Original Article

Ultrasound diagnostic value and clinical analysis of 61 uterine intravenous leiomyomatosis cases

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Background: Intravenous leiomyomatosis (IVL) is a rare benign smooth muscle tumor, for which the ultrasound features and diagnostic value have rarely been reported due to its infrequent presentation. This study aimed to analyze ultrasonographic characteristics and diagnostic value of uterine IVL and explore risk factors influencing postoperative recurrence.

Methods: A retrospective analysis was conducted of 61 patients who underwent surgical treatment from December 2014 to December 2023. Intraoperative or postoperative pathology confirmed uterine IVL in these patients. Clinical data and ultrasonographic features were analyzed, including IVL location, the International Federation of Gynecology and Obstetrics (FIGO) classification, shape, involved vessels, extent of involvement, internal blood flow, and ultrasound diagnostic accuracy. Cumulative recurrence rates were calculated using Kaplan-Meier method, and the survival curves for clinical factors were analyzed. Prognostic analysis of IVL recurrence was performed using Cox proportional hazard model.

Results: The diagnostic accuracy of ultrasound for IVL was 55.7% (34/61). The diagnostic accuracy of ultrasound was 76.7% for para-uterine IVL (P<0.001), 76.9% for FIGO 8 category (P<0.001), 84.4% for cord-like or beaded morphology (P<0.001), 92.3% for the involvement of the iliac vessels or inferior vena cava (IVC, P=0.003), and 66.7% for abundant internal blood flow (P=0.213). During the follow-up period, IVL in 10 cases (16.4%) recurred. The cumulative recurrence rates were 10.5%, 12.8%, and 18% at 1, 2, and 3 years, respectively. Patients aged ≤46.5 years (P=0.010), with IVL involving the iliac vein or IVC (P=0.017), and undergoing myomectomy (P<0.001) had a higher recurrence rate. Univariate analysis identified age (≤46.5 years) (P=0.035), IVL involving the iliac veins or IVC (P=0.029), and myomectomy (P<0.001) as risk factors for recurrence. Multivariate analysis showed that IVL involving the iliac veins or IVC [P=0.021, hazard ratio (HR) 6.407] and myomectomy (P<0.001, HR 77.360) were independent risk factors for recurrence.

Conclusions: The diagnostic accuracy of ultrasound was high for IVL located adjacent to the uterus and in FIGO 8 category, especially when it presented with cord-like or beaded morphology and involved the iliac vessels or IVC. Involvement of the iliac veins or IVC and myomectomy were independent risk factors for IVL recurrence. The risk of recurrence for IVL involving the iliac veins or IVC was 6 times higher than that confined to the uterus or para-uterine veins, and the risk of recurrence was 77 times higher for myomectomy than for hysterectomy with bilateral oophorectomy.

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Keywords: Ultrasonography; intravenous leiomyomatosis (IVL); uterus; recurrence

Submitted Aug 20, 2024. Accepted for publication Feb 24, 2025. Published online Mar 28, 2025.
doi: 10.21037/qims-24-1724
View this article at: https://dx.doi.org/10.21037/qims-24-1724

Introduction

Intravenous leiomyomatosis (IVL) is a rare and distinct smooth muscle tumor that originates primarily from the smooth muscle cells of the uterus. Unlike typical leiomyomas, IVL exhibits an invasive growth pattern, extending through the venous system and potentially reaching large blood vessels, such as the inferior vena cava (IVC) or the right atrium (1,2). The pathogenesis of IVL remains poorly understood, though several hypotheses suggest it may arise from a combination of hormonal, genetic, and vascular factors. The rarity and complexity of this condition present significant challenges in clinical diagnosis and treatment (3).

IVL can be classified into four stages based on disease progression: Stage I: lesions are confined to the uterus and its surroundings, with no involvement of major vessels. Patients may be asymptomatic or present with pelvic pain, irregular vaginal bleeding, or other gynecological symptoms. Stage II: tumors extend into the abdominal vessels but do not reach the level of the renal veins. Stage III: tumors extend beyond the renal veins into the IVC or invade the right atrium without reaching the pulmonary arteries. Stage IV: tumors invade pulmonary arteries or pulmonary metastasis, with patients potentially experiencing severe symptoms such as syncope or sudden death (4).

Early diagnosis and comprehensive treatment strategies are crucial for improving patient prognosis given the complexity and potential severity of IVL. Ultrasonography plays a crucial role in the initial evaluation and monitoring of IVL, providing a non-invasive, effective, and economical method for visualizing tumor characteristics and extent. However, due to the rarity of IVL, there is limited literature on its specific ultrasonographic features, and standardized diagnostic criteria are lacking.

This study retrospectively analyzed the clinical manifestations and ultrasonographic characteristics of 61 cases of IVL confirmed by surgical pathology over the past decade at The First Affiliated Hospital of Zhengzhou University, aiming to enhance understanding and diagnostic accuracy of this rare disease. Additionally, the study examined factors influencing postoperative recurrence, a crucial step in developing long-term management strategies and enhancing patient outcomes. Through this comprehensive analysis, we aimed to provide valuable insights into the effective diagnosis and treatment of IVL, ultimately striving to improve patient care and prognosis. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1724/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Scientific Research and Clinical Trials Ethics Committee of The First Affiliated Hospital of Zhengzhou University, China (No. 2024-KY-0933-001) and the requirement for individual consent for this retrospective analysis was waived.

Patients

A retrospective analysis was conducted on 61 patients diagnosed with IVL based on intraoperative or postoperative pathological findings between December 2014 and December 2023.

