Imaging techniques in the management of abnormal vaginal bleeding in non-pregnant women before and after menopause.

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Imaging techniques in the management of abnormal vaginal bleeding in non-pregnant women before and after menopause

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Abstract

Transvaginal ultrasound plays a pivotal role in the management of non-pregnant women with abnormal vaginal bleeding. No other imaging technique has a role in the triage of these women. In women with postmenopausal bleeding ultrasound is used to categorize women as being at low or high risk of endometrial cancer, the result of the ultrasound examination being the basis for further management. In women with abnormal vaginal bleeding before menopause the role of ultrasound is less clear, because some common causes of abnormal vaginal bleeding before menopause cannot be diagnosed with ultrasound, e.g. infection, dysfunctional bleeding or problems with intrauterine contraceptive devices or contraceptive pills. Nonetheless, transvaginal ultrasound may sometimes be helpful also in women with abnormal vaginal bleeding before menopause. In this chapter ultrasound findings in women with endometrial cancer, endometrial polyps, endometrial hyperplasia, adenomyosis, uterine myomas including submucuous myomas, and leiomyosarcoma will be presented and ultrasound based triage of women with postmenopusal bleeding described.

Key words Ultrasonography; endometrium; endometrial neoplasms; metrorrhagia

A. Introduction

The causes of abnormal vaginal bleeding differs between pre- and post-menopausal women. Endometrial cancer and other endometrial malignancies are relatively common causes in postmenopausal women but are rare before menopause. Myomas and adenomyosis may cause abnormal bleeding before menopause but rarely thereafter. Endometrial polyps, hyperplasia and uterine leiomyosarcomas may explain abnormal vaginal bleeding both before and after menopause, but leiomyosarcomas are extremely rare. Infection, dysfunctional bleeding or problems with contraceptives are common causes of abnormal vaginal bleeding before menopause.

Transvaginal ultrasound plays a pivotal role in the management of non-pregnant women with abnormal vaginal bleeding. No other imaging technique has a role in the triage of these women. In women with postmenopausal bleeding ultrasound is used to categorize women as being at low or high risk of endometrial cancer, the result of the ultrasound examination being the basis for further management. In women with abnormal vaginal bleeding before menopause the role of ultrasound is less clear, because some common causes of abnormal vaginal bleeding before menopause cannot be diagnosed with ultrasound, e.g. infection, dysfunctional bleeding or problems with intrauterine contraceptive devices or contraceptive pills. Nonetheless, transvaginal ultrasound may sometimes be helpful also in these women.

A gynaecological ultrasound examination in a woman with abnormal vaginal bleeding must be preceded by a thorough history and a careful speculum examination and gynaecological palpation. The role of ultrasound is to detect pathology not detectable at a clinical examination, for example endometrial pathology, small submucuous myomas, adenomyosis, cancer of the urinary bladder or small hormone producing ovarian tumours. The ultrasound examination is also used to confirm or

refute a diagnosis suspected on the basis of abnormal findings at palpation, for example uterine intramural or subserous myomas or adnexal masses. The clinician then needs to decide if an abnormal ultrasound finding is the likely cause of the abnormal bleeding or if it is an incidental finding unrelated to the woman´s symptoms.

The examination technique to be applied when scanning the uterus and the terminology to be used when describing ultrasound images of the endometrium and the uterine cavity are described in detail in reference [1]. An ultrasound examination performed because of abnormal vaginal bleeding should also include examination of the adnexa and the urinary bladder, because abnormal bleeding may be explained by a hormone producing ovarian tumour or a tumour in the urinary bladder (the woman confusing bleeding from the urinary tract with vaginal bleeding).

A. Imaging techniques in the management of postmenopausal bleeding

Ultrasound plays a very important role in the management of women with postmenopausal bleeding. About 10% of women with postmenopausal bleeding have endometrial cancer, but as many as 50% may not have any endometrial pathology at all [2]. There is strong scientific evidence that a transvaginal ultrasound examination with measurement of endometrial thickness can discriminate between those women with postmenopausal bleeding that are at high risk of endometrial cancer and those that are at low risk. The risk of finding an endometrial cancer in a woman with postmenopausal bleeding and endometrial thickness as measured by ultrasound $\leq$ 4 mm is very low. In a meta-analysis including almost 6000 women with postmenopausal bleeding this risk was estimated to be about 1 in 100 in women not using hormone replacement therapy and about 1 in 1000 in women using hormone

replacement therapy [2]. It is considered safe to refrain from endometrial sampling to obtain a histological diagnosis in women with postmenopausal bleeding and endometrial thickness ≤ 4 mm [2, 3, 4]. This endometrial thickness cutoff is applicable both in users and non-users of hormone replacement therapy [2]. Even though it has been suggested that it would be safer to use a cutoff of 3 mm to exclude endometrial cancer in women with postmenopausal bleeding [5], the 4 mm cutoff prevails in clinical practice.

In rare cases, a cervix cancer not detectable at speculum examination or palpation, a bladder tumour (Figure 1) or an ovarian tumour, e.g. a granulosa cell tumour, may be detected at the transvaginal ultrasound examination. Imaging of cervix cancer is described in another chapter of this issue.

B. How to measure endometrial thickness at transvaginal ultrasound?

Endometrial thickness is measured on a sagittal scan through the uterus. The uterus is scanned from one side to the other and the endometrial thickness is measured where it appears to be at its thickest from its outermost border on one side to that on the other [1]. The endometrium must not be measured on a transverse scan, because a transverse scan may be an oblique scan, and if so will yield to large a measurement. If there is spontaneous fluid in the uterine cavity, each endometrial layer is measured separately and the two measurements are added [1]. The measurement technique is illustrated in Figure 2.

In about 6-7% of women with postmenopausal bleeding the endometrium is not clearly visible and so is not measurable [6, 7]. In this situation saline contrast sonohysterography should be performed (see below).

B. Can the estimation of risk of endometrial malignancy be refined in women with postmenopausal bleeding and endometrial thickness ≥5mm?

A differentiation of risk in women with endometrial thickness ≥5 mm allows individualized management. A woman at relatively low risk of endometrial cancer despite her endometrium being thick will be managed differently from a woman at extremely high risk. Clinical information, the grey scale ultrasound morphology of the endometrium and the vascularization of the endometrium as assessed by colour Doppler or power Doppler ultrasound add information to endometrial thickness when estimating the risk of endometrial malignancy in women with postmenopausal bleeding and endometrial thickness ≥5 mm [7, 8, 9]. Irregular echogenicity of the endometrium (Figure 3) and irregularly branching vessels, densely packed vessels or colour splashes in the endometrium at power Doppler examination (Figure 3) increase the risk of malignancy [8]. High colour content in the endometrial scan at power or colour Doppler examination is also a sign of malignancy [7, 9] (Figure 3). The older the woman, the thicker the endometrium and the higher the colour content of the endometrial scan the higher the risk of malignancy, but if the woman uses hormone replacement therapy the risk decreases [7].

Mathematical formulas to calculate the individual risk of malignancy in women with postmenopausal bleeding and endometrial thickness ≥5 mm have been published [7, 8, 9]. However, there are no published studies describing their diagnostic performance on prospective validation. Therefore, it is too early to introduce these models into clinical practice.

B. Saline contrast sonohysterography

Infusion of saline into the uterine cavity during transvaginal scanning (saline contrast sonohysterography, saline infusion sonography or hydrosonography) clarifies whether there are focal lesions in the uterine cavity or not [10]. A focal lesion is anything that protrudes into the uterine cavity above the baseline endometrial surface [1] (Figure 4). Unless the cervical canal is stenotic, saline contrast sonohysterography is easy to perform. A thin plastic catheter (without a balloon) with a sterile 20 ml syringe filled with sterile saline attached to it is introduced into the uterine cavity through the cervical canal. Before introduction, the catheter must be flushed with saline to expel all air (air reflects the ultrasound beams making the ultrasound image difficult to interpret). Then the vaginal ultrasound transducer is introduced into the vagina and a few millilitres of saline is infused into the uterine cavity during scanning. If the cervical canal is stenotic, it may be necessary to use both a tenaculum and a small uterine sound before the catheter can be introduced into the uterus. Saline contrast sonohysterography fails in 10-20% of all women with postmenopausal bleeding [11, 12, 13].

Virtually all endometrial pathology grows focally in the uterine cavity [13]. If there are no focal lesions in the uterine cavity the odds of malignancy decrease 20 times and the odds of any endometrial pathology decrease 30 times [14]. Thus, a smooth endometrium outlining the uterine cavity at saline contrast sonohysterography is a strong sign of normality.

Irregular focal lesions in the uterine cavity at saline contrast sonohysterography in women with postmenopausal bleeding and endometrial thickness $\geq$5 mm is a very strong sign of endometrial malignancy [12] (Figure 4).

Because most focal lesions cannot be removed at all or can only be partially removed if a blind endometrial sampling technique is used, such as Pipelle ®

(Prodimed, Neulliy en Thelle, France), Endorette ® (MedScand AB, Malmö, Sweden), or dilatation and curettage, focal lesions should be hysteroscopically resected under direct visual control [6, 14]. This is to ensure that a representative sample is obtained.

B. Staging of endometrial cancer and discrimination between high risk and low risk endometrial cancer

If endometrial cancer is suspected at ultrasound examination when the woman first consults with her bleeding the spread of the cancer can be assessed at that primary consultation using a combination of vaginal and abdominal ultrasound. Moreover, the likelihood of a specific histological type of cancer (high risk or low risk) can be estimated. Computer tomography and magnetic resonance imaging can also be used for staging of endometrial cancer. Staging of endometrial cancer and discrimination between high risk and low risk endometrial cancer is discussed in another chapter in this issue.

B. Ultrasound based triage of women with postmenopausal bleeding

Based on the information provided above, women with postmenopausal bleeding can be managed as described in Figure 5. After a thorough history and clinical examination a vaginal smear is taken to try to rule out cervical cancer (because very small cervical cancers are unlikely to be detectable with transvaginal ultrasound). Then a transvaginal ultrasound examination is carried out with measurement of endometrial thickness. If the endometrial thickness is $\leq$ 4 mm the woman is dismissed without any endometrial sample being taken. If the endometrium measures $\geq$5mm, saline contrast sonohysterography is performed. If it reveals focal lesions the woman

is scheduled for operative hysterosocopy with removal of the focal lesion(s) under direct visual control. If there are no focal lesions an endometrial sample can be taken using an outpatient endometrial sampling device. If this fails the woman should be scheduled for dilatation and curettage in anaesthesia or analgesia.

If the endometrium is not seen well and so cannot be reliably measured, saline contrast sonohysterography should be performed to clarify the situation. If saline contrast sonohysterography fails the woman should undergo diagnostic hysteroscopy in anaesthesia (or analgesia).

B. Can other pathology than endometrial cancer be diagnosed with transvaginal ultrasound in women with postmenopausal bleeding?

C. Benign endometrial polyps

Benign endometrial polyps are often found in women with postmenopausal bleeding [2, 7, 8, 9, 13]. They are then supposed to be the cause of the abnormal bleeding, even though this is not necessarily the case [15]. The typical ultrasound appearance of a benign endometrial polyp is thick hyperechogenic endometrium with or without regular small cysts (cysts are common in atrophic polyps where the glands are cystically dilated [16]) and the presence of a “bright edge” [17, 18] (Figure 6). The bright edge is explained by the interface between the polyp (or any other focal lesion in the uterine cavity) and the endometrium [1,18]. However, when these ultrasound signs of endometrial polyp were prospectively validated in women with postmenopausal bleeding and endometrial thickness $\geq$5 mm they did not perform very well: sensitivity 49% (21/43), specificity 81% (50/62) [13]).

At Doppler ultrasound examination an endometrial polyp is characterized by the presence of a "pedicle artery" (also called "feeding vessel"), i.e. one big vessel seen to enter the endometrium from the surrounding myometrium [19] (Figure 6). In the article cited [19] the sensitivity of the pedicle artery with regard to endometrial polyp in women with postmenopausal bleeding was 78% (47/60) and the specificity 88% (88/100), i.e. the pedicle artery sign had at most moderate ability to correctly identify polyps in this patient group (positive likelihood ratio 6.5 and negative likelihood ratio 0.25). Alcazar et al [20] reported the presence of a single vessel penetrating into the endometrium from the myometrium (corresponding to the pedicle artery sign) to have a sensitivity with regard to endometrial polyp of 97% (33/34) and a specificity of 88% (38/43) in women with postmenopausal bleeding, i.e. in the hands of Alcazar and coworkers the pedicle artery sign performed better than in the hands of Timmerman et al [19]. To the best of my knowledge the ability of the pedicle artery sign to correctly identify polyps in postmenopausal women with vaginal bleeding has not been prospectively validated. However, on prospective external validation in women with abnormal vaginal bleeding either before or after menopause, the pedicle artery as a sign of endometrial polyp had a sensitivity of 67% (26/39) and a specificity of 98% (57/58) [21]. This corresponds to moderate diagnostic performance.

The typical appearance of an endometrial polyp at saline contrast sonohysterography is a polypoid focal lesion with regular hyperechogenic echotexture, with or without regular small cysts, and with a smooth surface [17] (Figure 6). When these criteria of endometrial polyp were prospectively validated in women with postmenopausal bleeding and endometrial thickness $\geq$5 mm they did not perform well: sensitivity 79% (26/33), specificity 76% (34/45) [13].

Some polyps may contain foci of malignancy [22, 23, 24, 25, 26, 27], but it is not known if such polyps manifest other ultrasound features than benign polyps, even though it has been suggested that in asymptomatic women polyps with malignant changes are larger than benign polyps [23]. Therefore, in women with postmenopausal bleeding and endometrial thickness ≥5 mm, all focal lesions irrespective of their ultrasound appearance at saline contrast sonohysterography should be hysteroscopically resected under direct visual control to ascertain their complete removal.

C. Endometrial hyperplasia

The ultrasound characteristics of endometrial hyperplasia have been described for women of any age not separating pre- from post-menopausal women and not separating asymptomatic from symptomatic women [28]. In the article cited the ultrasound characteristics of endometrial hyperplasia were described as thick, hyperechogenic endometrium (sometimes containing small cysts) with a polypoid surface at saline contrast sonohysterography [28]. To the best of my knowledge these ultrasound criteria of endometrial hyperplasia have not been prospectively validated. Ultrasound images of endometrial hyperplasia from my own clinical practice are shown in Figure 7.

C. Submucuous myomas

Submucuous myomas are sometimes detected at transvaginal ultrasound examination of women with postmenopausal bleeding [13]. The typical ultrasound appearance of a submucuous myoma is a solid tumour protruding into the uterine cavity from the surrounding myometrium and with the same echogenicity as the

surrounding myometrium (Figure 8). However, when these ultrasound criteria of submucous myoma were applied in women with postmenopausal bleeding and endometrial thickness ≥5 mm they did not perform well at unenhanced ultrasound examination. They were very specific (specificity 97%, 96/99) but not sensitive (sensitivity 33%, 2/6). This means that a submucuous myoma could be present even if the typical ultrasound signs of submucuous myoma were absent [13]. On the other hand, saline contrast sonohysterography was a good method for diagnosing submucuous myomas: sensitivity 80% (4/5), specificity 99% (72/73) [13]. In some cases, a submucuous myoma can be seen to be covered by endometrium at saline contrast sonohysterography [28] (Figure 8).

It has been suggested that submucuous myomas are surrounded by a ring of colour at colour or power Doppler ultrasound. On prospective validation in women with abnormal vaginal bleeding (proportion of pre- and post-menopausal women not reported) the colour ring sign had a sensitivity with regard to submucuous myoma of 67% (26/39) and a specificity of 98% (57/58) [21], i.e. it manifested moderate diagnostic performance.

C. Uterine leiomyosarcoma

Despite leiomyosarcoma being a very rare disease [29], in some cases the cause of postmenopausal bleeding is a uterine leiomyosarcoma. The largest series published comparing the ultrasound appearance of uterine leiomyosarcomas with that of benign leiomyomas includes eight leiomyosarcomas and 225 benign leiomyomas [30]. The menopausal status of the women in the study cited was not reported. The results showed that leiomyosarcomas were more often solitary lesions than benign leiomyomas (100% versus 53%) and that the leiomyosarcomas more often contained

cystically degenerated areas (50% versus 14%), and more often manifested marked central vascularization at power Doppler examination (87.5% versus 3%). Leiomyosarcomas were generally more richly vascularized than benign leiomyomas and they were larger, seven of eight being $\geq$ 8 cm in diameter. The combination of solid lesion $\geq$ 8 cm in diameter with ultrasound signs of cystic degeneration and marked central vascularization was a very specific (but not sensitive) ultrasound sign of leiomyosarcoma (sensitivity 50%, specificity 99%). These ultrasound signs of leiomyosarcoma need to be prospectively validated to better estimate their ability to distinguish leiomyosarcomas from benign leiomyomas. Ultrasound images of a benign uterine leiomyoma and of a leiomyosarcoma are shown in Figure 9.

The role of magnetic resonance imaging in the differential diagnosis between benign leiomyoma and malignant leiomyosarcoma is unclear. In one published series including four uterine leiomyosarcomas and 41 benign leiomyomas, magnetic resonance imaging correctly diagnosed all four leiomyosarcomas with no false positive result, the criterion of leiomyosarcoma being ill defined margins of the tumour [31]. In a more recently published article including five women with leiomyosarcoma and 76 women with benign leiomyomas, diffusion weighted magnetic resonance imaging was reported to discriminate between leiomyosarcoma and leiomyoma with a sensitivity of 100% and a specificity of 94% [32]. The diffusion weighted magnetic resonance imaging criteria for classifying a uterine nodule as being at high or low risk of leiomyosarcoma remain to be prospectively validated.

A. Imaging techniques in the management of abnormal vaginal bleeding in non-pregnant women before menopause

The first line imaging method to use in non-pregnant women with abnormal vaginal bleeding before menopause is ultrasound. However, the most common causes of abnormal vaginal bleeding in women before menopause, i.e. dysfunctional bleeding, infection and problems with contraceptives, cannot be diagnosed with any imaging technique. Causes of abnormal bleeding that can be detected with ultrasound in women before menopause are, for example, endometrial polyps, submucuous myomas, other types of myomas, leiomyosarcomas, possibly (but not certainly) endometrial hyperplasia, and adenomyosis. Endometrial cancer is rare before menopause [33].Cervix cancer is more common than endometrial cancer before menopause, but in most cases, a cervix cancer should be detectable at a clinical gynaecological examination. The ultrasound features of cervix cancer are described in another chapter of this issue.

B. Endometrial thickness measurements and saline contrast sonohysterography in premenopausal women

Endometrial thickness measurements with ultrasound have no role in the management of women with abnormal bleeding before menopause, because the endometrial thickness changes throughout the menstrual cycle. Immediately after menstruation the endometrium is thin and hyperechogenic, during the proliferative phase it increases in thickness and attains a triple layer appearance, in the secretory phase it remains thick and becomes homogenously hyperechogenic (often with posterior acoustic enhancement) [34, 35].Ultrasound images of normal endometrium in different phases of the menstrual cycle are shown in Figure 10.

