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Ultrasound for diagnosing acute salpingitis: a prospective observational diagnostic study

Running title: Ultrasound and salpingitis

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ABSTRACT

Study question: To estimate the sensitivity and specificity of ultrasound for diagnosing acute salpingitis in patients with clinical signs of pelvic inflammatory disease (PID).

Summary answer: In patients with a clinical suspicion of acute salpingitis, absence of bilateral adnexal masses at ultrasound decreases the odds of mild to severe acute salpingitis about five times, while the presence of bilateral adnexal masses increases the odds about five times.

What is known already: PID is difficult to diagnose because the symptoms are often subtle and mild. The diagnosis is usually based on clinical findings, and these are unspecific. Sensitivity and specificity of ultrasound with regard to salpingitis have been reported in one study (n=30) with appropriate design where most patients had severe salpingitis (i.e. pyosalpinx) or tubo-ovarian abscess.

Study design, size, duration: Diagnostic test study including 52 patients fulfilling clinical criteria of PID. Patients were recruited between October 1999 and August 2008. They underwent a standardised transvaginal gray scale and Doppler ultrasound examination by one experienced sonologist (index test) before diagnostic laparoscopy by a laparoscopist blinded to the ultrasound results. The final diagnosis was determined by laparoscopy, histology of the endometrium and other histology where relevant (reference standard).

Participants/materials, setting, methods: Twenty-three patients (44%) had a final diagnosis unrelated to genital infection, 29 had cervicitis (n=3), endometritis (n=9), or salpingitis (n=17; mild n=4, moderate n=8, severe, i.e. pyosalpinx n=5).

Main results and the role of chance: Bilateral adnexal masses and bilateral masses lying adjacent to the ovary were seen more often on ultrasound in patients with salpingitis than with other diagnoses (82% vs.17%, i.e.14/17 vs. 6/35, P = 0.000, positive likelihood ratio 4.8, negative likelihood ratio 0.22; 65% vs. 17%, i.e.11/17 vs. 6/35, P = 0.001, positive likelihood

ratio 3.8, negative likelihood ratio 0.42). In cases of salpingitis, the masses lying adjacent to the ovaries were on average 2-3 cm in diameter, solid (n=14), unilocular cystic (n=4), multilocular cystic (n=3), or multilocular solid (n=1) with thick walls and well vascularised at colour Doppler. In no case were the cog wheel sign or incomplete septae seen. All 13 cases of moderate or severe salpingitis were diagnosed with ultrasound (detection rate 100%, 95%CI 78% to 100%) vs. one of four cases of mild salpingitis. Three of six cases of appendicitis, and two of two ovarian cysts were correctly diagnosed with ultrasound, and one case of adnexal torsion was suspected and then verified at laparoscopy.

Limitations, reasons for caution: The sample size is small. This is explained by difficulties with patient recruitment. There are few cases of mild salpingitis, which means that we cannot estimate with any precision the ability of ultrasound to detect very early salpingitis.

Wider implications of the findings: The proportion of cases with salpingitis of different grade affects the sensitivity and specificity of ultrasound, and the sensitivity and specificity that we report here are applicable only to patient populations similar to ours. The information provided by transvaginal ultrasound is likely to be of help when deciding whether or not to proceed with diagnostic laparoscopy in patients with symptoms and signs suggesting PID, and if laparoscopy is not performed to select treatment and planning follow-up.

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Key words: salpingitis; ultrasonography; Doppler ultrasonography; emergency medicine, sensitivity/specificity

INTRODUCTION

Pelvic inflammatory disease (PID) is difficult to diagnose because the symptoms are often subtle and mild. Because there are no precise tests for PID, a diagnosis is usually based on clinical findings, but clinical diagnosis of PID is hampered by the lack of specificity of signs and symptoms. On physical examination, pelvic and abdominal tenderness, abnormal cervical secretions and fever are findings associated with PID (CDC, 2010). However, in a study by Jacobson and Weström (Jacobson and Westrom, 1969), only 65% of patients with a clinical diagnosis of PID had salpingitis confirmed when laparoscopy was performed, 23% had normal findings, and in the remaining 12% laparoscopy revealed pathologic conditions unrelated to PID (acute appendicitis, ectopic pregnancy, pelvic endometriosis and several other pelvic disorders) (Jacobson and Westrom, 1969). Palpable adnexal fullness or mass is a common finding in women with salpingitis and is related to the severity of inflammation as determined by laparoscopy. However, palpable adnexal fullness or mass is also reported in some women with normal findings on laparoscopy (Jacobson and Westrom, 1969).