The inclusion criteria were as follows: (I) all IVL patients underwent 3-dimensional transvaginal ultrasound examination before surgery. For patients with larger leiomyomas, abdominal ultrasound was also performed. In cases involving blood vessels or atria, right atria, or right ventricle, vascular and cardiac ultrasound examinations were conducted. (II) All patients received surgical treatment and were pathologically confirmed to have IVL. (III) There was no history of malignant tumors in the uterus or other parts of the body.

In addition, 26 patients underwent contrast-enhanced computed tomography (CT), 21 underwent enhanced magnetic resonance imaging (MRI), 3 underwent positron emission tomography-computed tomography (PET-CT), 2 underwent contrast-enhanced CT and enhanced MRI,

and 1 underwent PET-CT and contrast-enhanced CT before surgery.

Equipment, imaging protocols, and surgical technique

Examinations were performed using GE Voluson E8 and E10 color Doppler ultrasound diagnostic instruments (GE Healthcare, Pittsburgh, PA, USA). Vaginal ultrasounds were conducted with an intracavitary ultrasound probe (frequency 5.0–9.0 MHz), and abdominal and vascular ultrasounds were performed with a convex array probe (frequency 3.5–5.0 MHz). Echocardiography was carried out using Philips iE33 (Philips, Andover, MA, USA) or GE Logiq 9 ultrasound diagnostic instruments equipped with an M5S probe (frequency 2.0–5.0 MHz).

Observations included the location, shape, size, internal echogenicity, and internal blood flow of leiomyomas in the uterus or pelvis, as well as extent of involvement in the pelvic veins, iliac veins, IVC, and heart. IVL shape included cord-like, beaded, solid mass, and lobulated forms. Transvaginal ultrasound and abdominal ultrasound were performed by physicians from the obstetrics and gynecology ultrasound team. Cardiovascular ultrasound was performed by physicians from the cardiovascular ultrasound team, all of whom had more than 10 years of experience. The senior obstetric and gynecological ultrasound team physicians classified the location of IVL according to the International Federation of Gynecology and Obstetrics (FIGO) classification system (5).

The choice of surgical method and scope was based on the size of the tumor, the extent of involvement, and the preferences of the patient and their family. Options included myomectomy, hysterectomy with bilateral oophorectomy, and hysterectomy with bilateral salpingectomy. The primary goal was to remove all visible tumors as completely as possible.

Postoperative follow-up

Postoperative follow-up included gynecological examinations and transvaginal ultrasounds every 3 months, and CT or MRI scans every 6 months. Vascular and cardiac ultrasound examinations were conducted as needed. IVL recurrence was diagnosed if at least 2 of the following instruments (ultrasound, CT, or MRI) detected new masses. Recurrence and follow-up durations were calculated in months. Recurrence was considered the endpoint event, whereas no recurrence, loss to follow-up, or death were treated as censored observations, with the follow-up period ending in February 2024.

Statistical analysis

Data analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Data were expressed as mean ± standard deviation (SD) or median (interquartile range) as appropriate. For data conforming to a normal distribution, an independent sample *t*-test was used; for data not conforming to a normal distribution, the Mann-Whitney *U* test was employed. Categorical data were described using frequencies and percentages. The Pearson χ^2 test, continuity correction χ^2 test, or Fisher's exact test was chosen based on frequency for comparing differences between two groups. The optimal cutoff values for continuous variables were determined using receiver operating characteristic (ROC) curves and converted into binary variables for subsequent survival analysis. The cumulative recurrence rate was calculated using the Kaplan-Meier method, and the differences between groups were analyzed using the log-rank test. Univariate and multivariate prognostic analyses of IVL recurrence were conducted using Cox proportional hazards model. A P value of less than 0.05 was considered statistically significant.

Results

Clinical data of IVL patients

There were 61 IVL patients included in the study. The clinical data of the patients are shown in *Table 1*. Of 2 patients (3.3%) who had a history of uterine surgery, 1 had undergone a hysterectomy for uterine leiomyomas 14 years prior, and the other had given birth twice via cesarean.

Clinical data of IVL

Size and location of IVL

Among the 61 IVL patients, the median size of the IVL was 7.2 cm (range, 5.6–10.5 cm). Ultrasound showed that 15 leiomyomas were located on the left side of the uterus, 23 on the right side, and 4 on both sides. A total of 18 leiomyomas were confined to the uterus, with 4 involving the uterine cavity, 12 located in the myometrium and protruding outward, and 2 within the myometrium. One leiomyoma was in the pelvis following a hysterectomy.

According to the FIGO classification, there were 2 cases

Table 1 Clinical data of all 61 cases of uterine IVL patients

Clinical data	Values (n=61)
Patient characteristics	
Age (years)	46.6±5.4
Pregnancy history (times)	2 [2–3]
Birth history (times)	2 [1.5–2]
Uterine surgery history	2 (3.3)
Lung metastases	6 (9.8)
IVL with uterine leiomyomas	41 (67.2)
IVL with uterine adenomyosis	3 (4.9)
IVL with both conditions	10 (16.4)
Clinical manifestations	
Abdominal distension and pain	11 (18.0)
Increased menstrual flow	10 (16.4)
Chest tightness	5 (8.2)
Abnormal uterine bleeding	3 (4.9)
Urinary incontinence	2 (3.3)
Pelvic mass without clinical symptoms	30 (49.2)
Preoperative examinations	
Tumor markers	
Normal	43 (70.5)
Abnormal	18 (29.5)
TAP (↑)	4/18 (22.2)
CA125 (↑)	4/18 (22.2)
CA72-4 (↑)	2/18 (11.1)
CA19-9 (↑)	1/18 (5.6)
VEGF (↑)	2/18 (11.1)
NSE (↑)	2/18 (11.1)
SCCA (↑)	2/18 (11.1)
CYFRA 21-1 (↑)	1/18 (5.6)
Anemia	
No	43 (70.5)
Yes	18 (29.5)
Mild	10/18 (55.6)
Moderate	7/18 (38.9)
Severe	1/18 (5.6)

