Value of Preoperative Transvaginal Sonography (TVS) in the Description of Tumor Pattern in Ovarian Cancer Patients: Results of a Prospective Study

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Abstract. Background: This prospective study evaluates the predictive value of preoperative staging by transvaginal sonography (TVS) in ovarian cancer. Patients and Methods: In 39 patients presenting with clinical signs and symptoms of ovarian cancer, preoperative systematic staging regarding tumor size (T), presence of ascites (A), peritoneal carcinomatosis (PC), bladder invasion (BI), intestinal invasion (II) as well as pelvic lymph node involvement (LN), were evaluated by TVS. Findings combining conventional B-mode ultrasound and Color Doppler imaging were compared to preoperative findings and final histology results. Results: Preoperative staging was correctly achieved by TVS for T in 87%, for A in 97% (95% CI: 90-100), for PC in 96% (95% CI: 86-100), for BI in 99% (95% CI: 95-100), for II in 98% (95% CI: 93-100). The predictive value of TVS for LN was minor (sensitivity: 8%, 95% CI: 7-24). Conclusion: TVS is a sensitive and non-invasive method for preoperative staging of suspected ovarian cancer regarding tumor size, ascites, invasion of adjacent organs and peritoneal carcinomatosis, but not for detection of malignant lymph nodes. The need for invasive or more elaborate diagnostic tools such as CT and MRI, cystoscopy, rectoscopy and diagnostic ascites puncture can potentially be reduced by systematic use of TVS.

Ovarian cancer is the seventh most common malignancy and the fifth most common cause of death from cancer in women (1). The annual NCI report of 2005 emphasizes, that lack of early symptoms and absence of accurate screening tests for ovarian cancer can rather explain the delay for diagnosis and the usual unfavourable prognosis. Patients with ovarian cancer have the highest mortality rate among the female reproductive system cancers, and more than 70% of all patients with ovarian cancer will be diagnosed with an advanced tumor stage FIGO III/IV (2).

Primary surgery for histological diagnosis and maximal tumor debulking is the cornerstone of the clinical management of ovarian cancer (3, 4). Postoperative residual tumor is one of the most important prognostic factors in the operative treatment of ovarian cancer (5-7), therefore reducing tumor size as a goal in the preoperative plans is of great importance.

Because most patients present with advanced disease and metastasis, an interdisciplinary approach is necessary to achieve an optimal surgical outcome. Various non invasive (transabdominal, transvaginal sonography, CT, MRI and PET) as well as invasive preoperative diagnostic tools (cystoscopy, rectoscopy or ascites drainage) are routinely used. These methods differ significantly in their practicability, availability, side-effects and costs. Transvaginal sonography (TVS) is safe, widely available and cost effective (8). Nevertheless, most of the studies using TVS are retrospective and do not compare results with the surgical outcome and the actual tumor spread. We conducted this prospective study to determine the efficacy of TVS as a preoperative diagnostic tool in patients with suspected ovarian cancer.

Patients and Methods

A total of 39 consecutive patients with clinical suspicion of ovarian cancer were referred to and operated on at the Department of Gynaecology and Obstetrics of the Charité Campus Virchow-Klinikum. The most common clinical findings included palpable adnexal masses, increase of abdominal circumference, ascites, weight loss and elevated CA125 levels.

All relevant clinical variables such as patient’s age, FIGO stage, grading and histological type were documented. Only patients with a preoperative TVS, clinically suspicious ovarian cancer and an exact description of the intraoperative findings were included in

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the study. There was only one false positive case: the patient
presented with weight loss, elevated CA125 levels and was
sonographically diagnosed with two enlarged cystic ovaries
harbouring hyperperfused polyoid structures. In this case,
histological examination revealed severe ovarian endometriosis.
This patient was excluded from the statistical analysis.

