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(REVIEW ARTICLE)



Female genital vascular malformations: A comprehensive multimodal review of diagnosis, genetics, and minimally invasive treatment strategies

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#### **Abstract**

Vascular malformations of the female genitalia encompassing venous, lymphatic, and arteriovenous anomalies are rare yet clinically important, often causing pain, bleeding, and impaired reproductive function. These deformities may be congenital or acquired and present significant diagnostic and therapeutic challenges.

This literature review synthesizes evidence on classification, pathophysiology, and advances in diagnostic imaging and treatment. It also explores the role of genetics and targeted therapies.

With recent innovations in minimally invasive procedures and molecular diagnostics, this review aims to guide clinicians toward more personalized, effective interventions for these complex and underrecognized vascular conditions.

**Keywords:** Female Genital Vascular Malformations; Venous Malformations; Arteriovenous Malformations; Lymphatic Anomalies; Diagnostic Imaging; Gene Therapy; Embolization; Sclerotherapy; AI-Driven

#### 1. Introduction

Female genital vascular malformations are rare yet impactful conditions that disrupt normal blood or lymphatic vessel architecture. These anomalies can be congenital or acquired and are often categorized as high-flow (e.g., arteriovenous malformations) or low-flow (e.g., venous or lymphatic malformations) <sup>2</sup>. While some remain asymptomatic, others cause pain, swelling, ulceration, and sexual dysfunction, adversely affecting reproductive health and quality of life <sup>3</sup>

Advances in diagnostic imaging such as Doppler ultrasound and MRI have enhanced lesion identification and treatment planning  $^4$ . At the same time, genetic research has revealed mutations in pathways like PIK3CA, TEK, and GNAQ, opening new therapeutic directions through targeted agents  $^5$  and  $^6$ 

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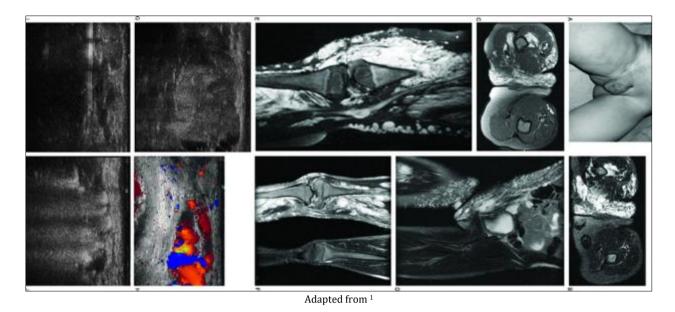


Figure 1 Vascular Malformations Involving the Female Pelvis (Rotation Form)

This review presents a structured overview of the classification, underlying mechanisms, diagnostic methods, and treatment approaches for vascular malformations affecting the female genital tract, aiming to improve clinical awareness and interdisciplinary management.

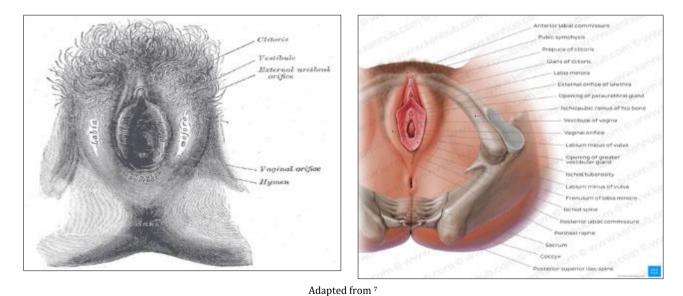


Figure 2 Vascular Anatomy of the Female Genitalia

# 2. Methods

### 2.1. Study Design and Data Sources

A structured literature review was conducted using PubMed, ScienceDirect, and the Journal of Vascular Surgery. Search terms included "female genital vascular malformations," "vulvar vascular anomalies," and "uterine arteriovenous malformations." Only peer-reviewed human studies from the last 10 years were included. 8

# 2.2. Eligibility Criteria

Eligible articles focused on adult female patients and covered diagnostic techniques, molecular pathogenesis, or treatment strategies. Excluded were pediatric, non-human, and non-clinical studies. Relevant case reports and clinical trials were reviewed for additional context. <sup>9</sup>

# 2.3. Assessment and Synthesis

Methodological quality was assessed using PRISMA guidelines. QUADAS-2 was used for diagnostic studies, and the Cochrane Risk of Bias tool was applied to intervention trials. Given the clinical and methodological heterogeneity, findings were summarized using thematic synthesis rather than meta-analysis.