Data are given as mean ± standard deviation, n (%), median [interquartile range] or n/N (%). ↑, an increase in variable. CA125, carbohydrate antigen 125; CA19-9, carbohydrate antigen 19-9; CA72-4, carbohydrate antigen 72-4; CYFRA 21-1, cytokeratin 21-1; IVL, intravenous leiomyomatosis; NSE, neuron-specific enolase; SCCA, squamous cell carcinoma antigen; TAP, tumor abnormal protein; VEGF, vascular endothelial growth factor.

of FIGO 1, 1 case of FIGO 2, 1 case of FIGO 3, 1 case of FIGO 4, 3 cases of FIGO 5, 22 cases (36.1%) of FIGO 6, and 26 cases (42.6%) of FIGO 8 (1 post-hysterectomy patient was included). The specific locations of FIGO 8 were as follows: 15 cases were in the broad ligament, 5 cases in the paracervical area, 3 cases in the retroperitoneum, 2 cases in the abdominopelvic cavity, and 1 case adjacent to the ovary. Additionally, there were 5 cases of hybrid leiomyoma, consisting of 4 cases of FIGO 3–5 and 1 case of FIGO 2–5.

Ultrasonographic features and involved vessels of IVL

Among the 42 IVL patients with leiomyomas located next to the uterus, 28 leiomyomas appeared as cord-like structures, with 13 showing abundant internal blood flow signals and 15 with poor internal blood flow signals (*Figure 1*). Two cases involved the IVC and right atrium both preoperatively and intraoperatively. Four cases involved the iliac veins intraoperatively, 19 involved the uterine or ovarian veins, and 3 did not show involvement of the veins next to the uterus intraoperatively. Four leiomyomas appeared beaded, with 1 showing abundant internal blood flow signals and 3 with poor internal blood flow signals (*Figure 1*). Three cases involved the uterine veins intraoperatively, and 1 involved the internal iliac vein. A total of 10 leiomyomas appeared as solid masses, with 2 showing abundant internal blood flow signals and 8 with poor internal blood flow signals. Two leiomyomas appeared lobulated, both involving the uterine veins intraoperatively, with 1 showing abundant internal blood flow signals (*Figure 1*). Five cases extended along the venous lumen, with 1 showing abundant internal blood flow signals. Four cases involved the iliac veins and IVC both preoperatively and intraoperatively, with 3 also involving the right atrium (*Figure 2*). One case involved the right ovarian vein both preoperatively and intraoperatively, and 3 cases involved the uterine veins intraoperatively, with 1 also involving the internal iliac vein.

Among the 18 cases of IVL confined to the uterus, 4 presented as solid masses involving the uterine cavity. One exhibited a lobulated morphology, and another had irregular cystic areas internally. A total of 12 were located within the myometrium and protruded outward. During surgery, 4 of these cases involved blood vessels: 3 involved the uterine veins, and 1 involved the ovarian vein. The remaining 8 cases showed no involvement of para-uterine veins during surgery. Among these, 3 had abundant internal blood flow signals, and 1 exhibited lipomatous degeneration of the leiomyoma both preoperatively and intraoperatively.

