

1 Good Practice Recommendations on terminology 2 and classification for adenomyosis

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27 Abstract

28 **STUDY QUESTION:** What insights does the collaborative document by ESGE, ESHRE, and WES
29 provide on adenomyosis terminology, classification, and diagnosis?

30 **SUMMARY ANSWER:** This Recommendations for Good Practice paper provides detailed
31 guidance on the terminology, classification, and diagnosis of adenomyosis in women of
32 reproductive age.

33 **WHAT IS KNOWN ALREADY:** Current literature on adenomyosis terminology is varied and
34 often contradictory. Multiple classification systems, primarily based on ultrasound and MRI,
35 have been suggested; however, none has achieved widespread international acceptance or
36 clinical validation. The lack of consensus on the diagnostic accuracy of these techniques adds
37 complexity to the diagnosis of adenomyosis in women of reproductive age.

38 **STUDY DESIGN, SIZE, DURATION:** A dedicated working group from ESGE, ESHRE, and WES
39 collaborated to develop comprehensive recommendations regarding the terminology,
40 classification, and diagnosis of adenomyosis.

41 **PARTICIPANTS/MATERIALS, SETTING, METHODS:** This Recommendations for Good Practice
42 paper focuses on the terminology, classification, and diagnosis of adenomyosis, setting the
43 stage for subsequent recommendations on its management and surgical interventions in
44 women of reproductive age.

45 **MAIN RESULTS AND THE ROLE OF CHANCE:** The document provides a comprehensive
46 overview of adenomyosis terminology and examines the various proposed reporting and
47 classification systems based on histology, ultrasound, and MRI, culminating in specific
48 diagnostic guidelines.

49 **LIMITATIONS, REASON FOR CAUTION:** Unpublished classification, staging or reporting
50 systems, or those published in books were not considered for inclusion in this paper.

51 **WIDER IMPLICATIONS OF THE FINDINGS:** The recommendations aim to refine and enhance
52 existing adenomyosis protocols.

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54 ESHRE, without any external financial contributions for the development process or
55 manuscript production.

56

57 Introduction

58 Adenomyosis is a non-cancerous gynaecological disorder, with an estimated prevalence that
59 varies significantly among populations. A recent systematic review estimated that the
60 prevalence of focal adenomyosis is around 17% (95% CI 7-30%) and 15% (95% CI 9-23%) for
61 the diffuse type (Wang et al., 2025). For women experiencing infertility, the prevalence was
62 estimated at 31% (95% CI 10-58%).

63 The histological description of adenomyosis dates back to the 18th century although the term
64 adenomyosis was adopted in the early 19th century. Non-histological diagnosis of the disease
65 began in the late 19th and the beginning of the 20th century with the advent of modern
66 imaging modalities. It is noteworthy that through the centuries, the reported prevalence of
67 adenomyosis has varied depending on the diagnostic modality used. The exact aetiology of
68 adenomyosis remains elusive, and both diagnosis and treatment continue to pose significant
69 challenges.

70 The presence of ectopic endometrial glands within the myometrium was first identified in
71 1860 by von Rokitansky, who described it as “cystosarcoma adenoids uterinum” (von
72 Rokitansky, 1860). In 1896, Von Recklinghausen further elaborated on this same
73 phenomenon, introducing the terms “adenomyomata” and “cystadenomata” of the uterus
74 and tubal wall (von Recklinghausen, 1896). He categorised adenomyomata into two types:
75 those localised in the periphery of the uterus and tubes, and those arising centrally within the
76 uterus. Initially, the diagnosis of adenomyosis was based predominantly on macroscopic and
77 microscopic examinations of surgical specimens, without the support of imaging
78 technologies. The first description of adenomyosis without imaging was made in 1898 by
79 Werth and Grusdew (Werth and Grusdew, 1898).

80 In 1908, Thomas Cullen refined the definition of adenomyosis as “the presence of endometrial
81 tissue in the myometrium” (Cullen, 1908). He was meticulous in describing how the “uterine
82 mucosa” invades the underlying myometrial tissue, differentiating between adenomyoma, a
83 tumour-like condition within the myometrium, and diffuse adenomyosis, where both
84 glandular and stromal elements are distributed throughout the myometrium. Cullen’s
85 seminal work laid the groundwork for the contemporary understanding of adenomyosis as a
86 pathologic condition characterised by the presence of endometrial tissue within the
87 myometrium.

88 In 1921, Sampson advanced the understanding of the pathogenesis of adenomyosis and
89 endometriosis, describing it as gland-like spaces forming small ‘haematomas’ that, when
90 invasive, evolve into “adenomyomas” (Sampson, 1921). He stated that these lesions could
91 extend between the rectum and vagina, forming an “adenomyoma of the rectovaginal
92 septum” and suggested that retrograde menstruation, in which “the menstrual blood flows
93 back through the fallopian tubes into the ovaries and peritoneal cavity”, could lead to extrinsic
94 adenomyosis. He was also the first to categorise adenomyomas into two different groups

95 “from the standpoint of their origin: (1) adenomyomas arising from an invasion of the “uterine
96 wall” by “the mucosa lining the cavity” (endometrium) described as invasion from “within”
97 the uterus and (2) adenomyomas arising from an “invasion of the serous surface by an
98 adenoma of endometrial type” secondary to “adenoma” of the ovary described as invasion
99 from “without” the uterus. Both entities had the same histological characteristics and were
100 similar to the recently described internal / intrinsic and external / extrinsic types of
101 adenomyosis. As a consequence of his theory, uterine adenomyosis could not be explained
102 by the regurgitation and implantation of endometrial-like cells in menstrual blood.
103 Adenomyosis and endometriosis were widely considered separate entities.

104 In 1925, Frankl coined the term “adenomyosis uteri”, distinguishing it from inflammatory
105 conditions like endometritis or adenomyositis (Frankl, 1925). He noted the connection
106 between ectopic glands in the myometrium and the endometrium, observing similarities
107 between adenomyosis and endometriosis, particularly the presence of blood within the
108 glands. In his description of adenomyosis, Frankl also referred to the sudden appearance of
109 heavy menstrual bleeding not connected to any endocrine disturbance.

110 In 1972, Bird et al. had defined adenomyosis as “the benign invasion of the endometrium into
111 the myometrium, producing a diffusely enlarged uterus which microscopically exhibits
112 ectopic, non-neoplastic, endometrial glands and stroma surrounded by the hypertrophic and
113 hyperplastic myometrium” (Bird et al., 1972). This definition advanced the understanding of
114 pathological features of adenomyosis and stimulated the development of modern diagnostic
115 methods.

116 More recently, Leyendecker et al. proposed a unifying theory of adenomyosis and
117 endometriosis pathogenesis, based on tissue injury and repair, termed archimetrosis
118 (Leyendecker et al., 2023a), although additional supportive evidence is required for the
119 theory to be accepted (Habiba et al., 2023).

120 Despite over a century of research and clinical observation, significant aspects of aetiology of
121 adenomyosis and its management remain poorly understood (Hao et al., 2020, Leyendecker
122 et al., 2023b, Wang et al., 2022). The recent advancements in non-invasive diagnostic
123 methods, such as transvaginal ultrasound and MRI, have markedly improved the
124 understanding and management of this challenging condition, providing insights that were
125 previously possible only through invasive techniques. However, continued research into more
126 effective diagnostic and therapeutic strategies is still necessary.

127 This Good Practice Recommendations paper critically assesses current methodologies for
128 diagnosing adenomyosis, spotlighting the heterogeneity in the literature concerning its
129 terminology, classification, and diagnostic approaches. Recommendations are provided
130 which can aid in the reduction of the observed heterogeneity.

131 Methods

132 Previously published guidelines have provided recommendations for the diagnosis and
133 management of adenomyosis, based on the highest quality evidence available (Dason et al.,
134 2023b, Harada et al., 2023). However, these guidelines did not address the technical specifics
135 of surgical interventions. Consequently, the European Society of Human Reproduction and
136 Embryology (ESHRE), the European Society for Gynaecological Endoscopy (ESGE), and the
137 World Endometriosis Society (WES) convened a working group to formulate a series of
138 practical recommendations concerning the classification, diagnosis of adenomyosis in a first
139 Good Practice Recommendations paper, as well as its clinical presentation, surgical and non-
140 surgical management and medically assisted reproduction in a second one. This document
141 represents the initial instalment in a series of practical recommendations aimed at detailing
142 the technical aspects of managing adenomyosis, encompassing terminology, classification,
143 diagnosis and treatment modalities, including surgical interventions. It is intended to
144 complement the existing evidence-based guidelines on the clinical management of
145 adenomyosis.

146 The current document was developed following the manual for development of ESHRE Good
147 Practice Recommendations (Vermeulen et al., 2019). The working group comprised experts
148 in reproductive medicine, reproductive surgery, and adenomyosis, ensuring diversity in
149 clinical expertise as well as geographical representation. A comprehensive literature search
150 was conducted using PUBMED and the Cochrane library, including articles published up to
151 September 11, 2025. The screening process involved reviewing all titles and abstracts to
152 identify pertinent studies, followed by a detailed examination of the full-text articles. Progress
153 was regularly reviewed in online meetings.

154 Results

155 Histopathology

156 Histopathology is to date considered the gold standard for the diagnosis of adenomyosis.
157 However, there is significant variability in terminology and diagnostic criteria used by
158 pathologists (McCaughey et al., 2025), as illustrated below.

159 Histopathological definition of adenomyosis

160 Adenomyosis is characterised by the presence of endometrial glands and stroma within the
161 myometrium, which may be accompanied by adjacent myometrial hyperplasia. The borders
162 of the endometrial-myometrial junction in adenomyosis are not distinctly linear, as the
163 endometrial glands from the basal layer of the endometrium penetrate the myometrium in a
164 manner akin to rhizomes. Furthermore, these borders are not clearly demarcated by an
165 intervening basal membrane, as is typical in other tissues. Consequently, it is common to
166 observe endometrial glands beneath what is traditionally identified as the endo-myometrial
167 junction in histological specimens (Antero et al., 2020). This has led to various descriptions

168 and proposals regarding the requisite depth of myometrial penetration by endometrial tissue
169 to qualify as adenomyosis.

170 **Diagnostic criteria for adenomyosis on histology**

171 The histopathological diagnosis of adenomyosis is predominantly based on the histological
172 identification of endometrial glands and/or stroma embedded within the myometrium,
173 specifically located at least 2.5 mm beyond the endometrial-myometrial junction, as indicated
174 in several studies (Acar et al., 2016, Bazot et al., 2001, Dakhly et al., 2016, Kara Bozkurt et al.,
175 2017). Due to the poorly defined nature of the endometrial-myometrial borders, more
176 nuanced definitions have been proposed by other researchers. For example, McCaughey *et*
177 *al.* (2022) suggested identifying endometrial glands and stroma at least 2-2.5 mm below the
178 endometrial-myometrial interface (McCaughey et al., 2022), and El Kattan *et al.* (2010)
179 proposed a range of 2-3 mm, also noting the occurrence of potential reactive hyperplasia of
180 the smooth muscle (ElKattan et al., 2010).

181 Alternative criteria focus on the relative depth of invasion into the myometrium. Ferenczy
182 (1998) used the relative invasion of the myometrium as a defining criterion for adenomyosis
183 (Ferenczy, 1998). Another method quantifies the invasion in terms of microscopic fields:
184 adenomyosis was defined as the presence of endometrial glands and stroma more than one
185 high-power microscopic field deeper than the endometrial-myometrial junction (Brosens et
186 al., 1995, Chiang et al., 1999, Reinhold et al., 1995, Reinhold et al., 1996). Others employed
187 low-power magnification, suggesting that endometrial glands and stroma located in at least
188 one field (da Silva et al., 2021) or half a field (Atri et al., 2000, Vercellini et al., 1998) from the
189 endo-myometrial junction qualify as adenomyosis. Another perspective considered
190 adenomyosis to be present if endometrial glands or stroma were found deeper than one
191 medium-power field (or >2 mm) from the junction (Dueholm et al., 2001). It needs to be
192 pointed out that the terminology of “high and low-power field” are ill-defined and not
193 standardised.

194 Additionally, the presence of surrounding muscle hypertrophy, along with multiple patches
195 or diffuse areas of endometrial glands and/or stroma within the myometrium, was noted as
196 an ancillary feature for the definition of adenomyosis by some authors (Atri et al., 2000,
197 Ferenczy, 1998, Vercellini et al., 1998).

198 Despite the variation in descriptions and histological criteria for definition of adenomyosis,
199 there appears to be a consensus on a minimum depth of myometrial invasion. A depth of 2 –
200 2.5 mm is generally accepted as a valid criterion.

201 **Recommendations**

**In histopathology, commonly used thresholds vary (2–3 mm or field-based definitions);
therefore, studies should explicitly report the threshold and sampling approach used.**

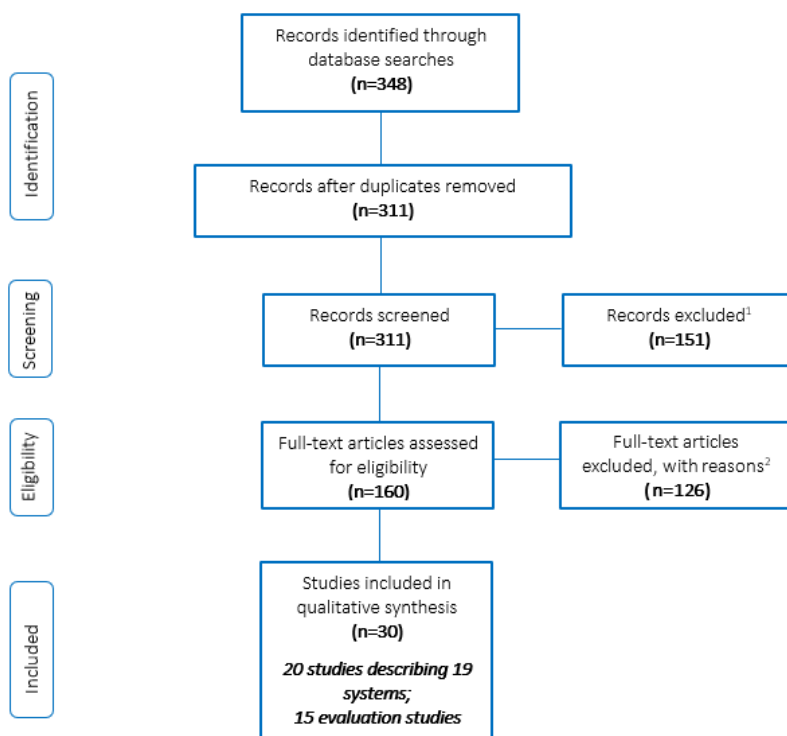
In histopathological analysis, the use of high-, medium- and low-power fields is not standardised terminology, and should be avoided in describing adenomyotic lesions. Rather, invasion depth should be reported in standardised metric units.

