or poorly differentiated according to the degree of differentiation by referring to the modified Broder's grading system (10, 11). According to this system, well differentiated cells were more than 75% of the tumor cells in grade 1 (well differentiated) carcinoma, they were 25%–75% of the tumor cells in grade 2 (moderately differentiated) carcinoma and they were less than 25% of the tumor cells in grade 3 (poorly differentiated) carcinoma (10, 11). Consequently, the number of patients with well, moderately and poorly differentiated carcinoma was 29, 31 and 64, respectively.

CT Examination

One hundred and eleven patients underwent CT examination at our institution, but 13 patients with one well differentiated carcinoma, eight with moderately differentiated carcinoma and four with poorly differentiated carcinoma had CT images obtained at other institutions. The imaging acquisition parameters of the CT images obtained at other institutions were variable, but all the images included contrast-enhanced scans with a 5–10 mm slice thickness. At our institution, the CT examinations were performed using a single-detector row helical CT scanner (Somatom Plus-S; Siemens Medical Systems, Erlangen, Germany) for 88 patients, including 26 with well differentiated carcinoma, 16 with moderately differentiated carcinoma and 46 with poorly differentiated carcinoma. Multi-detector row helical CT scanners (LightSpeed QX/i, General Electric Medical System, Milwaukee, WI) were used for the remaining 23 patients, including two with well differentiated carcinoma, seven with moderately differentiated carcinoma and 14 with poorly differentiated carcinoma. All patients received 500–900 mL of oral contrast material (E-Z-CAT [2% barium sulfate suspension]; E-Z-EM, Westbury, NY) 30 minutes prior to the CT examination. Intravenous contrast material (Ultravist 300 [iopromide]; Schering, Berlin, Germany or Iopamiro 300 [iopamidol]; Bracco, Milano, Italy) was administered into the antecubital vein with using a power injector at a dose of 2 mL/kg to a maximum dose of 160 mL at a rate of 3 mL/sec. The scan delay for contrast-enhanced scanning was 100–120 seconds for the single-detector row helical CT scanning and 90–100 seconds for the multi-detector row helical CT scanning. Scan coverage was from the diaphragmatic dome to the ischial tuberosities.

The scanning parameters for single-detector row helical CT were section collimation: 7 mm, pitch: 1.5, table speed: 7.5 mm per rotation (10 mm/sec), reconstruction interval: 5 mm, 120 kV and 210 mA. For multi-detector row helical CT, a section collimation of 5 mm $\times$4, a beam pitch of 1.5, a reconstruction interval of 5 mm, a X-ray tube voltage of 120 kV and a tube current of 210–240 mA were used.

Analysis of CT Findings

Two radiologists, who were unaware of the pathologic

Table 1. Histopathologic Diagnosis in 124 Patients

Diagnosis	Number
Serous adenocarcinoma	65
Mucinous adenocarcinoma	22
Endometrioid carcinoma	22
Transitional cell carcinoma	1
Mixed subtype	5
Undifferentiated carcinoma	9

reports of ovarian carcinoma, but who knew about the presence of ovarian cancer in each patient, evaluated the CT findings in a consensus fashion on the picture archiving and communication system, PetaVision (Asan Medical Center, Seoul, Korea); this made it possible to measure the tumor diameter and attenuation in a particular region of interest.

The reviewers evaluated the presence or absence of bilateral ovarian involvement and the nature of the tumor according to the ratio of the cystic portion in the tumor: this included cystic tumor (approximately 100%), predominantly cystic tumor (> 70%), mixed tumor (30 −70%), predominantly solid tumor (< 30%), and purely solid tumor (approximately 0%). The presence of a solid portion within the tumor was determined when an area showed an attenuation value greater than 60 HU. Then, in tumors with cystic, predominantly cystic or mixed nature, the presence or absence of septa, papillary projection and necrosis in the solid portion were evaluated. Furthermore, the presence or absence of a wall and/or septa greater than 3 mm at the maximum thickness was also evaluated. The ancillary findings were also evaluated, including lymphadenopathy, tumor seeding, organ invasion, metastasis and a large amount of ascites. Lymphadenopathy was considered to be present when the minimum diameter of a lymph node was greater than 1 cm. The presence of organ invasion was regarded to exist when an ovarian tumor encased more than 50% of the surface of an adjacent organ. A large amount of ascites was indicated when ascites was noted in both the abdomen and pelvis.