Transvaginal ultrasound has become increasingly common as an aid to establish a correct diagnosis in women with acute pelvic pain (Okaro and Valentin, 2004). Ultrasound findings suggestive of pyosalpinx have been described, i.e. a pear shaped fluid filled structure with thick walls, presence of incomplete septae, and cogwheel sign (Timor-Tritsch, et al., 1998). Moreover, increased vascularisation as determined by Doppler ultrasound has been reported in cases of inflammation-induced hyperemia in the tubes (Alatas, et al., 1996, Molander, et al., 2001).

The aim of this study was to 1) describe ultrasound findings in cases of acute mild, moderate and severe salpingitis verified by laparoscopy 2) to estimate the sensitivity and specificity of transvaginal ultrasound for diagnosing acute salpingitis in patients with clinical signs of PID.

METHODS

This is a prospective observational study. Consecutive patients scheduled for diagnostic laparoscopy at the department of Obstetrics and Gynecology, Skåne University Hospital, Malmö, Sweden, because of a clinical suspicion of acute salpingitis were eligible for inclusion. The clinical examination in the emergency room upon which the doctor based his/her clinical diagnosis included speculum examination, wet smear, and gynaecological palpation. Presenting symptoms and clinical findings were documented prospectively in a research protocol by the doctor in the emergency room. In addition, blood was drawn for analysis of C-reactive protein (CRP), and body temperature was measured. Salpingitis was suspected if the following criteria were fulfilled: acute abdominal pain for 1 – 14 days, cervical motion tenderness and adnexal tenderness at pelvic bimanual examination, negative pregnancy test and at least one of the following three signs: pathological saline prepared vaginal wet smear (more leucocytes than epithelial cells in the absence of clue-cells and inflammatory vaginitis) or pathological discharge at speculum examination, elevated C-reactive protein (CRP), oral temperature >38.0°C. These criteria are similar to the criteria of PID of the Centers for disease control and prevention, USA (CDC, 2010). According both to the policy of our department and our research protocol, all patients fulfilling these criteria should undergo diagnostic laparoscopy.

Tests for Neisseria gonorrhoea (N. Gonorrhoea) and Chlamydia trachomatis (C. trachomatis) were performed. N. gonorrhoea was detected by culture from a charcoal-treated cotton swab which was sent to the laboratory in Stuart's transport medium. First void urine together with cervical samples, or vaginal swabs together with urine, were collected to diagnose C.trachomatis using polymerase chain reaction, PCR (Roche Molecular Diagnostics, Pleasanton, CA, USA, or m2000, Abbott Molecular Inc. Des Plaines, IL, USA).

Our inclusion criteria were: age ≥18 years (the age of legal consent), signed informed consent, no unequivocal alternative diagnosis to PID on the basis of clinical evaluation, no ongoing treatment with antibiotics or anti-inflammatory drugs, but antibiotic therapy started <24 h before the laparoscopy was accepted. Exclusion criteria were violation of the study protocol or treatment with antibiotics >24 h before laparoscopy.

After a decision to perform laparoscopy had been taken by the physician in the emergency room, and after the patient had consented to participate in the study, a standardised transvaginal gray scale and colour and spectral Doppler ultrasound examination was performed by a gynaecologist with more than 10 years of experience in gynaecological ultrasound (LV). The ultrasound examiner knew that the eligibility criteria of the study were fulfilled but did not have access to any other clinical information. The ultrasound system used was a Sequoia 512 (Siemens Medical Solutions Inc., Ultrasound Division, Mountain View, CA, USA) equipped with a 5 – 8 MHz transvaginal transducer. All women were examined in the lithotomy position with an empty bladder. The uterus and adnexa were scanned systematically following the research protocol. The presence/absence of fluid in the endometrial cavity, the cervical canal and the pouch of Douglas was noted. The ovaries were described with regard to the presence of corpus luteum, polycystic appearance and any pathological intra-ovarian lesions. Any adnexal lesions were noted, and the gray scale morphology of any such lesion was described using the terminology of the International Ovarian Tumor Analysis group (Timmerman, et al., 2000). Subjective assessment, i.e. pattern recognition was also used for evaluation of ultrasound findings (Valentin, 1999, Valentin, 2004) ultrasound signs reported to be specific for pyosalpinx (Timor-Tritsch, et al., 1998, Valentin, 2004) being searched for. Three orthogonal diameters of any mass were measured. We report the size of masses as the mean of three orthogonal diameters. The dynamic and interactive nature of transvaginal ultrasound was made full use of for pain mapping and for