#### 3. Findings

# 3.1. Classification and Pathophysiology

#### 3.1.1. Types of Female Vascular Malformations

Female genital vascular malformations are classified based on flow dynamics and vessel type into four main categories: venous, lymphatic, arteriovenous, and capillary malformations. These may occur independently or as combined lesions, complicating diagnosis and management. Most cases are congenital, although acquired forms can result from trauma, surgery, or hormonal changes.  $^{10}$  and  $^{11}$ 

This table compares characteristics of venous, arterial, capillary, and lymphatic deformities.

 Table 1 Classification of Female Genital Vascular Malformations

Types	Pathophysiology	Common Symptoms	Genetic Associations	Severity Level	Frequency
Arteriovenous Malformations (AVMs)	High-flow abnormal connections between arteries and veins, bypassing capillary networks.	, ,,	RASA1, ENG	High	Rare
Venous Malformations (VMs)	Enlarged, slow-flow veins due to defective venous walls and valves.	Swelling, pain, heaviness.	TEK, PIK3CA	Moderate	Uncommon
Lymphatic Malformations (LMs)	Improper development of lymphatic vessels leading to fluid-filled cystic structures.	Lymphedema, recurrent infections.	GATA2, FOXC2	Variable	Rare
Capillary Malformations (CMs)	Dilated capillaries resulting in reddish or purplish skin discoloration.	Skin discoloration, potential ulceration.	GNAQ	Mild- Moderate	Common
Combined Malformations	Vascular malformations involving two or more vessel types.	Variable symptoms depending on malformation type.	PIK3CA	Variable	Rare

Adapted from <sup>3</sup>

# 3.1.2. Venous Malformations (VMs)

VMs are low-flow anomalies characterized by malformed, dilated venous channels. Clinically, they present as bluish, compressible soft tissue masses often located in the vulva or pelvic region. Patients may experience pain, swelling, dysmenorrhea, and superficial thrombosis. Hormonal influences, such as puberty or pregnancy, can exacerbate symptoms. In severe cases, venous stasis may lead to complications like deep vein thrombosis or dyspareunia. <sup>12</sup>

## 3.1.3. Lymphatic Malformations (LMs)

LMs consist of malformed lymphatic vessels that fail to connect properly to the central lymphatic system. They are typically cystic and affect the labia majora, perineum, or surrounding soft tissues. Symptoms include swelling, recurrent

infections, and localized discomfort. Histologically, they appear as fluid-filled spaces lined by endothelium. Genetic alterations involving the PIK3CA-AKT-mTOR pathway have been implicated in their development. <sup>13</sup>

### 3.1.4. Arteriovenous Malformations (AVMs)

AVMs are high-flow lesions where arteries shunt blood directly into veins, bypassing capillaries. This causes turbulent blood flow, vessel wall stress, and potential rupture. In the genital region, uterine or vaginal AVMs may manifest as unexplained bleeding, pelvic pain, or hemodynamic instability. These lesions can be life-threatening and are often treated with embolization or surgery. Imaging typically reveals serpentine vessels with early venous filling. <sup>14</sup>

#### 3.2. Genetic and Molecular Mechanisms

Recent discoveries have linked several gene mutations to the development of female genital vascular malformations. These mutations alter angiogenesis, vascular stability, and endothelial signaling, contributing to abnormal vessel proliferation and structure.

