VALUE OF COMBINED DETECTION OF AMH AND MRI IN DIAGNOSIS OF PATIENTS WITH ENDOMETRIOSIS

Sanyang Tan[1,#], Hong Li[1,#], Jun Zhang[2,*]
[1]Department of Clinical Laboratory, Haikou Maternal and Child Health Hospital, Hainan, 571100, China - [2]Department of Medical Imaging, The Fourth People's Hospital of Shaanxi, Xi'an, Shaanxi 710043, China
[#]*These authors are contributed equally to this work*

ABSTRACT

Introduction: *To explore the value of combined detection of anti-Mullerian hormone (AMH) and MR Imaging (MRI) in the diagnosis of patients with Endometriosis (EMS).*

Materials and methods: *116 patients with suspected endometriosis accepted at our hospital from February 2019 to December 2021 were selected for analysis, and each patient underwent serum AMH and MRI testing. The diagnostic efficacy of AMH and MRI was analyzed according to postoperative pathological findings. The diagnostic value of combined AMH and MRI for EMS was assessed using receiver operating characteristic (ROC) curves.*

Results: *The diagnosis was confirmed in 97 positive and 19 negative cases among 116 patients detected by laparoscopic surgery. The sensitivity, specificity and diagnostic value of serum AMH test for EMS were 68.04, 73.68, and 0.73% respectively. The sensitivity, specificity and diagnostic value of MRI for EMS were 90.72, 84.21, and 0.87% respectively. The sensitivity, specificity and diagnostic value of MRI combined with AMH test were 95.88, 94.74, and 0.95%.*

Conclusion: *MRI combined with serum AMH detection can improve the sensitivity and specificity of clinical diagnosis of EMS.*

Keywords: *AMH, MRI, EMS.*

DOI: 10.19193/0393-6384_2022_5_510

Received *March 15, 2022;* ***Accepted*** *June 20, 2022*

Introduction

Endometriosis (EMS) is an estrogen-dependent chronic disease that affects approximately 200 million women of reproductive age worldwide[(1)]. As the shed endometrial tissue enters the lower abdominal cavity, it leads to common symptoms such as pelvic pain, dysmenorrhea, and infertility[(2)]. The clinical diagnosis of EMS was complicated due to the similarity of these symptoms to other diseases, which seriously affects the physical and mental health of women in reproductive age[(3)]. Although many studies have been conducted around EMS biomarkers, they cannot be used as the main means of clinical identification due to low sensitivity and specificity[(4)]. Laparoscopic surgery is still the gold standard for determining the presence of EMS lesions[(5)]. However, this test is complex and invasive, and cannot be used to screen healthy people or patients in early stages. Anti-Müllerian hormone (AMH) is a common marker of ovarian function[(6)]. Since EMS affects ovarian reserve and results in lower serum AMH levels in patients, AMH testing can be used for EMS diagnosis[(7)]. The degree of EMS pathology can also be measured based on the degree of decrease in AMH levels[(8)]. In addition to hormone testing, imaging tests are also commonly used in clinical practice. Magnetic resonance imaging (MRI) is a

second-line screening technique after sonography and is often used as a complementary test in complex cases or before surgery[9]. MRI is also considered the best diagnostic imaging modality because it is more accurate than sonography in assessing deep infiltrative endometriosis (DIE)[10, 11].

Serum AMH and MRI are both non-invasive tools for differential diagnosis of EMS, and if used in combination, they may be effective in improving diagnostic accuracy and therapeutic management. The aim of this study was to evaluate the diagnostic value of combined serum AMH and MRI for endometriosis.

Materials and methods

Clinical data

The clinical data of 116 patients with suspected endometriosis admitted to our hospital from February 2019 to December 2021 were selected.

Inclusion criteria:

• Diagnosed by laparoscopic surgery;

• Patients had various complete medical records and signed informed consent forms.

Exclusion criteria:

• Patients with other malignant tumors, severe cognitive impairment or mental illness, congenital ovarian dysplasia were excluded;

• Patients who underwent endometriosis surgery prior to admission.

Serum AMH detection

Participating researchers drew 5 ml of venous blood, placed it at room temperature for 2 hours, and centrifuged at 3,000 r/min for 20 min to separate serum. Serum AMH levels were detected by ELISA (kits purchased from Abcam). The study was not conducted during menstruation.