estimating the mobility of organs and lesions. After the gray scale ultrasound examination had been completed, the ultrasound system was switched into the colour Doppler mode, and the colour content of the endometrium, myometrium and any adnexal mass suspected to be a diseased tube was estimated subjectively by the ultrasound examiner on a visual analogue scale (VAS) graded from 0 to 100. Standardised colour Doppler settings were used (frequency 6 MHz; power Doppler gain 50; dynamic range 10 dB; edge 1; persistence 2; colour map 1; gate 2; filter 3). Finally, blood flow velocities were measured in the uterine arteries, in the tubal arteries at the place where the tube leaves the uterus (Kirchler, et al., 1992) and in the wall of any adnexal mass. Angle correction was used when measuring blood flow velocities in the uterine arteries. For the other vessels angle correction was not used, but the highest achievable Doppler shift signals were sought for each vessel (Valentin, et al., 1994). Ultrasound images were documented on hard copies, on video tape or electronically. Based on subjective evaluation of ultrasound findings, the ultrasound examiner suggested a likely diagnosis. The ultrasound results were entered into a research protocol. The ultrasound examiner played no role in the clinical management of the patient, and all staff managing the patient including the laparoscopist was blinded to the ultrasound results.

After the ultrasound examination, laparoscopy was performed by gynaecologists with different levels of expertise (senior registrar or consultant). Immediately before the laparoscopy with the patient anaesthetised, any intrauterine contraceptive device was removed, and an endometrial sample was taken using both an Endorette^{TM} outpatient endometrial sampling device (Medscand AB, Malmö, Sweden) and a currette. The Endorette is a sterile device with a polyethylene piston which slides within a straight but flexible polypropylene sheath with four lateral holes near its tip. Its length is 285 mm and its outer diameter is 2.6 mm. The endometrial samples were analysed by one dedicated pathologist (LS) with the specific aim of confirming or excluding endometritis. At laparoscopy, cultures

were taken from the tubal fimbriae and from fluid in the pouch of Douglas for analysis of C. trachomatis and N. gonorrhea. The laparoscopy was documented on video tape or on DVD. Immediately after the laparoscopy, the laparoscopist described the laparoscopic findings in a standardised research protocol.

The final diagnosis was determined by the authors on the basis of the results of endometrial histology and findings at laparoscopy. A diagnosis of acute salpingitis was made if the laparoscopic criteria of mild, moderate or severe salpingitis as suggested by Hager et al. (Hager, et al., 1983) were fulfilled. The minimal criteria for a diagnosis of salpingitis were: tubal redness, tubal edema, and pus or exudate from the tubal fimbriae provoked by manipulation (salpingitis grade 1, i.e. mild salpingitis). If in addition to the minimal criteria, pus was present spontaneously and the tubes were fixed and closed, we classified the condition as salpingitis grade 2 (i.e. moderate salpingitis). If there was a pyosalpinx or a tubo-ovarian abscess the condition was classified as salpingitis grade 3 (i.e. severe salpingitis) (Hager, et al., 1983). The diagnosis of endometritis was made when there were neutrophlic microabscesses plus infiltration and destruction of glandular epithelium in the endometrial sample (acute endometritis) or infiltration of plasma cells, histiocytes, lymphocytes and lymphoid follicles (chronic endometritis) or both but no signs of salpingitis at laparoscopy (Blaustein and Kurman, 2002, Sellors, et al., 1991). A final diagnosis of cervicitis was made if there were clinical signs of cervicitis but neither the criteria of endometritis nor those of salpingitis were fulfilled.

We collected information regarding parity, gynaecological history, and use of contraceptives from the patient records retrospectively.

