Pulmonary Thromboembolism: Disease Recognition and Patient Management

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Effects of Anesthetic Techniques on Deep Venous Thrombosis

Pulmonary thromboemboli (PTE) impact the anesthesiologist most during an intraoperative or postoperative catastrophe. PTE are primarily responsible for 2–20% of postoperative deaths.1–5 Fatal PTE develop in 0.1–0.8% of general surgery patients, 0.3–2.4% of patients undergoing hip arthroplasties, and 4–7% of patients after surgery for hip fractures.4 Deaths from PTE in surgical patients actually decreased from 8.8% of the total deaths in 1966 to 2.3% in 1980.5 The lowered incidence may be due to anticoagulant use or changing patterns of the disease.

Diagnosis of Pulmonary Thromboemboli

Background information about PTE has been reviewed (table 1).5–9 The nonspecific cardiopulmonary symptoms occurring from minor PTE9,10 should be sought during the preoperative anesthetic evaluation of patients at high risk for PTE. Normal or abnormal results from laboratory tests, including a PaO2 above 80 or 85 mmHg, do not exclude the diagnosis of PTE.10,11 A retrospective study determined that 98% of patients with PTE have either an abnormal age corrected alveolar–arterial oxygen tension gradient or a PaCO2 below 36 mmHg while breathing room air.12 These tests are sensitive parameters, but their specificity was not studied. Chest x-rays and ECG exclude other acute diseases, but changes from PTE may be absent, nonspecific, transient, or delayed.7,10,13 Invasive hemodynamic monitoring or echocardiography show characteristic changes with massive PTE, but they cannot exclude submassive PTE.

Perfusion or ventilation/perfusion (V/Q) scans estimate the probability of PTE based on the anatomic patterns of injected radiolabeled albumin particles or inhaled inert radioactive xenon. A normal perfusion scan reliably excludes the diagnosis of PTE.14 However, the incidence of false-positive perfusion scans may be as high as 50%.10 A recent prospective study of 305 patients correlated the results from V/Q scans and pulmonary angiography.15 Segmental defects seen in perfusion scans predicted PTE in 71% of the pulmonary angiograms.15 The validity of high probability V/Q scans (segmental or larger perfusion defects with ventilation mismatch) was confirmed by angiography in 86% of these patients. However, V/Q mismatch at the subsegmental level was less reliable, and PTE was confirmed in only 37% of the cases. Unfortunately,
TABLE 1. Background Information

<table>
<thead>
<tr>
<th>Origin</th>
<th>Risk Factors for Deep Venous Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Origin: 4,7,8</td>
<td>Venous stasis, activation of blood coagulation, and vascular damage, from direct trauma or endothelial damage, increase the incidence of DVT, as first reported by Virchow in the 1850s. These conditions occur during surgery. Calf vein thromboses were diagnosed by radioabeled fibrinogen in 40 of 132 patients older than 40 yr undergoing intraabdominal surgery. The calf thrombi lyzed within 3 days in 14 patients, but they persisted in 26 patients, four of whom developed PTE. 20</td>
</tr>
<tr>
<td>Right atrium, with congestive heart failure, atrial fibrillation, or indwelling foreign bodies</td>
<td>Immobilization causes venous stasis after surgery, myocardial infarction, and acute paraplegia. 21,22 Primary or secondary hypercoagulability (table 2) induce DVT if abnormalities of venous flow or integrity are present, as recently reviewed. 22,23 Trauma to the femoral or pelvic veins occurs in 10–20% of hip fracture repair. 24,25; thus, proximal DVT can develop without calf vein thrombosis. The risk of developing DVT is based on the patients’ age and type of surgery. 4 Low-risk patients are younger than 40 yr of age having uncomplicated surgery or those older than 40 yr of age for minor surgery. General surgery patients older than 40 yr of age are at moderate risk if the procedures last more than 30 min. Their incidence of calf vein thrombosis is 10–40%, of proximal vein thrombosis is 2–10%, and fatal PTE is 0.1–0.7%. The high-risk group includes patients undergoing major orthopedic surgery on the lower limbs, patients with a recent history of thrombophlebitis, or those older than 40 yr of age for extensive pelvic or abdominal surgery for malig-</td>
</tr>
<tr>
<td>Hepatic and renal veins (rare)</td>
<td></td>
</tr>
<tr>
<td>Tricuspid endocarditis or upper extremity thrombi in intravenous drug abusers</td>
<td></td>
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<tr>
<td>Presentation</td>
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<tr>
<td>Uncomplicated embolus with dyspnea</td>
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<tr>
<td>Pulmonary infarction syndrome (pleuritic pain ± hemoptysis)</td>
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<tr>
<td>Circulatory collapse or syncope (&lt;10%)</td>
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</tr>
<tr>
<td>Signs and symptoms 4,9</td>
<td></td>
</tr>
<tr>
<td>Common (&gt;50%): dyspnea, tachypnea, tachycardia, apprehension, rales, cough, accentuated pulmonic heart sound, chest pain (pleuritic or angina-like)</td>
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</tr>
<tr>
<td>Less common (10–40%): hemoptysis, low-grade fever, cyanosis, diaphoresis, signs of elevated CVP, clinical DVT, syncope, altered mental status</td>
<td></td>
</tr>
<tr>
<td>Rare (&lt;10%): wheezing, disseminated intravascular coagulation, abdominal pain</td>
<td></td>
</tr>
<tr>
<td>Laboratory tests 4,10,12</td>
<td></td>
</tr>
<tr>
<td>No single or combination of laboratory tests predictive</td>
<td></td>
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<tr>
<td>Arterial blood gases, hypoxemia, hypocarbia</td>
<td></td>
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<tr>
<td>Cannot exclude PTE with normal PaO2</td>
<td></td>
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<tr>
<td>ECG changes 5,7,10</td>
<td></td>
</tr>
<tr>
<td>ST-T wave abnormalities</td>
<td></td>
</tr>
<tr>
<td>Rhythm disturbances: atrial or ventricular ectopic beats, atrial tachycardias</td>
<td></td>
</tr>
<tr>
<td>Right ventricular changes: right atrial strain, right bundle branch block, right (or left) axis deviation, S1Q3T3 (S-wave in I; Q-wave and inverted T-wave in III)</td>
<td></td>
</tr>
<tr>
<td>Chest x-ray changes 4,13</td>
<td></td>
</tr>
<tr>
<td>Atelectasis: planar or larger</td>
<td></td>
</tr>
<tr>
<td>Elevation of hemidiaphragm (loss of volume)</td>
<td></td>
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<tr>
<td>Pleural effusion</td>
<td></td>
</tr>
<tr>
<td>Focal oligemia (rare)</td>
<td></td>
</tr>
<tr>
<td>&quot;Knuckle sign&quot;: pulmonary artery tapars abruptly</td>
<td></td>
</tr>
<tr>
<td>Pulmonary infarction: preexisting cardiopulmonary disease</td>
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</tbody>
</table>

"low" probability scans, indeterminate scans (abnormal perfusion in conjunction with chest x-ray infiltrates), or matched defects due to PTE-induced bronchoconstriction do not exclude PTE because 25–40% of these angiograms were positive. 15 Diagnosis of proximal vein thromboses with the highly specific, noninvasive test of impedance plethysmography can decrease the need for angiograms. 15 Details and limitations of the noninvasive diagnostic techniques for deep vein thrombosis (DVT) have been discussed, 16,17 as well as the methodology for adequate phlebograms. 18

