

The value of transvaginal sonography in the preoperative assessment of myometrial invasion in high and low grade endometrial cancer and in comparison to frozen section in grade 1 disease

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Summary

Objective: To evaluate the diagnostic accuracy of preoperative transvaginal sonography (TVS) in the detection of deep myometrial invasion in endometrial cancer cases classified by the grade of disease, and in comparison to frozen section analysis in grade 1 cases.

Methods: In a prospective study, 91 patients with confirmed endometrial carcinoma underwent preoperative TVS for evaluation of myoinvasion. Sonographic results were categorized as superficial (less than or equal to 1/2 myometrial depth) and deep invasion (greater than 1/2 myometrial depth). TAH-BSO followed by retroperitoneal lymph node sampling were performed in all patients with grade 1-3 tumors. In patients with grade 1 disease, the surgical specimen was intraoperatively evaluated by frozen section, and lymph node sampling was carried out if deep invasion was determined. The preoperative sonographic findings and the frozen section results were compared to the final histopathology report of myoinvasion.

Results: In 77 of the 91 (84.6%) patients, the sonographic assessment of the depth of myoinvasion was in accord with the final histopathologic findings. TVS demonstrated a sensitivity of 87.8% and a specificity of 82.7% in detecting deep invasion in the entire study group (grade 1-3), with positive and negative predictive values (PPV, NPV) of 74.3% and 92.3%, respectively. TVS in grade 1 cases (n=47) showed a sensitivity of 77.7%, a specificity of 79%, PPV of 46.6% and NPV of 93.7%. TVS in cases with grade 2-3 tumors (n=44) showed a sensitivity of 90%, specificity of 91.6%, PPV of 90% and NPV of 91.6%. Thus, the accuracy of TVS in grade 2-3 cases was superior to that achieved in grade 1 cases (91% vs 78.7%; p=.002). The myometrial invasion was assessed by frozen section in 41 out of 47 patients with grade 1 disease and demonstrated a sensitivity of 85.7%, a specificity of 100%, PPV of 100% and NPV of 97.1%. The specificity (100%) and accuracy (97.5%) of the frozen section were found to be superior compared to that of the TVS (79% and 78.7%) in detecting deep invasion in grade 1 cases (p=.008, p=.005, respectively). No statistically significant difference was found between the sensitivity of either technique.

Conclusions: TVS appeared to be a more accurate method for preoperative assessment of myoinvasion in grade 2-3 endometrial cancer patients compared to grade 1 patients. In grade 1 cases, this method achieved lower accuracy in detecting deep invasion compared to the frozen section analysis. Based on these data, the value of preoperative TVS results as the sole criterion in the decision to perform extensive surgical procedures in grade 1 endometrial cancer is questionable and warrants further evaluation.

Key words: Endometrial cancer; Myoinvasion; Preoperative assessment; Transvaginal sonography.

Introduction

Myometrial invasion is one of the most important prognostic indicators in endometrial cancer. The depth of invasion correlates with the risk of lymph node metastasis and is usually considered when deciding the appropriate surgical staging approach in these patients. Most patients with superficially invasive grade 1 adenocarcinomas are unlikely to have extrauterine disease and a less extensive surgical approach may be justified in these patients [1-2]. A small percentage of patients with grade 1 disease will demonstrate significant myometrial invasion and, therefore, be at risk of retroperitoneal lymph

node metastasis [3]. These patients may benefit from a more extensive staging effort. Preoperative information of the depth of invasion could have an important implication in the selection of high risk patients who need lymph node sampling. Numerous studies have evaluated the use of abdominal and transvaginal sonography in assessing the depth of myometrial invasion with a reported concordance of 85-100% with the final histologic examination [4-11]. The results of these reports were based on an overall analysis of endometrial cancer patients with all grades. The aim of this study was to determine the accuracy of preoperative TVS in the detection of deep myometrial invasion in relation to the grade of disease, and to compare TVS and frozen section analysis in a sub-group of patients with grade 1 disease.

