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RESEARCH ARTICLE

Diagnostic Value of ADC Value and Choline Peak MR Spectroscopy in Patient with Uterine Tumors

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Abstract

Introduction: Accurate differentiation between benign and malignant uterine tumors is critical for determining therapeutic strategies. This study aims to evaluate the diagnostic performance of Apparent Diffusion Coefficient (ADC) values and Magnetic Resonance Spectroscopy (MRS)-derived choline (Cho) peaks in characterizing uterine tumors, using histopathology as the reference standard. **Methods:** A diagnostic accuracy study was conducted between February and August 2025, involving 35 patients with uterine tumors. All subjects underwent pelvic MRI, including diffusion-weighted imaging (DWI) and multivoxel MRS. ADC values and Cho peaks were measured from the solid portions of the lesions. Diagnostic performance, including sensitivity, specificity, and optimal cutoff values, was determined using Receiver Operating Characteristic (ROC) curve analysis. **Results:** Malignant tumors exhibited significantly lower mean ADC values (0.75×10^{-3} mm^2/s) compared to benign lesions (1.35×10^{-3} mm^2/s; p=0.001). Conversely, mean Cho peaks were significantly higher in the malignant group (3.33 ppm) than in the benign group (1.31 ppm; p=0.001). An ADC cut-off of 0.965×10^{3} mm^2/s yielded a sensitivity of 93.3% and a specificity of 100% (AUC=0.960). A Cho peak cut-off of 2.215 ppm demonstrated 100% sensitivity, 96.7% specificity, and 97.1% accuracy (AUC=0.967). Demographic factors such as age, parity, and contraceptive use showed no significant association with histopathological outcomes (p>0.05). **Conclusion:** Both ADC quantification and Cho peak MRS serve as highly accurate, non-invasive biomarkers for differentiating uterine malignancies. The integration of these functional MRI parameters significantly enhances diagnostic precision in the preoperative assessment of uterine tumors.

Keywords: Uterine tumor- magnetic resonance imaging- apparent diffusion coefficient- Magnetic resonance spectroscopy

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Introduction

Uterine tumors refer to abnormal tissue proliferation that arises within the uterus. Histologically, uterine tumors are broadly divided into benign and malignant categories, and may originate from one of the principal uterine layers, namely the endometrium (inner lining), myometrium (smooth muscle), or the surrounding subserosal connective tissue [1]. Benign tumors most frequently arise from the myometrium, where uterine leiomyoma represents the most common type, occurring in approximately 70–80% of women of reproductive age [1]. Leiomyomas originate from smooth muscle cells and are further classified by location as subserosal, intramural, or submucosal [1-3].

Within the endometrial layer, endometrial polyps and various endometrial tumors may develop, while adenomyosis represents ectopic endometrial glands within the myometrium. Malignant neoplasms of the endometrium predominantly manifest as endometrial carcinoma, which constitutes approximately 90% of malignant uterine tumors [1]. In the myometrial layer, leiomyosarcoma represents the principal malignant counterpart arising from smooth muscle tissue [2, 4].

Differentiating benign from malignant uterine tumors

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is essential to guide therapeutic strategies, yet clinical manifestations often overlap; therefore, accurate imaging is crucial [5]. Multiple radiologic modalities are utilized for diagnosis and pre-treatment assessment, including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Ultrasound is widely available, non-invasive, and cost-effective; however, its diagnostic utility is limited by lower spatial resolution, operator dependence, and inadequate assessment of invasion depth or extra-uterine spread [6]. Camponovo et al., [6] reported that ultrasound has limited accuracy for preoperative evaluation of uterine sarcoma, whereas MRI is superior due to enhanced soft-tissue contrast and improved ability to assess tumor morphology and perfusion.

Morphologic differences between benign and malignant tumors may remain ambiguous, even with contrast administration [7]. MRI is therefore considered the gold-standard modality for uterine malignancy assessment [6, 7]. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) maps have demonstrated diagnostic value for differentiating benign versus malignant neoplasms across multiple organs, including bowel, lung, breast, and ovary. Magnetic resonance spectroscopy (MRS) is a non-invasive technique that identifies metabolic signatures associated with malignant transformation and active tumor biology [5, 8].