A pulmonary angiogram definitively diagnoses PTE, and it is necessary before high-risk procedures, such as thrombolytic therapy, embolectomy, inferior vena cava ligation, or anticoagulating a patient with high bleeding risk. Mortality rarely occurs with pulmonary angiograms, especially if the procedure is avoided in patients with right ventricle end-diastolic pressures (RVEDP) over 20 mmHg. Morbidity occurs in 4–6% of patients. 14,19 However, the risks of pulmonary angiography may be less than the bleeding complications and deaths from unnecessary heparin. 14

TABLE 2. Hypercoagulable States

| Primary 22,23 | |
| Anticoagulant abnormalities or deficiencies of | |
| Antithrombin III: heparin cofactor, only heterozygotes survive | |
| Protein C or S: vitamin K-dependent cofactors, which inactivate Va and VIIIa | |
| Plasminogen or other factors in the fibrinolytic system | |
| Lupus anticoagulants: increased PT and paradoxically increased risk of thrombosis | |
| Secondary 22,23 | |
| Thrombosis and fibrinolysis altered by | |
| Surgery 8,9,11: increased tissue thromboplastin, fibrinogen, Factor VIII, decreased antithrombin III | |
| Pregnancy 27: decreased velocity of venous flow, fibrinolytic activity, and increased levels of coagulation factors | |
| Oral contraceptive agents 28: doubled risk of clinical DVT after surgery | |
| Adenocarcinoma 21,26: gastrointestinal tract, pancreas, prostate, lung, or breast | |
| Nephrosis: loss of anticoagulants in urine | |
| Disseminated intravascular coagulation: consumes anticoagulants | |
| Heparin therapy: antithrombin III levels decreased | |
| Thrombocytopenia 26,37: from antibodies induced by heparin, possible arterial and venous thrombosis | |
| Myeloproliferative disease: platelet abnormalities | |
| Behçet’s syndrome: venous abnormalities | |
| Homocystinuria: venous and platelet abnormalities | |
nant disease. Calf vein thrombosis occurs in 40–80%, proximal vein thrombosis in 10–20%, and fatal PTE in 1–5% of this high-risk group. However, an individual’s perioperative thrombotic risk is compounded by advanced age, obesity, presence of malignancy, congestive heart failure, acute myocardial infarction, prior DVT or PTE, estrogen use, or immobilization.21,22,26

Young patients with trauma, immobilization, surgery, cancer, pregnancy, or oral contraceptive use can develop DVT.21,27,28 DVT occur in children with trauma to the lower extremity, shunted hydrocephalus, congenital heart disease, infection, cancer, or chronic medical diseases.26,29

Hemodynamic Changes with PTE

McIntyre and Sasahara11 correlated the angiographic and hemodynamic findings in patients with no preexisting cardiopulmonary diseases. The correlation between the mean pulmonary artery pressure (PAP) and the mean pulmonary vascular obstruction (r = 0.677, P < 0.01) showed that a PAP of 22 mmHg correlated with 30% obstruction and a PAP of 36 mmHg occurred with 50% obstruction.11 The PAP did not exceed 40 mmHg in previously healthy patients, and PAP levels over 40 mmHg indicated the coexistence of chronic cardiopulmonary diseases.11,30 Central venous pressure (CVP) was over 5 mmHg in most patients with vessel obstruction over 35%, but the CVP was less than 5 mmHg in two patients with more than 50% of their vasculature obstructed. The cardiac index (CI), performed by Fick method, did not correlate with the magnitude of obstruction. Cardiac failure, defined as CI less than 2.3 L·min⁻¹·m⁻² and elevated CVP, occurred in three of five patients with vessel obstruction over 50%.11 Another series11 examined previously healthy patients with more than 50% of their vasculature obstructed. The CI averaged 2.2 L·min⁻¹·m⁻² with a mean RVEDP of 14 mmHg and CVP of 13 mmHg. The pulmonary capillary wedge pressures (PCWP) were normal. The gradients between the PA diastolic pressures and PCWP were always greater than 5 mmHg, but the gradients averaged 11 mmHg.‡

However, correlations did not exist between the angiographic findings, CI, or PAP in patients with chronic cardiopulmonary diseases. The CI was severely depressed in some patients with small PTE. The PCWP was commonly elevated in patients with histories of congestive heart failure and superimposed PTE.30

Clinical interpretation of some hemodynamic monitoring parameters is altered by massive PTE. The CVP, measuring the right sided preload, should be used to titrate volume infusion not the PCWP because the RV is susceptible to failure. The PAP may increase as cardiac output (CO) and pulmonary blood flow increase. Decreasing PAP indicates either less pulmonary obstruction or a deterioration in CO.31,32 The PaO₂ may initially decrease with higher CI. The CI was increased from 1.5 to 2.1 L·min⁻¹·m⁻² with inotropes or colloid infusion in conjunction with a PaO₂ decrease from 68 to 49 mmHg. The intrapulmonary shunt fraction increased with the higher CI, presumably from perfusion of areas with low V/Q ratios.32 However, the important parameters of oxygen tissue delivery and mixed venous oxygen tension (MVO₂) improved with the higher CI.32

Case reports described findings from Swan-Ganz catheterization that may aid in the diagnosis of PTE. These descriptions included sudden inability to measure CO due to occlusion of the thermistor,33 visualization of a kinked catheter on chest x-ray,34 the presence of both pulmonary hypertension and inability to attain PCWP,35 or an increase in PAP after deflation of the balloon, presumably from entry of the catheter tip into the embolus.36 These variations are not pathognomonic of PTE, but their occurrence could indicate that PTE needs to be in the differential diagnosis.

Right Ventricle Failure from PTE

The thin-walled, compliant right ventricle (RV) decompensates with acute increases in pulmonary vascular resistance.37–39 A massive PTE dramatically increases the RV afterload, enlarges the RV, and shifts the ventricular septum to the left. Echocardiography demonstrates shift of the ventricular septum and decreased left ventricle (LV) volume (preload).31,40 These changes decrease LV compliance and CO. The coronary perfusion pressure of the RV is reduced by both the low systemic blood pressure (BP) and high RVEDP. RV distension allows coronary flow only in diastole, instead of both systole and diastole.39 The resultant RV ischemia further decreases the ejection fraction, causes additional RV dilation, and further impedes LV function. This “vicious circle” of RV failure was first described by Guyton et al.39 and recently illustrated by Wiedemann and Matthay (fig. 1).41 Further decompensation occurs if the elevated right atrial and RV pressures cause flow through a patent foramen ovale or the tricuspid valve.31,42–44

RV function is difficult to assess because it is crescent shaped and has a posterolateral location. RV ejection fractions (RVEF) and stroke volumes can be calculated from Swan-Ganz catheters with rapid response thermistors that measure beat-to-beat temperature variations.45 No case reports detail use of these catheters in patients with PTE, but studies using normovolemic goats showed that the RVEF decreased from 51% to 26% after microem-
studies need to be interpreted with caution because the use of anesthesia can blunt the response of the sympathetic nervous system and therefore provide misleading information.

**HEPARIN**

Heparin (table 3) administration decreased mortality, mainly from recurrent PTE. A bolus of heparin is recommended before definitive diagnosis to improve cardiopulmonary function by preventing mediator-induced pulmonary vasoconstriction and bronchoconstriction from thrombin activation and platelet aggregation. The risks and benefits of this initial heparin bolus need to be carefully considered in a surgical patient with cardiovascular compromise from PTE.

Heparin induces antibodies active against platelets in about 5% of patients who may develop venous and arterial thromboses. Thrombocytopenia recurs with subsequent heparin use. Low molecular weight heparin may be safe, as recently reviewed. Individual patients with heparin-induced platelet antibodies have undergone cardiopulmonary bypass with preoperative plasmapheresis, received aspirin and dipyridamole pretreatment to minimize platelet aggregation with heparinization, or had prostacyclin substituted for heparin.

