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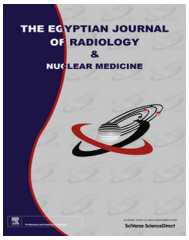

ORIGINAL ARTICLE

The significance of added ADC value to conventional MR imaging in differentiation between benign and malignant ovarian neoplasms

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KEYWORDS

ADC value;
MRI;
Ovarian tumors

Abstract *Purpose:* To highlight the role of ADC value measurement in differentiating benign from malignant ovarian tumors.
Materials and methods: Twenty patients with ovarian neoplasms underwent conventional MRI including ADC value calculation before surgery. Retrospective analysis of the pathological specimen with lesion morphology, signal characteristics, enhancement criteria and correlation with the appearance at DWI followed by ADC value measurement were obtained.
Results: Twenty patients with ovarian mass lesions were included. They were divided into purely solid, purely cystic and complex solid/cystic lesions. All solid malignant lesions showed diffusion restriction as well as the wall and septations of most malignant cystic lesion however, except one case. All benign lesions did not display diffusion restriction in DWI. The best cut off value of ADC to discriminate between benign and malignant lesions was 0.9 with specificity of 100%, sensitivity of 88.9%, NPV of 75%, PPV of 100% and accuracy of 91.7%.
Conclusion: Addition of ADC value measurement to conventional MRI increases its specificity from 78.6% to 85.7% which could be useful in differentiating benign from malignant lesions.

1. Introduction

Ovarian cancer is the seventh most common malignancy among women worldwide representing 3.7% of all cases of cancer in women and the second most common gynecological malignancy after cancer cervix (1). It is a disease of post-menopausal women and sometimes prepubescent girls. Risk factors include age more than 50, positive family history, infertility and previous cancer. Ovarian malignancy usually discovered at late stage (stages III and IV) with five year survival rate of 20%. Fortunately if the disease is discovered

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earlier (stage I), the five year survival rate will increases to 90%. Recurrence of cancer ovary in spite of aggressive treatment is common (2–4).

Most malignant ovarian tumors are primary (95%) usually of epithelial origin (90%). The epithelial tumors are classified into serous, mucinous, endometrioid, clear cell and undifferentiated. The non-epithelial tumors include sex cord stromal tumors and germ cell tumors (dysgerminoma, teratoma, yolk sac and choriocarcinoma). Most primary tumors which metastasize to the ovary includes gastric and colorectal (which are also called Krukenberg tumors), breast, pancreas and melanoma (5).

Cancer ovary metastasizes by several ways. Direct extension to the adjacent structures occurs after breaching the ovarian capsule. Intraperitoneal dissemination through implantation on the peritoneal surface, lymphatic spread to the para-aortic lymph nodes and hematogenous spread to distant organs are all known routes of metastasis (6,7).

Several tools are available for detecting ovarian cancer; however there is no single reliable diagnostic method. Ultrasonography plays a pivotal role in detecting ovarian lesions and differentiates solid, cystic and complex cystic lesions (1).

With its multiplanar capability, superior tissue contrast and different sequences, MRI becomes a crucial method of investigation of ovarian lesions. MRI has high sensitivity (97%) and specificity (84%) in characterizing malignant lesions and solves the problem of indeterminate lesion on Ultrasonography (1).

Conventional MR sequences include T1, T2 and fat suppressed images which provides anatomical and morphological criteria of the lesion. Lesions with high signal on T1 (fat or blood) and low signal in T2 (fibrous tissue) are likely to be benign (8). On the other hand, solid lesions with necrosis, cyst with irregular wall or septum or presence of solid and cystic component within the lesion are more likely to be malignant (9). Administration of contrast agent e.g. Gd-DTPA with the use of fat suppression can differentiate between the enhanced solid component and non-enhanced debris and blood clots (1).

Diffusion weighted (DWI) MR imaging is an in vivo functional method of investigation of various pathological conditions (10).

It can be obtained by ultrafast spin-echo echoplanar T2 WI with parallel imaging. As a modification of T2 sequence, DWI requires application of two diffusion sensitive gradients to the classic spin echo sequence (paired grandients). One of them is the dephasing gradient applied just before the 180° rephrasing pulse and the other gradient applied after the 180° rephrasing pulse. Both gradients should cancel each other and the tissue with restricted diffusion will be fully rephrased and hence preserve its T2 signal while the tissue with free diffusion, the water molecules move significantly between the two gradients and would not be fully rephrased which results in loss of its T2 signal intensity (11–13).

