Can Magnetic Resonance Spectroscopy reflect the Aggressiveness of Endometrial cancer?

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Target audience: Radiologists engaged in female pelvic MR and gynecologists.

Purpose: To investigate whether the choline-containing compounds (Cho) obtained from three-dimension ^{1}H magnetic resonance (MR) spectroscopy is associated with the aggressiveness of endometrial cancer (ECa).

Methods: Thirty-eight patients with ECa and 19 patients with benign lesions in endometria or in submucosa (BLs-ESm) confirmed by hysterectomy or lesions resection were included. They underwent preoperative multi-voxel ^{1}H MR spectroscopy (MRS) with a 3.0-T system. The MRS was performed with 3D CSI techniques based on PRESS with sufficient lipid. The average number of acquisition was 6 for the water suppression spectra and 2 for the unsuppressed water spectra. The voxels of interest with size of 7×7×7 mm^3 were selected in the lesions of solid components, avoiding cystic or necrotic areas. All the metabolite quantization was performed within jMRUI v.4.0 software. The ratio of sum of Cho to sum of water (Cho/water) was the statistical unit. $\text{Cho/water}=(\sum_{i=1}^{n}\text{Cho}_i)/(\sum_{i=1}^{n}\text{water}_i)$, where, n was the total number of included voxels for a patient. If the lesion was ECa, the tumor stage, grade, type (type I: estrogen-dependent; type II: estrogen-independent) and size (maximum diameter) were determined by a pathologist. The mean Cho/water was compared using independent sample t-test between two groups, and using ANOVA among three or more groups. The receiver operating characteristic (ROC) curve analyses was used to determine an optimal threshold to distinguish between ECa and BLs-ESm, as well as between type I ECa and type II ECa. The relationship between stage and mean Cho/water was analyzed with Spearman correlation analysis. The different grades tumors were analyzed using the same statistical methods with different stages tumors. The relationship between mean Cho/water and tumor size was analyzed with Pearson correlation analysis. $P < 0.05$ was considered to have a significant difference.

Results: The mean Cho/water (± standard deviation [SD]) was (3.02±1.43) × 10^{-3} for ECa and (1.68±0.33) × 10^{-3} for BLs-ESm ($P < 0.001$). The mean Cho/water was (4.42±1.53) × 10^{-3} for type II ECa (estrogen-independent) and (2.65±1.17) × 10^{-3} for type I ECa (estrogen-dependent) ($P = 0.001$). The area under the ROC curve to differentiate type I from type II ECa was 0.833 and the Yonden index was 0.517. When the threshold to differentiate type I from type II ECa was 3.41 × 10^{-3}, the sensitivity and specificity were 0.75 and 0.767, respectively. The mean Cho/water was 2.57 × 10^{-3} for Ia ECa; 3.02 × 10^{-3} for Ib ECa; 4.31 × 10^{-3} for II ECa; 3.52 × 10^{-3} for III ECa. There were no significant differences among different stages tumors ($P = 0.107$), but the Spearman coefficient between Cho/water and tumor stage was 0.386 ($P = 0.017$). The mean Cho/water was 2.43 × 10^{-3} for G1 ECa; 3.46 × 10^{-3} for G2 ECa; 2.85 × 10^{-3} for G3 ECa. There were no significant differences among different grades tumors ($P = 0.142$) and the Spearman coefficient between Cho/water and tumor grade was 0.235 ($P = 0.156$). The Pearson coefficient between Cho/water and tumor size was 0.333 ($P = 0.041$).

Discussion: It is important to differentiate the ECa from BLs-ESm. For diagnosis of complex or atypical endometrial hyperplasia, the results of intraoperative frozen section examination are not reliable. In this study, the mean Cho/water of ECa was significantly higher than that of BLs-ESm ($P < 0.001$). This may be a beneficial supplement to the pre- or intra- operative pathological examination. The type II ECa was often more aggressive than type I ECa. Type II ECa was closely related to lymph node metastasis and prognosis. Generally, lymph node resection was required for the type II ECa patients even the FIGO stage was low. Therefore, it was important to differentiate the two types ECa before operation. Generally, whether ECa was estrogen dependent was confirmed by immunohistochemistry in postoperative routine pathologic examination rather than in preoperative fractional D & C or intraoperative frozen section of endometrial lesions due to small tissue or limited time. In this study, the mean Cho/water of type II ECa was significantly higher than that of type I ECa ($P = 0.001$), which may contribute to differentiation of the two types ECa before operation. From the results, the Cho/water for different stages overlapped substantially, but there was a tendency for Cho/water to increase with an increase of tumor stage. In addition, Cho/water of ECa increased with the increase of tumor size ($P = 0.041$). However, no significant differences were found among mean Cho/water of different grades tumors; and no significant correlation was found between Cho/water and tumor grade.

Conclusions: the Cho/water obtained from MRS can differentiate ECa from BLs-ESm and differentiate type II ECa from type I ECa. There were no significant differences among different stages ECa, as well as among different grades ECa. However, Cho/water of ECa increased with the increase of tumor stage and tumor size. Therefore, Cho/water may reflect the ECa aggressiveness to some extent.