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Original Article

The added Value of Diffusion-weighted And T2 Star Weighted Magnetic Resonance Imaging in Accurate Detection and Diagnosis of Uterine Adenomyosis.

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ABSTRACT

Background: Uterine adenomyosis (UA) is a common noncancerous condition characterized by the presence of endometrial tissue within the myometrium. UA is often associated with adverse pregnancy outcomes and complications. Modern imaging techniques provide a non-invasive means of identifying UA, with Magnetic Resonance Imaging (MRI) being particularly effective due to its high precision. The aim of this study is to assess the diagnostic accuracy of MRI, specifically Diffusion-weighted image (DWI) and T2*WI, in detecting UA.

Methods: A total of 24 female participants underwent MRI using diagnostic protocol that included T1WI, T2WI, T1 FS WI, DWI and T2*WI. The results of (advanced MRI) sequences were compared to those of conventional MRI, with histopathological verification after surgery as the gold standard.

Results: Adenomyotic lesions showing restricted diffusion accounted for 75% of cases, while 83.3% of lesions exhibited signal voids on T2*WI. Additionally, 70.8% of lesions displayed typical signal intensities on conventional MRI. The inclusion of DWI improved the diagnostic performance of MRI which was further enhanced by addition of T2*WI compared to conventional MRI. Conventional MRI had sensitivity (SE) of 80% and specificity (SP) of 66.7%, but these values were not statistically significant ($p < 0.05$). On the other hand, DWI had SE of 85% and SP of 66.7%, which was statistically significant ($p< 0.05$). T2*WI had SE of 94.7% and SP of 75%, which was even more statistically significant and could be reliably correlated with laparoscopy.

Conclusions: T2*WI and DWI can serve as reliable supplementary diagnostic sequences to conventional MRI in detection of UA.

Keywords: DWI; T2*WI; adenomyosis; MRI; Pelvis

INTRODUCTION

Uterine adenomyosis (UA) is a common noncancerous gynecological condition where the endometrial glands and stroma are present in abnormal locations within the myometrium. This leads to an enlargement of the uterus and an increase in smooth muscle cells [1]. UA is associated with a wide range of clinical symptoms, ranging from no symptoms to debilitating complications such as severe menstrual pain, painful sexual intercourse, heavy and irregular menstrual bleeding, and even anemia [2-4]. Recent research has also explored its connection to infertility and negative pregnancy outcomes, including an increased risk of preeclampsia, miscarriage, and having a smaller gestational-aged child [5,6]. Therefore, there is a growing interest in identifying adenomyotic conditions in young women, which requires reliable and non-invasive diagnostic techniques. According to estimates, more than 20% of women who undergo hysterectomy for excessive uterine bleeding are found to have a histological diagnosis of UA [1]. The exact cause of UA is still not fully understood, but the most widely accepted theories suggest that endometrial glands infiltrate the myometrium, leading to the formation of new blood vessels and the growth of nearby smooth muscle tissue. The presence of abnormal hypertrophic muscle tissue within the

myometrium disrupts the normal uterine contractions that are important for blood clotting in the spiral arteries, which is believed to be the cause of heavy menstrual bleeding or dysfunctional uterine hemorrhage [7].

Currently, the main imaging methods used for diagnosing UA are magnetic resonance imaging (MRI) and transvaginal ultrasound (TV-US). These procedures are reliable and accurate diagnostic tools for evaluating young women with persistent pelvic pain or infertility [7]. However, one limitation of ultrasound is that it depends on the operator and can show significant variability between tests. Therefore, when ultrasound results are inconclusive, MRI is preferred as the imaging method. MRI is considered a secondary diagnostic tool for UA due to its limited availability and higher cost compared to ultrasound. However, MRI has higher Sensitivity (77%) and specificity (89%) and is less operator-dependent [8]. Moreover, MRI provides excellent diagnostic accuracy in distinguishing different types of soft tissues, allowing for the identification of other gynecologic conditions such as fibroids or endometriosis. It also enables the evaluation of the junctional zone (JZ), differentiation between different subtypes of UA, and assessment of the surrounding pelvic structures [9-11].