202

203 Classification/categorisation systems

204 The literature review retrieved 348 references. After removing duplicates, 160 full articles
 205 were assessed, of which 126 articles were excluded for the following reasons: full-text article
 206 could not be retrieved (n=9), not written in English (n=13), inappropriate publication types
 207 (case report, expert opinion, editorial) (n=43) and relevant patients and/or
 208 intervention/outcomes are not assessed (patients not diagnosed with adenomyosis or not a
 209 proposal for or validation of a classification system) (n=61). Thirty articles were included for
 210 either describing a classification, staging or reporting system in adenomyosis (n=20 studies
 211 describing 19 systems) or evaluating one (n=15) (Figure 1). The systems described in this
 212 paper have been published as reporting, classification or staging systems for adenomyosis,
 213 even though some were developed for diagnosis or subgrouping rather than classification.

214 Table 1 provides an overview of the 19 reporting, classification or staging systems identified
 215 in the literature and included in this report. Table 2 provides an overview of the criteria for
 216 the reporting or classification of the different systems described in Table 1. The fifteen studies
 217 reporting an evaluation of the different systems are listed in Table 3.



218

219 **Figure 1: PRISMA flow diagram for the selection of studies describing adenomyosis classification, staging and reporting**
 220 **systems.**

221 From the existing 20 proposals, 17 are reporting systems, 18 are classification systems, and
222 only two are staging systems. Each system employs distinct criteria.

223 It is evident that the diagnostic method used for documenting adenomyosis plays a crucial
224 role in the different proposals. Specifically, nine proposals are based on histology, five on
225 ultrasound, and six on MRI. This distribution is influenced by the historical evolution of
226 imaging modalities and the intended purpose of each proposal. Notably, the intended
227 purposes of these proposals vary; most are designed for diagnosis and categorization, while
228 others aim to correlate categories with symptoms, surgical difficulty, and/or treatment
229 outcomes.

Draft for pre-review

230 Table 1: Historical overview of adenomyosis reporting and/or classification systems.

Reference	Diagnostic modality used	Type of system			Intended purpose						Details	
		Reporting/ Descriptive	Classifica tion/ categoris ation	Staging	Diagnosis	Prediction of symptoms				Relation to treatment		
						Prediction of pain/ QoL	Prediction of AUB	Prediction of conception	Prediction of surgical difficulty	Pre - treatment assessment and selection		Response prediction
(Kobayashi and Matsubara, 2020)	MRI	√	√		√					√	√	Classification proposal based on MRI
(Bazot and Darai, 2018)	MRI	√	√		√					√	√	Classification proposal to distinguish between subtypes of adenomyosis with a potential relation for therapeutic strategy
(Gong et al., 2017)	MRI		√							√ HIFU	√ HIFU	The relationship between MRI features and response to HIFU treatment
(Dashottar et al., 2015)	MRI		√		√						√ Mirena	MRI findings of suspected adenomyosis
(Kishi et al., 2012)	MRI	√	√									Disclose characteristics and pathophysiology that are specific to subtypes of adenomyosis
(Gordts et al., 2008)	MRI	√	√		√	√	√	√				Establishing uniformity in both the terminology and classification of adenomyotic lesions
(Sinha et al., 2022)	USS		√		√							Sonological classification and scoring system for adenomyosis based on topography, type, size and extent.
(Exacoustos et al., 2020)	USS	√	√	√	√	√	√	√				
MUSA (Van den Bosch et al., 2019)	USS	√	√		√	√	√	√				A uniform reporting system for ultrasound findings of adenomyosis / DELPHI CONSENSUS, later revised in MUSA 2022 (Harmsen et al., 2022).
(Lazzeri et al., 2018)	USS	√	√	√		√	√	√	√	√		Adenomyosis mapping system based on USS / New schematic scoring system to assess the severity based on the extension of the disease considering all possible ultrasound adenomyosis features
MUSA (Van den)	USS	√			√					√		Consensus on Ultrasound finding for reporting uterine masses and adenomyosis

Bosch et al., 2015)												
(Grimbizis et al., 2014)	Histology	√	√			√ After surgery	√ After surgery	√ After surgery		√ Surgery	√ Surgery	Classification of adenomyosis to evaluate effect of treatment
(Pistofidis et al., 2014)	Histology	√	√		√				√	√ Surgery		Distinct types of uterine adenomyosis based on laparoscopic and histopathologic criteria
(Hulka et al., 2002)	Histology	√	√		√					√		Can TVUS characteristics indicate the extent of adenomyosis/ diagnostic accuracy of TVUS
(Sammour et al., 2002)	Histology	√	√			√	√					Correlation between the commonly associated symptoms and the presence, depth of penetration, and spread of adenomyosis.
(Levgur et al., 2000)	Histology	√	√			√	√			√	√	Correlation of pregnancy terminations with adenomyosis / Correlation of symptoms (menstrual bleeding and pain) with histology
(Siegler and Camilien, 1994)	Histology	√	√									
(Nishida, 1991)	Histology	√	√		√	√	√			√		The relationship between histologic findings of adenomyosis and onset of dysmenorrhea.
(Bird et al., 1972)	Histology	√	√		√							Categorisation of adenomyosis according to the depth of penetration and degree of involvement (glands per field)
(Sampson, 1921)	Histology	√	√		√							First attempt for histopathological classification, categorizing the disease into three groups according to the extent and the configuration of the lesions into the myometrium

231 HIFU: high intensity focussed ultrasound, UAE: uterine artery embolization, USS: ultrasound

232 Table 2: Criteria for diagnosis and for the reporting and/or classification of adenomyosis

Reference	Diagnostic modality used	Criteria for diagnosis	Type of system		Criteria for reporting / classification
			Reporting/ Descriptive	Classification/ Categorization	
(Kobayashi and Matsubara, 2020)	MRI	Intra-myometrial high-signal-intensity (SI) spots Thickening of the junctional zone (JZ) Asymmetry of the uterus	√	√	Affected area: Internal / External Pattern: Diffuse / Focal Size / Volume: <1/3, <2/3, >2/3 of myometrium Location: Anterior, Posterior, Left Lateral, Right Lateral, or Fundal
(Bazot and Darai, 2018)	MRI	US: MUSA Criteria MRI: <ul style="list-style-type: none"> T2 high-intensity myometrial foci embedded within the myometrium, Zonal anatomy of the uterus on T2-weighted imaging (WI) Smooth muscle cell hypertrophy / ill-defined T2-low SI 	√	√	Affected area <ul style="list-style-type: none"> Internal: focal / superficial / diffuse Adenomyomas: solid / cystic / submucosal / subserosal External: posterior / anterior
(Dashottar et al., 2015)	MRI	<ul style="list-style-type: none"> Diffuse or focal widening of the JZ on T2 WI. Poor definition of JZ borders or indistinct margins with the myometrium. High-SI foci within the JZ on T2-and/or T1-weighted images. JZ thickness with poor definition of borders with highSI foci on T1W and/or T2W 		√	Pattern: Diffuse / Focal
(Kishi et al., 2012)	MRI	<ul style="list-style-type: none"> Ill demarcated low-/mid-low intensity mass within the asymmetrically bulged uterine wall by T2-weighted MRI High-SI within the adenomyosis on T1- and T2-weighted images Teardrop deformity of the rectum 	√	√	Affected area <ul style="list-style-type: none"> Intrinsic / Extrinsic / Intramural / Indeterminate Location: Anterior / Posterior
(Gordts et al., 2008)	MRI		√	√	Pattern / Type / Size <ul style="list-style-type: none"> JZ hyperplasia: JZ thickness measuring (8-12 mm) on T2-weighted images. Partial or diffuse type

					<ul style="list-style-type: none"> • Adenomyosis JZ thickness ≥ 12 mm; high-SI myometrial foci; involvement of the outer myometrium: $< 1/3$, $< 2/3$, $> 2/3$ • Adenomyoma Myometrial mass with indistinct margins of primarily low-SI on all MR sequences. Retrocervical, retrovaginal, fallopian tube and bladder types
LAD (Sinha et al., 2022)	USS	<ul style="list-style-type: none"> • Topography: anterior, posterior, left lateral, right lateral or fundal • Type: localised, diffuse, adenomyoma, mixed • Size: largest diameter of the largest lesion was measured and in case of diffuse lesion, uterine size was measured • Extend: superficial, deep or full thickness 		√	<p>Step 1: diagnosis based on MUSA criteria</p> <p>Step 2: classification into different types</p> <p>Step 3: score based on the type, size and extent.</p>
MUSA (Harmsen et al., 2022)	USS	<ul style="list-style-type: none"> • Direct diagnostic findings: Myometrial cysts / Hyper echogenic islands / Echogenic sub endometrial lines and buds • Indirect diagnostic findings: Globular uterus / Asymmetrical myometrial thickening / Fan-shaped shadowing / Trans lesional vascularity / Irregular or Interrupted JZ 	√	√	No revision
(Exacoustos et al., 2020)	USS				USS diagnostic criteria / Classification into diffuse, focal adenomyosis, and the adenomyomas / Scoring based on USS criteria
MUSA (Van den Bosch et al., 2019)	USS	<ul style="list-style-type: none"> • Globular uterus • Asymmetrical myometrial thickening • Myometrial cysts • Hyper echogenic islands • Fan-shaped shadowing • Echogenic sub endometrial lines and buds • Trans lesional vascularity • Irregular or Interrupted JZ 	√	√	<ul style="list-style-type: none"> • Step 1; Diagnosis • Step 2; Location: Anterior, Posterior, Left Lateral, Right Lateral, or Fundal • Step 3; Differentiation (pattern): Focal (including adenomyomas) / Mixed / Diffuse • Step 4; Consistency: cystic / non-cystic • Step 5; Uterine layer involvement (affected area): inner JZ / middle / outer • Step 6; Extend: Mild ($< 25\%$) / Moderate (25-50%) / Severe ($> 50\%$) • Step 7: Size of lesion

(Lazzeri et al., 2018)	USS		√	√	<ul style="list-style-type: none"> • Classification based on Pattern: Diffuse / Focal / Adenomyoma • Staging based on: Uterine wall thickness / Locations involvement / Thickening of the inner myometrium (JZ) / Number of lesions / Size of lesions
MUSA (Van den Bosch et al., 2015)	USS	Differential diagnosis from myomas <ul style="list-style-type: none"> • Globular enlarged uterus • Asymmetrical myometrial thickening • Myometrial asymmetry • Ill defined lesion (exception adenomyoma) • Myometrial cysts / Hyper echogenic islands / Echogenic sub endometrial lines and buds • Fan-shaped shadowing • Trans lesional vascularity • Irregular or Interrupted JZ 	√		<ul style="list-style-type: none"> • No classification / only reporting of presence adenomyosis
(Grimbizis et al., 2014)	Histology		√	√	Pattern <ul style="list-style-type: none"> • Diffuse • Focal: Adenomyoma / Cystic • Polypoid: Typical / Atypical • Other: Endocervical / Retroperitoneal
(Pistofidis et al., 2014)	Histology		√	√	Pattern: laparoscopic and histopathologic criteria <ul style="list-style-type: none"> • Diffuse: The entire myometrium has a spongiform texture. • Sclerotic: lesion with off-white fibrotic appearance • Nodular: a well-defined spherical lesion • Cystic: adenomyotic cysts
(Hulka et al., 2002)	Histology	Presence of sub endometrial glands at least one-half to one low-power field (2–3 mm) below the endometrial junction with the myometrium.	√	√	Degree of involvement / Extend of penetration <ul style="list-style-type: none"> • Mild adenomyosis: only microscopic foci of adenomyosis present or only the inner one third of the myometrium was involved • Focal disease: focal adenomyomas • Severe or diffuse adenomyosis disease extending into the outer two thirds of the myometrium and up to gross involvement of the entire uterus
(Sammour et al., 2002)	Histology		√	√	Depth of penetration / density of adenomyotic foci (secondary characteristic) <ul style="list-style-type: none"> • Group A: up to 25%

					<ul style="list-style-type: none"> • Group B: 26–50% • Group C: 51–75%, • Group D: >75%.
(Levgur et al., 2000)	Histology	Endometrial glands or stroma within the myometrium at a depth of 2.5 mm or more	√	√	<p>Depth of penetration / Density of adenomyotic foci (secondary characteristic)</p> <ul style="list-style-type: none"> • Deep: >80% • Intermediate: 40–80% • Superficial: <40%
(Siegler and Camilien, 1994) From Zymberdikas et al 2020 and Vercelini 2006	Histology	Infiltration of the myometrium \geq 2.5 mm below the endo-myometrial border	√	√	<ul style="list-style-type: none"> • Depth of penetration: Grade1: Inner one-third / Grade 2: Two-thirds / Grade 3: Entire myometrium • Degree of the involvement: Mild: 1–3 adenomyotic foci per LPF / Moderate 4–9 foci per LPF / Severe: \geq 10 foci per LPF • Affected area (disease configuration): Diffuse / Nodular (focal)
(Nishida, 1991)	Histology		√	√	<p>(1) Localization of adenomyosis / (2) thickness of uterine muscle / (3) number of islands of adenomyotic lesions (including glands and stroma) / (4) number of glands / (5) mean number of glands contained in one island of adenomyosis / (6) distance between surface endometrium and the deepest portion of islands in the invaded tissue / (7) ratio of the depth of adenomyosis to uterine muscle thickness / (8) status of adenomyotic lesions; proliferative or secretory phase / (9) presence or absence of hemorrhage in adenomyotic lesions</p>
(Bird et al., 1972)	Histology	Endometrial glands and stroma > 1 LPF below the basal endometrium (endo-myometrial border)	√	√	<ul style="list-style-type: none"> • Depth of penetration: Grade I: Sub-basalis (up to one LPF below the “basal” endometrium) Grade II Penetration up to mid myometrium Grade III Penetration beyond mid myometrium • Degree of involvement (glands per field): Slight 1–3 (few) adenomyotic foci per LPF / Moderate 4–9 (several) foci per LPF / Severe: \geq 10 (many) foci per LPF
(Sampson, 1921)	Histology		√	√	<p>Extent and configuration of the lesions</p> <ul style="list-style-type: none"> • Invasion of the uterine wall by the mucosa lining (invasion from within the uterus) • Growth arising from the serous surface by endometrial tissue from an endometrial cyst (invasion from without the uterus) • Lesion arising from misplaced endometrial tissue in the uterine wall (adenomyoma)

