The Power Doppler Velocity Index, Pulsatility Index, and Resistive Index Can Assist in Making a Differential Diagnosis of Primary Ovarian Carcinoma and Krukenberg Tumors
A Preliminary Study

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Objective. The aim of this study was to compare the effectiveness of transvaginal power Doppler sonography with spectral Doppler analysis as an aid in preoperatively distinguishing primary ovarian carcinoma and metastatic carcinoma to the ovary (Krukenberg tumors). Methods. Fifty women with ovarian disease were preoperatively examined with transvaginal power Doppler sonography. Six basic parameters were measured, including intratumoral peak systolic velocity, end-diastolic velocity, time-averaged maximum velocity, pulsatility index (PI), resistive index (RI), and velocity index (VeI). Blood flow analyses were detectable in all patients. Twelve patients with metastatic carcinoma to the ovary were classified as group 1; 38 patients with primary ovarian carcinoma were classified as group 2. Comparison of intratumoral blood flow analyses between the two groups was performed. Results. The PI, RI, and VeI were significantly lower in patients with metastatic carcinoma to the ovary than those with primary ovarian carcinoma (P < .05). There were no significant differences in the peak systolic velocity (P = .871), end-diastolic velocity (P = .508), and time-averaged maximum velocity (P = .850) between the two groups. Conclusions. Transvaginal power Doppler sonography with spectral Doppler analysis is an effective method in evaluating intratumoral blood flow of Krukenberg tumors. Low impedance (PI, RI, and VeI) might assist us in making differential diagnoses between primary ovarian carcinoma and Krukenberg tumors according to our preliminary results.

Key words: Krukenberg tumor; metastatic ovarian cancer; power Doppler sonography; pulsatility index; resistive index; velocity index.

Abbreviations
EDV, end-diastolic velocity; PI, pulsatility index; PSV, peak systolic velocity; RI, resistive index; TAMXV, time-averaged maximum velocity; 3D, 3-dimensional; VeI, velocity index
Several reports in the literature have shown the possibility of differential diagnosis from the characteristics of sonography, computed tomography, and magnetic resonance imaging. The application of transvaginal sonography, color flow imaging, and Doppler waveform analysis allows a closer approach to pelvic hemodynamics. Various blood velocity measurements have been used to show the low impedance of intratumoral circulation in ovarian malignancy. Although excellent results in differentiating benign from malignant tumors have been reported by some authors, there are others who have described less encouraging findings. One previous report analyzed primary ovarian cancer and metastatic tumors to the ovary by transvaginal gray scale and color Doppler sonography. It revealed that the presence of a purely solid tumor indicates a higher probability of metastatic carcinoma than primary ovarian cancer. However, with the use of gray scale and color Doppler sonography, it is difficult to differentiate primary ovarian carcinomas from metastatic tumors to the ovary. To the best of our knowledge, none of the previous reports provided us with data from blood flow analysis within Krukenberg tumors. We assessed intratumoral blood flow analysis from 12 Krukenberg tumors using power Doppler sonography with spectral Doppler analysis and made comparisons with primary ovarian carcinoma.

Materials and Methods

We prospectively investigated 50 women with suggested ovarian carcinoma using transvaginal power Doppler sonography preoperatively from October 1997 through September 2000. All the patients with detectable intratumoral blood flow were examined within 3 days before laparotomy. Pathologic results revealed metastatic carcinoma to the ovary in 12 women who were classified as group 1; 38 women with primary ovarian carcinoma were classified as group 2.

All the patients were assessed with power Doppler sonography (Gateway; Diasonics, San Jose, CA) equipped for color Doppler imaging and power Doppler angiography. An intravaginal scanner with a 7.0-MHz curved array within a field of 112° was used. The ovarian tumors were first scanned and identified carefully in the gray scale mode. Then the tumors were shifted to the angiographic mode to evaluate the intratumoral blood vessels (Figure 1). The pulse repetition frequency was adjusted to filter out low-strength signals and set at less than 900 Hz; the temporal filter was set at 1.0. The detectable Doppler signals were processed and analyzed with a pulsed Doppler online spectrum (Figure 2). The detectable Doppler signals were defined as a series of reproducible similar arterial waveforms, which were obtained for at least 3 separate, consecutive cardiac cycles. All the Doppler signals were detected within the mass, and the angles of the detectable sample sites were set at less than 60°. The lowest detectable peak systolic velocity (PSV) and end-diastolic velocity (EDV) were 2.77 and 1.54 cm/s, respectively.

