Role of MR Spectroscopy in differentiating Benign from Malignant Ovarian Tumors

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Abstract

Background: Ovarian cancer stands as a greatly dangerous gynecological malignancy with elevated mortality rate. Imaging plays a pivotal role in identification and planning of treatment of accidentally detected ovarian lesions, as earlier diagnosis of ovarian malignancy has strong relation with good prognosis**.**

Objectives: This study goal is assessment of the effectiveness of proton magnetic resonance spectroscopy to discriminate the malignancy & the benign ovarian neoplasms.

Patients and methods: Twenty cases with histopathologically determined complex and solid ovarian tumors (10 benign ,8 malignant and 2 borderline) had traditional MRI and magnetic resonance spectroscopy. The integrals of the peak of creatine, choline, lipid and (NAA) N-acetyl aspartate evaluated. The choline to creatine, lipid to creatine and NAA to Creatine ratios had been detected and then compared among the groups of malignant and benign neoplasms.

Results: Our study showed mean of choline to creatine ratio was 4.29 ±1.7 in benign tumors in contrast to 8.06±1.4 in malignant ones, with significant differences in statics (PV of 0.000). There have been no significant statics differences of the malignancy or the benign neoplasms as regard NAA to creatine (PV of 0.12) and lipid to creatine ratio (PV of 0.19). An edge of 4.29 of choline to creatine for characterizing the benign and the malignant tumors had 91.7% sensitivity, 100% specificity and 95% accuracy**.**

Conclusion: This experimental research reached that proton magnetic resonance spectroscopy is different in malignancy and in benign complex and solid ovarian neoplasms and that choline to creatine ratio will help to differ the malignant and the benign ovarian neoplasms.

Keywords: Ovarian tumors; Spectroscopy; MRI**.**

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Introduction

Ovarian cancer stands as a greatly dangerous gynecological cancer that has high mortality rate, unless it is detected in early stages.

It is inappropriate for women having indeterminate ovarian lesions to have surgical exploration lacking clear treatment goal. For cases with such ovarian masses, magnetic resonance has the aptitude to cut back unnecessary surgeries in benign cases and lessen the hazards of neglecting malignant featuring ones **(John et al., 2010).** The accuracy of MRI to discriminate ovarian masses depending only on the standard sequences is nearly 80% **(Bazot et al., 2013).**

The dynamic contrast enhanced MRI also diffusion weighted image provides a perfect estimation of malignancies, especially prior to surgeries **(Dilks et al., 2006).** Proton MRS using Cho/Cr ratio added helpful information for the characterization of many ovarian neoplasms **(Elsorogy et al., 2012),** molecular imaging through magnetic resonance spectroscopy can distinguish metabolic structure that characterize the malignant masses. As chemical alterations frequently come first to gross changes, sensitivity predicted to be improved with such technique **(Belki´c et al., 2008***)*. For instance, benign neoplasms might be of solid or complex nature as malignant ones which can be of cystic nature and look like benign neoplasms**.**

Spectroscopy is non-intrusive modality that investigate biochemistry of breakdown via estimating proton including structures in different masses**.** It was cleared that spectroscopy will discriminate benign and malignancy masses outside human body **(Massuger et al., 2012**). Nevertheless, for the reason of its application restrictions, in vivo use of spectroscopy for characterization of ovarian neoplasms is yet in beginnings and limited experimental researches have informed variable outcomes **(Satoh et al.,2011).**

Patients and Methods

The study was Prospective cross-sectional study conducted on cases had ovarian masses at ultrasound referred from Radiodiagnosis Department & Gynecology Department.

The research included 20 patients with ovarian lesions that fulfilled the following criteria, with mean of age located at 50 years with the range between 20 and 80 years, patients with ovarian tumors (≥ 4 cm in maximal diameter) and solid or complex solid / cystic masses.

Exclusion criteria include purely cystic ovarian tumor, Patient with contraindication to perform MRI examination and Patient refusal.

Trans-abdominal ultrasound and trans-vaginal ultrasound were included in our routine protocol to obtain baseline information preceding MR examination which is performed with Philips Healthcare of 1.5 Tesla device using a pelvic coil. Nearly in all of cases (except one benign case) the diagnosis was proven by surgical and pathological examination.