234 Table 3: Overview of replication, validation and clinical value of published systems.

235 A: Studies using the MUSA classification system

Diagnostic accuracy for fertility-sparing treatment	Staging	Prediction of difficulty of surgery	Prediction of pain/QoL	Prediction of conception	Inter-observer agreement	Aim of the study	Sample size	Age mean (range or SD)	Population source	Adenomyosis definition	Main results	Reference
					√	Inter-rater agreement for diagnosing adenomyosis on USS by revised MUSA criteria	96	45.4±11.5	Single center	USS	An inter-rater reliability analysis showed that there was 72.9% agreement ($\kappa = 0.45$, 95% CI 0.27 to 0.63; $P < .001$). There were higher levels of inter-rater agreement for the presence or absence of myometrial cysts (91.7%) over other MUSA criteria components.	(Dosunmu et al., 2025)
					√	Inter- and intra-rater agreement for diagnosing adenomyosis on USS by revised MUSA criteria.	68	NR	Single center	USS	Fair level of inter-rater agreement ($\kappa = 0.28$, 95% CI 0.06-0.48). Among the direct features assessed, both myometrial cysts and hyperechogenic islands exhibited a fair level of agreement, ($\kappa = 0.21$, 95% CI -0.00-0.42 and $\kappa = 0.25$, 95% CI 0.01-0.47, respectively). However, subendometrial lines and buds demonstrated a poor level of agreement. Intra-observer agreement: the prevalence of adenomyosis after the first review and second review was 78% and 68%, respectively,	(Kadam et al., 2025)
					√	Inter-rater agreement for MUSA criteria for the	196	49 (34-80)	Single center	USS	Inter-rater agreement for direct signs varied between 87.7% (myometrial cysts)	(Yavuz et al., 2024)

						diagnosis of adenomyosis on USS						and 94.3% (hyperechogenic islands). For indirect signs, inter-rater agreement varied between 65.8% (irregular JZ) and 92.3% (globular uterus).	
				√		Inter-rater agreement for diagnosing adenomyosis on MRI and USS and for the individual imaging features	51	NR	Single center	MRI USS		The inter-rater agreement was higher for TVUS ($\kappa=0.42$, [0.417–0.422]) than for MRI ($\kappa = 0.28$, [0.28–0.287]). The inter-rater agreement for most individual imaging features was higher for MRI than for TVUS. Moreover, MRI showed clearly higher reliability than TVUS for continuous variables.	(Andersson et al., 2023)
				√		Effect of adenomyosis on reproductive outcomes in donor cycles	100	41.0 (35.5-44)	Single center	USS		The presence of ≥ 1 features (irregular/interrupted JZ and/or another feature) of adenomyosis was not associated with a change in the odds of live birth (OR 0.67, 95% CI 0.10–4.45; the same was observed for our secondary outcomes of clinical pregnancy and miscarriage. Specific features of adenomyosis, as well as feature location, were not associated with any change in outcome measures.	(Dason et al., 2023a)
		√				Evaluate accuracy of combined transvaginal USS and strain ratio elastography	79	45 \pm 4.9	Single center	USS, shear wave elastography, confirmation by histology		The statistical significance of each USS feature included in the study according to the presence or absence of adenomyosis at the histological examination. Significantly higher mean	(Sāsāran et al., 2021)

											and max strain ratio values in patients with histologically confirmed adenomyosis.	
√				√	√	(a) To assess the prevalence of USS markers of adenomyosis, (b) inter- and intra-rater agreement of 3D-USS assessment of adenomyosis, (c) to evaluate USS features of adenomyosis with respect to pregnancy outcome after sET of an euploid blastocyst.	638	37.1±5.2	Single center	Ultrasound, presence of ≥1 marker	(a) The prevalence of USS markers was low, no maker had a prevalence > 15%. (b) The overall inter-rater agreement in 3D USS was poor ($\kappa=0.23$). even when reviewers agreed regarding the diagnosis of adenomyosis, they agreed on the specific USS markers present in only 11.1% of cases. Intra-rater agreement was moderate ($\kappa=0.58$); reviewers agreed with their original assessment upon repeat evaluation 85.6% of the time. (c) no difference in clinical pregnancy, miscarriage rate or live birth rate	(Neal et al., 2020)
					√	Interrater agreement between expert and nonexpert raters in diagnosing adenomyosis by real-time 2D TVUS and offline 3D TVUS	96	45.3 (44-46)	Single center	2D and 3D TVUS, confirmation by histology	Diagnosis of adenomyosis with real-time 2D TVUS showed good inter-rater agreement ($\kappa = 0.69$), and the agreement was even better in the last period of patients ($\kappa = 0.74$). Diagnosis of adenomyosis with offline 3D TVUS showed poor inter-rater agreement ($\kappa = 0.21$) for individually recorded 3D volumes but slightly better inter-rater agreement ($\kappa = 0.40$) for expert-recorded 3D volumes, which also had	(Rasmussen et al., 2019b)

												better image quality (P < .05).	
					√	Intra- and inter-rater agreement in the reporting of benign myometrial lesions	30	45.3 (44-47)	Single center	USS, confirmation by histology		Poorly defined lesions and individual features showed low agreement, even among highly experienced raters. Additionally, in a few cases. the raters did not consider the poorly defined lesion as being adenomyosis, suggesting that how raters interpret the term “poorly defined” is highly subjective.	(Rasmussen et al., 2019a)
√						Develop a prediction model for the probability of adenomyosis	95	43.5±4.9	Single center	USS, confirmation by histology		LASSO analysis using these 13 variables yielded 9 variables and (unstandardized) β values. The β intercept value was – 1.11. The AUC of this model was 0.86 (95% CI 0.79–0.94). The optimal cutoff for predicting the probability of adenomyosis was 0.56, which gave a sensitivity of 85% and a specificity of 78%.	(Tellum et al., 2018)

236

237 B: Studies using a non-MUSA classification system

Diagnostic accuracy for fertility-sparing treatment	Staging	Prediction of difficulty of surgery	Prediction of pain/QoL	Prediction of conception	Inter-observer agreement	Aim of the study	Most important classification features	Sample size	Age mean (range or SD)	Population source	Adenomyosis definition	Main results	Reference
			√			Association between USS features of adenomyosis and the severity	asymmetrical myometrial thickening, myometrial cysts, linear striations,	718	38 (30-43)	Single center	USS, confirmation by histology	There was an independent statistically significant association between the USS features of adenomyosis and the	(Naftalin et al., 2016)

						of menstrual pain	parallel shadowing, adenomyomas, hyperechoic islands and an irregular endometrial-myometrial junction on either B-mode or 3D imaging					severity of menstrual pain. There was also a significant positive correlation between the number of USS features of adenomyosis and NRS score.	
			√		√	Correlation between clinical and pathologic characteristics of patients and adenomyosis subtypes	6 subtypes	678	43.7±5.4	Single center	MRI	The classification system by Kobayashi 2020 was best fitted classification system of adenomyosis severity from different classification criteria	(Tang et al., 2024)
√	√		√	√		Relation between MRI classification, clinical symptoms and corresponding therapeutic efficacy	4 types: intrinsic, extrinsic, intramural, penetrating	468	39.0±6.5	Single center	MRI	There was no significant difference in infertility incidence between intrinsic and intramural subtypes but both had lower rates than the extrinsic and penetrating subtypes. The total effective rate of progesterone treatment in intrinsic subtype was significantly lower than that in the extrinsic subtype. The effective rate of penetrating subtype was higher than that of intrinsic subtype.	(Han et al., 2023)
	√		√	√		To correlate type and degree of adenomyosis	5 types: diffuse (inner/outer), focal	108		Multi-center	USS	In patients trying to conceive, the presence of USS findings of focal	(Exacoustos et al., 2020)

						to symptoms and fertility	(inner/outer), adenomyoma					disease was associated with a higher percentage of infertility compared to diffuse disease. Tendency, although not significant, towards a higher percentage in patients with severe adenomyosis. compared to mild.	
√	√				√	(a) Inter-observer reproducibility of the USS adenomyosis mapping system (b) to define the type and extension of adenomyosis	3 types: diffuse, focal, or adenomyoma and a score of 1-4 for each type	70	37.8±7.2	Single center	USS, confirmation by histology	The level of agreement between both observers for the different diagnostic criteria was substantial ($\kappa=0.61$ to 0.80) to almost perfect ($\kappa=0.81$ to 0.99). The total score number, reflecting the total extent of the disease showed almost perfect agreement ($\kappa=0.969$).	(Lazzeri et al., 2018)

238

239 Despite differences in diagnostic methods and intended purposes, the criteria for reporting
240 and classifying adenomyosis share several similarities. Common criteria include the affected
241 myometrial layer (inner, middle, or outer), the location of the adenomyosis (anterior,
242 posterior, fundal, or lateral), the pattern (focal or diffuse), and, in some cases, whether the
243 glandular or muscular element is more prominent.

244 Several studies attempted to combine histologic and imaging findings into a reproducible
245 classification with correlation to clinical manifestation of the disease. Bird *et al.* was the first
246 to present such a classification based on measuring the depth of myometrial invasion using
247 histologic specimens after hysterectomy (Bird *et al.*, 1972). Later on followed a classification
248 scheme based on invasion with three distinct categories: deep (>80%), intermediate (40–
249 80%), and superficial (<40%) (Levgur *et al.*, 2000). Advances on imaging techniques resulted
250 in more complex classification schemes based on specific features like uterine size, detailed
251 extent of disease, configuration of lesions (diffuse, focal, and nodular), and degree of
252 junctional zone involvement (Exacoustos *et al.*, 2020). Lazzeri in his prospective study
253 evaluated the reproducibility of an MRI schematic mapping system based on the degree of
254 myometrial involvement, junctional zone thickening, and size of the lesion (Lazzeri *et al.*,
255 2018). Although the method was significantly accurate to the classification as focal, diffuse
256 with or without JZ involvement, no correlation with histology or clinical symptoms has been
257 evaluated. Another prospective observational study in 100 women undergoing hysterectomy
258 evaluated a prediction model for diagnosing adenomyosis by using preoperatively 2-D and 3-
259 D ultrasound, clinical questionnaires (Tellum *et al.*, 2018) and histopathology results. Authors
260 reported sensitivity of 85% and specificity of 78% for diagnoses and significant correlation
261 with symptoms, but this model needs a lot of clarifications and external validation.

262 The main disadvantage of the majority of studies is the fact that they have used a
263 retrospective method of correlating symptoms, imaging and histology. Retrospective analysis
264 of routine histology assessments implies no systematic investigation of the myometrium
265 regarding the diagnosis of adenomyosis. In addition, given the high comorbidity of
266 endometriosis, the severity of chronic pelvic pain due to adenomyosis is difficult to quantify.

267 These similarities in classification and reporting systems suggest a potential for
268 standardisation in the classification and reporting of adenomyosis, which could enhance
269 diagnostic accuracy and treatment planning. However, to date there is no universally
270 accepted classification system for adenomyosis.

271 Terminology for adenomyosis

272 Understanding the nuanced features indicative of adenomyosis on imaging is pivotal for
273 accurate diagnosis, especially for individuals who desire uterine preservation and/or fertility.
274 Terminology associated with each characteristic enhance clarity and facilitate effective
275 communication among healthcare professionals. As technology advances, a comprehensive

276 grasp of both MRI and ultrasound findings ensures a thorough assessment of adenomyosis,
277 guiding clinicians toward tailored and informed management strategies.

278 **Ultrasound**

279 The Morphological Uterus Sonographic Assessment (MUSA) group specified that the
280 junctional zone (JZ) on ultrasound is synonymous for the inner myometrium (Van den Bosch
281 et al., 2015). The JZ is seen as a hypoechoic halo within the myometrium, surrounding the
282 endometrial cavity. The differences in echogenicity between the uterine layers might be
283 explained by differences in vascularity or in tissue density. However, given that the JZ is
284 inconsistently depicted between imaging modalities and not always visible, it has been
285 proposed that the JZ, the endometrial-myometrial junction, and the inner myometrium
286 should not be used synonymously (Harmsen et al., 2023).

287 The MUSA statement is a consensus statement on terms, definitions and measurements that
288 may be used to describe and report the sonographic features of adenomyosis on ultrasound
289 (Van den Bosch et al., 2015). These criteria were later revised, making the distinction between
290 direct and indirect features of adenomyosis (Harmsen et al., 2022).

291 *Direct features of adenomyosis*

292 *Myometrial cysts*

293 These appear as rounded or oval cystic spaces of any size within the endo-myometrium. The
294 cystic contents may be anechoic or, of low-level echogenicity, of ground-glass appearance but
295 rarely of mixed echogenicity. A hyperechoic rim representing endometrium may be seen
296 but is not obligatory. Large myometrial cysts distinctly located laterally and under the
297 insertion of the round ligament and interstitial portion of the tube, represent an accessory
298 cavitated uterine malformation (ACUM) and should be distinguished from adenomyosis
299 (Timmerman et al., 2024).

300 *Hyperechoic islands*

301 These are hyperechoic areas within the myometrium. They may be regular, irregular or ill-
302 defined and represent ectopic endometrial-like tissue or haemorrhagic content.

303 *Echogenic subendometrial lines and buds*

304 Hyperechoic subendometrial lines or buds may be observed disrupting the JZ.
305 Hyperechoic subendometrial lines are (almost) perpendicular to the endometrial cavity
306 and are in continuum with the endometrium. These should be distinguished from small
307 vessels crossing the inner myometrium. Subendometrial buds are in continuity with the
308 endometrium and more round.

309 In research studies in literature, the term “echogenic striations” is sometimes used to refer
310 to subendometrial lines.

311 *Indirect features of adenomyosis*

312 *Globular uterus*

313 A globular uterus is present when the myometrial serosa diverges from the cervix in at least
314 two directions (anterior/posterior/lateral), instead of following a trajectory parallel to the
315 endometrium. The shape of the uterus should be assessed by pattern recognition.

316 In research studies in literature, the terms “enlarged globular fundus uterus” or “enlarged
317 spherical uterus” are sometimes used interchangeably instead of globular uterus. However,
318 enlarged is not a criterion for globular. In addition, globular uterus does not refer to the
319 fundus only, it starts from the cervix.