Statistical analysis

Statistical calculations were undertaken using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA, version 16.0 or 17.0). The statistical significance

of a difference in unpaired proportions was determined using the chi-squared test or Fisher´s exact test as appropriate, and the statistical significance of a difference in continuous unpaired data was determined using the Mann-Whitney test. Exact 95% confidence intervals (CI) for sensitivity and specificity were calculated. When sensitivity was 100%, positive and negative likelihood ratios were calculated by adding 0.5 to all four fields in the four-field table. A P-value <0.05 was considered statistically significant.

Ethical approval

The Ethics Committee of Lund University, Sweden, approved the study protocol. Written informed consent was obtained from all participants, after the nature of the procedures had been fully explained.

RESULTS

Recruitment was from October 1999 until August 2008. A total of 85 patients scheduled for diagnostic laparoscopy because of a clinical suspicion of salpingitis consented to be included in the study, but 33 had to be excluded: five because they were treated with antibiotics for >48h before the laparoscopy, one because the laparoscopy was carried out 13 days after the ultrasound examination, 11 because the planned laparoscopy was cancelled, and 16 because the ultrasound examiner was not available to perform the scan before the laparoscopy. Thus, 52 patients were included.

Eight of the 52 patients included received antibiotics during the 24h preceding the ultrasound examination and the laparoscopy (three cases with a final diagnosis of salpingitis or pyosalpinx and five cases with a final diagnosis of pelvic pain with unknown etiology). The time between the ultrasound examination and the diagnostic laparoscopy was median 4.9h (range 0.5 to 48).

The final diagnosis of the 52 patients included was: salpingitis (17/52, 32.7%), endometritis (9/52, 17.3%), cervicitis (3/52, 5.8%), and other (23/52, 44.2%). Four of the 17 cases of salpingitis were mild, eight were moderate and five were severe (i.e. pyosalpinx). No patient had a tubo-ovarian abscess. The other diagnoses were: pelvic pain with unknown etiology (7/52, 13.5%), appendicitis (6/52, 11.5%), peritoneal or ovarian endometriosis (2/52, 3.8%), ovarian cyst (2/52, 3.8%), urinary tract infection (2/52, 3.8%), adnexal torsion (2/52, 3.8%), i.e., one case of torsion of a hydrosalpinx and one of torsion of a Morgagni hydatid, mucinous cystadenocarcinoma in the appendix (1/52, 1.9%), and Crohn´s disease (1/52, 1.9%).

Demographic background data, symptoms, findings at clinical examination, results of cultures/PCR and endometrial histology are shown in Table I. No patient was diagnosed with N. Gonorrhea. More patients with salpingitis and endometritis than with other diagnoses

complained of discharge (17/25 vs. 8/26, P = 0.012), but there were no other obvious differences either in demographic background data, symptoms or clinical findings between women with laparoscopically confirmed salpingitis and those with other diagnoses. Patients with salpingitis had the highest CRP values (median 75, range 15 - 204 vs. 42, 8 - 374, P = 0.016).

Some ultrasound results are shown in Table II and III (Table III online only). There was no obvious difference in the presence of or in the amount of fluid in the pouch of Douglas between patients with salpingitis, endometritis and other diagnoses. Polycystic appearance of the ovaries was not more common in patients with salpingitis than in other patients. Bilateral adnexal masses and bilateral adnexal masses lying adjacent to the ovary were seen more often at ultrasound examination in patients with salpingitis than with other diagnoses (14/17 vs. 6/35, P = 0.000; 11/17 vs. 6/35, P = 0.001). The colour score of the endometrium was highest in patients with endometritis, pulsatility index (PI) values were lowest and time averaged maximum velocities (TAMXV) were highest in the uterine and tubal arteries in patients with salpingitis. However, there was substantial overlap in Doppler results between patients with different diagnoses.

