Can the Signal-to-Noise Ratio of Choline in Magnetic Resonance Spectroscopy Reflect the Aggressiveness of Endometrial Cancer?

Xue Han, MD, Jingxia Kang, MM, Jie Zhang, MD, Jianjun Xiu, MD, Zhaoqin Huang, MD, Chunrun Yang, MD, Xichao Sun, MD, Caixia Fu, SM, Qingwei Liu, MD

Rationale and Objectives: To differentiate endometrial cancer (ECa) from benign lesions in endometrial or in submucosa (BLs-ESm), and investigate whether the signal-to-noise ratio (SNR) of choline-containing compounds (Cho) obtained from three-dimensional ^{1}H magnetic resonance spectroscopy (MRS) is associated with the aggressiveness of ECa.

Materials and Methods: Thirty-three patients with ECa and 15 patients with BLs-ESm underwent preoperative multivoxel ^{1}H MRS at 3 T MR. The amplitude of Cho peak of each voxel was recorded, and the corresponding SNR of Cho peak (Cho_{SNR}) was calculated. The maximum Cho_{SNR} (max Cho_{SNR}) for each lesion was identified. The max Cho_{SNR} of ECa and BLs-ESm, as well as type I ECa and type II ECa, was compared. The relationship between max Cho_{SNR} and pathologic characteristics of tumors, including tumor grade, stage, type, and tumor size, was analyzed.

Results: The mean max Cho_{SNR} ($\pm$standard deviation [SD]) was 30.93 $\pm$ 16.89 for ECa and 10.40 $\pm$ 3.07 for BLs-ESm ($P < .001$). The mean max Cho_{SNR} for type II ECa (48.54 $\pm$ 21.46) was higher than that for type I ECa (26.19 $\pm$ 12.02, $P = .001$). There were no significant differences among different grades ($P = .449$). The Spearman coefficient between max Cho_{SNR} and stage was 0.423 ($P = .014$); the difference existed only between Ia and III ECa ($P = .048$). The Pearson coefficient between Cho_{SNR} and tumor size was 0.515 ($P = .002$).

Conclusions: The max Cho_{SNR} obtained from MRS can differentiate ECa from BLs and type I ECa and type II ECa, but cannot differentiate between each grade ECa and each International Federation of Gynecology and Obstetrics stage ECa. However, max Cho_{SNR} increased with the increase in International Federation of Gynecology and Obstetrics stage and size of ECa.

Key Words: Endometrial cancer; aggressiveness; magnetic resonance imaging; magnetic resonance spectroscopy; choline.

Endometrial cancer (ECa) is one of the three most common female genital tract malignancies in China. The incidence of ECa is rising worldwide in recent years. Correct diagnosis of ECa and benign lesions in endometrial or in submucosa (BLs-ESm) before surgery is very important to personalize treatment. The ECa type (type I, estrogen dependent; type II, estrogen independent), grade, stage, and tumor size were fundamental biological indicators of aggressiveness and prognosis of ECa (1). Type II ECa generally contains rare but aggressive subtypes of ECa, that is, squamous cell carcinoma, adenosquamous carcinoma, papillary serous carcinoma, and clear cell carcinoma, which closely related to lymph node metastasis and prognosis. The endometrial sampling is not sensitive enough to be used alone to exclude ECa. As a traditional method of diagnosis of ECa, the fractional dilatation and curettage cannot always exclude ECa when endometrial hyperplasia, especially atypical hyperplasia, was diagnosed because of limited samples (2). There were 16.7%–62.5% patients with atypical hyperplasia in dilatation and curettage having a diagnosis of ECa in the hysterectomy specimens (3–5).

Acad Radiol 2015; 22:453–459

From the Department of Radiology, Provincial Hospital Affiliated to Shandong University, 324#, Jingwu Weiqi Road, Jinan, PR China (X.H., J.Z., J.X., Z.H., Q.L.); Department of Radiology, Linyi People's Hospital, Linyi, PR China (J.K.); Department of Obstetrics and Gynecology, Provincial Hospital Affiliated to Shandong University, Jinan, PR China (C.Y.); Department of Pathology, Provincial Hospital Affiliated to Shandong University, Jinan, PR China (X.S.); and Siemens MRI Center, Shenzhen, PR China (C.F.). Received April 10, 2014; accepted December 9, 2014. This study was supported by Shandong Province Science and Technology Development Plan (2012GSF11820 and 2012YD18053) and Shandong Province Outstanding Young Scientist Award Fund (No. 2010BSB14072). **Address correspondence to:** Q.L. e-mail: doctorlqw@163.com

http://dx.doi.org/10.1016/j.acra.2014.12.010

TABLE 1. Parameters of Magnetic Resonance Imaging Sequences

Sequences	TR (ms)	TE (ms)	ST (mm)	Average	FOV (cm^2)	Matrix
Axial T2W	3110	101	3–4.5	2	20 × 20	320 × 256
Coronal T2W	3350	97	3–4	2	20 × 20	320 × 256
Sagittal T2W	2950	101	3–4	2	20 × 20	320 × 310
MRS*	750	145	—	6	—	—
DWI†	6200	63	3–4.5	6	20 × 20	160 × 120
T1W-DCE (VIBE)	5.21	1.8	3–4	1	26 × 26	224 × 161

