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Acoustic streaming cannot discriminate reliably between endometriomas and other types of adnexal lesion: a multicenter study of 633 adnexal masses

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KEYWORDS: acoustic streaming; endometrioma; ultrasonography; viscosity

ABSTRACT

Objective *To determine the ability of acoustic streaming to discriminate between endometriomas and other adnexal masses.*

Methods *We used data from 1938 patients with an adnexal mass included in Phase 2 of the International Ovarian Tumor Analysis (IOTA) study. All patients had been examined by transvaginal gray-scale and Doppler ultrasound following a standardized research protocol. Assessment of acoustic streaming was voluntary and was carried out only in lesions containing echogenic cyst fluid. Acoustic streaming was defined as movement of particles inside the cyst fluid during gray-scale and/or color Doppler examination provided that the probe had been held still for two seconds to ensure that the movement of the particles was not caused by movement of the probe or the patient. Only centers where acoustic streaming had been evaluated in > 90% of cases were included. Sensitivity, specificity, positive and negative likelihood ratios (LR+, LR−), and positive and negative predictive values (PPV and NPV) of acoustic streaming with regard to endometrioma were calculated.*

Results *460 (24%) masses were excluded because they were examined in centers where ≤ 90% of the masses with echogenic cyst fluid had been evaluated for the presence of acoustic streaming. Acoustic streaming was evaluated in 633 of 646 lesions containing echogenic cyst fluid. It was present in 19 (9%) of 209 endometriomas and in 55 (13%) of 424 other lesions. This corresponds to a sensitivity of absent acoustic streaming with regard to endometrioma of 91% (190/209), a specificity of 13% (55/424), LR+ of 1.04, LR− of 0.69, PPV of 34% (190/559) and NPV of 74% (55/74).*

Conclusions *Acoustic streaming cannot discriminate reliably between endometriomas and other adnexal lesions, and the presence of acoustic streaming does not exclude an endometrioma. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Acoustic streaming may be defined as the movement of particulate material within fluid due to energy transfer when an ultrasound wave is directed at it. The transfer of energy occurs when the sound wave strikes reflecting and absorbing obstacles in its path and is related to attenuation[1–3]. Edwards *et al.*[4] were the first to examine acoustic streaming in the cyst fluid of adnexal masses. They defined acoustic streaming as the visualization of movement of particles within the cyst away from the transducer during color Doppler imaging after the ultrasound probe had been held still for some time.

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They detected acoustic streaming in 15 of 29 cystic masses. None of seven endometriomas in their study population exhibited acoustic streaming, while this sign was seen in eight out of 10 (80%) cystadenomas. The authors concluded that 'acoustic streaming is the first sonographic feature that may be able to completely exclude endometrioma as a possible diagnosis for an adnexal cyst'. In a second prospective study, of 26 adnexal masses, they confirmed their findings: acoustic streaming was present in 10 of 16 (62.5%) non-endometriomas but in none of the 10 endometriomas in the study[5].

The correct preoperative identification of endometriomas with or without concomitant extraovarian endometriosis is important, at least in premenopausal patients, because endometriosis is a disease that may have a deleterious effect on fertility, and referral of patients with severe endometriosis to a specialized multidisciplinary team is advisable[6–8]. The aim of this study was to determine the ability of acoustic streaming to discriminate between endometriomas and other adnexal masses in a large prospective multicenter study.

METHODS

The presence of acoustic streaming in adnexal masses was examined in Phase 2 of the International Ovarian Tumor Analysis (IOTA) study. The IOTA group comprises a group of clinicians with a special interest in gynecological ultrasound. One aim of the group was to describe how an adnexal mass should be assessed during the ultrasound examination and what terms and definitions should be used to describe the ultrasound findings[9]. A second aim was to develop mathematical models that can be used to discriminate between benign and malignant adnexal masses. To this end the group created a multicenter database of more than 1000 adnexal masses that had all been scanned following the same standardized IOTA research protocol and for which the final histological diagnosis of the mass was available[10]; details of the IOTA studies can be found in references 9 and 10.