320 The measurement of a globular uterus as an indirect feature of adenomyosis showed high
321 heterogeneity as the presence of fibroids may also explain the globular shape of the uterus
322 (Harmsen et al., 2022).

323 *Asymmetrical myometrial thickening*

324 When the difference in thickness between the anterior and the posterior myometrial wall
325 appears significantly different, asymmetrical thickening is present. There is no evidence-
326 based cut-off to define asymmetry. A cut-off of ≥ 5 mm difference in myometrial wall
327 thickness, or a certain ratio between the anterior and posterior wall thickness should only be
328 used as a rule of thumb.

329 In research studies in literature, “asymmetrical walls” or “asymmetrical corpus myometrium”
330 is sometimes used to indicate asymmetrical myometrial thickening.

331 *Fan-shaped shadowing*

332 The presence of hypoechogenic stripes behind a myometrial lesion, sometimes alternating
333 with linear hyperechogenic stripes (echo enhancement). This feature is best assessed in
334 grayscale images without the use of colour Doppler.

335 In research studies in literature, “fan-shaped echo” or “radial shadow” is sometimes used
336 instead of fan-shaped shadowing.

337 *Translesional vascularity*

338 Vascularity within the lesion should only be assessed when a myometrial lesion is present.
339 Transmyometrial blood flow is normal and not an indicator of adenomyosis in the absence of
340 direct signs. It reflects the helical branches of the arcuate arteries that run from the outer
341 myometrium to the uterine cavity. However, in the presence of an adenomyoma or diffuse
342 adenomyosis, these vessels pass through the lesion, while in the case of fibroids, they are
343 pushed aside and form a circular pattern around the lesion.

344 *Irregular JZ*

345 The JZ can be irregular because of cystic areas, hyperechogenic dots, and hyperechogenic
346 buds and lines. Ultrasound measurement of JZ thickness has currently no role in clinical
347 practice.

348 *Interrupted JZ*

349 There is interruption of the JZ when a proportion of the JZ cannot be visualized on either 2D
 350 or 3D transvaginal ultrasound in any plane. An uninterrupted JZ means that the JZ is clearly
 351 seen in all planes on 2D ultrasound or in all planes on 3D ultrasound and is a negative predictor
 352 for adenomyosis in absence of other direct signs. The assessment of the JZ in 3D has a low
 353 inter-rater reproducibility and a low specificity for adenomyosis

354 Recommendations

The adenomyosis working group recommends following the revised MUSA criteria to diagnose adenomyosis by ultrasound.

The adenomyosis working group recommends differentiating between direct and indirect features to report on the diagnosis of adenomyosis.

Direct features included myometrial cysts, hyperechogenic islands and echogenic subendometrial lines and buds. Globular uterus, asymmetrical myometrial thickening, fan-shaped shadowing, translesional vascularity, irregular JZ and interrupted JZ are considered indirect features of adenomyosis.

355

356 **MRI**

357 MRI (magnetic resonance imaging) plays a crucial role in diagnosing adenomyosis due to its
 358 ability to visualize the different layers of the uterus distinctly (Balasubramanya R and C.,
 359 2025). Adenomyosis appears as ill-demarcated areas of low-signal intensity (SI) on T2-
 360 weighted images, focal thickening of the JZ, or invasion/interruption of the EMJ by high-SI
 361 areas. High-SI myometrial foci can be observed on T2-weighted and sometimes on T1-
 362 weighted images, representing haemorrhagic foci aiding in the identification of adenomyotic
 363 lesions.

364 *Direct features of adenomyosis*

365 *Foci of Increased Signal Intensity (SI) in JZ*

366 High-SI foci in the JZ are also expressed as "hyperintense JZ foci" or "signal alterations
 367 suggestive of adenomyosis". On T2-weighted images, punctuate high signal intensity foci can
 368 be found in the JZ. Corresponding high signal on T1-weighted images is less frequently
 369 observed but highly suggestive of adenomyosis.

370 In research studies in literature, "Intense JZ Signal Foci" or "Signal-Enhanced JZ Areas" is
 371 sometimes used instead of foci of increased SI in JZ.

372 *Finger like Indentations into JZ*

373 Finger like indentations, also referred to as myometrial tunnels or sulci, manifest as finger like
 374 projections or invaginations extending from the endometrium into the myometrium (Tellum
 375 et al., 2019a). On T2W images, they appear as high signal intensity linear striations extending
 376 from the endometrium into the myometrium as a result of direct invasion of the myometrium
 377 and result in pseudo-widening of the endometrium (Reinhold et al., 1999).

378 In research studies in literature, “JZ Cystic Configurations” or “Finger like JZ Impressions” is
379 sometimes used instead of Finger like indentations into the JZ.

380 *Myometrial cysts*

381 Myometrial (micro) cysts are a distinctive MRI finding, indicative of adenomyosis (Celli et al.,
382 2022).

383 In research studies in literature, “Uterine Cystic Lesions”, “Myometrial Fluid-Filled Pockets”
384 or “Cystic lesions in the myometrium” is sometimes used instead of myometrial cysts.

385 *Indirect features of adenomyosis*

386 The JZ on MRI, a key feature in pelvic MR imaging, represents the inner myometrium. It is
387 typically visualized on MRI as a low T2 SI layer beneath the endometrium. MRI and ultrasound
388 examinations reflect the JZ differently. Harmsen *et al.* (2023) explored the discrepancies and
389 diagnostic challenges in defining and visualizing the uterine JZ across MRI, transvaginal
390 ultrasound (TVUS), and histology, particularly in the context of adenomyosis (Harmsen et al.,
391 2023). This manuscript highlights that while MRI provides a distinct, low-SI band depiction of
392 the JZ and TVUS identifies it as a hypoechogenic layer, histological analysis reveals more
393 gradual transitions. These differences complicate the standardization of JZ assessment. The
394 study emphasizes the importance of understanding the JZ’s structure and alterations for
395 accurate diagnosis and management of adenomyosis.

396 *JZ thickness and ratio*

397 JZ Thickness \geq 12 mm

398 Although a JZ thickness of 12 mm has frequently been cited as a key diagnostic criterion for
399 adenomyosis, this cut-off has not consistently been validated in prospective studies that use
400 histopathology as the gold standard. Originally selected in a post-hoc analysis (Reinhold et al.,
401 1999), this cutoff was not found to be a reliable predictor of adenomyosis in premenopausal
402 women (Dueholm et al., 2001, Tellum et al., 2019a). Importantly, none of these studies
403 advocated using JZ thickness in isolation. In addition, it is important to note that the
404 measurement of JZ thickness is not consistently done in research studies, as some also include
405 the adenomyotic lesions.

406 In research studies in literature, “thickened myometrial junction” or “excessive JZ width” or
407 “JZ hypertrophy” is sometimes used instead of thickened JZ.

408 JZ to Myometrium Ratio 40-50%

409 The JZ to myometrium ratio represents the ratio between the JZ at maximum thickness and
410 the corresponding thickness of the myometrium thickness, measured at the same
411 measurement level. It can be indicated as "increased JZ-to-myometrium ratio," signifying the
412 disproportionate prominence of the JZ. On MRI, the JZ is found occupying 40-50% of the
413 myometrium (Rees et al., 2021).

414 In research studies in literature, “Ratio of JZ to Myometrial Dominance” or “Myometrial Zone
415 Proportion” is sometimes used instead of increased ratio of JZ to myometrium.

416 *Structural JZ irregularities*

417 Irregular JZ

418 MRI reveals irregularities in the JZ, manifesting as an uneven, disrupted pattern, often
419 denoted as "distorted JZ" in literature, characterizing the pathological changes associated
420 with adenomyosis. On MRI, the JZ is found exhibiting irregularities in thickness or appearance
421 (Tellum et al., 2019a).

422 In research studies in literature, "Anomalous JZ" or "Irregular Myometrial Transition" is
423 sometimes used instead of irregular JZ.

424 JZ Differential > 5 mm

425 JZ differential is the difference between maximum and minimum JZ thickness. MRI visualizes
426 JZ differentials, with a threshold of ≥ 5.5 mm indicating adenomyosis. The threshold of a 5
427 mm differential in the JZ thickness as an indicator of adenomyosis in MRI imaging is a specific
428 criterion used in diagnostic radiology. This cut-off is utilized to differentiate between normal
429 and abnormal JZ thickness, with a measurement greater than 5 mm suggesting the presence
430 of adenomyosis (Rees et al., 2021). This criterion helps in distinguishing adenomyosis from
431 other uterine conditions by highlighting disproportionate or thickened areas in the JZ.

432 In research studies in literature, "Thickened JZ differentials", "Disproportionate JZ thickness",
433 "JZ Thickness Disparity" or "Differential JZ Expansion" are sometimes used instead of
434 increased JZ differential.

435 *Uterine morphology*

436 MRI discerns enlarged and globular uterine contour, emphasizing the characteristic shape
437 change associated with diffuse adenomyosis, often cited as "globular uterus", reflecting
438 structural deformities (Tellum et al., 2019b).

439 Asymmetric uterine wall thickening is more often found in the posterior uterine wall than the
440 anterior and is associated with focal adenomyosis (Byun et al., 1999).

441 Heterogenous myometrium

442 This can also be described as a "heterogeneous myometrial appearance," emphasizing the
443 non-uniformity typically observed on MRI (Jain et al., 2023).

444 In research studies in literature, "Heterogeneous myometrial appearance" is sometimes used
445 instead of heterogeneous myometrium.

446 Asymmetry of Myometrium with Cystic-like Foci

447 Asymmetry of the Myometrium with Cystic-like Foci: MRI identifies characteristic asymmetry
448 in the myometrium, often accompanied by cystic-like foci, indicative of adenomyosis (Vinci et
449 al., 2017).

450 In research studies in literature, "Myometrial Imbalance" or "Cystic Myometrial Anomalies"
451 is sometimes used instead of asymmetry of myometrium with cyst-like foci.

452 Poorly Defined Margins

453 Lesions with poorly defined margins on MRI, which may also be characterized in literature as
 454 "indistinct boundaries" or "ill-defined margins". Adenomyoma also fit within this description.
 455 Adenomyoma is a histological diagnosis. MRI identifies adenomyoma as an uterine mass with
 456 ill-defined margins with possible haemorrhagic content, referred to as "focal adenomyosis"
 457 in literature, distinguishing it from diffuse adenomyosis (Byun et al., 1999).

458 In research studies in literature, "Indistinct Lesion Edges", "Marginally Defined Structures",
 459 "Uterine Mass Lesion" or "Adenomyotic Tumour" are sometimes used instead of lesions with
 460 poorly defined margins.

461 Globular Corpus Uteri

462 MRI discerns globular uterine contour alterations, emphasizing the characteristic shape
 463 change associated with adenomyosis, often cited as "globular uterus," reflecting structural
 464 deformities (Tellum et al., 2019b).

465 In research studies in literature, "Spherical Uterine Morphology" or "Round Corpus Uteri" is
 466 sometimes used instead of globular corpus uteri.

467 Recommendations

The main direct MRI finding of adenomyosis are the presence of high signal intensity myometrial foci, linear striations (finger like indentations) and tiny myometrial and subendometrial cysts and the others remain as indirect findings.

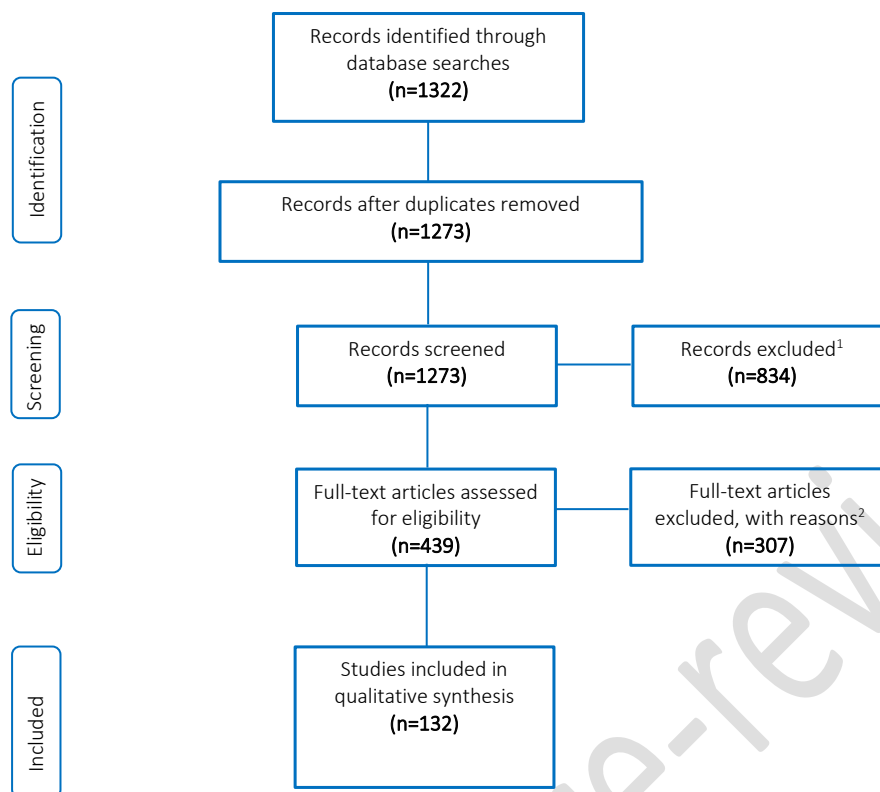
The adenomyosis working group recommends not using the JZ thickness ≥ 12 mm as the sole adenomyosis feature to diagnose adenomyosis on MRI.

468

469 Assessment of diagnostic accuracy

470 The literature review retrieved 1322 references. After removing duplicates, 1273 full articles
 471 were assessed, of which 1141 articles were excluded for the following reasons: full-text article
 472 could not be retrieved (n=8), not written in English (n=124), inappropriate publication types
 473 (case report, expert opinion, editorial, conference abstract, study protocol) (n=299) and
 474 relevant patients and/or intervention/outcomes are not assessed (patients not diagnosed
 475 with adenomyosis or not a diagnostic accuracy study) (n=750). Ultimately, 132 articles were
 476 included for either describing diagnostic accuracy of ultrasound or MRI in patients with
 477 adenomyosis (Figure 2).

