The accuracy of transvaginal sonography to detect endometriosis cyst

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Abstract. Endometriosis is common in women of reproductive age. Late diagnosis is still the main concern. Currently, noninvasive diagnostic testing, such as transvaginal sonography, is recommended. The aim of the current study was to evaluate the accuracy of transvaginal sonography in diagnosing endometrial cysts in patients in Cipto Mangunkusumo Hospital, Jakarta, Indonesia. This diagnostic study was carried out at Cipto Mangunkusumo Hospital between January 2014 and June 2015. Outpatients suspected have an endometrial cyst based on the patient history and a clinical examination was recruited. The patients were then evaluated using transvaginal sonography by an experienced sonologist, according to the research protocol. The gold standard test was a histological finding in the removed surgical mass. Ninety-eight patients were analyzed. An endometrial cyst was confirmed by histology in 85 patients (87%). The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of transvaginal sonography was established to be 85% (a range of 71-99%), 93%, 77%, 96%, and 63%, respectively. A significantly higher area under the curve was identified using transvaginal sonography compared to that achieved with a clinical examination alone (85% versus 79%). Transvaginal sonography was useful in diagnosing endometrial cysts in outpatients and is recommended in daily clinical practice.

1. Introduction
Endometriosis is one condition that occurs when the endometrial tissue grows outside the uterus. The etiology of endometriosis remains unknown [1]. The clinical features vary, making it difficult to diagnose, especially as surgery is the only method through which a definitive diagnosis of endometriosis can be obtained. It is uncommon for surgery to be performed without the symptoms or physical characteristics suggestive of endometriosis. If a patient is suspected to have endometriosis, laparoscopy or laparotomy are carried out, in conjunction with histological and biopsy examinations to establish the diagnosis [2]. Common symptoms in woman with endometriosis include pelvic pain, dysmenorrhea, dyspareunia, dyschezia, and infertility. However, several patients with endometriosis are asymptomatic. Thus, occasionally, a diagnosis of endometriosis is made incidentally. The presenting symptoms in patients with endometriosis are similar to those in patients with other gynecological disease or with gastrointestinal or urogenital disturbances. This can result in a delayed diagnosis of endometriosis, often in association with the initial administration of incorrect treatment for another mistaken diagnosis. Hence, high suspicion of endometriosis is advised [3].

There is no easy way of diagnosing endometriosis when there is high suspicion of the condition in a patient. A laparoscopy, with or without confirmation of an anatomical pathology, is considered to be the
gold standard diagnostic method to use to identify endometriosis. However, the effective use thereof depends on the experience of the surgeon conducting the laparoscopy, intra-observer variability, the technique used for lesion excision (for the purpose of an anatomical pathology examination), and the experience of the relevant pathologist in conducting it [4]. Although laparoscopy is a minimally invasive procedure, sufficient skill is required to perform it owing to the potential for complications. General anesthesia is required for laparoscopy and is associated with minor complications, such as nausea and vomiting in 3% of patients, as well as major risks, such as intestinal perforation, in 1% of them [5]. Many patients do not consent to laparoscopy, especially as it is a relatively expensive procedure. Thus, other noninvasive examinations are warranted to diagnose endometriosis in patients [6].

In the current research, endometrial cysts were diagnosed via anamnesis, a vaginal and rectal physical examination, and other supporting examinations, such as transvaginal ultrasonography and histopathology, as standard procedures. If the degree of accuracy of all of these was determined, a guideline on the selection of the most optimal diagnostic method could be applied. Ultrasonography is readily available in state hospitals, is more economic than diagnostic laparoscopy, is virtually free of side-effects, and general practitioners can be trained to use it. Thus, more patients suspected to have endometriosis can be screened using this method [7–9].

2. Materials and Methods
Diagnostic research was performed with a cross-sectional design. The selection of subjects with a suspected endometriosis cyst based on anamnesis and a physical examination was made on the basis of consecutively presenting patients. Inclusion criteria were: (1) female patients with high suspicion of an endometriosis cyst based on anamnesis, a physical examination, and transvaginal ultrasonography; (2) Patients undergoing laparotomy or laparoscopy; (3) Patients with medically traceable records. Exclusion criteria were patients not yet menstruating, menopausal patients and those who had not yet lost their virgity owing to the difficulties in examining such patients with genital tract malformation via vaginal examination and transvaginal ultrasonography.