The IOTA Phase 2 study included 1938 patients with an adnexal mass who were prospectively recruited from 19 ultrasound centers in nine countries. All patients underwent a standardized transvaginal ultrasound examination using the IOTA research protocol and all were operated on ≤120 days after the ultrasound examination. All the ultrasound examiners were experienced, and high-quality ultrasound equipment was used. The ultrasound examiners prospectively collected information on more than 40 ultrasound and demographic variables and used the IOTA terms and definitions[9] to describe their findings. In addition, the ultrasound examiner classified each mass as benign or malignant using subjective evaluation of ultrasound findings (pattern recognition) and suggested a histopathological diagnosis, e.g., endometrioma, dermoid cyst, or hydrosalpinx. The evaluation of acoustic streaming was optional. Acoustic streaming is the movement of the material in the cyst fluid away from the transducer due to energy transfer from the ultrasound wave. For this study we used the same definition of acoustic streaming and the same method to determine the presence of acoustic streaming as described in the original paper by Edwards *et al.*[4]. Acoustic streaming was considered to be present whenever the ultrasound examiner found that particles inside the cyst fluid were moving away from the probe, provided that the probe had been held still for 2 seconds to ensure that the movement of the particles was not caused by movement of the probe or the patient. Before concluding that acoustic streaming was absent, the gain was increased to ensure that even the smallest particles in the cyst fluid had been seen, and the color Doppler function was switched on to maximize the energy transfer of the ultrasound wave (Videoclips S1–S3). The gray-scale ultrasound settings of the ultrasound systems were not standardized. The Doppler settings were standardized to allow detection of low blood-flow velocities without artifacts, the settings usually allowing detection of blood-flow velocities of around 5 cm/s (depending on the ultrasound system used). These settings were not changed when we looked for acoustic streaming.

To minimize selection bias, in this study only centers that had evaluated the presence of acoustic streaming in $> 90\%$ of their masses containing cyst fluid with internal echoes were included. The gold standard was the histological diagnosis of the surgically removed adnexal mass. In patients with more than one adnexal mass, only the mass with the most complex gray-scale ultrasound morphology was included. If all the tumors had similar gray-scale ultrasound morphology, the largest one or the one most easily accessible with ultrasound was included.

Statistical analysis

Statistical analysis was carried out using SAS 9.2 (SAS Institute Inc., Cary, NC, USA). The sensitivity, specificity, positive and negative likelihood ratio (LR+ and LR−), and the positive and negative predictive value (PPV and NPV) for 'absent acoustic streaming' with regard to endometrioma were calculated. The same calculations were done to determine the diagnostic performance of pattern recognition with regard to discriminating endometriomas from other types of tumor. The statistical significance of differences in continuous data was determined using Wilcoxon's rank sum test and that of differences in proportions using the χ^2-test or Fisher's exact test, as appropriate. Two-tailed $P < 0.05$ was considered statistically significant.

RESULTS

Of the 1938 patients in the IOTA Phase 2 study, 460 (24%) were excluded because they were examined in 10 centers where $\leq 90\%$ of the masses with echogenic cyst fluid were evaluated for the presence or absence of acoustic streaming. An additional 833 women were excluded because their masses were solid without cyst fluid ($n = 319$) or contained only anechoic cyst fluid ($n = 514$). Acoustic streaming was evaluated in 633 of the remaining 645 (98%) cases. Of the 633 patients included, 162 (26%) were postmenopausal. The histology of the masses included is shown in Table 1; 507 (80%) were benign and 126 (20%) were malignant.

The prevalence of acoustic streaming in masses with different histology is shown in Table 1. Acoustic streaming was present in 12% of the benign masses (60/507) and in 11% (14/126) of the malignant ones. The benign masses that most often exhibited acoustic streaming were serous cystadenomas (44%), rare benign tumors (29%), mucinous cystadenomas (18%) and hydrosalpinges (17%). Acoustic streaming was seen least often in endometriomas (9%), teratomas (6%), fibromas, abscesses and peritoneal inclusion cysts (none of 20). There was no clear difference in acoustic streaming between different types of malignancy.