Six basic measurements were recorded from each pulsed Doppler spectral analysis: PSV, EDV, time-averaged maximum velocity (TAMXV), pulsatility index (PI), resistive index (RI), and velocity index (VeI). The PI was defined as the difference between the PSV and EDV divided by the mean velocity. The RI was defined as the difference between the PSV and EDV divided by the PSV. The VeI was defined as the PSV divided by the EDV. The examination was performed by 1 author (Y.-C.W.) to avoid the interobserver variation. The entire statistical analysis included an unpaired Student t test and Fisher exact test. The study was approved by the Institutional Ethics Committee Board of our department, and the patients gave informed consent before participation.

Results

We accessed the 6 basic parameters obtained from intratumoral blood flow analysis using power Doppler angiography between these two groups. The mean age ± SD of the patients in group 1 was 45.2 ± 11.8 years (range, 33.4–57.0 years), and that in group 2 was 53.5 ± 10.8 years (range, 32.0–75.0 years). In the 12 patients in group 1, the cancer originated from the stomach in 8 patients, from the colon in 2, from the breast in 1, and from the pancreas in 1. The general characteristics of group 2 are listed in Table 1. In group 2, there were 18 premenopausal patients and 20 postmenopausal patients. After laparotomy, the International Federation of Gynecology
and Obstetrics surgical stages of the patients included 9 Ia, 5 Ic, 1 Ila, 3 IIc, 16 IIIc, and 4 IV. From histologic examination, 31 patients were classified as having epithelial types, and 7 were classified as having nonepithelial types. For the patients with epithelial types, 7 had mucinous adenocarcinoma; 5 had serous adenocarcinoma; 13 had endometrioid carcinoma; 5 had peritoneal serous papillary carcinoma; and 1 had clear cell carcinoma. For the patients with nonepithelial types, 2 had germ cell tumors (1 dysgerminoma and 1 mixed germ cell tumor); 4 had sex cord tumors (2 granulosa cell tumors, 1 leydig cell tumor, and 1 cystadenocarcinofibroma); and 1 had angiosarcoma.

The intratumoral blood flow analysis for group 1 is listed in Table 2 (12 cases of metastatic carcinoma to the ovary). The mean PI ± SD of patients with epithelial types (31 patients) was 0.59 ± 0.18, and that of patients with nonepithelial types (7 patients) was 0.58 ± 0.25. The mean RI of patients with epithelial types was 0.40 ± 0.11, and that of patients with nonepithelial types was 0.41 ± 0.10. The mean VeI of patients with epithelial types was 1.74 ± 0.33, and that of patients with nonepithelial types was 1.73 ± 0.41. The residual analyses including PSV, EDV, and TAMXV are listed in Table 3.

Intratumoral blood flow analysis between group 1 and group 2 is listed in Table 4. The PI was significantly lower in patients with metastatic ovarian carcinoma (mean ± SE, 0.39 ± 0.05; 95% confidence interval, 0.14–0.64) than in patients with primary ovarian carcinoma (0.59 ± 0.04; 0.16–1.11) (P < .01). The RI was significantly lower in patients with metastatic ovarian carcinoma (0.25 ± 0.04; 0.03–0.46) than in patients with primary ovarian carcinoma (0.40 ± 0.02; 0.15–0.67) (P < .005). The VeI was significantly lower in patients with metastatic ovarian carcinoma (1.43 ± 0.08; 1.09–1.85) than in patients with primary ovarian carcinoma (1.74 ± 0.07; 1.18–3.00) (P < .05). There were no significant differences between the PSV (P = .871), EDV (P = .508), and TAMXV (P = .850).

Discussion

Krukenberg tumors are widely defined as the presence of any metastasis to the ovaries. Among the primary lesions in the gastrointestinal tract, the colon is the most common site in Western countries, and the stomach is the most common site in Asian countries. The other sites of primary tumors include the breast, pancreas, lung, gallbladder, small intestine, and kidney, as well as melanoma, sarcoma, and carcinoid tumors.
The clinical incidence is approximately 5% to 10% in the United States and 15% to 20% in Asia.\textsuperscript{18–20} The presence of ovarian metastasis is universally a poor prognostic sign and commonly occurs during a woman’s reproductive years. Early, prompt, and aggressive therapy is beneficial for the patient’s quality of life and symptom relief. Asymmetrically enlarged bilateral encapsulated masses, variable intratumoral echogenic density, and ascites are the major characteristics on sonography.