During the examination protocol, person lied in flat posture and respired without restrictions throughout examination. First standard noncontrast MR then examinations obtained after contrast injection. Axial T1&T2 WIs, coronal and sagittal T2WIs were acquired. After contrast injection (IV gadolinium), T1WI with fat suppression taken in sagittal and axially views. Axial DWI obtained. After the detection of the ovarian masses on T2WIs, spectroscopic voxel positioned on the directed part of the lesion without noticeable fluidy element via checking standard images. Analysis of the images was reviewed. The characteristics of the lesions including (extent and dimensions, intensity signal, form, diffusion restriction and contrast uptake pattern) in addition to accompanying changes (Nodal involvement, fluid collections, peritoneal seeding, and other organs Mets) were evaluated. Analysis of spectroscopic examination of neoplasms was done through evaluating the indicators from creatine at 3.03 ppm, NAA at 2.01 ppm, lipid at 1.32 ppm and choline at 3.20 ppm. Every region under exact resonance integrals had been detected for these four metabolites. A comparatively steady creatine peak had been applied to be an interior reference and indicator, as well as the Cho/Cr, lip/Cr and NAA/Cr ratios of every voxel have been calculated.

Statistical study

Values were proven, implied and evaluated by IBM-SPSS 23.0. Statistical descriptions: Means, medians, standard deviations, proportions and ranges had been estimated. Test of Chi² applied to judge the alteration in frequencies between various sets. ANOVA assessment was done in cases of continuous variables. Correlation study applied to detect the link between variables (correlation of Spearman's rank). The PV is taken into account once it is equivalent to or smaller than 0.05.

Results

The characteristics of morphology of the 20 cases of the solid and complex ovarian masses are demonstrated in (**Table.1**). With noticed significant statics differences among the malignant and the benign tumor groups considering diameter, consistency and pattern of enhancement. The spectral values had been detected for the 20 cases. Pathological types and ratios Cho/Cr, NAA /Cr, and Lip/Cr of the benign, borderline and the malignant masses were demonstrated in (**Table. 2**). Mean of Cho/Cr was 8.06± 1.4 in malignant neoplasms versus 4.29 ±1.7 in benign ones with the PV equals 0.000. on the other hand, no differences are significant in statics of Lip /Cr with PV of 0.19 and NAA/Cr with PV of 0.12 between the two groups of neoplasms.

The analysis of the curve of ROC of Cho/Cr ratio produced a threshold of 4 for discriminating the benign and the malignant masses, with a 100% specificity, 91.7% sensitivity, and 95% accuracy.

Table 1. Distribution of age and MRI Features among the studied group

Variables	Benign (N=8)	Malignant (N=10)	Borderline (N=2)	*PV*
Age	40.3± 11.6	52.8± 13.6	42.5± 3.5	0.2
Max. dimension	4.1± 1.6	9.3±3.5	8.5± 3.5	0.006
Outline Regular	8 (100%)	9 (90%)	2 (100%)	0.5[a]
Irregular	0 (0%)	1 (10%)	0 (0%)	
SI on T2WI Hypointense	6 (75%)	2 (20%)	0 (0%)	0.18[a]
Hyperintense	0 (0%)	1 (10%)	0 (0%)	
Mixed	2 (25%)	7 (70%)	2 (100%)	
Enhanced No	3 (37.5%)	0 (0%)	0 (0%)	0.02
Minor	2 (25.0%)	2 (20%)	5 (50%)	
Modest	2 (25.0%)	2 (20%)	0 (0%)	
Marked	1 (12.5%)	6 (60%)	5 (50%)	
Pattern of enhancement Homogenous	4 (100%)	1 (10%)	5 (50%)	0.007
heterogeneous	0 (0%)	9 (90%)	5 (50%)	
Consistency Solid	5 (62.5%)	2 (20.0%)	0 (0%)	0.01
Complex	3 (37.5%)	8 (80%)	2 (100%)	

SD= (standard deviation); N=number; Data was expressed in form of frequency (Percentage). PV was significant if < 0.05 (by Chi² test).

