Risk Factors for Venous Thromboembolism in General Surgical Patients

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Venous thromboembolism is a common disease with an annual incidence of 1 per 1,000 in the general population [1]. Patients undergoing general surgery are at considerable risk of developing venous thromboembolic disease [2]. VTE is associated with 2% of all deaths in general surgical patients [3], and surgery accounts for 24.2% of the cases of VTE occurring in the population [4]. However, VTE is preventable. Randomized controlled studies in patients undergoing general surgery have shown that chemical prophylaxis (low molecular weight heparin/unfractionated heparin) reduces the rate of postoperative deep vein thrombosis from 25.2% to 6.9% [2], a relative risk reduction of 72% (RR 0.28, 95% confidence interval 0.26 to 0.30; P < 0.001).

Since the risk for VTE is multifactorial, recognizing individual risk factors provides surgeons with the opportunity to stratify patients into low, moderate, and high risk categories [5]. This stratification allows the surgeon to target prophylaxis towards those at risk. All risk factors can be related to Virchow’s triad, which describes three groups of conditions that affect the pathophysiology of VTE. Most risk factors (Table 1) are associated with either hypercoagulability or venous stasis; however in general surgery, vessel damage may be one of the most important causes of increased thromboembolic risk.

Surgical procedure and technique

Damage to muscle and vascular endothelium during surgery stimulates the release of tissue factor, which results in the local activation of the coagulation cascade. This contributes to the high incidence of DVT (25%) in general surgical patients not receiving thromboprophylaxis [2]. The duration and type of surgery also have well-established influences on VTE risk [6,7]. An operative time of more than 45 minutes is thought to increase VTE risk [8]. Minimally invasive surgery is now used extensively, but although it results in less tissue damage than open surgery, VTE is known to occur [9,10]. In some cases this may be due to increased operation times, and in others to abdominal sufflation causing venous compression. However, clotting activation may be less of a problem, as shown in a study on patients undergoing laparoscopic surgery for cholecystectomy [11].

Advanced age

Increasing age [12] or age above 40 years [8] has been shown to be an independent risk factor for VTE. With the average age of the general surgical patient on the increase – 70% of general surgical patients were over the age of 70 in 1998–1999 [3] – the risk for VTE and the prevalence of premorbid conditions and poor mobility will also increase.

Venous stasis and Immobility

Many of the conditions listed in Table 1 share the tendency to form thrombi as a result of venous stasis, which contributes to thrombogenesis by allowing activated coagulation factors to accumulate. In addition, stagnation of the blood may lead to local hypoxia, which stimulates endothelial cells to release an activator of factor X. Immobility, venous obstruction, increased venous pressure, venous dilatation, and increased blood viscosity can all contribute to venous stasis. Venous thrombosis occurs in immobilized patients because blood pools in the intramuscular sinuses of the calf that are dilated when the patient is recumbent. A patient’s ability to mobilize postoperatively is affected by the impact of the surgical procedure, co-morbidity, and the occurrence of postoperative complications. Over 50% of people undergoing surgery have a co-morbid cardiac or respiratory complaint and 10%

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Table 1. Risk factors for venous thromboembolism

<table>
<thead>
<tr>
<th>Surgical procedure/technique</th>
<th>Physical condition</th>
<th>Thrombophilas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal</td>
<td>Age</td>
<td>Antithrombin deficiency</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>Hydration</td>
<td>Protein C or S deficiency</td>
</tr>
<tr>
<td>Urologic</td>
<td>Immobilization</td>
<td>Activated protein C resistance</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Trauma</td>
<td>Heparin co-factor II deficiency</td>
</tr>
<tr>
<td>Benign or malignant</td>
<td>Delay in surgery</td>
<td>Lupus anticoagulants</td>
</tr>
<tr>
<td>Infection</td>
<td>Infection</td>
<td>Paroxysmal nocturnal hemoglobinuria</td>
</tr>
<tr>
<td>General anesthetic</td>
<td></td>
<td>Myeloproliferative syndromes</td>
</tr>
</tbody>
</table>

VTE = venous thromboembolism

RR = relative risk
DVT = deep vein thrombosis
have a musculoskeletal disorder. This is reflected by the increasing numbers of surgical patients with American Society of Anesthesiologists (ASA) grade III and IV [3]. Postoperatively, one-third of patients have cardiorespiratory complications [3], which decrease their ability to mobilize early. Mechanical methods of thromboprophylaxis such as graduated compression stockings and intermittent pneumatic compression are used to overcome stasis and potentially protect the vessel wall. These techniques, being physiologic, are beneficial in those patients with an increased risk of bleeding.

**Infection**

Postoperatively there is an increased risk of infection, with 30% of patients developing a respiratory complication, 14% a generalized sepsis, 3% a wound infection, and 2% a urinary tract infection [3]. Since the presence of acute infection can initiate thrombogenesis [13,14], prevention of such infections is vital. Postoperative mobilization may help prevent some infective complications by improving respiratory function and decreasing the need for venous cannulae and urethral catheters.

