The Role of Diffusion Weighted Imaging in suspected cases of ovarian cancer

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Abstract

Background: Ovarian cancer is a common gynecological malignancy and often diagnosed late with extensive peritoneal and nodal metastasis. Diffusion-weighted imaging (DWI) provides valuable information about the structural properties of the tissue and has shown great value in cancer imaging. Recently developed post-processing three-dimensional apparent diffusion coefficient (3D ADC) map has a significant value in variable tumors yet its role in ovarian cancer is not well established. We aim to evaluate the added value of DWI and 3D ADC maps in the diagnosis of ovarian masses, detection of nodal and peritoneal deposits, and so appropriate management planning.

Results: Conventional MRI and DWI were performed to fifty-one patients with complex cystic or solid adnexal lesions depicted by gynecological ultrasonography. Results were compared with surgical and histopathologic findings revealing 23/51 (45%) had malignant ovarian tumors and 28/51 (55%) had benign ovarian pathologies. The mean 3D ADC values were 0.977 ± 0.32, 0.934 ± 0.27, and 0.956 ± 0.25 × 10−3 mm²/s for ovarian, nodal, and peritoneal malignancy respectively which were significantly lower than the mean 3D ADC values of benign ovarian lesions, non-metastatic lymph nodes and benign peritoneal lesions/fat which were measured 1.516 ± 0.6, 1.208 ± 0.25, and 1.46 ± 0.43 × 10−3 mm²/s respectively.

Conclusion: Adding DWI and 3D ADC maps to routine MRI improves the sensitivity, specificity, and accuracy for detecting ovarian malignancy, nodal, and peritoneal metastasis. They also provide qualitative data helping in the differentiation of malignant and non-malignant entities.

Keywords: Conventional MRI, DWI, 3D ADC map, Ovarian malignancy, Peritoneal carcinomatosis

Background

Of all gynecological malignancy ovarian cancer represents about 2.5% and representing about 5% of female cancer death [1]. Primary ovarian tumors are divided into epithelial-stromal tumors, sex cord-stromal tumors, and germ cell tumors [2].

Malignant epithelial tumors account for 90% of all ovarian malignancy and include high grade serous ovarian cancer, low grade serous ovarian cancer, endometrioid carcinoma, clear cell carcinoma, and mucinous carcinoma [3]. Up to 65% of patients with epithelial carcinoma are diagnosed at FIGO stages III and IV with peritoneal and nodal deposits [4].

Secondary ovarian tumors mostly originate from the endometrium, the pancreas, the gastrointestinal tract, and the breast. Most of them are clinically and pathologically mimic the primary tumors [5].

Although staging laparotomy and histopathological examination are the gold standard methods for staging in all women suspected of having ovarian carcinoma, it is necessary to explore less invasive preoperative methods for staging and detection of nodal and peritoneal deposits [6].

The major roles of diagnostic imaging have been to characterize the ovarian mass, determine the extent of...
preoperative disease, predict tumor resectability, and evaluate response to chemotherapy [7].

Pelvic and abdominal CT with both oral and intravenous (IV) contrast is the modality of choice in the pre-operative assessment of disease extension as well as predicting the success of surgical cytoreduction [8].

The doses of ionizing radiation to which the population has been exposed are increasingly higher due to its use in medical applications for the diagnosis and treatment of diseases. In 2008, the CT scan in the USA was the diagnostic technique that showed the highest dose deposition in the population [9]. So we are in need to use imaging techniques with low or no radiation hazards.

Ovarian cancer as other malignant tumors is characterized by neovascularization which predicts the metastatic properties of the tumor. Newly developed radiolabeled monoclonal antibodies have been settled for both the diagnosis and treatment of tumors in targeted radiotherapy [10].

MRI has flexibility for imaging anatomy, physiological parameters, and biochemical function, through appropriate choice of pulse sequences [11].

Diffusion MRI measures the diffusivity of endogenous water molecules in a tissue that reflects the mean size of the tissue microstructure that restricts and/or hinders the Brownian random motion of water molecules [12].

DWI allows the construction of 3D ADC maps of water molecules, that are promising markers of internal tumor pores and cellular gaps in which water molecules can migrate [11].

The primary focus of the research was the assessment of DWI for the qualitative evaluation of certain tumors. This focus has gradually shifted toward more quantitative methods of DWI assessment, including a large number of studies on the use of the main quantitative measure of DWI (ADC maps) [13].

