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Junctional zone endometrium as a risk factor for symptom recurrence of adenomyosis after ultrasound-guided high-intensity focused ultrasound ablation surgery

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Abstract

Background

Symptom recurrence remains a clinically significant concern, highlighting the need for reliable prognostic markers to guide patient management. This study focused on evaluating the association of the maximum junctional zone thickness (JZmax) with symptom recurrence among patients with intrinsic adenomyosis following ultrasound-guided high-intensity focused ultrasound ablation surgery (FUAS).

Methods

The present retrospective analysis enrolled 326 patients with intrinsic adenomyosis who underwent FUAS between June 2017 and March 2024. Factors related to symptom recurrence were identified by binary logistic regression. The optimum JZmax cutoff was determined by receiver operating characteristic (ROC) analysis. Cox regression alongside Kaplan–Meier (K-M) curve analysis was performed to assess the relationship between JZmax and time to recurrence. Multiple linear regression identified factors influencing JZmax.

Results

Symptom recurrence occurred in 58 patients with intrinsic adenomyosis (17.8%). Multivariate logistic regression showed that JZmax was the independent risk factor related to recurrence (OR = 1.060, 95% CI: 1.026–1.095, P < 0.001). The optimal JZmax cutoff was 23.1 mm, with 98.3% sensitivity. Cox regression showed JZmax significantly influenced time to recurrence (HR = 1.158, 95% CI: 1.009–1.330, P = 0.037). K-M analysis revealed a shorter median recurrence time in the high-JZmax group (44.5 months) compared to the low-JZmax group (53 months, P = 0.001). Preoperative menorrhagia, adenomyotic lesion volume and uterine volume were positively related to JZmax.

Conclusion

Elevated JZmax was related to a higher risk and earlier symptom recurrence onset after FUAS for intrinsic adenomyosis.

Tweetable abstract: Preoperative JZmax >23.1mm may predict adenomyotic symptom recurrence following FUAS.

1. Background

Adenomyosis is the frequently seen gynecological condition characterized by ectopic endometrial tissue present inside the myometrium, frequently manifesting as dysmenorrhea and menorrhagia(1, 2). While hysterectomy remains the definitive treatment, it is not suitable for women wishing to preserve fertility(3, 4). Ultrasound-guided high-intensity focused ultrasound ablation surgery (FUAS) is the non-invasive therapeutic alternative, demonstrating favorable efficacy and safety in symptom control(1, 5, 6). However, symptom recurrence remains a clinically significant concern, often occurring within 12 months post-treatment(7–9), highlighting the need for reliable prognostic markers to guide patient management.

The junctional zone (JZ)—the inner layer of the myometrium—plays a central role in the pathophysiology of adenomyosis(10). According to MRI-based JZ of intrinsic adenomyosis, adenomyosis occurrence was directly

associated with junctional zone thickness(11), besides, normal muscular structure is a well-established diagnostic criterion and has been reported as a potential marker of clinical success after uterine artery embolisation (UAE) in adenomyosis(10, 12–14). Although the maximal JZ thickness (JZmax) has been investigated on vaginal bromocriptine for treatment of adenomyosis(13), its value in predicting symptom recurrence after FUAS for adenomyosis remains underexplored.

This study aimed to evaluate the relation of preoperative JZmax with symptom recurrence among intrinsic adenomyosis patients undergoing FUAS, and to further explore its relationship with clinical indicators of disease burden, such as menorrhagia, adenomyotic lesion volume and uterine volume.

2. Materials and methods

2.1 Ethical considerations and Patients

The current retrospective cohort analysis extracted data from 359 symptomatic adenomyosis patients at Affiliated Nanchong Central Hospital of North Sichuan Medical College between June 2017 and June 2024. The study protocol was approved by the Ethics Committee of the Affiliated Nanchong Central Hospital, North Sichuan Medical College (Approval No: 2021/104). Informed consent was waived due to the retrospective nature of the study and full anonymization of patient data. After applying inclusion and exclusion criteria, 326 cases with sufficient clinical information and follow-up period were included in the final analysis.

Inclusion criteria: (a) patients reporting dysmenorrhea or menorrhagia; (b) intrinsic adenomyosis confirmed by preoperative MRI(11, 15); (c) completion of standardized JZ thickness assessment; (d) treatment with FUAS.