Saline contrast sonohysterography should not be performed in the secretory phase of the menstrual cycle, because of the risk that there is a fertilized egg in the uterine

cavity. Moreover, in the secretory phase, the endometrium often has a polypoid outline at saline contrast sonohysterography, and endometrial folds may be confused with pathological lesions [Jokubkiene et al, unpublished].

C. Endometrial polyps

The typical ultrasound feature of an endometrial polyp in a woman before menopause is a hyperechogenic area in the endometrium surrounded by a bright edge. Cystic areas are much more rarely seen than in polyps in postmenopausal women (personal experience). At colour or power Doppler ultrasound examination a pedicle artery is often detectable [19]. In the study cited the sensitivity of the pedicle artery with regard to endometrial polyp in women before menopause with abnormal vaginal bleeding was 96% (26/27) and the specificity 91% (89/98) [19], i.e. the pedicle artery was an excellent test for correctly identifying polyps in this group of women.

At saline contrast sonohysterography a polyp in a woman before menopause is typically seen as a polypoid focal lesion with regular hyperechogenic echogenicity - very rarely containing regular small cysts - and with a smooth surface (personal experience of the author). Endometrial folds, which are common in the secretory phase of the menstrual cycle [Jokubkiene et al., unpublished] or blood clots may be confused with endometrial polyps in premenopausal women with abnormal vaginal bleeding [36].

To the best of my knowledge, neither the grey scale nor the colour or power Doppler ultrasound criteria for endometrial polyp either at unenhanced ultrasound or at saline contrast sonohysterography have been prospectively validated specifically in premenopausal women either with or without abnormal vaginal bleeding. However, in a study of premenopausal women with bleeding problems, where all the above criteria

of endometrial polyp seem to have been applied, the ultrasound diagnosis of endometrial polyp was not confirmed at operative hysteroscopy in 19 (25%) of 75 women [37].

It is important to emphasize that if a lesion with the typical appearance of an endometrial polyp is detected at ultrasound in a woman with abnormal bleeding before menopause it is not necessarily the polyp-like lesion that is the cause of the bleeding. Polyps are common in asymptomatic women [15], and polyps may regress spontaneously in women before menopause [38]. Hysteroscopic resection of endometrial polyps in women with irregular vaginal bleeding before menopause has questionable effect on the bleeding problems [37, 39].

C**.** *Endometrial hyperplasia*

The ultrasound appearance of endometrial hyperplasia has been described but not separately for pre-and post-menopausal women, not separately for women with and without abnormal bleeding, and not separately for different types of hyperplasia, nor have the ultrasound criteria been prospectively validated, see above [28].

C**.** *Submucuous myomas*

Submucuous myomas may well be the cause of abnormal vaginal bleeding in women before menopause, even though the prevalence of submucuous myomas in women with no gynaecological symptoms is not known. The typical ultrasound appearance of a submucuous myoma is likely to be the same in women before and after menopause (Figure 8). However, as far as I know the sensitivity and specificity of transvaginal ultrasound (with or without saline contrast sonohysterography) with regard to submucuous myoma in premenopausal women with abnormal uterine

bleeding has not been reported. Polyps and submucuous myomas may sometimes be confused with each other at ultrasound examination in women with abnormal bleeding before menopause [36].

Results of observational studies suggest that hysteroscopic resection of submucuous myomas in women with irregular vaginal bleeding before menopause ameliorates the bleeding problems [40]. However, to the best of my knowledge there are no randomized controlled trials comparing hysteroscopic resection with no treatment or with medical treatment.

C. Intramural and subserous myomas

Intramural myomas may cause menorrhagia. The typical ultrasound appearance of intramural or subserous uterine leiomyomas is a round, oval, or lobulated solid tumor casting stripy shadows (Figure 9). Ultrasound is as good as magnetic resonance imaging for detecting uterine myomas [41]. However for determination of the exact number and location of the myomas ("myoma mapping") magnetic resonance imaging is superior to transvaginal ultrasound if the uterus is very large (volume > 375 ml) or if it contains five or more myomas [41]. Myoma mapping is clinically important if myoma enucleation is considered as treatment.

C. *Adenomyosis*

Adenomyosis is traditionally considered to be associated with menorrhagia [42]. However, this association has been questioned in a recent publication [43]. Adenomyosis may be confidently diagnosed using transvaginal ultrasound. As long as there are no big myomas in the uterus, ultrasound is as good as magnetic resonance imaging for diagnosing adenomyosis [42]. In women examined both with ultrasound

and magnetic resonance imaging, the sensitivity of the two methods with regard to adenomyosis varied between 65% and 89 % and the specificity between 65 % and 98% [42]. Typical ultrasound signs of adenomyosis are described in another chapter of this issue.

C. Endometrial cancer

To the best of my knowledge there is no publication describing the typical ultrasound appearance of endometrial cancer in premenopausal women. On the other hand there is little reason to believe that endometrial cancer in premenopausal women manifests ultrasound features different from those of endometrial cancer in postmenopausal women.

An endometrium with irregular internal echogenicity that is richly vascularized at colour or power Doppler ultrasound with irregularly branching vessels, densely packed vessels or colour splashes in the endometrium should raise the suspicion of endometrial cancer both in pre- and post-menopausal women (Figure 3). So should the presence of irregular intracavitary focal lesions at saline contrast sonohysterography (Figure 4), see above.

C. Uterine leiomyosarcoma

In very rare cases the cause of abnormal vaginal bleeding in a woman before menopause is a uterine leiomyosarcoma. The ultrasound appearance of uterine leiomyosarcomas has been described but not separately for pre-and post-menopausal women [30]. Whether magnetic resonance imaging is superior to ultrasound for distinguishing leiomyosarcomas from leiomyomas is currently not known, see above.

A. Summary

The role of transvaginal ultrasound for triaging women with postmenopausal bleeding is indisputable. Endometrial thickness ≤ 4 mm as measured by transvaginal ultrasound (on a sagittal section through the uterus) entails a low risk of endometrial cancer, while endometrial thickness ≥ 5 mm entails a high risk. It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness ≤ 4 mm, while it is necessary to obtain a representative endometrial sample in women with postmenopausal bleeding and endometrial thickness ≥ 5mm. In women with postmenopausal bleeding and endometrial thickness ≥ 5mm irregular echogenicity of the endometrium and high colour content in the endometrial scan at power or colour Doppler examination increase the risk of malignancy. The presence of at least one irregular focal lesion in the uterine cavity at saline contrast sonohysterography is a strong sign of endometrial cancer. The typical ultrasound features of endometrial polyps, submucuous myomas, endometrial hyperplasia and leiomyosarcomas have been described. However, we do not know to what extent the ultrasound appearance of these lesions differ between pre-and postmenopausal women. Moreover, the ultrasound features suggested to be typical of various pathologies in the endometrial cavity are based on personal experience, and studies prospectively validating them are very few. Adenomyosis and uterine leiomyomas may cause abnormal vaginal bleeding in premenopausal women. Ultrasound and magnetic resonance imaging have similar ability to diagnose adenomyosis and uterine benign leiomyomas, but magnetic resonance imaging is superior to ultrasound for "myoma mapping" if the uterus is very large (> 375ml) or contains five myomas or more. Endometrial sonographic thickness measurements have no role in the

management of women with abnormal vaginal bleeding before menopause, because endometrial thickness changes throughout the menstrual cycle.

A. Practice points

- Transvaginal ultrasound plays a pivotal role in the management of non-pregnant women with abnormal vaginal bleeding; no other imaging technique has a role in the triage of these women.
- Endometrial thickness $\leq$ 4 mm as measured by transvaginal ultrasound in women with postmenopausal bleeding entails a low risk of endometrial cancer
- It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness $\leq$ 4 mm
- Endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound in women with postmenopausal bleeding entails a high risk of endometrial cancer
- A representative endometrial sample for histological diagnosis must be obtained in women with postmenopausal bleeding and endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound
- Focal lesions in the uterine cavity in women with postmenopausal bleeding and endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound should be hysteroscopically resected under direct visual control to ascertain their complete removal
- Only if there are no focal lesions in the uterine cavity at saline contrast sonohysterography will a blind endometrial sampling technique yield a representative endometrial sample

- The typical ultrasound features of endometrial polyps, submucuous myomas and endometrial hyperplasia have been described, but it is not known if these features are the same in pre-and post-menopausal women, nor have these features been prospectively validated
- Ultrasound and magnetic resonance imaging have similar ability to diagnose adenomyosis and benign uterine leiomyomas
- Magnetic resonance imaging is superior to ultrasound for "myoma mapping" if the uterus is very large (> 375ml) or contains five or more myomas.
- Endometrial sonographic thickness measurements have no role in the management of women with abnormal vaginal bleeding before menopause, because endometrial thickness changes throughout the menstrual cycle.

A. Research agenda

- To establish on the basis of a large amount of prospectively collected data the typical ultrasound appearance of endometrial cancer, endometrial polyps, submucuous myomas, different types of hyperplasia, leiomyosarcomas and endometrial cancer in premenopausal women
- To establish on the basis of a large amount of prospectively collected data the typical ultrasound appearance of different types of endometrial cancer, endometrial polyps, submucuous myomas, different types of hyperplasia and leiomyosarcomas in postmenopausal women
- To prospectively validate ultrasound criteria established as described above for endometrial cancer, polyps, submucuous myomas, different types of

hyperplasia and leiomyosarcomas in pre- and post- menopausal women separately

- To prospectively validate published mathematical models to calculate the risk of endometrial cancer in women with postmenopausal bleeding and endometrial thickness as measured by ultrasound ≥5mm.
- To estimate interobserver agreement when using the International endometrial Tumor Analysis (IETA) terminology to describe ultrasound images of the endometrium

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Legends

Figure 1. Ultrasound images of the uterus (sagittal scan) (a) and of the urinary bladder containing a bladder cancer (b, c) in a woman with postmenopausal bleeding. The grey scale ultrasound image of the urinary bladder is shown in (b) and the colour Doppler image in (c). The tumour is extremely well vascularized. The asterisk denotes the bladder cancer. U, urinary bladder.

Figure 2. Ultrasound measurement of endometrial thickness. The thickness of the endometrium is measured on a longitudinal scan through the uterus where the endometrium appears to be at its thickest (a). If there is fluid in the uterine cavity the two opposite endometrial layers are measured separately and the two measurements are added (b). The callipers denote the measurements.

Figure 3. Ultrasound images of endometrial cancer. The grey scale ultrasound image shows heterogeneous echogenicity of the endometrium (a). The power Doppler image shows high colour content in the endometrium, densely packed vessels and colour splashes (b). The thin green line circumscribes the endometrium. These ultrasound findings are highly suggestive of endometrial cancer. The histological diagnosis here is endometroid cancer of adenopapillary type.

Figure 4. Ultrasound image illustrating intrauterine focal lesions. Using the terminology of the International Endometrial Tumour Analysis group a focal lesion is anything that protrudes into the uterine cavity above the baseline endometrial surface [1]. A very small focal lesion is seen in (a), a larger one in (b), and an irregular one indicating malignancy in (c).

Figure 5. Schematic drawing showing the recommended management of women with postmenopausal bleeding.

* If the endometrium is not seen well and so cannot be reliably measured, saline contrast sonohysterography should be performed to clarify the situation. If saline contrast sonohysterography fails the woman should undergo diagnostic hysteroscopy in anaesthesia or analgesia.

** If the endometrium has heterogenous echogenicity and is richly vascularized so that a diagnosis of endometrial cancer is almost certain one can refrain from saline contrast sonohysterography and take a blind endometrial sample using an outpatient endometrial sampling device. If endometrial cancer is not histologically confirmed then hysteroscopy should be performed.

*** If the sampling fails dilatation and curettage should be performed

Figure 6. Ultrasound images of the uterus showing the typical signs of endometrial polyps in postmenopausal women. In (a) the thick hyperechogenic endometrium is surrounded by "bright edges" (arrows); in (b) the thick endometrium contains cysts and is surrounded by "bright edges" (arrows). The pedicle artery sign, i.e. one big vessel seen to penetrate into the endometrium from the surrounding myometrium [19] is illustrated in (c). At saline contrast sonohysterography a polyp typically appears as a polypoid focal lesion with regular hyperechogenic echotexture with (d) or without (e) regular small cysts, and with a smooth surface.

Figure 7. Ultrasound images obtained at saline contrast sonohysterography of histologically confirmed endometrial hyperplasia. The histological diagnosis in (a) is polypous endometrial hyperplasia (thick, hyperechogenic endometrium with polypoid surface). The histological

diagnosis in (b) is simple hyperplasia (thick, hyperechogenic endometrium with some discrete cysts inside).

Figure 8. Ultrasound image of a submucuous myoma at saline contrast sonohysterography. A solid tumour protruding into the uterine cavity from the surrounding myometrium and with the same echogenicity as the surrounding myometrium is seen (a). In (b) the submucuous myoma is seen to be covered by endometrium (asterisks).

Figure 9. Ultrasound images of a benign uterine leiomyoma (a) and a malignant leiomyosarcoma (b, c). The benign uterine leiomyoma is a round, well demarcated solid tumour casting stripy shadows (a). The leiomyosarcoma is a solid tumour with irregular internal echogenicity and no stripy shadows (b). This leiomyosarcoma is poorly vascularized at power Doppler examination (c), probably because of tumour necrosis.

Figure 10. Ultrasound images of normal endometrium in different phases of the menstrual cycle. Shortly after menstruation the endometrium is thin, sometimes with a faint triple layer appearance as in this case (a), during the proliferative phase it increases in thickness and attains a clear triple layer appearance (b). In the late proliferative phase a thick hyperechogenic rim surrounds the thick triple layer endometrium (c). In the secretory phase the endometrium remains thick and becomes homogenously hyperechogenic (d). Acoustic enhancement, which is common in the secretory phase, is not seen in (d).

MCQ

MCQ 1 Which of the following statements is/are correct?

a) It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness ≤ 4 mm

b) It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness ≥ 5 mm if the endometrium has regular echogenicity and is poorly vascularized at colour or power Doppler ultrasound

c) The absence of focal lesions at saline contrast sonohysterography in women with postmenopausal bleeding is a strong sign of normality

d) In women with postmenopausal bleeding and endometrial thickness ≥5 mm focal lesions in the uterine cavity should be hysteroscopically resected under direct visual control

e) If the endometrium is not seen at transvaginal ultrasound in a woman with postmenopausal bleeding it means that it is thin, and so the risk of endometrial malignancy is low and no endometrial sampling is needed.

Correct answers: a) T b) F c) T d) T e) F

Explanations to the answers to question 1

The risk of finding an endometrial cancer in a woman with postmenopausal bleeding and endometrial thickness as measured by ultrasound ≤ 4 mm is very low. Prospective observational follow-up studies show that it is safe to refrain from endometrial sampling in these women. However, if the endometrial thickness is ≥5 mm, a representative endometrial sample must always be obtained. Regular endometrial echogenicity at grey

scale ultrasound and poor vascularization at colour or power Doppler do decrease the risk of malignancy, but this information should be used mainly for prioritizing women on a waiting list for a diagnostic procedure, not to decide if a diagnostic procedure is needed or not (unless the woman is at extremely high operative risk and surgery is necessary to obtain a histological diagnosis). Almost all endometrial pathology grows focally in the uterine cavity. Therefore, a smooth endometrium with no signs of focal pathology at saline contrast sonohysterography (or hysteroscopy) is a strong sign of normality. Because 87% of focal lesions cannot be removed at all or only partially removed if a blind endometrial sampling technique is used [1], they must be resected under direct visual control to ensure their complete removal. Malignancy is sometimes found in benign polyps. Therefore, it is important to remove focal lesions in toto. An endometrium that cannot be seen at ultrasound cannot be measured and cannot be evaluated with regard to its echogenicity or vascularity. Indeed, endometrial cancer is sometimes diagnosed in women with an invisible endometrium at ultrasound. To clarify the situation, saline contrast sonohysterography should be performed. If it fails the woman should be referred for hysteroscopy and endometrial sampling in anaesthesia or analgesia.

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MCQ2. Which of the following statements is/are correct?

a) Endometrial thickness measurements with transvaginal ultrasound play a pivotal role in the triage of women with irregular bleeding before menopause

b) At ultrasound examination the endometrium is hyperechogenic throughout the menstrual cycle

c) Endometritis has typical appearance at transvaginal ultrasound examination

d) Intracavitary lesions with the appearance of an endometrial polyp at saline contrast sonohysterography may regress if left in situ

e) In premenopausal women, endometrial polyps are typically surrounded by a ring of colour at power Doppler ultrasound examination

Correct answers a) F b) F c) F d) T e) F

Explanations to the answers to question 2

Endometrial thickness measurements with transvaginal ultrasound have no role in the triage of women with irregular bleeding before menopause, because the endometrial thickness changes during the menstrual cycle. Immediately after menstruation the endometrium is thin, during the proliferative phase it increases in thickness and it remains thick in the secretory phase. The ultrasound appearance of the endometrium in case of endometritis is not well known. Despite extensive literature search I have found only one published ultrasound image of reasonably good quality illustrating endometritis. However, this was a special case of anaerobic endometritis after surgery on the uterus, where the uterine cavity was filled with gas [1]. I have found no published high quality ultrasound images of more common types of endometritis or of tuberculous endometritis. Indeed, endometritis in women with clinical signs of pelvic inflammatory disease does not seem to manifest any specific ultrasound features [2]. Benign polyps may regress spontaneously in women before menopause. Whether this is explained by misdiagnosis or

by true polyps regressing is unknown. Polyps are characterized by the presence of a feeding vessel at colour or power Doppler ultrasound examination, i.e. one big vessel entering into the endometrial echo from the surrounding myometrium, while submucuous myomas are reported to be surrounded by a ring of colour.