Statistical Analysis

The frequency of bilateral ovarian involvement, the tumor nature, septa, papillary projection, necrosis, lymphadenopathy, tumor seeding, organ invasion, ascites and metastasis were all compared in well, moderately, and poorly differentiated ovarian carcinomas by using Fisher's exact test. *P* values < 0.05 were considered statistically significant.

RESULTS

Bilateral Ovarian Involvement

Among 124 patients, 46 patients had bilateral ovarian involvement. Only two (7%) of the 29 patients with well differentiated carcinoma had bilateral ovarian involvement, whereas 13 (42%) of the 31 patients with moderately differentiated carcinoma and 31 (48%) of the 64 patients with poorly differentiated ovarian carcinoma showed bilateral ovarian involvement. The frequency of bilateral ovarian involvement was greater in the moderately and poorly differentiated carcinomas than in the well differentiated carcinomas ($p = 0.002$ and $p < 0.0001$, respectively), whereas the frequency was not significantly different between moderately and poorly differentiated carcinomas ($p = 0.662$) (Figs. 1, 2).

Tumor Nature

A total of 170 ovarian tumors from 124 patients were analyzed. The number of well, moderately and poorly differentiated carcinomas was 31, 44 and 95, respectively. Comparison of the tumor nature in the well, moderately and poorly differentiated carcinomas is summarized in Table 2. Well differentiated carcinomas showed a strong tendency to be cystic or predominantly cystic nature, as was demonstrated by 25 (81%) of 31 tumors (Fig. 1). In contrast, the moderately or poorly differentiated carcinomas tended to be mixed, predominantly solid or solid in nature with a frequency of 73% (32/44) for the moderately differentiated carcinomas and 88% (84/95) for

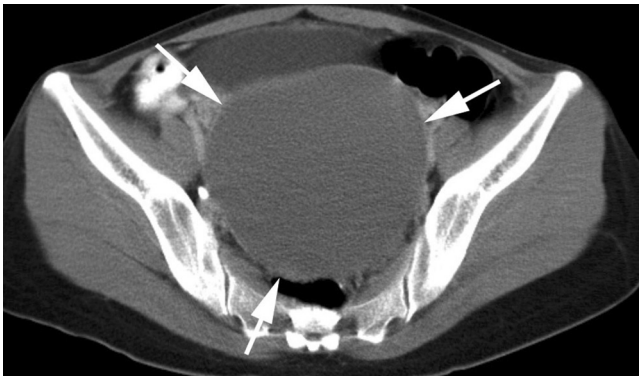

Fig. 1. 30-year-old female patient with well differentiated ovarian carcinoma. Transverse CT image shows 12-cm-sized unilocular cystic mass (arrows). Mass originates from the right ovary and the left ovary (not shown) is normal.

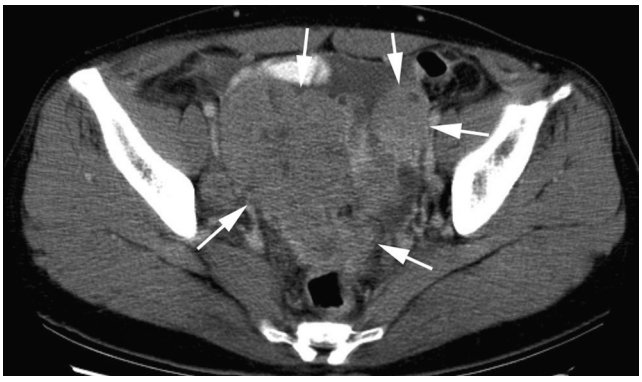

Fig. 2. 46-year-old female patient with poorly differentiated ovarian carcinoma. Transverse CT image shows two masses involving bilateral ovaries (arrows). Both masses show solid nature.

the poorly differentiated carcinomas (Fig. 2). The frequency of a cystic or predominantly cystic nature was greater in the well differentiated carcinomas than in the moderately differentiated ($p < 0.0001$) or poorly differentiated carcinomas ($p < 0.0001$). This frequency was also greater in the moderately differentiated carcinomas than in the poorly differentiated carcinomas ($p = 0.028$). In contrast, the frequency of a predominantly solid or solid nature was greater in the moderately and poorly differentiated carcinomas than in the well differentiated carcinomas ($p < 0.0001$).