#### 3.2.1. PIK3CA Mutations

Somatic mutations in *PIK3CA* activate the PI3K/AKT/mTOR pathway, driving cell overgrowth and vascular anomalies. This mutation is often found in syndromes like CLOVES and Klippel-Trénaunay, both of which can involve the genital region. <sup>15</sup>

#### 3.2.2. GNAO and GNA14 Mutations

*GNAQ* mutations are implicated in capillary malformations such as port-wine stains, while *GNA14* is linked to tufted angiomas and kaposiform hemangioendotheliomas tumors that may affect reproductive and pelvic tissues. <sup>16</sup>

#### 3.2.3. TEK (TIE2) Mutations

Mutations in the endothelial-specific tyrosine kinase receptor gene TEK contribute to abnormal venous development. TEK mutations are particularly associated with localized venous malformations and may explain recurrent lesions in the pelvic or vulvar region.  $^{17}$ 

These genetic findings support the use of targeted molecular therapies. Inhibitors of mTOR and PI3K, as well as anti-VEGF agents, are currently under investigation. Genetic testing is also emerging as a diagnostic adjunct to distinguish between malformation subtypes and guide personalized treatment strategies.

# 3.3. Implications for Diagnosis and Treatment

Understanding these genetic mutations has significant implications for the diagnosis and management of vascular deformities in the female genitalia. Genetic testing can aid in accurate diagnosis, allowing for personalized treatment approaches. Targeted therapies, such as PI3K inhibitors, have shown promise in treating PIK3CA-related vascular anomalies, offering potential non-surgical treatment options for affected individuals <sup>18</sup>

Incorporating genetic analysis into clinical practice enhances the ability to diagnose and manage vascular malformations effectively, ultimately improving patient outcomes.

# 3.4. Imaging and Diagnostic Techniques

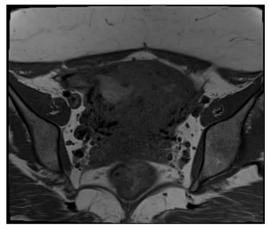
Accurate imaging is essential for diagnosing female genital vascular malformations and guiding treatment planning. The selection of modality depends on lesion depth, flow characteristics, and available technology.

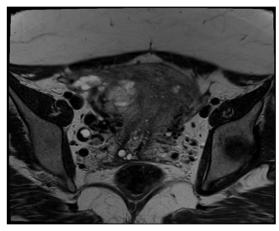
# 3.5. Ultrasonography (US)

US, especially with Doppler enhancement, is a first-line, non-invasive tool for differentiating between solid and cystic lesions. However, its sensitivity decreases with deeper or complex malformations. <sup>19</sup>

#### 3.6. Magnetic Resonance Imaging (MRI)

MRI offers superior soft tissue contrast and helps define lesion extent, flow patterns, and tissue involvement. It is especially useful for pelvic and deep vulvar anomalies. <sup>19</sup>





Adapted from 20

**Figure 3** T1 and T2 weighted MRI scans demonstrating uterine arteriovenous malformations with serpentine flow-related signal voids, characteristic of high-flow vascular lesions

# 3.6.1. Computed Tomography Angiography (CTA)

CTA provides high-resolution vascular mapping using contrast and X-rays. Though effective in assessing arteriovenous shunting, it poses risks related to radiation and contrast exposure.  $^{21}$ 