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MCQ 3 Which of the following statements is/are correct?

a) Magnetic resonance imaging is superior to ultrasound for diagnosing adenomyosis

b) Transvaginal ultrasound is as good as magnetic resonance imaging in detecting uterine leiomyomas

c) Malignant uterine leiomyosarcomas have an ultrasound appearance that is distinctly different from that of benign uterine leiomyomas

d) Magnetic resonance imaging is superior to ultrasound for discriminating between uterine leiomyosarcomas and benign uterine leiomyomas

e) The typical ultrasound features of endometrial hyperplasia are the same in pre-and post-menopausal women

Correct answers a) F b) T c) F d) F e) F

Explanations to the answers to question 3

In three studies where women underwent both ultrasound and magnetic resonance imaging before hysterectomy, ultrasound was as good as magnetic resonance imaging for diagnosing adenomyosis provided that the uterus was not very large (> 400ml) and did not also contain myomas [1]. In a meticulously designed prospective study where women underwent both transvaginal ultrasound and magnetic resonance imaging before hysterectomy, the two methods had equal ability to detect uterine leiomyomas (magnetic resonance imaging sensitivity 99%, specificity 86%; transvaginal ultrasonography sensitivity 99%, specificity 91%). However, magnetic resonance imaging was superior to transvaginal ultrasound for myoma mapping (determination the exact number, location and size of the myomas) if the uterus was > 375 ml or contained five or more myomas [2]. In typical cases benign leiomyomas are solid tumours characterized by regular internal echogenicity and stripy shadows at ultrasound examination, while leiomyosarcomas are solid tumours that often contain areas of necrosis and therefore have a more irregular internal echogenicity. However, there is too little information in the literature about the typical ultrasound appearance of malignant uterine leiomysosarcomas to know to what extent the ultrasound features of uterine leiomyosarcomas and leiomyomas overlap. In my personal experience, both benign leiomyomas and malignant leiomyosarcomas may appear either richly or poorly vascularized. Poor vascularization of leiomyosarcomas is often explained by necrosis. Unfortunately, there are no studies that are large enough to estimate with any precision the ability of either ultrasound or magnetic resonance imaging to discriminate between benign uterine leiomyomas and leiomyosarcomas. This is natural because of the rarity of this disease. To the best of my knowledge there are also no studies comparing ultrasound with magnetic resonance imaging for discriminating between uterine leiomyosarcomas and leiomyomas. It is not known if the ultrasound appearance of endometrial hyperplasia is the same in pre- and post-menopausal women.

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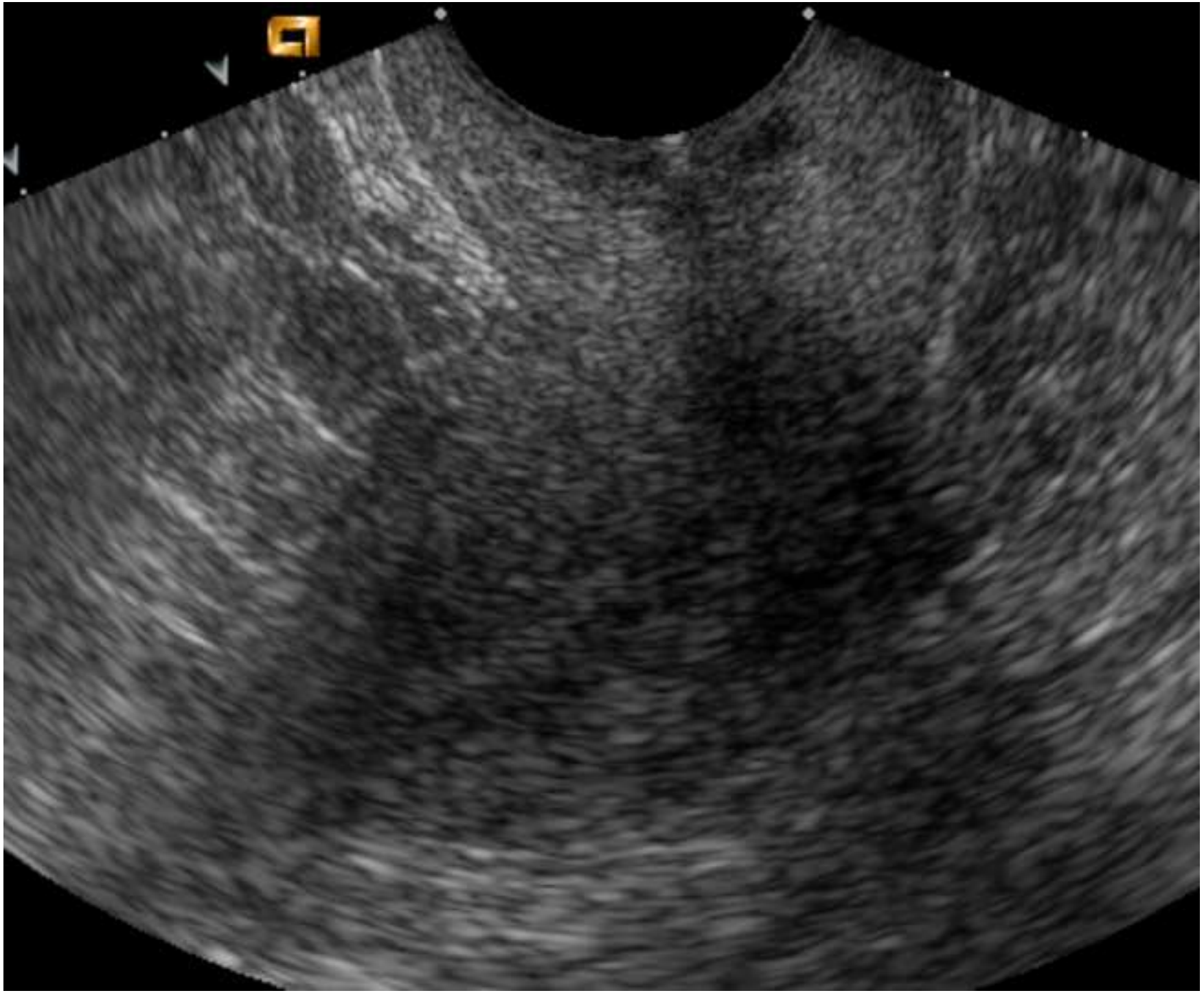