Diffusion-weighted imaging (DWI) is a technique that provides both structural and functional information about biological tissues without the need for ionizing radiation or contrast agents. UA may exhibit restricted diffusion on DWI [12]. DWI plays a unique role in differentiating between UA and fibroids by showing significantly decreased apparent diffusion coefficient (ADC) values in fibroids compared to adenomyoma at all b values [13]. T2*-weighted images (T2*WI) can detect areas of signal loss due to magnetic susceptibility effects, allowing for the identification of ancient hemorrhagic material in UA [14]. Therefore, our aim is to highlight the importance of unenhanced advanced MRI techniques of the pelvis (UE-MRI), including T2*WI and DWI, in the detection and characterization of UA compared to histopathology.

METHODS

This study was conducted at the Radiodiagnosis Department of Zagazig University Hospital in Egypt from June 2023 to December 2023. It was a cross-sectional prospective investigation focused on the diagnostic stage or pre-operative UA assessment. The study included 24 female patients aged between 25 and 58 years who reported chronic pelvic pain, abnormal uterine hemorrhage, or infertility. The inclusion criteria consisted of women who complained of abnormal uterine bleeding with typical UA signs observed through ultrasound (US) and chronic pelvic pain, as well as infertile females seeking fertility with suspicious UA signs detected through the US. Individuals with contraindications to MRI examination, such as those with aneurysmal clips and pacemakers, were excluded.

Ethical considerations

Participants were provided with a detailed explanation of the study and were required to sign an informed consent form. The study received approval from the Faculty of Medicine, Zagazig University Institutional Review Board (#10671/4-4-2023) The study adhered to the guidelines of the Declaration of Helsinki Code of Ethics for research involving human subjects.

Patient preparation

Patients underwent a full clinical examination, including a complete medical history, as well as the following procedures:

- Pelvis-abdominal ultrasound examination
- Transvaginal ultrasound (TV-US) when necessary
- MRI of the pelvis

For MRI preparation, patients were instructed to:

- Fast for 4-6 hours before the imaging
- Follow a low-residue diet for 1-2 days
- Receive intravenous administration of an anti-peristaltic drug prior to the examination
- Have a moderately filled bladder
- Take 2 doses of an oral laxative or undergo a bowel enema 2-3 hours before the MRI

Patient position

The patient was positioned in a supine position with their head towards the magnet. Then the pelvic coil is placed, with the coil positioned over the abdomen and pelvis. To prevent respiratory artifacts, the coil was tightened.

Protocol: Table 1 summarizes the sequences used in the study.

Image analysis: MR sequences were performed using a 1.5 Tesla superconducting MR imager (Philips medical system) with a pelvic coil

MRI interpretation:

The MR features of UA were assessed using the criteria suggested by **Foti et al. (2018) (14)**, whichinclude:

1. Thickened endometrial myometrial junction > 12mm
2. Indistinct endometrial myometrial junction
3. Sub endometrial cystic lesions
4. T1WI high signal intensity foci and striations
5. Punctate or scattered signal voids on T2*WI
6. Restricted diffusion on DWI may be observed inUA

Data analysis focused on the DWI and T2*WI signals to study the adenomyotic lesions.

The gold standard: histopathological verification after surgery.

STATISTICAL ANALYSIS

Data analysis was performed using IBM SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Quantitative variables were presented as frequencies and percentages. The diagnostic performance was measured by determining the SE, SP, positive predictive value (PPV), and negative predictive value (NPV). The adenomyotic lesions in patients who underwent surgery were evaluated to assess the diagnostic accuracy of conventional MRI, DWI, and T2*WI sequences. The comparison was based on percentages. A statistically significant result was defined as $P < 0.05$.

RESULTS

In this cross-sectional study, MRI was performed on a sample of 24 female patients aged 25–58 years with the mean age was 41.1 ± 9.16 who were either at the diagnostic stage or undergoing pre-operative assessment for UA. (Table 2). However, only 23 patients underwent surgical or laparoscopic examination. Out of the 24 patients included in the study, 11 (45.8%) reported pelvic pain, 9 (37.5%) reported abnormal uterine bleeding, 5 (20.8%) reported infertility, and 4 (16.7%) reported dysmenorrhea. Additionally, 12.5% of the patients were asymptomatic and came for routine check-ups. Among the 24 patients with UA, 17 (70.8%) had diffuse UA, 5 (20.8%) had localized UA, and 2 (8.4%) had cystic UA. (Table 3).