Apparent diffusion coefficient (ADC) is a quantitative derivative of DWI that can be expressed as a map or calculated as a value. Multiple *b*-values should be obtained to reduce the error in ADC calculation and improve tissue characterization (14).

Kwee et al. observed that inter- and intraobserver variation of ADC measurements may not always be sufficient to discriminate malignant from nonmalignant lymph nodes. Furthermore, ADC values tend to vary if different scan parameters or methods of measurement are applied, which may limit reproducibility and comparability of ADC values between centers (15).

The aim of the work is to highlight the role of ADC value measurement in differentiating benign from malignant ovarian tumors (Figs. 1–3).

2. Subjects and methods

2.1. Patients

The study was conducted in university hospital from January 2013 to September 2013. Twenty patients with ovarian tumors were included. Their age ranged from 17 to 71 years (mean age 40.5 ± 13.6). Their symptomatology ranged from abdominal enlargement, non-specific pelvic pain and loss of weight. All patients were subjected to full history taken and clinical examination. Informed consents were obtained from all study participants. Abdominal and Transvaginal Ultrasonographic examination with Doppler study were performed to all patients to exclude normal individuals, patients with functional cysts and to select cases for MRI referral. All patients underwent surgical excision of the tumor and histopathology.

2.2. MR Protocol and Parameters

All studies were performed using a 1.5T MR imaging unit (Achiva, Philips medical system, Best, the Netherlands). All patients were imaged in supine position using a pelvic phased array coil. Conventional pelvic MRI was performed followed by DWI sequence. Conventional T2 axial, sagittal and coronal were obtained with TR range/TE range: 3000–5000/90–100 and FOV (288×350 mm, 290×290 mm and 300×300 mm respectively), T2 Axial SPAIR, T1 axial with TR/TE: 500/10 and FOV 260×216 mm. Fat suppressed T1 axial and coronal post contrast images were obtained after injection of IV contrast (gadoterate meglumine (Dotarem, Guerbet) 0.1 ml/kg) with TR range/TE range: 420–500/10 and FOV 260×216 mm and 280×280 mm, respectively. DW axial images were obtained with *b*-values of 0, 1000 and 1500 s/mm^2, TR/TE was 5000/77, FOV of 240×240 mm, matrix size 124×100 and slice thickness was 6 mm with 1 mm slice gap. Axial T2WI and DWI of the abdomen were obtained to verify hepatic and peritoneal mets in ovarian malignancy.

2.3. Image analysis

Two radiologists with at least 6 years of experience in MRI served as study coordinators. They determined the lesions and correlated the findings with the pathological specimens after surgery. First, the conventional MR images were analyzed to detect the location, morphology, signal intensity and post enhancement criteria of the lesion. Second, DWI and ADC map were compared with the conventional MR findings. High signal in T1 was considered due to blood or fat. Persistence of high signal in fat suppressed images confirmed its bloody nature. Lesions with high signal on T2, high signal on DWI and low signal on ADC were considered restricted diffusion. Lesions with high signal on T2, DWI and ADC map