**Table 2** Imaging Modalities for Diagnosing Vascular Malformations

Imaging Modality	Description	Advantages	Limitations
Ultrasonography (US)	Uses high-frequency sound waves to produce real-time images of vascular structures	Non-invasive, widely available, cost-effective.	Limited penetration depth, operator-dependent results.
Magnetic Resonance Imaging (MRI)	Provides detailed soft tissue contrast and multiplanar imaging.	No radiation exposure, excellent lesion characterization.	High cost, long scan time, contraindicated in some patients.
Computed Tomography (CT) Angiography	Uses X-rays and contrast dye to visualize blood vessels.	Rapid imaging, detailed vascular mapping.	Ionizing radiation exposure, potential contrast nephropathy.
Doppler Ultrasound	Evaluates blood flow and hemodynamics of vascular structures.	Real-time imaging, useful for assessing flow abnormalities.	Limited by patient body habitus and deep lesions.
3D Ultrasonography	Generates three-dimensional reconstructions of vascular anomalies.	Enhanced spatial visualization of complex lesions.	Limited clinical availability, requires specialized equipment.
Elastography	Measures tissue stiffness to assess vascular lesion properties.	Helps differentiate between normal and pathological tissues.	Operator variability, requires expertise for interpretation.
Contrast-Enhanced Ultrasound (CEUS)	Uses microbubble contrast agents to enhance visualization of blood flow.	No radiation exposure, real-time imaging.	Less commonly available, potential contrast reaction in some patients.
Photoacoustic Uses laser-induced ultrasound waves to generate high-resolution vascular images.		Provides functional and structural information on blood vessels.	Still experimental, limited clinical accessibility.
Artificial Intelligence (AI) Integration	AI-powered analysis of imaging data for automated detection.	Enhances diagnostic accuracy, reduces human error.	Requires validation and regulatory approval before widespread use.

Adapted from  $^{\rm 10}$  and  $^{\rm 11}$  with additional insights from  $^{\rm 22}$ 

#### 3.6.2. Doppler Ultrasound

Doppler ultrasound assesses blood flow within vessels, enabling the detection of abnormal flow patterns associated with vascular malformations. It is a non-invasive, first-line imaging modality that provides real-time information about hemodynamics. Color Doppler can help in distinguishing between high-flow and low-flow lesions, which is crucial for accurate diagnosis and management <sup>23</sup>

#### 3.6.3. 3D Ultrasonography

Allows spatial visualization of vascular structures, improving diagnostic confidence for complex cases. Limitations include cost and limited availability.  $^{24}$ 

### 3.6.4. Elastography

Measures tissue stiffness, helping to distinguish between normal and abnormal vessels. It may aid in monitoring treatment response.

- **Ultrasound Elastography in Venous Malformations**: A study evaluated the effectiveness of different ultrasound elastography techniques in patients with venous malformations. The findings suggest that qualitative Acoustic Radiation Force Impulse (ARFI) elastography can reliably detect changes induced by sclerotherapy within venous malformations. Quantitative ARFI measurements may also assist in therapy planning and monitoring outcomes, as well as assessing the effects of sclerosing agents on both the malformation and surrounding tissues 25
- **Elastography Imaging in Vascular Anomalies**: Research has been conducted to assess the utility of ultrasound elastography in imaging vascular anomalies. The study presents experiences with various cases, highlighting the application of elastography in these pathologies 26
- **Intravascular Elastography**: The development of intravascular elastography techniques has enabled the assessment of mechanical properties of diseased arteries. These methods have been validated through studies involving porcine aortas, demonstrating the potential of elastography in characterizing arterial wall mechanics 27

# 3.6.5. Contrast-Enhanced Ultrasound (CEUS)

CEUS improves visualization of microvascular flow in real time, particularly in low-flow venous malformations. <sup>28</sup>

# 3.6.6. Photoacoustic Imaging

A hybrid technology combining light and ultrasound to provide detailed vascular imaging. PAI is still experimental but shows promise for superficial genital lesions.:

- Ovarian Cancer Diagnosis: Researchers at Washington University in St. Louis have integrated PAI with traditional ultrasound to improve diagnostic accuracy for ovarian and adnexal lesions. By illuminating tissues with near-infrared light, PAI enhances the visualization of functional biomarkers, potentially reducing unnecessary surgical interventions <sup>29</sup>
- **Cervical Lesion Detection**: A study investigated the clinical application of PAI for detecting precursor lesions in the uterine cervix. The findings suggest that PAI could serve as a supportive or alternative technique to colposcopy, offering improved accuracy and reproducibility in early diagnosis <sup>30</sup>

These advancements underscore PAI's potential in enhancing the detection and characterization of vascular anomalies within the female reproductive system.