The probability of a type I error was set at 5% using two-way hypothesis, so $Z_\alpha = 1.96$. The expected sensitivity to be obtained using the diagnostic method being researched was set at 85%. The absolute deviation ($d$) that could be tolerated was set at 10%. The expected prevalence of endometriosis, based on the clinical symptoms of pelvic pain, dysmenorrhea, dyspareunia, dyschezia, and infertility, was determined to be 50%. Thus, 98 subjects were needed in this study.

Data collection was performed for the subjects who fulfilled the inclusion and exclusion criteria, and included the use of patient registration numbers, identities, primary presenting symptoms, intra-examination findings, and the transvaginal ultrasonography and histopathology results. The establishment of a picture of homogeneous internal echoes assists the diagnosis of an endometrial cyst diagnosis.

A clinical examination, ultrasonography, and tissue processing for histology were performed. The histology examination was carried out in the Department of Anatomy, Faculty of Medicine, Universitas Indonesia. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of each diagnostic method was determined. The histopathology examination was used as the reference method. Diagnostic anamnesis and the physical examination findings were compared with their effect in conjunction with the addition of transvaginal ultrasonography using receiving operating characteristic (ROC) curve analysis. A comparison of the area under curve was made for all of the research methods. SPSS version 22 was used for the statistical analysis. Ethical clearance was sought and obtained prior to commencement of the study.

3. Results and Discussion
3.1 Results
Ninety-eight women participated in the study. The mean age of the subjects was 37.4 ± 8.1 years, half of whom had not yet had children (Table 1). The primary presenting symptom was dysmenorrhea ($n = 63, 64\%$), followed by infertility ($n = 38, 39\%$). Twenty-two patients had dysmenorrhea with infertility
(22%), 20 had dysmenorrhea only (20%), 11 had pelvic pain (11%), and eight had abdominal distension with pelvic pain (8%). An analysis of the clinical findings and the histopathological interpretation is provided in Table 2. A comparison of the transvaginal ultrasonography and histopathological findings is detailed in Table 3.

Table 1. The characteristics of the study subjects and clinical findings

| Characteristics                  |     |
|----------------------------------|-----|
| Age (years) (mean ± SD)          | 37.4 ± 8.1 |
| Parity (n, %)                    |     |
| 0                                | 50 (51.0) |
| 1                                | 13 (13.3) |
| ≥ 2                              | 35 (35.7) |
| Clinical findings n(%)           |     |
| Dysmenorrhea                      | 63 (64.3) |
| Infertility                       | 38 (38.8) |
| Pelvical pain                     | 30 (30.6) |
| Distended stomach                 | 27 (27.6) |
| Dispareunia                       | 10 (10.2) |
| Dyschezia                         | 4 (4.1) |

(a) SD: standard deviation

Table 2. Analysis of the clinical findings and the histopathological interpretation

| Histopathology | Total |
|----------------|-------|
|                | Endometriosis | Other |      |
| Clinical findings |     |       |      |
| Suspected endometriosis | 62 | 2 | 64 |
| Non-endometriosis     | 23  | 11  | 34  |
| Total                 | 85  | 13  | 98  |

Table 3. Analysis of the ultrasonographic findings and the histopathological interpretation

| Histopathology | Total |
|----------------|-------|
|                | Endometriosis | Other |      |
| Transvaginal ultrasonography | 79 | 3 | 82 |
| Suspected endometriosis         |     |       |      |
| Non-endometriosis                 | 6   | 10  | 16  |
| Total                            | 85  | 13  | 98  |

Endometrial cysts were confirmed in 85 of the 98 subjects (87%). The mean diameter of the detected cysts was 7.8 ± 4.1 cm. The diagnostic accuracy of transvaginal ultrasonography was 85% (95% confidence interval [CI]: 71.0–98.8). Sensitivity, specificity, PPV, and NPV were 93%, 77%, 96%, and 63%, respectively (Table 4). The accuracy of transvaginal ultrasonography was 6%. The positive likelihood and negative likelihood ratios recorded with transvaginal ultrasonography were 4.0 and 0.09.
Table 4. The accuracy, sensitivity, specificity, and positive and negative predictive values

| Examination                  | AUC (95% CI) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|------------------------------|--------------|-----------------|-----------------|---------|---------|
| Clinical finding             | 78.8 (66.0–91.6) | 72.9            | 84.6            | 96.8    | 32.4    |
| Clinical finding + TVS       | 84.9(71.0–98.8) | 92.9            | 76.9            | 96.3    | 62.5    |