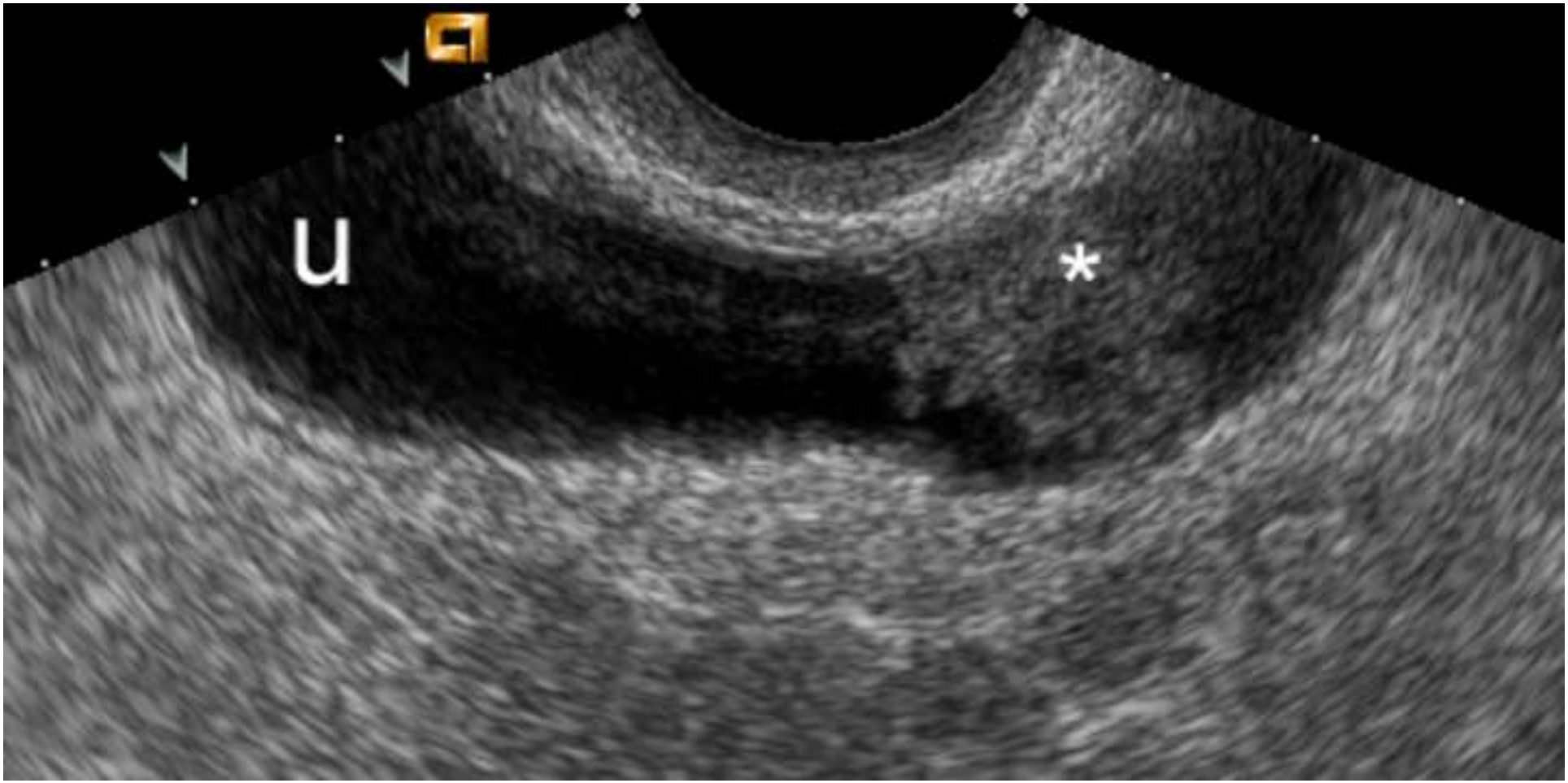

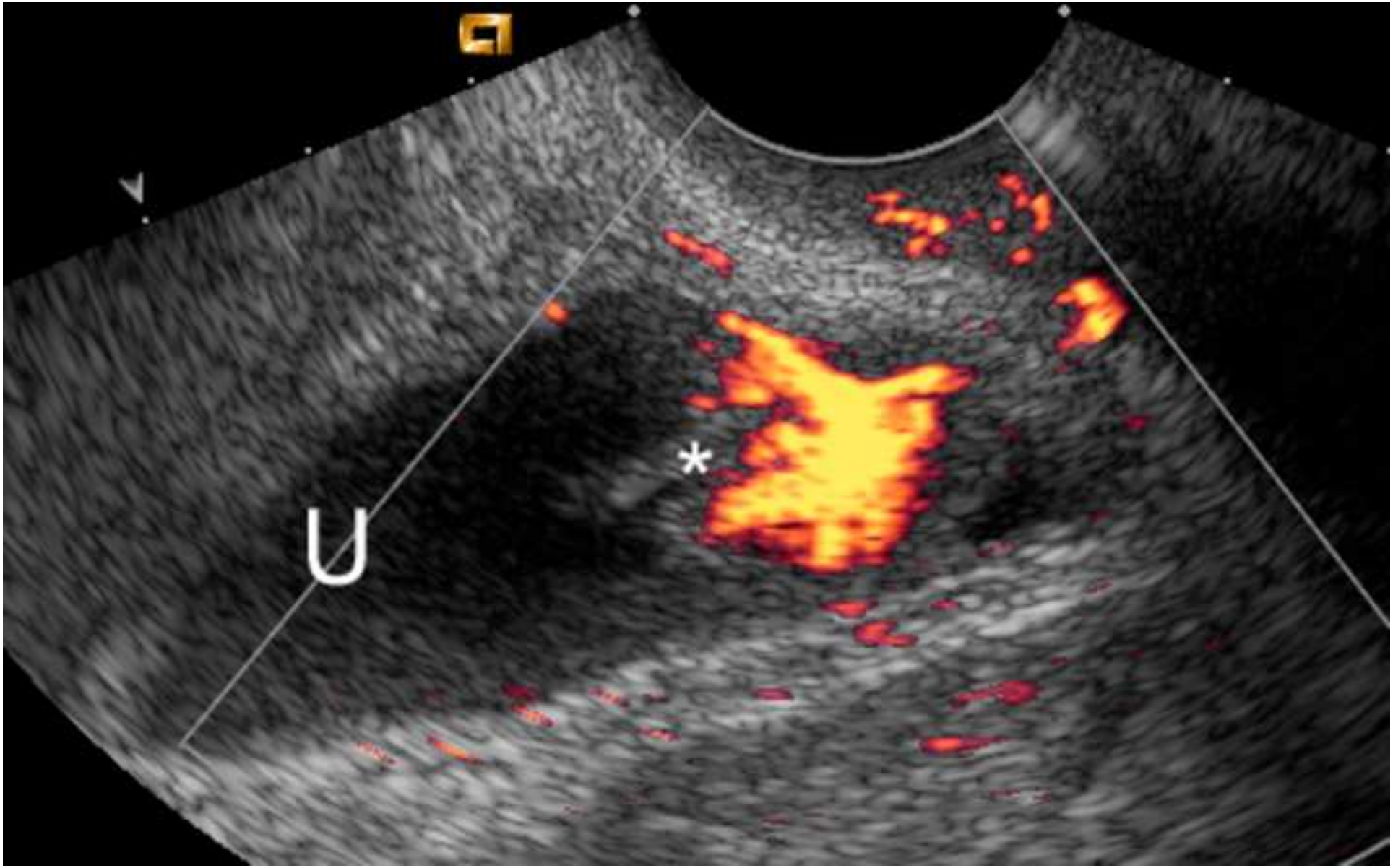

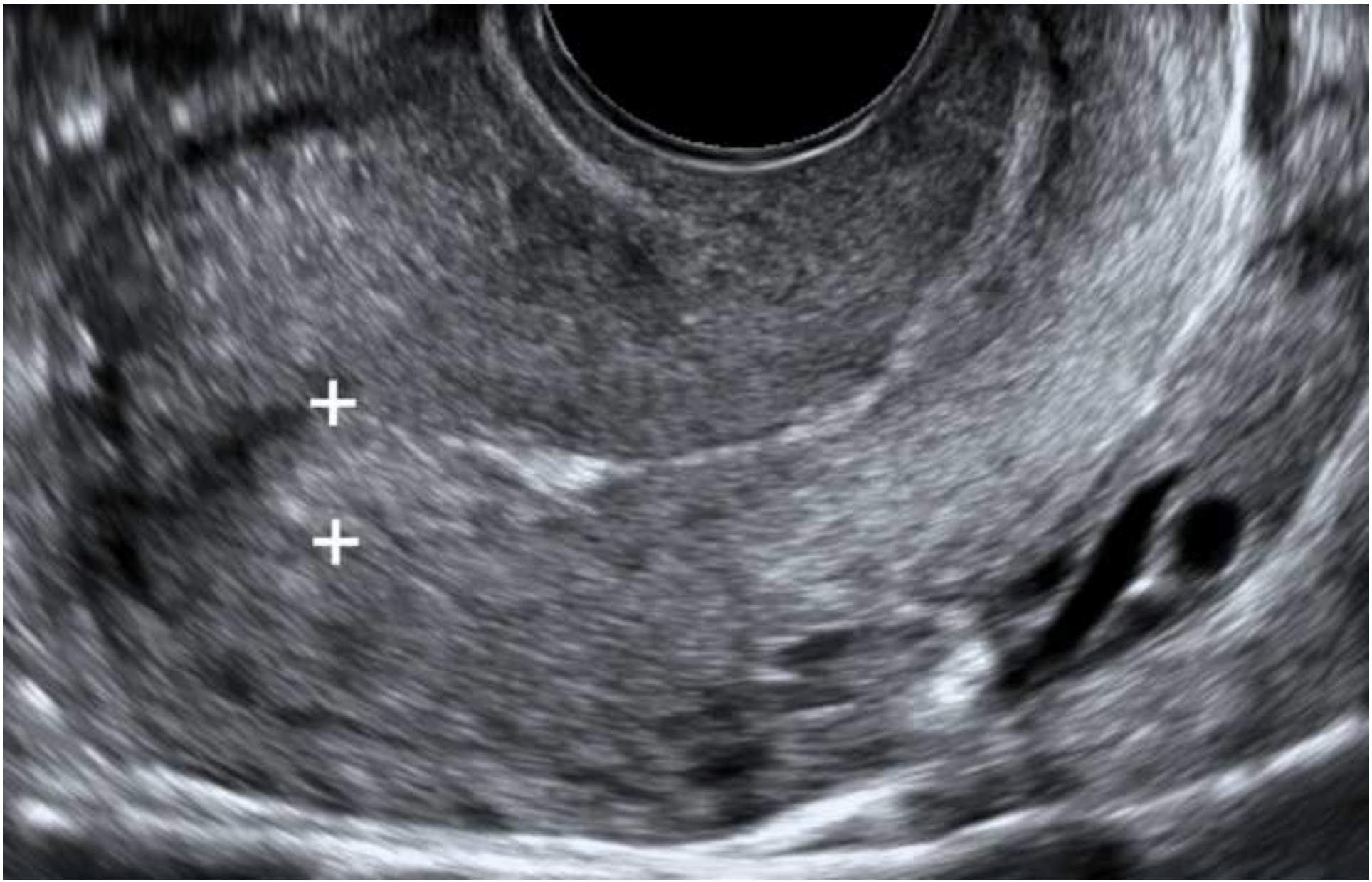

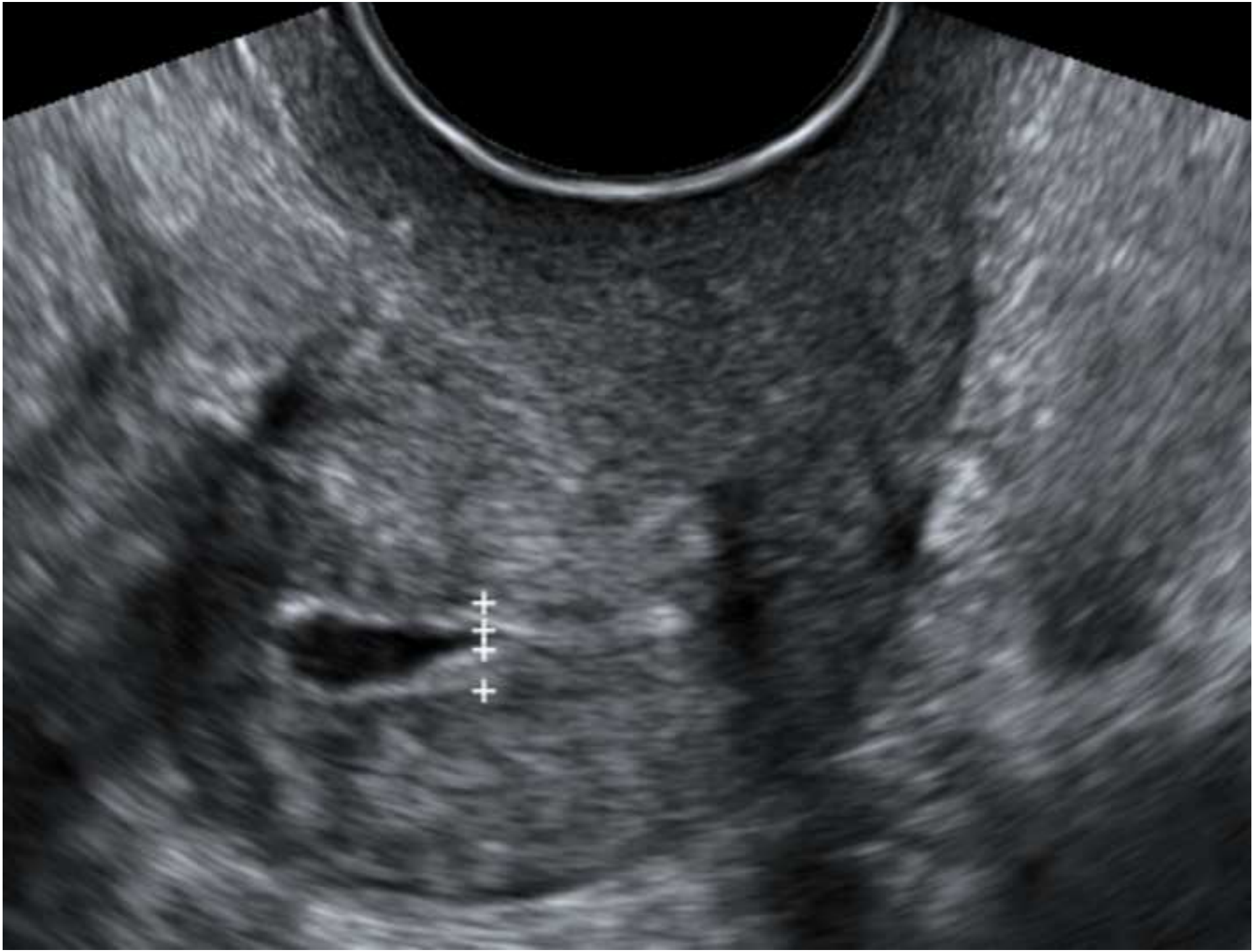

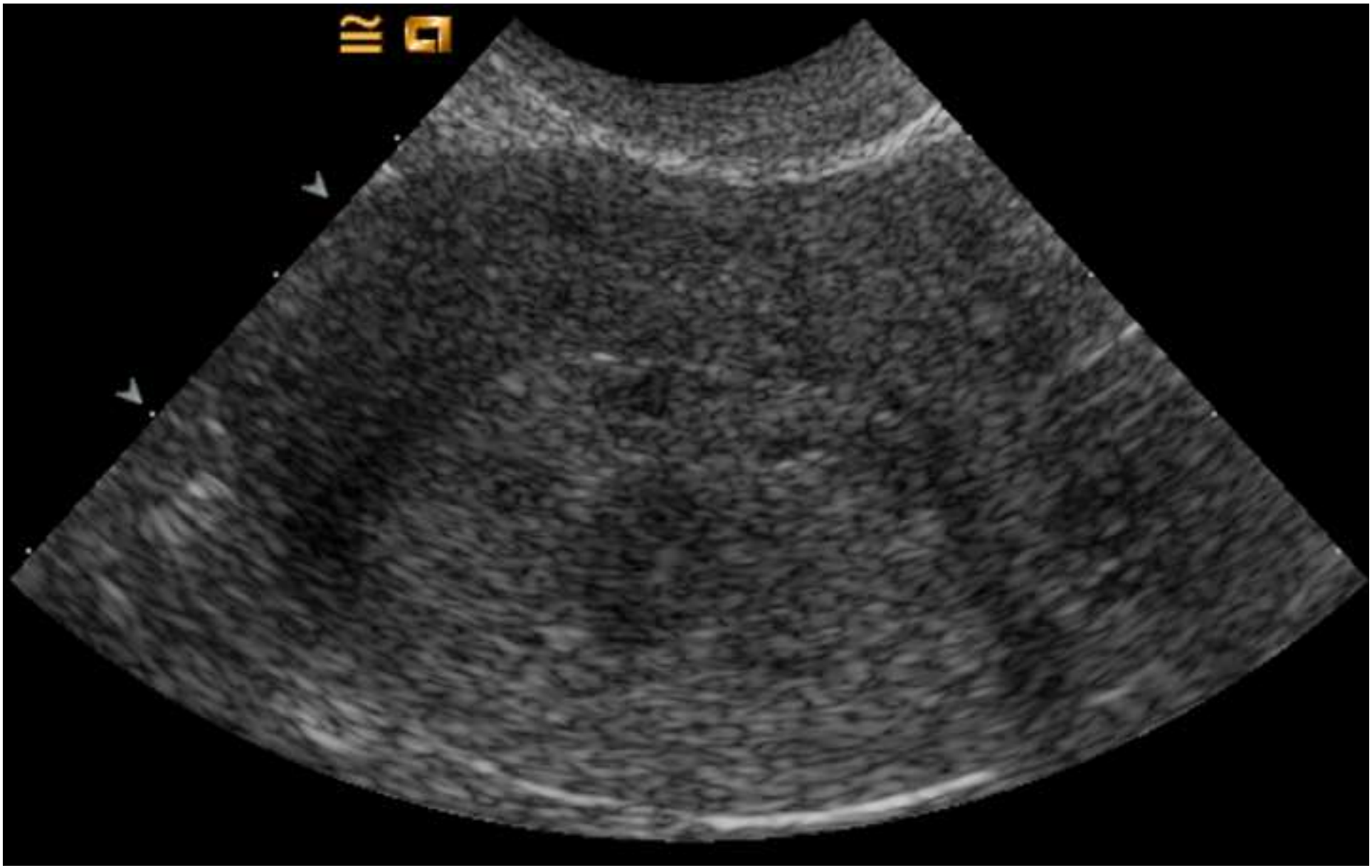

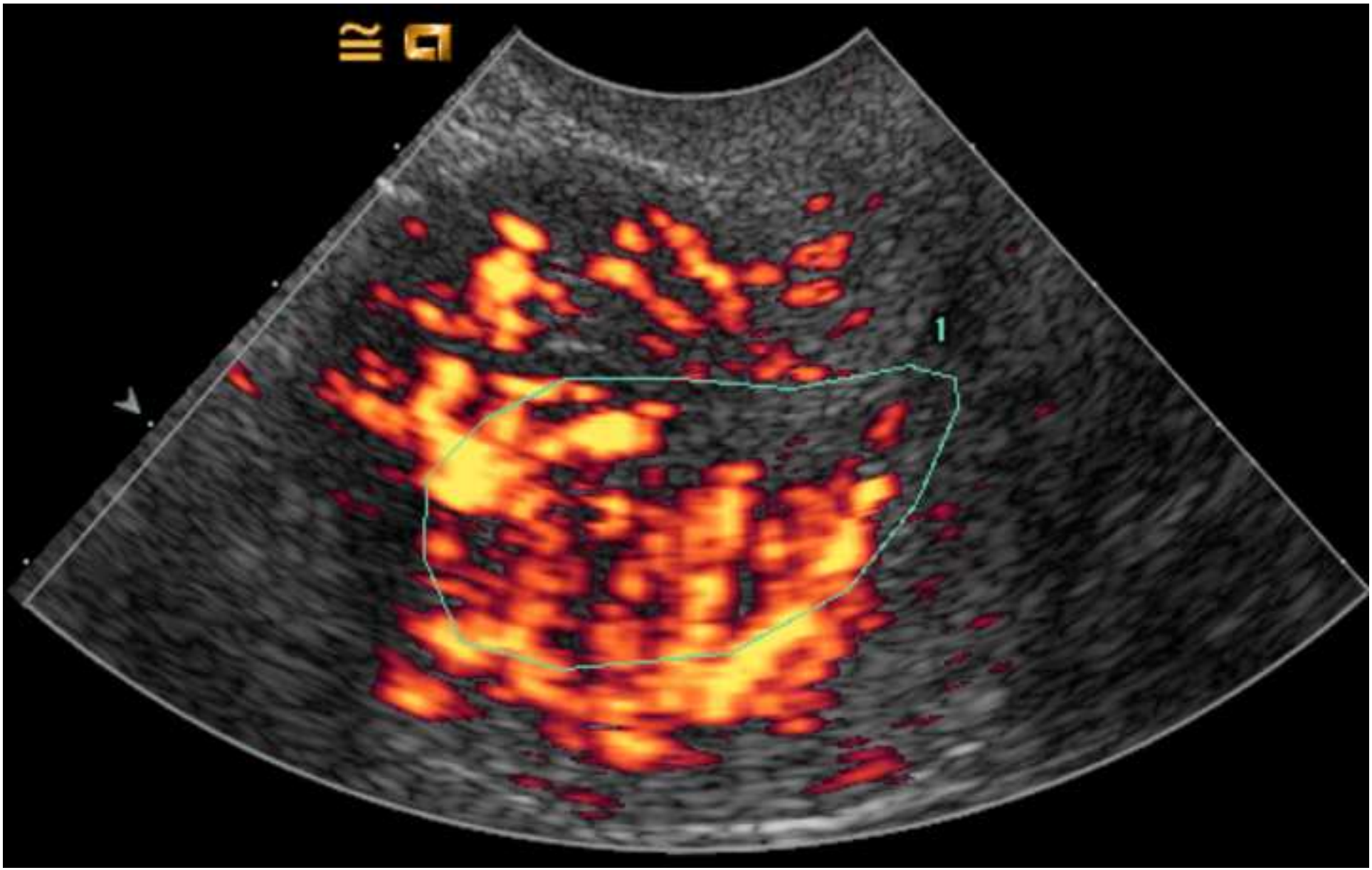

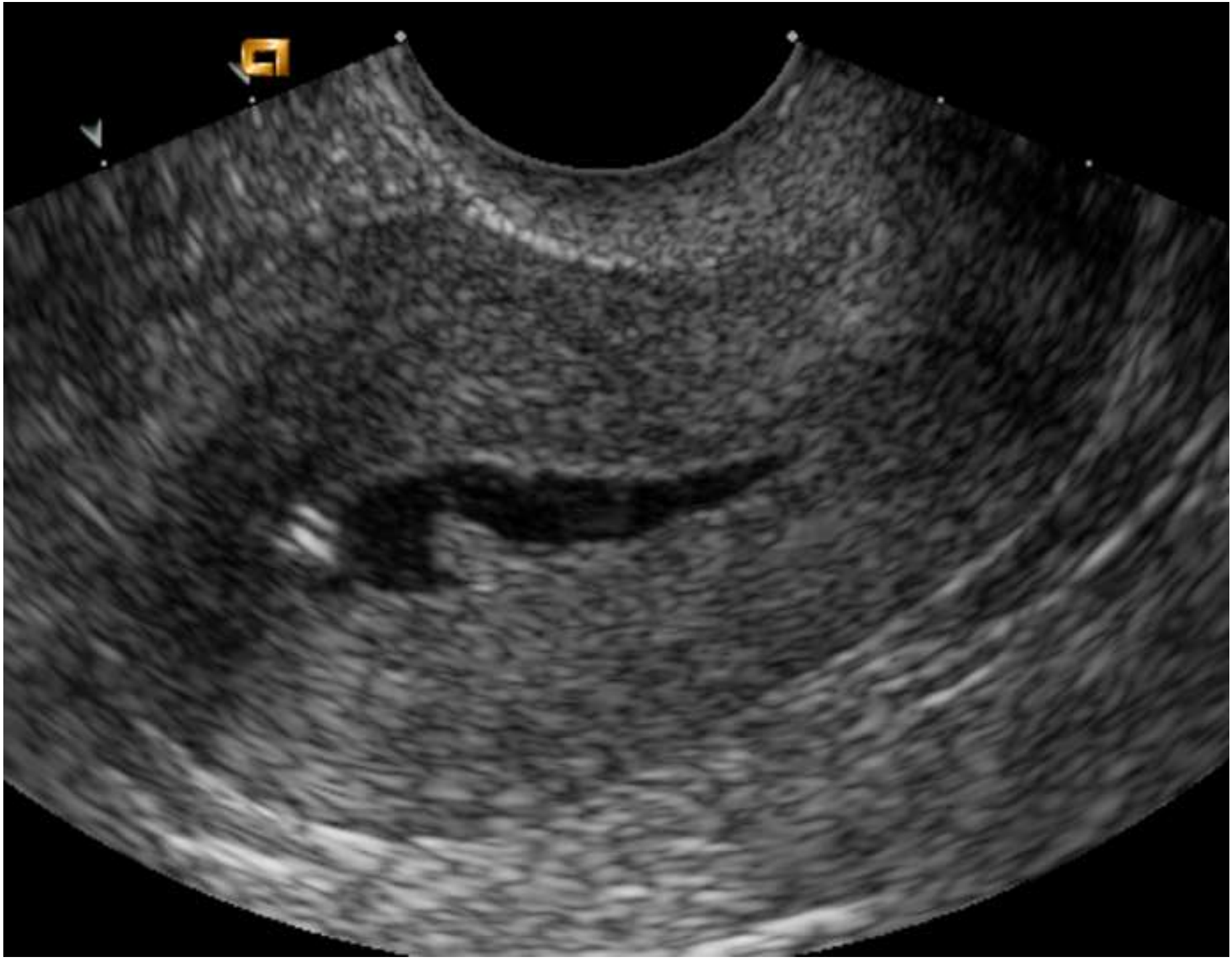

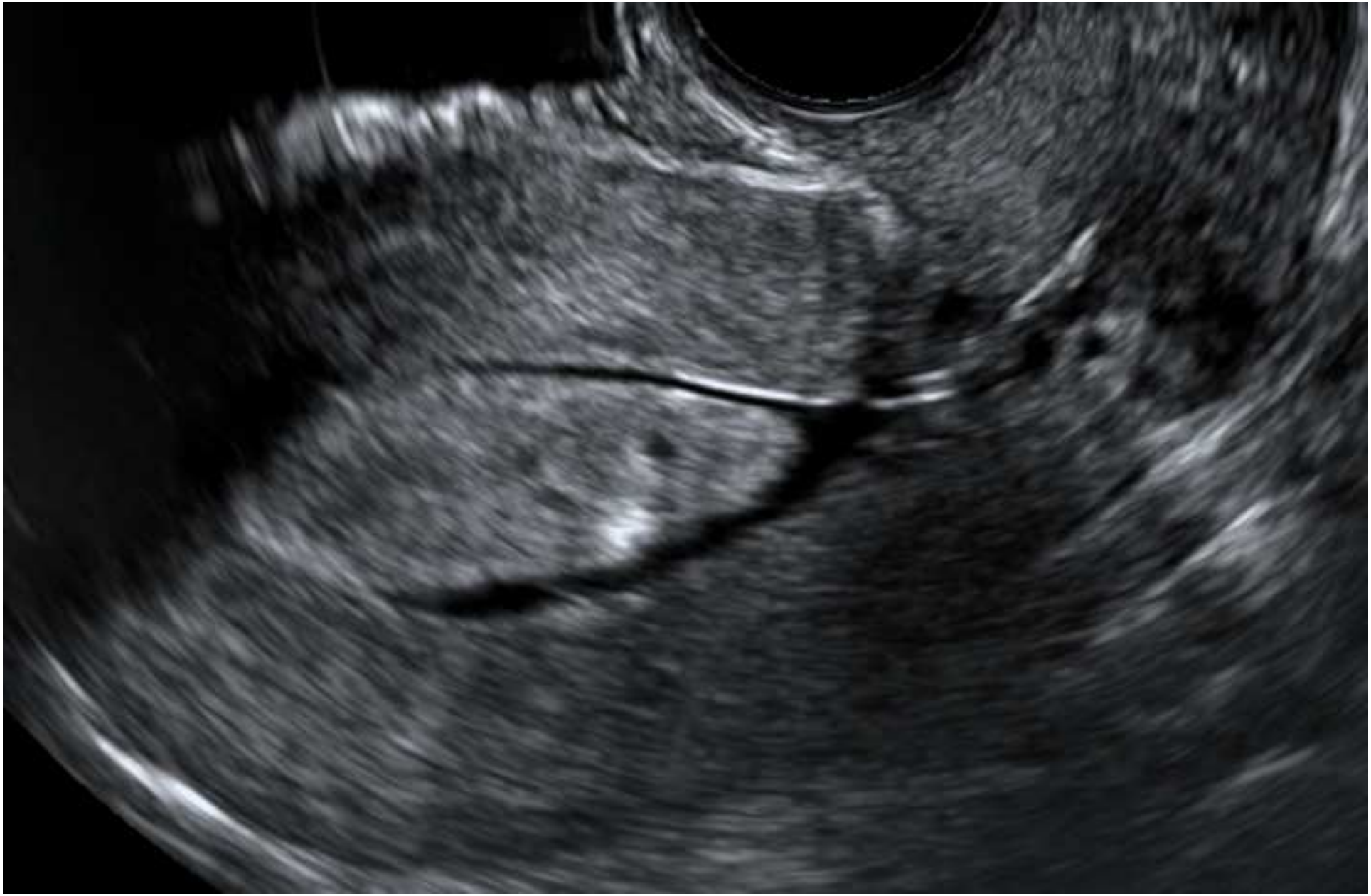

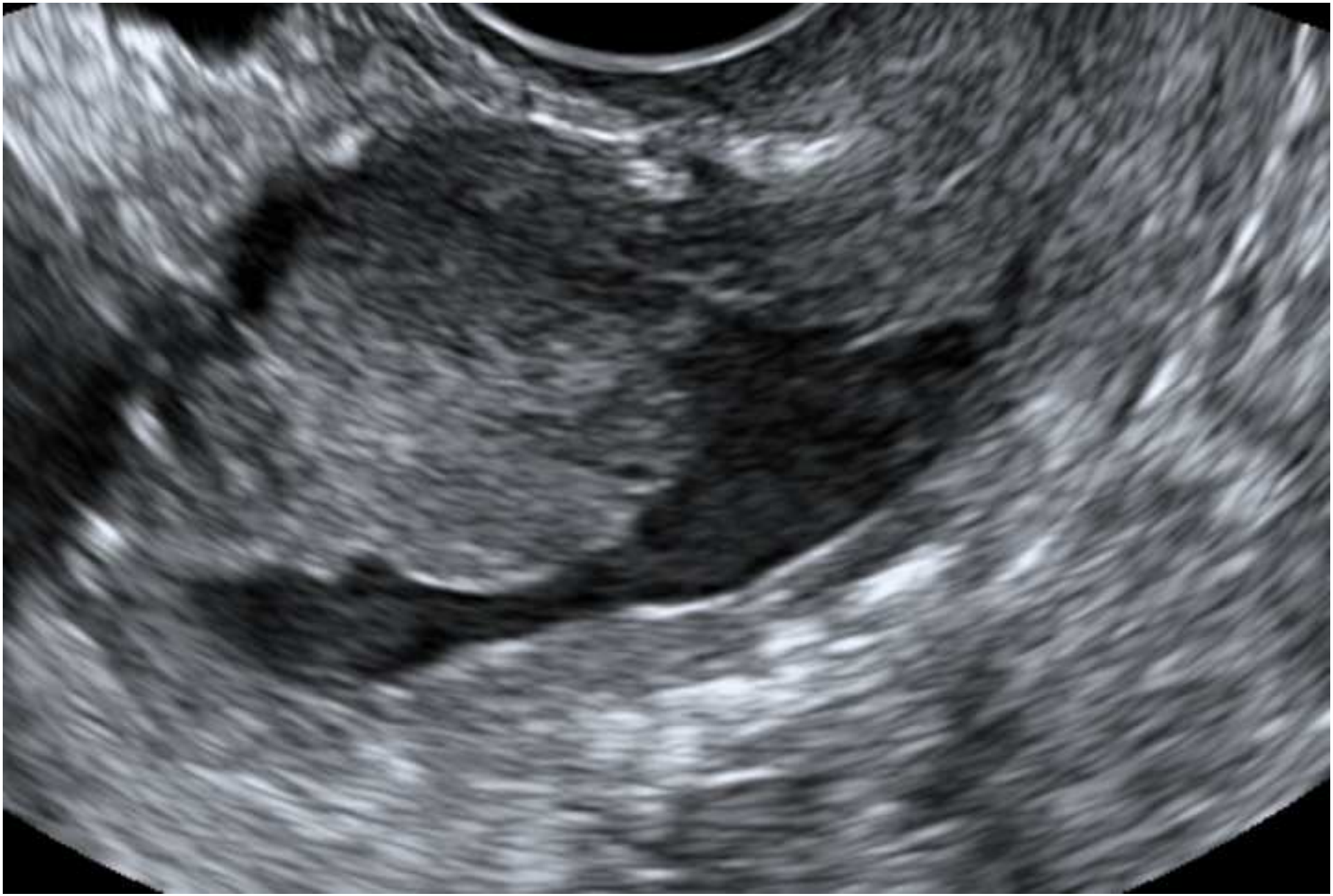

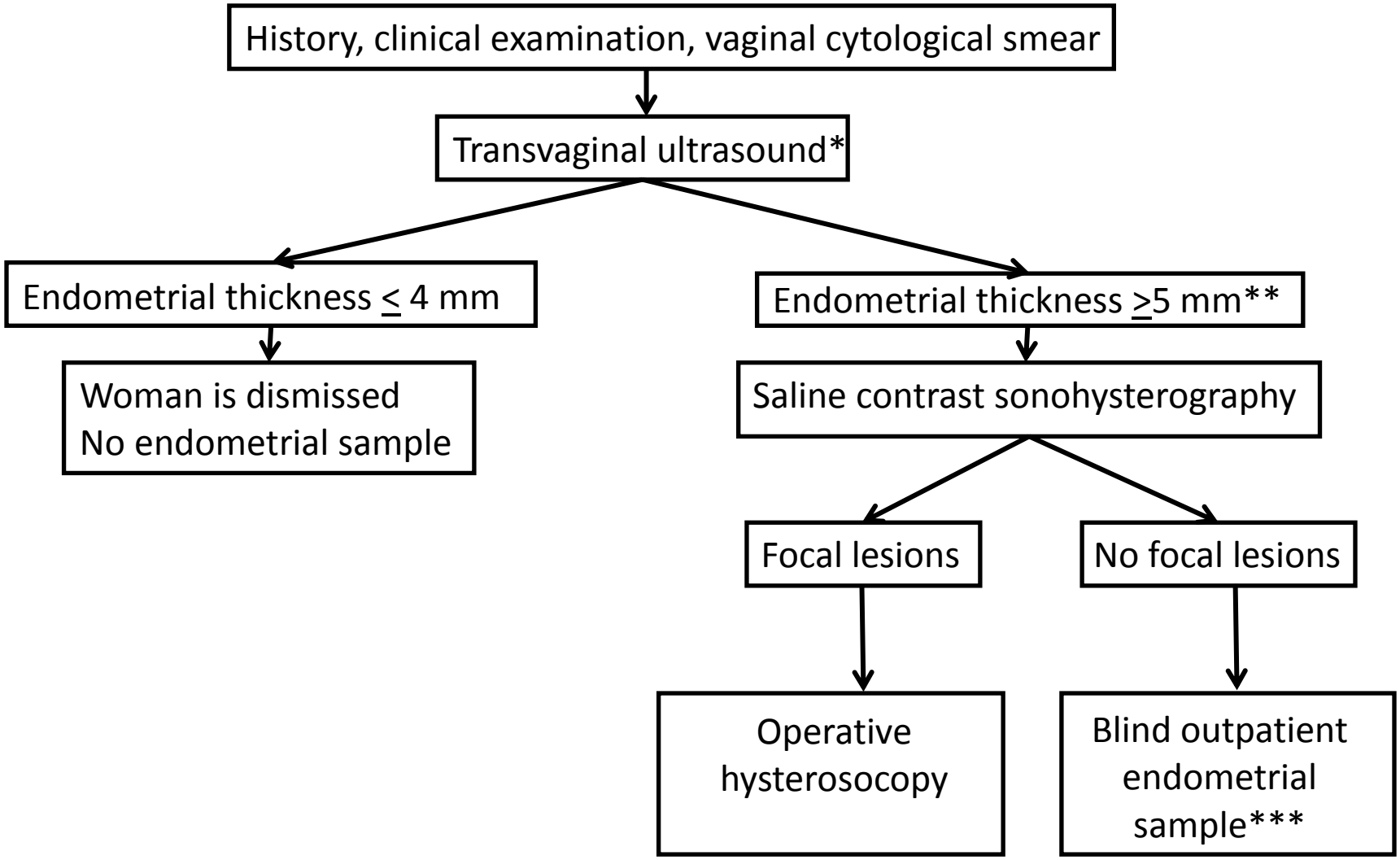

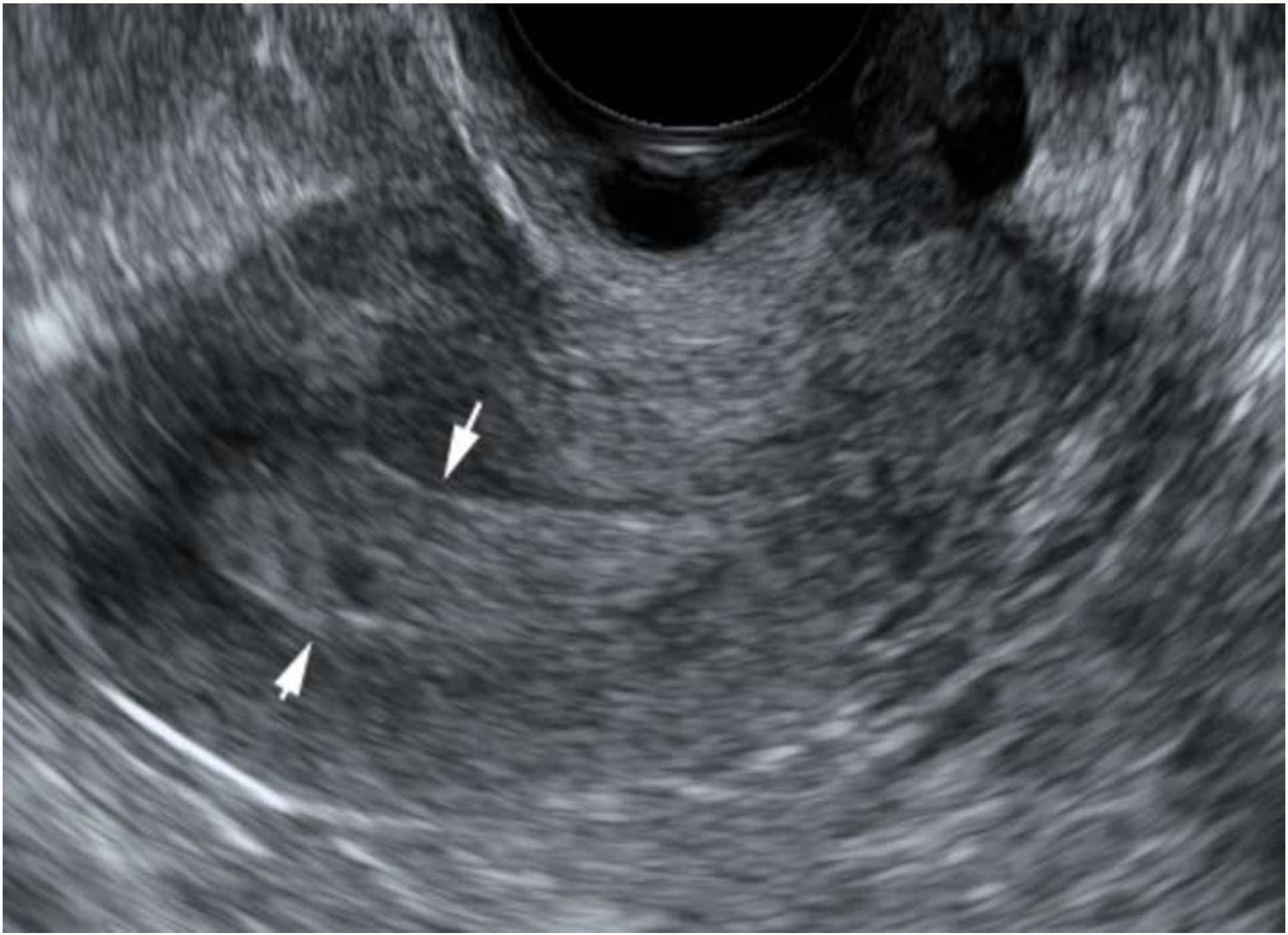

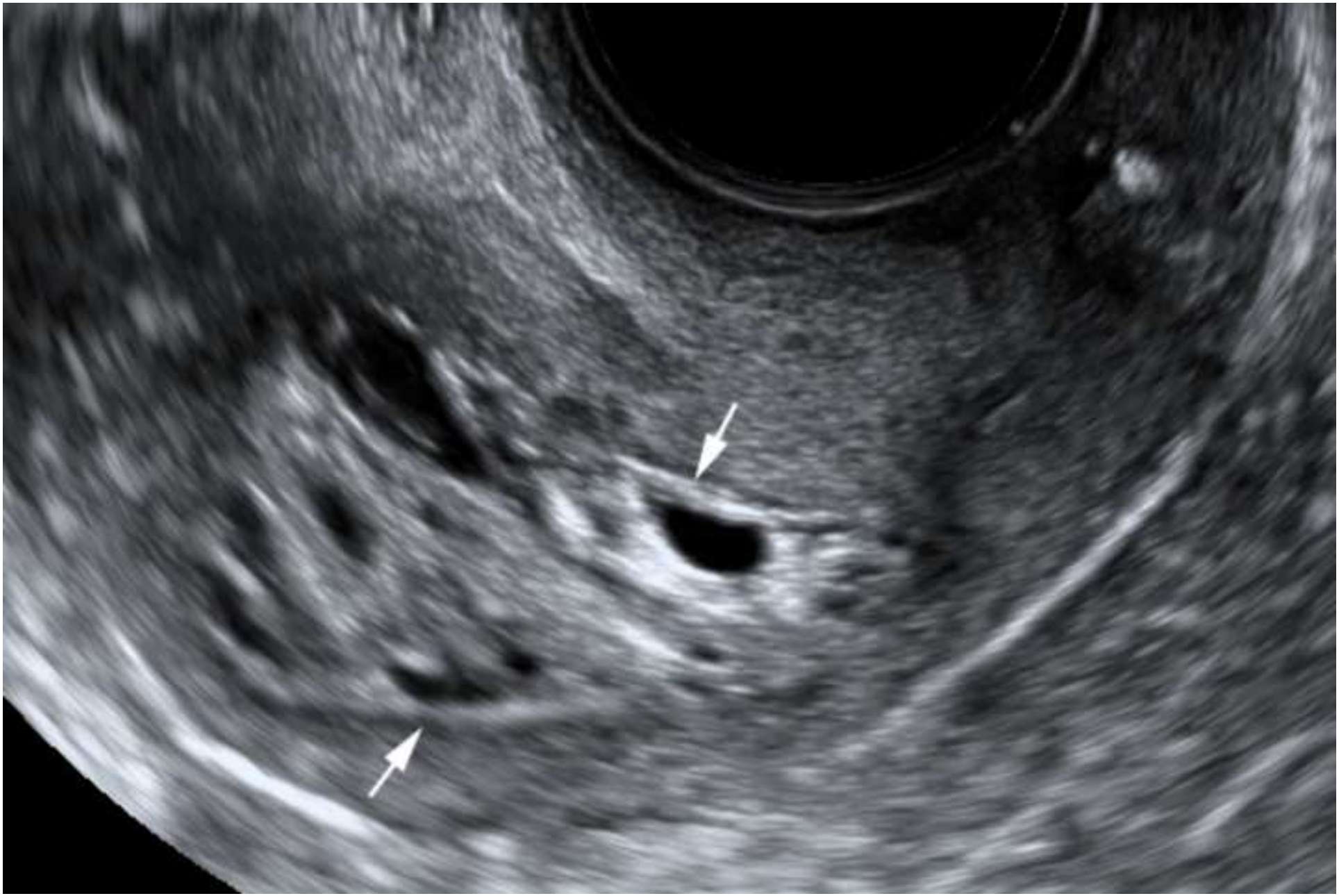

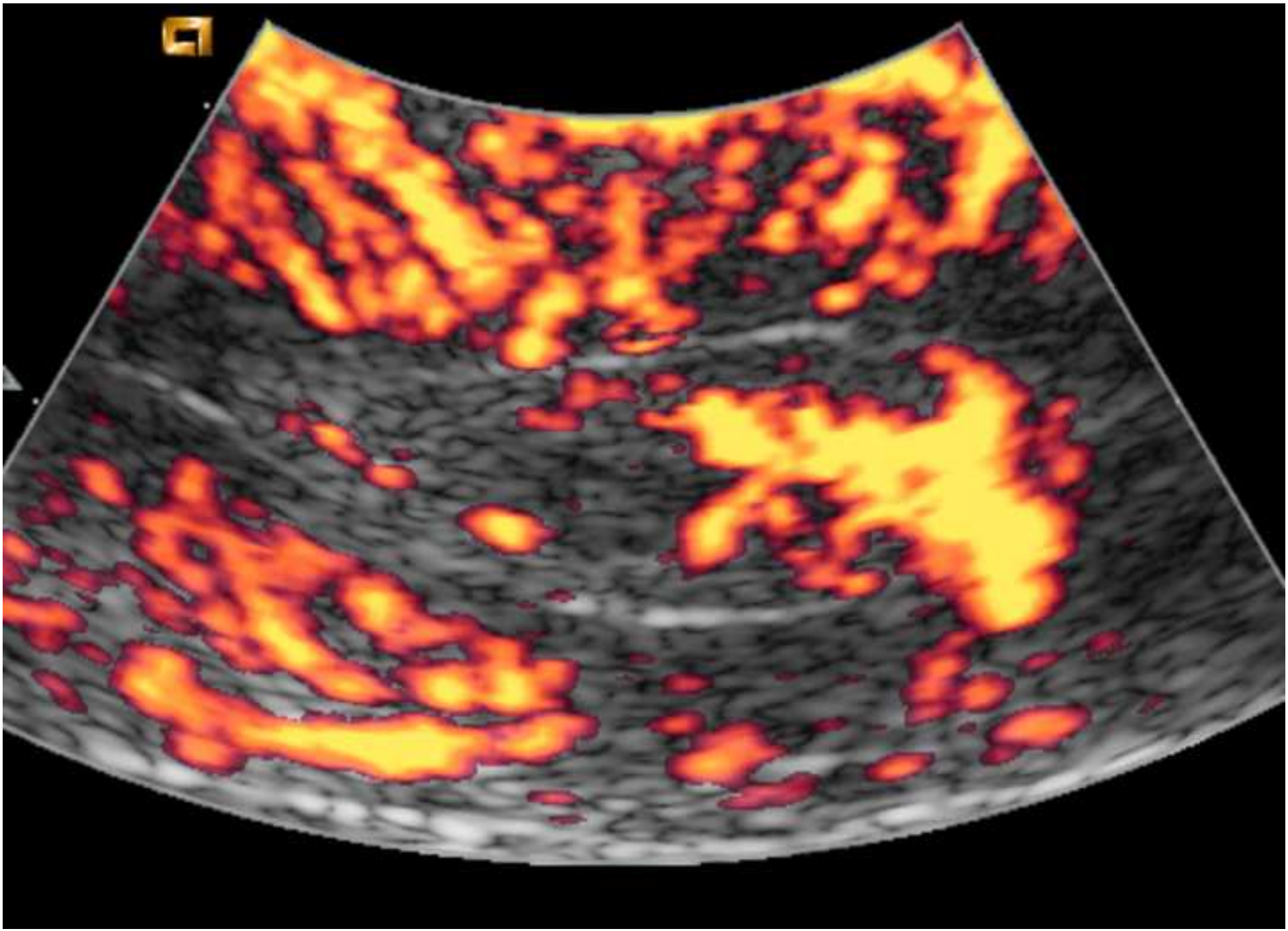

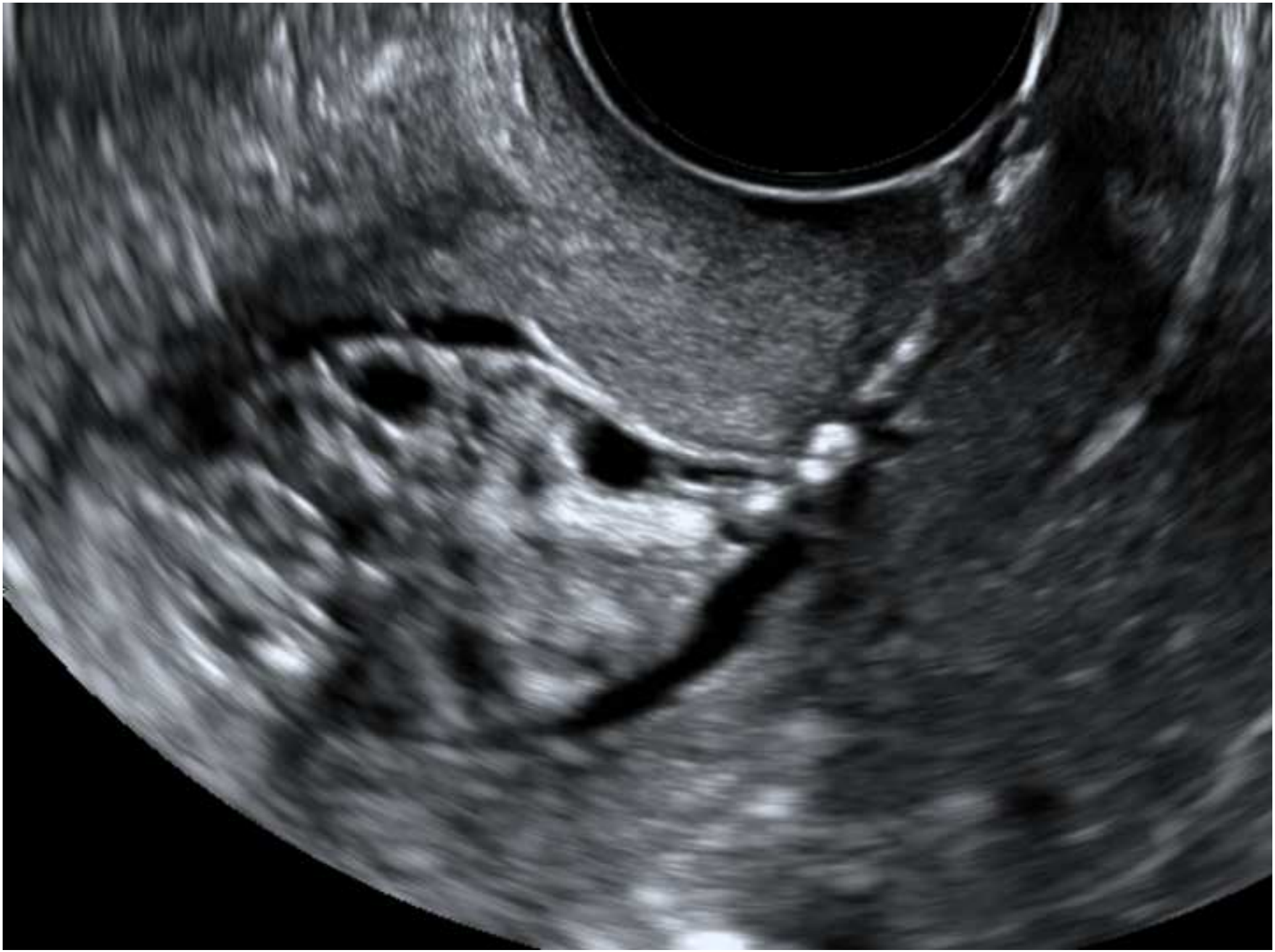

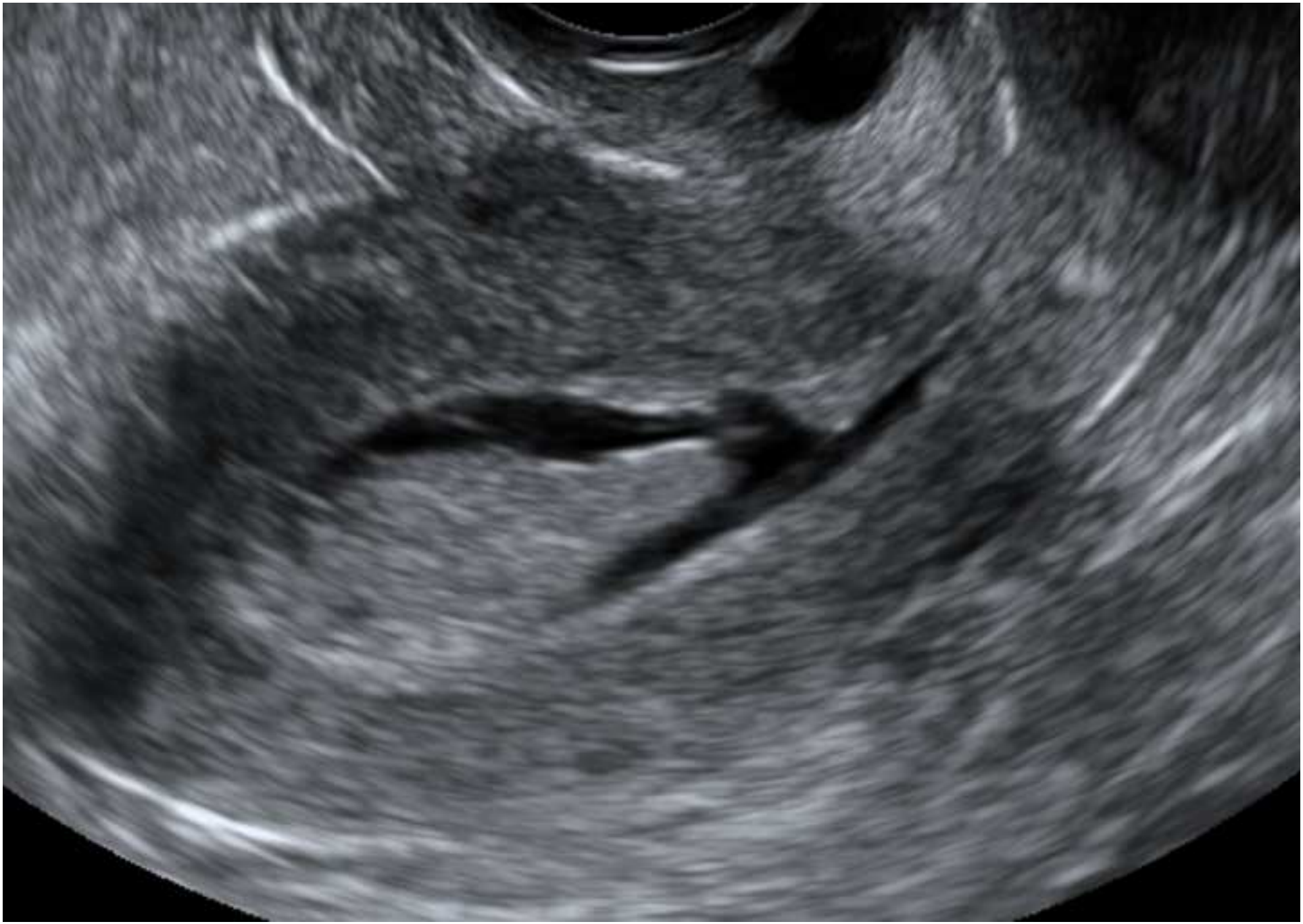

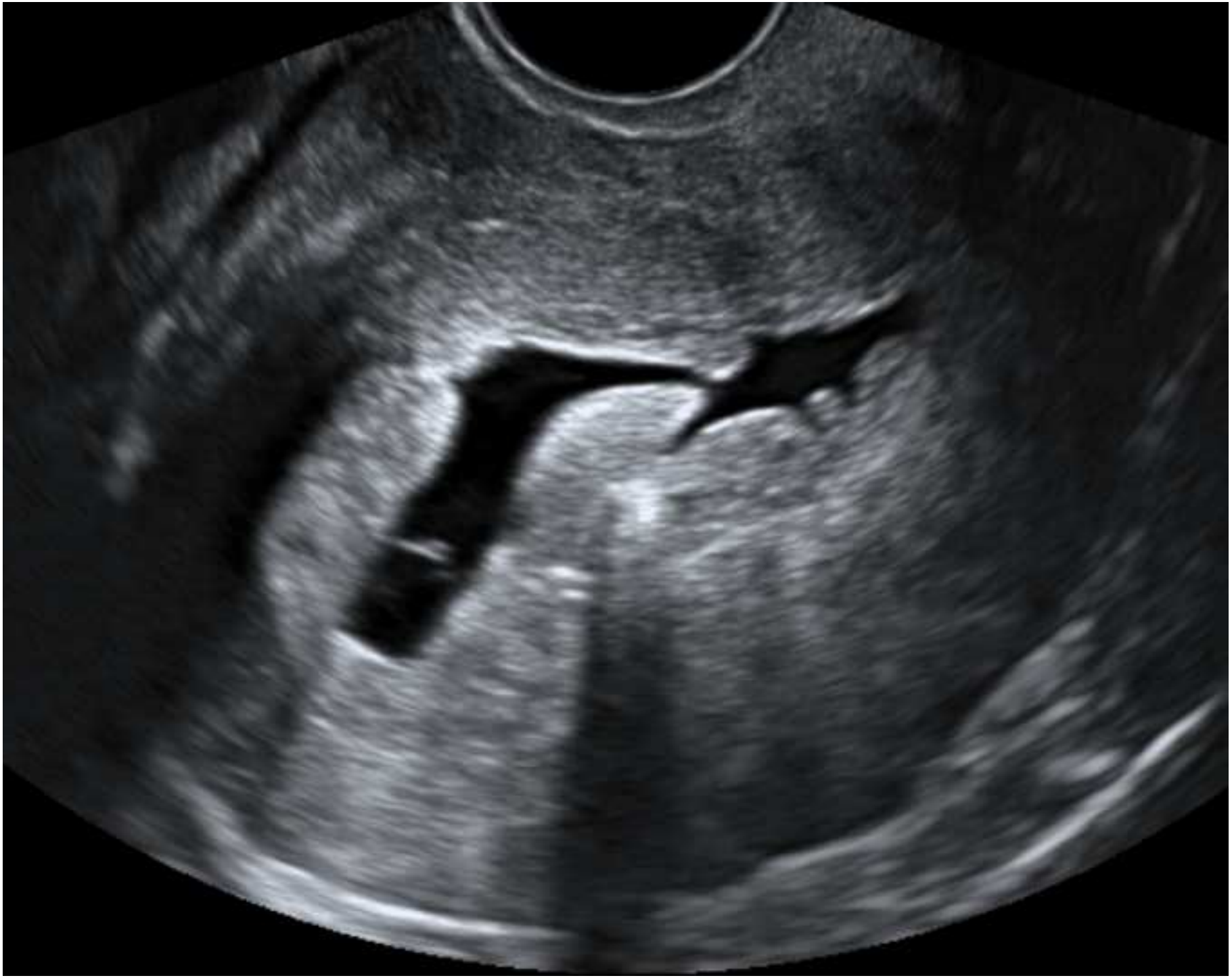

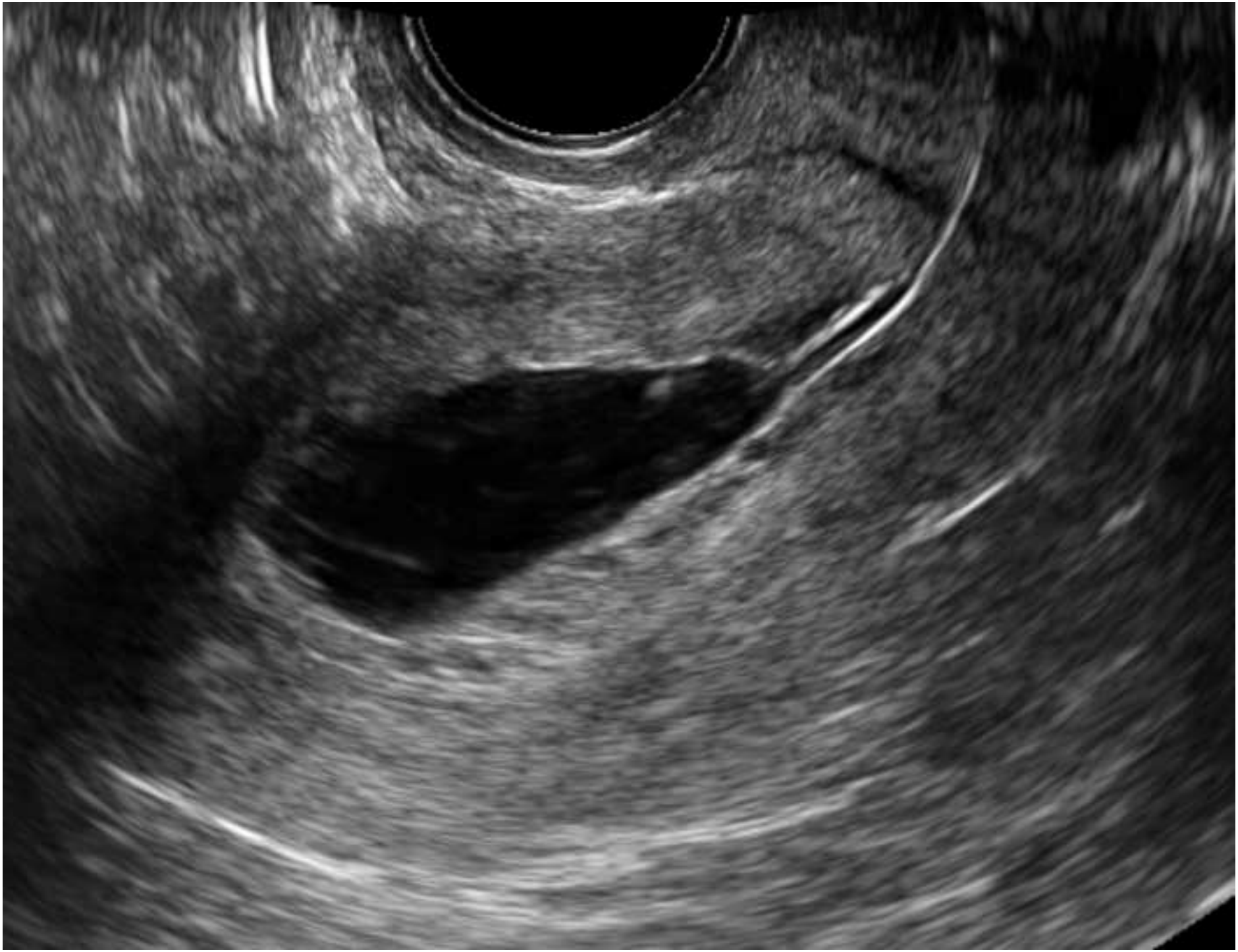

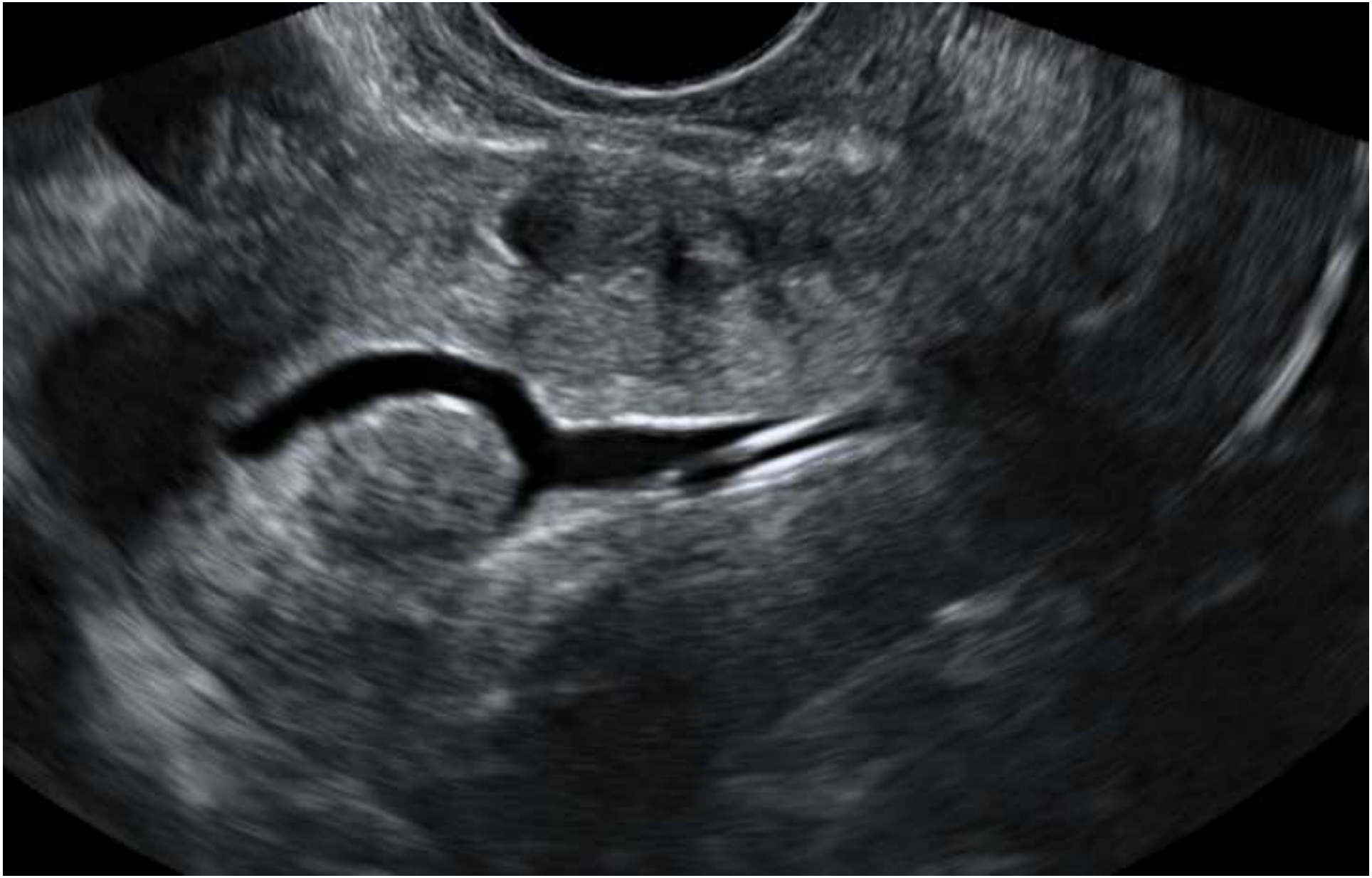

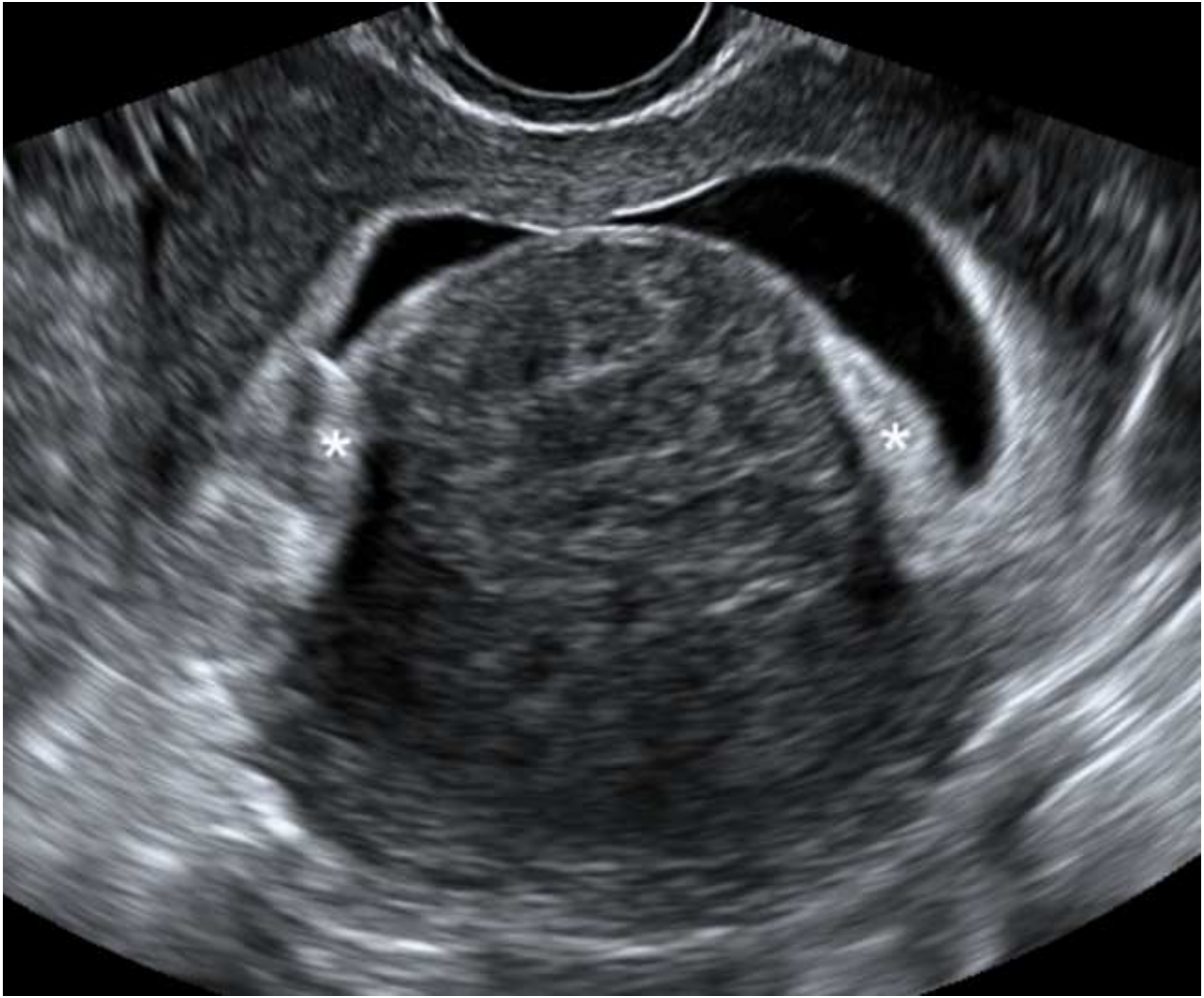

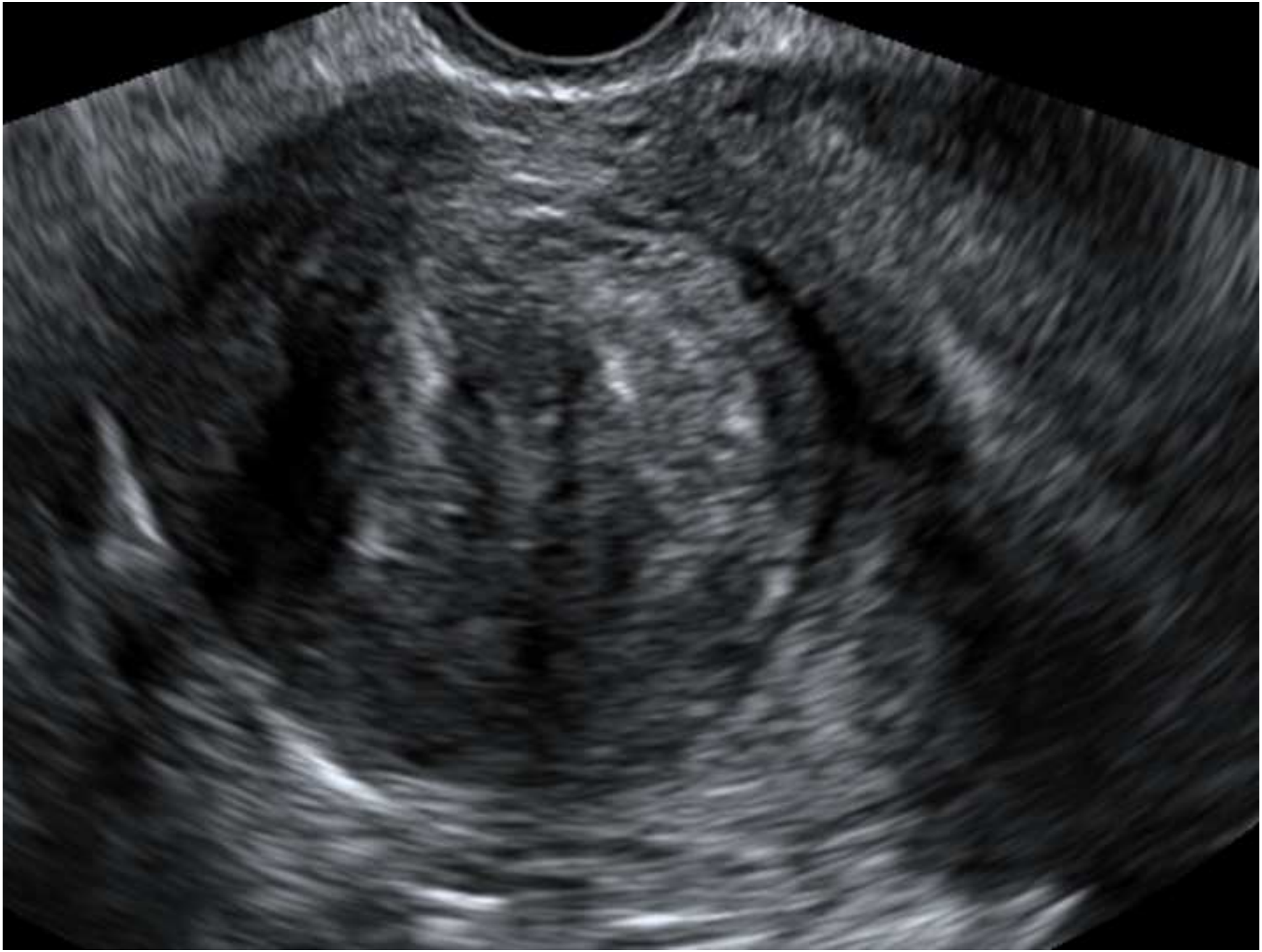

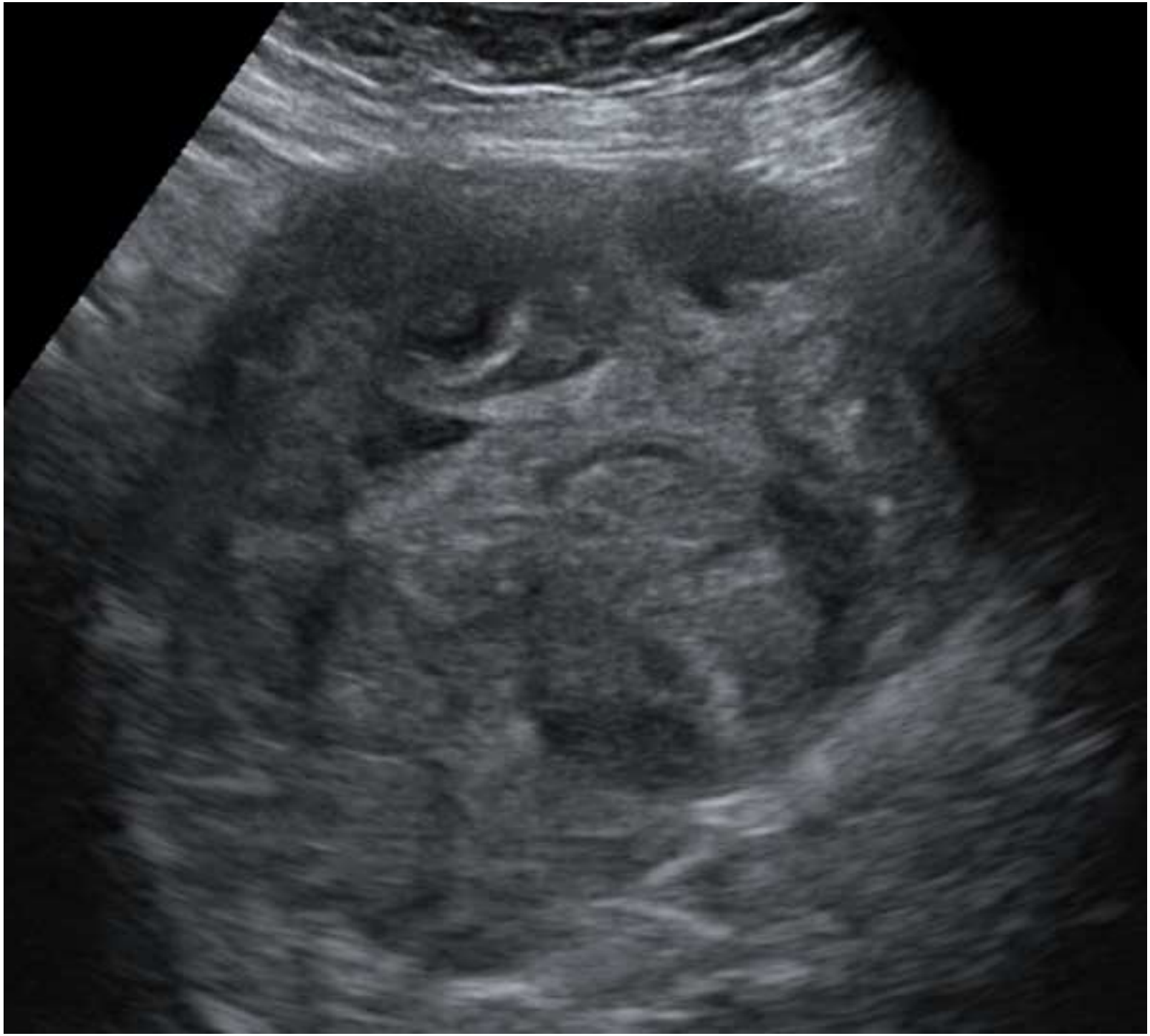

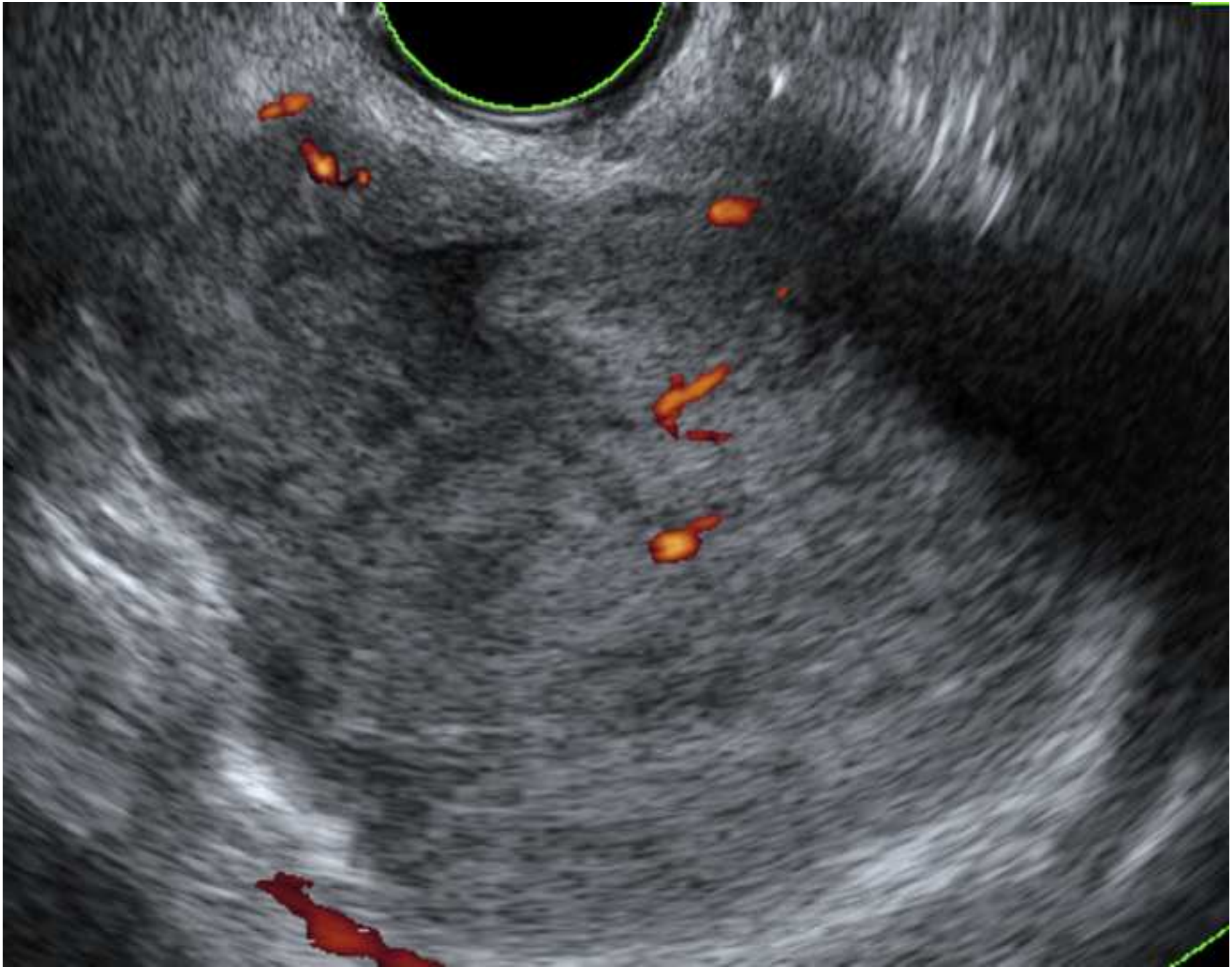

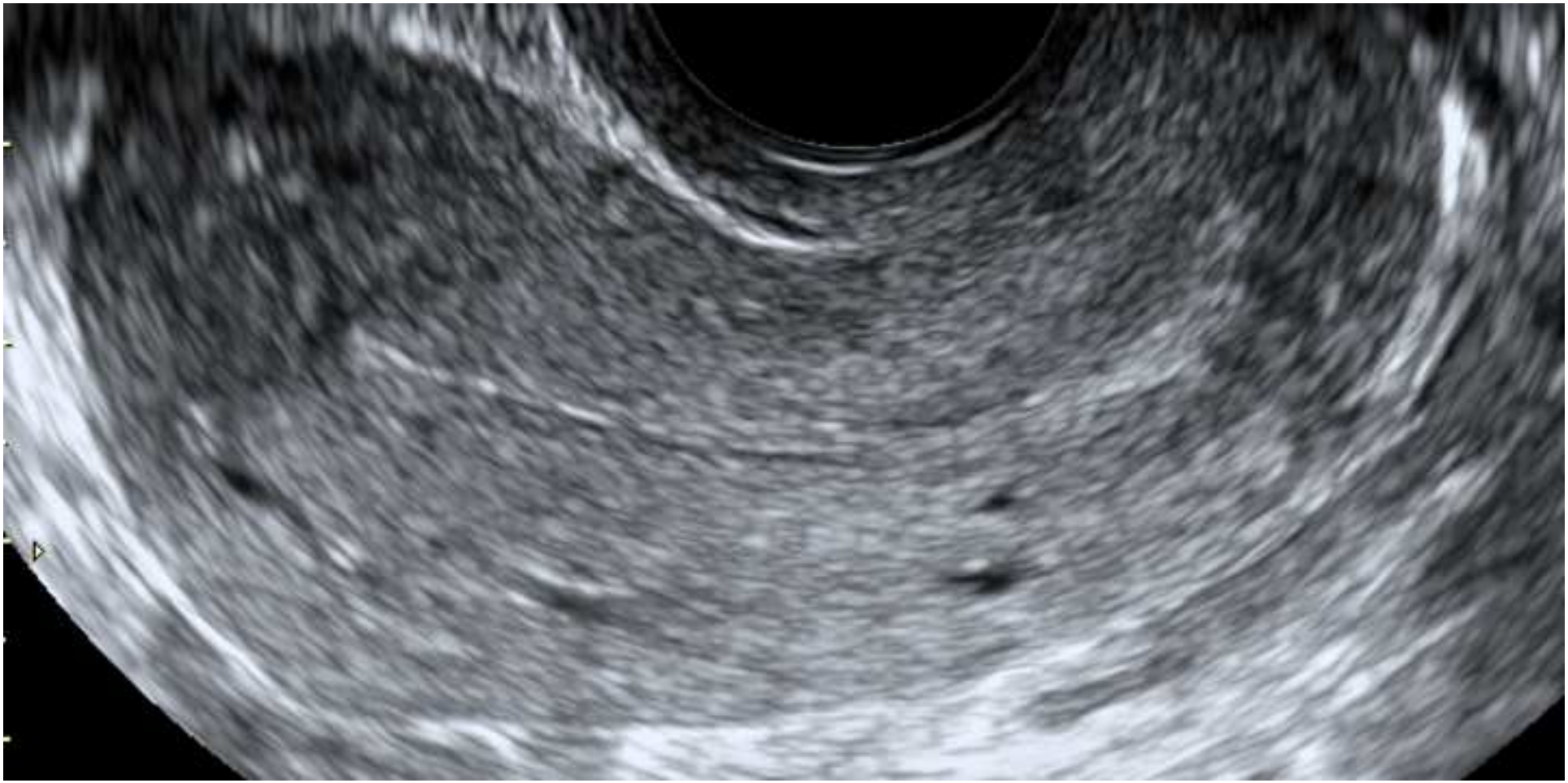

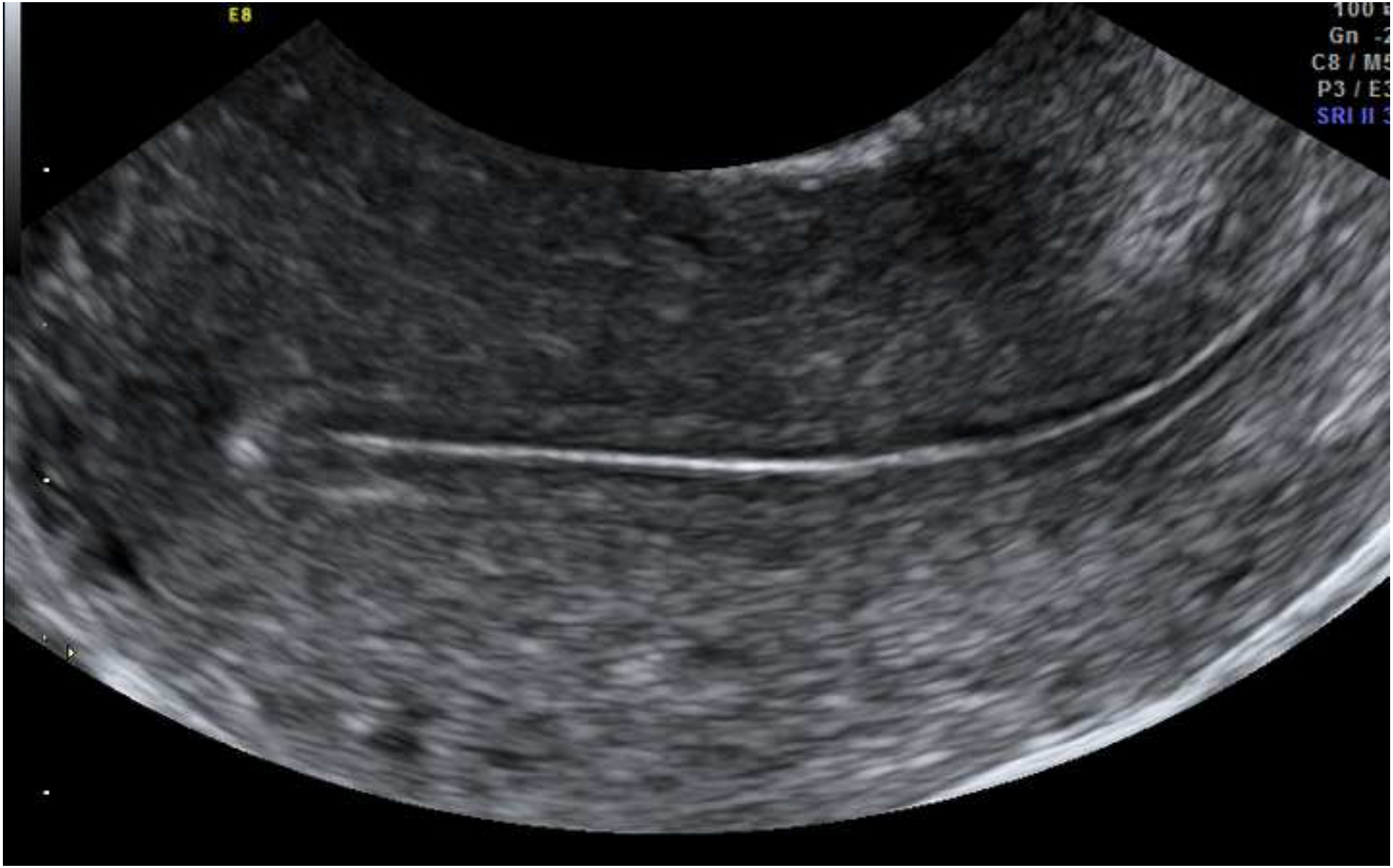

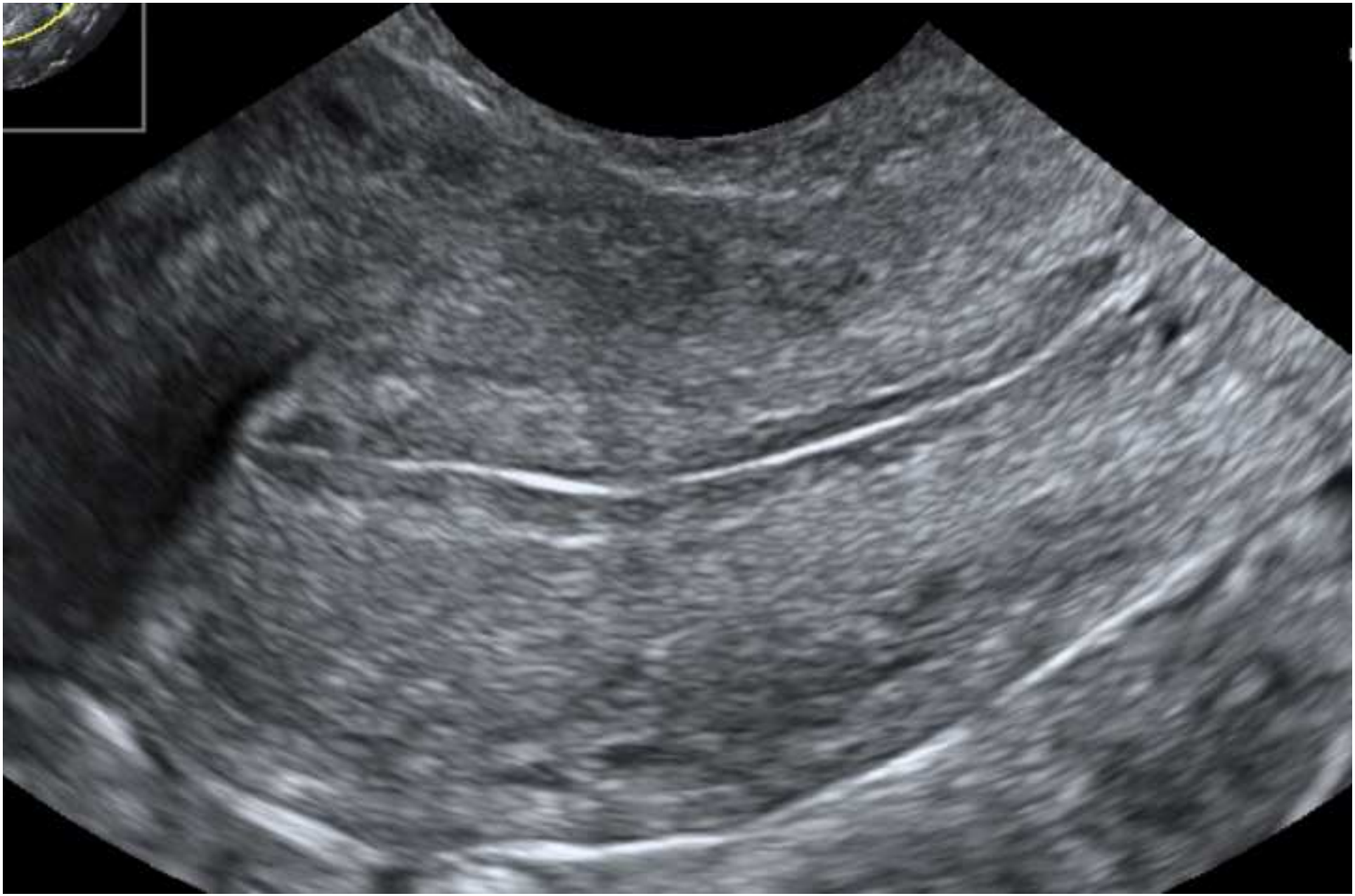

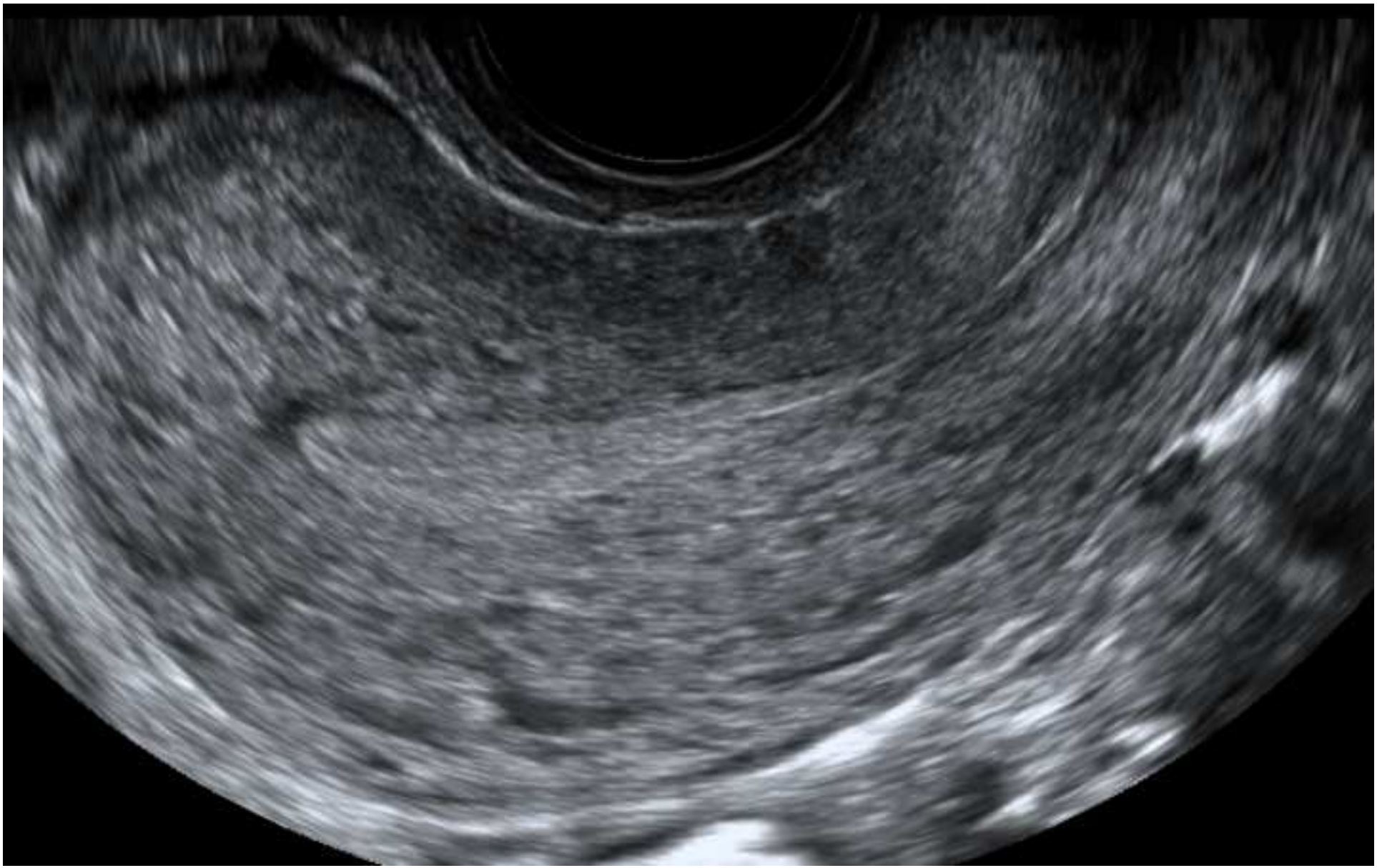

A. Practice points

- Transvaginal ultrasound plays a pivotal role in the management of non-pregnant women with abnormal vaginal bleeding; no other imaging technique has a role in the triage of these women.
- Endometrial thickness $\leq$ 4 mm as measured by transvaginal ultrasound in women with postmenopausal bleeding entails a low risk of endometrial cancer
- It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness $\leq$ 4 mm
- Endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound in women with postmenopausal bleeding entails a high risk of endometrial cancer
- A representative endometrial sample for histological diagnosis must be obtained in women with postmenopausal bleeding and endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound
- Focal lesions in the uterine cavity in women with postmenopausal bleeding and endometrial thickness $\geq$ 5 mm as measured by transvaginal ultrasound should be hysteroscopically resected under direct visual control to ascertain their complete removal
- Only if there are no focal lesions in the uterine cavity at saline contrast sonohysterography will a blind endometrial sampling technique yield a representative endometrial sample
- The typical ultrasound features of endometrial polyps, submucuous myomas and endometrial hyperplasia have been described, but it is not

known if these features are the same in pre-and post-menopausal women, nor have these features been prospectively validated

- Ultrasound and magnetic resonance imaging have similar ability to diagnose adenomyosis and benign uterine leiomyomas
