Deep-Vein Thrombosis Is Associated with Large Uterine Fibroids

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Pulmonary thromboembolism (PE) may occur upon a patient's first postoperative attempt of ambulation. PE is a serious complication, often leading to shock or sudden death. Reported rates of PE following gynecologic surgery are between 0.3% and 0.8%, while the incidence of postoperative deep-vein thrombosis (DVT), the major cause of PE, is between 17% and 20%. Therefore, effective preventive measures, such as preoperative assessment for asymptomatic DVT, should be considered. It is well known that DVT and/or PE are associated with large uterine fibroids, the common, benign tumor of myometrium. Here, to establish the statistical relationship between DVT risk and uterine fibroid size/weight, we assessed the preoperative DVT rate with respect to three possible risk factors: age, obesity level, and uterine size/weight. A total of 361 patients with uterine fibroids undergoing hysterectomy between July, 2003 and December, 2009 were enrolled. All patients were evaluated for preoperative DVT; the results were stratified for statistical comparison by patient age, BMI, and uterine weight. There was no statistical difference in the DVT rate for patients stratified by age (below age 45 years or older) or BMI (below 25 or higher). By contrast, the rate of DVT was significantly higher for patients with uterine weights of 1,000 gm or more (11.5% [7/61]) compared with weights below 1,000 gm (3.0% [9/300]). None of the patients studied developed PE. In conclusion, the incidence of DVT is significantly higher in cases where uterine weight is 1,000 gm or more (ie, adult head size on pelvic examination).

Keywords: D-dimer; deep vein thrombosis; pulmonary thromboembolism; uterine fibroid; weight of uterus
has been routine at our hospital since July, 2003 for all surgical candidates, followed by lower extremity venous ultrasonography at D-dimer levels exceeding the DVT trigger reference value (0.5 µg/ml). A 5- to 10-MHz linear electronic ultrasonographic probe is used and Doppler scanning technique is applied to patients in the supine, slight open-leg, or sitting position. When DVT has been excluded, intraoperative and postoperative compression stockings and intraoperative intermittent pneumatic compression (IPC) are implemented. Otherwise, intraoperative and postoperative compression stockings are the rule for cases of DVT, but not IPC. Heparin sodium is also used preoperatively and for 5-7 days postoperatively for DVT. The starting dose of 12,000 units/day is maintained, until the activated partial thromboplastin time (APTT) is 1.5 to 2.5 times the control.

Accrued patient data altogether included age, uterine weight, BMI, average D-dimer level, D-dimer positive rate (0.5 µg/ml or higher) and incidence of DVT. Differential rates of developing DVT were ultimately evaluated for ages below 45 years and at 45 years or older, for BMI below 25 and at 25 or higher, and for uterine weights below 1,000 gm and at 1,000 gm or more. The reasons of these delimitations are explained below in the discussion section. Results were subjected to Chi-Square analysis, with a P value < 0.05 delimiting statistical significance.

### Results

Mean patient parameters were as follows: age, 45.5 years; uterine weight, 656 gm; BMI, 22.7; and D-dimer level, 0.42 µg/ml. Overall, 18.6% (67/361) of the cohort had preoperative D-dimer levels of 0.5 µg/ml or higher, and 4.4% (16/361) had documented DVT.

There was no statistical difference in the DVT rate for patients stratified by age (below age 45 years, 3.2% [5/154]; age 45 years or older, 5.3% [11/207]) or BMI (below 25, 3.5% [10/282]; 25 or higher, 7.6% [6/79]). However, the rate of DVT was significantly higher for patients with uterine weights of 1,000 gm or more (11.5% [7/61]) compared with weights below 1,000 gm (3.0% [9/300]). None of the patients studied developed PE.