Of the 633 tumors included, 177 (28%) had low-level echogenicity of the cyst fluid, 217 (34%) ground-glass echogenicity, 30 (5%) hemorrhagic echogenicity, and 209 (33%) mixed echogenicity. Acoustic streaming was significantly more common in cyst fluid with low-level echogenicity (26% (46/177)) than in cyst fluid with ground-glass echogenicity (9% (19/217); $P < 0.0001$), hemorrhagic cyst fluid (7% (2/30); $P = 0.0191$) and cyst fluid with mixed echogenicity (3% (7/209); $P < 0.0001$). Masses with acoustic streaming were significantly larger than masses without acoustic streaming (median largest diameter 86 (range, 17–278) vs. 67 (range, 14–450) mm; $P = 0.0002$).

Table 1 Final histology of all masses included and their relation to presence of acoustic streaming ($n = 633$)

Histology (n)	*Acoustic streaming present* (n *(%))*
Benign ($n = 507$)	60 (12)
Serous cystadenoma ($n = 32$)	14 (44)
Mucinous cystadenoma ($n = 56$)	10 (18)
Rare benign tumor ($n = 7$)*	2 (29)
Hydrosalpinx ($n = 18$)	3 (17)
Functional cyst ($n = 27$)	3 (11)
Simple cyst ($n = 10$)	1 (10)
Endometrioma ($n = 209$)	19 (9)
Teratoma ($n = 128$)	8 (6)
Abscess ($n = 14$)	0 (0)
Ovarian fibroma ($n = 5$)	0 (0)
Peritoneal pseudocyst ($n = 1$)	0 (0)
Borderline ($n = 40$)	5 (13)
Serous borderline ($n = 18$)	2 (11)
Mucinous borderline ($n = 22$)	3 (14)
Invasive ($n = 73$)	8 (11)
Clear cell ($n = 11$)	2 (18)
Endometrioid ($n = 9$)	1 (11)
Serous ($n = 35$)	4 (11)
Mucinous ($n = 9$)	0 (0)
Mixed ($n = 1$)	0 (0)
Other ($n = 8$)†	1 (13)
Metastatic ($n = 13$)	1 (8)
Colon/rectum/appendix ($n = 2$)	0 (0)
Biliary tract ($n = 1$)	0 (0)
Stomach ($n = 3$)	0 (0)
Breast ($n = 2$)	0 (0)
Endometrium ($n = 2$)	0 (0)
Other ($n = 3$)	1 (33)
All tumors ($n = 633$)	74

*For example, Brenner tumor or struma ovarii. †For example, anaplastic carcinoma or granulosa cell tumor.

Of the 209 endometriomas included, 19 (9%) demonstrated acoustic streaming vs. 55 of 424 (13%) non-endometriomas ($P = 0.1530$). This corresponds to a sensitivity with regard to endometrioma of absent acoustic streaming of 91% (190/209), a specificity of 13% (55/424), LR+ of 1.04, LR− of 0.69, a PPV of 34% (190/559), and an NPV of 74% (55/74).

The results for masses with ground-glass echogenicity are shown in Table 2. Among 217 masses with ground-glass echogenicity, 175 (81%) were endometriomas, 33 (15%) were other benign tumors, three (1%) were borderline tumors and six (3%) were malignancies. Acoustic streaming was absent in 93% (163/175) of the endometriomas, 85% (28/33) of the other benign masses, 100% (3/3) of the borderline tumors and 67% (4/6) of the invasive malignancies with ground-glass echogenicity. This corresponds to a sensitivity of absent acoustic streaming with regard to endometrioma in tumors with ground-glass echogenicity of cyst fluid of 93% (163/175), a specificity of 17% (7/42), LR+ of 1.12, LR− of 0.41, PPV of 82% (163/198) and NPV of 37% (7/19). For pattern recognition the sensitivity with regard to endometrioma was 86% (180/209), specificity 94% (400/424), LR+ 15.1, LR− 0.15, PPV 88% (180/204) and NPV 93% (400/429).