Table 2. Pathological natures and Metabolite ratios for groups of studied neoplasms

Case	Cho/Cr	NAA/Cr	Lip/Cr
Benign			
Endometrioma 1	5.67	2.16	5.63
Endometrioma 2	5.13	1.7	6.74
Endometrioma 3	5.52	2.31	5.82
Fibroma 1	2.21	1.29	3.65
Fibroma 2	2.17	1.31	3.32
Dermoid	4.67	2.33	3.57
Fibrothecoma	5.75	1.16	6.61
Sclerosing stromal tumor	5.71	1.15	9.44
Malignant			
Serous cystadenocarcinoma1	8.95	1.89	8.89
Serous cystadenocarcinoma2	8.9	2.45	8.99
Serous cystadenocarcinoma3	8.69	1.38	6.77
Serous cystadenocarcinoma4	5.53	2.24	12.99
Mucinous cystadenocarcinoma	9.6	7.17	5.37
Spindle cell carcinoma	10.1	2.22	7.14
Endometrioid carcinoma	6.94	2.76	8.22
Malignant teratoma	7.15	1.55	5.72
Granulosa cell tumor	6.56	2.89	5.22
Sertoli-Leydig cell tumor	8.24	2.24	7.5
Borderline			
Borderline serous cystadenocarcinoma	8.66	1.02	5.61
Borderline mucinous cystadenocarcinoma	10.52	1.39	5.27