The TVUS examination of the cases revealed that the most frequent US finding among the 17 cases with diffuse UA was globular enlargement of the uterus (88.2%), followed by indistinct endometrial (70.5%) and sub-endometrial cysts (58.8%). The least frequent finding was striation (41.2%). The conventional MRI sequences showed that the most frequent finding among the 17 cases with diffuse UA was thickened endo-myometrial junction (82.3%), followed by distinct endo-myometrial junction (70.5%), sub-endometrial cysts (58.8%), and the least frequent finding was T1WI high SI foc2i and striations (41.17%). Regarding the gold standard diagnosis, 85% of the lesions were UA, 5% were endometrial hyperplasia, and 10% were uterine fibroids.

In our study, the conventional MRI had 80%, 66.7%, 78.3%, 94.1%, and 33.3% SE, SP, DA, PPV, and NPV, respectively. The DWI findings among the studied lesions showed that 75% of the lesions were restricted (High SI at DWI and low SI at ADC map), while 25% were not restricted (Low SI at DWI and high SI at ADC map). After confirmation by histopathology, the MRI analysis, along with the DWI sequence, exhibited better outcomes with SE, SP, PPV, and NPV of 85%, 66.7%, 94.4%, and 40%, respectively. Thus, DWI, when compared to conventional MRI, had increased SE, PPV, and NPV but had a similar SP.

The T2*WI findings among the studied lesions showed that 19 out of 23 cases (83.3%) showed signal voids (blooming), while 16.7% of the lesions did not show blooming. Accordingly, the SE and SP improved from 80% and 66.7% with conventional MRI to 94.7% and 75% with the addition of T2*WI, respectively. (Table 4)

Table 1: MRI protocol performed in the current study

Sequence	TR (ms)	TE (ms)	FOV (mm)	Matrix	Slice thickness (mm)	Flip angle
T2 sagittal	3000	90	290 × 290	208 × 205	4	90
T2 axial	3700	100	288 × 350	292 × 180	5	90
T1 axial	500	10	260 × 216	263 × 171	5	90
T1 FS axial	530	8	240 × 240	240 × 190	5	90
T2 coronal	3000	90	300 × 300	272 × 200	4.5	90
DWI (b0, 500, 1000)	2000	77	240 × 240	124 × 100	5	90
T2*	500	4.6	240 × 240	256 × 256	4	20

1. Slice gap is one mm and flip angle 90° in all sequences, except T2*, 20°

2. Abbreviations: FOV field of view, FS fat suppression, DWI diffusion-weighted imaging

Table (2): Age distribution among studied patients

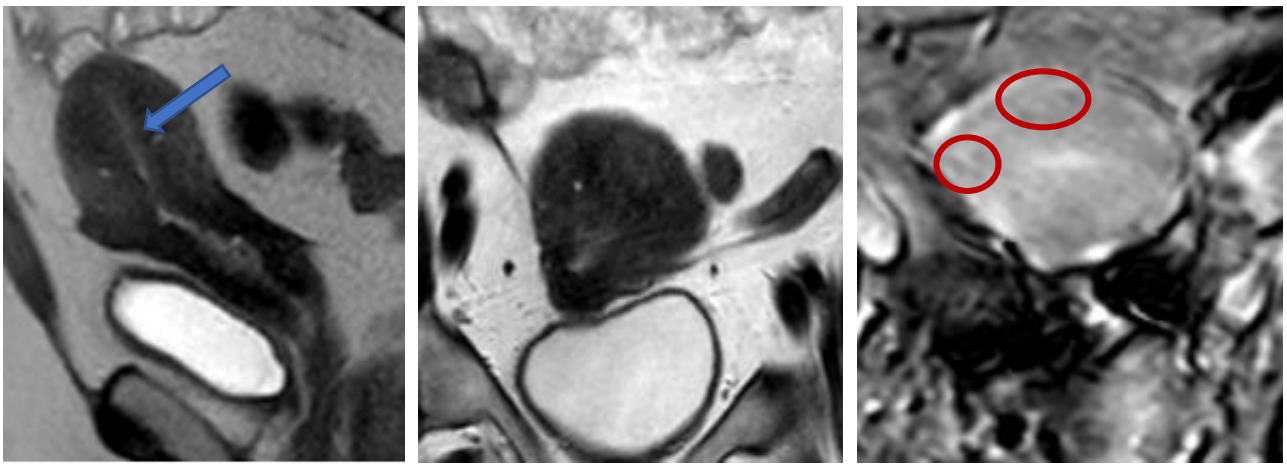
Variable	All patients (n=24)
Age (years) **Mean ± SD** **(range)**	 **41.1 ± 9.16** **(25 – 58)**
Age groups (N.%) **<30** **30 – 40** **40 – 50** **>50**	 **2 (8.3%)** **9 (37.5%)** **9 (37.5%)** **4 (16.7%)**

Table (3): Types of uterine adenomyosis.