The characteristics of endometriomas with and without acoustic streaming are shown in Table 3. Endometriomas with acoustic streaming more often contained cyst fluid of low-level echogenicity (21 vs. 6%, $P = 0.0351$) and were larger than those that did not manifest acoustic streaming (median largest diameter of the lesion 70.5 vs. 55 mm; $P = 0.0387$). However, there was no difference between endometriomas with and without acoustic streaming with regard to type of tumor, vascularization as determined by color score, the patient's age or pain during the ultrasound examination.

Table 2 Presence of acoustic streaming within the group of tumors with ground-glass echogenicity of the cyst fluid

Tumor group	*Masses with acoustic streaming* (n *(%))*
Endometriomas ($n = 175$)	12 (7)
Non-endometriomas ($n = 42$)	7 (17)
Benign tumors ($n = 33$)	5 (15)
Teratoma ($n = 3$)	0 (0)
Simple cyst ($n = 3$)	0 (0)
Functional cyst ($n = 6$)	1 (17)
Hydrosalpinx ($n = 4$)	2 (50)
Abscess ($n = 3$)	0 (0)
Fibroma ($n = 1$)	0 (0)
Serous cystadenoma ($n = 3$)	2 (67)
Mucinous cystadenoma ($n = 10$)	0 (0)
Borderline tumors ($n = 3$)	0 (0)
Invasive cancer ($n = 6$)	2 (33)

Table 3 Sonographic, clinical and demographic characteristics of endometriomas with and without acoustic streaming

Variable	*Endometriomas with acoustic streaming* (n = *19)*	*Endometriomas without acoustic streaming* (n = *190)*	P
Type of tumor			0.5230
Unilocular ($n = 147$)	13 (68)	134 (71)	
Unilocular-solid ($n = 16$)	1 (5)	15 (8)	
Multilocular ($n = 30$)	2 (11)	28 (15)	
Multilocular-solid ($n = 16$)	3 (16)	13 (7)	
Maximum diameter of lesion (mm)	70.5 (17–180)	55 (15–166)	0.0387
Echogenicity of cyst fluid			0.0321
Low-level ($n = 15$)	4 (21)	11 (6)	0.0351
Ground-glass ($n = 175$)	12 (63)	163 (86)	0.0192
Hemorrhagic ($n = 9$)	1 (5)	8 (4)	0.5834
Mixed ($n = 10$)	2 (11)	8 (4)	0.2271
Color score			0.1990
1 ($n = 69$)	3 (16)	66 (35)	
2 ($n = 104$)	13 (68)	91 (48)	
3 ($n = 34$)	2 (11)	32 (17)	
4 ($n = 2$)	1 (5)	1 (0.5)	
Age (years)	34 (19–61)	35 (18–50)	0.3423
Pain during the ultrasound examination	7 (37)	73 (38)	0.8926

Data are given as *n* (%) or median (range). Color score: 1, no color content; 2, minimal color content; 3, moderate color content; 4, high color content.

When using pattern recognition, 88% (167/190) of the endometriomas without acoustic streaming were correctly classified as endometriomas vs. 68% (13/19) of those with acoustic streaming ($P = 0.0313$, Fisher's exact test). Of the six endometriomas with acoustic streaming that were misclassified, none had ground-glass echogenicity of the cyst fluid and all were rather large masses (median of the largest diameter 88.5 (range, 64–180) mm).

Acoustic streaming was present in 7% (13/180) of the endometriomas correctly diagnosed by pattern recognition, 8% (2/24) of the false-positive cases, 21% (6/29) of the false-negative cases and 13% (53/400) of the true negative cases.