• Artificial Intelligence (AI) Integration: AI-assisted platforms are being integrated into imaging workflows to improve detection, classification, and segmentation. While still in development, AI holds potential for reducing diagnostic delays and operator variability.

# 3.7. Applications in Medical Imaging

# 3.7.1. Image Interpretation

AI systems can assist radiologists by automatically detecting and characterizing vascular anomalies, reducing the likelihood of human error and expediting the diagnostic process.

#### 3.7.2. Segmentation and Classification

Advanced AI models can accurately segment complex vascular structures and classify different types of malformations, aiding in precise treatment planning.

#### 3.7.3. Predictive Analytics

AI can analyze vast datasets to predict disease progression and potential complications, facilitating proactive patient management.

#### 3.8. Advantages

#### 3.8.1. Enhanced Accuracy

AI algorithms can process large volumes of imaging data, identifying subtle patterns that may be overlooked by the human eye, thus improving diagnostic accuracy.

# 3.8.2. Efficiency

Automated image analysis reduces the workload on radiologists, allowing for faster diagnosis and treatment initiation.

#### 3.8.3. Personalized Medicine

By integrating patient-specific data, AI can tailor treatment strategies to individual needs, optimizing outcomes.

#### 3.9. Challenges

#### 3.9.1. Data Quality

The effectiveness of AI depends on the quality and diversity of the data used for training. Inadequate datasets can lead to biased or inaccurate results.

#### 3.9.2. Integration into Clinical Practice

Incorporating AI tools into existing clinical workflows requires careful planning to ensure compatibility and user acceptance.

#### 3.9.3. Ethical Considerations

The use of AI in healthcare raises ethical questions regarding patient privacy, data security, and decision-making transparency.

Incorporating AI into the imaging and diagnosis of vascular deformities in female genitalia holds significant promise. Continued research and development are essential to fully harness its potential while addressing the accompanying challenges <sup>23</sup>. Accurate diagnosis is fundamental to selecting the most effective treatment approach for vascular deformities in the female genitalia. While imaging techniques such as MRI, ultrasound, and AI-driven analysis improve lesion detection and classification, treatment selection depends on the nature, location, and severity of the vascular anomaly. The following section explores the available therapeutic strategies, ranging from minimally invasive procedures to surgical interventions.

# 3.10. Treatment Strategies

Management of female genital vascular malformations depends on lesion type, location, flow characteristics, and clinical severity. While conservative observation may suffice for stable or asymptomatic cases, symptomatic lesions often require intervention. Recent advances have enabled less invasive and more targeted treatment options.

#### 3.10.1. Endovascular Embolization

Embolization is a minimally invasive technique that occludes abnormal vessels using agents like ethanol or coils. It is particularly effective for high-flow lesions, such as AVMs. <sup>31</sup> demonstrated both midterm and long-term success using ethanol embolization for AVMs. Though originally developed for fibroid management, <sup>32</sup> showed uterine artery embolization (UAE) to be a valuable alternative for other vascular conditions, including those of the genital tract. Embolization can significantly reduce symptoms and lesion size but should be tailored to individual vascular anatomy and fertility considerations.

Table 3 Comparative Efficacy of Treatment Strategies

Treatment Modality	Lesion Type and Severity	Success Rate (%)	Recurrence Rate (%)	Patient Outcomes	Notable Complications
Endovascular Embolization	AVMs, moderate to severe	93.5%	15.2%	Significant symptom reduction; high patient satisfaction	Risk of non-target embolization, vessel rupture
Sclerotherapy	VMs, small to moderate	81%	98%	Effective in symptom relief; high recurrence rate	-
Surgical Resection	AVMs, extensive lesions	19%	81%	Variable outcomes; high recurrence rate	High risk of intraoperative hemorrhage
Laser Therapy	Superficial CMs	Data not specified	Data not specified	Effective for superficial lesions	Skin pigmentation changes, multiple sessions required
Pharmacotherapy	Symptomatic management	Data not specified	Data not specified	Adjunctive therapy; variable efficacy	Systemic side effects