- Magnetic resonance imaging is superior to ultrasound for “myoma mapping” if the uterus is very large (> 375ml) or contains five or more myomas.
- Endometrial sonographic thickness measurements have no role in the management of women with abnormal vaginal bleeding before menopause, because endometrial thickness changes throughout the menstrual cycle.

A. Research agenda

- To establish on the basis of a large amount of prospectively collected data the typical ultrasound appearance of endometrial cancer, endometrial polyps, submucuous myomas, different types of hyperplasia, leiomyosarcomas and endometrial cancer in premenopausal women
- To establish on the basis of a large amount of prospectively collected data the typical ultrasound appearance of different types of endometrial cancer, endometrial polyps, submucuous myomas, different types of hyperplasia and leiomyosarcomas in postmenopausal women
- To prospectively validate ultrasound criteria established as described above for endometrial cancer, polyps, submucuous myomas, different types of hyperplasia and leiomyosarcomas in pre- and post- menopausal women separately
- To prospectively validate published mathematical models to calculate the risk of endometrial cancer in women with postmenopausal bleeding and endometrial thickness as measured by ultrasound $\geq$5mm.
- To estimate interobserver agreement when using the International endometrial Tumor Analysis (IETA) terminology to describe ultrasound images of the endometrium

MCQ

MCQ 1 Which of the following statements is/are correct?

a) It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness ≤ 4 mm

b) It is safe to refrain from endometrial sampling in women with postmenopausal bleeding and endometrial thickness ≥ 5 mm if the endometrium has regular echogenicity and is poorly vascularized at colour or power Doppler ultrasound

c) The absence of focal lesions at saline contrast sonohysterography in women with postmenopausal bleeding is a strong sign of normality

d) In women with postmenopausal bleeding and endometrial thickness ≥5 mm focal lesions in the uterine cavity should be hysteroscopically resected under direct visual control

e) If the endometrium is not seen at transvaginal ultrasound in a woman with postmenopausal bleeding it means that it is thin, and so the risk of endometrial malignancy is low and no endometrial sampling is needed.

Correct answers: a) T b) F c) T d) T e) F

Explanations to the answers to question 1