Flowchart



¹ Non-English language studies, animal studies and papers not focusing on adenomyosis

² Exclusion criteria included: full text not able to be retrieved (n=8); publication types [case report, expert opinion, editorial] (n= 299);

478

479 **Ultrasound**480 *Accuracy of ultrasound as a diagnostic tool*

481 Ultrasound, particularly transvaginal ultrasound, has been extensively utilised due to its
 482 increased accessibility and lower cost relative to MRI for the initial evaluation of adenomyosis.
 483 The technique is lauded for its ability to detect characteristic signs of adenomyosis, such as
 484 myometrial cysts, echogenic heterogeneity, and irregular JZ. Results from two recent meta-
 485 analyses that evaluated the performance of transvaginal ultrasound imaging against histology
 486 on hysterectomy specimens showed that transvaginal ultrasound can achieve a sensitivity of
 487 78% (95% CI 73-82%) and 75% (95% CI 63 –84%) and specificity of 78% (95% CI 74-81%) and
 488 81% (95% CI 60 – 92%) respectively (Alcázar et al., 2023, Tellum et al., 2020). There was
 489 however, some heterogeneity between the included studies, although the majority of these
 490 studies came from expert centres. One of the causative factors for heterogeneity may be that
 491 the diagnostic accuracy is highly dependent on the operator's skill and experience,
 492 particularly in complex cases or among postmenopausal women, where tissue characteristics
 493 may differ significantly (Dueholm et al., 2001, Tellum et al., 2020). In addition, post hoc
 494 selection of parameters for the diagnosis of adenomyosis and the use of hysterectomy
 495 specimens may have led to overestimation of accuracy. Characteristics of the patient

496 population included, such as age and use of medical therapy, may have influenced the
497 accuracy of imaging in these studies.

498 Table 4 summarises all other studies included as evidence on the comparison between
499 ultrasound and histology that were not included in the meta-analysis mentioned above. The
500 sensitivity ranged between 10.9% and 89% and the specificity between 24.9% and 98.3%.

501 A 2023 systematic review and meta-analysis reporting on 294 patients across five studies,
502 investigated the use of ultrasound elastography for the diagnosis of adenomyosis (Brunelli et
503 al., 2023). Elastography was compared with histology in 3 of the 5 studies, with conventional
504 ultrasound in 1 of the 5 and with magnetic resonance imaging in the remaining study.
505 Sensitivity ranged from 80.6% to 98.7% across the included studies, and specificity valued
506 from 92.9% to 99.7%. The pooled sensitivity was 87.2% (79.1- 92.4) and pooled specificity was
507 98% (93.3-99.4) (Brunelli et al., 2023).

508 Table 5 includes studies investigating the diagnostic accuracy of 3D colour Doppler or shear
509 wave elastography to diagnose adenomyosis, with histology as the reference standard. The
510 sensitivity and specificity ranged between 48.7% and 100% and 79% to 100%, respectively.
511 However, the sensitivity and specificity were both over 70% in all studies except one.

512 Table 6 includes studies investigating the diagnostic accuracy of ultrasound to diagnose
513 adenomyosis, with MRI as the reference standard. The sensitivity of ultrasound ranged
514 between 36.8% and 70%, and the specificity between 79% and 92.7%.

515 Table 4: Accuracy of ultrasound compared to reference standard histology for diagnosis of
516 adenomyosis.

Reference	No of patients	No of criteria		Sensitivity	Specificity	PPV	NPV	Accuracy
Meta-analysis								
(Alcázar et al., 2023)	595		AUC: 0.83	75%	81%	3.9	0.31	
(Tellum et al., 2020)	827		AUC: 0.73	78%	78%	3.52	0.28	
Other studies								
(Maghsoudlou et al., 2025)	26	NR	AUC: 0.54	66.7%	42.9%	50%	60%	
(Jain et al., 2023)	365	≥3		77.8%	64.3%	84.9%	52.9%	74%
(Krentel et al., 2023)	202	NR		71.5%	48.6%	71.5%	48.6%	63.4%
(Maudot et al., 2023)	456	NR		52%	87%	77%	70%	
(Raimondo et al., 2023)	100	≥2		72%	69%	44%	88%	70%
(McCaughey et al., 2022)	317	NR		53.8%	66.2%	NR	NR	
(Zanolli et al., 2022)	180	NR		10.9%	98.3%	77.8%	66.7%	
(da Silva et al., 2021)	192	≥2		84.4%	24.9%			41.1%
(Zannoni et al., 2020)	78	≥2		77%	96%	91%	89%	90%
(Kara Bozkurt et al., 2017)	90	≥1		70.8%	62.1%	40.4%	85.4%	
(Dakhly et al., 2016)	292	≥2		84%	60%	72.3%	75%	73.29%
(Hanafi, 2013)	123	2		84.6%	43.4%	75.6%	57.5%	
(Naftalin et al., 2012)	985	NR		81.8%	81.3%	75%	86.7%	
(Abdel Hak, 2010)	50	NR		83.3%	86.8%	66.7%	94.3%	86%
(ElKattan et al., 2010)	352	NR		75.7%	90.8%	49.1%	97.0%	89.2%
(Atri et al., 2000)	102	NR	Reviewer 1	80%	73%	55%	90%	75%
			Reviewer 2	85%	69%	54%	92%	74%
(Chiang et al., 1999)	78	NR	Morphologic TVUS	79%	80%	75%	83%	
(Botsis et al., 1998)	206	3		82%	88.3%	84.6%	87.5%	
(Vercellini et al., 1998)	102	NR		82.7%	67.1%	50%	90.7%	
(Atzori et al., 1996)	58	NR		86%	96.2%	68.4%	98%	
(Reinhold et al., 1996)	119	NR		89%	89%	71%	96%	
(Brosens et al., 1995)	56	NR		86%	50%	86%	77%	
(Reinhold et al., 1995)	100	NR		86%	86%	71%	94%	
(Siedler et al., 1987)	80	NR		63%	97%	71%	NR	

517 NR: not reported, PPV: positive predictive value, NPV: negative predictive value.

518 Table 5: Accuracy of ultrasound colour Doppler/shear wave elastography compared to reference standard histology for diagnosis of adenomyosis.

Reference	No of patients		Cut-off value	ROC	Sensitivity	Specificity	PPV	NPV	Accuracy	Remarks
(Li et al., 2025)	58	SWE	20.642 kPa	0.853	73%	100%	NR	NR		
(Ren et al., 2023)	96	SR	>1.36	0.987	94.7%	100%	NR	NR		
(Pongpunprut et al., 2022)	75	SWE	3.465 m/s	0.80	80%	80%	NR	NR		
(Säsäran et al., 2022)	63	SRmean	>5.42	1.00	100%	100%	NR	NR		
		SRmax	>5.80	1.00	100%	100%	NR	NR		
(Görgülü and Okçu, 2021)	147	SRmean	>1.54	0.918	74.4%	100%				
		SRmax	>2.4	0.934	84.6%	94.7%				
		ADC	≤1.51	0.870	82.1%	79.0%				
		SWE	>50 kPa	0.706	48.7%	92.1%				
(Säsäran et al., 2021)	79	SRmean	>7.71	0.99	100%	96.2%	NR	NR		To distinguish between fibroids and adenomyosis
		SRmax	>8.91	0.98	96%	96.2%	NR	NR		
(Kara Bozkurt et al., 2017)	90	PI	>1.21		92.3%	96.2%	85.7%	97%		
		RI			86.4%	82.6%	75.1%	86.5%		
		Vmax			78.2%	84%	73.9%	85.9%		
(Sharma et al., 2015)	100	PI	>1.2	95.6	93.4	88.6	97.6	93.8		
		RI	>0.7							
(Chiang et al., 1999)	78	PI	>1.17		82%	84%	80%	86%		
		Pattern (intratumoral signals)			88%	93%	91%	91%		
(Hirai et al., 1995)	51	RI	0.43		100%	83%			96%	
		Vmax	23.4 em/s		91%	83%			93%	

519 ADC: apparent diffusion coefficient, NPV: negative predictive value, NR: not reported, PI: lowest pulsatility index PPV: positive predictive value, RI: resistive index, SR: strain ratio, SWE: shear wave
520 elastography, Vmax: peak systolic velocity.

Draft for pre-review

521 Table 6: Accuracy of ultrasound compared to MRI for diagnosis of adenomyosis.

Reference	No of patients	No of criteria		Sensitivity	Specificity	PPV	NPV
(Shaikh et al., 2023)	208	NR		74.4%	96.2%	98.3%	55.6%
(Sam et al., 2020)	649	NR	Uterine fibroids cases included	36.8	91.8	81.3	60.2
			Without uterine fibroids cases	30.9	92.7	80.0	58.8
(Konrad et al., 2018)	88	NR		70%	79%	73%	76%
(Alborzi et al., 2007)	81	NR		55.6%	88.9%	38.5%	94.1%

522 NR: not reported, PPV: positive predictive value, NPV: negative predictive value.

523 *Accuracy of different ultrasound characteristics*

524 Table 7 provides an overview of the accuracy (in terms of sensitivity, specificity, positive
525 predictive value and negative predictive value) of ultrasound criteria that are used to diagnose
526 adenomyosis, compared to histology on hysterectomy specimens.

527 Table 8 provides an overview of the prevalence of ultrasound criteria among women with
528 histopathological proven adenomyosis.

529 Overall, there are wide variations in the accuracy and prevalence of the ultrasound finding
530 studied. Therefore, the MUSA group carried out a Delphi procedure to determine direct and
531 indirect features of adenomyosis on ultrasound examination (Harmsen et al., 2022).

532 Table 7: Accuracy of ultrasound characteristics for the diagnosis of adenomyosis.

533 Studies indicated in red have MRI as the reference test.

534 Da Silva 2021 (in purple): data on the narrative reporting have been extracted from the study.

535 Bazot 2002: group 1: women with recurrent menometrorrhagia but no evidence of leiomyomata and endometrial diseases, group 2: all other women.

Feature	Reference	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy
Features of the uterus						
Globular shape/enlarged globular uterus	(Maghsoudlou et al., 2025)	33.3 (6.7-60.0)	85.7 (67.4-100.0)	66.7 (28.9-100.0)	60 (38.5-81.5)	
	(Yavuz et al., 2024)	57.7	60.2	27	84.6	59
	(Jain et al., 2023)	63.9 (47.5-77.5)	42.9 (21.3-67.4)	74.2 (56.8-86.3)	31.6 (15.4-54.0)	58 (44.2-70.6)
	(Krentel et al., 2023)	79.1	37.1	76.6	40.6	67.5
	(Shaikh et al., 2023)	71.8 (62.6-78.6)	88.5 (75.9-95.2)	94.2 (88.8-97.9)	51.1 (40.4-61.7)	
	(da Silva et al., 2021)	11.1 (3.7-24)	72.1 (64-79)	NR	NR	
	(Säsäran et al., 2021)	68 (48.41-82.79)	41.51 (29.26-54.91)	NR	NR	
	(Sam et al., 2020)	76.7 (71.7-81.3)	58.6 (53.1-64.0)	64.0 (50.7-67.2)	72.4 (57.8-76.6)	
	(Zannoni et al., 2020)	77	46	42	80	61.5
	(Tellum et al., 2018)	61 (46-75)	83 (65-94)	86 (72-93)	57 (47-65)	70 (58-80)
	(Abdel Hak, 2010)	41.67	100	100	84.44	86
	(Sun et al., 2010)	50.6	78.1	60.6	70.4	67.1
	(Kepkep et al., 2007)	69.2	86.4	75	82.6	80
	Group 1 (Bazot et al., 2002)	52.3	100	100	20	
	Group 2 (Bazot et al., 2002)	92.3	96.2	40	76.2	
(Bazot et al., 2001)	30.0	96.3	80.0	73.3	74.0	
Asymmetrical walls	(Maghsoudlou et al., 2025)	41.7 (13.8-69.6)	85.7 (67.4-100.0)	71.4 (38.0-100.0)	63.2 (41.5-84.8)	
	(Yavuz et al., 2024)	55	60	26.1	83.9	59
	(Krentel et al., 2023)	76.5 (68.4-84.7)	30.6 (21.7-39.5)	67.5 (58.5-76.5)	40.7 (31.3-50.2)	60.6 (51.2-70.0)
	(Shaikh et al., 2023)	62.8 (54.7-70.3)	84.6 (71.4-92.7)	92.5 (85.2-96.5)	43.1 (33.5-53.3)	
	(da Silva et al., 2021)	6.7 (1.4-18.2)	98.6 (95.1-99.8)	NR	NR	NR
	(Zannoni et al., 2020)	80	70	72	78	78.9
	(Rasmussen et al., 2019a)	72 (53-86)	64 (52-75)	NR	NR	
	(Dakhly et al., 2016)	56.8	70.8	70.8	56.8	63.0
	(Luciano et al., 2013)	62	67	29	89	63
	(Exacoustos et al., 2011)	47 (30-65)	80 (64-90)	65 (43-83)	65 (50-78)	65 (54-75)
	(Sun et al., 2010)	58.8	75	61	73.3	68.5
	(Kepkep et al., 2007)	61.5	63.6	50.0	73.7	62.9
	Group 1 (Bazot et al., 2002)	23.8	100	100	11.1	
	Group 2 (Bazot et al., 2002)	23	82.5	70	76.7	

