The Role of Diffusion Weighted MRI Study and Its Quantitative Parameter, Apparent Diffusion Coefficient Value, In the Differentiation of Complex Adnexal Masses

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Abstract: Purpose was to get judgment for the utilized MRI tools and find out whether diffusion weighted imaging is a necessity or luxury in case we need to asses an adnexal mass. This study was conducted in Fayoum university hospital radiology department & some cases from National cancer institute. Thirty patients with detected complex cystic or solid adnexal masses on preliminary pelvic US examination after ethical consideration at the period from 4-2017 to 10-2017 including patients from Surgery & gynecology outpatient -clinic, after approval of research and ethical committee. **Conclusion:** The solo performance of DWI is not an applicable way to discriminate benign from malignant adnexal masses due to its low specificity. According to us, DWI has sensitivity of (87.5%), but didn't improve the specificity (66.6%) or the accuracy (75%), while post –contrast MRI improved the specificity (100%) and the overall accuracy (95%). DWI can help and increase confidence of MRI in assessment or exclude potential malignancy in complex adnexal masses; provided i) inclusion of the conventional MRI data, ii) combined analysis of DWI quantitative and qualitative criteria and iii) awareness of the possible sequence pitfalls. So, in our study we recommend to do DWI as adjuvant and complementary sequence in post-contrast MRI study for these complex ovarian masses to increase the confidence level of diagnosis.

1. Introduction

Ovarian Cancer is the second most common gynecological malignancy with the highest mortality rate of all gynecological malignancies and an overall five years survival rate of 46%. An important reason for this high mortality is the extensive disease at the time of diagnosis which makes it important to characterize these lesions early in its course. (Zhang P, et al., 2012)

The primary goal of imaging in the evaluation of an adnexal mass is to differentiate malignant from benign. Proper diagnoses will direct patients to the appropriate treatment algorithm to reduce the number of women unnecessarily undergoing cancer surgery, to preserve fertility in young women (by allowing laparoscopy), and, when necessary, to enable the referral of patients to a tertiary referral center with a specialist gynecologic oncologist. (Adusumilli S, et al., 2006)

The aim of work was to get judgment for the utilized MRI tools of assessment and to find out whether diffusion weighted imaging is a necessity or luxury in case we need to asses an adnexal mass.

2. Patients and Methods

This prospective study was conducted in Fayoum university hospital radiology department & some cases from National cancer institute. Thirty patients with detected complex cystic or solid adnexal masses on preliminary pelvic US examination after ethical consideration at the period from 4-2017 to 10-2017 including patients from Surgery & gynecology outpatient - clinic, after approval of research and ethical committee.

Included thirty patients that showed up with complex cystic or solid adnexal masses selected after a preliminary pelvic ultrasound examination. The patients age ranged from 22 to 60 years.

We had analyzed DWI and post contrast-MR imaging regarding their diagnostic performance in the evaluation of complex adnexal masses.

The histopathologies of the evaluated masses were listed (16 benign, two borderline and 12 malignant).

Benign tumors included: mature cystic teratoma, serous cystadenoma, pedunculated subserous fibroid, mucinous cystadenoma, papillary serous cystadeno fibroma, tubo-ovarian abscess, pelvic abscess.

Borderline tumor was: borderline papillary serous cystadenoma.

Malignant tumors included: papillary serous cystadeno carcinoma, mucinous cystadeno carcinoma, juvenile granulosa cell tumor, clear cell carcinoma.

We compared the number of cases which was diagnosed by post contrast MR images as benign or malignant tumors according to the criteria mentioned before, with those diagnosed depending on the DWI. The results were compared with the pathology which is considered the main reference.

For the sake of statistical evaluation, the borderline tumor with low potential malignancy (papillary serous cystadenoma) was categorized in our study with the malignant tumors.

Enhanced-MRI was able to diagnose 11 malignant tumors, one of the malignant tumors showed delayed enhancement and was diagnosed as benign (FN).

Diffusion-weighted (DWI) magnetic resonance suggested malignancy in 21 tumors compared to only 12 stated by the pathology.

The DWI and post contrast MRI sequences in the estimation of complex adnexal masses had elicited the same sensitivity value, yet regarding specificity; the post contrast images showed more enhanced value of almost 100% compared with only 66.7% for the DW images effect. Not to mention the accuracy percentage that was also increased from 75% for the DWI to 95% for the enhanced-MRI.

Cases showed discrepancy between the post-contrast MRI and DWI in their diagnosis:

3. Results
In our study:
There are benign masses misdiagnosed by the DWI as malignant (as mentioned earlier); these masses were mature cystic teratoma, tubo-ovarian abscess, pedunculated subserous fibroid.

For post contrast-MRI; only one true malignant mass (mucinous cystadenocarcinoma) with uniformly thickened septations & no gross solid component, was misinterpreted as being benign.