MRI protocol

A 1.5T MRI scanner from Siemens, Germany, was used for the abdominal scan with a torso phased array coil and the pelvic scan with a pelvic array coil. The scans were performed from the level of both iliac crests to the level of the pubic symphysis. The tests were not performed during menstruation. Scan sequences included axial, sagittal T1-weighted imaging (T1WI), axial T1WI with fat suppression; sagittal, axial and coronal T2-weighted imaging (T2WI) scans. The contrast agent was Magnevist solution at a dose of 0.2 mmol/kg. MRI features of EMS (hyperintense on T1 and T1 with fat suppression, hypointense on T2, and shadow sign on T2) were used to determine whether the study subjects had EMS. Image analysis was assessed by two diagnostic imaging physicians, with a third physician consulted in case of disagreement.

Statistical analysis

The data were analyzed using SPSS 22.0 software. The measurement data were expressed as mean ± standard deviation, and the data were compared using a t-test.

Results

Clinical characteristics

A total of 116 patients with suspected EMS participated in this study, and the clinical characteristics are shown in Table 1. Using the diagnostic results of laparoscopic surgery as the gold standard, 97 were confirmed as positive for EMS and 16 were confirmed as negative for EMS after surgery.

Characteristics	Total (n=116)
Age (years)	31.7±4.1
BMI (kg/m2)	22.9±4.5
Number of Pregnancies (%)	
0	72 (62.1%)
1	38 (32.8%)
≥2	6 (5.1%)
Endometriosis	
Positive	97 (83.6%)
Negative	19 (16.4%)

Table 1: Baseline characteristics of participants.

Diagnostic efficacy of serum AMH levels in EMS

Serum AMH levels were (2.88±1.03) ng/mL in EMS-positive women and (3.78±1.14) ng/mL in EMS-negative patients. As shown in the Figure 1, serum AMH was significantly lower in patients with confirmed EMS than in controls (P<0.01). The diagnostic value of serum AMH for EMS was 0.73 (95%CI 59.61%-86.35%), with a sensitivity of 68.04 % and specificity of 73.68 %. And the best cut off is 3.40 ng /ml.

Diagnostic efficacy of MRI in EMS

Patient images were detected using MR. The images of EMS are characterized by high signal intensity on T1-weighted imaging (T1WI) and low signal intensity in the form of shading on T2-weighted imaging (T2WI). Ninety-one patients with

EMS were diagnosed using MRI, of which 88 were true positives and 3 were false positives. There were 16 true negatives and 9 false negatives among the 25 negative patients detected by MRI (Table 2). The sensitivity and specificity of MRI in the diagnosis of EMS were 90.72%, 84.21% respectively.

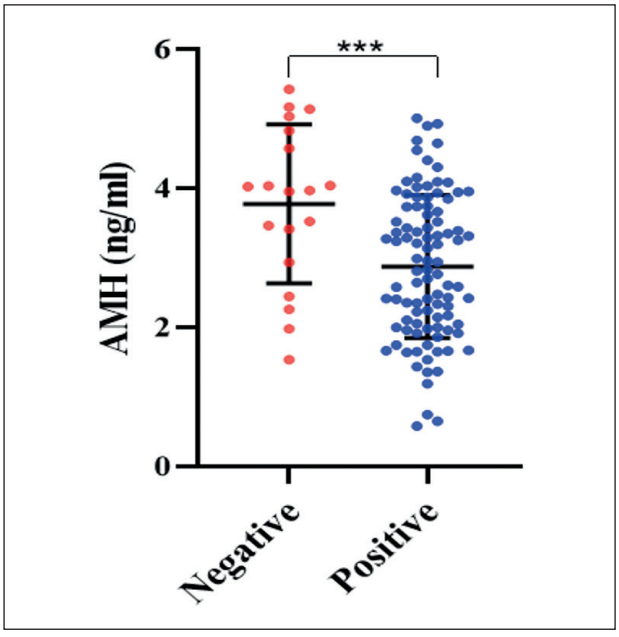

Figure 1: Serum AMH levels in EMS-positive and EMS-negative patients.