Few articles have been reported; the diagnostic application of the DWI and ADC maps in the characterization and staging of ovarian tumors yet most of these studies have used the 2D ADC maps [14, 15].

This study evaluated the usefulness of diagnosis and preoperative staging of ovarian cancer (including characterization of ovarian lesions, detection of nodal, and peritoneal metastasis), using qualitative and quantitative analysis of DWI, and recently developed post-processing method (3D ADC maps).

Methods

Patients

This prospective study was performed from June 2018 till January 2020, and it included fifty-one adult females who had a complex cystic or solid adnexal lesion by transvaginal or trans-abdominal ultrasound examination with a mean age 45 ± 13.9-year-old (range of 16-74). Patients were referred to our radiology department in El-Demerdash Hospital for further assessment of the adnexal lesions.

Non-contrast MRI studies including conventional pelvic-abdominal images and DWI were done for all participants, after written consent was taken, according to the rules of our ethical committee. The results were confirmed by histopathology (Fig. 1).

The proper exclusion criteria were the following:

- Patients with previous adnexal surgical intervention
- Patients who received RTH or CTH or any treatment before MRI examination
- Patient with contraindication to MRI e.g. non-MRI compatible pacemaker

MRI examination

- Patients were injected with Buscopan intramuscularly 20 min before the examination to suppress bowel contractions, thereby avoiding DWI misreading of intestinal serosal deposits.
- MRI examination including conventional and DW images was done for all participants using 1.5 T Philips Achieva MRI unit with body Torso coil. The following conventional images were included:
  - Pelvis MRI included
    - Axial T1w-TSE (TR/TE, 550/24 ms), slice thickness 5 mm, gap 1 mm, and FOV 36 cm. Matrix 576 × 576.
    - Axial T2w-TSE (TR/TE, 7649/115 ms), slice thickness 5 mm, gap 1 mm, and FOV 36 cm. Matrix 560 × 560.
    - Sagittal and coronal T2-weighted, slice thickness 8-10 mm, gap 1 mm, and FOV 72-80 cm.
- DW-MRI was acquired in the axial plane by using a single-shot echo-planar imaging sequence with \( b \) values 0, 200, and 800, TR/TE 4274/63, slice thickness 5 mm, gap 1 mm, FOV 36 cm. Matrix 384 × 384.
- Abdomen MRI included
  - Axial T2w-TSE (TR/TE, 450/80 ms), slice thickness 6 mm, gap 1 mm, and FOV 36 cm. Matrix 480 × 480.
  - DW-3b (TR/TE 3793/65 ms), Slice thickness 6 mm, gap 1 mm, FOV 36 cm. Matrix 288 × 288.
  - DWI at \( b \) value 800 was processed into inverted grayscale DWI using synapse. The SYNAPSE, Product Release Specification, Software Version 4.4, ENG-0034171-A, March 13th, 2015, SYNAPSE is a registered trademark of FUJIFILM Medical Systems, USA.
3D apparent diffusion coefficient (ADC) map was generated on the 3D synapse.

The mean ADC values measured for the solid component of the ovarian lesions, lymph nodes, and peritoneal deposits.

**Analysis of data**

- The images were then reviewed by two gynecological radiologists (with 10 and 5 years’ experience in female radiology) with specific points to comment on qualitative, and quantitative analysis of ovarian lesions, lymph nodes, and peritoneal carcinomatosis:
  - Ovarian masses—unilateral or bilateral, solid or complex cystic (with septations, papillary projection, or soft tissue component), restricted or facilitated diffusion, and 3D ADC value of the solid component.
  - Nodal assessment—site, size, restriction pattern compared to the solid component of ovarian masses, and 3D ADC value.
  - Peritoneal thickening—presence or absence, size of nodules, anatomical site including omentum, peritoneal surface and serosa, and 3D ADC values.
  - The two radiologists viewed the DWI and MRI data via a 3D synapse system without any knowledge of the pathological information. When there was a difference between them, a final decision was made by consensus.
  - Forty-five patients underwent a total abdominal hysterectomy, oophorectomy, omentectomy, and lymph nodes biopsy. Six cases underwent unilateral oophorectomy. All results were correlated to the final post-operative histopathological data.