All preoperative TVS examinations were performed by Professor
W. Henrich. KRETZ-Technik-Combiyon 420 and Siemens Sonoline
Elegra ultrasound systems with a 5-7.5 MHz vaginal probe and 3.5-
5 MHz abdominal probe were used. Color and Power Doppler were
used in addition to the conventional b-mode. The following
parameters were examined systemically: i) maximal tumor size (T)
determined as: T1: <1 cm; T2: 1-<3 cm; T3: 3-<5 cm; T4: 5-<10
cm; T5: >10 cm); ii) laterality (L): unilateral versus bilateral tumor
involvement; iii) invasion of adjacent organs (uterus, bladder (BI),
peritoneum (PC) and intestinal segments below the arcuate line
(II)); iv) detection of ascites (A); and v) enlarged pelvic lymph nodes
(LN).

Intraoperatively, all sites of the primary tumor and metastases
as well as all macroscopically affected solid organs and structures
were documented in detail using specific ovarian cancer tumor
mapping by an independent person who was not involved either in
the preoperative ultrasound examination or in the surgical
management (19). All histological results were analysed
independently by an independent examiner. Macroscopic tumour
invasions were described by the surgeon and the pathologist.

Statistical analysis. Analyses were conducted in an exploratory
fashion. Results are presented in raw numbers, rates, or medians
and ranges, according to the underlying distribution.

Sensitivity, specificity, negative and positive predictive values
were obtained from the underlying distribution. Binomial-exact 95%
confidence intervals (CI) are also reported. STATA 8.0 statistical
software (STATA Corp., TX, USA) was used for all analyses.

Results

The median age of the examined patients was 61.5 years
(range: 38-87 years), with a 25th percentile of 52 years and a
75th percentile of 68.5 years. The FIGO stage was distributed
as follows: FIGO I: 9 patients (23%), FIGO II: 3 patients
(37.7%), FIGO III: 25 patients (64%), FIGO IV: 2 patients
(5.1%).

Twenty-one patients (52.4%) had bilateral carcinoma of
the ovaries, whereas in 18 patients (47.6%) the carcinoma
was unilateral. The histological infiltration of the organs
adjacent to the ovaries were as follows: uterus, 2 patients
(5.1%); bladder, 1 patient (2.5%); peritoneum, 27 patients
(69%); intestine (small and large bowel), 13 patients
(33.3%); and lymph nodes (pelvic and paraaortal), 10 patients
(25.6%). Twenty-two patients had ascites (56.4%). TVS
staging showed a high predictive value regarding tumor
size (T), laterality (L), ascites (A), bladder invasion (BI) and
intestinal invasion (II).

Laterality. Ovarian cancer was sonographically detected in
a total of 38 out of 39 (97%) patients (sensitivity: 97%; 95%
CI: 92-100%). Twenty-one women (54%) had bilateral
carcinoma. Bilaterality was correctly diagnosed preoperatively
in only 11 patients (sensitivity: 52.4%; 95% CI: 31-74%),
whereas in the other 9 patients with bilateral carcinoma only
a unilateral tumor was falsely diagnosed (42.9%). In a single
patient (2.6%), both ovaries were incorrectly diagnosed as
normal. Eighteen women had unilateral carcinoma, similar in
all cases with the TVS findings (sensitivity: 95%, 95% CI: 85-
100% and specificity: 57%, 95% CI: 36-78%).

Tumor size. TVS estimation of tumor size (T 1-5) was
congruent with the macroscopic findings in 34 out of
39 cases (sensitivity: 87%, 95% CI: 77-98%). In 4 cases
(2x5.3%) tumor size was misjudged as being one category too
low or too high (Figure 1). There was no misclassification
greater than by 1 category.

Involvement of adjacent organs. Information about the presence
or not of a uterine involvement could be preoperatively given
in 34 of the 39 examined patients (87, 2%), since the 5
remaining patients did not have a uterus. In 2 patients,
macroscopic uterine invasion was histologically proven. In 32
patients, uterine tumor invasion was correctly excluded by TVS
and confirmed by macroscopic findings and histology. One
patient with sonographical uterine invasion was correctly
diagnosed by TVS, while a minimal invasion of the uterus was
missed by TVS (one false negative case) (specificity: 100%,
95% CI: 100 and sensitivity: 50%, 95% CI: 19-100%).

Sensitivity for bladder invasion was 100% (n=1). One
patient had invasion of the bladder that was diagnosed
preoperatively by TVS. Thirty-eight patients had no
preoperative sonographic findings of involvement and no
invasion of the bladder.