Comparison of having a septa or wall in the 87 tumors with a cystic, predominantly cystic or mixed nature is summarized in Table 3. The distribution of having a maximum wall thickness was similar in these three groups ($p > 0.05$). A septa greater than 3 mm for the maximum thickness was more frequently noted in the poorly differentiated carcinomas (91%) than in the well (63%) or moderately differentiated carcinomas (64%) ($p < 0.0001$ and $p = 0.015$, respectively) (Figs. 3, 4).

In 87 cystic, predominantly cystic and mixed tumors, papillary projection was noted in 14 (47%) of the 30 well differentiated carcinomas, in 15 (68%) of the 22 moderately differentiated carcinomas and in 32 (91%) of the 35 poorly differentiated carcinomas. Papillary projection was more frequently noted in the poorly differentiated carcinomas than in the well differentiated ($p < 0.0001$) or moderately differentiated carcinomas ($p = 0.035$), whereas this frequency was similar in well differentiated and moderately differentiated carcinomas ($p = 0.162$).

In 87 cystic, predominantly cystic and mixed tumors, necrosis in the solid portion was observed in eight (27%)

Table 3. Comparison of the Walls and Septa in Well, Moderately and Poorly Differentiated Carcinoma

Differentiation	Wall Thickness < 3 mm	Wall Thickness > 3 mm
Well (n = 30)	3 (10)	27 (90)
Moderate (n = 22)	4 (18)	18 (82)
Poor (n = 35)	5 (14)	30 (86)

	No septa	Septa < 3 mm	Septa ≥3 mm
Well (n = 30)	5 (17)	6 (20)	19 (63)
Moderate (n = 22)	5 (23)	3 (14)	14 (64)
Poor (n = 35)	1 (2)	2 (6)	32 (91)

Note.—Numbers in parentheses are percentages.

Table 2. Comparison of the Tumor Nature in Well, Moderately and Poorly Differentiated Carcinomas

Differentiation	Cystic	Predominantly Cystic	Mixed	Predominantly Solid	Solid
Well (n = 31)	11 (35)	14 (45)	5 (16)	1 (3)	0 (0)
Moderate (n = 44)	6 (14)	6 (14)	10 (23)	8 (18)	14 (32)
Poor (n = 95)	4 (4)	7 (7)	24 (25)	17 (18)	43 (45)

Note.—Numbers in parentheses are percentages.

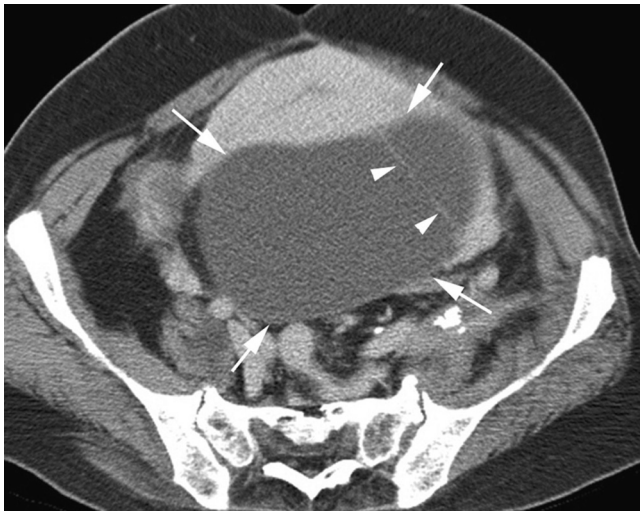

Fig. 3. 50-year-old female with moderately differentiated ovarian carcinoma. Tansverse CT image shows cystic mass from the left ovary (arrows), which shows septa thinner than 3 mm in diameter (arrowheads) but no papillary projection or necrosis in the solid protion.