Malignant tumors typically demonstrate increased cellularity and reduced extracellular space, resulting in lower ADC values relative to benign lesions [8]. Thus, ADC quantification has value in distinguishing benign from malignant uterine tumors [9]. MRS provides complementary metabolic analysis, specifically quantifying metabolites such as choline, which reflects membrane turnover and cellular proliferation [5]. Elevated choline peaks are typically associated with cancer and higher proliferative activity [5, 7]. When integrated, ADC measurements and choline peaks yield a more comprehensive assessment of both structural and metabolic tumor characteristics, thereby improving diagnostic accuracy [5, 8].

Recent studies support the combined use of ADC and MRS to enhance characterization of uterine tumors [5, 7, 10, 11]. Based on this evidence, the present study aims to evaluate the diagnostic performance of ADC values and MRS-derived choline peaks, compared with histopathology, in patients presenting with uterine tumors.

Materials and Methods

Study design and patient characteristics

This study is a diagnostic accuracy test designed to determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of apparent diffusion coefficient (ADC) measurements and choline peak magnetic resonance spectroscopy (MRS) compared to histopathological findings in patients with uterine tumors. The study conducted from February until August 2025.

Eligible subjects were patients diagnosed with uterine tumors who were willing to participate, had undergone anatomical pathology examination, and had completed pelvic gynecological MRI that included both routine MRI sequences and MR spectroscopy. Patients were excluded if they had previously undergone surgery, chemotherapy, or radiotherapy for uterine tumors, or if the largest tumor lesion measured less than 0.5 cm in diameter. Sampling was performed using a consecutive sampling technique from the accessible clinical population.

Definition

Uterine tumors are diagnosed based on clinical referral, MRI examination, and results from histopathology. Examples include leiomyoma, adenomyosis, endometrial polyps and hyperplasia, leiomyosarcoma, and endometrial carcinoma.

Research protocol

Prior to data collection, the research proposal underwent ethical review by the Research Ethics Committee, Research and Development Unit, Faculty of Medicine, Hasanuddin University. After approval was granted, permission to conduct the study was issued, and data collection commenced. All study data were obtained from secondary sources, including electronic medical records (EMR), MRI workstation data, and PACS archives at Hasanuddin University Hospital, with access granted under Ethics Committee approval.

Patients who met eligibility criteria were identified based on clinical referral, MRI results, and histopathology confirmation. For cases with multiple lesions, ADC and choline measurements were taken from the largest tumor. Mass localization was performed in axial, coronal, and sagittal views. Conventional images included T1-weighted and T2-weighted sequences, with slice thickness 3–4 mm, 1 mm interslice gap, field of view 250 mm, and 90° flip angle.

ADC values were automatically generated by the workstation software. Round regions of interest were placed at three points in the solid portion of each lesion, with diameters of 0.5–1.0 cm, avoiding normal parenchyma, necrotic areas, and hemorrhagic components. The mean ADC value obtained was used for analysis and was compared with histopathological results.

MRS acquisition used the PRESS sequence and multivoxel water-suppressed technique with automatic shimming. The volume-of-interest was positioned over the solid portion of the mass while avoiding cystic or hemorrhagic regions, calcification, and large vessels. ADC and choline peak interpretation was carried out by the principal investigator under supervision and was validated by two board-certified radiologists. All results were recorded in standardized data collection sheets and subsequently processed for statistical evaluation.

Statistical analysis

Data analysis was performed using SPSS version 25.0, with the threshold for statistical significance set at $p<0.05$. Categorical variables were expressed as frequencies and percentages, while continuous variables,

including ADC and choline peak measurements, were described using minimum, maximum, mean, and standard deviation. Bivariate analysis was conducted to evaluate differences between benign and malignant tumor groups. For categorical clinico-demographic factors, associations with histopathological outcomes were analyzed using the Fisher's exact test. Continuous variables were assessed for normality, with group differences determined via independent t-tests for normally distributed data and the Mann-Whitney U test for non-normal distributions. Furthermore, Receiver Operating Characteristic (ROC) curve analysis was employed to determine the diagnostic performance and optimal cutoff values for ADC and choline peaks in differentiating benign from malignant pathology.