The diagnoses suggested by the ultrasound examiner are shown in Table IV (online only). The sensitivity with regard to acute salpingitis of subjective interpretation of the ultrasound findings by the ultrasound examiner was 82% (14/17, 95% CI 57-96%), the specificity 77% (27/35, 95%CI 60-90%), the positive likelihood ratio 3.6 and the negative likelihood ratio 0.23. The sensitivity and specificity of ultrasound findings of bilateral masses lying adjacent to the ovary were 65% (11/17, 95%CI 38-86%) and 83% (29/35, 95%CI 66-93%), and the positive and negative likelihood ratios 3.8 and 0.42. The corresponding figures for bilateral adnexal masses were 82% (14/17, 95% CI 57-96%), 83% (29/35, 95%CI 66-93%), 4.8 and 0.22. Bilateral adnexal masses were found in all 13 patients with moderate or severe

salpingitis but in only one of four patients with mild salpingitis. Thus, the sensitivity and specificity of bilateral adnexal masses with regard to moderate or severe salpingitis were 100% (13/13, 95% CI 78-100%) and 82% (32/39, 95% CI 67-91%) and the positive and negative likelihood ratios 5.1 and 0.04.

Ultrasound findings in patients with mild salpingitis (red, swollen tubes and pus or exudate from the tubal fimbriae provoked only by manipulation at laparoscopy)

The only patient with mild salpingitis that was diagnosed with ultrasound had bilateral solid masses with a diameter of 19 mm and 23 mm, respectively, lying adjacent to the ovary. The colour score was 14 and 65, PSV 4 cm/s and 23 cm/s, TAMXV 2 cm/s and 10 cm/s, and PI 1.60 and 2.03 in the smallest and largest mass, respectively. In the remaining three patients with mild salpingitis, no adnexal masses were seen with ultrasound.

Ultrasound findings in patients with moderate salpingitis (red, swollen, fixed and closed tubes, pus present spontaneously at laparoscopy)

Seven of the eight patients with moderate salpingitis had bilateral masses lying adjacent to the ovary, and one had a mass lying adjacent to the ovary on one side and a mass with no discernable ovary on the other side. Ten of the 15 masses lying adjacent to the ovary were solid, four were unilocular cystic (sausage shaped, thick walled unilocular structure with echogenic fluid inside, no cogwheel sign, no incomplete septae) and one was multilocular solid (thick walled roundish lesion filled with echogenic fluid, no cogwheel sign, no incomplete septae). The mass without a discernable ovary was solid. The size of the smallest mass lying adjacent to the ovary was median 18 mm (15-23) and that of the largest mass 28 mm (24-32). Median colour score in the smallest and largest mass was 75 (45-99) and 92 (5-97), median PSV17 cm/s (9-26) and 15 cm/s (8-47), median TAMXV 9 cm/s (5-16) and 9 cm/s (4-27) and median PI 1.15 (0.78-2.00) and 1.16 (0.80-1.46). The mass without a

discernable ovary measured 60 mm, had a colour score of 18, a PSV of 17 cm/s, a TAMXV of 12 cm/s and a PI of 0.63.

Ultrasound images from patients with laparoscopically confirmed moderate salpingitis are shown in Figure 1, 2 and 3.

Ultrasound findings in patients with severe salpingitis (pyosalpinx at laparoscopy)

Three of the five patients with severe salpingitis had bilateral masses lying adjacent to the ovary: three of the six masses were solid and the other three were roundish or elongated multilocular thick-walled cystic structures containing echogenic fluid without cogwheel sign or incomplete septae. Two patients had bilateral adnexal masses without a discernable ovary: two were solid masses, and two were multilocular solid masses with thick walls and septae and with cyst locules containing homogenously echogenic fluid or fluid with echogenicity similar to what is seen in haemorrhagic corpora lutea (Valentin, 2004). Neither cogwheel sign nor incomplete septae were seen. The median size of the smallest and biggest adnexal mass lying adjacent to the ovary was 21 (19-30) and 33 (27-46) mm, the median colour score 87 (29-95) and 76 (56-97), the median PSV 20 cm/s (12-21) and 14 cm/s (13-37), the median TAMXV 8 cm/s (7-14) and 6 cm/s (6-22), and the median PI 0.98 (0.69-2.06) and 2.06 (1.07-2.07). The median diameter of the smallest mass without a discernable ovary was 32 mm (30 - 34) and of the biggest 48 (40-60) mm. The median colour score was 71 and 73 (65-81), the median PSV 35 cm/s and 30 cm/s (18-41), the median TAMXV 10 cm/s and 15 cm/s (8-21) and the median PI 3.22 and 1.68 (1.30-2.07) (velocimetry results were missing for one of the smallest masses).