Case presentation

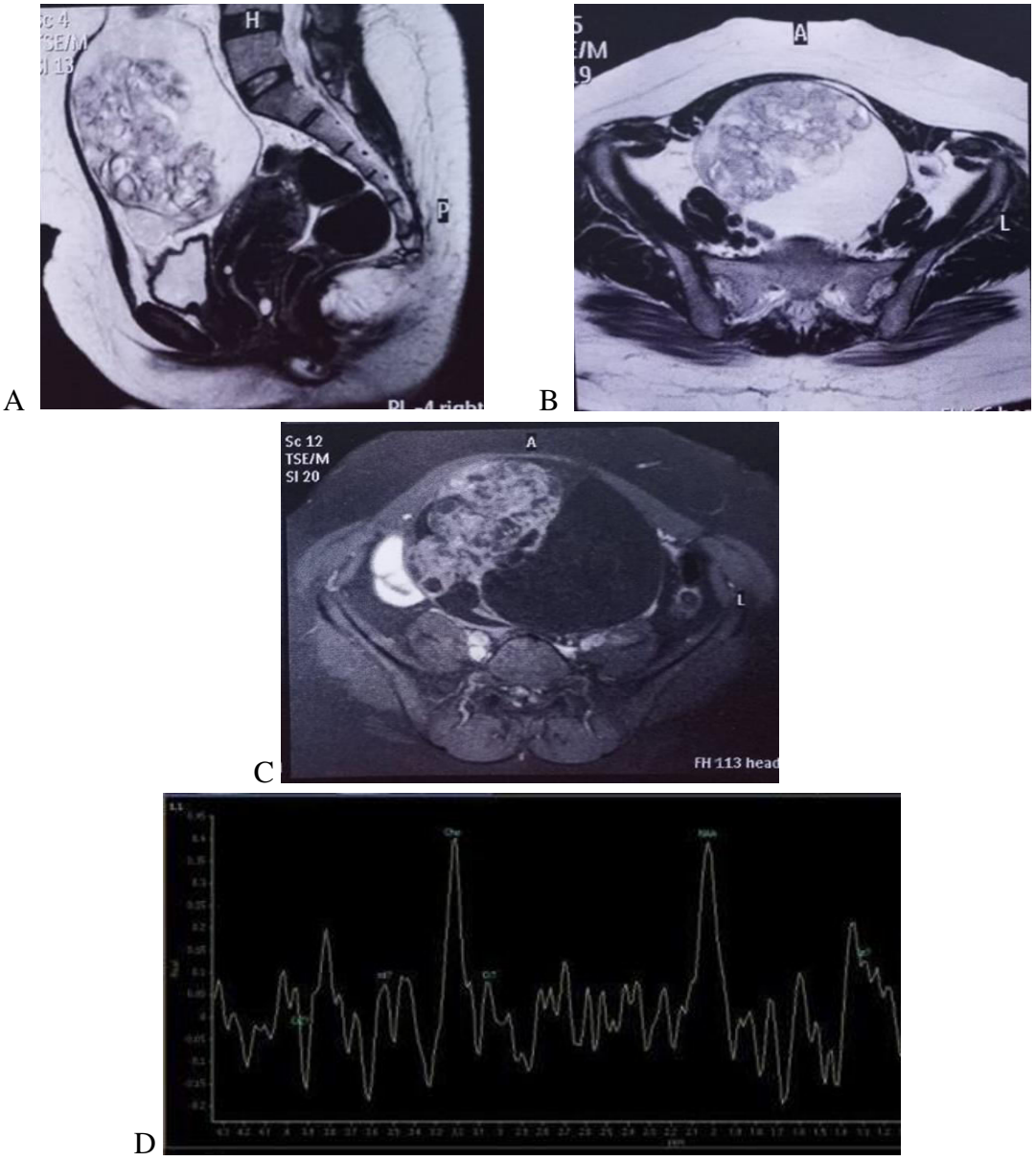

Fig.1. 45 years old woman with diagnosed malignant teratoma.A: Sagittal T2WI shows complex (solid / cystic) heterogenous lesion. B: T2WI (Axial).C: Post GAD T2WI (axial) with fat suppression that exhibits markedly and heterogeneously enhanced mass. D: Spectroscopic exam exhibits choline surge (70.3) and Cho/Cr is 7.15.