To be fair; the inclusion of both complex cystic and solid masses; although provided practical outfit to the current study and eliminated the probability of selection bias, yet that have affected the specificity value of the DWI performance (66.6%) in comparison to that of enhanced-MRI (100%). This should not underestimate the added value of DWI being a non-invasive method of investigation of ovarian masses provided knowledge of the current sequence pitfalls.

The technique is easy to be repeated, allowing close follow-up during and after tumor treatment.

Table (1): Correlation between the number of cases diagnosed as benign or malignant by the post contrast MR imaging, DWI and their pathological diagnosis

	Post contrast-MR	DWI	Pathology
Benign	19	9	18
Malignant	11	21	12
Total	30	30	30

Then we compared diffusion weighted imaging (DWI) to post contrast enhanced MRI to detect differences in sensitivity, specificity, PPV, NPV and accuracy.

Table (2) showing sensitivity, specificity, PPV, NPV and accuracy of (DWI) compared to (post contrast MRI)

	DWI	Enhanced MRI
Sensitivity	87.5%	87.5%
Specificity	66.66%	100%
PPV	63.63%	100%
NPV	88.88%	92.3%
Accuracy	75%	95%

4. Discussion
Ovarian cancer is the second most common gynecological malignancy with the highest mortality rate of all gynecological malignancies and an overall five years survival rate of 46%. An important reason for this high mortality is the extensive disease at the time of diagnosis which makes it important to characterize these lesions early in its course. **(Zhang P, et al., 2012)**

The primary goal of imaging in the evaluation of an adnexal mass is to differentiate malignant from benign. Proper diagnoses will direct patients to the appropriate treatment algorithm to reduce the number of women unnecessarily undergoing cancer surgery, to preserve fertility in young women (by allowing laparoscopy), and, when necessary, to enable the referral of patients to a tertiary referral center with a

specialist gynecologic oncologist. **(Adusumilli S, et al., 2006)**

For years, (MRI) had helped in identifying malignant lesions before surgery, particularly when US findings are suboptimal or indeterminate. MRI can reveal morphologic characteristics such as papillary projections, nodularity, septa, solid portions and signal intensity on T1- and T2-weighted images, but none of these criteria reliably distinguish between benign and malignant tumors. **(Zhang P, et al., 2012)**

DWI is one of the promising new functional imaging techniques that have shown to be effective in the differentiation of benign from malignant adnexal masses **(Thomassin-Naggara, et al., 2011).**

The aim of work was to get judgment for the utilized MRI tools of assessment and to find out whether diffusion weighted imaging is a necessity or luxury in case we need to asses an adnexal mass.

This prospective study was conducted in Fayoum university hospital radiology department & some cases from National cancer institute. at the period from 4-2017to 10-2017 including patients from Surgery & gynecology outpatient –clinic, after approval of research and ethical committee.

Included thirty patients that showed up with complex cystic or solid adnexal masses selected after a preliminary pelvic ultrasound examination. The patients age ranged from 22 to 60 years (mean age 38.625 +/-10.676 SD).

We had analyzed DWI and post contrast-MR imaging regarding their diagnostic performance in the evaluation of complex adnexal masses.

The histopathologies of the evaluated masses were listed (16 benign, two borderline and 12 malignant).

Benign tumors included: mature cystic teratoma, serous cystadenoma, pedunculated subserous fibroid, mucinous cystadenoma, papillary serous cystadeno fibroma, tubo-ovarian abscess, pelvic abscess.

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The DWI and post contrast MRI sequences in the estimation of complex adnexal masses had elicited the same sensitivity value, yet regarding specificity; the post contrast images showed more enhanced value of almost 100% compared with only 66.7% for the DW images effect. Not to mention the accuracy percentage that was also increased from 75% for the DWI to 95% for the enhanced-MRI.

DWI:

According to us, DWI had shown 87% sensitivity in its individual performance during the assessment of the included adnexal masses, yet the specificity was very low (45.45%).

In the quantitative assessment, the mean ADC values for malignant lesions were ($0.74 \times 10^{-3} \pm 0.38$ SD mm^2/s), while that for benign lesions were ($1.45 \times 10^{-3} \pm 0.5$ SD mm^2/s).

Such low specificity elicited in our research is explained by the presence of six benign masses that have mimicked malignancy on DWI; starting from their misleading signal intensities of restricted diffusion, down to the low ADC values measured.

Such masses included:

Mature cystic teratomas showed restricted diffusion and mean ADC values 0.6×10^{-3} mm^2/s. (false positive), due to mixed cellularity of the teratoma. Other masses such as tubo-ovarian abscess and pedunculated subserous fibroid showed restricted diffusion due to the mixed cellularity of such tumors with mean ADC values ($0.8 - 1.1 \times 10^{-3}$ mm^2/s) respectively.