**Statistical analysis**

The data analysis was performed using the IBM SPSS statistics (V. 25.0, IBM Corp., USA, 2017-2018). For
quantitative parametric measurements, the data were expressed as mean ± SD. A receiver operating characteristic (ROC) curve was performed to assess the diagnostic accuracy of the measured ADC value for diagnosing malignant ovarian and nodal lesions using diagnostic validity tests which included sensitivity and specificity. *P* value < 0.05 was considered a statistically significant value. *P* value < 0.001 was considered a highly statistically significant value.

**Results**

This study included fifty-one female patients, their ages ranged between 16 and 74 years with mean age 45 ± 13.9 years old.

**Characterization of ovarian lesions**

From fifty-one cases, twenty-three cases showed malignant histopathology (45%) (Fig. 2) and twenty-eight cases showed benign histopathology (55%) (Table 1). Four cases showed bilateral ovarian lesions yet the most suspicious lesion of both ovarian lesions only included in this study to avoid bias.

The conventional MR combined with DW images were accurate in detecting ovarian malignancy yet 8 false-positive cases with solid components, intermediate or heterogeneous T2wi SI and low ADC values were reported, these cases were cases of necrotizing casing granuloma, tubo-ovarian abscesses, mature cystic teratomas, infarcted ovary, and cystadenofibroma (Table 2).

These combined images showed 100% sensitivity, 71.4% specificity, 100% NPV, 74.2% PPV, and 84.3% efficacy. Yet the accuracy of conventional MRI alone without DWI in the characterization of the ovarian lesion was 80% with 91.3% sensitivity, 64.29% specificity, 90% NPV, and 67.7% PPV.

In this study, two false-negative cases were reported, which were detected by the combined MRI/DWI yet were missed on conventional MRI alone, the first one was a very small malignant epithelial tumor, and the second one was ovarian surface small deposits secondary to malignant mesothelioma. Both of these malignant lesions were missed by conventional MRI images, yet restricted in the DWI.

Regarding ovarian lesions signal intensity in both DWI and 3D ADC map, 21/23 of malignant pathologies (91.3%) were restricted and only 2/23 pathologies (8.7%) were facilitated. The facilitated pathologies were metastatic from the colon with complex cystic morphology. Yet 17/28 benign lesions were restricted (60.7%) and 11/28 pathologies (39.3%) were facilitated. The restricted benign cases were cases of mature cystic teratomas, tubo-ovarian abscess, fibromas, fibrothecomas, cystadenofibroma, tubo-ovarian abscesses, and infarcted ovary.

The mean value of ADC of the malignant ovarian lesions was statistically significantly lower than that of the benign ovarian lesions (0.977 ± 0.3 and 1.516 ± 0.6 respectively) (Table 3).

Based on the area under the ROC curve of 0.756, the cutoff value below which malignancy is expected is less than $1.17 \times 10^{-3}$ mm²/s with 69.9% sensitivity, and 75% specificity (Fig. 3).

**Detection of nodal deposits**

The histopathological results assessed only in forty-seven patients out of the fifty-one patients, and it revealed metastatic LN in eleven cases, yet the LN was benign in thirty-six cases.

The conventional MR combined with DW images were accurate in detecting metastatic LNs yet 5 false-positive cases with low ADC values were reported, three of them were associated with benign ovarian pathologies (necrotizing casing granuloma and tubo-ovarian abscesses) and two associated with malignant ovarian pathologies.
pathologies with histopathologically proven free lymph nodes (Table 2).

The combined images showed 100% sensitivity, 86.1% specificity, 100% NPV, 68.8% PPV, and 89.4% efficacy in detecting LNs deposits. Yet the accuracy of conventional MRI alone without DWI was 76.6% with 63.64% sensitivity, 80.56% specificity, 87.88% NPV, and 50% PPV.

Conventional MRI images showed lower sensitivity than that of combined images in the detection of nodal metastasis as 4/11 (36.37%) of metastatic lymph nodes were small and missed by conventional images.

The mean 3D ADC value of malignant nodal deposits was statistically significantly lower than that of the non-metastatic lymph nodes (measured 0.934 ± 0.27 and 1.208 ± 0.25 respectively) (Table 3).