**OXYGENATION AND VENTILATION**

The etiology of hypoxemia may be different in patients with acute or subacute PTE. Two studies have used the sophisticated multiple gas elimination technique to determine the abnormalities in acute PTE. The first study examined seven patients with embolic obstruction averaging 55% and with PaO₂ of 67 ± 11% on supplemental oxygen. The ten patients in the second study demonstrated pulmonary vascular obstruction of 49%, PaO₂ of 61 mmHg (FIO₂ 21%), lower mean cardiac output, and included some patients with chronic diseases. As expected, alveolar ventilation to perfusion (VA/Q) mismatches occurred. The dead space ventilation was over 50%. An unexpected abnormality was the amount of perfusion distributed to lung units with VA/Q ratios of less than 1. This regional hypventilation and excess perfusion presumably resulted from redistribution of blood flow or from bronchoconstriction in nonemobilized lung areas. The true intrapulmonary shunt fraction averaged 5% or 9% in the two studies using inert gases, but the true shunt was below 1% in two patients with PTE less than 48 h old. (The 2–3% left-to-right shunt from the bronchial and thebesian vessel blood flow are not measured.) However, the venous admixture, calculated by the Berggren formula, was elevated (16 ± 5%), and the MVO₂ averaged 27 ± 5 mmHg. A mathematical simulation demonstrated that increasing the cardiac output

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Table 3. Heparin and Thrombolytic Therapy

<table>
<thead>
<tr>
<th>Indications</th>
<th>Thrombolytic Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary emboli</td>
<td>Pulmonary emboli: central, or peripheral if patient is unstable</td>
</tr>
<tr>
<td>Suspected pulmonary emboli</td>
<td>? Improved pulmonary microcirculation</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>? Improved venous circulation (48–72 h)</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Absolute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preexisting bleeding tendency</td>
<td>Active internal bleeding</td>
</tr>
<tr>
<td>Bacterial endocarditis</td>
<td>Recent (&lt;10 days) major surgery, obstetrical delivery, organ</td>
</tr>
<tr>
<td>Subarachnoid or cerebral hemorrhage</td>
<td>biopsy, previous puncture of noncompressible vessels</td>
</tr>
<tr>
<td>Malignant hypertension</td>
<td>Recent serious gastrointestinal bleeding</td>
</tr>
<tr>
<td>Recent central nervous system, ocular, or spinal surgery</td>
<td>Severe arterial hypertension (systolic &gt; 200 mmHg,</td>
</tr>
<tr>
<td>Heparin hypersensitivity</td>
<td>diastolic &gt; 110 mmHg)</td>
</tr>
</tbody>
</table>

| Relative | |
|---------|
| Major vascular procedures with grafts | Recent minor trauma, including cardiopulmonary resuscitation |
| Recent surgeries | Possible left heart thrombus (atrial fibrillation, mitral valve |
| Pericarditis | disease) |

<table>
<thead>
<tr>
<th>Complications</th>
<th>Anticoagulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Antibody formation (SK)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Allergic reaction (SK)</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>Fever (SK)</td>
</tr>
<tr>
<td>Resistance</td>
<td>Resistance to thrombolytic state</td>
</tr>
</tbody>
</table>

SK = streptokinase.

raised the $M_{O_2}$ to 40 mmHg and the $P_{aO_2}$ from 61 to 87 mmHg.62 This simulation supports the use of inotropes to improve oxygenation.

Rarely, intracardiac shunting through a patent foramen ovale causes severe hypoxemia.51,42,43 An infusion of the α-agonist metaraminol (3 μg·kg⁻¹·min⁻¹) reversed the presumed intracardiac shunting in two patients with acute PTE.43

Positive end-expiratory pressure (PEEP) must be administered cautiously to treat the hypoxemia because PEEP has detrimental hemodynamic effects. PEEP shifts the-ventricular septum, increases RV wall stress, and also decreases venous return, LV volume, and CO.63–65 Mechanically ventilated, unstable patients with PTE received small tidal volumes (7 ml/kg), rapid respiratory rates, and no PEEP.31,32 PEEP may be beneficial if PEEP increases ventilation of lung areas receiving excessive perfusion without decreasing the $M_{O_2}$ or CO.

PEEP (20 cmH₂O) returned the $P_{aO_2}$ to baseline, when the right heart output was maintained by a mechanical pump, in open chested dogs infused with autologous clots.50 This study supports the utility of PEEP when CO is maintained. The lower airway pressures from high frequency jet ventilation in dogs embolized with autologous muscle resulted in a higher $P_{aO_2}$ and CI than did conventional mechanical ventilation (tidal volume 15 ml/kg).66 The etiology of the hypoxemia in subacute PTE differs from acute PTE. Hypoxemia in subacute PTE is caused by increased shunt fraction and atelectasis from local hypoxia, hypocarbia, or decreased surfactant production.42,53,61,67 The intrapulmonary shunt fractions, determined by the multiple inert gas elimination technique, ranged from 3% to 39% in patients. The shunt fractions also correlated with the severity of pulmonary atelectasis on chest x-ray.61 Oxygenation was improved by intermittent positive pressure breaths, oxygen, or breathing carbon dioxide in air.42,67 Standard ventilatory techniques should therefore treat the hypoxemia from subacute PTE.

**VOLUME RESUSCITATION**

Controlled administration of fluids, usually colloid solutions, improved the hemodynamic status and tissue oxygenation in patients with PTE.31,32,68,69 Volume infusions should be titrated when the CVP is less than 12–15 mmHg and stopped if a large increase in the CVP occurs. Fluids...
boluses have induced hemodynamic collapse in patients critically ill with PTE.\textsuperscript{41,68,70} Laver \textit{et al.}\textsuperscript{65} called this phenomenon “LV end-diastolic tamponade” because the RV fills the available pericardial space and impedes LV function. Volume infusion caused detrimental effects in dogs with RV failure from microemboli\textsuperscript{71} or autologous clots.\textsuperscript{72}

Microemboli were infused until the CO decreased by 50% (1.4 l/min) with a mean PAP of 55 mmHg. Dextran (100 ml) significantly decreased the mean BP from 97 to 65 mmHg with a nonsignificant decrease in CO to 0.9 l/min.\textsuperscript{71} The autologous clots were infused until the CO was about 0.8 l/min, with a mean PAP of 55 and RVEDP of 8 mmHg. Repeated boluses of 100 ml of dextran caused severe hypotension and increased the RVEDP to 17 mmHg, and all the dogs died. The myocardial decompensation was attributed to increased oxygen consumption from increased RV wall tension and inadequate coronary perfusion pressure.\textsuperscript{72}

\section*{Inotropes}

Isoproterenol is an inotrope, pulmonary vasodilator, and bronchodilator. Isoproterenol appears beneficial in mild cases and detrimental in severe cases of clinical and experimental PTE.\textsuperscript{46,54} Isoproterenol infusion (1.5–6 µg·kg\textsuperscript{-1}·min\textsuperscript{-1}) increased CO from 4.9 to 7.1 l/min, the heart rate from 115 to 135, and decreased mean BP from 79 to 72 mmHg with no change in PAP. Only two of nine patients in this study had a CO below 3 l/min.\textsuperscript{73} Isoproterenol infusion in patients with more severe hemodynamic compromise changed the CI minimally from 1.4 ± 0.4 to 1.8 ± 0.3 l·min\textsuperscript{-1}·m\textsuperscript{-2}, but the mean BP decreased from 73 to 57 mmHg.\textsuperscript{58} Systemic vasodilation, excessive tachycardia, or arrhythmias can complicate isoproterenol use.\textsuperscript{68} Hemodynamic collapse and death occurred after isoproterenol infusion in dogs with severe RV failure (CO 0.8 l/min) from embolization of autologous clots.\textsuperscript{72}