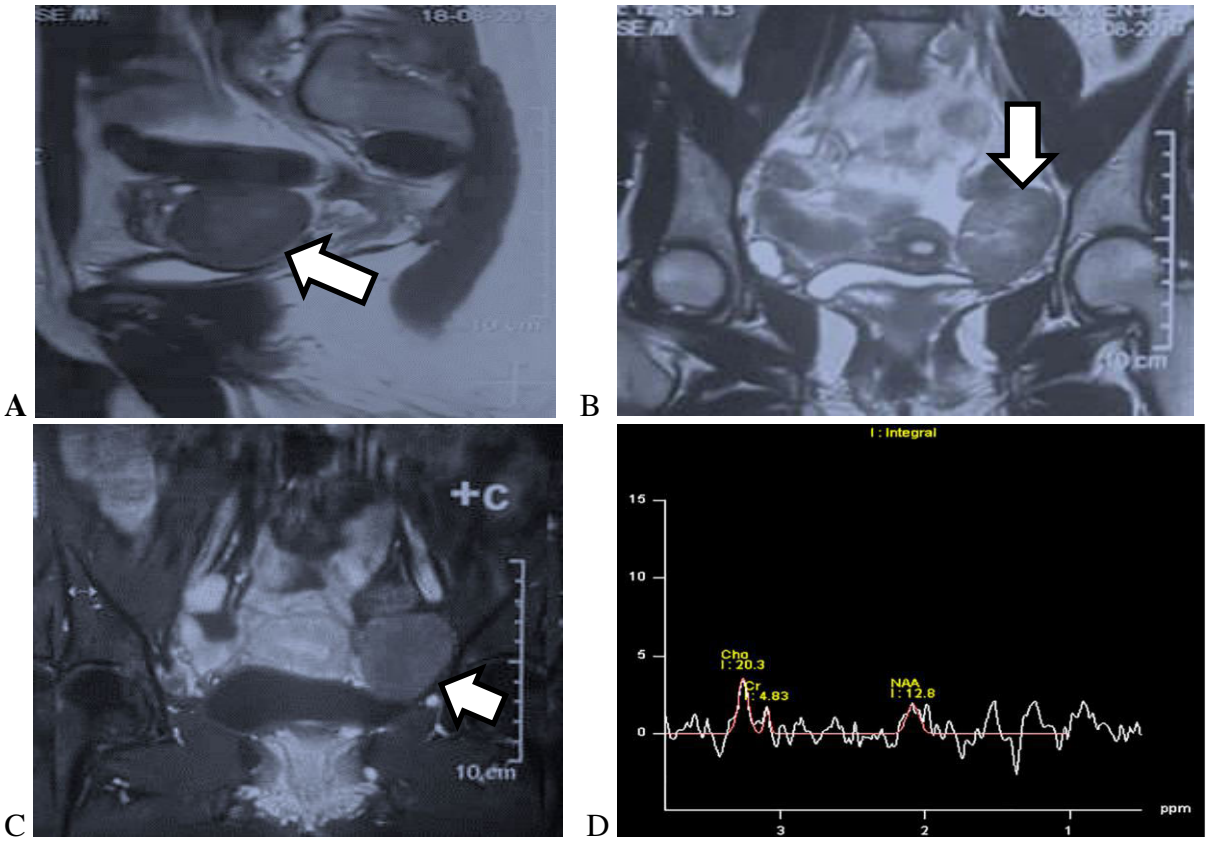

Fig.2. 50 years with proven left sided ovarian fibroma. A: T2WI sagittal exhibits a regular outlined isointense homogenous mass lesion of solid nature. B: T2WI (Coronal). C: Coronal T1WI with fat suppression after GAD injection exhibits an isointense mass lesion (solid) that mildly and homogenously enhanced. D: Spectroscopic exam demonstrate choline surge of 20.3 and Cho/Cr ratio of 4.2.

Discussion

Since a solid feature or a complex mass is considered one of the foremost significant features of malignancies in the ovarian neoplasms, several benign neoplasms, like adenofibromas and sex cord stromal tumors frequently look as complex or solid natures. Consequently, they could show significant overlapping morphology alongside with the malignancies which develops drawbacks in diagnosis. Standard magnetic resonance examination can assess the gross characters of a mass, for example mural thickness, internal growth, septations and intensity signals on T1W and T2W images, but then nothing of these features dependably can distinguish the malignancy and the benign lesions **(Schmidt et al., 2015).**

Magnetic resonance spectroscopic examination could be nonintrusive investigative instrument aimed at the examination of tumor breakdown with purposeful addition to traditional examinations. Also was cleared that magnetic resonant spectroscopy is helpful in identification, follow up observation in cases of brain and prostate cancers **(Bulik et al., 2013)**. As regard its use in cases of ovarian neoplasms, it continues to be in experimental steps with variable outcomes likely because of the narrow range of trials as well as the overlapping and complexed characteristics of masses.

Many researches revealed that quantities of choline in malignancies are seriously superior to those of benign ones. The interior mass spectroscopic examination being less accurate than if it was exterior, so the researches took in account the integral ratios to investigate and compare metabolite variations of various neoplasms. Lipid could be detected in numerous malignant masses of the ovary. **(Cho et al., 2002)** proved a strong lipid surge on 1.3 ppm in cancerous neoplasms also in benign featuring teratomas of the ovary, in contrast, benign featuring epithelial neoplasms displayed no lipid surge.

NAA could be monitored on 2.01 ppm. No significant statics difference was detected among groups in our research as regard the NAA/Cr ratio.

Our research matched with that directed by **(Aliaa et al.,2019).** It was on 24 cases, with the Cho/Cr edge was 3.6 for characterizing the benign from the malignant adnexal masses, with the sensitivity of 69.2% and the specificity of 90.9%.

Our search agreed with that done by **(Rania et al.,2019)** on 57 cases and ended that the mean CHO/Cr ratio was higher in the malignant than in the benign lesions, and MRS separable implementations in diagnosis having sensitivity of 89%, specificity of 100% and accuracy of 95%.

Our research matched with research directed by **(Feng et al., 2014)**. It was on 69 cases, 42 malignancy & 27 benign solid neoplasms. The choline to creatine ratio among both groups shows PV equals 0.000, that of difference significant in statics and an edge of 7.46 of Cho/Cr for characterizing benign neoplasms from malignancies had 97.1% of specificity, 94.1% of sensitivity, and 91.2% of accuracy. Also, no detected differences significant in statics within the lip/Cr and NAA/Cr ratios as PV of 0.12 & 0.26, in order. So, spectroscopic examination of the solid adnexal tumors varies as regard the malignant or the benign natures. Cho/Cr ratio would be of help in discrimination the malignancy from the benign masses. Our research matched with one directed by **(Stanwell et al., 2008)** demonstrated Cho/Cr relation in malignancy is higher than in benign ovarian neoplasms. He informed that ratio of Cho/Cr higher than 3.09 suggested malignant neoplasm, while a ratio less than 1.15 indicated a non-malignant neoplasm.