Results

A total of 35 subjects met the study criteria and were included in the analysis. The distribution of respondent characteristics is presented in Table 1. Analysis revealed that 60% of patients with benign histopathology were under 45 years of age, while 80% of those in the malignant group were aged 65 years or older; however, these age-related distributions did not reach statistical significance (p=0.499). Similarly, neither contraceptive use nor age at marriage demonstrated a significant association with tumor histopathology (p=0.447 and p=0.195, respectively), with the majority of subjects in both cohorts being non-users of contraception and having married after the age of 18.

Hormonal and reproductive factors, specifically age at menarche and parity, also showed no significant correlation with histopathological outcomes. Most subjects in the benign (90%) and malignant (100%) groups experienced menarche at or after 12 years of age (p=1.000). Furthermore, nulliparity was observed in 56.7% of benign cases and 60% of malignant cases, yet parity status remained statistically independent of histopathology (p=0.995). Collectively, these findings indicate that the histopathological differentiation in this study cohort was not significantly influenced by traditional clinico-demographic or reproductive risk factors, thereby shifting the diagnostic focus to functional imaging parameters.

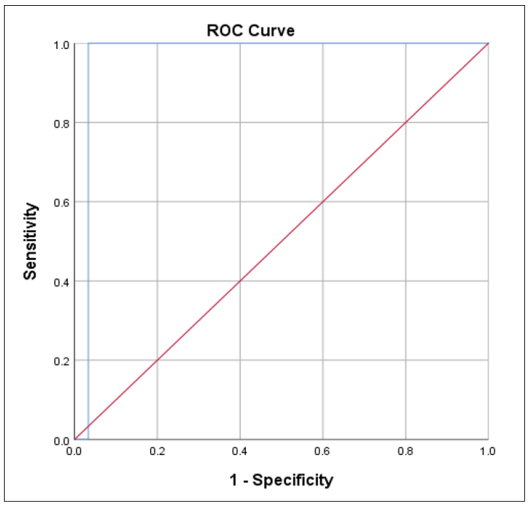

Figure 1. Receiver Operating Characteristic (ROC) Curve of Apparent Diffusion Coefficient (ADC) Values. The blue line represents the diagnostic performance of ADC in differentiating malignant from benign uterine tumors, achieving an Area Under the Curve (AUC) of 0.960 (95% CI: 0.893–1.000; p=0.001). At the optimal cutoff of 0.965×10^{3} mm²/s, the parameters demonstrate 93.3% sensitivity and 100% specificity. The red dashed line represents the reference diagonal (AUC=0.5).

Based on the MRI findings presented in Table 2, ADC values ranged from 0.61 to 1.87 (median 1.25) with a mean of $1.26\pm0.33\times10^{-3}$ mm²/s. Choline peak values ranged from 0.21 to 5.99 ppm with a mean of 1.66±1.13

Table 1. Patient Characteristics

Variables		Histopathology		p-value
		Malignant (%)	Benign (%)	
Age (years)				
	<45	18 (60)	1 (20)	0.499*
	≥65	12 (40)	4 (80)	
Contraceptive use				
	Yes	8 (26.7)	2 (40)	0.447*
	No	22 (73.3)	3 (60)	
Marital aged (years)				
	≤18	4 (13.3)	2 (40)	0.195*
	>18	26 (86.7)	3 (60)	
Menarche age (years)				
	< 12	3 (10)	0 (0)	1.000*
	≥12	27 (90)	5 (100)	
Parity				
	Nullipara	17 (56.7)	3 (60)	0.995*
	Primipara/ Multiparous	13 (43.3)	2 (40)	