Ultrasound findings in patients with endometritis

In six (66.6%) of the nine patients with a final diagnosis of endometritis no adnexal masses were seen at ultrasound examination, while bilateral solid masses lying adjacent to the ovary were described in three patients. The median size of the smallest of the bilateral masses was

16 mm (15-16) and that of the largest 19 mm (16-23). The colour content of the masses lying adjacent to the ovary in women with endometritis was lower than in patients with confirmed salpingitis while PI values were higher, the median colour score in the smallest and largest mass in the patients with endometritis being 51 (20-81) and 54 (20-88) and the median PI 1.63 (0.97-2.31) and 1.31 (1.00-1.63). PSV and TAMXV in masses lying adjacent to the ovary were similar in women with salpingits and endometritis, the median PSV and TAMVX in the women with endometritis being 14 cm/s (8-16) and 6 cm/s (3-10) in the smallest mass and 14 cm/s (7-21) and 6 cm/s (3-13) in the largest mass.

Ultrasound findings in patients with a final diagnosis other than salpingitis or endometritis

In 15 of the 26 patients with a final diagnosis other than salpingitis or endometritis no masses were detected at ultrasound examination. The final diagnosis in these 15 cases were pain of unknown etiology (n=4), cervicitis (n=3), appendicitis (n=3), urinary tract infection (n=2), peritoneal endometriosis (n=1), Crohn´s disease (n=1), and cystadenocarcinoma of the appendix (n =1).

In two of the 26 patients, unilateral ovarian lesions were seen at ultrasound examination and suggested by the ultrasound examiner to be a haemorrhagic corpus luteum cyst and a 50 mm bilocular ovarian cyst. The two diagnoses of ovarian cyst were confirmed at laparoscopy.

A unilateral mass lying adjacent to the ovary was seen in six of the 26 patients. In one of these six cases no mass was found at laparoscopy (the final diagnosis was pain of unknown etiology, and in retrospect the mass seen at ultrasound was probably a bowel loop). In four cases the ultrasound image of the mass was judged to be compatible with acute appendicitis. This diagnosis was confirmed in three of the four cases. In the fourth case the appendix was judged to be normal at laparoscopy, and the final diagnosis was peritoneal endometriosis. In the last case a multilocular solid mass was suggested by the ultrasound examiner to be either torsion of a diseased tube, a pyosalpinx or - very unlikely - a malignancy. This mass was the

only one manifesting the cogwheel sign (Figure 4). The correct diagnosis was torsion of a hydrosalpinx.

In three of the 26 patients, bilateral small diffusely delineated solid masses lying adjacent to the ovary were seen at ultrasound examination. In two of these cases the ultrasound examiner suggested a diagnosis of acute salpingitis, but no pathology was judged to be present at laparoscopy, and the final diagnosis was pain of unknown etiology (size of smallest mass 15 mm and 26 mm, colour score 70 and 12, PSV 13 cm/s and 22 cm/s, TAMXV 5 cm/s and 9 cm/s, PI 1.88 and 1.75; size of largest mass 18 mm and 27 mm, colour score 95 and 87, PSV 8 cm/s and 13 cm/s, TAMXV 4cm/s and 8cm/s and PI 1.58 and 0.88). In the third case torsion of a gangrenous hydatid of Morgagni was found at laparoscopy, while no mass was confirmed on the contralateral side. At ultrasound examination the mass corresponding to the hydatid of Morgagni was solid and had a size of 12 mm, a colour score of 22, PSV 16 cm/s, TAMXV 9 cm/s and PI 0.69. The mass that was not confirmed at laparoscopy was also considered to be solid, and had a size of 14 mm, a colour score 70, PSV 17 cm/s, TAMXV 8 cm/s and PI 1.64.

DISCUSSION

Our results showed that ultrasound findings suggestive of moderate or severe acute salpingitis were the presence of bilateral adnexal masses or the presence of bilateral adnexal masses lying adjacent to the ovary, 100% and 77% of the patients with moderate to severe salpingitis confirmed by laparoscopy manifesting these signs vs. one of the four patients with mild salpingitis and 17 % of the patients with other diagnoses. Most masses lying adjacent to the ovaries in cases of salpingitis were solid, fewer were thick-walled elongated unilocular cystic masses or roundish or elongated multilocular or multilocular solid masses containing echogenic fluid but not manifesting the cogwheel sign or incomplete septae. Most of these lesions were 2 -3 cm in size and well vascularised at colour Doppler ultrasound examination.