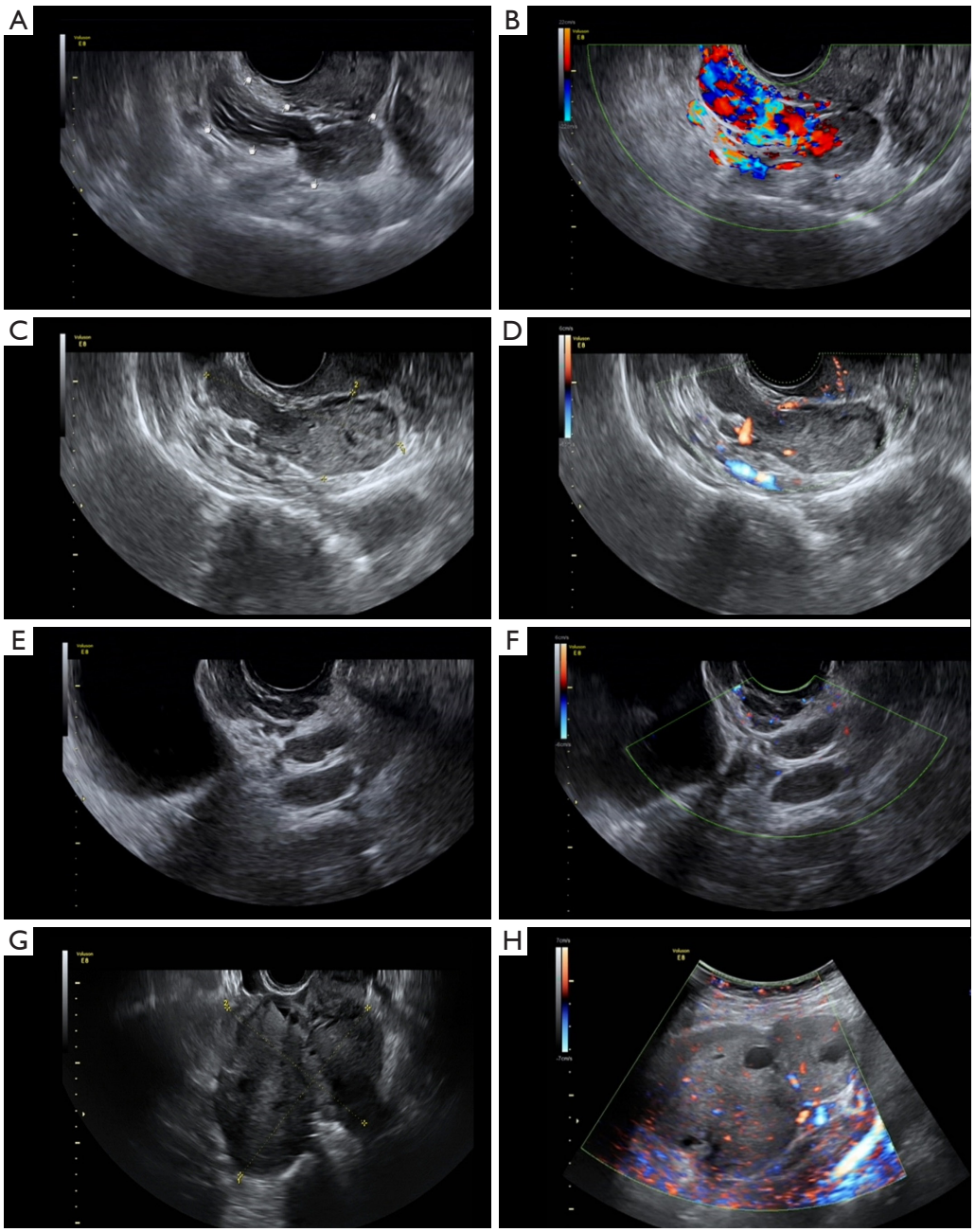

Figure 1 Transvaginal ultrasound and color Doppler ultrasound findings of IVL. (A) A cord-like hypoechoic mass approximately 6.2 cm in length was observed adjacent to the right side of the uterus. Multiple hyperechoic lines were seen within the hypoechoic area. (B) CDFI showed abundant blood flow signals within the mass. (C) A cord-like hypoechoic mass approximately 6.3 cm in length was observed adjacent to the right side of the uterus. (D) CDFI showed poor blood flow signals within the mass. (E) Multiple hypoechoic masses adjacent to the uterus were observed, presenting as beaded structures. One of the masses had a long axis diameter of approximately 3.6 cm. (F) CDFI showed poor blood flow signals within the mass. (G) A solid hypoechoic mass adjacent to the right side of the uterus was observed, approximately 13.6 cm in length. It exhibited a solid mass morphology resembling lobulated shapes, with small cystic areas visible internally. (H) CDFI showed poor blood flow signals within the mass. CDFI, color Doppler flow imaging; IVL, intravenous leiomyomatosis.

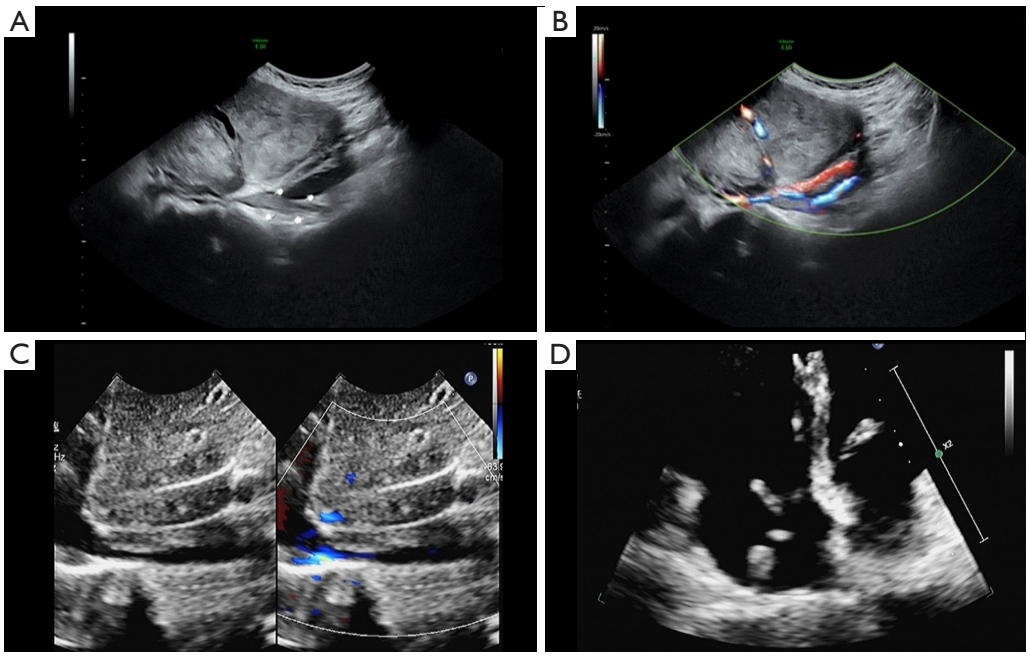

Figure 2 Conventional ultrasound and color Doppler ultrasound findings of IVL. (A) A large hypoechoic mass measuring approximately 20.6 cm in length was visible on the right side of the uterus. It closely adhered to the right uterine wall, and within the right internal iliac vein, there were hypoechoic mass (indicated by the small hand symbol). (B) CDFI showed blood flow filling defects within the right internal iliac vein. (C) Longitudinal section of the inferior vena cava displayed hypoechoic mass extending along the venous lumen. CDFI depicted fine blood flow bundles between the hypoechoic mass and the venous wall. (D) A cord-like hypoechoic structure was visible in the right atrium, continuous with the hypoechoic mass in the inferior vena cava. It exhibited movement with the cardiac cycle, partially passing through the tricuspid valve into the right ventricle during diastole. CDFI, color Doppler flow imaging; IVL, intravenous leiomyomatosis.