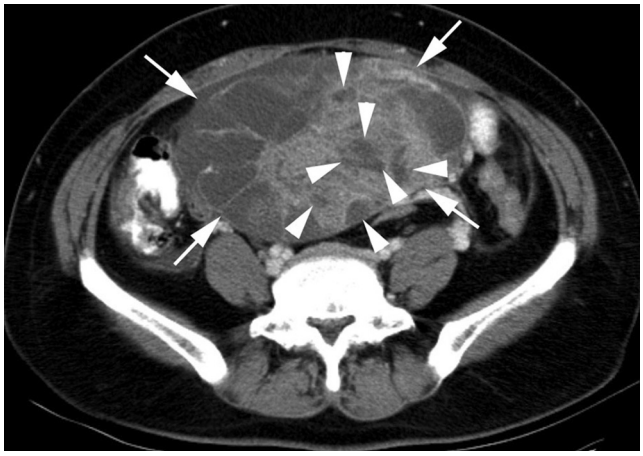

Fig. 4. 53-year-old female patient with pooly differentiated ovarian carcinoma. Transverse CT image shows mass with mixed pattern (arrows). Mass shows necrosis in the solid portion (arrowheads).

of the 30 well differentiated carcinomas, in eight (34%) of the 22 moderately differentiated carcinomas, and in 27 (77%) of the 35 poorly differentiated carcinomas. The frequency of necrosis was greater in the poorly differentiated carcinomas than in the well differentiated ($p < 0.0001$) or moderately differentiated carcinomas ($p = 0.005$). This frequency was similar in the well differentiated and moderately differentiated carcinomas ($p = 0.548$) (Figs. 3, 4).

Ancillary Findings

The results of the ancillary findings are summarized in Table 4. Lymphadenopathy was more common in the poorly differentiated carcinomas than in the well differentiated ($p < 0.0001$) or moderately differentiated carcinomas ($p = 0.016$), whereas this frequency was similar in the well differentiated and moderately differentiated carcinomas ($p = 0.355$). Adjacent organ invasion was also more common in the poorly differentiated carcinomas than in the well differentiated carcinomas ($p = 0.001$). This frequency was not significantly different in the poorly differentiated or moderately differentiated carcinomas ($p = 0.066$) or in the well differentiated and moderately differentiated carcinomas ($p = 0.238$). The frequency of tumor seeding was greater in the poorly differentiated carcinomas than in the well differentiated ($p < 0.0001$) or moderately differentiated carcinomas ($p < 0.0001$). This frequency was also greater in the moderately differentiated carcinomas than in the well differentiated carcinomas ($p = 0.017$). A large amount of ascites was more frequently noted in the poorly differentiated carcinomas than in the well differentiated ($p < 0.0001$) or moderately differentiated carcinomas ($p = 0.043$), although this frequency was not significantly different in the well differentiated and moderately differentiated carcinomas ($p = 0.058$). Metastasis was only noted in three patients, including one with moderately differentiated carcinoma and two with poorly differentiated carcinoma. Metastasis was noted in the liver of two patients, including one with moderately differentiated carcinoma and one with poorly differentiated carcinoma, and in the lung of one patient with poorly differentiated carcinoma. The frequency of metastasis was not significantly different in any comparative pair from the well, moderately and poorly differentiated carcinomas ($p > 0.05$).

DISCUSSION

Our results show that the CT findings of epithelial origin ovarian carcinoma vary according to the degree of differentiation. The frequency of bilateral ovarian involvement and a solid or predominantly solid nature were greater in the poorly and moderately differentiated carcinomas than in the well differentiated carcinomas. Tumor seeding was noted in the following order in the poorly, moderately and well differentiated carcinomas. The poorly differentiated carcinoma group was different from the other groups for the tumor morphology, that is, the frequency of thick septa (> 3 mm), papillary projection and necrosis in the solid portion was greater in the poorly differentiated carcinoma than in the other tumor types. The tumor behavior for the poorly differentiated carcinoma was more aggressive than that of the other groups, that is, lymphadenopathy, tumor

Table 4. Frequency of Lymphadenopathy, Adjacent Organ Invasion, the Extent of Tumor Seeding, the Amount of Ascites and Distant Metastasis in Well, Moderately and Poorly Differentiated Carcinomas

	Well Differentiated (n = 29)	Moderately Differentiated (n = 31)	Poorly Differentiated (n = 64)
Lymphadenopathy			
Absent	28 (97)	27 (87)	40 (63)
Present	1 (3)	4 (13)	24 (38)
Adjacent organ invasion			
Absent	29 (100)	28 (90)	47 (73)
Present	0 (0)	3 (10)	17 (27)
Tumor seeding			
Absent	23 (79)	15 (48)	8 (13)
Present	6 (21)	16 (52)	56 (87)
Large amount of ascites			
Absent	23 (83)	17 (55)	20 (31)
Present	6 (17)	14 (45)	44 (69)
Metastasis			
Absent	29 (100)	30 (97)	62 (97)
Present	0 (0)	1 (3)	2 (3)

Note.—Numbers in parentheses are percentages.

seeding and a large amount of ascites were more frequently noted in the poorly differentiated carcinoma than in the other tumor types.