AUC: area under the curve, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value, TVS: transvaginal ultrasonography

The researcher reported on three subjects with false positive, and on six subjects with false negative, transvaginal ultrasonography examination results. The false positive results were for a mucinous tumor and mesenteric attachment (ovarian carcinoma and non-Hodgkin lymphoma). The false negative results pertained to an allegedly functional ovarian cyst, a suspected malignant neoplasm with papillary features, a tubo-ovarian abscess, mucinous cystadenocarcinoma, and two cases of hydrosalpinx.

3.2 Discussion
The demographic characteristics of the 98 patients were similar to those identified in previous research. The median age of the subjects was 37.4 years, similar to that of 33 years reported in the study by Jermy et al. for patients with endometriosis [10]. Previous study also reported an age range of 17–42 years for such patients, half of whom were nulliparous [1]. The patients in the current study were also mostly nulliparous, and dysmenorrhea was cited as the most common presenting symptom. Eighty-seven percent of the cysts (85 of the 98 patients versus 96% identified in the research by Jermy et al.) were shown to be endometriosis [10]. In this study, the accuracy of the clinical examinations, i.e., anamnesis and the physical examination, was determined to be 79% (95% CI: 66.0–91.6). The most common symptoms with which patients present at the obstetrics and gynecology clinic at Cipto Mangunkusumo Hospital are dysmenorrhea and infertility (22 patients, 22%).

Transvaginal ultrasonography was found to be a noninvasive imaging modality with which to diagnose endometrial cysts, with reported sensitivity of 93%, specificity of 77%, PPV of 96%, NPV of 63%, and 85% accuracy. It was a more effective diagnostic tool than the physical examination alone. In this regard, the increase in accuracy based on the area under the curve was found to be 6%. Transvaginal ultrasonography is an additional examination to use in patients suspected to have endometriosis following the clinical examination (anamnesis and the physical examination). Thus, it is recommended as the first-line examination for endometriosis. Aside from its sound diagnostic ability, it is cost-effective and is easily performed at various health facilities. The sensitivity of transvaginal ultrasonography is also superior to that of transabdominal ultrasonography [11]. Moore et al. concluded that transvaginal ultrasonography was effective in diagnosing endometrial cysts in their meta-analysis. The range of false positive scores was demonstrated to be 0–8% and that of false negative scores to be 2–14%. This corresponds with the findings of the current research in which false positive results for three of the 98 subjects (3%), and false negative results for six of the 98 subjects (6%), were demonstrated [12]. The reported sensitivity of transvaginal ultrasonography ranged from 64–89%, with specificity of 89–100%. The patients in this study had adnexal masses so the prevalence of endometrial cysts was 13–28%. The approach of the previous studies differed to that of the current research, where an attempt was made to diagnose endometrial cysts based on the clinical findings [13,14].

Three cases with false positive and six cases with false negative results were identified in the current study. The former were a mucinous tumor and malignancy involving mesenteric attachment (ovarian carcinoma and non-Hodgkin lymphoma). Pascual et al. identified eight false positive cases, i.e. a borderline tumor, serosa cysts (two cases) and hemorrhagic cysts (four cases), all confirmed by anatomical pathology. Four false negative cases of dermoid cyst, eight cases of malignancy and one case of a cyst with septa were also found [15]. In their meta-analysis, Moore et al. reported errors in the diagnosis, especially regarding the dermoid cysts and functional cysts [12]. This supports the current
research findings. False negative cases were also reported in the study by Pascual et al., mostly owing to suspicions about ovary malignancy (in three of the six cases). As many as 19% of patients with endometriosis have septa. Meanwhile, the feature of 29% malignancy cases shows homogeneous internal echoes [15]. The features of an endometrial cyst are typical to those of an unilocular cyst, with homogeneous internal echoes (a “ground glass” appearance), and with or without vascularization. Endometriosis cysts are identified based on caliper projection without blood flow. In practice, what may appear to be papillary features on ultrasonography might be false positive. The finding of a clot or fibrin near the cyst wall can resemble papillary projection on ultrasonography [16]. A “ground glass” appearance is typical of an endometriosis cyst. This feature was demonstrated in 6% of benign and in 6% of malignant tumors in the study by Holsbeke et al. [13].