Question mark sign		(Krentel et al., 2023)	93.3 (82.9-103.7)	14.3 (0.3-28.9)	70.0 (50.9-89.2)	50.0 (29.1-70.9)	68.2 (48.7-87.7)	
		(da Silva et al., 2021)	0	0	NR	NR		
		(Zannoni et al., 2020)	41	96	83	77	68.8	
Features of the myometrium								
Presence of myometrial cysts		(Maghsoudlou et al., 2025)	25.0 (0.5-49.5)	85.7 (67.4-100.0)	60 (17.1-100.0)	57.1 (36.0-78.3)		
		(Yavuz et al., 2024)	17.5	79	22.5	80	70	
		(Jain et al., 2023)	19.5 (9.8-35.0)	92.9 (68.5-98.7)	87.5 (52.9-97.8)	31.0 (19.1-46.0)	40 (27.6-53.8)	
		(Krentel et al., 2023)	88.1 (81.3-94.9))	14.3 (7.0-21.6)	76.6 (67.8-85.4)	27.3 (18.0-36.6)	70.5 (61-80)	
		(Shaikh et al., 2023)	37.2 (29.7-45.3)	100 (91.4-100)	100 (92.3-100)	34.7 (27.2-42.9)		
		(da Silva et al., 2021)	17.8 (8-32)	98 (94.1-99.6)	NR	NR		
		(Sam et al., 2020)	33.3 (28.2–38.8)	88.5 (84.6–91.8)	73.5 (66.6–79.6)	58.0 (55.9–60.1)		
		(Zannoni et al., 2020)	30	92	67	73	61.5	
		(Rasmussen et al., 2019a)	47 (29-65)	90 (81-96)	NR	NR		
		(Tellum et al., 2018)	51 (38-64)	86 (71-95)	86 (72-93)	75 (44-59)	64 (54-74)	
		(Dakhly et al., 2016)	54.3	80	77.2	58.4	65.8	
		(Hamimi, 2015)	35	88	88	35		
		(Luciano et al., 2013)	35	83	23	90	44	
		(Exacoustos et al., 2011)	53 (35-70)	98 (85-100)	94 (70-100)	72 (58-83)	78 (67-86)	
		(Abdel Hak, 2010)	41.67	100	100	84.44		
		(ElKattan et al., 2010)	70.27	54.29	15.29	93.96	55.97	
		(Sun et al., 2010)	82.4	45.3	50	79.5	60	
		(Kepkep et al., 2007)	61.5	81.8	66.7	78.3	74.3	
		Group 1	(Bazot et al., 2002)	80.9	100	100	66	
		Group 2	(Bazot et al., 2002)	65.3	97.5	81.8	82.1	
			(Bazot et al., 2001)	60	98.8	96.0	83.2	84.2
	Heterogenous echotexture of the myometrium		(Jain et al., 2023)	58.3 (42.2-72.9)	64.3 (38.8-83.7)	80.8 (62.1-91.5)	37.5 (21.2-57.3)	60 (46.2-72.4)
			(Krentel et al., 2023)	88.8 (83.7-94.0)	23.9 (16.9-30.9)	71.3 (63.9-78.7)	50.0 (41.8-58.2)	68.1 (60.8-75.7)
		(Shaikh et al., 2023)	71.8 (63.9-78.6)	96.2 (85.7-99.3)	98.3 (93.2-99.7)	53.2 (42.7-63.5)		
		(da Silva et al., 2021)	82.2 (68-92)	19.1 (13-26.3)	NR	NR		
		(Sam et al., 2020)	74.5 (59.4–79.2)	56.5 (51.0–61.9)	62.2 (58.9–65.4)	69.8 (65.2–74.0)		
		(Zannoni et al., 2020)	100	7	35	100	53.9	
		(Rasmussen et al., 2019a)	84 (67-95)	31 (21-42)	NR	NR		
		(Dakhly et al., 2016)	50.6	69.2	67.2	52.9	59.0	
		(Hamimi, 2015)	100	75	88	100		
		(Luciano et al., 2013)	92	67	67	92	88	
		(Exacoustos et al., 2011)	88 (70-95)	65 (48-79)	67 (50-80)	87 (68-96)	75 (64-84)	
		(Abdel Hak, 2010)	75	86.84	64.29	91.67	84	

		(ElKattan et al., 2010)	94.59	44.44	16.67	98.59	49.72
		(Sun et al., 2010)	87.1	60.1	59.2	87.5	70.9
		(Kepkep et al., 2007)	80.8	61.4	55.3	84.4	68.6
	Group 1	(Bazot et al., 2002)	100	50	95.4	100	
	Group 2	(Bazot et al., 2002)	88.4	30	29.1	88.8	
		(Bazot et al., 2001)	52.5	90.0	33.8	40.1	90.0
Focal abnormal myometrial echotexture	Group 1	(Bazot et al., 2002)	42.8	100	100	14.2	
	Group 2	(Bazot et al., 2002)	19.2	98.7	83.3	21	
		(Bazot et al., 2001)	38.0	99.0	94.0	77.0	79.0
Echogenic linear striations or nodules		(Maghsoudlou et al., 2025)	83.3 (62.2-100.0)	64.3 (39.2-89.4)	66.7 (42.8-90.5)	81.8 (59.0-100.0)	
		(Yavuz et al., 2024)	15	95.5	46	81	79
		(Jain et al., 2023)	25 (13.8-41.1)	85.7 (60.1-96.0)	81.8 (52.3-94.9)	30.8 (18.6-46.4)	42 (29.4-55.8)
		(Krentel et al., 2023)	91.9 (84.1-99.7)	0	77.3 (65.3-89.3)	0	72.3 (59.5-85.1)
		(da Silva et al., 2021)	2.2 (0.06-11.7)	96.6 (92-98.9)	NR	NR	
		(Sam et al., 2020)	31.5 (26.4-36.9)	92.8 (89.4-95.3)	80.7 (73.3-86.4)	58.5 (56.5-60.4)	
		(Rasmussen et al., 2019a)	52 (33-71)	87 (76-94)	NR	NR	
		(Dakhly et al., 2016)	56.8	67.7	68.7	55.7	61.7
		(Luciano et al., 2013)	54	83	29	93	59
		(Abdel Hak, 2010)	41.67	100	100	84.44	86
		(ElKattan et al., 2010)	48.65	90.79	38.30	93.77	
		(Sun et al., 2010)	91.8	71.1	67.8	92.9	79.3
		(Kepkep et al., 2007)	30.8	95.5	80.0	70.0	71.4
	Group 1	(Bazot et al., 2002)	66.6	100	100	77.7	
	Group 2	(Bazot et al., 2002)	3.8	98.7	50	75.9	
Hyperechoic islets		(Maghsoudlou et al., 2025)	83.3 (62.2-100.0)	50.0 (23.8-76.2)	58.8 (35.4-82.2)	77.8 (50.6-100.0)	
		(Yavuz et al., 2024)	17.5	94	43	94	78
		(Krentel et al., 2023)	88.6 (82.0-94.4)	23.7 (16.0-31.4)	70.7 (62.5-79.0)	50.0 (40.9-59.1)	67.5 (59.0-76.0)
		(Tellum et al., 2018)	51 (38-64)	78 (61-90)	79 (66-88)	49 (42-57)	61 (51-71)
Streaky myometrium		(Shaikh et al., 2023)	68.0 (59.9-75.1)	88.5 (75.9-95.2)	94.6 (88.2-97.2)	47.9 (37.7-58.3)	
		(Sam et al., 2020)	34.0 (28.8-39.5)	93.1 (89.8-95.5)	82.4 (75.5-87.8)	59.5 (57.4-61.5)	
Features of the junctional zone							
Ill-demarcated endometrial-myometrial border/interrupted junctional zone		(Yavuz et al., 2024)	30	80	28.5	81.8	70
		(Jain et al., 2023)	58.3 (42.2-72.9)	78.6 (52.4-92.4)	87.5 (69-95.7)	42.3 (25.5-61.1)	64 (50.1-75.9)
		(da Silva et al., 2021)	0	0	NR	NR	
		(Sam et al., 2020)	44.0 (38.5-49.7)	81.3 (76.6-85.3)	69.3 (63.6-74.5)	60.2 (57.5-62.8)	
		(Zannoni et al., 2020)	70	88	78	82	78.8

		(Rasmussen et al., 2019a)	48 (29-68)	87 (76-94)	NR	NR	
		(Tellum et al., 2018)	53 (41-67)	39 (23-57)	64 (51-67)	39 (24-46)	48 (38-59)
		(Dakhly et al., 2016)	45.7	73.9	68.5	52.2	58.2
		(Hamimi, 2015)	79	68	81	65	
		(Luciano et al., 2013)	92	67	67	92	88
		(Exacoustos et al., 2011)	88 (70-96)	78 (61-89)	76 (58-88)	89 (72-96)	82 (72-89)
		(ElKattan et al., 2010)	75.68	54.29	16.28	95.00	56.53
		(Sun et al., 2010)	62.4	70	56.4	73.1	65.7
JZ thickness (JZmax)	>12 mm	(Krentel et al., 2023)	100	0	77.8 (62.1-93.5)	0	77.8 (62.1-93.5)
	≥8 mm	(Zannoni et al., 2020)	40	99	100	73	70
	>10.5 mm	(Rasmussen et al., 2019a)	76 (57-90)	73 (61-83)	NR	NR	
	≥5.1 mm	(Tellum et al., 2018)	58 (34-80)	78 (56-93)	69 (48-84)	69 (56-80)	69 (53-82)
	>8 mm	(Luciano et al., 2013)	58	83	31	94	63
	≥8 mm	(Exacoustos et al., 2011)	84 (67-94)	75 (58-87)	73 (56-86)	86 (69-95)	79 (68-87)
JZ diff	≥4 mm	(Zannoni et al., 2020)	60	87	75	76	73.8
	≥5 mm	(Rasmussen et al., 2019a)	79 (59-92)	77 (65-87)	NR	NR	
	≥1.5 mm	(Tellum et al., 2018)	43 (28-58)	84 (66-95)	80 (63-91)	49 (42-56)	
	>4 mm	(Luciano et al., 2013)	85	67	50	92	81
	≥4 mm	(Exacoustos et al., 2011)	88 (70-96)	83 (67-92)	80 (63-91)	89 (74-97)	85 (75-91)
Subendometrial buds		(Krentel et al., 2023)	91.1 (84.4-97.8)	23.1 (13.2-33.0)	83.6 (74.9-92.3)	37.5 (26.1-48.9)	78.3 (68.6-88.0)
		(Tellum et al., 2018)	12 (5-23)	89 (74-97)	64 (36-85)	38 (35-42)	41 (31-52)
"poorly defined interface"/ poor endometrial delineation		(Zannoni et al., 2020)	85	56	50	88	70.3
Other features							
Fan-shaped shadowing		(Maghsoudlou et al., 2025)	33.3 (6.7-60.0)	64.3 (39.2-89.4)	44.4 (12.0-76.9)	52.9 (29.2-76.7)	
		(Yavuz et al., 2024)	55	61	26.8	84.2	60
		(Säsaran et al., 2021)	48 (30.03-66.5)	52.83 (39.7-65.6)	NR	NR	
		(Rasmussen et al., 2019a)	41 (24-59)	85 (75-92)	NR	NR	
		(Tellum et al., 2018)	36 (24-49)	92 (78-98)	88 (69-96)	47 (42-57)	57 (46-67)
		(Zannoni et al., 2020)	54	96	88	81	75

536 JZ: junctional zone, NPV: negative predictive value, NR: not reported, PPV: positive predictive value.

537 Table 8: Prevalence of ultrasound characteristics for the diagnosis of adenomyosis.

538 Studies indicated in red have MRI as the reference test.

539 Da Silva 2021 (in purple): data on the narrative reporting have been extracted from the study.

Feature	Reference	Number of patients	Prevalence (%)
Features of the uterus			
Globular shape/enlarged globular uterus	(Yavuz et al., 2024)	40	57.5
	(Haj Hamoud et al., 2023)	25	32
	(Krentel et al., 2023)	202	57.1
	(Maudot et al., 2023)	90	40
	(Raimondo et al., 2023)	25	72
	(da Silva et al., 2021)	45	11.1
	(Zannoni et al., 2020)	26	77
	(Tellum et al., 2018)	59	51
	(Sharma et al., 2015)	28	73
	(ElKattan et al., 2010)	37	67.6
	(Sun et al., 2010)	85	50.6
	(Kepkep et al., 2007)	26	69.2
(Bromley et al., 2000)	43	95.7	
Asymmetrical walls	(Yavuz et al., 2024)	40	39.7
	(Haj Hamoud et al., 2023)	25	80
	(Krentel et al., 2023)	202	51.5
	(Maudot et al., 2023)	90	17.8
	(Raimondo et al., 2023)	25	60
	(da Silva et al., 2021)	45	6.7
	(Zannoni et al., 2020)	26	62
	(Dakhly et al., 2016)	162	56.8
	(Pinzauti et al., 2015)	53	56.6
	(Sharma et al., 2015)	28	60
	(Luciano et al., 2013)	26	61.5
	(Exacoustos et al., 2011)	32	46.9
	(ElKattan et al., 2010)	37	32.4
	(Sun et al., 2010)	85	58.8
	(Kepkep et al., 2007)	26	61.5
Question mark sign	(Haj Hamoud et al., 2023)	25	32
	(Krentel et al., 2023)	202	10.9
	(Raimondo et al., 2023)	25	28
	(da Silva et al., 2021)	45	0
	(Zannoni et al., 2020)	26	38
Features of the myometrium			
Presence of myometrial cysts	(Yavuz et al., 2024)	40	17.5
	(Krentel et al., 2023)	202	43.6
	(Maudot et al., 2023)	90	34.4
	(Raimondo et al., 2023)	25	48
	(da Silva et al., 2021)	45	17.8
	(Zannoni et al., 2020)	26	31
	(Tellum et al., 2018)	59	51
	(Vinci et al., 2017)	27	47
	(Dakhly et al., 2016)	162	54.3
	(Hamimi, 2015)	45	33
	(Pinzauti et al., 2015)	53	49.1
	(Sharma et al., 2015)	28	83
	(Luciano et al., 2013)	26	34.6
(Exacoustos et al., 2011)	32	53.1	
(ElKattan et al., 2010)	37	70.3	