The risk of finding an endometrial cancer in a woman with postmenopausal bleeding and endometrial thickness as measured by ultrasound ≤ 4 mm is very low. Prospective observational follow-up studies show that it is safe to refrain from endometrial sampling in these women. However, if the endometrial thickness is ≥5 mm, a representative endometrial sample must always be obtained. Regular endometrial echogenicity at grey

scale ultrasound and poor vascularization at colour or power Doppler do decrease the risk of malignancy, but this information should be used mainly for prioritizing women on a waiting list for a diagnostic procedure, not to decide if a diagnostic procedure is needed or not (unless the woman is at extremely high operative risk and surgery is necessary to obtain a histological diagnosis). Almost all endometrial pathology grows focally in the uterine cavity. Therefore, a smooth endometrium with no signs of focal pathology at saline contrast sonohysterography (or hysteroscopy) is a strong sign of normality. Because 87% of focal lesions cannot be removed at all or only partially removed if a blind endometrial sampling technique is used [1], they must be resected under direct visual control to ensure their complete removal. Malignancy is sometimes found in benign polyps. Therefore, it is important to remove focal lesions in toto. An endometrium that cannot be seen at ultrasound cannot be measured and cannot be evaluated with regard to its echogenicity or vascularity. Indeed, endometrial cancer is sometimes diagnosed in women with an invisible endometrium at ultrasound. To clarify the situation, saline contrast sonohysterography should be performed. If it fails the woman should be referred for hysteroscopy and endometrial sampling in anaesthesia or analgesia.

Reference

1. Epstein E, Ramirez A, Skoog L, Valentin L. Dilatation and curettage fails to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding. Acta Obstet Gynecol Scand 2001; **80**: 1131-1136.

MCQ2. Which of the following statements is/are correct?

a) Endometrial thickness measurements with transvaginal ultrasound play a pivotal role in the triage of women with irregular bleeding before menopause

b) At ultrasound examination the endometrium is hyperechogenic throughout the menstrual cycle
c) Endometritis has typical appearance at transvaginal ultrasound examination
d) Intracavitary lesions with the appearance of an endometrial polyp at saline contrast sonohysterography may regress if left in situ
e) In premenopausal women, endometrial polyps are typically surrounded by a ring of colour at power Doppler ultrasound examination

Correct answers a) F b) F c) F d) T e) F