Adapted from 33

### 3.10.2. Sclerotherapy

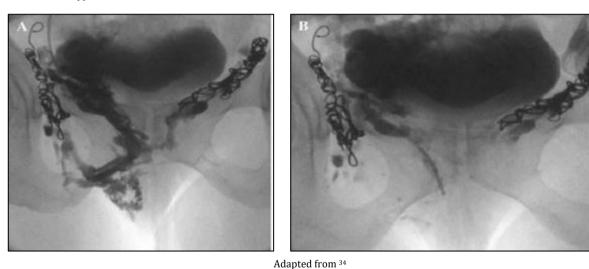


Figure 4 A and B Vulval varices treated with foam sclerotherapy and coil embolization

Sclerotherapy involves injecting sclerosants directly into vascular malformations to induce fibrosis and shrinkage. This approach is especially useful for venous malformations in the vulvar region. Case reports by <sup>35</sup> and <sup>36</sup> described notable cosmetic and symptomatic improvements in pediatric patients. Though effective, it may require multiple sessions due to recurrence. Side effects like ulceration or tissue necrosis are uncommon but possible.

This method is particularly effective for treating venous malformations (VMs) in the vulvar region. A case report by  $^{35}$  demonstrated successful treatment of a vulvar VM in an 11-year-old girl using sclerotherapy, resulting in significant symptom improvement and cosmetic satisfaction.  $^{36}$ 

# 3.10.3. Laser Therapy

Nd:YAG laser therapy has emerged as a non-invasive treatment for superficial venous malformations. <sup>37</sup> reported successful outcomes using this modality in genital vascular lesions, noting favorable safety and cosmetic profiles. However, limitations include the need for multiple treatments and potential pigmentation changes.

#### 3.10.4. Combined Endovascular and Surgical Approaches

In more extensive or refractory cases, a combination of embolization followed by surgical resection has proven beneficial. <sup>38</sup> detailed a successful staged approach for managing slow-flow vulvar malformations, resulting in favorable long-term outcomes and reduced recurrence.

#### 3.10.5. Pharmacotherapy

Antiangiogenic and targeted pharmacologic agents are gaining traction as adjunct treatments. Drugs such as mTOR inhibitors and  $\beta$ -blockers have been explored in cases with diffuse, non-operable lesions. <sup>22</sup> emphasized the need for case-by-case evaluation due to the systemic risks associated with long-term use.

Table 4 Treatment Strategies for Female Genital Vascular Malformations

Treatment Modality Description		Primary Indications	Potential Risks	
Endovascular Embolization  Catheter-based procedure that blocks abnormal blood vessels using embolic agents.		AVMs, PCS.	Recurrence, non-target embolization, vessel rupture.	
Sclerotherapy	Injection of sclerosants to shrink malformed veins and lymphatic vessels.	VMs, LMs.	Pain, ulceration, potential allergic reactions.	
Surgical Resection	Direct excision of the malformation when other therapies fail.	Refractory or extensive cases.	Scarring, nerve damage, long recovery time.	
Laser Therapy	Uses high-energy light to coagulate or reduce vascular lesions.	Superficial vascular anomalies.	Skin burns, pigment changes, incomplete response.	
Pharmacotherapy	Medications targeting vascular growth and inflammation, including $\beta$ -blockers and mTOR inhibitors.	AVMs, complex malformations.	Side effects from long-term drug use, systemic reactions.	

Adapted from 32 and 37 and 38

Overall, treatment strategies should be personalized based on lesion characteristics, symptom burden, and patient goals. A multidisciplinary approach remains critical in optimizing outcomes while minimizing procedural risks and recurrence.

## 4. Discussion

Female genital vascular malformations are rare but clinically significant, presenting unique challenges due to their association with hormonal cycles, pregnancy, and reproductive anatomy. Their complexity requires careful diagnostic and therapeutic strategies, yet standard approaches remain limited.