DCE, dynamic contrast–enhanced imaging; DWI, diffusion-weighted imaging; FOV, field of view; ST, slice thickness; T1W, T1-weighted; T2W, T2-weighted; TE, echo time; TR, repetition time; VIBE, volume interpolated body examination.

*Resolution was 7 × 7 × 7 mm^3.

†b Value = 0, 100, 400, 800 s/mm^2.

Magnetic resonance (MR) imaging is considered as the optimal imaging modality in assessing the invasion of uterine cancers (6,7). The accuracy of staging ECa using MR imaging was high (8). MR imaging has also been used in determining the origin of uterine cancer (9) and differentiation of malignant tumors from benign lesions of uterus (10). As a noninvasive examination, MR spectroscopy (MRS) can provide the tissue biochemical information. The clinical application of MRS has been steadily increasing in recent years. MRS contributes to the diagnosis, differentiation of malignant tumors from benign lesions, and assessing tumor aggressiveness in brain (11,12), breast (13), and prostate (14,15). Choline-containing compounds (Cho) increased in actively proliferating tumors (16). The differentiation of malignant tumors from benign lesions of uterus with single voxel MRS has been reported in a study by Takeuchi et al. (17). The size of single voxel was often large. The large volume of a voxel may result in the restriction of measurement of small tumor, although a signal-to-noise ratio (SNR) of single voxel MRS was relatively high. However, the differentiation of ECa from BLs-ESm and the assessment of ECa aggressiveness with multivoxel MRS have not been systematically investigated.

The purpose of this study is to differentiate ECa from BLs-ESm and investigate whether the SNR of Cho (Cho_{SNR}) obtained from three-dimensional ^1H MRS is associated with the aggressiveness of ECa.

MATERIALS AND METHODS

Patients

This prospective study was approved by Ethical Committee of our hospital and the informed consent was obtained from each patient before performing MRS. Patients with primary untreated ECa or BLs-ESm diagnosed by hysterectomy or resection of the lesion were included. Patients who had no voxel with satisfactory MRS in lesions were excluded. From March 2012 to May 2013, 33 patients with ECa and 15 patients with BLs-ESm were included. Mean age of the 33 patients with ECa was 57.4 years (range, 34–75 years). Mean age of the 15 patients with BLs-ESm was 54.2 years (range, 35–78 years).

MR Imaging

All MR examinations were performed with a 3 T system (MAGNETOM Verio; Siemens, Erlangen, Germany). An eight-channel pelvic phased-array surface coil and integrated spine coils were used for signal reception. The patients were required to fast for 4 hours before MR imaging. Raceanisodamine hydrochloride injection (Minsheng Pharma, Hangzhou, China) was administered before image acquisition to reduce bowel motion. The bladder was partially filled.

MR sequences included T2-weighted (T2W) imaging, MRS, T1-weighted (T1W) imaging, diffusion-weighted imaging, and dynamic contrast–enhanced imaging. The parameters of these sequences are shown in Table 1. Using these images, the voxels of interest were placed in the lesions of solid components, avoiding cystic or necrotic areas. MRS data were overlaid on the corresponding axial T2W images. The MRS (repetition time, 750 milliseconds; echo time, 145 milliseconds; flip angle, 90°; bandwidth, 1250 Hz) was performed with three-dimensional chemical shifting imaging techniques based on point-resolved spectroscopic sequence with sufficient lipid suppression by using frequency selective saturation fat suppression. Chemical shift selective suppression water suppression scheme was used in water suppression. Eight saturation bands were used to minimize the contamination from peripheral structures of uterine. The number of average was 6 for the acquisition with water suppression spectra and 2 for unsuppressed water spectra. The scan matrix was 12 × 12 × 12 and interpolated to 16 × 16 × 16. The scan time was 9 minutes 54 seconds for MRS acquisition with water suppression, and 5 minutes 51 seconds for MRS acquisition with unsuppressed water. The voxel size was 7 × 7 × 7 mm^3, which may be small enough to measure the smaller tumors. The amplitude and the integration of Cho peak were recorded. MRS data with unsuppressed water and the integration of Cho were not investigated in this article.

MRS Data Analysis

The analysis of MRS data was performed with the spectroscopy software on Syngo workstation (Siemens). The MRS data obtained from MR scanner needed to be processed further, including further water suppression, baseline