Thirteen women had invasion of adjacent intestinal
segments (small and large bowel). This was diagnosed by
TVS in five cases (38.5%). The other 26 women presented
no intestinal involvement. In all cases, TVS had correctly
predicted invasion.

Twenty of the 27 patients (74.1%) with peritoneal
carcinomatosis were correctly diagnosed preoperatively by
TVS. In the remaining 12 patients TVS correctly predicted
the absence of peritoneal carcinomatosis (specificity: 96% and
sensitivity: 27%) (Figure 3). Intraoperatively, 22 patients were
found to have ascites. Preoperative TVS correctly described ascites in the pouch
of Douglas in 18 of the 22 patients (81.8%). In the
remaining 17 patients TVS correctly predicted the absence
of ascites (specificity: 97% and sensitivity: 21%).

Histology revealed lymph node metastases in 22 of the 39
patients. In the remaining 17 patients, lymphadenectomy was
avoided, either because of an increased bleeding tendency or
because of an advanced tumor disease. Intraoperatively, 10
of these 22 patients had macroscopic pelvic lymph node
metastases. Preoperatively, TVS was unable to show any lymph node metastases (specificity: 93% and sensitivity: 8%) (Table I; Figure 2).

**Discussion**

Radical tumor surgery has been shown to significantly improve the outcome of patients with ovarian cancer (4, 5, 7). Surgery comprises cytology, bilateral adnectomy, hysterectomy, infragastral omentectomy, appendectomy, peritoneal biopsies and systematic pelvic and paraaortic lymphadenectomy (3, 4, 7). In advanced stages of the tumor disease, partial resection of organs or structures (e.g. intestine, liver and spleen) is frequently required to achieve an optimal tumor debulking. In specialized ovarian cancer centres, precise preoperative evaluation of the tumor burden and metastatic tumor pattern are the main prerequisite in order to plan multivisceral surgery (9).

TVS is cost-effective, safe, easily available and requires minimal diagnostic effort. Other imaging modalities (computed tomography, magnetic resonance imaging) are much more cost-intensive, more time-consuming, and with potential side-effects such as radiation exposure (10-14). Nevertheless, only few prospective studies are initiated to compare these different methods.

Invasive examinations such as colonoscopy, barium/gastrographin study and cystoscopy put a strain on patients. In different studies, sensitivities range between 62% and 100% and specificities between 83% and 95% for the differentiation between benign and malignant ovarian lesions (11, 15-18). Best results are achieved when combining grey scale ultrasound Color or Power Doppler techniques (especially when three-dimensional ultrasound is used) and localization of the vessels in the adnexal masses (i.e. central localization as unfavourable criterion) (20-24). TVS allows reliable differentiation between malignant and benign disease, which can decrease unnecessary surgical interventions. The decision to proceed with laparoscopy or laparotomy is made easier and more accurate (25). In our study, 97% of patients were correctly diagnosed with ovarian cancer using the preoperative TVS, which turned out to be very suitable for the determination of tumor size:

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**Table I. Predictive value of sonography for tumor infiltration of different organs/structures.**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Sens. (95% CI)</th>
<th>Spec. (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder (n=1)</td>
<td>100% (15-100)</td>
<td>99% (95-100)</td>
<td>75 (15-100)</td>
<td>99% (95-100)</td>
</tr>
<tr>
<td>Ascites (n=22)</td>
<td>21% (9-52)</td>
<td>97% (90-100)</td>
<td>75 (15-100)</td>
<td>76% (59-94)</td>
</tr>
<tr>
<td>Peritoneum (n=27)</td>
<td>27% (10-43)</td>
<td>96% (86-100)</td>
<td>94 (77-100)</td>
<td>38% (21-54)</td>
</tr>
<tr>
<td>Intestinum (n=13)</td>
<td>39% (14-65)</td>
<td>98% (93-100)</td>
<td>92 (70-100)</td>
<td>76% (62-90)</td>
</tr>
<tr>
<td>Lymph nodes (n=10)</td>
<td>8% (7-24)</td>
<td>93% (79-100)</td>
<td>50 (19-100)</td>
<td>54% (34-74)</td>
</tr>
</tbody>
</table>