# 4.1. Comparison with Existing Literature

Vascular malformations of the female genitalia are underreported, particularly when compared to similar anomalies in other regions. Uterine AVMs have been more thoroughly investigated due to their effects on reproductive health and bleeding risk  $^{22}$ . In contrast, vulvar and vaginal lesions remain poorly studied, contributing to frequent misdiagnoses and delays in care.  $^{38}$ 

Uterine artery embolization (UAE) has shown efficacy for uterine AVMs and fibroids, offering a minimally invasive option with fewer complications <sup>32</sup>. However, its role in treating external genital lesions is less explored. Sclerotherapy and laser therapy especially in vulvar cases have demonstrated strong outcomes in symptom relief and lesion shrinkage, making them valuable front-line options when preserving function is essential. <sup>37</sup>

# 4.2. Current Gaps and Challenges

Despite diagnostic advances, the field continues to face several limitations:

### 4.2.1. Limited Epidemiological Data

Most studies are small-scale or case-based, making it difficult to determine true prevalence, long-term outcomes, or treatment algorithms.

#### 4.2.2. Diagnostic Ambiguities

Many vascular malformations present with symptoms similar to endometriosis or chronic pelvic pain. Conditions like pelvic congestion syndrome (PCS) are frequently misdiagnosed, delaying effective treatment. <sup>22</sup>

#### 4.2.3. Treatment Standardization

Embolization, sclerotherapy, and laser therapy have all shown promise, but standardized guidelines for treatment selection by lesion type are lacking. There's also insufficient head-to-head data comparing long-term outcomes or recurrence risk.

Table 5 Long-Term Outcomes & Recurrence Risks of Treatment Modalities

Treatment Modality	Average Success Rate (%)	Recurrence Risk (%)	Long-Term Complications	Follow-Up Recommendations
Endovascular Embolization	80-90%	10-30%	Vessel recanalization, ischemia	Routine imaging at 6-12 months
Sclerotherapy	75-85%	15-40%	Tissue necrosis, fibrosis	Repeat treatments if needed
Surgical Resection	85-95%	5-20%	Scarring, infection	Postoperative Doppler monitoring
Laser Therapy	70-80%	20-35%	Skin discoloration, pain	Multiple sessions may be needed
Pharmacotherapy	60-75%	30-50%	Hormonal side effects	Long-term hormonal evaluation

Adapted from 31 and 33

These comparative outcomes emphasize the importance of selecting treatment modalities based on lesion type, recurrence risk, and long-term patient well-being. While embolization, sclerotherapy, and laser therapy demonstrate high success rates, ongoing research is essential to optimize patient-specific approaches.

# 4.3. Future Directions

Continued research is needed to support more personalized and effective care

### 4.3.1. Personalized Treatment Approaches

Genetic findings, such as mutations in PIK3CA and TEK, may enable more personalized treatment plans and reduce reliance on invasive procedures.  $^{18}$ 

# 4.3.2. AI-Assisted Diagnosis

Artificial intelligence and machine learning hold promise in imaging interpretation and early-stage lesion classification, potentially reducing misdiagnoses. <sup>23</sup>

### 4.3.3. Long-Term Outcome Studies

More prospective studies on fertility, recurrence, and quality of life are needed. Patient registries and real-world data collection could help refine treatment pathways and enable predictive analytics for individualized care.

#### 5. Conclusion

Vascular malformations of the female genitalia are rare but clinically significant, often presenting with complex diagnostic and therapeutic challenges. Advances in imaging, interventional radiology, and molecular research have

improved lesion classification and treatment planning. Minimally invasive options such as embolization, sclerotherapy, and laser therapy have shown promising outcomes, particularly when personalized to lesion type and patient needs. Future progress will depend on standardized protocols, long-term outcome studies, and greater integration of genetic diagnostics and AI-assisted imaging. A multidisciplinary, patient-centered approach remains essential for improving clinical outcomes in this underrecognized area of female health.

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