The presence of papillary projection and a solid portion in the tumor are known as the most predictive findings for ovarian carcinoma (9). In this study, these findings were noted in less than half of the well differentiated carcinomas, whereas most of the cases of poorly differentiated carcinoma showed these findings. Moreover, the frequency of these findings in the moderately differentiated carcinoma was between those frequencies of the well differentiated and poorly differentiated carcinomas. With these results, our study shows that the frequency of the well-known CT findings that are predictive of ovarian carcinoma is heavily related to the degree of differentiation.

The fact that many cases of well differentiated carcinoma do not show papillary projection or necrosis in the solid portion means that there may be a high risk for misinterpreting well differentiated carcinoma from benign cystic neoplasms in daily practice. Therefore, any decision on distinguishing benign from malignant ovarian neoplasms should be reached not only according to the imaging findings, but also according to the clinical findings such as the CA-125 level and the patient's signs and symptoms.

In our study, nearly half the cases of moderately or poorly differentiated carcinomas showed bilateral ovarian involvement. This result suggests the difficulty in differentiating primary ovarian carcinoma from metastatic ovarian cancer. Brown et al. (12) reported that the frequency of multilocularity was significantly higher in primary ovarian tumors than in the metastatic ovarian cancers in bilateral ovarian tumors. However, many cases of moderately and poorly differentiated carcinomas in this study had a predominantly solid or purely solid nature that seemed to be unrelated to multilocularity. Therefore, this differentiation is very difficult when bilateral ovarian masses show a solid nature, and in these cases, more effort must be given in these cases to detect primary tumors in organs other than the ovaries.

Various imaging modalities such as ultrasonography, CT and MR are used for evaluating ovarian tumors. It has been reported that gadolinium-enhanced MR imaging is superior to CT and US for tissue characterization and that CT may miss a small solid portion; further, it cannot differentiate solid nodules from high-attenuation fluid such as mucin or hemorrhage (6, 9). Nevertheless, we believe that CT is still widely used for patients with presumed ovarian tumor because it is superior to MR in terms of the scanning time, cost and range of scan coverage. Furthermore, CT is undoubtedly better than MR for detecting a possibly hidden primary tumor in organs other than the ovaries. Therefore, radiologists should be mindful of the spectrum of CT imaging of ovarian carcinoma according to the degree of differentiation.

There are limitations and possible controversy regarding this study. First, this study evaluated only cases of malignant ovarian epithelial neoplasms and it did not include other malignant tumors such as granulosa cell tumor and germ cell tumors, which usually manifest as predominantly solid or purely solid tumors (13, 14). Therefore, the CT findings of solid ovarian masses do not always suggest moderately or poorly differentiated ovarian carcinoma, and it is mandatory to consider the clinical or serologic findings such as CA-125, alphafetoprotein and beta human chorioglobin levels when interpreting CT images.

Second, CT has a widely known limitation for assessing solid lesions. The decision for a solid lesion can be made on the basis of enhancement between the unenhanced and contrast-enhanced scans. Unfortunately, as all of our patients did not have both these types of images, we could not accurately estimate the extent of the solid portions of the tumors, although we considered a portion with a CT number greater than 60 HU as a solid portion. Therefore, there may have been a potential study drawback that mucin or hemorrhage in the tumor was interpreted as a solid portion.

Third, as we judged the presence of adjacent organ invasion and peritoneal carcinomatosis only by the CT findings, but not by the pathology reports, there might have been false negative or positive cases when evaluating those findings.