The strength of our study is that it contributes information to an area where scientific evidence is very scarce. To the best of our knowledge the ultrasound findings in cases of mild or moderate salpingitis - but not distinguishing between the two - verified by laparoscopy have been described in only one publication. It includes six cases of mild or moderate salpingitis and shows ultrasound images of two of these cases (Molander, et al., 2001). We are aware of only two published studies reporting on the sensitivity and specificity of ultrasound with regard to laparoscopically confirmed acute salpingitis (Molander, et al., 2001, Tukeva, et al., 1999). Both include mainly patients with pyosalpinx or tuboovarian abscess, and only one of them has a design appropriate for estimating sensitivity and specificity (Table V) (Tukeva, et al., 1999). Details on published studies reporting on the sensitivity and specificity of ultrasound for diagnosing “upper genital tract infection” are shown in Table VI (Boardman, et al., 1997, Cacciatore, et al., 1992) .

Our study has limitations. First, the sample size is small. This is explained mainly by difficulties with patient recruitment (doctors in the emergency ward forgetting to recruit patients, patients declining to undergo diagnostic laparoscopy). According to our hospital

statistics, 245 patients had a diagnosis of acute salpingitis either as inpatients or outpatients in our hospital during the study period. Our study sample includes only 17 of these. Second, there were few cases of mild salpingitis in our study sample. This means that we cannot estimate with any precision the ability of ultrasound to detect very early salpingitis. Clearly, the proportion of cases with salpingitis of different grade affects the sensitivity and specificity of ultrasound, and the sensitivity and specificity that we report here are generalizable only to patient populations similar to our study population. Moreover, one can expect results similar to ours only if ultrasound is carried out by experienced ultrasound examiners using high end ultrasound systems. The small number of patients with mild salpingitis may reflect either that doctors did not recommend laparoscopy to all patients fulfilling our eligibility criteria (which they should have done both according to the policy of our department and our study protocol), that a higher proportion of patients with mild salpingitis than moderate or severe salpingitis declined to participate in the study, or that few patients with mild salpingitis fulfilled our eligibility criteria. A third limitation – and one that we share with other studies trying to estimate the sensitivity and specificity of ultrasound with regard to acute salpingitis - is the lack of an obvious gold standard. Salpingitis may be present in the absence of histological signs of endometritis (Sellors, et al., 1991). In our opinion, the best gold standard is diagnostic laparoscopy. Still, diagnostic laparoscopy is not ideal. Sellors et al (Sellors, et al., 1991) found laparoscopy to have low sensitivity (58%) with regard to histologically confirmed salpingitis, and Molander et al (Molander, et al., 2003) reported poor intra-and inter-observer agreement with regard to PID when six gynecologists evaluated laparoscopic images of the female pelvis.

The ultrasound image of early salpingitis has been described by Molander et al (Molander, et al., 2001) as a solid mass with high colour content at power Doppler examination located close to the ovary. Our results agree fairly well. However, neither we nor Broadman et al

(Boardman, et al., 1997) were able to confirm the findings of Cacciatore et al (Cacciatore, et al., 1992) that fluid in the pouch of Douglas and polycystic appearance of the ovaries are reliable signs of ´upper genital tract infection´. Even though our results confirm that inflamed tubes are richly vascularised at Doppler examination (Alatas, et al., 1996, Molander, et al., 2001, Tinkanen and Kujansuu, 1992), all our Doppler results overlapped too much between patients with different diagnoses for them to be clinically useful. This is in accordance with the findings in the case-control study by Molander et al. (Molander, et al., 2001) where ultrasound images of acute salpingitis (cases) were compared with those of hydrosalpinx (controls). Possibly, the inability of Doppler ultrasound to distinguish upper genital tract infections from other conditions in the pelvis is explained by Doppler measurements not being sufficiently precise or accurate.

Two studies (Molander, et al., 2001, Tukeva, et al., 1999) reported very high sensitivity and specificity of ultrasound for diagnosing PID. The higher sensitivity in these studies than in ours is likely to be explained by a much higher prevalence of pyosalpinx and tuboovarian abscess in the other studies (Table V). The sensitivity and specificity reported by Molander et al. (Molander, et al., 2001) are not applicable to patients with clinical signs of acute PID, because they calculated sensitivity using patients with laparoscopically confirmed PID (cases) and specificity using patients with hydrosalpinx (control group).