Two cases were located entirely within the myometrium; both had abundant internal blood flow signals, and 1 was found to have a soft, friable tumor mass during surgery.

Additionally, 1 IVL patient had a tumor located in the pelvis. The leiomyoma appeared as a large, lobulated solid mass, involving the bilateral common iliac veins, IVC, right atrium, and pulmonary artery both preoperatively and intraoperatively.

Evaluation of the accuracy of ultrasound diagnosis

Among the 61 cases, 34 were diagnosed with IVL, resulting in an ultrasound diagnostic rate of 55.7% (34/61). Clinical and ultrasonographic characteristics of the IVL are summarized in *Table 2*. When IVL was located adjacent to the uterus (76.7% *vs.* 5.6%), FIGO category was 8 (76.9% *vs.* 59.1% *vs.* 7.7%), exhibited a cord-like or beaded ultrasonographic morphology (84.4% *vs.* 24.1%), and involved the iliac veins or the IVC (92.3% *vs.* 45.8%), the diagnostic accuracy of ultrasound was significantly higher, with the difference being statistically significant (P<0.05).

Evaluation of therapeutic outcomes after IVL surgery

After surgical resection, the median follow-up period was 38 months (range, 1–110 months). Among the patients, 10 experienced recurrences (16.4%); the cumulative recurrence rates were 10.5%, 12.8%, and 18% at 1, 2, and 3 years, respectively. One patient (1.6%) died due to extensive pelvic tumor extension involving the iliac veins, IVC, and pulmonary arteries, which was complicated by severe intra-abdominal adhesions. Following severe postoperative bleeding and difficulty in maintaining blood pressure, the patient's family decided to discontinue further treatment. Additionally, 1 patient (1.6%) was lost to follow-up.

Among the 10 patients with recurrence, 7 were in the myomectomy group. Of these, 4 had recurrences in the uterus, with 1 case involving metastasis to both lungs; 2 had recurrences in the right side of the uterus; and 1 had a recurrence in the left side of the uterus with metastasis

Table 2 Diagnostic accuracy of ultrasonographic characteristics for uterine IVL

Characteristics	Total cases (n=61)	Correct diagnosis	Not diagnosed	χ^2	P value
Shape				22.375	<0.001
Cord-like/beaded	32 (52.5)	27 (84.4)	5 (15.6)		
Solid mass	29 (47.5)	7 (24.1)	22 (75.9)		
Location				23.259	<0.001
Adjacent to the uterus	43 (70.5)	33 (76.7)	10 (23.3)		
Within the uterus	18 (29.5)	1 (5.6)	17 (94.4)		
FIGO classification				16.994	<0.001
FIGO 1–5 and hybrid leiomyoma	13 (21.3)	1 (7.7)	12 (92.3)		
FIGO 6	22 (36.1)	13 (59.1)	9 (40.9)		
FIGO 8	26 (42.6)	20 (76.9)	6 (23.1)		
Extent of vascular involvement				8.956	0.003
Uterine or para-uterine veins	48 (78.7)	22 (45.8)	26 (54.2)		
Iliac vein or inferior vena cava	13 (21.3)	12 (92.3)	1 (7.7)		
Internal blood flow				1.550	0.213
Abundant blood flow	21 (34.4)	14 (66.7)	7 (33.3)		
Poor blood flow	40 (65.6)	20 (50.0)	20 (50.0)		

Data are given as n (%). FIGO, the International Federation of Gynecology and Obstetrics; IVL, intravenous leiomyomatosis.

to the IVC and iliac vein. After recurrence, 5 patients underwent hysterectomy with bilateral oophorectomy, whereas 2 patients underwent hysterectomy with bilateral salpingectomy. In the 2 patients from the hysterectomy with bilateral salpingectomy group, recurrences were in the pelvis, involving the left internal iliac vein and ovarian vein, with 1 case also involving metastasis to both lungs. After recurrence, both patients underwent tumor resection and oophorectomy. In the 1 patient from the hysterectomy with bilateral oophorectomy group, the recurrence was in the pelvis, and the patient refused further surgery. Pathology confirmed that all recurrences were IVL. As of the follow-up period, these patients have not experienced further recurrence.

Survival analysis of IVL recurrence

The recurrence-free survival curves were plotted using Kaplan-Meier survival analysis (*Figure 3*). The log-rank results showed statistically significant differences in recurrence-free survival rates based on age (P=0.010), extent of vascular involvement (P=0.017), and surgery type (P<0.001). Patients aged ≤46.5 years, with IVL involving the iliac vein or IVC, and undergoing myomectomy had a higher recurrence rate. The tumor size ≥6.25 cm approached the threshold of statistical significance (P=0.05). No statistically significant differences in recurrence-free survival rates were found with respect to pregnancy history, birth history, menopausal status, tumor markers, or anemia (P>0.05) (*Table 3*).

Analysis of risk factors influencing IVL recurrence

Univariate analysis showed that age ≤46.5 years (P=0.035), IVL involving iliac vein or IVC (P=0.029), and myomectomy (P<0.001) were significant risk factors influencing IVL recurrence (*Table 4*).

Further multivariate analysis revealed that involvement of the iliac vein or IVC [P=0.021, hazard ratio (HR) 6.407] and myomectomy (P<0.001, HR 77.360) were independent risk factors for recurrence. No statistically significant differences were detected in in risk of recurrence between hysterectomy with bilateral oophorectomy and hysterectomy with bilateral salpingectomy (P=0.175) (*Table 4*).