Explanations to the answers to question 2

Endometrial thickness measurements with transvaginal ultrasound have no role in the triage of women with irregular bleeding before menopause, because the endometrial thickness changes during the menstrual cycle. Immediately after menstruation the endometrium is thin, during the proliferative phase it increases in thickness and it remains thick in the secretory phase. The ultrasound appearance of the endometrium in case of endometritis is not well known. Despite extensive literature search I have found only one published ultrasound image of reasonably good quality illustrating endometritis. However, this was a special case of anaerobic endometritis after surgery on the uterus, where the uterine cavity was filled with gas [1]. I have found no published high quality ultrasound images of more common types of endometritis or of tuberculous endometritis. Indeed, endometritis in women with clinical signs of pelvic inflammatory disease does not seem to manifest any specific ultrasound features [2]. Benign polyps may regress spontaneously in women before menopause. Whether this is explained by misdiagnosis or

by true polyps regressing is unknown. Polyps are characterized by the presence of a feeding vessel at colour or power Doppler ultrasound examination, i.e. one big vessel entering into the endometrial echo from the surrounding myometrium, while submucuous myomas are reported to be surrounded by a ring of colour.

Reference

1. Savelli L, Pilu G, Valeri B, Bovicelli L. Transvaginal sonographic appearance of anaerobic endometritis. Ultrasound Obstet Gynecol 2003; **21**: 624-625.

2. Romosan G, Bjartling C, Skoog L, Valentin L. Ultrasound for diagnosing acute salpingitis: a prospective observational diagnostic study. Hum Reprod 2013; **28**: 1569-1579.

MCQ 3 Which of the following statements is/are correct?

a) Magnetic resonance imaging is superior to ultrasound for diagnosing adenomyosis
b) Transvaginal ultrasound is as good as magnetic resonance imaging in detecting uterine leiomyomas
c) Malignant uterine leiomyosarcomas have an ultrasound appearance that is distinctly different from that of benign uterine leiomyomas
d) Magnetic resonance imaging is superior to ultrasound for discriminating between uterine leiomyosarcomas and benign uterine leiomyomas
e) The typical ultrasound features of endometrial hyperplasia are the same in pre-and post-menopausal women

Correct answers a) F b) T c) F d) F e) F

Explanations to the answers to question 3