**Malignancy**

In addition to the general surgical procedure and the occurrence of potential complications, the physical condition and co-morbid state of a surgical patient has an impact on the overall risk of VTE. The rate of VTE in a patient undergoing abdominal surgery for cancer is 29% as compared to 20% in a patient without cancer. Cancer may trigger a hypercoagulable state due to the release of procoagulants from tumor cells and overexpression of tissue factor, leading to excess thrombin production. Malignancy of the pancreas, liver, and gastrointestinal tract are strongly associated with an increased risk of VTE. The likelihood of thromboembolic events occurring in cancer patients is further increased by interventions such as chemotherapy and insertion of central venous lines. Chemotherapy appears to induce a prothrombotic state by reducing the number of circulating anticoagulant proteins, while central lines damage the vascular endothelium [15].

**Previous VTE and varicose veins**

Previous venous thrombosis can lead to valvular damage in the deep veins, causing turbulent flow and increased venous stasis. Varicose veins may occur as a result of such damage, and in conjunction with a history of previous VTE are associated with an increased risk of subsequent DVT [13]. Recurrent VTE occurs frequently, and is of greatest risk in the first 6–12 months after the initial event. The risk of recurrence continues for at least 10 years after the initial VTE and never falls to zero [16].

**Obesity and body mass index**

The presence of obesity (body mass index = 30 kg/m² for males and = 28.6 kg/m² for females) may affect the duration of a surgical procedure, venous return, postoperative mobilization, and therefore increase the risk of VTE [13]. Obesity is also an independent predictor of recurrent VTE [16]. The World Health Organization estimates that approximately 300 million adults worldwide are currently obese, and that 20 million children are overweight (body mass index 25–29.9 kg/m²), and that these figures are bound to increase.

**Thrombophilia**

Alterations in the coagulation-fibrinolytic system can induce a hypercoagulable state and play a significant role in the pathogenesis of VTE [17]. Present in a significant proportion of those who develop VTE disease [17], these changes can be divided into two groups—hereditary and acquired. Of the acquired disorders, two of the most important are the “stress” response to surgery, associated with an elevation of procoagulant factors and a shut-down of the fibrinolytic process; and hyperviscosity associated with perioperative fluid loss. Others include acute infection, inflammatory bowel disease, nephrotic syndrome, and cardiorespiratory failure. Resistance to activated protein C resistance is the most common of the inherited hypercoagulable disorders and usually results from a point mutation of the factor V Leiden gene. Deficiencies of protein C, protein S and antithrombin III are other important causes of congenital thrombophilia.

**Oral contraceptives and pregnancy**

There is an increased risk of VTE in users of the oral contraceptive pill [18], which increases after age 39 [19], but this risk remains lower than that associated with pregnancy (60 per 100,000) [18]. The risk of VTE associated with the use of third-generation OCPs, such as desogestrel (25 per 100,000), is higher than with the use of second-generation OCPs, e.g. levonorgestrel (15 per 100,000) [18]. Some guidelines suggest that estrogen-containing OCPs should be stopped 4 weeks before major surgery or surgery to the legs, and should only be restarted 2 weeks after full mobilization [18]. Other guidelines recommend continuing OCPs together with effective thromboprophylaxis, since the risks of pregnancy and subsequent complications including VTE may be higher.

**Conclusion**

Recognition of the pathophysiology and the associated risk factors for VTE in general surgical patients allows a preventive strategy to be targeted to those at risk. A preventive strategy should include patient education, anticoagulant and mechanical therapy, early active perioperative mobility, and the active prevention of postoperative complications.

**References**


OCP = oral contraceptive pill

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**Capsule**

**Capsule endoscopy reduces costs and improves quality of life**

Investigators at Thomas Jefferson University’s Office of Health Policy and Clinical Outcomes recently reported in Disease Management that the MA2 capsule endoscope offers a potential net cost savings through early diagnosis of obscure intestinal bleeding. In addition to economic benefits, the authors show that capsule endoscopy has a higher diagnostic yield than other modalities for the small intestine. Moreover, use of the capsule results in less pain, discomfort and anxiety for the patient. Early diagnosis also averts needless worry, inconvenience and out-of-pocket costs to the patient.

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**Capsule**

**Express thyself!**

Most T cells that react to self-antigens are deleted in the thymus during development, but how does a multitude of tissue-restricted self-proteins find their way to the thymus in the first place? One proposed solution to this puzzle has been that cells of the thymus also express certain “tissue-restricted” genes. Anderson et al. show that a transcription factor, termed autoimmune regulator or Aire, controls ectopic gene expression in thymic epithelial cells. In the absence of Aire, mice developed autoimmunity against target organs, such as salivary gland and ovary, with a corresponding loss of expression of target tissue-specific genes by the thymic epithelial cells.

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