Our research matched with that conducted by (**Li et al., 2008**) demonstrated that an edge of 2 within Cho to noise ratio can perfectly distinguish adnexal malignancies and benign neoplasms of adnexa. During our research, Cho/Cr ratio of 4.29 ± 1.7 within the benign group against 8.06 ± 1.4 of the malignancy set.

In our research there had been two weak points. The First one, metabolites to creatine ratio was only assessed and related. The other one, unavoidable bias in selection were thanks to the retrospective research.

Conclusion

Finally, Cho/Cr ratio is widely accepted parameter for malignancy evaluation over other magnetic resonance spectroscopic metabolites investigated, where Cho/Cr ratio over 4 is an indicator of the tumor malignancy nature.

References

- **Aliaa S. Sheha, Nermeen N. Keriakos and Malames M. Faisal. (2019).** The role of magnetic resonance spectroscopy in the differentiation of benign and malignant adnexal masses. Egyptian Journal of Radiology and Nuclear Medicine ,50:112-122.
- **Bulik M, Jancalek R, Vanicek J, Skoch A, Mechl M. (2013).** Potential of MR spectroscopy for assessment of glioma grading. Clin Neurol Neurosurg, 115:146-153.
- **Belki´c D, Belki´c K. (2008).** The general concept of signal–noise separation (SNS): mathematical aspects and implementation in magnetic resonance spectroscopy. J Mathemat Chem, 44:884–912.
- **Dilks P, Narayanan P, Reznek R, Sahdev A, Rockall A. (2006).** Can quantitative dynamic contrast-enhanced MRI independently Characterize an ovarian mass? EurRadiol, l:1–8.
- **Iorio E, Mezzanzanica D, Alberti P. (2010).** Activation of phosphatidylcholine cycle enzymes in human ovarian cancer cells. Cancer Res, 70:2126–2135.
- **John A. Spencer, Rosmarie Forstner, Teresa M. Cunha and Karen Kinkel. (2010).** MR imaging of the songraphically indeterminate adnexal mass. EurRadiol, 20: 25–35.
- **Lamiaa El sorogy, Nahed Abd El gaber, Eman Omran, Maged Elshamy and Hamed Youssef. (2012).** Role of diffusion MRI and proton magnetic resonance spectroscopy in characterization of ovarian neoplasms.

The Egyptian Journal of Radiology and Nuclear Medicine, 43: 99–106.

- **Li HM, Qiang JW, Xia GL. (2015).** MRI for differentiating ovarian endometrioid adenocarcinoma from high-grade serous adenocarcinoma. J Ovarian Res, 8(26).
- **M. Bazot, D. Haouy, E. Dara¨ı, A. Cortez, I.Thomassin-Naggara.(2013).** ―Is MRI a useful tool to distinguish between serous and mucinous borderline ovarian tumours? ‖. Clinical Radiology, vol. 68, no. 1, pp. e1–e8.
- **Rania S. M. Ibrahim, Marwa Sh. Abd El Fattah, Zeinab M. Metwally and Lamiaa A. S. Eldin.(2019).** Value of magnetic resonance spectroscopy in assessment of adnexal lesions. Egyptian Journal of Radiology and Nuclear Medicine, 50:90-102.
- **Satoh T, Tanaka YO, Okada S. (2011).** Solid non-invasive ovarian masses on MR: histopathology and a diagnostic approach. Eur J Radiol, 80: e91–e97.
- **Schmidt S, Meuli RA, Achtari C, and Prior JO. (2015).** Peritoneal Carcinomatosis in Primary Ovarian Cancer Staging Comparison Between MDCT, MRI, and 18 F-FDG PET/CT. ClinNucl Med,40: 371–377.
- **Stanwell P, Russell P, Carter J, Pather S, Heintze S, Mountford C. (2008).** Evaluation of ovarian tumors by proton magnetic resonance spectroscopy at three Tesla. Invest Radiol, 43:745–751.