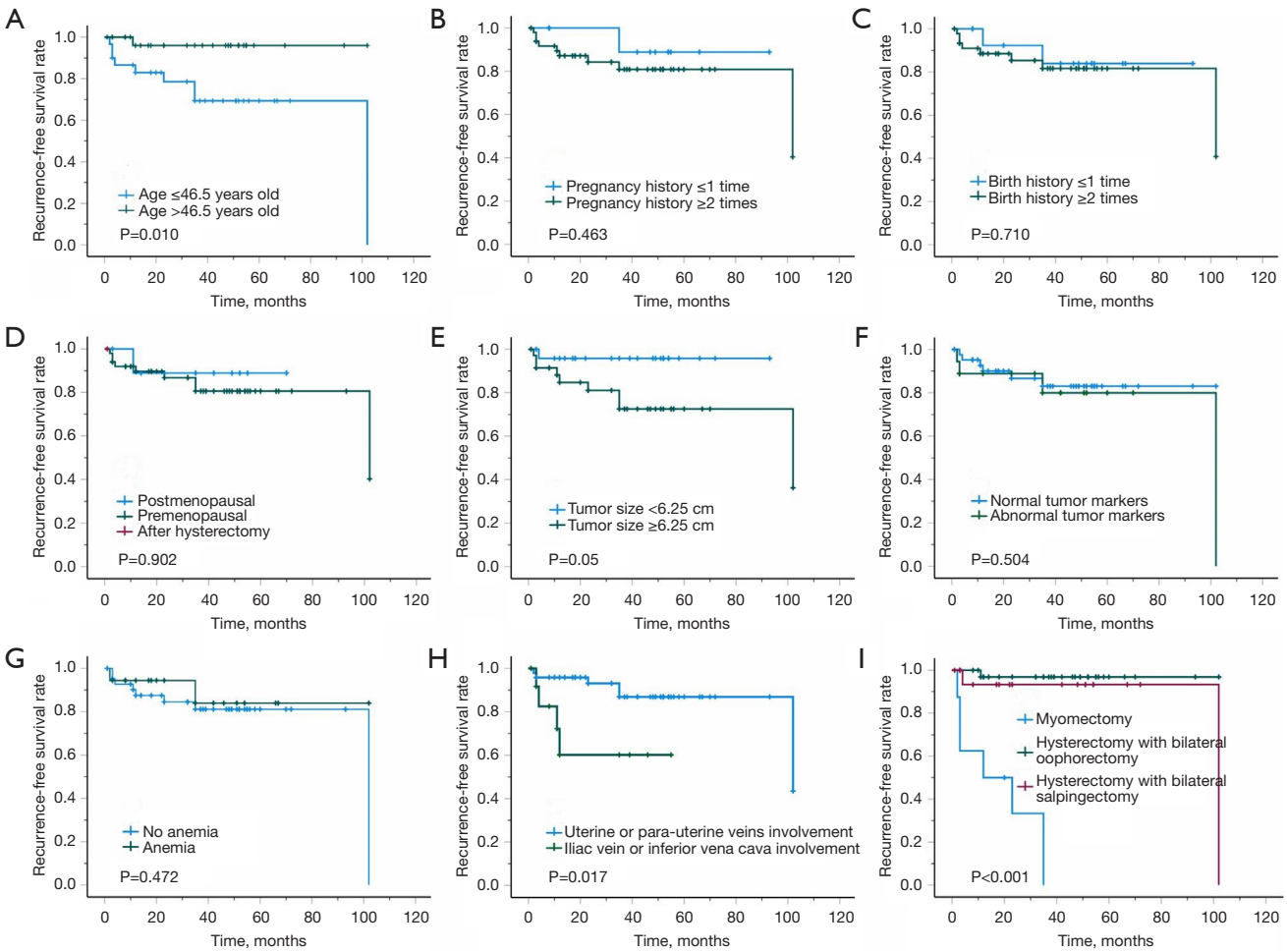

Figure 3 Kaplan-Meier curve for recurrence-free survival. (A) Age. (B) Pregnancy history. (C) Birth history. (D) Menopausal status. (E) Tumor size. (F) Tumor markers. (G) Anemia. (H) Extent of vascular involvement. (I) Surgery type.

Discussion

IVL is a rare, histologically benign but biologically invasive tumor (6). There are currently 2 main theories regarding its pathogenesis: 1 suggests that it originates from uterine smooth muscle leiomyomas, whereas the other proposes that it stems from the walls of uterine veins, though most studies support the former (7,8). This study found that among 61 patients, 51 had concurrent uterine leiomyomas, accounting for 83.6% of the total, which further supports the theory of origin being from uterine smooth muscle leiomyoma.

IVL often extends beyond the uterus, invading surrounding venous vessels. It can spread along the uterine veins, internal iliac veins, common iliac veins, IVC, and may even extend to the right atrium, right ventricle, and pulmonary arteries. Additionally, it can spread via the left ovarian vein to the left renal vein or the right ovarian vein to the IVC, eventually reaching the right atrium, right ventricle, and pulmonary arteries (1,2,9). Occasionally, IVL may exhibit skip lesions or metastatic-like dissemination, presenting as multiple lung nodules (10,11). Rarely, it involves spinal bone metastasis, potentially through hematogenous spread from the pelvic veins via the Batson venous plexus (12,13).