Note: * Fisher's exact test

Table 2. Quantitative Imaging Parameters and Histopathological Distribution

Variable	Category	n (%)	Mean ± SD	Median (Min–Max)
ADC Value (10^3 mm^2/s)	—	—	1.26±0.33	1.25 (0.61–1.87)
Choline Peak (ppm)	—	—	1.66±1.13	1.37 (0.21–5.99)
Histopathology	Malignant	5 (14.3)	—	—
	Benign	30 (85.7)	—	—

Table 3. Mean ADC Value with Histopathology Results in Patients with Uterine Tumors

Histopathology	n	ADC value		p-value
		Mean	SD	
Malignant	5	0.75	0.07	<0.001*
Benign	30	1.35	0.28	

Note: *independent t-test

Table 4. Comparison of MRI ADC Values (cut-off values) with Histopathology Results

ADC Value	Histopathology	
	Benign	Malignant
≥ 0.965	28 (93.3%)	0 (0%)
< 0.965	2 (6.7%)	5 (100%)

ppm. Histopathological results showed that benign uterine tumors predominated (85.7%), while malignant tumors comprised 14.3% of cases.

Table 3 shows that the mean ADC value was significantly higher among benign tumors (1.35×10^{-3} mm^2/s) compared to malignant tumors (0.75×10^{-3} mm^2/s), with p=0.001, indicating a significant association between ADC value and histopathology status. The ROC curve for ADC value is shown in Figure 1, which yielded an AUC of 0.960 (p=0.001; 95% CI: 0.893–1.000). The optimal ADC cutoff point for distinguishing benign from malignant histopathology was 0.965×10^{-3} mm^2/s.

As shown in Table 4, all malignant cases (100%) were correctly identified below the ADC threshold of 0.965×10−3 mm^2/s, while 93.3% of benign lesions were correctly identified above this value. The diagnostic performance for the ADC cutoff demonstrated a sensitivity of 93.3%, specificity of 100%, a positive predictive value of 71.4%, and a negative predictive value of 100%.

Table 5 presents findings for the choline peak. Mean choline peak values were 3.33 ppm in the malignant group and 1.31 ppm in the benign group, with p=0.001 indicating a statistically significant difference between the two groups. The ROC curve for choline peak is presented in Figure 2, yielding an AUC of 0.967 (p=0.001; 95% CI: 0.902–1.000). The optimal choline peak cutoff was 2.215 ppm.

Diagnostic test results based on the choline cutoff value are summarized in Table 6. Malignant tumors most frequently demonstrated choline peak values ≥2.215 ppm (100%), while benign tumors most frequently demonstrated values <2.215 ppm (96.7%). The diagnostic performance of the choline peak cutoff resulted in sensitivity of 100%, specificity of 96.7%, positive predictive value of 83.3%, negative predictive value of 100%, and accuracy of 97.1%.

Discussion

In this study, 35 subjects were evaluated to determine whether demographic and clinical characteristics were associated with uterine tumor histopathology. Demographic and clinical characteristics including age, parity, and contraceptive use were evaluated as potential confounders; however, no statistically significant associations with uterine tumor histopathology were identified. While prolonged estrogen exposure, nulliparity, and advanced age are established risk factors for gynecologic malignancies in larger epidemiological cohorts, the lack of significance in this analysis suggests that in a clinical diagnostic setting, these clinical markers may overlap considerably between benign and malignant lesions. Consequently, the diagnostic emphasis shifts to functional imaging biomarkers, which provide a more objective and direct reflection of tumor biology than clinical history alone.

The diagnostic efficacy of the ADC and Cho peak MRS underscores their role in capturing the physical and metabolic hallmarks of malignancy. The observed reduction in ADC values among malignant tumors (0.75×10−3 mm2/s) is a direct result of hypercellularity, which restricts the Brownian motion of water molecules within the neoplastic tissue. Complementing this, the significantly elevated choline peaks observed

Table 5. Mean Choline Peak Value with Histopathology Results in Uterine Tumor Patients

Histopathology	n	Choline peak		p-value
		Median	Min-Max	
Malignant	5	3.33	2.46-3.66	0.001*
Benign	30	1.31	0.21-5.99	