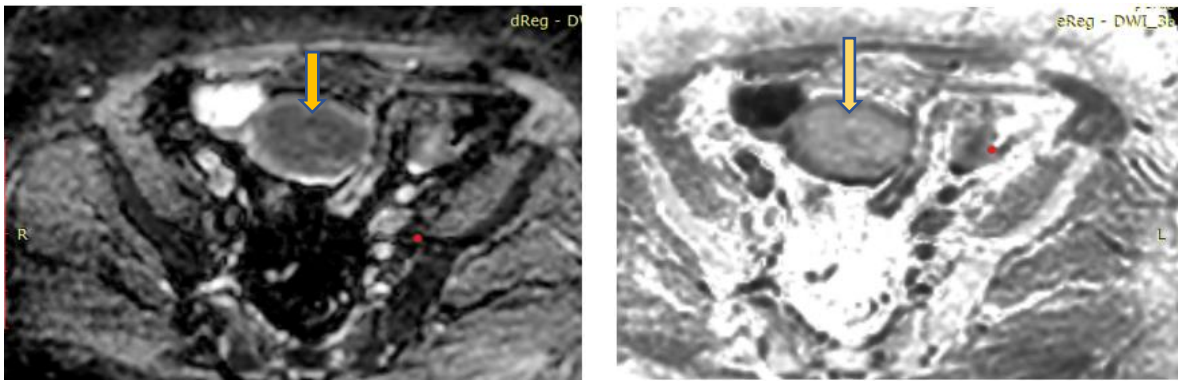
Variable (N. %)	Patients (n=14)
Diffuse	**17 (70.8%)**
Focal	**5 (20.8%)**
Cystic	**2 (8.4%)**

Table (4): Sensitivity, specificity, positive predictive value, negative predictive values of conventional MRI; DWI and signal void in T2* images

	Conventional MRI	DWI	T2 *WI
Sensitivity	**80%**	**85%**	**94.7%**
Specificity	**66.7%**	**75%**	**75%**
Accuracy	**78.3%**	**82.6%**	**91.3%**
Positive Predictive value	**94.1%**	**94.4%**	**94.7%**
Negative predictive value	**33.3%**	**40%**	**75%**
Positive likelihood ratio	**2.40**	**2.55**	**3.78**
Negative likelihood ratio	**0.300**	**0.225**	**0.07**



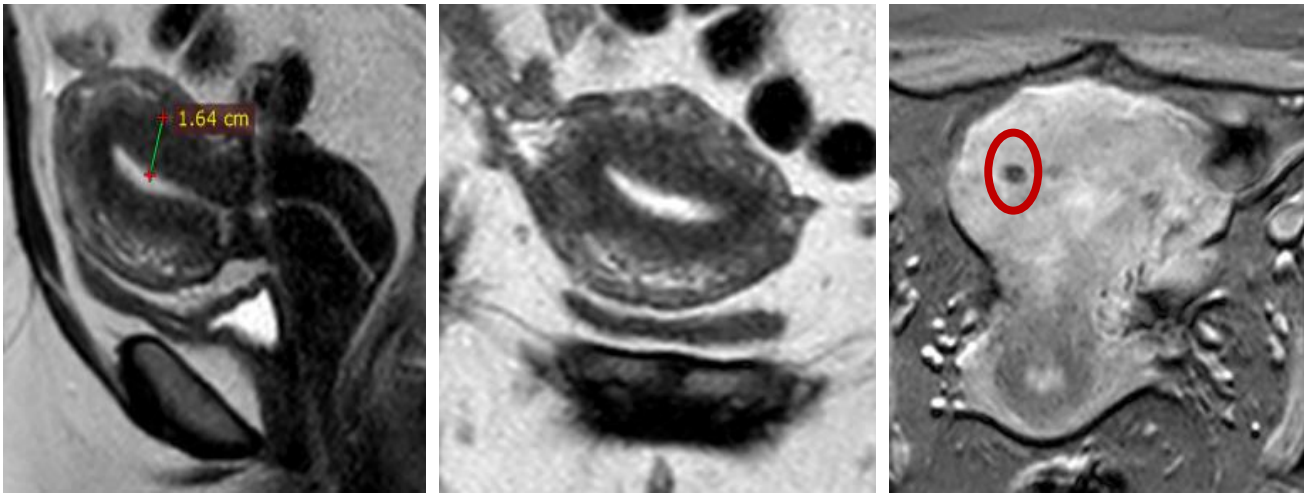
(A) **(B)** **(C)**



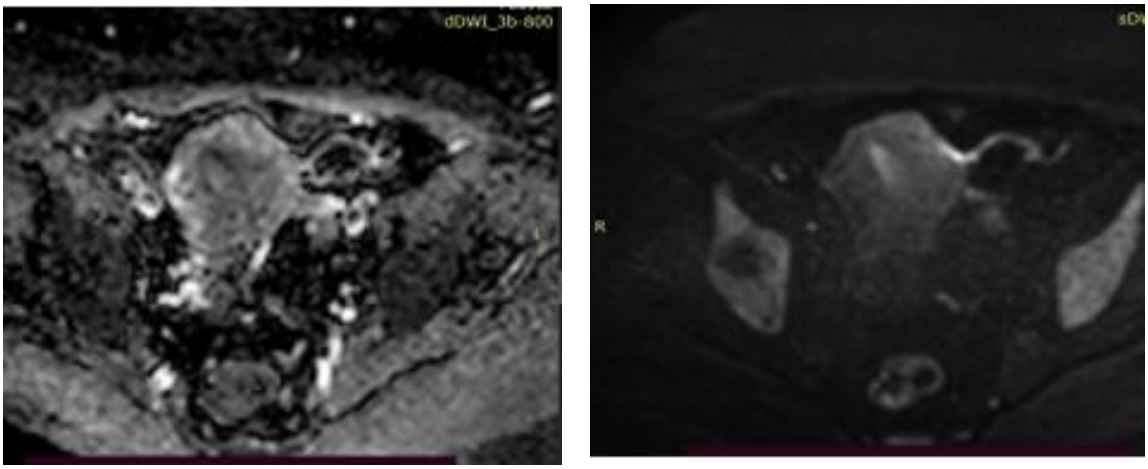
(D) (E)

Figure (1): A case of 45-year-old female patient complaining of abnormal uterine bleeding.

- **(A & B) Sagittal and coronal T2WI:** showing thickened endometrial myometrial junction with sub-endometeric cystic changes display high SI. (blue arrow)
- **(C) Susceptibility weighted image (T2*)**: showing blooming of some of these cysts. (Red circles)
- **(D& E) DWI**: sub-endometric cysts displaying low SI at ADC map and high SI at DWI consistent with Restricted diffusion of the sub-endometerial cysts.(Yellow arrow)



(A) (B) (C)



(D) (E)

Figure(2): A case of 56-year-old female patient complain of severe pelvic pain.

- **(A&B) sagittal and coronal T2WI: showing** enlarged bulky uterus with increased endometrial myometerial junction >12 mm.
- **(C) T2* WI:** showing subendometerial blooming (red circle).
- **(D& E) DWI: shows** no diffusion restriction.

DISCUSSION

In 1860, Rokitansky was the first to identify UA, which refers to the presence of endometrial glands and stromal cells within the myometrium, and endometriosis, which refers to their occurrence beyond the uterine cavity (15). In 1925, Frankl used the term "adenomyosis" to describe a pathological condition of the muscular uterine tissue that involves endometrial glands [15]. UA is a chronic and heterogeneous disease characterized by ectopic endometrium. Although it is a benign condition that depends on estrogen, it does share certain similarities with malignant tissue. However, the prognosis for this condition remains quite favorable despite its adverse effect on women's quality of life due to chronic pain and infertility [16]. The classification of UA depends on the distribution of endometrial glands inside the myometrium, distinguishing between diffuse and localized variants. Diffuse UA is characterized by multiple distributed foci within the myometrium, while focal UA presents as localized nodules of hypertrophic myometrium with ectopic endometrium [17,18].

MRI is considered an essential imaging technique for accurately diagnosing and pre-operatively planning UA. While ectopic endometrium can have various imaging characteristics, its hemorrhagic nature is the primary feature that aids in its diagnosis [19]. T2-weighted images are highly sensitive to hemosiderin, and the presence of a signal void indicates the presence of the ancient hemorrhagic substance in UA [14]. The study included 24 female patients aged between 25 and 58 years. Among the patients, 45.8% experienced pelvic discomfort, 37.5% experienced abnormal uterine bleeding, 20.8% experienced either primary or secondary infertility, 16.7% experienced dysmenorrhea, and 12.5% came for routine check-ups. Another study by Gordts et al. (2018) [20] yielded similar results, indicating that the most prevalent clinical manifestation of UA was pelvic discomfort, accounting for 45.3% of the patients included in the study. Among the 24 patients with UA in our study, 17 patients (70.8%) had diffuse UA, 5 patients (20.8%) had focal UA, and 2 patients (8.3%) had cystic UA. These results are consistent with those of Chapron et al., (2020) [17], who identified that the most common type of adenomyosis is the diffuse type by 64.5% and the least common is the cystic type by 6.5%. Our study found that among 17 cases with diffuse UA, the most common conventional MRI finding was a thickened endo-myometrial junction, observed in 82.3% of the patients. This was followed by a distinct endo-myometrial junction in 70.5% of the patients, sub-endometrial cysts in 58.8%, and the least frequent finding was T1WI high SI foci and striations, observed in 41.2% of the patients. Templeman et al. [22] also found similar results and stated that the most common diagnostic sign for UA is JZ thickening, with a thickness greater than 12 mm in 80 % of patients. This sign has positive predictive value (95%) for diagnosis of UA.

In our study, conventional MRI with T2WI showed 80% SE and 66.7% SP in UA diagnosis. This agrees with Outwater and Dunton [23], who demonstrated the SE and SP of conventional MRI as 83% and 68%, respectively. However, our findings disagree with those of Aki Kido et al. [21], who reported an overall diagnostic value of 90% SE, 98% SP, and 96% diagnostic accuracy using conventional sequences.

Regarding DWIs, 75% of the examined lesions showed hyperintensity on DWI and hypointensity on the ADC map. This is consistent with restricted diffusion caused by increased cell density. 25% of the lesions exhibited hypointensity on DWI and hyperintensity on the ADC map, indicating facilitated diffusion. In our study, the SE was approximately 85%, and the SP was 66.7%. This is somewhat aligned with Raafat M et al. [19], who observed favorable results in MRI analysis using diffusion sequences, resulting in an increase in SE, positive predictive value, and negative predictive value while maintaining a comparable SP compared to traditional MRI.

When T2*WI was added to our study, 20 out of 24 cases of UA displayed signal voids. This led to an enhancement in SE and SP from 80% and 66.7% with conventional MRI to 94.7% and 75% with the inclusion of T2*WI. Similar findings were proposed by Pin et al. [24], suggesting that T2*WI can be used as a complementary tool for conventional MRI, with overall diagnostic performance improvements in SE and SP from 88.2% to 94.1% and 68.8% to 73.3%, respectively.

In terms of associated pathology, our study found that ovarian cysts were present in 20.8% of the patients, fibroids in 12.5% of the patients, and malignancy in one patient (4.2%). This disagrees with (offers from Gordts S et al. [20], who reported that fibroids were found in 23%–34% of patients with UA. Our study demonstrated that MRI with T2* and DWI sequences can be a reliable and effective tool for detecting UA. Our results are consistent with those of Raafat et al.

[19], who also found that T2* and DWI sequences had high values of SE (94.7%), SP (75%), diagnostic accuracy (91.3%), positive predictive value (94.7%), and negative predictive value (75%). Conversely, conventional MRI sequences had lower values of SE (80%), SP (66.7%), diagnostic accuracy (78.3%), positive predictive value (94.1%), and negative predictive value (33.3%), but the difference between advanced and conventional MRI sequences was not statistically significant.

CONCLUSIONS

This work greatly improves the comprehension of UA by integrating both traditional and cutting-edge MRI methods. The results of our study confirm the efficacy of MRI, particularly when combined with T2*WI and DWI sequences, in the diagnosis of UA. The study illustrates that the utilization of sophisticated imaging techniques can lead to enhanced diagnostic precision, SE, and SP in comparison to merely depending on traditional MRI. These insights help improve the accuracy of diagnosis and the care of patients with this disease as part of larger therapeutic initiatives.

Limitations and Future Perspectives

This study highlights the potential of sophisticated MRI methods to enhance the accuracy of diagnosing UA. However, it is important to note that the study has several limitations, which indicate areas that should be explored in future research. The limited sample size and single-center design of the study may restrict the applicability of the findings, indicating the necessity for bigger, multicenter investigations to confirm and build upon these results. Furthermore, due to the cross-sectional design of the investigation, it is not possible to examine long-term clinical outcomes related to various MRI results. This emphasizes the need for further longitudinal studies.

Conflict of interest: Nil.

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