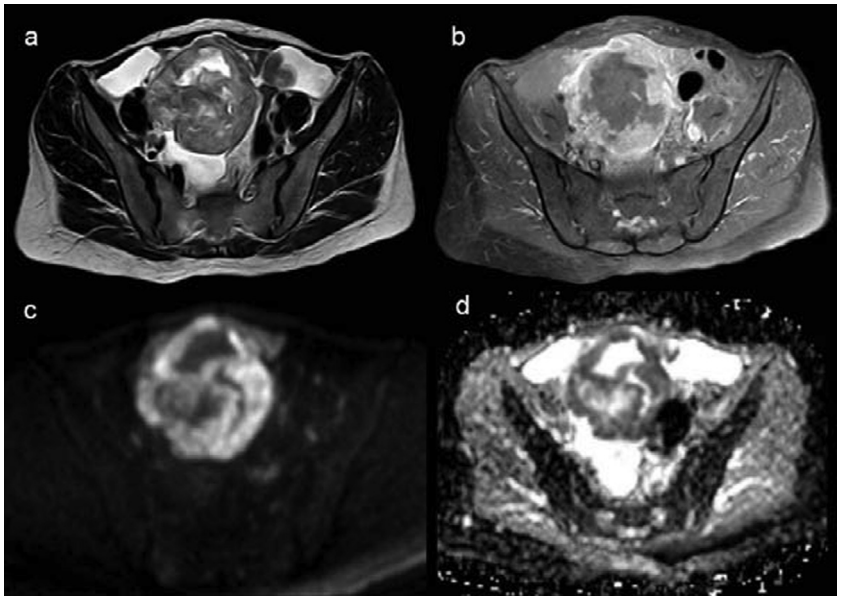

Fig. 1 Axial images of the pelvis, (a) T2, (b) Post contrast T1 fat suppressed image, (c) DWI (*b*-value 1000 s/mm^2) and (d) ADC map. A right ovarian solid lesion with central breaking down is noted. The solid component displays intermediate signal in T2, avid enhancement in post contrast sequence, bright signal in DWI and low signal in ADC map denoting diffusion restriction. The calculated ADC value of the solid component was 0.8×10^{-3} mm^2/s and diagnosis of mucinous cystadenocarcinoma was made on pathology.

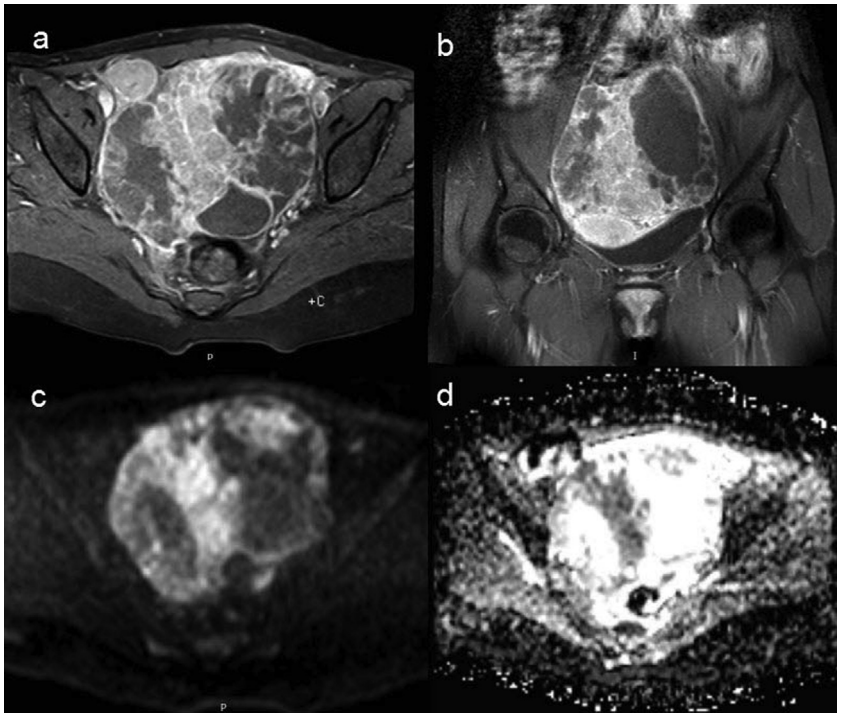

Fig. 2 Large bilateral ovarian complex solid/cystic lesions. The solid component displays avid enhancement in axial (a) and coronal (b) post contrast fat suppressed T1 WIs. It exhibits bright signal in DWI (*b* value 1000 s/mm^2) (c) and low signal in ADC map (d). The cystic component shows facilitated diffusion displaying low signal in DWI and bright signal in ADC map. ADC value of the solid component was 0.74×10^{-3} mm^2/s and of the cystic component was 2.2×10^{-3} mm^2/s. Pathological specimen revealed mucinous cystadenocarcinoma.

were attributed to T2 shine through effect and not true diffusion restriction. Lesions with low signal in DWI and high signal in ADC were considered facilitated diffusion.

Quantitative analysis of the lesions was obtained via plotting a region of interest (ROI) on expected location of the solid component of the lesion on ADC map and measuring its ADC