Note: *Mann-Whitney test

Table 6. Comparison of Choline Peak MRI Values (cut-off values) with Histopathological Types

Choline Peak	Histopathology	
	Malignant	Benign
≥ 2.215	5 (100)	1 (3.3)
<2.215	0 (0)	29 (96.7)

in malignant lesions (mean 3.33 ppm) highlight the accelerated membrane turnover inherent in aggressive cellular proliferation. The integration of these parameters demonstrating a sensitivity of 100% and accuracy up to 97.1% allows for a comprehensive metabolic and structural characterization, transforming the preoperative assessment from a purely morphological description to a high-precision "imaging biopsy".

The largest proportion of subjects with malignant tumors were aged 36–45 years, which is consistent with previous findings suggesting that uterine malignancies tend to occur in women of older reproductive age (mean 51.25 years) compared to benign tumors (mean 46.74 years) [12]. Zhao et al., [13] also reported that the mean age for malignancy was higher (54.33 years) than non-malignant lesions (46.12 years). During the reproductive period, benign uterine tumor incidence increases with age, and prevalence reaches 30–40% among women >40 years [14]. Although age is widely reported to influence uterine tumor biology, particularly in malignant transformation, this study did not identify a statistically significant association between age and histopathology.

The distribution of age at marriage in this study showed that most malignant cases occurred in women married at >18 years. Previous studies have not yet fully explained this association; however, marital status has been associated with cancer outcomes, where unmarried

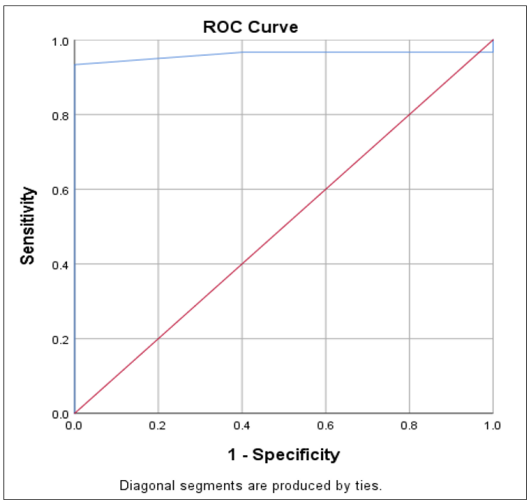

Figure 2. Receiver Operating Characteristic (ROC) Curve of Choline Peak Values. The green line illustrates the diagnostic performance of MRS-derived choline peaks in distinguishing malignant from benign uterine tumors, yielding an Area Under the Curve (AUC) of 0.967 (95% CI: 0.902–1.000; p=0.001). At the optimal threshold of 2.215 ppm, the parameter demonstrates 100% sensitivity and 96.7% specificity. The red dashed line represents the reference diagonal (AUC=0.5).

individuals may experience higher psychosocial stress, impaired immune regulation, and increased tumor invasion risk [15]. Bunga et al. reported that the average age at marriage among benign uterine tumors was <20 years [16]. Nevertheless, in this study age at marriage was not significantly correlated with histopathological outcomes.

Age at menarche is an established hormonal risk factor for gynecologic malignancy. Prior studies demonstrated earlier menarche (≤13 years) in both benign and malignant uterine tumors [12, 17, 18], and prolonged estrogen exposure is believed to promote uterine tumor development [12, 17-20]. Early menarche increases cumulative ovulatory cycles and metabolic alterations that may influence endometrial proliferation. Despite this, our analysis did not identify a significant association between age at menarche and histopathology.

Contraceptive use was more frequently absent in both malignant and benign groups. Several studies have reported a protective effect of oral contraceptives against uterine cancer, with risk reductions persisting decades after discontinuation [21, 22]. However, other studies have demonstrated either minimal effect or inconsistent association in benign uterine tumors [20]. In this study, contraceptive use was not significantly related to histopathological outcome.