The lymph node restriction degree compared to that of the solid component of the ovarian masses was statistically significant in differentiating metastatic and non-metastatic lymph nodes with \( p = 0.000 \) (Table 4). As 45.5% of metastatic lymph nodes had the same degree of restriction compared to the solid component of ovarian masses and 36.4% were restricted more than the solid component. This compared to 8.3% of the non-metastatic lymph nodes which had the same degree of restriction as to the solid component and 2% of them were restricted more than the solid component of ovarian masses.

Based on the area under the ROC curve of 0.868 the cutoff value below which malignancy is expected is less than 0.9 \( \times 10^{-3} \) mm\(^2\)/s with 63.6% sensitivity, and 80.6% specificity (Fig. 3).

### Table 1 Ovarian masses pathological classification

| Ovarian lesions subtypes                  | Malignant NB (%) | Benign NB (%) |
|------------------------------------------|------------------|---------------|
| *Primary ovarian tumors                  |                  |               |
| High-grade papillary serous              | 6 (11.7)         | 7 (13.7%)     |
| Low-grade papillary serous               | 4 (7.8%)         | 3 (5.9%)      |
| Mucinous adenocarcinoma                  | 1 (1.9%)         | 3 (5.9%)      |
| Endometrioid adenocarcinoma              | 1 (1.9%)         | 2 (3.9%)      |
| Malignant germ cell tumor                | 2 (3.9%)         | 1 (1.9%)      |
| Malignant granulosa cell                 | 1 (1.9%)         | 1 (1.9%)      |
| Malignant endodermal sinus tumor         | 1 (1.9%)         | 2 (3.9%)      |
| *Metastatic ovarian tumors               |                  |               |
| Endometrial cancer                       | 2 (3.9%)         | 1 (1.9%)      |
| Uterine leiomyosarcoma                   | 1 (1.9%)         | 1 (1.9%)      |
| Colon adenocarcinoma                     | 2 (3.9%)         |               |
| Gastric carcinoma                        | 1 (1.9%)         |               |
| Malignant mesothelioma                   | 1 (1.9%)         |               |

### Table 2 Conventional MRI combined with DWI in detection of ovarian malignancy, nodal, and peritoneal deposits correlated to histopathology

| Conventional MRI and DWI | Histopathology | Pearson chi-square |
|--------------------------|----------------|--------------------|
|                          | Malignant      | Non-malignant      | Value   | \( P^* \) |
| Ovarian Masses           | Malignant      | 23 (100%)          | 8 (26.9%) | 27.028* | 0.000 |
|                          | Benign         | 0 (0%)             | 20 (71.4%) |        |      |
|                          | Total          | 23 (100%)          | 28 (100%) |        |      |
| Lymph nodes              | Metastatic     | 11 (100%)          | 5 (13.9%) | 27.825* | 0.000 |
|                          | Non-metastatic | 0 (0%)             | 31 (86.1%) |        |      |
|                          | Total          | 11 (100%)          | 36 (100%) |        |      |
| Peritoneal deposits      | Carcinomatosis | 18 (100%)          | 3 (9%)    | 39.7403* | 0.000 |
|                          | No carcinomatosis | 0 (0%)           | 30 (90.9%) |        |      |
|                          | Total          | 18 (100%)          | 33 (100%) |        |      |

Chi-square tests—\( P \) value > 0.05, non significant; \( P \) value < 0.05, significant; \( P \) value < 0.001, highly significant

*the significance level
Assessment of peritoneal deposits

Peritoneal carcinomatosis was histopathologically confirmed in 18 cases (35.3%) (Fig. 4), other thirty-three cases (64.7%) had no carcinomatosis with only three cases showing benign peritoneal thickening on histopathology (Figs. 5 and 6).

The combined conventional MR and DW images were accurate in detecting peritoneal carcinomatosis (Table 2) with 100% sensitivity, 90.91% specificity, 100% NPV, 85.71% PPV, and 94.12% efficacy.

Yet the accuracy of conventional MRI alone without DWI in the detection of peritoneal deposits was 90.2% with 88.89% sensitivity, 90.91% specificity, 93.75% NPV, and 84.21% PPV.

Three false-positive cases associated with benign ovarian pathologies two of them were diffuse granulomatous and inflammatory thickening in cases of necrotizing caseating granuloma, tubo-ovarian abscess. The third one showed small nodular thickening (peritoneal particulates) which was seen in the case of ovarian infarction.

Two false-negative cases in the form of tiny peritoneal metastatic deposits were missed by conventional MRI alone and detected by DWI.