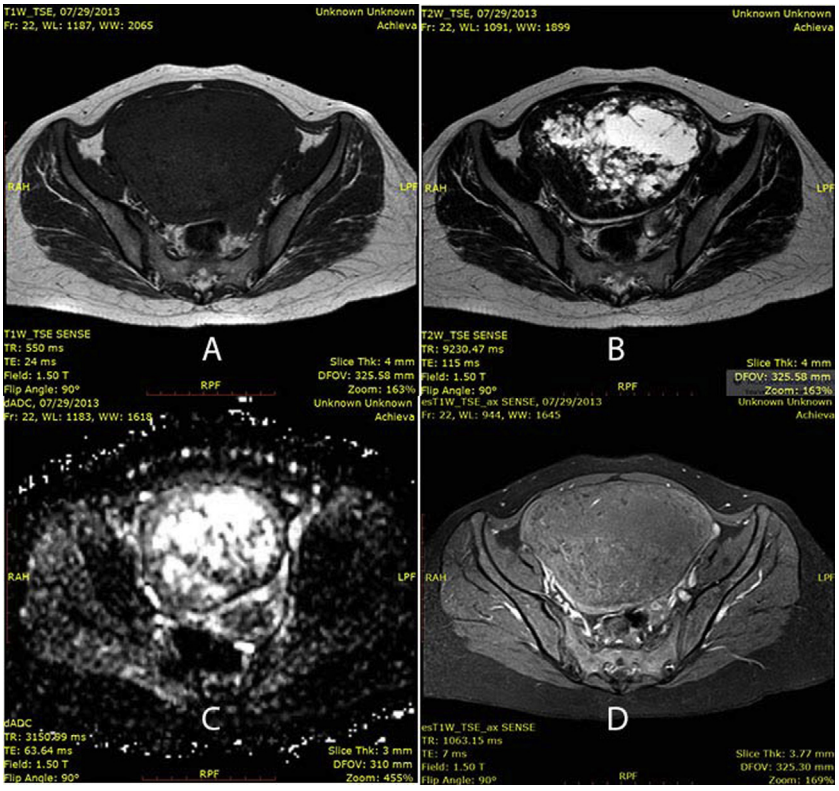

Fig. 3 Axial T1WI (A), axial T2WI (B) and post contrast T1 with fat suppression (D) display mixed solid/cystic lesion with T2 bright signal of the cystic component, low signal of the solid portion and mild enhancement of its wall and septa on post contrast scan. The lesion displays bright signal on ADC (C), which favors benign nature of the lesion. ADC value was 2.4×10^{-3} mm^2/s. Histopathology revealed atypical mature cystic teratoma.

value. The high ADC value was the more diffusion that occurred in this ROI and vice versa.

3. Results

Ten patients had benign lesions and ten patients had malignant tumors. The benign tumors included 4 serous cystadenoma, 3 mucinous cystadenoma, 2 mature cystic teratoma and 1 ovarian fibroma. The malignant tumors included 4 serous cystadenocarcinoma, 3 mucinous cystadenocarcinoma, 2 metastatic deposits and 1 granulosa cell tumor. The benign lesions ranged in size from 4.2 to 16 cm (mean size 9.3 cm) and the malignant lesion ranged in size from 4 to 19 cm (mean size 11.4 cm).

Ten cases of the study were malignant. They were classified into complex solid/cystic (7 cases), cystic (2 cases) and purely solid (1 case). Two cases of the complex lesions were cysts with intramural nodule >1 cm, one case was solid with cystic degeneration and the rest were mixed solid and cystic. Four cases showed moderate ascites and two were associated with significant pelvic lymphadenopathies. The enlarged internal iliac lymph nodes display diffusion restriction yet the limited number of cases with enlarged lymph nodes (2/20) has no statistical significance could be addressed in our study. All solid components of this group showed diffusion restriction on DWI.

The two cystic lesions were multilocular cysts with thick enhancing wall. The cyst contents did not express diffusion restriction but their wall and septa did.

The case with pure solid lesion (granulose cell tumor) showed enhancement of post contrast study and diffusion restriction on DWI.

The benign lesions were classified as 9 multilocular cystic tumors and 1 purely solid lesion. The multilocular cystic lesions showed faint enhancement of their wall and septa with no diffusion restriction on DWI. The solid lesion (fibroma) exhibited low signal in T1 and T2, faint enhancement in post contrast study with no restricted diffusion on DWI.

Two cases (atypical mature cystic teratoma) were false positive by MRI and showed no diffusion restriction on DWI which favor benignity. One case (serous cystadenocarcinoma) was false negative by DWI which could be attributed to the well differentiated nature of the lesion. The sensitivity, specificity, NPV, PPV and accuracy were compared between conventional MRI and DWI and expressed in Table 1.

So, addition of DWI to the conventional MR images did not improve the sensitivity, but increased the specificity,

Table 1 Comparison between mri and dwi results.

	MRI results (%)	DWI results (%)
Sensitivity	100	83.3
Specificity	78.6	85.7
PPV	62.5	71.4
NPV	91.7	92.3
Accuracy	80	85

Table 2 Differences between ADC values in solid component in benign and malignant tumors.