A French group studied dobutamine and dopamine in unstable patients with PTE and no preexisting cardiopulmonary diseases.\textsuperscript{58,74} Volume loading was initially performed, and the CVP averaged 13 mmHg. Dobutamine infusion (8 ± 3 µg·kg\textsuperscript{-1}·min\textsuperscript{-1}) increased the CI from 1.7 to 2.3 l·min\textsuperscript{-1}·m\textsuperscript{-2} and reversed the systemic hypotension. In addition, the pulmonary vascular resistance and heart rate decreased.\textsuperscript{74} Dopamine (5–17 µg·kg\textsuperscript{-1}·min\textsuperscript{-1}) induced similar increases in CO and mean BP, but the PAP rose by about 30%, and some patients developed tachycardia.\textsuperscript{68} Dopamine was the preferred drug for elevating cerebral and coronary perfusion pressures.\textsuperscript{74}

Even though no clinical series have been reported, norepinephrine should be tried when other inotropes do not raise coronary and cerebral perfusion pressures.\textsuperscript{31} The case report of a 65-yr-old man with PTE showed the efficacy of norepinephrine.\textsuperscript{70} His CO of 2.2 l/min, PCWP of 17, systolic PAP of 70, and RVEDP of 12 mmHg were initially treated with furosemide (40 mg) and dopamine (8 µg·kg\textsuperscript{-1}·min\textsuperscript{-1}). The systolic BP later decreased to 100 mmHg, and infusion of 300 ml normal saline decreased the systolic BP to 70 and PAP to 50 mmHg. Dopamine infusion of approximately 200 µg·kg\textsuperscript{-1}·min\textsuperscript{-1} was ineffective. However, a 100-µg bolus of norepinephrine and a titrated infusion of norepinephrine increased CO to 5.5 l/min and systolic BP to 150 mmHg, with decreased CVP and PCWP.\textsuperscript{70}

The importance of increasing coronary perfusion pressure has been emphasized in experimental acute RV failure. Norepinephrine increased the CO and decreased the RVEDP in dogs with severe RV failure (CO averaging 0.8 l/min) after embolization with blood clots. The norepinephrine bolus of 100–200 µg was followed by a continuous infusion (0.08–0.16 µg·kg\textsuperscript{-1}·min\textsuperscript{-1}).\textsuperscript{72} An aortic balloon counterpulsation device reversed the severe RV failure by increasing the LV afterload and RV coronary perfusion pressure in dogs infused with autologous clots.\textsuperscript{75} Progressive constriction of the pulmonary arteries induced hemodynamic decompensation when the systolic PAP reached 60–80 mmHg in dogs. A small supplementation of right coronary flow by pump dramatically reversed the RV failure and systemic hypotension,\textsuperscript{58} even though the flow was already twice that of baseline. Phenylephrine infusion in a similar dog model also reversed the right sided ischemia, decreased the RVEDP, and increased BP, CO, and right coronary blood flow.\textsuperscript{57}

\section*{Vasodilators}

Administration of inotropes and pulmonary vasodilators, such as norepinephrine and PGE\textsubscript{1},\textsuperscript{76} would seem logical in PTE. However, no selective pulmonary vasodilators are known, and systemic or venous dilation are potentially detrimental to patients with severe, acute PTE. Oral administration of hydralazine to patients with chronic pulmonary hypertension either increased CO and decreased PAP\textsuperscript{77,78} or induced symptomatic, systemic hypotension.\textsuperscript{79} No clinical studies have examined hydralazine use in acute PTE. The case report of a previously healthy 71-yr-old woman detailed hydralazine use after acute PTE.\textsuperscript{80} Dopamine (14 µg·kg\textsuperscript{-1}·m\textsuperscript{-2}) improved the CI to 1.81·min\textsuperscript{-1}·m\textsuperscript{-2} with a PAP of 30/20 mmHg. Her CI deteriorated to 1.31·min\textsuperscript{-1}·m\textsuperscript{-2} over the next 24 h. Hydralazine (100 mg initially and then 50 mg po every 6 h) increased her CI to 1.81·min\textsuperscript{-1}·m\textsuperscript{-2} and decreased the pulmonary vascular resistance from 788 to 444 dynes·s·cm\textsuperscript{-5} with minimal changes in BP or heart rate. When the patient was stable and receiving no hydralazine, another dose of hydralazine induced further hemody-
namic improvement. Intravenous hydralazine (10–20 mg) or nifedipine (10 mg) are anecdotally used by an-

Hydralazine and nitroprusside have been compared in
dogs with CO decreased by 40–50% from autologous clot
infusion. Hydralazine returned the CO to baseline,
whereas nitroprusside induced systemic hypotension
without improving the CO or pulmonary vascular resis-
tance. The pressure–flow relationship of the pulmonary
vasculature was studied in this model by opening arterio-
venous fistulas to provide different levels of CO at base-
line, after embolization, and after hydralazine treat-
ment. Hydralazine aliquots were infused in 2–3 mg al-

of the onset of acute symptoms, but even some patients
with recurrent PTE responded. Stellate ganglion blockade
reverses pulmonary artery vasospasm and decreases pres-

MANIPULATION OF VASOACTIVE MEDIATORS

Blockade of vasoactive mediators is a theoretically ap-
pealing treatment modality. Pretreatment with aspirin, a
prostaglandin synthesis inhibitor, or methysergide, a se-

Benefits from kentaserin were less dramatic in ten hepa-
arinized patients with non–life-threatening PTE. The
P_{A\text{O}_2} increased by 6 mmHg (Fi_{O_2} 21%) and the PAP and
MAP decreased by 3 and 9 mmHg, respectively, with no
change in CI. However, four of the five patients whose
PAP decreased by 4–5 mmHg also increased their P_{A\text{O}_2}
by 5–14 mmHg. These patients tended to have more
recent, larger PTE, but not all similar patients responded
to kentaserin. Kentaserin may serve as a pulmonary vas-
dilator that improves oxygenation in certain acutely ill
patients with PTE, but an inotrope may be needed.

Case reports from the 1940s and 1950s demonstrated
that stellate ganglion blocks, performed on the symptom-

† Braun SD, Newman GE, Ford K, Miller GA, Coleman RE, Dunnick
NR: Ventilation–perfusion scanning and pulmonary angiography:
Correlation in a clinical high probability pulmonary embolism. Amer-

Treatment of Unstable Patients with PTE

Treatment options for massive PTE are as follows: 1) thrombolytic therapy; 2) pulmonary embolectomy per-
formed with or without cardiopulmonary bypass (CPB);
3) transvenous catheter embolectomy; or 4) an inferior
cava (IVC) filter. The management algorithms for
stable and unstable patients, with and without contrain-
dications to anticoagulants, are presented (figs. 2 and 3).
The distinction between central or peripheral PTE is criti-

cal because peripheral emboli induce shock only in pa-

FIG. 2. No contraindications to anticoagulants. *VQ scan useful if
negative. **PTT must be normal in patients after SK-UK.
PULMONARY THROMBOEMBOLISM

binds to the plasminogen associated with fibrin in tissue clots, which include surgical wounds. t-PA (50 mg over 2 h) effectively lyzed the PTE, but t-PA still induced a systemic fibrinolytic state, with lowered fibrinogen levels.99 A higher dose of t-PA (80–90 mg over 6 h) improved angiographic scores and RV function in seven stable patients with acute pulmonary hypertension from PTE.44 Echocardiography showed decreased RV size and elimination of systolic septal flattening, hypokinetic wall movement, and tricuspid regurgitation.44