Peritoneal carcinomatosis deposits were smaller than 10 mm in two cases (11.1%) and larger than 10 mm in five cases (27.8), yet it was confluent in eleven cases (61.1%). Non-malignant peritoneal thickening was smaller than 10 mm in one case (3%) and confluent in two cases (6.1%) (Table 5).

The mean 3D ADC value of peritoneal carcinomatosis was statistically significantly lower than that of non-carcinomatosis (including the ADC value of peritoneal fat in cases where there were no peritoneal thickening and the ADC value of benign peritoneal thickening) measuring 0.956 ± 0.25 and 1.46 ± 0.43 respectively (Table 3).

Discussion

Ovarian cancer is often diagnosed late with extensive peritoneal metastases [FIGO stages IIIc and IV], decreasing the patient’s survival rate to 10% in FIGO stage IV and 20–40% in FIGO stage IIIc disease [16] (Fig. 3).

Cancer staging is a fundamental principle and one of the first and most important steps used to predict the patient outcomes as well as to plan the most appropriate treatment [17].

In this study, DWI combined with conventional MR images were used for staging of ovarian cancer aiming that these non-contrast MRI images may become the exam of choice in patients with absolute or relative contraindications to contrast media, e.g., pregnant females (this study included two pregnant cases).
To our knowledge, this was the first study that used a 3D ADC map in preoperative staging of ovarian cancer. This study included quantitative and qualitative analysis of ovarian masses, lymphatic metastasis, and peritoneal deposits. Yet other studies used 2D ADC maps in the staging of ovarian malignancy.

In this study, combined DW and conventional MRI images showed a high sensitivity (100%) for the detection of ovarian pathology yet low specificity (71.4%). This low specificity could be explained by the presence of eight false-positive cases (eight benign adnexal masses that mimicked malignancy). All these cases showed solid adnexal lesions components displayed intermediate or heterogeneous T2wi SI and low ADC values. These cases included necrotizing caseating granuloma, tubo-ovarian abscesses, mature cystic teratomas, infarcted ovary, and cystadenofibroma with mean 3D ADC values of $1.3 \times 10^{-3}$ mm$^2$/s, $0.63 \times 10^{-3}$ mm$^2$/s, $0.9 \times 10^{-3}$ mm$^2$/s, $0.53 \times 10^{-3}$ mm$^2$/s, and $1.2 \times 10^{-3}$ mm$^2$/s respectively. Few cases of them were also associated with benign peritoneal thickening and enlarged lymph nodes with low 3D ADC values as in cases of necrotizing caseating granuloma and case of tubo-ovarian abscess.

| Nodal/solid component restriction | Histopathogy |
|----------------------------------|--------------|
|                                 | Benign       | Malignant  |
| < Solid component                | 31 (86.1%)   | 2 (18.2%)  |
| = Solid component                | 3 (8.3%)     | 5 (45.5%)  |
| > Solid component                | 2 (5.6%)     | 4 (36.4%)  |
| Value                            | $P^*$        | 0.000      |

Pearson chi-square: 19.434

Chi-square test

*P value > 0.05, non significant; $P$ value < 0.05, significant; $P$ value < 0.01: Highly significant

![Fig. 4 a](image1) Inverted DWI and 3D ADC map showing hepatic surface deposits in case of malignant endodermal sinus tumor (a and b). b Diffuse peritoneal deposits in a case of metastatic leiomyosarcoma as demonstrated by red arrows in inverted DWI and 3D ADC map (c and d)
In this study, the mean 3D ADC values for benign ovarian lesions were $1.516 \pm 0.6 \times 10^{-3} \text{mm}^2/\text{s}$ and for malignant lesions were $0.977 \pm 0.3 \times 10^{-3} \text{mm}^2/\text{s}$ and the cutoff value below which malignancy is expected is less than $1.17 \times 10^{-3} \text{mm}^2/\text{s}$ with 69.9% sensitivity, 75% specificity, 75% NPV, and 69.6% PPV.