DISCUSSION

We have prospectively evaluated the presence of acoustic streaming in adnexal masses and found that although acoustic streaming was not commonly seen in endometriomas, it could not be used in isolation as a test to exclude endometriomas. Acoustic streaming was present in 7% (12/175) of endometriomas with ground-glass echogenicity. Endometriomas with acoustic streaming more often contained cyst fluid with low-level echogenicity and were larger than those without acoustic streaming. Overall, acoustic streaming was most often associated with larger masses and masses with low-level echogenicity.

The strength of our study is that it is a very large prospective multicenter study that includes consecutive patients with an adnexal mass for which final histology is available. A weakness is the lack of specific training in assessing acoustic streaming before the start of the study and the lack of consensus agreement among the examiners regarding when to classify acoustic streaming as present or absent in equivocal cases. A further criticism is that the primary aim of the IOTA study was not to evaluate the presence of acoustic streaming. Therefore, the examiners might not have spent sufficient time examining the lesions for the presence of acoustic streaming. On the other hand, Edwards *et al.*[4] presented the evaluation of acoustic streaming as a simple ultrasound test, and we used their method of assessing acoustic streaming as well as their definition of acoustic streaming.

Our results confirm the impression of Edwards *et al.*[4] that acoustic streaming is more common in cyst fluid with low-level echogenicity than in cyst fluid with ground-glass echogenicity. In the original studies by Edwards *et al.*[4] and Clarke *et al.*[5], acoustic streaming was found in 52% (15/29) and 38% (10/26) of all masses but not in any endometrioma. In our study acoustic streaming was found in only 12% of all masses (74/633) but in 9% (19/209) of endometriomas. In the study by Clarke *et al.*[5], 87.5% (7/8) of cystadenofibromas demonstrated acoustic streaming vs. only 27% (24/88) in our study. The discrepant results might be explained by subtle differences in interpretation of acoustic streaming between operators. Unfortunately, studies on interobserver agreement when assessing acoustic streaming have not been published, and the interobserver agreement cannot be determined retrospectively using our data. Differences in output energy might be another explanation for the discrepant results. Edwards *et al.*[4] and Clarke *et al.*[5] did not specify the output energy of their color Doppler ultrasound examinations, nor did we prospectively collect information on it. The energy output was not standardized either in our study or in those by Edwards *et al.*[4] and Clarke *et al.*[5].

Our finding that the presence or absence of acoustic streaming in cyst fluid depends on the size of the cyst is in agreement with the results presented in the *in-vitro* study by Clarke *et al.*[11]. This can be explained by fluid mechanics resulting in higher streaming velocities for the same energy input, or by the fact that a longer path through the cyst results in more energy transfer from the ultrasound beam to the cyst fluid[12]. The viscosity of the cyst fluid, which is determined by the size of the particles it contains (e.g. red or white blood corpuscles, crystals, cells, amorphous material), will influence the streaming velocities. Higher velocities are obtained in less viscous fluids[11–14]. In an *in-vitro* study, Clarke *et al.*[11] demonstrated differences in acoustic streaming in different cyst media. The physical properties are likely to vary from one endometrioma to another depending on, for example, whether there has been recent (menstrual) bleeding into the cyst. Variations in the properties of the cyst fluid may explain why acoustic streaming is absent in most endometriomas but not in all.

Our data show that acoustic streaming is not related to any specific histology and that the presence of acoustic streaming in a cyst cannot be used to exclude endometrioma. However, pattern recognition is a good method for distinguishing endometriomas from other types of adnexal mass.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Videoclip S1 Clip demonstrating no acoustic streaming in a unilocular endometrioma ($52 \times 60 \times 90$ mm) with ground-glass echogenicity in a 53-year-old premenopausal patient.

Videoclip S2 Clip demonstrating acoustic streaming in a unilocular endometrioma ($51 \times 46 \times 32$ mm) with ground-glass echogenicity in a 29-year-old patient.

Videoclip S3 Clip demonstrating acoustic streaming in a unilocular-solid lesion with ground-glass echogenicity and a color score of 4 (high vascularization) in a 55-year-old patient. On final histology it proved to be a Stage Ic serous Fallopian tube carcinoma.