Revised manuscript accepted for publication November 22, 1999

Materials & Methods

In a prospective study, 91 patients with histologically confirmed endometrial carcinoma underwent preoperative TVS for assessment of myometrial invasion. Patients analyzed for this study were those with clinical stage I carcinoma who were candidates for surgery. We included only patients with a histologic subtype of endometrioid carcinoma, in all grades. All patients underwent a standard preoperative evaluation to assess the clinical extent of the disease and the operative risk. This consisted of history and physical examination, Papanicolaou smear, review of endometrial biopsy specimen, laboratory studies, chest radiograph, electrocardiogram and anesthetic consultation. Additional laboratory and diagnostic studies, as well as medical consultation, were ordered when indicated by the clinical situation.

TVS was performed by a single experienced examiner (R.T.), using a 5-7.5 MHz transducer probe, Acuson 128, XP 10 (Acuson, Mountain View, CA). TVS was performed within three days of surgical intervention. The physician who performed the scans was unaware of the endometrial cancer grade. Longitudinal and transverse sections of the uterus were obtained, and the endometrium was measured in the longitudinal plane at the level of its maximal thickness. The invasion was assessed at the point of its maximal depth. Sonographic findings were categorized as superficial invasion (less than or equal to 1/2 the myometrium), or deep invasion (greater than 1/2 the myometrium). Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and systematic exploration of the abdominal cavity with sampling of peritoneal washing for cytology were performed in all patients. Selective retroperitoneal lymph node sampling was carried out in all grade 2 and 3 tumors. In patients with grade 1 tumors, myometrial invasion was intraoperatively evaluated by frozen section; if deep invasion was determined, retroperitoneal lymph node sampling was performed. The pathologist was unaware of the sonographic findings. The final histologic results of the uterine specimens were considered to be the gold standard for the study, to which the TVS findings of all cases and frozen section analysis of the grade 1 cases were compared.

Fisher's exact test and the Pearson Chi-Square test were used for statistical analyses.

Results

The mean age of the patients was 62 years (range 40-83). The sonographic assessment and final histologic results of myometrial invasion are shown in Table 1. The sonographic evaluation was accurate in 77 out of 91 patients (84.6%). Ninety-two percent of the cases (48/52) in which ultrasound detected superficial invasion were confirmed by the final histologic findings. There were four cases underestimated by TVS where final histopathology revealed deep invasion. In 10 out of 14 cases with disagreement between the TVS and the histology, the TVS overestimated deeper myometrial involvement. Six of these specimens contained intramural leiomyomas and one had adenomyosis. In three other cases, we were unable to explain the error. TVS demonstrated a sensitivity of 87.8% (29/33) and a specificity of 82.7% (48/58) in detecting deep invasion in the entire study group (grade 1-3), with a PPV of 74.3% (29/39) and NPV of

92.3% (48/52). TVS in the subgroup of patients with grade 1 disease (n=47) showed a sensitivity of 77.7% (7/9), a specificity of 79% (30/38), PPV of 46.6% (7/15) and NPV of 93.7% (30/32) (Table 2). TVS in cases with grade 2-3 disease (n=44) demonstrated a sensitivity of 90% (18/20), a specificity of 91.6% (22/24), PPV of 90% (18/20) and NPV of 91.6% (22/24) (Table 3). Thus, the accuracy of TVS in detection of deep invasion in grade 2-3 cases was superior to that achieved in grade 1 cases [91% (40/44) vs 78.7% (37/47); p=.002]. The myometrial invasion was assessed by frozen section in 41 out of 47 patients with grade 1 disease, and was omitted in six cases at the discretion of the physician. The frozen section correctly showed deep invasion in six patients with grade 1, while only one case was falsely diagnosed as being superficially invasive, with a sensitivity of 85.7% (6/7), a specificity of 100% (34/34), PPV of 100% (6/6) and NPV of 97.1% (34/35) (Table 4). The frozen section was found to be superior compared to TVS in specificity (p=.008) and accuracy [97.5% (40/41) vs 78.7% (37/47); p=.005] in detecting deep invasion in grade 1 cases. No statistically significant difference was found between the sensitivity of either technique.