Surgery within 7–10 days was classified as a major relative contraindication by the NIH Consensus Conference because thrombolytic therapy also lyzes other tissue blood clots (table 3).96 Clinically significant bleeding (transfusion required or 5% decrease in hematocrit) occurred in 9% with urokinase and in 4% with heparin therapy during the initial 24-h infusions.10 The rate of bleeding over 2 weeks in both groups was 13–18%.100 The 1% incidence of intracranial bleeding was twice the rate developing with heparin.10,92 Unfortunately, bleeding from thrombolytic therapy cannot be predicted from laboratory tests.10,93 Cryoprecipitate or fresh frozen plasma should be transfused to elevate the fibrinogen level.93,94 The thrombolytic inhibitor e-aminocaproic acid may be given to treat central nervous system bleeding or before emergency surgery.95 However, using e-aminocaproic acid has been questioned because the active factor plasmin is not affected and only plasminogen activation is antagonized.94

Multiple dosing regimens of thrombolytic agents have been developed to optimize clot lysis and minimize bleeding complications.100,101 The protocols discussed here involved hemodynamically significant emboli102 or t-PA use within 3 days of surgery.103 A lower dose of urokinase (15,000 IU/kg) was infused through the pulmonary angiography catheter or right atrium of 14 patients with life-threatening PTE (clinical shock, RV failure, syncope, or seizures).102 A 30% improvement in the hemodynamic and angiographic parameters occurred by 3 h in the 12 patients with a fibrinolytic state. One of the two deaths (7%) occurred in a patient with no fibrinolytic activity.102 No serious bleeding complications occurred in these 14 unstable patients and in nine other hemodynamically stable patients.102,104

Both intravenous and intrapulmonary administration of t-PA (50 mg over 2 h, and then 50 mg over 5 h) decreased the magnitude of the embolism by 38% in 34 heparinized patients with vessel obstruction over 48%.103 The mean PAP decreased from 31 to 12–18 mmHg within 5 h.103 Eighteen of these 34 patients were within 3–15 days of surgery. Bleeding complications, mainly at puncture or operation sites, were present in 16 patients, including five postoperative patients. The 12% incidence of major bleeding was the same as that in nonsurgical patients in the Urokinase Pulmonary Embolism Trial.10,103

monary embolectomy is contraindicated for peripheral PTE because surgical mortality is high.90–92

THROMBOLYTIC THERAPY

The thrombolytic agents streptokinase and urokinase (Table 3) activate the natural fibrinolytic system to speed lysis of PTE.10,95,94 Urokinase (loading dose 4,400 IU/kg, then 4,400 IU·kg⁻¹·h⁻¹ for 12–24 h) converts the inactive plasminogen to plasmin. Streptokinase (loading dose 250,000 IU, then 100,000 IU/h for 24 h) first complexes with plasminogen, and the complex then activates plasminogen. Thrombolytic agents are indicated when hemodynamic compromise makes the rate of clot resolution critical.92,95,96 Delayed benefits, such as improved pulmonary capillary diffusing capacity,97 or patency of lower extremity veins,98 may also occur.

Tissue plasminogen activator (t-PA) more specifically

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**FIG. 3.** Contraindications to anticoagulants. Patients with contraindications to either streptokinase-urokinase (SK-UK) and heparin or contraindications just to SK-UK are indicated by the large X through the anticoagulants.
Bolus administration of urokinase\textsuperscript{102} or t-PA administration to heparinized patients\textsuperscript{103} may be better for hemodynamically compromised postoperative patients, but few reports exist of standard thrombolytic regimens in postoperative patients.

PULMONARY EMBOLOCTOMY

The controversies about pulmonary embolectomy (table 4) have been recently detailed.\textsuperscript{105,106} The difficult goal is to avoid embolectomies in patients who would survive anyway while not allowing irreversible organ damage in those needing the procedure. The patient population for embolectomy is difficult to define because two of three fatalities from PTE occur within the first 2 h.\textsuperscript{106} Proponents of thrombolytic therapy believe embolectomy should be performed only when thrombolytic therapy is contraindicated or ineffective.\textsuperscript{52,95,107} By contrast, the liberal guidelines for embolectomy proposed by Sasahara et al.\textsuperscript{5} include obstruction of more than 50% of the vasculature, PaO\textsubscript{2} less than 60 mmHg, systolic BP less than 90 mmHg, and urine output less than 20 ml/h after 1 h of maximal medical therapy. The mortality rates for embolectomies 10–15 yr earlier ranged from 29% to 63%, but recently they are 11–31%.\textsuperscript{108} The improved survival rates have been attributed to the initiation of partial, sometimes portable, CPB before embolectomy in patients near cardiac arrest.\textsuperscript{90,109,111} Patients with chronic pulmonary hypertension, medical diseases,\textsuperscript{90–92} or with symptoms of more than 7 days duration had higher mortality rates.\textsuperscript{108} Lower mortality rates occurred in studies with many postoperative patients.\textsuperscript{90–92,108,109,112}

No multi-institutional prospective studies have compared embolectomy and thrombolytic therapy, and comparison between studies is difficult. Two older retrospective studies concluded that survival from thrombolytic therapy was equal to or better than an embolectomy.\textsuperscript{107,113} A recent prospective Danish study in mainly postoperative patients with PTE concluded that embolectomy was life saving and effective.\textsuperscript{108} The patients treated with streptokinase (n = 28) had only 30–55% obstruction of the PA. The embolectomy patients (n = 25) had more severe injury, with 55–75% of the PA obstructed or had contraindications to streptokinase. Seven of the 25 patients in the embolectomy group came to the operating room with cardiac arrest, and four of these seven patients survived. The hospital mortality rate was 21% in the streptokinase group. The hospital mortality rate was 20% in the embolectomy group, but it was only 11% if the patients with cardiac arrest were excluded. Cerebral impairment and fatal hemorrhage occurred in 18% of patients given streptokinase, and cerebral impairment developed in 8% of patients after embolectomy.\textsuperscript{108} The good results from embolectomy in this Danish study\textsuperscript{108} are probably attributable to the general, underlying healthy state of the postoperative patients.

Clinical judgment about the urgency of the situation, contraindications to thrombolytic therapy, and the availability of local resources are the deciding factors for management of a specific patient. Critical information is not available when considering the difficult clinical decision between pulmonary embolectomy or thrombolytic therapy in a postoperative patient. Individual postoperative patients have received thrombolytic therapy because it is a relative major (not absolute) contraindication.\textsuperscript{96} The risk of bleeding, size of PTE, days after surgery, and clinical outcome have never been retrospectively correlated or prospectively studied in postoperative patients.

An erroneous preoperative diagnosis resulted in mortality rates of 70–100% after embolectomy.\textsuperscript{112,114} Because pulmonary angiograms cannot always be performed before embolectomies,\textsuperscript{92,105} urgent diagnoses have been made by echocardiography or by injecting contrast dye in central venous or Swan-Ganz catheters, sometimes while on CPB.\textsuperscript{8,92,109,115,116}

The embolectomy series encouraged femoral vessel cannulation under local anesthesia to initiate partial CPB in patients with cardiogenic shock before anesthetic induction.\textsuperscript{90,109,111} Cardiac arrests occurred with anesthetic

<table>
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<td>PTE &gt; 50% in unstable patient with maximal medical therapy</td>
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<td>Contraindications</td>
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<td>Chronic venous insufficiency of lower extremities</td>
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<td>Filter migration</td>
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induction in these surgical series, two of which were published in the early 1980s.\textsuperscript{90,111} Patients with acute PTE are extremely sensitive to the vasodilating and negative inotropic effects of anesthetic agents,\textsuperscript{117,118} but specific studies are lacking. These patients may "tolerate" only oxygen, neuromuscular paralysis, and amnestic drugs, such as scopolamine, low doses of a benzodiazepam, or ketamine. It is not known if low doses of ketamine aggravate the pulmonary hypertension of acute PTE. Opioids or low levels of inhalation agents may be added. Respiratory alkalis are used as a nonspecific pulmonary vasodilator in other types of pulmonary hypertension\textsuperscript{116}; thus, hyperventilation with small tidal volumes may be beneficial.