		(Sun et al., 2010)	85	82.4
		(Kepkep et al., 2007)	26	61.5
		(Reinhold et al., 1995)	25	40
Heterogenous echotexture of the myometrium		(Krentel et al., 2023)	202	71.3
		(Maudot et al., 2023)	90	53.3
		(da Silva et al., 2021)	45	82.2
		(Zannoni et al., 2020)	26	100
		(Vinci et al., 2017)	27	57
		(Dakhly et al., 2016)	162	50.6
		(Hamimi, 2015)	45	78
		(Pinzauti et al., 2015)	53	26.4
		(Sharma et al., 2015)	28	73
		(Luciano et al., 2013)	26	92.3
		(Exacoustos et al., 2011)	32	87.5
		(ElKattan et al., 2010)	37	94.6
		(Sun et al., 2010)	85	87.1
		(Kepkep et al., 2007)	26	80.8
		(Bromley et al., 2000)	43	100
		(Reinhold et al., 1995)	25	44
Echogenic linear striations or nodules		(Yavuz et al., 2024)	40	15
		(Krentel et al., 2023)	200	23.5
		(Maudot et al., 2023)	90	20.0
		(da Silva et al., 2021)	45	2.2
		(Vinci et al., 2017)	27	57
		(Dakhly et al., 2016)	162	56.8
		(ElKattan et al., 2010)	37	48.6
		(Sun et al., 2010)	85	91.8
		(Kepkep et al., 2007)	26	30.8
	(Raimondo et al., 2023)	25	28	
Hyperechoic islets		(Yavuz et al., 2024)	40	17.5
		(Krentel et al., 2023)	202	57.9
		(Raimondo et al., 2023)	25	28
		(Tellum et al., 2018)	59	51
Hypoechoic striations		(Pinzauti et al., 2015)	53	17
		(Exacoustos et al., 2011)	32	50
Features of the junctional zone				
Ill-demarcated endometrial-myometrial border/interrupted junctional zone		(Yavuz et al., 2024)	40	30
		(Haj Hamoud et al., 2023)	25	52
		(Maudot et al., 2023)	90	32.2
		(Raimondo et al., 2023)	25	32
		(da Silva et al., 2021)	45	0
		(Zannoni et al., 2020)	26	54
		(Tellum et al., 2018)	59	54
		(Vinci et al., 2017)	27	33
		(Dakhly et al., 2016)	162	45.7
		(Hamimi, 2015)	45	67
		(Sharma et al., 2015)	28	86
		(Luciano et al., 2013)	26	92.3
		(Exacoustos et al., 2011)	32	87.5
		(ElKattan et al., 2010)		
		(Sun et al., 2010)	85	62.4
	(Bromley et al., 2000)	43	78.7	
	(Kepkep et al., 2007)	26	53.8	
JZ thickness (JZmax)	>12 mm	(Krentel et al., 2023)	202	13.4

	≥8 mm	(Zannoni et al., 2020)	26	31
		(Pinzauti et al., 2015)	53	17
	≥5.1 mm	(Tellum et al., 2018)	59	19
JZ diff	≥4 mm	(Zannoni et al., 2020)	26	46
		(Pinzauti et al., 2015)	53	47.2
		(Tellum et al., 2018)	59	43
“poorly defined interface”/ poor endometrial delineation		(Zannoni et al., 2020)	26	85
		(ElKattan et al., 2010)	37	75.7
Other features				
Fan-shaped shadowing		(Yavuz et al., 2024)	40	55
		(Raimondo et al., 2023)	25	60
		(Zannoni et al., 2020)	26	54
		(Tellum et al., 2018)	59	35
Translesional vascularization		(Haj Hamoud et al., 2023)	25	80
		(Maudot et al., 2023)	90	14.4
		(Vinci et al., 2017)	27	68
		(Sun et al., 2010)	85	93

540 JZ: junctional zone.

541

542 MRI

543 *Accuracy of MRI as a diagnostic tool*

544 MRI stands out for its superior imaging capabilities, particularly in visualizing the JZ. A recent
545 meta-analysis showed that compared to histology as the reference standard, MRI can achieve
546 a sensitivity of 69% (95% CI 54 – 80%), and specificity of 80% (95% CI 67 – 89%) (Alcázar et al.,
547 2023). The depth and clarity offered by MRI allow for a detailed assessment of the JZ features,
548 including appearance on T2 and T1 sequences and thickness measurements.. MRI’s advantage
549 over ultrasound lies in its improved capacity to provide consistent results across different
550 operators, minimising the variability seen with ultrasound. However, the utilization of MRI is
551 often limited by factors such as higher costs and reduced accessibility, which may not make
552 it suitable for first-line diagnostic use but rather reserved for inconclusive ultrasound cases or
553 pre-surgical planning (Gordts et al., 2008, Grimbizis et al., 2014).

554 Table 9 includes all other studies included as for evidence on the comparison between MRI
555 and histology that were not included in the meta-analysis.

556 Table 9: Accuracy of MRI compared to reference standard histology for diagnosis of
557 adenomyosis.

Reference	No of patients		ROC	Sensitivity	Specificity	PPV	NPV	Accuracy
Meta-analysis								
(Alcázar et al., 2023)	595		0.81	69%	80%	3.5	0.39	
Other studies								
(Jain et al., 2023)	365			91.7%	85.7%	94.3%	80%	90%
(Maudot et al., 2023)	147			58%	81%	75%	67%	
(Zanolli et al., 2022)	180			29.7%	85.3%	52.8%	68.8%	65.6%
(Görgülü and Okçu, 2021)	147	ADC	0.870	82.1%	79.0%	NR	NR	

558 PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio.

559

560 Accuracy of different characteristics

561 JZ Thickness ≥ 12 mm

562 Tellum *et al.* assessed the diagnostic accuracy of this criterion with histopathological analysis
563 as the reference (Tellum et al., 2019a). The authors reported that a maximum JZ thickness
564 (JZ_max) of ≥ 12 mm was not positively correlated with adenomyosis diagnosis, with
565 histopathology as the reference, in a premenopausal study population. They concluded that
566 measuring the JZ thickness had limited value for diagnosing adenomyosis with MRI, especially
567 in premenopausal women with moderate disease severity. Instead, direct signs of
568 adenomyosis, such as irregularities of the JZ, provided better diagnostic accuracy.

569 Another study on MRI characteristics of the uterine JZ noted that while adenomyosis can be
570 diagnosed using MRI with a diagnostic accuracy of 85% with histological diagnosis as the
571 reference, the principal limitation is the absence of a definable JZ on imaging, which occurs in
572 20% of premenopausal women (Novellas et al., 2011). Additionally, a study comparing
573 endovaginal USS and MRI imaging against histopathologic findings in women with diffuse
574 adenomyosis found that endovaginal ultrasound was as accurate as MR imaging in diagnosing
575 uterine adenomyosis (Reinhold et al., 1996). It suggested that the use of a JZ thickness of ≥ 12
576 mm could optimize the diagnostic accuracy of MR imaging for this condition.

577 These studies indicate that while the 12 mm cutoff for JZ thickness is a useful guideline, it
578 should be considered in conjunction with other diagnostic criteria and imaging findings for a
579 comprehensive evaluation of adenomyosis.

580 JZ Differential ≥ 5.5 mm

581 The definition of a 5.5 mm threshold in JZ thickness for diagnosing adenomyosis via MRI is
582 explored in two significant studies. Dueholm *et al.* compared the efficacy of MRI and
583 transvaginal ultrasonography in diagnosing adenomyosis with histopathological analysis as
584 the reference (Dueholm et al., 2001). The sensitivity and specificity of calculating the

585 maximum difference between the thinnest and thickest JZ (JZ_{diff}) were as follows; sensitivity:
586 MRI 70% (95% CI 46–87%) and TVUS 68% (95% CI 44–86%); specificity: MRI 86% (95% CI 76–
587 93%) and TVUS 65% (95% CI 50–77%). The combination of MRI and TVUS was most sensitive
588 (89%, 95% CI 64–98%), but produced the lowest specificity (60%, 95% CI 44–73%).
589 Adenomyosis was not detected by either MRI or TVUS at uterine volumes >400 mL. Exclusion
590 of uteri >400 mL from the analysis improved the diagnostic precision of MRI, but not that of
591 TVUS. The diagnostic accuracy at MRI was improved by JZ_{diff} (i.e. ≥ 5 –7 mm).

592 In a systematic review, Rees and colleagues provided a comprehensive analysis of the
593 diagnostic accuracy of various MRI measures for adenomyosis compared to histopathology,
594 including JZ thickness (Rees et al., 2021). This review may offer insights into the rationale
595 behind specific JZ thickness thresholds like the 5.5 mm cutoff and how it was established as a
596 diagnostic marker for adenomyosis.

597 Table 10 provides an overview of the accuracy (in terms of sensitivity, specificity, positive
598 predictive value and negative predictive value) of MRI criteria that are used to diagnose
599 adenomyosis.

600 Table 11 provides an overview of the prevalence of MRI criteria among women with
601 histopathologically proven adenomyosis.

602 Overall, the main direct MRI finding of adenomyosis is the presence of tiny myometrial cysts,
603 and the others remain as indirect findings (Bazot and Darai, 2018).

604 Recommendation

Both MRI and ultrasound have high sensitivity and specificity in detecting adenomyosis when histology is used as the benchmark. Transvaginal ultrasound should be considered the first-line diagnostic modality. MRI should be regarded as a second-line imaging modality, indicated in selected clinical scenarios. It plays an important role in assessing disease extent, detecting concomitant gynaecologic conditions, supporting the differential diagnosis, and potentially informing therapeutic planning.

605

606 Table 10: Accuracy of MRI characteristics for the diagnosis of adenomyosis.

Feature		Reference	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy
JZ thickness ≥ 12 mm		(Jain et al., 2023)	97.2 (85.8-99.5)	78.6 (52.4-92.4)	92.1 (79.2-97.3)	91.7 (64.6-98.5)	92 (81.2-96.9)
		(Tellum et al., 2019a)	53 (39-66)	56 (38-72)	65 (55-74)	43 (33-53)	54 (43-64)
		(Hamimi, 2015)	95	94	98	88	
		(Bazot et al., 2001)	62.5	96.3	89.3	83.7	85
		(Reinhold et al., 1996)	93 (75-99)	91 (79-95)	79 (68-95)	98 (93-100)	
JZ differential	> 5 mm	(Jain et al., 2023)	77.8 (61.9-88.3)	85.7 (60.1-96.0)	93.3 (78.7-98.2)	60 (38.7-78.1)	80 (67.0-88.8)
	≥ 5.5 mm	(Tellum et al., 2019a)	53 (39-66)	75 (58-88)	77 (64-86)	50 (42-58)	61 (51-71)
JZ to myometrium ratio	>40%	(Jain et al., 2023)	88.9 (74.7-95.6)	78.6 (52.4-92.4)	91.4 (77.6-97.0)	73.3 (48.1-89.1)	86 (73.8-93.1)
		(Bazot et al., 2001)	65	92.5	81.3	84	83.3
	$\geq 50\%$	(Tellum et al., 2019a)	42 (29-56)	58 (41-75)	50 (50-72)	39 (31-48)	48 (38-60)
Presence of irregular JZ		(Tellum et al., 2019a)	74 (60-85)	83 (67-94)	88 (77-94)	67 (51-80)	77 (68-86)
Globular corpus uteri		(Tellum et al., 2019a)	51 (37-64)	64 (46-79)	69 (57-79)	45 (36-54)	56 (45-66)
Enlarged uterus		(Bazot et al., 2001)	22.5	97.5	81.8	72.5	72.5
Myometrial cysts		(Tellum et al., 2019a)	70 (57-82)	89 (74-97)	91 (80-96)	65 (55-74)	77 (68-86)
		(Hamimi, 2015)	50	75	80	43	
High-SI myometrial spots		(Jain et al., 2023)	72.2 (56.0-84.2)	100 (78.5-100)	100 (87.1-100)	58.3 (38.8-75.5)	80 (67.0-88.8)
		(Bazot et al., 2001)	47.5	98.8	95	79	81.7
Heterogeneous myometrium usually heterogeneously hyperintense		(Jain et al., 2023)	91.7 (78.2-97.1)	50 (26.8-73.2)	82.5 (68.1-91.3)	70 (39.7-89.2)	80 (67.0-88.8)
		(Hamimi, 2015)	95	75	88	88	
Cysts and/or fingerlike indentations in the JZ		(Tellum et al., 2019a)	39 (26-52)	94 (81-99)	92 (73-98)	49 (44-55)	60 (50-70)
Presence of adenomyoma		(Tellum et al., 2019a)	32 (20-45)	94 (81-99)	90 (69-97)	47 (42-51)	56 (45-66)

607 JZ: junctional zone, NPV: negative predictive value, PPV: positive predictive value.

608 Table 11: Prevalence of MRI characteristics for the diagnosis of adenomyosis.

Feature		Reference	Number of patients	Prevalence (%)
JZ thickness ≥ 12 mm		(Tellum et al., 2019a)	57	53
		(Vinci et al., 2017)	22	81
		(Hamimi, 2015)		93
		(Reinhold et al., 1996)	28	93
		(Byun et al., 1999)	45	78.6 (>10 mm)
JZ differential	≥ 5.5 mm	(Tellum et al., 2019a)	57	53
JZ to myometrium ratio	$\geq 50\%$	(Tellum et al., 2019a)	57	62
Presence of irregular JZ		(Tellum et al., 2019a)	57	74
Globular corpus uteri		(Tellum et al., 2019a)	57	66
Myometrial cysts		(Tellum et al., 2019a)	57	70
		(Hamimi, 2015)		44
High-SI myometrial spots		(Hamimi, 2015)		38
		(Reinhold et al., 1996)	28	50
		(Byun et al., 1999)	45	42.9
Heterogeneous myometrium usually heterogeneously hyperintense		(Jain et al., 2023)		
		(Hamimi, 2015)		
Asymmetry of the myometrium with cystic-like foci		(Vinci et al., 2017)	22	72
Subendometrial halo		(Reinhold et al., 1996)	28	64
Poorly defined margins		(Byun et al., 1999)	45	93
Cysts and/or fingerlike indentations in the JZ		(Tellum et al., 2019a)	57	39
Presence of adenomyoma		(Tellum et al., 2019a)	57	32

609 JZ: junctional zone.

610 **Ultrasound vs MRI**

611 A systematic review and meta-analysis compared the diagnostic accuracy of ultrasound to
612 MRI with histopathology as the reference standard. The Fagan nomograms showed that a
613 positive test for TVUS and MRI significantly increases the pre-test probability for
614 adenomyosis, from 52% to 81% in the case of TVUS and from 52% to 79% in the case of MRI.
615 On the other hand, a negative test result significantly decreases the pre-test probability for
616 adenomyosis from 52% to 25% in the case of TVUS and from 52% to 30% in the case of MRI
617 (Alcázar et al., 2023). Three studies were identified that were not included in the systematic
618 review. Zanolli *et al.* reported 79.4% (143/180) agreement between MRI and ultrasound on
619 the presence or absence of adenomyosis, with a sensitivity for concordant imaging of 6.8%,
620 specificity 99% and 70.6% accuracy (Zanolli et al., 2022). Maudot *et al.* reported that in their
621 study, the correlation between the results of ultrasound and MRI was poor in both patients
622 with and without adenomyosis on pathological analysis with Pearson coefficients between
623 0.25 and 0.44 (n=60 patients) (Maudot et al., 2023). Finally, Jain et al reported kappa
624 agreement coefficients of 0.246 (68.67%) between transvaginal ultrasound and MRI, and
625 0.324 (71.24%) for transvaginal ultrasound with Doppler and MRI in 233 patients (Jain et al.,
626 2023).