Parity has also been widely reported as a hormonal and structural determinant in tumor biology. Nulliparity increases lifetime estrogen exposure and is associated with increased risk of both benign and malignant uterine tumors [14, 20, 23]. In the present study, most malignant and benign cases occurred among nulliparous women, although this association was not statistically significant.

This study demonstrated that ADC values significantly differed between benign and malignant tumors, with malignant tumors showing lower ADC values. These findings are in agreement with prior investigations where malignant uterine tumors exhibit reduced diffusivity due to increased cellular density [24-28]. The diagnostic performance in this study (AUC 0.960; accuracy 94.2%) is consistent with meta-analytic data reporting AUC values around 0.94 [25]. In atypical endometrial hyperplasia, there is an increase in apparent diffusion coefficient (ADC) value and a decrease in choline peak. However, in one sample of atypical endometrial hyperplasia with EIN type, the results were different. Specifically, there was a decrease in ADC value and an increase in choline peak.

Furthermore, choline peak values on MR spectroscopy were significantly higher in malignant lesions. Choline elevation indicates increased cell membrane turnover, a hallmark of malignant proliferation [29-33]. Our diagnostic performance (AUC 0.967; accuracy 97.1%) is consistent with findings by Takeuchi et al., [29] and Malek et al., [31] confirming the diagnostic utility of choline MRS.

Despite the high diagnostic accuracy demonstrated, several limitations must be addressed to contextualize these findings. The primary constraint is the relatively modest sample size of 35 subjects and the single-center design conducted at Hasanuddin University Hospital,

which may introduce selection bias. Although the results reached statistical significance (p=0.001), the small cohort size potentially limits the ability to detect more nuanced correlations between clinico-demographic variables such as age, parity, and contraceptive use and specific histopathological subtypes. Furthermore, the specific 3T MRI hardware and software configurations utilized, alongside the incomplete standardization of acquisition protocols, may influence the absolute quantification and reproducibility of these biomarkers.

Technical factors, including the sensitivity of ADC values to b-value selection and the dependence of MRS choline peaks on shimming efficiency or echo time (TE), can lead to discrepancies across different centers. Consequently, the specific cutoff values proposed in this study 0.965×10−3 mm^2/s for ADC and 2.215 ppm for Cho, should be regarded as preliminary, center-specific benchmarks rather than universal thresholds. The lack of a standardized, multi-vendor consensus for uterine MRS remains a challenge for broader clinical adoption, emphasizing the need for established reporting and acquisition standards similar to the PI-RADS framework for prostate imaging to ensure reliable integration into multicenter diagnostic workflows.

To enhance external validity, larger-scale prospective multicenter trials are necessary to standardize imaging protocols across diverse hardware platforms and validate diagnostic thresholds across a broader demographic spectrum. Future clinical protocols should consider the integration of routine choline peak MRS in the evaluation of uterine tumors to improve preoperative diagnostic precision.

In conclusion, the mean ADC value in uterine tumors was significantly higher in benign histopathology than in malignant cases, while mean choline peak values were significantly higher in malignant tumors than benign lesions. The optimal ADC cutoff value for distinguishing benign from malignant histopathology was 0.965×10^{-3} mm^2/s, yielding a sensitivity of 93.3% and a specificity of 100%. These findings, alongside a choline peak sensitivity of 100%, support the clinical value of combining these functional MRI parameters.

While our findings demonstrate exceptional sensitivity and specificity within the study cohort, the single-center design and limited sample size necessitate caution in broad clinical application. We recommend that future research focuses on multicenter validation to refine these diagnostic thresholds and establish them as standardized biomarkers in oncological imaging.

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Contributors

NP (Concept, Design, Resources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Writing Manuscript), MM (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), RR (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), AAZ (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), NUP (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), and ISR (Concept, Design, Analysis and Interpretation, Critical Review). All authors read and approved the final version of the manuscript.

Competing interests

No competing interests were reported.

Ethics approval

All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudirohusodo Hospital Faculty of Medicine, Hasanuddin University (letter no. 460/UN4.6.4.5.31/PP.36/2025).

Data availability statement

The data presented in this study are available on request from the corresponding author.

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