In this study, 6 patients (9.8% of the total) developed bilateral lung metastases. Among them, 5 patients (excluding 1 who died postoperatively) underwent total hysterectomy with bilateral oophorectomy, and no pulmonary nodules enlarged during follow-up. This outcome may result from the combined effects of tumor resection and bilateral oophorectomy. Immunohistochemical analysis showed positive estrogen receptor (ER) and progesterone receptor

Table 3 Log-rank test analysis of factors for recurrence that are associated with uterine IVL

Characteristic	Total cases (n=61)	Recurrence (n=10)	χ^2	P value
Age (years)			6.620	0.010
>46.5	31 (50.8)	1 (10.0)		
≤46.5	30 (49.2)	9 (90.0)		
Pregnancy history (times)			0.538	0.463
≤1	11 (18.0)	1 (10.0)		
≥2	50 (82.0)	9 (90.0)		
Birth history (times)			0.139	0.710
≤1	15 (24.6)	2 (20.0)		
≥2	46 (75.4)	8 (80.0)		
Menopause			0.207	0.902
Postmenopausal	10 (16.4)	1 (10.0)		
Premenopausal	50 (82.0)	9 (90.0)		
After hysterectomy	1 (1.6)	0		
Tumor size (cm)			3.848	0.05
<6.25	25 (41.0)	1 (10.0)		
≥6.25	36 (59.0)	9 (90.0)		
Tumor markers			0.446	0.504
Normal	43 (70.5)	6 (60.0)		
Abnormal	18 (29.5)	4 (40.0)		
Anemia			0.518	0.472
No	43 (70.5)	8 (80.0)		
Yes	18 (29.5)	2 (20.0)		
Extent of vascular involvement			5.729	0.017
Uterine or para-uterine veins	48 (78.7)	6 (60.0)		
Iliac vein or inferior vena cava	13 (21.3)	4 (40.0)		
Surgery type			49.575	<0.001
Hysterectomy with bilateral oophorectomy	35 (57.4)	1 (10.0)		
Hysterectomy with bilateral salpingectomy	18 (29.5)	2 (20.0)		
Myomectomy	8 (13.1)	7 (70.0)		

Data are given as n (%). IVL, intravenous leiomyomatosis.

(PR) expression in 4 patients, whereas 2 others were not tested due to financial constraints, suggesting that hormonal levels may influence the progression or stabilization of pulmonary nodules. Considering the recurrence risk of IVL, long-term follow-up is planned to further investigate this relationship and identify factors affecting pulmonary nodule behavior.

Ultrasound features of IVL have rarely been reported in previous studies, which mainly focused on cases involving IVC or the heart (3,14-17). This study extensively analyzed the location, FIGO classification, shape, extent of vascular involvement, and internal blood flow characteristics of IVL.

Table 4 Univariate and multivariate analysis of prognostic factors for recurrence that are associated with uterine IVL

Characteristic	Univariate analysis			Multivariate analysis		
	P value	HR	95% CI	P value	HR	95% CI
Age (years)						
>46.5		1				
≤46.5	0.035	9.178	1.163–72.447			
Pregnancy history (times)						
≤1		1				
≥2	0.476	2.132	0.265–17.113			
Birth history (times)						
≤1		1				
≥2	0.712	1.345	0.279–6.489			
Menopause						
Postmenopausal		1				
Premenopausal	0.630	1.666	0.208–13.325			
After hysterectomy						
Tumor size (cm)						
<6.25		1				
≥6.25	0.088	6.123	0.766–48.975			
Tumor markers						
Normal		1				
Abnormal	0.509	1.538	0.428–5.527			
Anemia						
No		1				
Yes	0.479	0.568	0.119–2.717			
Extent of vascular involvement						
Uterine or para-uterine veins		1			1	
Iliac vein or inferior vena cava	0.029	4.404	1.165–16.652	0.021	6.407	1.319–31.135
Surgery type						
Hysterectomy with bilateral oophorectomy		1			1	
Hysterectomy with bilateral salpingectomy	0.298	3.651	0.318–41.866	0.175	6.025	0.450–80.702
Myomectomy	<0.001	63.153	7.204–553.596	<0.001	77.360	8.584–697.199

CI, confidence interval; HR, hazard ratio; IVL, intravenous leiomyomatosis.

The results indicate that IVL located adjacent to the uterus, FIGO 8, appearing as cord-like or beaded structures on ultrasound, and involving iliac vessels or IVC significantly enhances the accuracy of ultrasound diagnosis. When IVL involves iliac vessels or IVC, the ultrasound diagnostic accuracy can reach 92.3%. Approximately 34.4% of tumors in this study exhibited rich internal blood flow, contrasting with Zhang *et al.*'s (18) reported rate of 60% for tumors involving the heart. However, the diagnostic accuracy for IVL with abundant internal blood flow was only 66.7%,

possibly due to the insensitivity of conventional ultrasound to slow blood flow within lesions. Ge *et al.*'s (19) analysis of IVL lesions involving the IVC demonstrated that contrast-enhanced ultrasound (CEUS) could better depict fine blood flow within the lesions.