Takeuchi et al. [18], in their study which included 49 ovarian tumors, 39 of them were malignant/borderline malignant and 10 were benign tumors, found that the mean 2D ADC value for malignant tumors was significantly lower than that in benign tumors (measured $1.03 \pm 0.19$ and $1.38 \pm 0.30$ respectively). They also

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**Fig. 5** 23-year-old female with bilateral adnexal necrotizing caseating granuloma (b) associated with peritoneal and hepatic involvement. Bilateral complex adnexal cystic lesions are seen in axial T2WI of the pelvis (a). Solid components showing restricted diffusion (red arrows) in both inverted DWI and 3D ADC maps (b and c). Inverted DWI and 3D ADC map of the pelvis (d and e) showing diffuse peritoneal surface (blue arrows) and bowel serosal thickening (orange arrows)

**Fig. 6** 58-year-old patient with right ovarian infarction and peritoneal particulates. A right complex adnexal lesion with heterogeneous SI in T2wi as seen in figure a. Lesion is truly restricted (blue arrows) with ADC value $= 0.53 \times 10^{-3} \text{mm}^2/\text{s}$ as seen in inverted DWI and 3D ADC map (b and c). Small peritoneal lesions also noted (green arrow)
found the cutoff ADC value of 1.15 malignant lesions had 74% sensitivity, 80% specificity, 94% PPV, and 44% NPV. The mean ADC value for malignancy was higher than that of this study as this study included malignant ovarian lesions with low ADC values as leiomyosarcoma, and uterine adenocarcinoma with metastatic deposits to ovaries with ADC values 0.4, and 0.6 respectively.

Michielsen et al. [14] found that DWI/MRI was accurate in detecting peritoneal carcinomatosis with 100% sensitivity, 90.91% specificity, 100% NPV, 85.71% PPV, and 94.12% efficacy. The size of peritoneal carcinomatosis was smaller than 1 cm in 11.1% and larger than 1 cm in 27.8% and 61.1% showed confluent disease.

Other studies also concluded the accuracy of DWI in the characterization of ovarian masses and detection of nodal deposits [8, 19, 21].

In this study, the conventional MR combined with DW images were accurate in detecting peritoneal carcinomatosis with 100% sensitivity, 90.91% specificity, 100% NPV, 85.71% PPV, and 94.12% efficacy. The size of peritoneal carcinomatosis was smaller than 1 cm in 11.1% and larger than 1 cm in 27.8% and 61.1% showed confluent disease.

Michielsen et al. [14] found that DWI/MRI was accurate in detecting peritoneal carcinomatosis with 91% sensitivity, 91% specificity, 89% PPV, 93% NPV, and 91% accuracy. The size of peritoneal carcinomatosis in their study was smaller than 1 cm in 36% and larger than 1 cm in 29% and 35% showed confluent disease. Higher sensitivity in this study may be attributed to a greater percentage of cases with confluent peritoneal disease and may be also attributed to the sensitivity of 3D ADC colored maps.

Other studies also showed the accuracy of DWI in the detection of peritoneal carcinomatosis (qualitative analysis) [25–28]. Yet few studies concerned with quantitative analysis of peritoneal carcinomatosis.

In this study, the mean 3D ADC value of peritoneal carcinomatosis at $b$ value 800 was 0.956 ± 0.25 × 10^{-3} mm$^2$/s. Onur et al. [29], in their study which included 28 oncology patients six of them had ovarian cancer, found that the mean ADC value at $b$ value 1000 was 1.09 ± 0.4 × 10^{-3} mm$^2$/s. A lower mean ADC value for peritoneal carcinomatosis in this study may be attributed to low ADC value peritoneal deposits as in cases of metastatic leiomyosarcoma and peritoneal mesothelioma.

In this study, the mean ADC value of both peritoneal carcinomatosis and malignant lymphadenopathy is

| Table 5 The size of peritoneal thickening/ deposits correlated to histopathology |
|---------------------------------------------------------------|
| **Histopathology** | **No carcinomatosis** | **Carcinomatosis** | **Total** |
| Size of peritoneal nodules by MRI | No nodules | 30 (90.9%) | 0 (0%) | 30 (58.8%) |
| | nodules < 10 mm | 1 (3%) | 2 (11.1%) | 1 (2%) |
| | nodules > 10 mm | 0 (0%) | 5 (27.8%) | 5 (9.8%) |
| | Confluent | 2 (6.1%) | 11 (61.1%) | 15 (29.4%) |
| Total | 33 (100%) | 18 (100%) | 51 (100%) |

To our knowledge, few studies exploring relationships between ADC values of lymph nodes and lymphatic metastasis were done, one of them performed by Wang et al. [24], including 49 patients with 29 negative cases (59.2%) and 20 positives (40.8%). They agreed with us regarding the statistical significance of ADC values in the detection of metastatic nodal deposits with $p = 0.000$. Yet their study showed a higher cut off value (1.003 × 10^{-3} mm$^2$/s) with higher specificity (93.1%). Such lower specificity in this study can be attributed to the presence of acute lymphadenitis in cases of necrotizing caseating granuloma and tubo-ovarian abscesses showed low ADC values and reported as malignant lymph nodes.