Last, for determining the grade of differentiation in ovarian carcinoma, several grading systems have been introduced based on various findings such as the percentage of undifferentiated or well differentiated cells, the architectural features and the nuclear features (15 −18). This study used Broder's grading system, which is mainly based on the percentage of well differentiated cells, because this system is generally used in the pathology department of our institution. Therefore, the composition of our study population might have changed if another grading system were applied.

In summary, our results demonstrate that epithelial origin ovarian carcinoma has various imaging findings according to the degree of differentiation. We suggest radiologists should keep in mind that well differentiated carcinoma may not show the typical findings of ovarian carcinomas and that moderately or poorly differentiated carcinomas may mimic metastatic ovarian cancers.

References

1. Landis SH, Murray T, Bolden S, Wingo PA. Cancer statistics, 1998. *CA Cancer J Clin* 1998;48:6-29
2. Herrmann UJ, Jr, Locher GW, Goldhirsch A. Sonographic patterns of ovarian tumors: prediction of malignancy. *Obstet Gynecol* 1987;69:777-781
3. Ghossain MA, Buy JN, Ligneres C, Bazot M, Hassen K, Malbec L, et al. Epithelial tumors of the ovary: comparison of MR and CT findings. *Radiology* 1991;181:863-870
4. Komatsu T, Konishi I, Mandai M, Togashi K, Kawakami S, Konishi J, et al. Adnexal masses: transvaginal US and gadolinium-enhanced MR imaging assessment of intratumoral structure. *Radiology* 1996;198:109-115
5. Yamashita Y, Hatanaka Y, Torashima M, Takahashi M, Miyazaki K, Okamura H. Characterization of sonographically indeterminate ovarian tumors with MR imaging: a logistic regression analysis. *Acta Radiol* 1997;38:572-577
6. Kurtz AB, Tsimikas JV, Tempany CM, Hamper UM, Arger PH, Bree RL, et al. Diagnosis and staging of ovarian cancer: comparative values of Doppler and conventional US, CT, and MR Imaging correlated with surgery and histopathologic analysis--Report of the Radiology Diagnostic Oncology Group. *Radiology* 1999;212:19-27
7. Kawamoto S, Urban BA, Fishman EK. CT of epithelial ovarian tumors. *Radiographics* 1999;19:S85-102
8. Jeong YY, Outwater EK, Kang HK. Imaging evaluation of ovarian masses. *Radiographics* 2000;20:1445-1470
9. Hricak H, Chen M, Coakley FV, Kinkel K, Yu KK, Sica G, et al. Complex adnexal masses: detection and characterization with MR imaging-Multivariate analysis. *Radiology* 2000;214:39-46
10. Khoo SK, Battistutta D, Hurst T, Sanderson B, Ward BG, Free K. The prognostic value of clinical, pathologic, and biologic parameters in ovarian cancer. *Cancer* 1993;72:531-537
11. Nascimento AG, Meis-Kindblom J.M. Recent advances and controversies in soft tissue pathology. *Rev Esp Patol* 1999;32:424-430
12. Brown DL, Zou KH, Tempany CM, Frates MC, Silverman SG, McNeil BJ, et al. Primary versus secondary ovarian malignancy: imaging findings of adnexal masses in the Radiology Diagnostic Oncology Group Study. *Radiology* 2001;219:213-218
13. Morikawa K, Hatabu H, Togashi K, Kataoka ML, Mori T, Konishi J. Granulosa cell tumor of the ovary: MR findings. *J Comput Assist Tomogr* 1997;21:1001-1004
14. Pretorius ES, Outwater EK, Hunt JL, Siegelman ES. Magnetic resonance imaging of the ovary. *Top Magn Reson Imaging* 2001;12:131-146
15. Barber HR, Sommers SC, Synder R, Kwon TH. Histologic and nuclear grading and stromal reactions as indices for prognosis in ovarian cancer. *Am J Obstet Gynecol* 1975;121:795-807
16. Lieberman MW, Lebovitz RM. *Anderson's pathology*, 10th ed. St. Louis: Mosby, 1996:513-547
17. Cotran RS, Kumar V, Collins T. *Robbins pathologic basis of disease*, 6th ed. Philadelphia: WB Saunder, 1999:260-327
18. Giacomarra V, Tirelli G, Papanikolla L, Bussani R. Predictive factors of nodal metastases in oral cavity and oropharynx carcinomas. *Laryngoscope* 1999;109:795-799