	Minimum	Maximum	Mean ± SD	*p*-Value
ADC ($\times 10^{-3} \times mm^2/s$) in malignant tumors	0.13	0.90	0.56 (±0.26)	0.013
ADC ($\times 10^{-3} \times mm^2/s$) in benign tumors	1.1	1.55	1.18 (±0.24)	

Table 3 Differences between ADC values in cystic component in benign and malignant lesions.

	Minimum	Maximum	Mean ± SD	*p*-Value
ADC ($\times 10^{-3} \times mm^2/s$) in malignant tumors	0.9	2.66	2.416 (± 0.73)	0.21
ADC ($\times 10^{-3} \times mm^2/s$) in benign tumors	1.8	2.9	2.54 (± 0.35)	

PPV, NPV and accuracy from 78.6%, 62.5, 91.7% and 80% to 85.7%, 71.4%, 92.3% and 85%, respectively.

ADC values of solid and cystic components of benign and malignant tumors were calculated and expressed in Tables 2 and 3, respectively which demonstrated a significant statistical difference between solid component malignant and benign tumors (*p*-value of 0.013). As regards the cystic component there was no significant difference between benign and malignant lesions with *p*-value of 0.21 (*p*-value is considered significant if < 0.05)

The best cut off value of ADC to discriminate between benign and malignant lesions was 0.9 with specificity of 100%, sensitivity of 88.9%, NPV of 75%, PPV of 100% and accuracy of 91.7%.

4. Discussion

DWI is a new promising diagnostic tool that can be added to conventional MRI to increase its specificity to better characterize and differentiate benign from malignant lesions (16).

In 2009, Thomassin-Naggara et al. evaluated the contribution of DWI in conjunction with morphological criteria to characterize 77 complex adnexal masses (30 benign and 47 malignant). In their results, low signal intensity both on DWI and T2-weighted images in the solid component of mixed adnexal masses would predict benignity and could help in differentiating benign from malignant lesion. This result matched with our result (17).

A similar study carried out by Takeuchi and colleagues in 2010 on 49 ovarian tumors (39 malignant and 10 benign), all solid malignant tumors showed diffusion restriction as well as two of the benign tumors (thecomas) which was attributed to their highly cellular content. He concluded that the presence of low signal in DWI may suggest benign nature and it was difficult to differentiate between benign and malignant tumors on the basis of DWI alone (18). Again our study suggested that low signal in T2 and DWI favors benignity of the lesion.

Another study was carried out by Li and colleagues in 2011 on 127 patients with 131 pelvic masses, (46 benign and 85 malignant). The purpose of this study was to evaluate differences in ADC values for the solid component of benign and malignant ovarian surface epithelial tumors to differentiate benign from malignant ovarian tumors preoperatively. The mean ADC value measured for the cystic component did not differ significantly between benign and malignant masses. Unlike that measured for the solid component which significantly differed between the benign and malignant lesions. Mean ADC value for benign lesions was $1.69 \times 10^{-3} \pm 0.25$ SD mm^2/s, and for the malignant was $1.03 \times 10^{-3} \pm 0.22$ SD mm^2/s. The lower ADC value associated with the malignant group was found to be statistically significant. Their results suggest that an ADC value $\geqslant 1.25 \times 10^{-3}$ mm^2/s may be an optimal cutoff value for differentiating benign and malignant ovarian tumors.

While in our study, the mean ADC value for solid malignant lesions was $0.56 \times 10^{-3} \pm 0.26$ SD mm^2/s, while that for solid benign lesions was $1.18 \times 10^{-3} \pm 0.24$ SD mm^2/s with *p*-value = 0.013 that was considered statistically significant.

Also in their study, the sensitivity, specificity, PPV, NPV and accuracy of conventional MR imaging increased from 91.8%, 78.3%, 88.6%, 83.7% and 87.0%, respectively to 96.5%, 89.1%, 94.3%, 93.2% and 93.1% after adding DWI to the conventional MR. This was comparable to our study as addition of DWI to conventional raised the specificity, PPV, NPV and accuracy from 78.6%, 62.5, 91.7% and 80% to 85.7%, 71.4%, 92.3% and 85% with no improvement for the sensitivity (19).

In our study we could not predict a definite cutoff value due to our small number of cases, but when regarding solid lesion only the best ADC cut off value between malignant and benign lesion is 0.947×10^{-3} mm^2/s, with sensitivity of 88.9%, specificity of 100%, PPV of 100%, and NPV of 75%.