Exclusion criteria: (a) absence of preoperative MRI or incomplete measurement of JZ thickness; (b) presence of concurrent uterine fibroids, endometriosis, or pelvic malignancy; (c) diagnosis of acute pelvic inflammatory disease; (d) inability to exclude malignancy; (e) history of surgical or medical treatment for menorrhagia within 6 months prior to FUAS.

2.2 Diagnostic and Follow-up Criteria

For every patient, pelvic magnetic resonance imaging (MRI) examination was conducted with 1.5 T, turbo spin-echo T2-weighted as well as single-shot echo-planar diffusion-weighted imaging sequence. The MRI procedure was implemented in line with Brown MA(16). Before FUAS, preoperative MRI images were independently evaluated by two radiologists, ZJ (10-year) and JZ (11-year experience), any disagreements were resolved through consensus discussion(17). The observed imaging indicators included diagnosis, the lesion's location and size, the measurement of JZ thickness, as well as its signal characteristics on T2-weighted imaging (T2WI). The radiologists had no knowledge of patients' clinical information. The diagnosis of adenomyosis was made by MRI: JZmax ≥12 mm, JZmax/entire myometrium >40%, or JZ differential >5 mm based on MRI(9, 10). An intrinsic subtype of adenomyosis was defined as adenomyosis featured by basal endometrial invagination in myometrium with no influence on the outer myometrium(11, 15). JZmax was calculated as the average value of multiple measurements taken by ZJ and JZ(18), any disagreements were resolved through consensus discussion(17).The subcutaneous fat diameter on MRI was determined to be subcutaneous fat thickness(5, 17). Uterine and adenomyotic-lesion volumes were determined by 0.52 × length × anteroposterior diameter× transverse diameter (9, 19).

Symptom recurrence post-FUAS referred to the presence of menorrhagia and/or dysmenorrhea 12 months following a period with symptom relief for ≥3 months post-FUAS self-reported by the patient (8, 9, 19). Dysmenorrhea secondary to adenomyosis obtained in the medical record referred to patient-reported pain during the menstrual cycle documented at clinical visits prior to FUAS(17, 19). Menorrhagia secondary to adenomyosis referred to an elevation of menstrual blood volume reported by patients and documented in clinical records at visits prior to FUAS(17, 19).

For assessing symptom relief and ablation efficacy, all patients were encouraged to pay follow-up visits regularly(17, 19). Between June 2017 and June 2024, 326 cases finished the questionnaire on the spot or via telephone (for those unable to return to our center).

2.3 FUAS procedure

The pre-FUAS preparation and FUAS procedure were carried out following the Focused Ultrasound Tumor Therapeutic System guideline (Model-JC200, Chongqing Haifu Medical Technology Co., Ltd.)(20, 21). Treatment details including total sonication time and average sonication power were recorded by computer(17, 21). Each patient must be hospitalized for 24 h post-FUAS to observe their conditions(17, 21).

2.4 Statistical analysis

Continuous variables were presented as mean ± standard deviation and proportion. Differences in basic features between recurrence and non-recurrence groups were analyzed by Chi square test and Student's t-test. The relations of clinicopathological variables (age, menorrhagia dysmenorrhea, JZmax pre-FUAS) with symptom recurrence were analyzed with the logistic regression model through odds ratios (ORs) and 95% confidence intervals (CIs). The best threshold of JZmax for recurrence was determined by areas under the receiver operating characteristic curves (ROCs; MedCalc Software bvba [ver. 15.2.1], Ostend, Belgium). Additionally, the association strength of JZmax with symptom recurrence timing was determined through Cox regression with hazard ratio (HR) as well as 95% CI. The median recurrence time for diverse JZmax levels for adenomyosis was predicted by K-M curves. Factors (age, diffuse adenomyosis, menorrhagia, adenomyotic lesion volume, uterine volume) affecting JZmax were analyzed by linear regression. SPSS 22.0 (IBM, Armonk, NY) was employed for statistical analysis, with $p<0.05$ suggesting statistical significance.

3. Results

3.1 Clinicopathological features

Table 1 presents basic features of 326 cases enrolled into the present work. Their median follow-up length was 25 (15-46.5) months. There were 58 (17.8%) and 268 (82.2%) cases in recurrence and non-recurrence groups separately. The JZmax (38.1±13.0 mm) of recurrence group increased relative to that of non-recurrence group (33.5±10.8 mm) (P□0.05, shown in table 1).

3.2 Factors influencing symptom recurrence of adenomyosis

During multivariate logistic regression, JZmax was related to adenomyosis symptom recurrence (OR=1.060, 95%:1.026□1.095, P<0.001), while age, BMI, uterus volume, adenomyosis volume, subcutaneous fat thickness showed no such relation (P□0.05, shown in table 2).

3.3 Identification of JZmax for symptom recurrence

According to ROC curve analysis on JZmax for adenomyosis symptom recurrence, the optimum cut-off point, sensitivity, specificity, and AUC of JZmax were 23.1 U/mL, 98.2%, 19.8%, 0.612, respectively (95% CI: 0.556-0.665, P=0.006, Figure 1). Accordingly, 271 patients were included into high-JZmax (JZmax level≥23.1 mm) group (83.1%) and 55 patients in low-JZmax (JZmax level ≤23.1 U/ml) group (16.9%).

3.4 Magnitude of JZmax for symptom recurrence

In the multivariate cox regression analysis, JZmax was related to timing of symptom recurrence (HR=1.158, 95% CI 1.009–1.330, P=0.037, shown in table 3). K-M curve analysis revealed the shorter median recurrence time in high-JZmax group (44.5 months) than that in low-JZmax group (53 months) (P=0.042, Figure 2).

3.5 The factors impacting JZmax

Age, diffuse adenomyosis, preoperative menorrhagia, adenomyotic lesion volume and uterus volume were incorporated in linear regression model for JZmax. As a result, preoperative menorrhagia, adenomyotic lesion volume and uterus volume pre-FUAS showed positive association with JZmax (P<0.05, shown in Table 4).

4. Discussion

4.1 Summary

Our findings in the present work identified an elevated JZmax as the significant risk factor related to symptom recurrence in patients with adenomyosis following FUAS. A cutoff value of 23.1 mm was established as a clinically useful threshold to identify high-risk patients. Moreover, higher JZmax was associated with earlier recurrence, underscoring its prognostic relevance. Further analysis revealed that preoperative menorrhagia, uterine volume and adenomyotic lesion volume were significantly correlated with JZmax, indicating that JZmax serves not merely as an isolated metric but as an imaging biomarker reflective of overall disease burden.

4.2 Comparison with existing literature and clinical implications

While the association between JZ thickening and adenomyosis has been widely recognized(13, 14), our research extended this understanding by highlighting its specific role in predicting symptom for recurrence after FUAS. In contrast to prior studies that primarily emphasized diagnostic criteria or clinical outcomes(13, 14), this study repositioned JZmax as a prognostic tool for intrinsic adenomyosis after FUAS. By integrating JZmax with uterine and lesion volume measurements, we confirmed its utility as an integrative parameter for assessing global disease severity. Preoperative JZmax evaluation thus might offer a practical means of risk-adaptive management, enabling tailored follow-up and adjunctive treatment for high-risk patients.

The prognostic significance of JZmax may be explained by its central role in sustaining a pathological cycle within the uterine microenvironment. We proposed that JZ thickening drives recurrence through three interrelated mechanisms. Firstly, at the functional level, estrogen-dependent hyperperistalsis and structural disruption of myometrial smooth muscle led to abnormal uterine contractions(22, 23). These irregularities contributed to dysmenorrhea and impaired hemostasis during menstruation, aggravating menorrhagia(10, 24). Secondly, chronic tissue injury and repair (TIAR), potentiated by local hyperestrogenism—possibly mediated by

GPR30 overexpression—induced a pro-inflammatory and pro-fibrotic state(25, 26). This environment promoted ectopic endometrial survival and proliferation(10, 24). Thirdly, resultant hypoxia and inflammation stimulated vascular endothelial growth factor (VEGF)-mediated angiogenesis, establishing a pro-angiogenic milieu that further sustained adenomyotic lesions and menstrual abnormalities(27–29).

Within the context of FUAS, these mechanisms clarify why elevated preoperative JZmax was associated with recurrence after FUAS. Even after ablation of the dominant lesion, the persistent dysfunctional state of the residual JZ—marked by disordered contractility, inflammation, and angiogenesis—likely enable microscopic disease regrowth and symptom relapse. JZmax thus represents not a passive indicator but an active driver of disease chronicity and recurrence.

4.3 Strengths and limitations

Notwithstanding our study showed that elevated JZmax was related to a higher risk and earlier symptom recurrence onset after FUAS for intrinsic adenomyosis, several limitations must be acknowledged. Firstly, due to our cross-sectional nature, the conclusion of JZmax as a factor leading to adenomyosis symptom recurrence could not be made, even though our results verified the relation of JZmax with symptom recurrence. Clinicians may be interested in this conclusion to predict FUAS consequences and make relevant prevention measures. Second, exclusion of patients due to incomplete follow-up may have introduced selection bias, despite efforts to ensure comprehensive data collection. Third, symptom recurrence was assessed through patient self-reporting using a binary (yes/no) classification rather than a graded system such as the Numerical Rating Scale, which may affect accuracy in evaluating symptom severity. Future multicenter prospective studies incorporating standardized symptom metrics should be performed for verifying the above results and refining risk prediction models.

5. Conclusions

Collectively, this study illustrated the relation of an increased JZmax (> 23.1 mm) with the increased risk and early symptom recurrence post-FUAS for Intrinsic adenomyosis.

Abbreviations

JZmax, junctional zone thickness

FUAS, ultrasound-guided high-intensity focused ultrasound ablation surgery

ROC, receiver operating characteristic

K-M, Kaplan–Meier

MRI, magnetic resonance imaging

ORS, ds ratios

TIAR, tissue injury and repair

VEGF, vascular endothelial growth factor

CI, confidence intervals

Declarations

Author contributions

This research was developed by Ying Tang, Huai-qin Tang, and carried out by Ying Tang, Huai-qin Tang and Zhi-jun Jiang. Ying Tang, Li-ming Shen, Xue-jiao Zhong and Ying Song contributed information from medical records. Ying Tang assisted all authors in drafting the original manuscript. The article's final form was written and approved by all of the writers.

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Availability of data and material

Due to the sensitive nature of the interview scripts and privacy concerns of study participants, we will share qualitative data only upon reasonable request by the corresponding author.

Ethics approval and consent to participate

This retrospective cohort study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the Institutional Review Board of the Affiliated Nanchong Central Hospital, North Sichuan Medical College (Approval No. 2021/104). Due to the retrospective nature of the study and the use of anonymized patient data, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Informed consent

Due to the study was retrospective in nature and fully anonymous, the requirement for written informed consent was waived.

Competing interests

The authors declare no competing interests.

Clinical trial number: not applicable.

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Tables

Table1 Clinicopathological features.

Variable	Total cohort (n=326)	Recurrence group (n=58)	Non-Recurrence group (n=268)	Test value	P
Age (years)	43.3±5.4	42.5±5.0	43.4±5.5	-1.137	0.256
BMI (kg/m2)	23.6±3.0	23.5±2.9	43.4±5.5	0.704	0.483
Pre-FUAS dysmenorrhea				2.134	0.144
Yes (%)	258 (79.1)	50(86.2)	208(77.6)		
No (%)	68 (20.9)	8 (13.8)	60 (22.4)		
Pre-FUAS menorrhagia				1.900	0.168
Yes (%)	293 (89.9)	55 (94.8)	238(88.8)		
No (%)	33 (10.1)	3 (5.2)	30 (11.2)		
Uterus position				5.736	0.057
Ante-verted (%)	204 (62.6)	32(55.2)	172 (64.2)		
Retro-verted (%)	107 (32.8)	20 (34.5)	87(32.5)		
Neutral (%)	15 (4.6)	6 (10.3)	9(3.4)		
Type of adenomyotic lesions				2.470	0.116
Focal (%)	174 (34.7)	11(19.0)	78 (29.1)		
Diffuse (%)	328 (65.3)	47 (81.0)	190 (70.9)		
Adenomyosis location				2.140	0.544
Anterior (%)	100 (30.7)	15 (25.9)	85 (31.7)		
Posterior (%)	126 (38.7)	27 (46.6)	99 (36.9)		
Fundus (%)	37 (11.3)	5 (8.6)	32 (11.9)		
Anterior-Posterior (%)	63 (19.3)	11(19.0.0)	52 (19.4)		
Subcutaneous fat thickness (mm)	18.4±6.5	18.8±9.1	19.5±9.6	-0.291	0.772
Distance (mm)	20.3±14.8	23.5±14.6	24.1±14.7	-1.425	0.155
Uterus volume (cm3)	252.2±142.1	247.2±156.5	225.1±122.7	0.225	0.822
Adenomyosis volume (cm3)	53.6±55.7	78.7±68.9	69.6±83.0	0.851	0.397
JZmax（mm）	34.5±11.4	38.1±13.0	33.5±10.8	3.067	0.003
Depth of myometrial invasion（mm）	38.7±11.1	43.1±13.0	37.8±10.4	2.935	0.004

Total sonication time (s)	427.9±302.3	428.3±302.3	427.9±300.5	0.011	0.991
Average sonication power (s/h）	431.1±300.4	440.1±114.7	447.8±247.4	-0.356	0.722

BMI, body mass index; FUAS, focused ultrasound ablation surgery; distance, from the posterior surface of the adenomyosis lesion to the sacrum; JZmax, maximal thickness of junctional zone endometrium

Table 2 Binary logistic regression analysis of factors impacting symptom recurrence of adenomyosis.

Variable	Univariate			Multivariate		
Age (year)	0.972	0.923-1.023	0.280	0.959	0.906-1.015	0.147
BMI (kg/m2)	1.037	0.923-1.023	0.466	1.072	0.963-1.193	0.204
JZmax（mm）	1.041	1.016-1.607	0.001	1.060	1.026-1.095	<0.001
Uterus volume（cm3）	1.000	0.998-1.002	0.937	0.998	0.995-1.001	0.143
Adenomyosis volume（cm3）	1.000	0.998-1.004	0.513	1.000	0.995-1.004	0.852
Subcutaneous fat thickness（mm	0.995	0.961-1.031	0.778	0.992	0.952-1.033	0.698
Distance(mm)	0.983	0.962-1.005	0.134	0.986	0.962-1.011	0.267

BMI, body mass index; JZmax, maximal thickness of junctional zone endometrium（distance, from the posterior surface of the adenomyosis lesion to the sacrum

Table 3 Multivariate cox regression analysis of factors for symptom recurrence of adenomyosis.

Variable	B	SE	Wald	Exp(B)	95%CI	P
Age (year)	-0.063	0.039	2.644	0.939	0.870-1.013	0.104
BMI (kg/m2)	0.010	0.082	0.016	1.010	0.860-1.187	0.900
JZmax（mm）	0.147	0.071	4.328	1.158	1.009-1.330	0.037
Depth of myometrial invasion（mm）	-0.137	0.076	3.252	0.872	0.752-1.012	0.071
Uterus volume（cm3）	-0.001	0.002	0.109	0.999	0.995-1.004	0.741
Adenomyosis volume (cm3）	<0.001	0.005	0.008	1.000	0.990-1.011	0.927
Subcutaneousfatthickness (mm	0.019	0.036	0.299	1.020	0.951-1.093	0.585
Distance(mm)	-0.030	0.023	1.797	0.970	0.928-1.014	0.180
Sonication time（s）	-0.001	0.001	0.586	0.999	0.997-1.001	0.444
Average sonicationpower（sh）	0.001	0.002	0.192	1.001	0.997-1.005	0.661

BMI, body mass index; JZmax, maximal thickness of junctional zone endometrium; distance, from the posterior surface of the adenomyosis lesion to the sacrum

Table 4 Coefficient of multivariable regression model of maximal thickness of junctional zone endometrium.

Model	Non-standardized coefficients		standardized coefficients	t	P	Collinearity Statistics	
	B	SE	Beta			Tolerance	VIF
Constant	17.956	4.641		3.869	<0.001		
Age (years)	-0.023	0.100	-0.011	-0.227	0.821	0.993	1.007
Type of adenomyosis (diffuse vs. focus)	1.135	1.223	0.044	0.928	0.354	0.976	1.025
Preoperative menorrhagia	10.598	1.823	0.280	5.815	<0.001	0.966	1.036
Uterus volume (cm3)	0.018	0.004	0.240	4.072	<0.001	0.647	1.547
Adenomyotic lesions volume (cm^3)	0.036	0.008	0.257	4.389	<0.001	0.650	1.538

Figures

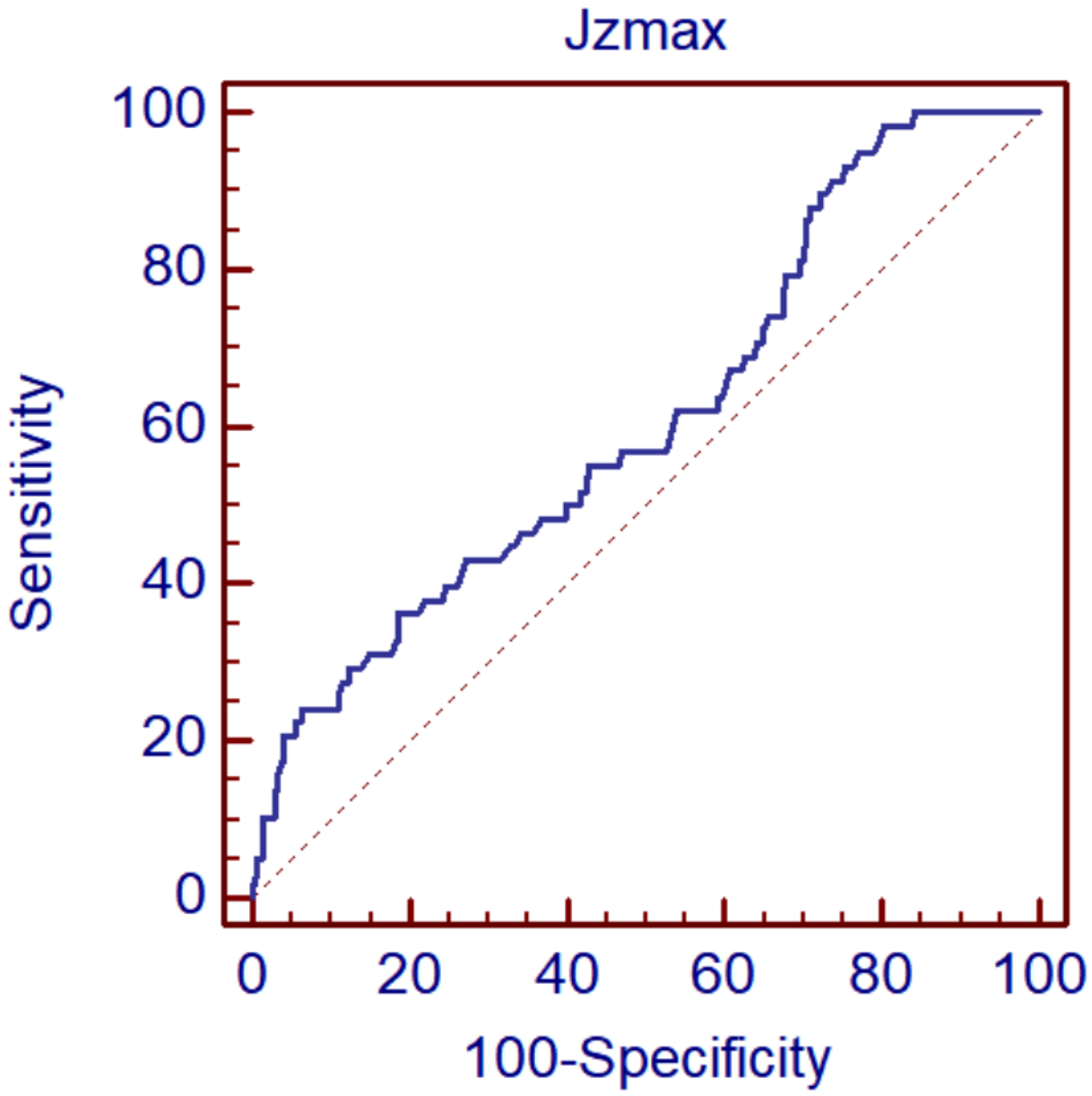


Figure 1

ROC curve of JZmax for symptom recurrence in adenomyotic patients

The optimum cut-off point, sensitivity, specificity, and AUC of JZmax were 23.1 U/mL, 98.2%, 19.8%, 0.612, respectively (95% CI: 0.556-0.665, P=0.006) in the ROC curve analysis on JZmax for adenomyosis symptom recurrence.