Our study results agreed with a study was carried out by Fujii and colleagues in 2008 on 123 ovarian masses that included 42 malignant and 81 benign lesions. In this study, the majority of the malignant tumors, mature cystic teratomas, and almost half of the endometriomas, showed abnormal signal intensity on DWI, whereas most fibromas and other benign lesions did not. The main locations of abnormal signal intensity were solid portions in malignant ovarian tumors, keratinoid substances and Rokitansky protuberance in mature cystic teratomas, and intracystic clots in endometriomas, they finally concluded that DWI of ovarian lesions and the elicited ADC values are not useful for differentiating benign from malignant ovarian lesions.

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). According to them, low signal intensity on T2-weighted images and disappearance of restricted diffusion signal in the solid component of the mixed adnexal masses may predict benignity. They attributed the presence of low mean ADC values elicited by benign fibrous tumors as fibromas, Brenner tumors, and cystadeno fibromas are due todense network of collagen fibers within the extracellular matrix.

A similar study was carried out by Takeuchi and colleagues in 2010 on 49 ovarian tumors (39 malignant/borderline malignant, and 10 benign), it stated that the solid portions of all the 39 malignant tumors showed homogenous or heterogeneous high intensity on DWI, whereas only 3 of the 10 benign tumors (3 the comas) showed high intensity, the mean ADC value in the 39 malignant tumors 1.03×10^{-3} mm^2/s and was significantly lower than that of the 10 benign tumors 1.38×10^{-3}, they concluded low DWI and high ADC intensity may suggest benign lesion, however, it may be occasionally difficult to differentiate benign and malignant lesions only on the basis of DWI.

(Such suggestion agrees with our study that showed that abundant cellular masses).

Another study was carried out by Zhang P and colleagues in 2012 on one hundred and 91 patients with 202 ovarian masses; the purpose of this study was to evaluate differences in ADC values for the solid component of benign and malignant ovarian surface epithelial tumors with the goal of differentiating benign versus malignant ovarian tumors preoperatively. The results of that study showed that DWI appears to be a useful method for differentiating between benign epithelial ovarian tumors with solid components and malignant ovarian tumors, and is associated with high sensitivity and specificity, however, after exclusion of endometriomas, mature cystic teratomas and pure cystic adenomas from the analysis.

Considering such exclusion may have elevated the specificity of the DWI in our study yet this was not applicable; first because our analysis is a prospective evaluation and second such action would have subjected our evaluation to a major bias and unreliable data for use in the clinical practice.

Another study was carried out by Zhoa SH and colleagues in 2014 to investigate diffusion- weighted (DW) magnetic resonance (MR) imaging for differentiating borderline from malignant epithelial tumors of the ovary, the study included 60 borderline epithelial ovarian tumor (BEOTs) in 48 patients and 65 malignant epithelial ovarian tumors (MEOTs) in 54 patients, results of the study showed, the majority of MEOTs to be of high signal intensity on DW imaging, whereas most of BEOTs showed low or moderate signal intensity. The mean ADC value of the solid component of BEOTs ($1.562 \pm 0.346 \times 10^{-3}$ mm^2/s) was significantly higher than in MEOTs ($0.841 \pm 0.209 \times 10^{-3}$ mm^2/s).

Our study included only one borderline tumor (papillary serous neoplasm of low malignant potential), on DWI the tumor showed persistent high signal intensity, intermediate signal intensity on ADC map and a rather high ADC value (1.2×10^{-3} mm^2/s).

Enhanced-MRI:

In our study the sensitivity of MRI on individual basis was the same as post contrast-MRI (88.88%). The specificity was higher for enhancement (100%) compared to pre-contrast MRI sequences (72.73%), as well as the accuracy which was 95% and 80% for post contrast-MRI and MRI respectively.

Enhanced-MRI was able to diagnose 11 malignant tumors, one of the malignant tumors showed uniformly thickened septations with no gross solid components.

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In our study:

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Conclusion

- The solo performance of DWI is not an applicable way to discriminate benign from malignant adnexal masses due to its low specificity.

- According to us, DWI has sensitivity of (87.5%), but didn't improve the specificity (66.6%) or the accuracy (75%), while post –contrast MRI improved the specificity (100%) and the overall accuracy (95%).

- DWI can help and increase confidence of MRI in assessment or exclude potential malignancy in complex adnexal masses; provided i) inclusion of the conventional MRI data, ii) combined analysis of DWI quantitative and qualitative criteria and iii) awareness of the possible sequence pitfalls.

- So, in our study we recommend to do DWI as adjuvant and complementary sequence in post-contrast MRI study for these complex ovarian masses to increase the confidence level of diagnosis.

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