627 **Biopsy**

628 As adenomyosis is characterized by the presence of ectopic endometrial glands and stroma
629 within the myometrium in histopathological specimens, it seems reasonable that histology

630 should be considered the gold standard of diagnosis. However, in cases of conservative uterus
 631 sparing management, where uterus is not available for histological examination, biopsies
 632 from the myometrium might be used to confirm diagnosis of adenomyosis. Various tissue-
 633 sampling techniques were proposed for microscopic examination and include intra-uterine
 634 route via hysteroscopic needle biopsy or myometrial resection extra-uterine route via blind
 635 percutaneous, ultrasound guided percutaneous, ultrasound guided transvaginal or
 636 laparoscopic guided needle biopsy; ex-vivo tissue sampling.

637 *Accuracy of biopsy as diagnostic tool*

638 A systematic review and meta-analysis, including 683 women in 6 cohort studies investigated
 639 the sensitivity and specificity of uterine biopsy in the diagnosis of adenomyosis, using
 640 histology as the reference standard (Movilla et al., 2020). The sensitivity of extra-uterine
 641 needle biopsies varied significantly and appeared dependent on the route of biopsy and total
 642 number of biopsies performed per patient. The lowest sensitivity (22.2%) was found with
 643 transvaginal ultrasound guided needle biopsy and 4 biopsies per patient targeted at
 644 suspicious adenomyosis lesions identified via pelvic ultrasound. Highest sensitivity (up to
 645 97.8%) was reported for laparoscopic needle biopsy with 10 biopsies performed per patient
 646 targeted at suspicious adenomyosis lesions identified via preoperative pelvic ultrasound. All
 647 5 studies demonstrated a high specificity via extra-uterine needle biopsy, ranging from 95.9%
 648 -100.0% for all of routes of the extra-uterine needle biopsy described.

649 It is obvious that in cases of diffuse severe adenomyosis the pathological diagnosis is easy
 650 with high diagnostic accuracy reaching almost 100%. However, the microscopic diagnosis is
 651 more difficult in cases of more limited disease affecting part of the myometrium. False
 652 negative results might be due to unsuccessful sampling of the adenomyotic area and false
 653 positive results might be due to hysteroscopic biopsies of tangential sampling of the endo-
 654 myometrial interface. Although guided sampling is used to overcome the above mentioned
 655 diagnostic errors, still diagnostic accuracy is not ideal with varying degrees of sensitivity and
 656 specificity.

657 Table 12 provides an overview of the accuracy (in terms of sensitivity, specificity, positive
 658 predictive value and negative predictive value) of biopsy compared to reference standard
 659 histology to diagnose adenomyosis.

660 Recommendation

Uterine biopsy is not recommended for the diagnosis of adenomyosis due to its marked variability in accuracy and invasive nature.

661

662 Table 12: Accuracy of biopsy compared to reference standard histology for diagnosis of
663 adenomyosis.

Reference	No of patients	Sampling technique	Sensitivity	Specificity	PPV	NPV
(Laban et al., 2025)	60	Hysteroscopy guided biopsy of the posterior wall	86.4%	N/A	66.7%	N/A
(Dakhly et al., 2016)	292	Hysteroscopic Scissors / graspers Single biopsy form the posterior wall	54.3%	78.5%	75.9%	58.0%
(Jeng et al., 2007)	100	Laparoscopy-guided myometrial biopsy	98%	100%	100%	80%
(Vercellini et al., 1998)	102	Ex-vivo uterine needle biopsy	44.8%	95.9%	81.2	81.4
(Brosens and Barker, 1995)	40	Ex-vivo uterine needle biopsy	44%	NR	NR	NR
(Popp et al., 1993)	68	Laparoscopic, vaginal ultrasound guided myometrial biopsy	14%	NR	NR	NR

664 PPV: positive predictive value, NPV: negative predictive value.

665

666 Discussion

667 This Recommendations for Good Practice paper critically assesses current methodologies for
668 diagnosing adenomyosis, spotlighting the heterogeneity in the literature concerning its
669 terminology, classification, and diagnostic approaches. It integrates classic insights of
670 histology with advanced diagnostic technologies such as ultrasound and MRI (Bird et al., 1972,
671 Brosens et al., 1995). This Good Practice Recommendations paper reviews seminal historical
672 descriptions, such as those by Cullen (Cullen, 1908) and Sampson (Sampson, 1921), and also
673 describes contemporary research that pushes the frontiers of molecular and imaging
674 diagnostics in adenomyosis (Kishi et al., 2012, Leyendecker et al., 2023b, Yamaguchi et al.,
675 2021).

676 In a first step, the working group decided to review all existing classification and
677 categorisation systems in literature, rather than developing a new one. Specifically, nine
678 proposals were identified based on histology, five on ultrasound, and six on MRI. This
679 distribution is influenced by the historical evolution of imaging modalities and the intended
680 purpose of each proposal. Despite differences in diagnostic methods and intended purposes,
681 the criteria for reporting and classifying adenomyosis share several similarities, highlighting
682 the potential to arrive at an internationally accepted universal classification systems. For
683 ultrasound, the MUSA criteria (Van den Bosch et al., 2015) have been internationally accepted
684 as the best available standardised terminology and reporting framework for adenomyosis on
685 ultrasound, and several validation studies have been published in the past years (Andersson
686 et al., 2023, Dosunmu et al., 2025, Kadam et al., 2025, Yavuz et al., 2024). Nevertheless, it fails
687 to provide any information regarding the classification of morphological subtypes of the

688 disease. This classification system although it is very descriptive fails to prove the correlation
689 between histological, clinical, and ultrasound findings and severity of the disease. While the
690 MUSA criteria have their shortcomings, the use of standardised terminology and reporting of
691 adenomyosis features in international research studies is of key importance towards a higher
692 quality evidence base and a better understanding of the disease. For MRI, currently, an
693 internationally accepted reporting system is still missing.

694 Adenomyosis was long seen as a benign pathology in post-menopausal women, as diagnosis
695 was made histopathologically after hysterectomy. However, it has become increasingly clear
696 that it also affects women of reproductive age who desire uterine preservation, highlighting
697 the need of non-invasive diagnostic methods. Diagnosis of adenomyosis on imaging is
698 however complicated by the lack of universally accepted reporting and classification systems
699 and the variability in diagnostic accuracies of different imaging modalities, such as ultrasound
700 and MRI. In addition, currently, the reference standard or diagnostic accuracy studies is
701 histopathologic diagnosis and there is still no international agreement between pathologists
702 on how to diagnose adenomyosis (McCaughey et al., 2025). Diagnosing adenomyosis through
703 histological examination relies on a variety of criteria detailed in the literature, each with
704 specific advantages and drawbacks. The commonly cited 2-2.5 mm threshold for myometrial
705 invasion of adenomyosis is largely consensus-based and derived from microscopic field
706 approximations, rather than from prospective outcome-based studies. The selection of a
707 diagnostic criterion can influence the reported prevalence rates of adenomyosis, the
708 detection of sub-endometrial cases, and the accuracy of non-invasive diagnostics.
709 Establishing a consensus on diagnostic criteria is crucial to standardise research findings and
710 enhance the management of this condition.

711 Several reporting and classification systems for adenomyosis have been proposed based on
712 transvaginal ultrasonography (Exacoustos et al., 2020, Lazzeri et al., 2018, Sinha et al., 2022,
713 Van den Bosch et al., 2019, Van den Bosch et al., 2015). The reporting system by the MUSA
714 group has received the greatest international acclaim (Van den Bosch et al., 2015). After their
715 first publication, they were revised by Delphi consensus among experts, making the
716 distinction between direct and indirect criteria (Harmsen et al., 2022). The direct features of
717 adenomyosis are features indicating presence of ectopic endometrial tissue in the
718 myometrium, and indirect features are described as features reflecting changes in the
719 myometrium secondary to presence of endometrial tissue in the myometrium.

720 Transvaginal ultrasound has been shown to be sufficiently accurate compared to
721 histopathology as the reference standard in recent meta-analyses (Alcázar et al., 2023, Telling
722 et al., 2020). However, diagnostic accuracy of ultrasound for adenomyosis is highly dependent
723 on the operator's skill and experience, and many of the diagnostic accuracy studies have been
724 conducted in expert centers, resulting in unrealistically high accuracy for ultrasound diagnosis
725 of adenomyosis. Indeed, most recent validation studies of the MUSA criteria have shown that
726 the inter- and intra-observer agreement is only modest (Dosunmu et al., 2025, Kadam et al.,

727 2025). In addition, the accuracy of the presence of one direct and/or indirect feature to
728 diagnose adenomyosis needs further investigation.

729 Unlike for transvaginal ultrasound, several authors have proposed different MRI reporting
730 and classification systems, without reaching an international consensus (Gordts et al., 2008).
731 Similar to ultrasound, some researchers also distinguish between direct and indirect signs of
732 adenomyosis for its diagnosis on MRI (Celli et al., 2022). A direct diagnostic sign of
733 adenomyosis is the presence of tiny myometrial cysts in the inner myometrium. Indirect
734 criteria of adenomyosis are based on JZ thickening (Celli et al., 2022).

735 Irrespective of the lack of internationally accepted reporting and classification system, MRI
736 has shown to have comparable diagnostic accuracy as transvaginal ultrasound in recent meta-
737 analyses (Alcázar et al., 2023, Tellum et al., 2020). MRI's advantage over ultrasound lies in its
738 improved capacity to provide consistent results across different operators, minimising the
739 variability seen with ultrasound. Still, there is variation in protocols, and variation in
740 radiologist training and interpretation. In addition, it is important to be aware of the
741 hormone-dependent nature of the JZ, influencing its thickening, reducing the MRI sensitivity
742 for the diagnosis of adenomyosis (Celli et al., 2022). MRI can be very useful in cases of
743 concomitant uterine diseases, such as leiomyomas and endometriosis, making the imaging
744 diagnosis more complex. Furthermore, the utilisation of MRI is often limited by factors such
745 as higher costs and reduced accessibility, which may not make it suitable for first-line
746 diagnostic use but rather reserved for inconclusive ultrasound cases or pre-surgical planning
747 (Gordts et al., 2008, Grimbizis et al., 2014).

748 In addition to modality-specific difficulties to take into account, it is important to highlight
749 that diagnostic accuracy studies are performed in women undergoing hysterectomy for
750 histopathological confirmation. While this approach is sensible, it also introduces
751 considerable bias, as women undergoing hysterectomy often have more advanced or
752 symptomatic disease. In addition, the main group of women suffering from adenomyosis
753 symptoms and infertility are a younger population, further skewing the results of diagnostic
754 accuracy. Furthermore, these diagnostic accuracy studies are often retrospective in nature
755 and single-center, therefore, the resulting quality of this evidence is considered low to very
756 low.

757 Concerning the role of biopsy for diagnosis confirmation in patients with suspected
758 adenomyosis, based on the existing data no definite recommendations can be provided. This
759 is due mainly to the heterogeneity of the sampling techniques and the variety of the evidence,
760 which is actually quite limited. Although the theoretical strength of myometrial biopsy is the
761 recognition of endometrial tissue within the myometrium and the definite diagnosis of the
762 disease, the main limitation is that the sample is not always representative in cases of disease
763 covering part of myometrium; laparoscopic and/or ultrasound guidance might contribute in
764 overcoming this limitation. Thus, more data are needed on safety, the technical aspects, the
765 route, the number of biopsies needed and the guidance in targeting the right area. At the

766 moment, laparoscopic ultrasound guided extra-uterine biopsy might be used in patients
767 whom diagnosis confirmation might alter their management.

768 To conclude, this Good Practice Recommendations paper provides a historical overview of
769 histopathological definitions of adenomyosis, combined with a thorough review of current
770 reporting and classification systems, highlighting the need for future research to standardise
771 diagnostic criteria across imaging modalities. A solid evidence base underlying the diagnostic
772 criteria and a unified terminology for adenomyosis is of critical importance to support further
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1087 **Supplementary data**

- 1088 - S1: Abbreviations
 1089 - S2: List of recommendations
 1090 - S3: List of participants to the stakeholder review

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1092 **S1: Abbreviations**

Abbreviation	Explanation
ACUM	Accessory cavitated uterine malformation
ADC	Apparent diffusion coefficient
AUB	Abnormal uterine bleeding
AUC	Area under the curve
CI	Confidence interval
HIFU	High-intensity focused ultrasound
JZ	Junctional zone
LPF	
MR	Magnetic resonance
MRI	Magnetic resonance imaging
MUSA	Morphological Uterus Sonographic Assessment
NR	Not reported
NRS	
NVP	Negative predictive value
OR	Odds ratio
PI	Pulsatility index
PPV	Positive predictive value
QoL	Quality of life
RI	Resistive index
SI	Signal intensity
SR	Strain ratio
SWE	Shear wave elastography
TVUS	Transvaginal ultrasound
USS	Ultrasound
Vmax	Peak systolic velocity

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1095 **S2: List of recommendations**

Histopathology	
	In histopathology, commonly used thresholds vary (2–3 mm or field-based definitions); therefore, studies should explicitly report the threshold and sampling approach used.
	In histopathological analysis, the use of high-, medium- and low-power fields is not standardised terminology, and should be avoided in describing adenomyotic lesions. Rather, invasion depth should be reported in standardised metric units.
Terminology	
	The adenomyosis working group recommends following the revised MUSA criteria to diagnose adenomyosis by ultrasound.
	The adenomyosis working group recommends differentiating between direct and indirect features to report on the diagnosis of adenomyosis. Direct features included myometrial cysts, hyperechogenic islands and echogenic subendometrial lines and buds. Globular uterus, asymmetrical myometrial thickening, fan-shaped shadowing, translesional vascularity, irregular JZ and interrupted JZ are considered indirect features of adenomyosis.
	The main direct MRI finding of adenomyosis are the presence of high signal intensity myometrial foci, linear striations (finger like indentations) and tiny myometrial and subendometrial cysts and the others remain as indirect findings.
	The adenomyosis working group recommends not using the JZ thickness ≥ 12 mm as the sole adenomyosis feature to diagnose adenomyosis on MRI.
Diagnosis	
	Both MRI and ultrasound have high sensitivity and specificity in detecting adenomyosis when histology is used as the benchmark. Transvaginal ultrasound should be considered the first-line diagnostic modality. MRI should be regarded as a second-line imaging modality, indicated in selected clinical scenarios. It plays an important role in assessing disease extent, detecting concomitant gynecologic conditions, supporting the differential diagnosis, and potentially informing therapeutic planning.

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