MRI diagnosis	Histopathology		
	Positive	Negative	Total
Positive	88	3	91
Negative	9	16	25
Total	97	19	116

Table 2: Diagnostic efficacy of MRI in EMS.

Comparison of diagnostic efficacy between MRI combined with AMH and MRI or AMH alone

As shown in Table 3, combine the patient's two test results to determine if the patient has EMS. The sensitivity and specificity of the combined of MRI and AMH was 95.88% and 94.74% (Table 4). The diagnostic value of the combination was 0.95 (Figure 2). The results showed that the diagnostic value of MRI combined with AMH testing was higher than that of one test alone (P<0.01).

Combination diagnosis	Histopathology		
	Positive	Negative	Total
Positive	93	1	94
Negative	4	18	22
Total	97	19	116

Table 3: Diagnostic efficacy of combination of AMH and MRI in EMS.

Factors	AMH	MRI	Combination	p.Value
Sensitivity (%)	68.04 (66/97)	90.72 (88/97)	95.88 (93/97)	<0.01
Specificity (%)	73.68 (14/19)	84.21 (16/19)	94.74 (18/19)	<0.01

Table 4: Comparison of MRI and AMH combined or single diagnosis.

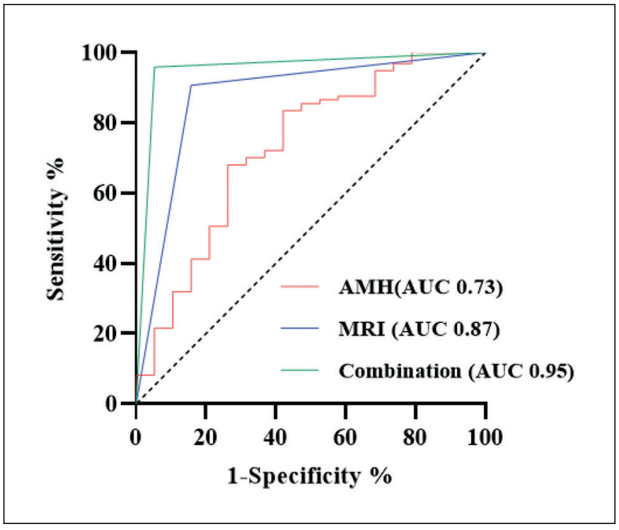

Figure 2: ROC curve of diagnostic efficacy of combined diagnosis with MRI or AMH alone.

Discussion

Endometriosis is a complex clinical syndrome with a high prevalence in women of childbearing age. EMS is an important cause of physical and mental health impairment in young women. Prevalence of EMS is as high as 35-50% among women with pelvic pain and unexplained infertility[12]. Because the clinical symptoms of this gynecological disease are not specific, it is often confused with diseases with similar symptoms such as chronic pelvic inflammatory disease leading to delayed diagnosis[13, 14]. In addition, the current gold standard for EMS diagnosis still relies on invasive surgery to observe lesions, which causes a significant increase in physical burden and financial cost compared to minimally invasive or non-invasive diagnostic modalities. And it further exacerbates the EMS diagnosis delay. Statistically, there is a 6-7 year delay between the onset of symptoms and surgical confirmation of the diagnosis[15]. Since most patients begin to experience symptoms around puberty, early differential diagnosis can reduce physical pain and avoid loss of fertility. Therefore, reliable non-invasive diagnostic tools can improve the screening and treatment of EMS. In clinical practice, serum AMH examination and MRI are commonly used

to determine whether a patient has EMS. The main objective of this study was to evaluate the diagnostic value of the combined application of MRI and serum AMH for EMS.

AMH responds to the number of primary follicles and regulates follicular maturation. It is expressed steadily during the menstrual cycle. Pacchiarotti et al. suggested that AMH, as a marker of ovarian reserve, could identify ovarian damage due to endometriosis and assess the decrease in ovarian reserve[16]. According to Kasapoglu and Romanski's study, serum AMH levels were significantly lower in women with EMS than in healthy women, and patients had a more rapid decline in AMH levels[17, 18]. In addition, serum AMH levels were lower in patients with advanced EMS (stage IV) than in patients with early-stage[8, 19]. Serum AMH in patients with endometriosis negative and 97 patients with confirmed EMS were analyzed in this study, and based on the critical value of 3.40 ng /ml could be used for differential diagnosis of EMS. However, there are some drawbacks in the diagnosis of EMS by AMH. AMH levels in patients with early EMS (stage I-II) did not change significantly and were almost identical to healthy controls, which may lead to misdiagnosis of patients in early stage[20].