### Previous studies

Michielsen et al. [14] found that DWI/MRI was accurate in detecting peritoneal carcinomatosis with 91% sensitivity, 91% specificity, 89% PPV, 93% NPV, and 91% accuracy. The size of peritoneal carcinomatosis in their study was smaller than 1 cm in 36% and larger than 1 cm in 29% and 35% showed confluent disease. Higher sensitivity in this study may be attributed to a greater percentage of cases with confluent peritoneal disease and may be also attributed to the sensitivity of 3D ADC colored maps.

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In this study, the mean ADC value of both peritoneal carcinomatosis and malignant lymphadenopathy is
slightly lower than that of ovarian cancer. In certain cases as cases of tubo-ovarian abscesses, necrotizing caseating granuloma, and ovarian infarction especially in elderly patients, ovarian lesions were mimetic of that ovarian cancer as they had low ADC values, associated with peritoneal nodules, and enlarged lymphadenopathy, especially in first two cases so proper history and clinical data are very important for proper diagnosis and management.

In this study, the 3D ADC map was helping in proper assessment of ovarian masses, peritoneal, and nodal deposits. Few studies were done to evaluate the role of 3D ADC maps in discrimination of different tumor histological grading and other studies compared the role of 3D and 2D ADC maps.

Moryia and colleagues [30] used 3D ADC histogram in the differentiation of different histological types of hepatocellular carcinomas and they found that the minimum ADC was the most promising parameter for distinguishing poorly differentiated HCC from the other histological grades.

Tamada et al. [31], in their study which compared the reproducibility and diagnostic performance of 2D and 3D ROIs for prostatic ADC measurements, found that the use of 3D ROI did not improve the intrareader or inter-reader reproducibility or the diagnostic performance compared with the use of 2D ROI.

This was in contrary to the study done by Lui and colleagues [32] comparing the whole tumor 3D and 2D center-slice analysis in both ADC maps of b800 and b1000 and they suggested that the whole tumor 3D analysis of ADC maps provide reliable results and a more comprehensive evaluation of tumor histological grade.

Another study done by Souza and colleagues [33] in which they compared mean ADC values calculated in 2D and 3D for differentiating healthy brain tissues, glioblastoma, and meningioma and they found that 2D and 3D ADC maps could possibly differentiate meningiomas and glioblastomas or glioblastomas from normal tissues. However, meningiomas and normal tissues can be confused in the 3D analysis because of different cellularity and cellular type variability.

This study had several limitations such as the unequal distribution of ovarian pathologies included in the study and the limited number of cases with primary ovarian malignancy. Our study depended on 3D ADC maps and 2D maps were not included. Furthermore, a limitation related to the cost, availability, and the contraindication of MRI examination was encountered.

A future comparative study comparing and evaluating the diagnostic performance of 2D and 3D ovarian ADC maps with a larger sample number and better pathological distribution is recommended.

Conclusion
Adding DWI and recently developed processed 3D ADC maps to the conventional MR images provides quantitative and qualitative analysis of the ovarian masses, lymph nodes, and peritoneal deposits and hence, increasing the sensitivity, specificity, and accuracy of the non-contrast conventional images. Therefore DWI, and recently developed post-processing 3D ADC, may become promising techniques with applications in various areas of ovarian cancer imaging including diagnosis, staging, and treatment planning especially in patients with relative or absolute contraindications to the use of contrast material.

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RA and HN Suggest and develop the research idea. RF wrote the manuscript. HN and AI analyzed and interpreted the patient data. NC and AM reviewed all patients’ magnetic resonance images. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was approved by the Research Ethics Committee of the Faculty of Medicine at Ain Shams University in Egypt on 27 May 2018; reference number of approval: FWA 000017585. All patients included in this study gave written informed consent to participate in this research.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests
The authors declare that they have no competing interest.

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