In 1975, Ingersoll and Scully\textsuperscript{21} first described a patient with ovarian carcinoma, metastatic from the colon, with a complex lesion containing cystic and solid features on combined B-scan and A-mode sonography. Rochester et al\textsuperscript{5} also described a patient with a Krukenberg tumor (colon origin) that showed homogeneous low-level echoes with the usual gain, and excellent transmission of sound was seen on low-gain and high-frequency (3.5-MHz) sonography. Later, Choi et al\textsuperscript{15} studied 16 Krukenberg tumors from patients with gastric carcinoma. They found varied echogenicity within tumors on sonography: solid in 8 patients, mixed in 6, and predominantly cystic in 2. Shimizu et al\textsuperscript{22} further classified Krukenberg tumors in 9 patterns by the tumor wall, solid part, and cystic part. They found that 14 of 15 Krukenberg tumors had clear tumor margins, irregular hyperechoic solid patterns, and “moth-eaten” cyst formations on real-time gray scale sonography.\textsuperscript{22} In our study, 5 Krukenberg tumors had clear tumor margins, but only 2 patients (40%) had irregular hyperechoic solid parts; 3 patients (60%) had diffuse homogenous solid parts around internal small clear cystic formations. Only 1 patient had a moth-eaten cyst formation; the others had irregular cystic formations.

Transabdominal color Doppler sonography has provided us with a new assessment method in Krukenberg tumors. An abnormal vascular pattern with high-velocity, low-impedance signals within heterogeneous solid masses was the important sonographic characteristic.\textsuperscript{23} Moreover, Cho et al\textsuperscript{24} showed that power Doppler sonography was superior to conventional color Doppler sonography in detecting slow blood flow, especially in showing relatively prominent vascular signals along the walls of intramural cysts, which were located in solid masses in 2 patients with Krukenberg tumors from gastric carcinoma. Additionally, 3-dimensional (3D) transvaginal power Doppler imaging better defined the morphologic and vascular characteristics of ovarian lesions.\textsuperscript{25} The ovarian malignancies were correctly identified by both 2-dimensional and 3D imaging; however, the specificity significantly improved with the addition of 3D power Doppler sonography. To the best of our knowledge, no previous studies reported that 3D power Doppler indices could be useful tools in differentiating primary ovarian cancer and metastatic ovarian tumors. Alcázar\textsuperscript{26} reported that vascularization, as assessed by 3D power Doppler sonographic indices, was higher in advanced stage and metastatic ovarian cancers than in early-stage ovarian cancer. However, no differences were found in the PI, RI, and PSV in early-stage ovarian cancers.

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Total</th>
<th>Unilateral</th>
<th>Bilateral</th>
<th>Mean PI</th>
<th>Mean RI</th>
<th>Mean TAMXV</th>
<th>Mean PSV</th>
<th>Mean EDV</th>
<th>Mean Vel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>8</td>
<td>2</td>
<td>6</td>
<td>0.395</td>
<td>0.236</td>
<td>13.934</td>
<td>16.711</td>
<td>12.515</td>
<td>1.420</td>
</tr>
<tr>
<td>Colon</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0.390</td>
<td>0.290</td>
<td>8.805</td>
<td>11.080</td>
<td>7.660</td>
<td>1.493</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0.310</td>
<td>0.220</td>
<td>20.700</td>
<td>24.450</td>
<td>19.130</td>
<td>1.278</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0.470</td>
<td>0.360</td>
<td>8.330</td>
<td>10.600</td>
<td>7.070</td>
<td>1.499</td>
</tr>
</tbody>
</table>

**Table 1.** General Characteristics of 38 Primary Ovarian Carcinomas

**Table 2.** Intratumoral Blood Flow Analysis in Group 1 (12 Cases of Krukenberg Tumors of the Ovary)

FIGO indicates International Federation of Gynecology and Obstetrics.
In our study, the mean PI and RI in the group with primary ovarian cancer showed no significant differences with previous reports. However, the mean PI and RI values of Krukenberg tumors were lower than those of primary ovarian tumors (P < .05). We may assume that the vasculature of metastatic ovarian cancer is much different from that of primary ovarian tumors and normal ovarian vessels. Active angiogenesis might be the key factor of these findings. After attaching to ovaries, the metastatic cells activate the quiescent vasculature to produce new blood vessels with wall structures that have little or no smooth muscle support. These abnormal vessels, along with arteriovenous shunting in some metastatic tumors, contribute to diminished vascular resistance and, therefore, are reflected by PI and RI values that are much lower than those of primary ovarian tumors. Furthermore, increased permeability of abnormal vessels could cause stasis of blood flow and short shunts, which result in low impedance.

In this study, the patients with Krukenberg tumors had a significantly lower Vel (PSV/EDV) than those with primary ovarian tumors. This result might indicate that metastatic tumors could not establish organized intratumoral vasculature, especially when they seeded on other organs or tissues. The unhealthy vasculature reflected the lower Vel. On the contrary, primary ovarian tumors could have been directly and abundantly nourished by ovarian vessels, which resulted in the higher PSV.

In conclusion, power Doppler sonography might be a useful tool in evaluating intratumoral blood flow analysis of ovarian carcinoma before surgery. According to our results, lower impedance (such as a lower PI, RI, and Vel) could be a guideline when making differential diagnoses between primary and metastatic ovarian carcinoma. However, further studies are needed to determine the cutoff values of the PI, RI, and Vel for differentiating primary and metastatic ovarian tumors.