Sens., sensitivity; Spec., specificity; PPV, positive predictive value; NPV, negative predictive value.
87% of the carcinomas were accurately categorized, 10% were assigned to an adjacent category, while gross false judgement did not occur. Similar results are also presented by several study groups: Grischke et al. reported a size deviation of more than 20% in only 15% of the assessed carcinomas (12), while uterine invasion by the ovarian cancer was correctly detected in 50% of the patients. In another study, Buy et al. were able to correctly predict (sensitivity 25%) the invasion of the uterus (3 in 3) in a total of 12 patients; bladder invasion was described in one case and was correctly diagnosed by preoperative TVS (14). The specificity (99%, 95% CI: 95-100%) and negative predictive value (99%; 95% CI: 95-100%) that have been determined in our study support the fact that in these cases cystoscopy is not superior to TVS and are congruent with our results. We therefore believe that the routine preoperative use of cystoscopy should be revised.

Intestinal invasion was present in 13 patients but only 5 patients (38.5%) showed preoperative sonographic indications for intestinal involvement. TVS was proven to be unreliable for the accurate diagnosis of intestinal invasion. Guidozzi et al. reported 5% sensitivity when using TVS for intestinal invasion assessment (13). Only Houvenaeghel et al. achieved better results, combining transvesical and transrectal ultrasound (26, 27). The small and large bowel located in the upper abdomen can also be affected in advanced ovarian cancer and we therefore believe that TVS is not an adequate method to exclude bowel involvement. Nevertheless, TVS can give indirect signs of bowel involvement (e.g. subileus, ileus, peritoneal carcinomatosis, ascites); the value of these predictive factors was not systematically analysed in our study though. Further studies addressing this topic are warranted.

CT and MRI also have limitations for the assessment of bowel involvement (28). In a prospective study, Ricke et al. 2003 (10) found that MRI has a sensitivity ranging from 73% to 77% for accurate staging of advanced carcinoma involving the bowel and mesentery. Sensitivity was very low regarding involvement of pelvic lymph nodes (28%) and greater omentum (38%) and omental bursa invasion (43%). TVS proved to be accurate in diagnosing the presence of ascites with a sensitivity of 81.8% and a specificity of 100%. Conte et al. and Guidozzi et al. also reported a 97.4% and 91% sensitivity, respectively (13, 29). We report two false negative results; in both cases the actual quantity of ascites was less than 0.5 l.

TVS was 74.1% sensitive and 100% specific when assessing peritoneal involvement. Even if the direct comparison with other studies is limited because of different definitions and patient selection, MRI does not seem to provide any considerable advantage for peritoneal carcinomatosis assessment (30). An explanation for the relatively high sensitivity of TVS could possibly be the high coincidence of ascites present with peritoneal carcinomatosis which improves the visualisation of the peritoneal layers.

As expected, TVS was not accurate in diagnosing lymph node involvement. Tempany et al. showed that preoperative
abdominal CT or MRI were not accurate for lymph node staging either (31). Systematic pelvic and paraaortic lymph node dissection remains the gold standard for tumor staging even in macroscopic unsuspicious conditions (3-5), since 50% of all infiltrated lymph nodes measure <2 mm diameter. Moreover there are positive paraaortic lymph nodes through skip metastases in at least 20-30% of cases with negative pelvic lymph nodes (32). Preoperative determination of the lymph node status is therefore clinically not relevant (33, 34).

In conclusion, based on our results, TVS is an effective method for the preoperative staging of suspected ovarian cancer and should be performed routinely. The size of the carcinoma, the presence of uterine or bladder invasion, peritoneal carcinomatosis and presence of ascites can be assessed precisely. Routine invasive examinations (e.g. rectoscopy, cystoscopy, ascites puncture) for suspected primary ovarian cancer are not justified. Prospective studies should focus on the combination of vaginal and transabdominal ultrasound to optimize the preoperative description of the tumor. Additionally, cost-benefit analyses and patient satisfaction should be defined as secondary objectives in such trials.

References

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