4. Conclusion
Transvaginal ultrasonography was demonstrated to have good diagnostic accuracy in the current study. The adjuvant use thereof increased the accuracy of the clinical examination by 6% (95% CI: 71.0–98.8). Dysmenorrhea with infertility is the primary presenting symptom of endometriosis. The false positive result obtained on transvaginal ultrasonography pertained to a mucinous tumor. The false positive malignancy result pertained to a previously diagnosed functional cyst, hydrosalpinx, and a tubo-ovarian abscess. Endometriosis cysts have homogeneous internal echoes that resemble those of mucinous and functional cysts. Multilocus sequence typing, papillae, thick septum, and attachments with a surrounding structure complicate a diagnosis of malignancy. The inflammation process and attachments were also contributory to the false negative result with respect to the hydrosalpinx and tubo-ovarian abscess.

References
[1] Fassbender A, Burney RO, O DF, D’Hooghe T, Giudice L 2015 Update on Biomarkers for the Detection of Endometriosis BioMed Research International 2015 130854.
[2] Jacoeb T Z and Hadisaputra W 2009 Penanganan Endometriosis Panduan Klinis dan Algoritme. (Jakarta: Sagung Seto).
[3] Overton C, Davis C, McMillan L and Shaw R W 2007 An Atlas Of Endometriosis. 3 ed. (United Kingdom: Informa Healthcare).
[4] Filho D PdA, Oliveira L Jd and Amaral V Fd 2008 Accuracy of laparoscopy for assessing patients with endometriosis. Sao. Paulo. Med. J. 126 305-8.
[5] Moore J, Copley S, Morris J, Lindsell D, Golding S and Kennedy S 2002 A systematic review of the accuracy of ultrasound in the diagnosis of endometriosis. Ultrasound. Obstet. Gynecol. 20 630–4.
[6] Moore J, Copley S, Morris J, Lindsell D, Golding S and Kennedy S 2002 A systematic review of the accuracy of ultrasound in the diagnosis of endometriosis. Ultrasound. Obstet. Gynecol. 20 630–4.
[7] Tamer H, Amal Z 2014 Prediction of endometriosis by transvaginal ultrasound in reproductive-age women with normal ovarian size Middle East Fertility Society Journal 19 197-207.
[8] Hsu AL, Khachikyan I, Stratton P 2010 Invasive and non-invasive methods for the diagnosis of endometriosis Clinical obstetrics and gynecology 53 413-419.
[9] Szabo T L 2004 Ultrasound and other Diagnostic Imaging Modalities. In: Szabo TL, (ed.) Diagnostic Ultrasound Imaging: Inside Out. (United States of America: Elsevier) p. 22-6.
[10] Jermy K, Luise C and Bourne T 2001 The characterization of common ovarian cysts in premenopausal women. Ultrasound. Obstet. Gynecol. 17 140-4.
[11] Monte G L, Wenger J M and Petignat P 2014 Imaging in Practice. Cleveland. Clin. J. Med. 81 361.
[12] Moore J, Copley S, Morris J, Lindsell D, Golding S and Kennedy S 2002 A systematic review of the accuracy of ultrasound in the diagnosis of endometriosis. Ultrasound. Obstet. Gynecol. 20 630-4.
[13] Van Holsbeke C, Van Calster B, Guerriero S, et al. 2010 Endometriomas: their ultrasound characteristics. Ultrasound. Obstet. Gynecol. 35 730-40.
[14] Agarwal N, Subramanian A 2010 Endometriosis – Morphology, Clinical Presentations and Molecular Pathology *Journal of Laboratory Physicians* **2** 1-9.

[15] Pascual M A, Tresserra F, López-Marín L, Ubeda A, Grases P J and Dexeus S 2000 Role of color Doppler ultrasonography in the diagnosis of endometriotic cyst. *J. Ultrasound. Med.* **19** 695-9.

[16] Exacoustos C, Manganaro L and Zupi E 2014 Imaging for the evaluation of endometriosis and adenomyosis. *Best. Pract. Res. Clin. Obstet. Gynecol.* **28** 655-81.