Our finding that 44% (23/52) of the patients with clinical signs of PID had normal laparoscopy findings or a final diagnosis unrelated to PID agrees with those of others, the corresponding figures in other studies being 30% (9/30) (Tukeva, et al., 1999), 35% (282/814) (Jacobson and Westrom, 1969), 39% (13/33) (Molander, et al., 2000) and 33% (10/30) (Molander, et al., 2001). In our study as well as in others, common diagnoses unrelated to PID in patients with clinical signs of PID were appendicitis (Jacobson and Westrom, 1969, Molander, et al., 2000) adnexal torsion (Molander, et al., 2000, Tukeva, et al., 1999), ovarian

cysts (Jacobson and Westrom, 1969, Molander, et al., 2000, Tukeva, et al., 1999) and endometriosis (Jacobson and Westrom, 1969, Molander, et al., 2000, Tukeva, et al., 1999).

Our results support that ultrasound is likely to be helpful when managing patients with symptoms and clinical signs of acute PID, because symptoms and signs of PID overlap with those of several diagnoses unrelated to genital infection. Ultrasound signs of affected tubes changed the odds of salpingitis only moderately (about five times) (Jaeschke, et al., 1994), but even a small change in odds may be helpful in patients presenting a diagnostic dilemma (Jaeschke, et al., 1994). Moreover, in the absence of bilateral adnexal masses the odds of moderate or severe salpingitis decreased more than 20-fold, while mild salpingitis could not be excluded. This information provided by transvaginal ultrasound is likely to be of help when deciding on whether or not to proceed with diagnostic laparoscopy in patients with symptoms and signs suggesting PID and, if laparoscopy is not performed, for selecting treatment and planning follow-up. In addition, ultrasound may reveal diagnoses unrelated to PID, e.g. appendicitis, ovarian cysts including endometriomas, and torsion of the adnexa.

Author's roles:

GR recruited patients, performed the statistical analysis, drafted the manuscript and approved the final version submitted for publication. CB recruited patients, revised the manuscript critically for important intellectual content and approved the final version submitted for publication, LS examined all endometrial biopsies, revised the manuscript critically for important intellectual content and approved the final version submitted for publication, LV designed the study, performed all the ultrasound examinations, participated in the statistical analysis and interpretation of the results, revised the manuscript critically for important intellectual content and approved the final version submitted for publication

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Legends

Figure 1. Ultrasound images from one patient with moderate acute salpingitis verified by laparosocopy. a) and b) show gray scale ultrasound images of the left tube, c) and d) show colour Doppler images of the same tube. The lesion is a sausage shaped thick-walled unilocular cystic structure with a very small amount of echogenic fluid inside. We interpret the white oval ring in (b) as the mucosa of the inflamed tube. As seen in (c) and (d), the tube is extremely well vascularised at Doppler ultrasound examination. Please, note the ring of colour in (d). We interpret this as rich vascularisation surrounding a transverse section through the inflamed tube. We observed this finding also in other cases of moderate salpingitis, see Figure 2 and 3.

Figure 2. Ultrasound images of moderate acute salpingitis verified by laparosocopy in a second patient a) shows a sausage shaped solid structure corresponding to the inflamed tube b) shows the rich vascularisation of the same structure; rings of colour are discernable, see also Figure 1 and 3.

Figure 3. Ultrasound images of moderate acute salpingitis verified by laparosocopy in a third patient a) shows a unilocular sausage shaped thick-walled structure corresponding to the inflamed tube with a very small amount of echogenic fluid inside b) shows a transverse section through the same tube c) shows the rich vascularisation of the same tube; please, note the ring of colour surrounding the transverse section of the tube, see also Figure 1 and 2..

Figure 4. Ultrasound images of a hydrosalpinx that has undergone torsion. This is a 3 cm multilocular solid mass lying adjacent to the ovary. Swollen mucosal folds protrude into the fluid filled lumen of the mass. This is the only mass in our series manifesting the cogwheel sign. The ultrasound examiner suggested three possible diagnoses: torsion of a diseased tube, pyosalpinx, or - very unlikely - a malignancy.