### Table 3. Intratumoral Blood Flow Analysis by Histologic Type in Group 2 (38 Cases of Primary Ovarian Carcinoma)

<table>
<thead>
<tr>
<th>Histologic Type</th>
<th>n</th>
<th>PSV</th>
<th>EDV</th>
<th>TAMXV</th>
<th>PI</th>
<th>RI</th>
<th>VeI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial*</td>
<td>31</td>
<td>16.31 ± 9.67</td>
<td>9.61 ± 5.73</td>
<td>12.22 ± 7.29</td>
<td>0.59 ± 0.18</td>
<td>0.40 ± 0.11</td>
<td>1.74 ± 0.33</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma*</td>
<td>7</td>
<td>13.72 ± 4.57</td>
<td>7.84 ± 2.16</td>
<td>10.01 ± 2.86</td>
<td>0.62 ± 0.24</td>
<td>0.40 ± 0.15</td>
<td>1.83 ± 0.51</td>
</tr>
<tr>
<td>Serous adenocarcinoma*</td>
<td>5</td>
<td>16.65 ± 9.35</td>
<td>10.13 ± 6.11</td>
<td>12.68 ± 7.50</td>
<td>0.59 ± 0.19</td>
<td>0.39 ± 0.12</td>
<td>1.73 ± 0.34</td>
</tr>
<tr>
<td>Endometrioid carcinoma*</td>
<td>13</td>
<td>15.86 ± 12.14</td>
<td>8.98 ± 6.49</td>
<td>11.67 ± 8.84</td>
<td>0.61 ± 0.16</td>
<td>0.41 ± 0.09</td>
<td>1.75 ± 0.26</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
<td>1</td>
<td>42.87</td>
<td>31.53</td>
<td>35.35</td>
<td>0.43</td>
<td>0.26</td>
<td>1.36</td>
</tr>
<tr>
<td>PSPC*</td>
<td>5</td>
<td>17.35 ± 6.44</td>
<td>10.04 ± 4.24</td>
<td>13.22 ± 5.39</td>
<td>0.56 ± 0.17</td>
<td>0.41 ± 0.10</td>
<td>1.73 ± 0.30</td>
</tr>
<tr>
<td>Nonepithelial*</td>
<td>7</td>
<td>17.59 ± 7.22</td>
<td>11.97 ± 6.55</td>
<td>14.25 ± 7.09</td>
<td>0.58 ± 0.25</td>
<td>0.38 ± 0.16</td>
<td>1.73 ± 0.41</td>
</tr>
<tr>
<td>Germ cell tumor*</td>
<td>2</td>
<td>28.30 ± 3.50</td>
<td>22.65 ± 1.55</td>
<td>25.60 ± 2.60</td>
<td>0.22 ± 0.06</td>
<td>0.20 ± 0.05</td>
<td>1.24 ± 0.07</td>
</tr>
<tr>
<td>Sex cord tumor*</td>
<td>4</td>
<td>12.36 ± 4.54</td>
<td>6.24 ± 2.87</td>
<td>8.56 ± 3.89</td>
<td>0.80 ± 0.19</td>
<td>0.52 ± 0.07</td>
<td>2.08 ± 0.32</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>1</td>
<td>17.12</td>
<td>13.52</td>
<td>14.28</td>
<td>0.44</td>
<td>0.21</td>
<td>1.27</td>
</tr>
</tbody>
</table>

PSPC indicates peritoneal serous papillary carcinoma.
*Values are mean ± SD.

### Table 4. Comparison of Intratumoral Blood Flow Analysis Between Group 1 (12 Cases of Krukenberg Tumors of the Ovary) and Group 2 (38 Cases of Primary Ovarian Carcinoma)

<table>
<thead>
<tr>
<th>Index</th>
<th>Group 1 (n = 12) Mean</th>
<th>SE</th>
<th>95% CI</th>
<th>Group 2 (n = 38) Mean</th>
<th>SE</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>0.393</td>
<td>0.046</td>
<td>0.140–0.640</td>
<td>0.589</td>
<td>0.038</td>
<td>0.161–1.110</td>
<td>.009</td>
</tr>
<tr>
<td>RI</td>
<td>0.254</td>
<td>0.043</td>
<td>0.030–0.460</td>
<td>0.395</td>
<td>0.022</td>
<td>0.149–0.670</td>
<td>.003</td>
</tr>
<tr>
<td>Vel</td>
<td>1.427</td>
<td>0.075</td>
<td>1.086–1.850</td>
<td>1.737</td>
<td>0.068</td>
<td>1.175–3.000</td>
<td>.019</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
Power Doppler Sonography in Krukenberg Tumors

References