### Discussion

Suzuki et al. (2010) have reported an incidence rate of 3.17% for perioperative DVT, including patients with malignant tumors. Fletcher et al. (2009) have also remarked that relatively uncomplicated cases of uterine fibroids in younger patients carry no increased risk of DVT. While these observations suggest uterine fibroids per se seldom induce DVT, higher rates of DVT and related PE in patients with large uterine fibroids have been substantiated by a number of case reports (Chong et al. 1998; Dekel et al. 1998; Nishikawa et al. 2000; Tanaka et al. 2002; Khilanani and Dandolu 2007; Asciutto et al. 2008). The pathogenesis is embodied in the classic etiologic triad of Virchow (1854): 1) stasis of blood, 2) hypercoagulability, and 3) vessel wall abnormality. Hence, it is compression of the inferior vena cava and other veins in the pelvis by these large masses that creates the vascular stasis leading to DVT. There are, however, no formal investigations that link the risk of DVT definitively to a large uterus size/weight. In this study, we defined uterus ≥ 1,000 gm (as large as an adult head size in pelvic examination) at large size. This weight is clinically critical because uterine fibroid cases with uterine weight ≥ 1,000 g are usually accompanied by other conditions, including abdominal edema, that may cause difficulty during surgery. This threshold seems relevant as shown in this study that the incidence of DVT is significantly higher in cases where uterine weight is 1,000 gm or more. Conversely, we found no significant difference in DVT risk with varying age or obesity level, both considered DVT risk factors in general patient populations (Anderson et al. 2003). Suzuki et al. (2010) considered age ≥ 50 as risk factor for DVT in women with gynecologic disease. However, because hysterectomy for fibroids is largely performed on premenopausal patients in their 40s, age alone would not appear to dictate DVT risk. Few patients underwent hysterectomy for fibroids during our study. Therefore, we divided our study population at the age of 45, and found that age was not a risk factor. Regarding the obesity level, purportedly only 2% of the Japanese population reaches a

### Table 1. Patient Parameters.

<table>
<thead>
<tr>
<th>(patients with DVT/all those with fibroids)</th>
<th>Mean (range) or rate</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>45.5 years (29-76)</td>
</tr>
<tr>
<td>Weight of uterus</td>
<td>656 g (50-7000)</td>
</tr>
<tr>
<td>BMI</td>
<td>22.7 (16.0-38.3)</td>
</tr>
<tr>
<td>D-dimer</td>
<td>0.42 µg/ml (0.06-9.81)</td>
</tr>
<tr>
<td>D-dimer positive rate</td>
<td>18.6% (67/361)</td>
</tr>
<tr>
<td>DVT incidence</td>
<td>4.4% (16/361)</td>
</tr>
</tbody>
</table>

### Table 2. DVT Rate by Category.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 45 years</td>
<td>≥ 45 years</td>
</tr>
<tr>
<td>Weight of extracted uterus</td>
<td>&lt; 1,000 g</td>
<td>≥ 1,000 g</td>
</tr>
<tr>
<td></td>
<td>3.0% (9/300)</td>
<td>11.5% (7/61)</td>
</tr>
<tr>
<td>BMI</td>
<td>&lt; 25</td>
<td>≥ 25</td>
</tr>
<tr>
<td></td>
<td>3.5% (10/282)</td>
<td>7.6% (6/79)</td>
</tr>
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</table>
BMI ≥ 30, as opposed to 20% in Europe or the US. Our BMI-related risk of DVT would therefore skew much lower with obesity defined by BMI ≥ 30. The majority of reports defines obesity in the Asian races as BMI ≥ 25 (Ko et al. 1999). In this study, BMI ≥ 25 was not a significant risk factor for preoperative DVT.

Nonetheless, DVT has an established role in perioperative PE, so its presence warrants preventative measures. We do not use intraoperative IPC with DVT, but intra- and postoperative compression stockings are employed, and heparin sodium is administered for 5–7 days postoperatively, adjusting dosage for a target APTT of 1.5 to 2.5 times the control (Karmy-Jones et al. 2007; Kim et al. 2008). With this protocol, none of the patients in our study developed PE.

To summarize, our findings indicate that in patients with uterine fibroids (as benign disease), larger tumors are more often complicated by DVT. Consequently, it may be important to monitor D-dimer levels closely, performing more often complicated by DVT. As such, the protocol above appears to be effective at reducing the risk of PE, as none of the patients in our study developed PE.

Conflict of Interest
All authors have no conflict of interest in this study.

References