In a more recent study in 2012, Zhang et al. studied 191 patients with 202 ovarian masses and measured the ADC values of their solid components. The study included 74 benign and 128 malignant lesions. The ADC values between benign and malignant lesions were statistically significant with cut off point of 1.2×10^{-3} mm^2/s (20). These results matched our study however our cut off value was 0.9×10^{-3} mm^2/s.

The small number of population in our study provided a significant limitation.

5. Conclusion

Addition of ADC value measurement to the conventional MRI sequences increases the specificity and accuracy of MRI to discriminate between benign and malignant lesions. It is easy to perform with short scan time and simple to interpret which is finally reflected on patient's outcome and prognosis.

Conflict of interest

No conflict of interest.

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References

(1) Mohaghegh P, Rockall AG. Imaging strategy for early ovarian cancer: characterization of adnexal masses with conventional and advanced imaging techniques. Radiographics 2012;32(6):1751–73.
(2) Hongju S, Shahid M, Jamal R, et al. Role of FDG PET/CT in staging of recurrent ovarian cancer. RadioGraphics 2011;31:569–83.
(3) Hippisley-Cox J, Coupland C. Identifying women with suspected ovarian cancer in primary care: derivation and validation of algorithm. BMJ 2012;344:1–11.
(4) Chu C, Kim S, June C, et al. Immunotherapy opportunities in ovarian cancer. Expert Rev Anticancer 2008;8:243–57.
(5) Mironov S, Akin O, Pandit-Taskar N, et al. Ovarian cancer. Radiol Clin North Am 2007;45(1):149–66.
(6) Kapadia AS, Devi KU. Epithelial ovarian cancer. In: Basu P, Singh A, Pandey A, editors. A practical approach to gynecologic oncology. New Delhi: Jaypee Brothers; 2005. p. 153–71.
(7) Jemal A, Murray T, Samuels A, et al. Cancer statistics, 2004. CA Cancer J Clin 2004;53:5–26.
(8) Thomassin-Naggara I, Daraï E, Cuenod CA, et al. Dynamic contrast-enhanced magnetic resonance imaging: a useful tool for characterizing ovarian epithelial tumors. J Magn Reson Imaging 2008;28(1):111–20.
(9) Sohaib SA, Sahdev A, Van Trappen P, et al. Characterization of adnexal mass lesions on MR imaging. AJR Am J Roentgenol 2003;180(5):1297–304.
(10) Koh D, Collins D. Diffusion-weighted MRI in the body: applications and challenges in oncology. AJR 2007;188:1622–35.
(11) Qayyum A. Diffusion-weighted imaging in the abdomen and pelvis: concepts and applications. RadioGraphics 2009;29:1797–810.
(12) Charlotte S, Andy C, Linda C, et al. Diffusion-weighted MR imaging of female pelvic tumors: a pictorial review. RadioGraphics 2009;29:759–78.
(13) Aliya Q. Diffusion-weighted imaging in the abdomen and pelvis: concepts and applications. RadioGraphics 2009;29:1797–810.
(14) Malayeri AA, El Khouli RH, Zaheer A, et al. Principles and applications of diffusion-weighted imaging in cancer detection staging and treatment follow-up. Radiographics 2011;31(6):1773–91.
(15) Kwee TC, Takahara T, Luijten PR, Nievelstein RA. ADC measurements of lymph nodes: inter- and intra-observer reproducibility study and an overview of the literature. Eur J Radiol 2010;75(2):215–20.
(16) Fujii S, Kakite S, Nishihara K, et al. Diagnostic accuracy of diffusion-weighted imaging in differentiating benign from malignant ovarian lesions. J Magn Reson Imaging 2008;28:1149–56.
(17) Thomassin-Naggara I, Daraï E, Cuenod CA, et al. Contribution of diffusion-weighted MR imaging for predicting benignity of complex adnexal masses. Eur Radiol 2009;19(6):1544–52.
(18) Takeuchi M, Matsuzaki K, Nishitani H. Diffusion-weighted magnetic resonance imaging of ovarian tumors: differentiation of benign and malignant solid components of ovarian masses. J Comput Assist Tomogr 2010;34(2):173–6.
(19) Li W, Chu C, et al. Diffusion-weighted MRI: a useful technique to discriminate benign versus malignant ovarian surface epithelial tumors with solid and cystic components. Abdom Imaging 2012;37(5):897–903.
(20) Zhang P, Cui Y, Li W, et al. Diagnostic accuracy of diffusion-weighted imaging with conventional MR imaging for differentiating complex solid and cystic ovarian tumors at 1.5T. World J Surg Oncol. 2012;10(1):237.