Mortality rates are higher for embolectomies performed without CPB (Trendelenburg procedure).\textsuperscript{105,112} A preceding cardiac arrest was associated with mortality rates of 74\%, and patients with systolic BP under 100 mmHg had mortality rates of 20\%.\textsuperscript{112} The anesthesiologist should be prepared to give sustained positive pressure inflation to help extract distal thrombi during a Trendelenburg procedure.\textsuperscript{117}

**Transvenous Catheter Embolectomy, IVC Procedures**

Patients with contraindications to anticoagulants may require an IVC plication or a transvenous catheter embolectomy. This recently designed steerable catheter has a suction cup to remove central PTE. It is inserted into the femoral or jugular veins under local anesthesia.\textsuperscript{110,120} The mortality rate was 27\% in unstable patients undergoing catheter embolectomy.\textsuperscript{120} Femoral venoarterial CPB can be initiated to maintain hemodynamic stability during the procedure.\textsuperscript{119} Anesthetic management must consider the possibility of bleeding from percutaneous punctures or cutdowns due to prior anticoagulants, intrapulmonary bleeding from reperfusion of the lungs, ventricular arrhythmias, bradycardia, or perforation of the pulmonary artery.\textsuperscript{121}

The IVC can be ligated or partially occluded to prevent thrombi from reaching the lungs, but the mortality rates averaged 14\% (table 4).\textsuperscript{8,95} Transvenous placement of filters, such as the Greenfield filter, through the femoral or jugular veins using local anesthesia has predominantly replaced the intraabdominal procedures.\textsuperscript{119}

**Chronic PTE**

Recurrent PTE can lead to chronic pulmonary hypertension and cor pulmonale in a small number of patients.\textsuperscript{122} Embolectomies can successfully treat chronic PTE.\textsuperscript{123a,123b} A hospital mortality rate of 12\% was reported for patients, which compares to an estimated 25\% mortality for heart lung transplant.\textsuperscript{123a} The protocol used CPB, extreme hypothermia, a cooling jacket on the right and left ventricle, cardioplegia, and intermittent circulatory arrest to minimize backbleeding from hyperplastic bronchial arteries.\textsuperscript{123a} The anesthesia management of chronic PTE has also been discussed.\textsuperscript{124}

**Presentation of Intraoperative PTE**

Case reports\textsuperscript{115,116,125–131} describe the intraoperative presentation of PTE. Only cases with definitive diagnostic end points for PTE are detailed. Risk factors, such as obesity, older age, and immobilization, were present. Leg manipulation or changes in position characteristically induced the episodes. Application of Esmarch bandages led to massive PTE in two patients undergoing delayed repair of lower extremity trauma.\textsuperscript{132,133} Tourniquet inflation caused cyanosis and death despite 30 min of cardiopulmonary resuscitation.\textsuperscript{133} Another patient developed ventricular bigeminy, which progressed to a slow idioventricular pulse and cardiac arrest despite resuscitative efforts. An emergency embolectomy was performed using CPB, and this patient survived.\textsuperscript{132}

A respiratory arrest occurred while the upper femoral fragment was being reamed in a young woman anesthetized with halothane 4 days after a motor vehicle accident.\textsuperscript{125} No resistance to positive pressure ventilation was present, but cyanosis, neck vein distension, and electromechanical dissociation developed. Closed and open chest cardiac massage and resuscitation drugs were ineffective. A saddle embolus was found at autopsy.\textsuperscript{125}

A 67-yr-old man, undergoing a posterior fossa exploration for a cerebellar tumor, developed sinus tachycardia and hypoxemia (P_{\text{aCO}_2}, 40 mmHg).\textsuperscript{127} A second episode of hypoxemia recurred, but he was neurologically intact after surgery. An episode of supraventricular tachycardia converted to atrial fibrillation, and cyanosis, hypotension, and loss of consciousness ensued. He was reintubated and regained consciousness. Digitalis was given to treat the tachycardia and furosemide because the CVP doubled. A perfusion lung scan demonstrated multiple defects. An IVC ligation was performed because heparin was contraindicated after the intracranial procedure.

A 66-yr-old man with a 6-cm abdominal aortic aneurysm was stable for 20 min after division of the lumbar sympathetic chains.\textsuperscript{129} His BP suddenly decreased from 120/70 to 50/40 mmHg with tachycardia and no changes in ECG, airway pressure, breath sounds, or PCWP. The CVP rose from 7 to 16 and the PAP from 18/8 to 44/38 mmHg. Arterial blood gases (\text{FiO}_2, 100\%) with a minute ventilation of 10 l/min were \text{pH} 7.09, \text{P}_{\text{aCO}_2} of 579, and \text{P}_{\text{aCO}_2} of 77 mmHg, with a base deficit of 5 mEq/L. The
patient stabilized after ephedrine, dopamine (2–4 µg · kg⁻¹ · min⁻¹), sodium bicarbonate, calcium chloride, and heparin (10,000 U). It was not reported how this diagnosis was confirmed or if the patient was heparinized in the postoperative period.

A 76-yr-old woman with steroid-dependent rheumatoid arthritis and asthma was undergoing repair of a 48-h-old hip fracture under spinal anesthesia with a sensory block to the sixth thoracic dermatome. She had received oral prednisone preoperatively and was stable until the surgeon elevated her leg. The BP dropped to 40/10 mmHg, and tachycardia, cyanosis, labored breathing, neck vein distension, QRS widening, and T-wave inversion developed. Phenytoine was administered. A Swan-Ganz catheter was inserted, the PAP was 75/24, and the PCWP was 16 mmHg. A bedside angiogram through the Swan-Ganz catheter showed filling defects. Improvement occurred after heparin and bronchodilator administration. A fatal cardiopulmonary arrest occurred 4 days later despite continuation of heparin.

A 64-yr-old man with a 14-cm abdominal aortic aneurysm and a distal aortocaval fistula was in high output failure (CO, 11 l/min; PAP, 41/24; PCWP, 21; BP, 115/20 mmHg). The BP decreased (70/20 mmHg) with metabolic acidosis, and additional increases in the CVP and PAP occurred before surgery. Cross-clamping of the aorta increased the BP to 92/60 mmHg. The PAP then acutely increased to 90/40 and BP decreased to 30 mmHg with bradycardia. No improvement followed infusion of whole blood for abdominal hemorrhage, calcium, atropine, dopamine, epinephrine, norepinephrine, and isoproterenol. The EEG became isoelectric. Internal cardiac massage generated only 5 mmHg of pulse pressure after sternotomy. A 45-g saddle embolus was removed during a Trendelenburg procedure. The patient stabilized and was subsequently discharged with no sequelae.

An artificial bladder sphincter was being inserted in an 11-yr-old child with a sacral myelomeningocele and shunted hydrocephalus. Tachycardia and mild hypotension developed when the surgeon mobilized the bowel and bladder. The heart rate increased to 180 beats per min, the systolic BP decreased to 45 mmHg, and cyanosis, diaphoresis, and fixed pupils developed, which did not respond to volume infusion and ephedrine. External cardiac massage relieved the cyanosis temporarily, and gradual hemodynamic improvement occurred. Heparin was given after a perfusion scan demonstrated minimal perfusion of the left lung and smaller defects in the right lung. This PTE occurred unexpectedly in an ambulating child who had her ventriculoatrial shunt removed 3 years previously.