Various imaging diagnostic methods are used to detect EMS, including MRI. MRI is radiation-free and can scan the body locally or systemically. According to several meta-analyses, MRI has a high specificity and sensitivity for diagnosing EMS[21, 22]. Especially for DIE, MRI is more reliable compared to transvaginal sonography and rectal endoscopic sonography[23]. The use of MRI in this study to diagnose patients with suspected EMS also showed a better sensitivity (90.72%) and specificity (84.21%). Since there is no internationally accepted optimal imaging protocol for EMS with MRI, the diagnostic results are largely dependent on the subjective judgment of the physician. Physician's experience largely influences MRI diagnostic performance[24, 25]. In addition, despite the greater diagnostic advantage of MRI for advanced endometriosis, imaging is limited by the machine detection threshold, and it is difficult to identify superficial peritoneal lesions[26]. Thomeer et al. reported that the diagnostic sensitivity of MRI for EMS in stages II-IV was 100%, whereas for stage I was only 42% sensitive[27].

In this study, the results of the combination of MRI and serum AMH were analyzed to evaluate the diagnostic value. The results showed that the sensitivity (95.88%), specificity (94.74%), and diagnostic value (0.95) of MRI combined with AMH test were better than the diagnostic results of one method alone. Serum AMH is used to evaluate ovarian reserve, reflecting the impairment of ovarian function due to EMS. And MRI is characterized by visualization, allowing adjustment of imaging parameters to improve contrast. According to our results, the combination of both methods can effectively improve the diagnostic accuracy. Since both AMH and MRI have some limitations in the diagnosis of early stage, even if they are combined, it may cause a delay in diagnosis in some patients[20, 26]. We will continue to explore non-invasive diagnostic modalities with a wider range of validity and higher accuracy in our follow-up study. In addition, this study also has some limitations. First, the small sample size may affect the reliability of the data. Second, the test method may be subject to errors due to instrument or subjective judgment.

In conclusion, this study explored that the combined MRI and serum AMH test can effectively improve the sensitivity and specificity of EMS diagnosis compared to single-method testing. And it improves clinical diagnostic accuracy and contributes to the timely treatment for EMS patients.

References

1) Vallvé-Juanico J, Houshdaran S, Giudice LC. The endometrial immune environment of women with endometriosis. Hum Reprod Update 2019; 25(5): 564-591.
2) Bulun SE, Yilmaz BD, Sison C, et al. Endometriosis. Endocr Rev 2019; 40(4): 1048-1079.
3) Sims OT, Gupta J, Missmer SA, et al. Stigma and Endometriosis: A Brief Overview and Recommendations to Improve Psychosocial Well-Being and Diagnostic Delay. Int J Environ Res Public Health 2021; 18(15).
4) Anastasiu CV, Moga MA, Elena Neculau A, et al. Biomarkers for the Noninvasive Diagnosis of Endometriosis: State of the Art and Future Perspectives. Int J Mol Sci 2020; 21(5).
5) Kiesel L, Sourouni M. Diagnosis of endometriosis in the 21st century. Climacteric 2019; 22(3): 296-302.
6) Broer SL, Broekmans FJ, Laven JS, et al. Anti-Müllerian hormone: ovarian reserve testing and its potential clinical implications. Hum Reprod Update 2014; 20(5): 688-701.

7) Seyhan A, Ata B, Uncu G. The Impact of Endometriosis and Its Treatment on Ovarian Reserve. Semin Reprod Med 2015; 33(6): 422-428.
8) Dong Z, An J, Xie X, et al. Preoperative serum anti-Müllerian hormone level is a potential predictor of ovarian endometrioma severity and postoperative fertility. Eur J Obstet Gynecol Reprod Biol 2019; 240: 113-120.
9) Bazot M, Bharwani N, Huchon C, et al. European society of urogenital radiology (ESUR) guidelines: MR imaging of pelvic endometriosis. Eur Radiol 2017; 27(7): 2765-275.
10) Bazot M, Kermarrec E, Bendifallah S, et al. MRI of intestinal endometriosis. Best Pract Res Clin Obstet Gynaecol 2021; 71: 51-63.
11) Marcal L, Nothaft MA, Coelho F, et al. Deep pelvic endometriosis: MR imaging. Abdom Imaging 2010; 35(6): 708-715.
12) Bulletti C, Coccia ME, Battistoni S, et al. Endometriosis and infertility. J Assist Reprod Genet 2010; 27(8): 441-447.
13) Lea R, Bancroft K, Whorwell PJ. Irritable bowel syndrome, chronic pelvic inflammatory disease and endometriosis: a comparison of symptomatology. Eur J Gastroenterol Hepatol 2004; 16(12): 1269-1272.
14) Yang M, Abdalrahman H, Sonia U, Mohammed AI, Vestine U, Wang M, Ebadi AG, Toughani M. The application of DNA molecular markers in the study of Codonopsis species genetic variation, a review. Cell Mol Biol 2020; 15(2): 23-30.
15) Nnoaham KE, Hummelshoj L, Webster P, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril 2011; 96(2): 366-373.
16) Pacchiarotti A, Frati P, Milazzo GN, et al. Evaluation of serum anti-Mullerian hormone levels to assess the ovarian reserve in women with severe endometriosis. Eur J Obstet Gynecol Reprod Biol 2014; 172: 62-64.
17) Kasapoglu I, Ata B, Uyaniklar O, et al. Endometrioma-related reduction in ovarian reserve (ERROR): a prospective longitudinal study. Fertil Steril. 2018; 110(1): 122-127.
18) Romanski PA, Brady PC, Farland LV, et al. The effect of endometriosis on the antimüllerian hormone level in the infertile population. J Assist Reprod Genet 2019; 36(6): 1179-11784.
19) Wen L, Zhang Y, Yang B, Han F, Ebadi AG, Toughani M. Knockdown of Angiopoietin-like protein 4 suppresses the development of colorectal cancer. Cell Mol Biol 2020; 66(5): 117-124.
20) Shebl O, Ebner T, Sommergruber M, et al. Anti muellerian hormone serum levels in women with endometriosis: a case-control study. Gynecol Endocrinol 2009; 25(11): 713-716.
21) Guerriero S, Saba L, Pascual MA, et al. Transvaginal ultrasound vs magnetic resonance imaging for diagnosing deep infiltrating endometriosis: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2018; 51(5): 586-595.
22) Noventa M, Scioscia M, Schincariol M, et al. Imaging Modalities for Diagnosis of Deep Pelvic Endometriosis: Comparison between Trans-Vaginal Sonography, Rectal Endoscopy Sonography and Magnetic Resonance Imaging. A Head-to-Head Meta-Analysis. Diagnostics (Basel) 2019; 9(4).
23) Bazot M, Lafont C, Rouzier R, et al. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. Fertil Steril 2009; 92(6): 1825-1833.
24) Bruyere C, Manitou I, Habre C, et al. Pelvic MRI for Endometriosis: A Diagnostic Challenge for the Inexperienced Radiologist. How Much Experience Is Enough? Acad Radiol 2021; 28(3): 345-353.
25) Yang M, Shi D, Wang Y, Ebadi AG, Toughani M. Study on Interaction of Coomassie Brilliant Blue G-250 with Bovine Serum Albumin by Multispectroscopic. Int J Peptide Res Therapy 2021; 27(1): 421-431.
26) Mason BR, Chatterjee D, Menias CO, et al. Encyclopedia of endometriosis: a pictorial rad-path review. Abdom Radiol (NY) 2020; 45(6): 1587-1607.
27) Thomeer MG, Steensma AB, van Santbrink EJ, et al. Can magnetic resonance imaging at 3.0-Tesla reliably detect patients with endometriosis? Initial results. J Obstet Gynaecol Res 2014; 40(4): 1051-1058.

Corresponding Author:
Jun Zhang
Department of Medical Imaging, The Fourth People's Hospital of Shaanxi, No. 512, Xianning East Road, Xi'an, Shaanxi 710043, China
Email: zjsxsy_doctor@163.com
(China)