Table 1. — Postoperative histologic results of myometrial invasion in relation to preoperative TVS assessment in the entire study group (grades 1-3; n=91).

Sonography finding	n	Histopathology finding	
		deep invasion	superficial invasion
Deep invasion	39	29	10
Superficial invasion	52	4	48

Table 2. — Postoperative histologic results of myometrial invasion in relation to preoperative TVS assessment in patients with grade 1 endometrial carcinoma (n=47).

Sonography finding	n	Histopathology finding	
		deep invasion	superficial invasion
Deep invasion	15	7	8
Superficial invasion	32	2	30

Table 3. — Postoperative histologic results of myometrial invasion in relation to preoperative TVS assessment in patients with grade 2-3 endometrial carcinoma (n=44).

Sonography finding	n	Histopathology finding	
		deep invasion	superficial invasion
Deep invasion	20	18	2
Superficial invasion	24	2	22

Table 4. — Postoperative histologic results of myometrial invasion in relation to intraoperative frozen section assessment of grade 1 endometrial carcinoma (n=41).

Frozen section	n	Histopathology finding	
		deep invasion	superficial invasion
Deep invasion	6	6	0
Superficial invasion	35	1	34

Discussion

Efforts to define the components of surgical staging procedures in endometrial cancer and target them toward "at risk" subgroups are highly important. It is routine in many cancer centers to limit an extended surgical staging effort (including retroperitoneal lymph node sampling) to patients with grade 2 or 3 adenocarcinomas, to those with high risk variant cell types, and to those with deep myometrial invasion because these are the women most likely to have extrauterine disease [12]. The decision to perform lymph node sampling in grade 1 tumors is left to the discretion of the surgeon and is usually reserved for cases with deep myoinvasion. An acceptable approach is to select the grade 1 subjects by estimating myometrial invasion intraoperatively using a combination of gross visual inspection and frozen-section [13-15]. Preoperative knowledge of apparent deep invasion would benefit surgical planning. Efforts to use preoperative assessment of myometrial invasion by TVS have previously been reported with promising results [4-11]. These studies comprised patients with all grades of endometrial carcinoma. In accordance with these studies, we found TVS to be accurate in predicting myoinvasion in 84.6% of endometrial cancer cases in the non-selected group. However, the current study shows that incorporation of TVS into the standardized preoperative work-up recommended for grade 1 tumors is premature. When we consider a method for myoinvasion assessment in grade 1 disease, whereby current approach clinicians are likely to perform lymph node sampling only if deep invasion is determined, the results showed the superiority of frozen section analysis compared to TVS. In grade 1 cases, if we had relied on the TVS results as the sole criterion for making the decision, we would have failed to detect the need for retroperitoneal lymph node sampling in two of nine patients, and would have performed unnecessary procedures in eight cases overestimated by TVS. Alternatively, basing the decision in this group of grade 1 subjects on the frozen section results, we would have failed to detect one of seven cases that needed surgical staging, however, we would have not performed any unnecessary procedure. The previous reported results of TVS accuracy, based on the combined analysis of all grades of endometrial cancer, do not necessarily apply to grade 1 cases – the actual group that needs it. The observed lower accuracy of TVS in grade 1 cases compared to grade 2-3 cases needs further evaluation. Intramural leiomyoma and adenomyosis, which were diagnosed in a few of these cases, are very often indistinguishable from true deep invasion by sonography [4]. Nevertheless, these benign pathologies seem to be uniformly present in the entire study population, therefore, they should not have a significant effect on the different results obtained in the different grades. Grade 1 cases commonly presented with superficial invasion in this study (38/47; 81%), hence, a plausible explanation for the diverse accuracy of TVS between low and high grades is that this method, in the face of superficial invasion presents poor tumor/myometrium contrast identification. Further investigation needs to be

carried out to define if there are any other morphologic or histologic characteristics in the endometrium, or within the adjacent myometrium of grade 1 cases, which result in the unique sonographic features that contribute to overestimation of myometrial invasion in this group.

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