In three studies where women underwent both ultrasound and magnetic resonance imaging before hysterectomy, ultrasound was as good as magnetic resonance imaging for diagnosing adenomyosis provided that the uterus was not very large (> 400ml) and did not also contain myomas [1]. In a meticulously designed prospective study where women underwent both transvaginal ultrasound and magnetic resonance imaging before hysterectomy, the two methods had equal ability to detect uterine leiomyomas (magnetic resonance imaging sensitivity 99%, specificity 86%; transvaginal ultrasonography sensitivity 99%, specificity 91%). However, magnetic resonance imaging was superior to transvaginal ultrasound for myoma mapping (determination the exact number, location and size of the myomas) if the uterus was > 375 ml or contained five or more myomas [2]. In typical cases benign leiomyomas are solid tumours characterized by regular internal echogenicity and stripy shadows at ultrasound examination, while leiomyosarcomas are solid tumours that often contain areas of necrosis and therefore have a more irregular internal echogenicity. However, there is too little information in the literature about the typical ultrasound appearance of malignant uterine leiomysosarcomas to know to what extent the ultrasound features of uterine leiomyosarcomas and leiomyomas overlap. In my personal experience, both benign leiomyomas and malignant leiomyosarcomas may appear either richly or poorly vascularized. Poor vascularization of leiomyosarcomas is often explained by necrosis. Unfortunately, there are no studies that are large enough to estimate with any precision the ability of either ultrasound or magnetic resonance imaging to discriminate between benign uterine leiomyomas and leiomyosarcomas. This is natural because of the rarity of this disease. To the best of my knowledge there are also no studies comparing ultrasound with magnetic resonance imaging for discriminating between uterine leiomyosarcomas and leiomyomas. It is not known if the ultrasound appearance of endometrial hyperplasia is the same in pre- and post-menopausal women.

References

1. Dueholm M. Transvaginal ultrasound for diagnosis of adenomyosis: a review. Best Pract Res Clin Obstet Gynaecol 2006; **20:** 569-582.

2. Dueholm M, Lundorf E, Hansen ES et al. Accuracy of magnetic resonance imaging and transvaginal ultrasonography in the diagnosis, mapping, and measurement of uterine myomas. Am J Obstet Gynecol 2002; **186**: 409-415.

Malmö 14th March 2014

Please, find enclosed my manuscript for **Re: Best Practice and Research Clinical Obstetrics and Gynaecology – Issue 28.5 (Imaging in Gynaecology*)***

Best regards
Lil Valentin