Traumatic injuries to a 22-yr-old woman included severely displaced pelvic and hip fractures and pancreatitis, which necessitated parenteral nutrition. The hip fracture was repaired in left lateral position 8 days after trauma. The PaO₂ was 72 after induction and improved to 349 mmHg with increasing PEEP from 5 to 7 cmH₂O, the FiO₂ from 0.33 to 1.0, and the tidal volume from 800 to 900 ml. The PaO₂ acutely deteriorated to 58 mmHg and the PaCO₂ increased to 85 mmHg. Bilateral end-expiratory wheezes were treated by increasing the isoflurane concentration, administering orciprenaline (2.25 mg) via the endotracheal tube, and infusing isoproterenol (1 µg/min). Cyanosis developed, and the CVP increased from 15 to 19 mmHg and airway pressure from 22 to 25 cmH₂O. A digital subtraction angiogram showed no blood flow to the right lung. A Greenfield filter was placed. Heparinization was delayed 1 day due to the extensive surgery. The patient was discharged 14 days after surgery.

The typical presentations of PTE in anesthetized patients included cyanosis, hypoxemia, hypotension, neck vein distension, pulmonary hypertension, increased CVP, and normal PCWP. However, hypotension, hypoxemia, or hypocarbia did not uniformly occur. Wheezing or decreased compliance developed under anesthesia. End-tidal CO₂ decreased, but this was not a specific change because the patient was also severely hypotensive. The PCWP increased in patients with preexisting cardiac disease. Heparin administration induced hemodynamic or symptomatic improvement. Adequate cardiopulmonary resuscitation did not always prevent death. A pulmonary embolectomy should be attempted when PTE is the most likely diagnosis for an intraoperative catastrophe. The use of CPB is optimal, but a Trendelenburg procedure may be necessary.

Prophylaxis of Deep Venous Thrombosis in Surgical Patients

Prevention of DVT and PTE is the ideal but underutilized solution. Recent review articles and the NIH Consensus Conference strongly recommend the use of prophylactic techniques in moderate- and high-risk surgical patients. Numerous randomized studies have been combined to evaluate the efficacy and cost of these prophylactic techniques. The selection of prophylactic technique(s) must consider the risk factors specific to an individual patient, type of surgery, and length of immobilization to avoid inadequate prophylaxis or unnecessary complications. These techniques are briefly summarized so that an anesthesiologist can undertake a preoperative discussion of prophylaxis with the surgeon (table 5).

Heparin for Moderate-risk Surgical Patients

Kakkar organized a multicenter, randomized study of more than 4,000 patients and demonstrated that low-dose heparin (5,000 units) administered subcutaneously 2 h
before surgery and then every 8 h decreased the incidence of DVT and fatal PTE. However, the overall surgical mortality was not decreased. This small dose of heparin potentiates antithrombin III to inactivate Factor Xa and prevents the formation of large amounts of thrombin in the cascade system. Collins et al. performed a meta-analysis of the randomized trials of prophylactic heparin because the controversy is ongoing and thousands of patients are needed to detect changes in postoperative mortality. This overview showed that perioperative subcutaneous heparin decreased calf vein thromboses diagnosed by radiolabeled fibrinogen by 67 ± 4% and proximal DVT by 56 ± 12% in general surgery patients. The nonfatal PTE decreased by 47 ± 10% and fatal PTE by 64 ± 15% in combined populations of general surgery, urologic, and elective or traumatic orthopedic surgery patients. Fatal PTE occurred in 39 of 7,486 patients receiving heparin (0.52%) and in 98 of 8,112 control patients (1.1%). Administration of heparin either 2 or 3 times daily affected neither the efficacy nor bleeding risk. "Excessive" bleeding increased by 62 ± 11% and involved almost 2% of those receiving heparin. However, wound hematomas, which did not require surgical drainage, increased from 15% to 32% in a double-blind randomized trial of patients undergoing hernia repair. The use of low-dose heparin is contraindicated before surgical procedures on the spinal cord, eye, and brain or for open procedures of the prostate.

Different regimens, formulations of heparin, or addition of other drugs have been tried for perioperative prophylaxis. "Ultra-low dose" heparin (1 U·kg⁻¹·min⁻¹) was infused in the operating room and for 2–5 days postoperatively. This regimen decreased the incidence of fibrinogen diagnosed DVT from 22% to 4% (n = 100). Alternatively, adding dihydroergotamine (0.5 mg) improved the efficacy of low-dose heparin given twice daily. Dihydroergotamine is a smooth muscle vasoconstrictor with predominant effects on the venous circulation. Dihydroergotamine is contraindicated in patients with hypovolemia from trauma or sepsis to avoid arteriolar vasospasm. Low molecular weight fractions of heparin may have fewer bleeding complications, be as effective as standard heparin, and may be given only once a day. Low molecular weight heparin binds more specifically to Factor X and antithrombin and less tightly to thrombin and platelets.

Despite the demonstrated efficacy of perioperative heparin administration, it is not universally used due to the rarity of death from PTE, the incomplete protection offered, iatrogenic bleeding complications, patient discomfort, and the use of a technique unnecessary for the majority of patients. The diagnosis of calf vein thromboses by radiolabeled fibrinogen may be too sensitive of an end point because at least 80% of calf vein thrombi resolved in general surgical patients. The significance of calf vein thromboses has been reviewed, with the conclusion that asymptomatic patients can be followed with serial impedance plethysmography to detect proximal extension before starting anticoagulants. Anticoagulants are indicated for symptomatic calf vein thromboses because the high incidence of recurrent DVT indicates that this is probably a more severe disease process.

**Perioperative Prophylactic Heparin and Regional Anesthesia**

Authorities state that preoperative heparin is a contraindication to spinal anesthesia. The variable response to the fixed-dose heparin regimen must be recognized before considering regional anesthesia. The partial thromboplatin time (PTT) was 1.5 times normal in 15% of the general surgery patients 2–4 h after the preoperative heparin dose. The PTT also remained elevated in 15% of gynecologic surgery patients in the postoperative period. Similar changes occurred with the activated clotting time (ACT), which increased an average of 10 s for up to 5 h after subcutaneous heparin. Full anticoagulation occurred in 1–2% of patients.
tients with elevated preoperative ACT or PTT can be excluded, but the safety of performing spinal anesthesia in patients on prophylactic heparin with normal clotting times has not been studied. A recent review found no cases of spinal hematomas in patients receiving low-dose heparin. Lumbar epidurals have been performed with no neurologic sequelae in 58 patients receiving low-dose heparin and 951 patients receiving oral anticoagulants. However, the lack of reported complications does not exclude a low incidence of this serious complication, especially if PTT or ACT are not measured before performance of a regional technique.

OTHER PROPHYLACTIC TECHNIQUES FOR MODERATE-RISK SURGICAL PATIENTS

Prophylactic techniques, other than heparin and dextran, have not been studied in adequate numbers of patients to show decreased incidence of fatal PTE. Dextran (500 ml, molecular weight 40,000 or 70,000) is infused during surgery and for 1–5 days postoperatively. Dextran decreases platelet aggregation and viscosity, increases blood flow, and the thrombi formed are more easily lysed. A large randomized multicenter study (n = 4,352) showed that dextran was as effective as low-dose heparin in decreasing the incidence of fatal PTE. Three 500-ml doses of dextran 70 were given during and after surgery and on the next day. Wound hematomas occurred almost twice as often in the dextran group, but blood loss and explorations for bleeding complications were not changed. Problems with dextran include volume overload, renal failure from the osmotic diuresis, and need for venous access. Pretreatment with a hapten prevented the rare anaphylactic reactions (0.008%) to dextran.