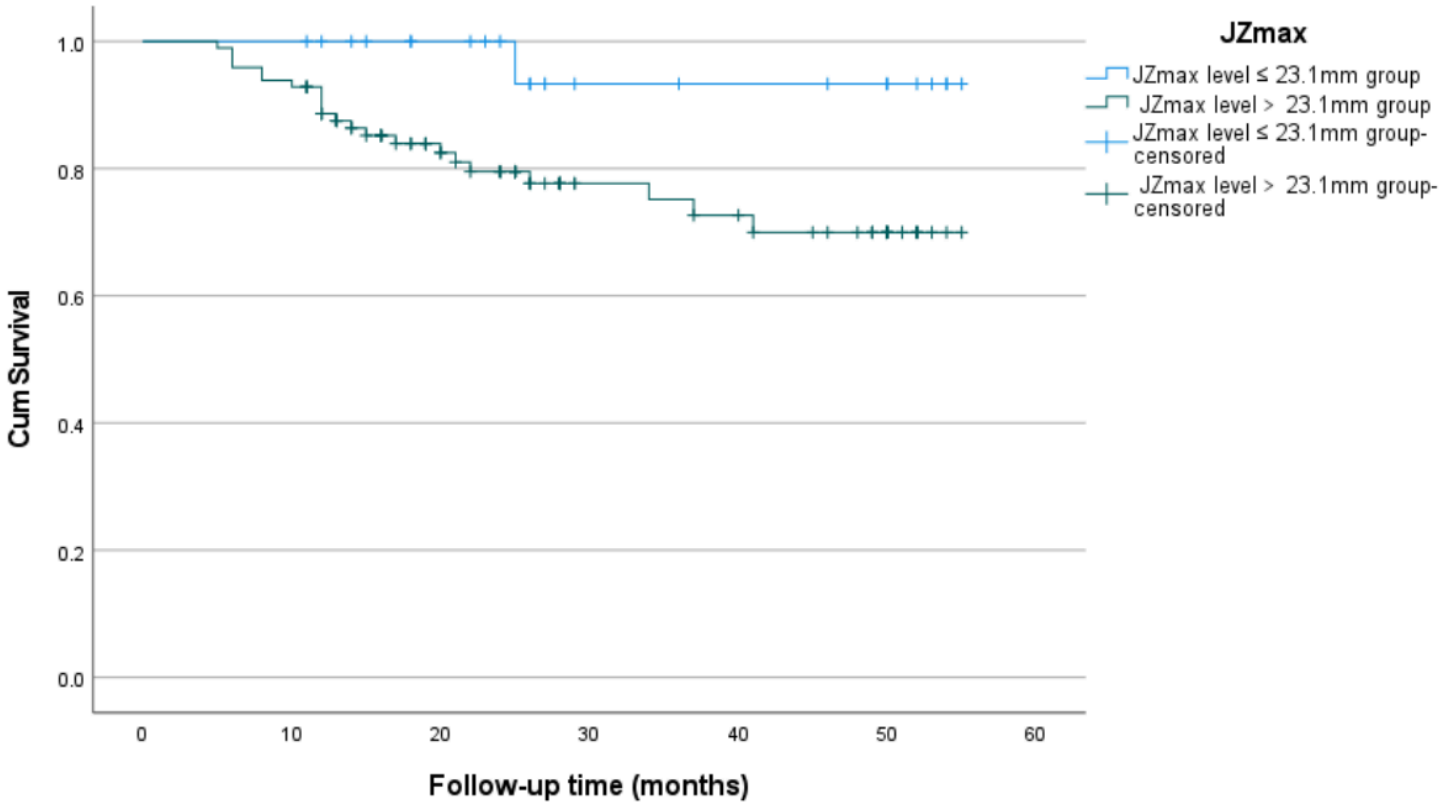


Figure 2

Magnitude of serum JZmax for predicting symptom recurrence

K-M curve showed when serum JZmax level≤ 23.1mm, adenomyotic patients were more likely to relapse, medium recurrence time was 44.5 month vs. 53 month (P<0.05).