Given the low incidence and clinical rarity of IVL, it is prone to misdiagnosis. This study shows that IVL confined to the uterus (18 cases) had a very low ultrasound diagnostic rate of only 5.6%. Some studies indicate that early ultrasound features of IVL are atypical and often misdiagnosed as uterine leiomyoma, primarily because the tumor remains within small vessels of the muscle layer (8,20). A definitive diagnosis requires the integration of intraoperative findings and postoperative pathological results. A retrospective study of 27 IVL cases found that ultrasound had a misdiagnosis rate of 85.7% for intrapelvic IVL, underscoring the challenges of early diagnosis. CT was primarily used to evaluate extrapelvic involvement, whereas MRI was valuable in evaluating para-uterine vascular involvement. However, the role of MRI in early diagnosis requires further validation due to limited case studies (14). Wang *et al.* (21) retrospectively analyzed 11 IVL cases and found that ultrasound revealed uterine or para-uterine venous tortuosity in 4 cases. Subsequent MRI and CT scans identified para-uterine/uterine vein or iliac vein involvement in 6 cases and extrapelvic lesions in 5 cases. Their findings emphasized the complementary roles of ultrasound and MRI, with MRI being particularly useful for assessing extensive venous involvement. They concluded that pelvic ultrasound is valuable for early screening, whereas contrast-enhanced CT and MRI are essential for diagnosis and evaluation of venous involvement.

Ultrasound is a fast, simple, cost-effective, and radiation-free imaging modality, making it ideal for the initial screening of IVL. It provides key information on tumor location, shape, internal blood flow, and vascular involvement, with the added benefit of dynamic observation. However, its limitations in detecting deeper or complex lesions and reliance on physician expertise can lead to underdiagnosis. In contrast, MRI offers superior soft tissue contrast and excels in evaluating venous involvement and complex anatomical regions, such as the internal iliac vein, making it valuable for confirming diagnoses and preoperative planning. Despite its advantages, MRI is more expensive, time-consuming, and often requires intravenous contrast, adding to its cost and complexity. Its limited availability in certain settings is another limitation. When ultrasound suggests or confirms IVL, contrast-enhanced CT or MRI is recommended for precise diagnosis and comprehensive vascular assessment, which are critical for treatment planning and multidisciplinary collaboration.

This study shows a recurrence rate of 16.4% for IVL, which closely aligns with the rates in previous reports ranging from 11.4% to 27.8% (4,8,22). Yu *et al.* (23) demonstrated through log-rank analysis that major vessel involvement was a significant risk factor for IVL recurrence. Additionally, Zhang *et al.* (24) highlighted that incomplete tumor resection, tumor size, and involvement of the iliac vein, gonadal veins, or IVC are critical factors contributing to IVL recurrence and progression. Patients under 45 years of age and those undergoing uterine leiomyoma resection have higher recurrence rates (25). Peng *et al.* (26), in their multivariate regression analysis, identified surgical type as the sole factor influencing IVL recurrence, with a 20-fold higher risk associated with myomectomy compared to total hysterectomy with bilateral oophorectomy. This study indicates that patients aged ≤46.5 years, with IVL involving the iliac vein or IVC, and undergoing myomectomy had a higher recurrence rate. Cox multivariate analysis confirmed that involvement of the iliac vein or IVC and myomectomy are independent risk factors for recurrence, consistent with previous reports.

Currently, surgery remains the most effective treatment for IVL, with the optimal approach involving multidisciplinary collaboration to achieve complete tumor resection (27,28). Reports have indicated that patients undergoing total hysterectomy with bilateral salpingo-oophorectomy and complete visible tumor resection had a recurrence rate of 7.6%. Those undergoing only total hysterectomy had a recurrence rate of 25%, whereas those going through only myomectomy, preserving the uterus and bilateral ovaries, experienced a high recurrence rate of 75% (29). In this study, recurrence rate was 10% for patients undergoing total hysterectomy with bilateral oophorectomy and complete tumor resection, 20% for those undergoing only total hysterectomy, and 70% for those undergoing myomectomy while preserving the uterus and ovaries, consistent with previous reports. For patients with suspected IVL, total hysterectomy with bilateral oophorectomy and complete tumor resection is recommended if their general condition is good and the tumor has not involved major vessels or the heart, or if it is easily removable despite such involvement. Young patients wishing to preserve their ovaries should be informed of the recurrence risk and advised on regular follow-ups. For patients with poor health or tumors that are large, severely adherent, and difficult to separate, staged

surgery may be considered to minimize postoperative mortality.

The limitations of this study lie in its retrospective nature, where the accuracy of ultrasound diagnosis is influenced by the physician's experience and sensitivity to the condition. Therefore, in this study, we selected diagnostic cases from ultrasound physicians with over 10 years of experience to minimize the impact on diagnostic accuracy. Moreover, the internal blood flow of IVL is inconsistent with some literature, and in the future, it is hoped to assess the subtle blood flow and enhancement patterns within tumors through CEUS.

Conclusions

IVL is a rare but invasive tumor, often originating from uterine smooth muscle leiomyomas. This study found that 83.6% of patients had concurrent uterine leiomyomas, supporting this origin theory. IVL frequently extends beyond the uterus, involving major venous structures and occasionally metastasizing to the lungs. Ultrasound diagnostic accuracy was highest when IVL involves major vessels, but early-stage IVL was often misdiagnosed. Recurrence rates were influenced by factors such as age, vessel involvement, and surgery type, with complete tumor resection being the most effective treatment. Total hysterectomy with bilateral oophorectomy offers the lowest recurrence rates, though younger patients desiring ovarian preservation must be informed of higher recurrence risks and require regular follow-up. Multidisciplinary collaboration is crucial for optimal patient management.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-1724/rc

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1724/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Scientific Research and Clinical Trials Ethics Committee of The First Affiliated Hospital of Zhengzhou University, China (No. 2024-KY-0933-001) and the requirement for individual consent for this retrospective analysis was waived.

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Cite this article as: Zhang TT, Zhou JY, Li HL, Zhang XL, Chang L. Ultrasound diagnostic value and clinical analysis of 61 uterine intravenous leiomyomatosis cases. Quant Imaging Med Surg 2025;15(4):3347-3359. doi: 10.21037/qims-24-1724