The external pneumatic compression device is a boot that applies intermittent pressure to the calf, with mild patient discomfort as the only complication. These devices decrease stasis, induce fibrinolysis, and are as effective as low-dose heparin in decreasing DVT. The cost analysis studies estimated that external compression decreased the incidence of DVT to either 8% (n = 270) or 18% (n = 395) from 27% (n = 2,860 controls). External pneumatic compression in only the operating and recovery rooms was as effective as compression performed for 2–3 days postoperatively in urologic patients undergoing abdominal procedures and ambulating early. The efficacy of this limited perioperative use has not been verified in general surgery patients, but 50% of their calf vein thrombi formed in the operating room. Compression devices are especially useful if heparin is contraindicated. However, compression needs to be continued during the entire period of immobilization in neurosurgical patients.

The NIH Consensus Conference stated that graduated compression stockings were inadequately studied to recommend their use in moderate- and high-risk patients. Eight randomized trials with well-fitting stockings designed to exert more pressure on the ankles and calves showed that the incidence of DVT decreased from 27% (n = 2,860 controls) to 11% in moderate-risk surgical patients (n = 532). Platelet antiaggregatory drugs did not prevent DVT in general surgery patients. Surveillance by radiolabeled fibrinogen effectively diagnoses DVT at an early stage, but it is too expensive for routine use.

PROPHYLAXIS FOR HIGH-RISK SURGICAL PATIENTS

Preventing DVT is even more challenging in the high-risk group (table 5), which includes patients undergoing lower extremity, pelvic, or open prostate surgery or patients with prior PTE, age more than 60 yr, or cancer. Low-dose heparin provided inadequate protection for proximal vein thrombosis and increased the incidence of wound hematomas in elective or emergency hip surgery. However, the combined statistical analyses of orthopedic studies showed that heparin significantly decreased the incidence of calf vein thromboses diagnosed by radiolabeled fibrinogen from 46% to 20%. This finding ignores the fact that 10–20% of thrombi, which are also the most likely to embolize, arise directly in the femoral or pelvic veins in these patients. The wound radioactivity interferes with their detection. Low-dose heparin is generally not recommended in hip surgery patients.

Other dosing regimens or types of heparin may be effective in orthopedic patients. Subcutaneous heparin, titrated to increase PT to 31.5–36 s in elective hip surgery patients, decreased the incidence of proximal DVT from 39% to 13% with no increase in bleeding complications in a single study (n = 79). Heparin and dihydroergotamine, low molecular weight heparin, or low molecular weight heparin with dihydroergotamine also effectively decreased DVT with minimal increase in bleeding complications in patients undergoing elective hip surgery.

Both fatal and nonfatal PTE in hip surgery patients were decreased by coumadin, with elevation of the prothrombin time (PT) to 1.5–2.0 times normal. These benefits existed even when coumadin was started on the day before or day of elective hip surgery. Oral anticoagulants are rarely used because bleeding complications occurred in 10–20% of the patients, and this coagulopathy is difficult to reverse. However, administering coumadin at two different intensities to elective hip surgery patients decreased bleeding complications and the
incidence of proximal DVT from 16% to 2%.\textsuperscript{171} The PT was initially prolonged by 1.5–3 s over control, 10–14 days before surgery. The dosage was increased after surgery to prolong the PT to 1.5 times the control value.\textsuperscript{171}

External pneumatic compression was effective in patients undergoing knee surgery\textsuperscript{174} but not for hip surgery.\textsuperscript{172} The use of both dextran and sequential calf and thigh compression decreased the incidence of DVT in hip surgery patients by their effect on both hypercoagulability and stasis.\textsuperscript{172}

The incidence of DVT was lowered by intravenous dextran given for 4–7 days in orthopedic patients.\textsuperscript{24,25,135,173} Increased bleeding was reported when more than 500 ml dextran was given during hip surgery.\textsuperscript{172} Prolonged venous access and careful monitoring of the volume status are necessary. The efficacy of aspirin in hip surgery is controversial. Harris et al.\textsuperscript{172} demonstrated that aspirin (1.2 g) effectively decreased the incidence of DVT in males only, but these results have not been confirmed by others.\textsuperscript{4,135} The NIH Consensus Conference did not recommend graduated compression stockings for orthopedic patients,\textsuperscript{135} but a cost analysis study found that stockings decreased the incidence of DVT diagnosed by radiolabeled fibrinogen from 53% (n = 728) to 24% (n = 173).\textsuperscript{136} The limitations of this diagnostic technique in hip surgery patients minimizes the importance of this observation.

High incidences of DVT and PTE occur in patients undergoing pelvic surgery for gynecologic malignancy. Low-dose heparin did not decrease the incidence of calf or proximal vein thromboses in a randomized study of patients with gynecologic malignancy.\textsuperscript{174} Pelvic origin of thrombi was suspected in three patients with PTE and negative screening tests.\textsuperscript{174} Significant increases in the retroperitoneal drainage and decreases in the platelet count occurred, and 15% of these patients developed an elevated PTT bleeding complications.\textsuperscript{150} External pneumatic compression used in the operating room and the first 5 postoperative days decreased DVT in gynecologic malignancy,\textsuperscript{175} but it was not effective when used only in the operating and recovery rooms.\textsuperscript{176} Prophylactic heparin also did not decrease the incidence of DVT diagnosed by \textsuperscript{125}I-fibrinogen uptake in patients undergoing open prostate or bladder surgery.\textsuperscript{177}

Recommendations for prophylaxis are difficult to formulate in terms of the risk/benefit ratio for an individual patient. Dextran given over 2 days provided prophylaxis as effective as a longer course of low-dose heparin in moderate-risk patients.\textsuperscript{156} External pneumatic compression is effective at decreasing DVT in moderate-risk patients, but not enough patients have been studied to show decreased mortality from PTE.\textsuperscript{4} As discussed, low-dose heparin is recommended for moderate-risk surgical patients, but it provides inadequate prophylaxis for most high-risk patients undergoing orthopedic, open prostate, or gynecologic malignancy procedures.

**Effects of Anesthetic Techniques on Deep Venous Thrombosis**

The incidence of DVT and PTE decreased if hip surgery was performed with epidural anesthesia and analgesia provided in the postoperative period.\textsuperscript{178,179} Epidural anesthesia increased blood flow to the lower extremities and decreased stasis and activation of coagulation factors.\textsuperscript{178,179} In vitro local anesthetics increased fibrinolytic activity and decreased platelet aggregation.\textsuperscript{180} Epidural anesthesia also lowered the incidence of DVT from 51% to 12% in patients undergoing open prostatectomies.\textsuperscript{181} Three studies showed less DVT with the use of spinal anesthesia for hip surgery.\textsuperscript{182–184} By contrast, thoracic epidural anesthesia with no lower extremity vasodilation did not diminish DVT in moderate-risk patients undergoing abdominal procedures.\textsuperscript{185,186}

Pulmonary thromboembolism is a nebulous and fatal disease, which anesthesiologists can ignore as a "medical" disease. However, anesthesiologists can improve surgical patient care by early recognition of DVT or PTE, use of appropriate prophylaxis in patients at risk, and by initiating the proper treatment and hemodynamic management.

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**References**

9. Stein PD, Willis PW, DeMeis DL: History and physical examination in acute pulmonary embolism in patients without preex-
isting cardiac or pulmonary disease. Am J Cardiol 47:218–223, 1981
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71. Ghignone M, Girling L, Prewitt RM: Volume expansion versus norepinephrine in treatment of a low cardiac output complicating an acute increase in right ventricular afterload in dogs. ANESTHESIOLOGY 60:132–135, 1984


95. Kinaszewiz GT, George RB: Management of thromboembolism:


