Learning Objectives: After studying this article, the participant should be able to: 1. Understand and appreciate the incidence of venous thromboembolism in plastic surgery. 2. Understand and describe the cause and natural history of venous thromboembolism in the setting of plastic surgery. 3. Understand the important patient risk factors for venous thromboembolism and perform an individualized assignment of venous thromboembolism risk. 4. Select a method of venous thromboembolism prophylaxis based on a patient’s venous thromboembolism risk assignment and the overall thromboprophylaxis guidelines by the American College of Chest Physicians.

Summary: This Maintenance of Certification module reviews the incidence, cause, and natural history of venous thromboembolism in plastic surgery patients and highlights one algorithm for approaching venous thromboembolism risk assignment and choice of thromboprophylaxis.

The Maintenance of Certification module series is designed to help the clinician structure his or her study in specific areas appropriate to his or her clinical practice. This article is prepared to accompany practice-based assessment of preoperative assessment, anesthesia, surgical treatment plan, perioperative management, and outcomes. In this format, the clinician is invited to compare his or her methods of patient assessment and treatment, outcomes, and complications with authoritative, information-based references.

This information base is then used for self-assessment and benchmarking in parts II and IV of the Maintenance of Certification process of the American Board of Plastic Surgery. This article is not intended to be an exhaustive treatise on the subject. Rather, it is designed to serve as a reference point for further in-depth study by review of the reference articles presented. (Plast. Reconstr. Surg. 122: 1, 2008.)

Venous thromboembolism, a spectrum of disease ranging from deep vein thrombosis to pulmonary embolism, is a complication relevant to all practicing plastic surgeons. In one survey of board-certified plastic surgeons, pulmonary embolism was found to be the leading cause of death following liposuction, accounting for 23 percent of all deaths. In a prospective series of office-based surgical procedures, 63.6 percent of postoperative deaths were secondary to thromboembolism. Surprisingly, however, a recent survey of current members of the American Society of Plastic Surgeons found that only 48.7 percent of surgeons performing face lifts, 43.7 percent of surgeons performing liposuction, and 60.8 percent performing a combined procedure use thromboprophylaxis all the time. This hesitancy in instituting thromboprophylaxis may be attributable to the belief that there is a low incidence of venous thromboembolism or to the

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concern over bleeding complications secondary to chemoprophylaxis.

**INCIDENCE OF VENOUS THROMBOEMBOLISM**

Plastic surgery is not immune to the dangers of venous thromboembolism, with rates of venous thromboembolism ranging from less than 1 percent to nearly 10 percent, depending on the surgical procedure. In a survey of members of the American Society for Aesthetic Plastic Surgery, Reinisch et al. reported a 0.49 percent rate of venous thromboembolism in face-lift procedures. Chen et al. found a 0.57 percent incidence of venous thromboembolism in patients undergoing head and neck reconstruction. In a series of pedicled transverse rectus abdominis myocutaneous flaps for breast reconstruction, Erdmann et al. observed a 1.3 percent rate of venous thromboembolism. Concerning large-volume liposuction procedures, one series reported a 1.7 percent incidence of venous thromboembolism in patients undergoing 5 liters or more of fat aspiration. Grazer and Goldwyn cited a 1.9 percent incidence of venous thromboembolism in a series of abdominoplasty patients. Belt lipectomy procedures are associated with the highest rate of venous thromboembolism, approximately 9.4 percent in a recent study by Aly et al.

**CAUSE OF VENOUS THROMBOEMBOLISM**

As described by the German pathologist Rudolf Virchow, venous thrombus formation is driven by a triad of factors: (1) venous stasis; (2) vascular injury; and (3) hypercoagulability. At least one part of the triad is necessary to initiate the coagulation cascade (Fig. 1). During surgery, the combination of general anesthesia, supine positioning, and immobilization promotes venous stasis. Decreased venous return prevents clearance of activated clotting factors, leading to thrombus accumulation behind venous valve cusps. Intimal damage is also a byproduct of surgery, secondary to venous traction during muscle and tissue retraction and the vasodilatory effect of anesthesia. At these intimal sites of microscopic injury, platelets collect and initiate the coagulation cascade.

Hypercoagulability can be secondary to inherited or acquired coagulation disorders. Common inherited prothrombotic disorders include factor V Leiden; prothrombin 20210A; and deficiencies of protein C, protein S, and antithrombin III. Factor V Leiden, present in roughly 4 to 6 percent of Caucasians, represents the most common genetic prothrombotic defect. The mutated factor V resists inactivation by activated protein C and drives unchecked clot formation. Prothrombin 20210A, a variant found in 1.7 to 3 percent of people of European descent, results in elevated prothrombin levels and hypercoagulability. Acquired hypercoagulable disorders can stem from pharmacologic interaction or disease sequelae and include antiphospholipid antibody syndrome, hyperhomocysteinemia, and cancer. In cancer, there are multiple mechanisms by which the prothrombotic machinery is jump-started. Malignancies, such as gastric and pancreatic types, express tissue factor–like material that activates coagulation. By means of an acute inflammatory phase reaction, tumor-infiltrating macrophages can promote thrombus formation through interleukin-1 and tumor necrosis factor-α production. Malignancies can also down-regulate endothelial cell anticoagulant activity and stimulate release of fibrinogen and factor VIII.

**NATURAL HISTORY OF VENOUS THROMBOEMBOLISM**

The natural history of surgery-associated venous thromboembolism events has been well described by Kearon and is summarized below. Up to all three components of Virchow’s triad may be present at the time of surgery to promote venous thrombosis, explaining how perhaps 50 percent of deep vein thromboses associated with surgery start intraoperatively. Most of these intraoperative deep vein thromboses begin in the distal veins, specifically, in the calf region. Approximately 50 percent of deep vein thromboses formed intraoperatively may resolve spontaneously within 72 hours, with venous thromboprophylaxis facilitating lysis of perioperative deep vein thromboses and preventing formation of new thrombi. Isolated calf deep vein thromboses rarely cause leg symptoms or clinically important pulmonary embolisms. Of more concern, approximately 25 percent of untreated symptomatic calf deep vein thromboses extend to the proximal veins (at or above the popliteal vein) within 1 week of presentation. The majority of patients with a symptomatic proximal deep vein thrombosis and without chest symptoms have evidence of a pulmonary embolism on lung scan. The highest risk period for fatal postoperative pulmonary embolism occurs 3 to 7 days after surgery, with approximately 10 percent of symptomatic pulmonary embolisms fatal within 1 hour of first symptoms. Furthermore, the risk of symptomatic venous thromboembolism is highest within 2 weeks of surgery and...
Fig. 1. Coagulation cascade.
remains elevated for approximately 2 to 3 months. After a diagnosed pulmonary embolism, 50 percent of patients have right ventricular dysfunction on echocardiography. After a symptomatic deep vein thrombosis, there is an approximately 10 percent cumulative incidence of severe postthrombotic syndrome after 5 years.

RISK ASSIGNMENT FOR VENOUS THROMBOEMBOLISM

Given that up to two-thirds of patients with a venous thromboembolism may appear clinically silent, leading to a substantial delay in diagnosis and treatment and resulting in significant morbidity and mortality, the need for thromboprophylaxis is paramount. Because of the elective nature of many plastic surgical procedures, it is of paramount importance that the surgeon allow for appropriate planning and risk-reduction strategies. Based on the authors’ preference, choice of thromboprophylaxis is dependent on venous thromboembolism risk assignment and the 2004 American College of Chest Physicians overall recommendations on prophylaxis for surgical patients within each venous thromboembolism risk category.

In approaching venous thromboembolism risk assignment, we advocate an individualized assessment of thrombotic risk, as described by Bergqvist et al. (Fig. 2). This approach takes into account a patient’s unique set of predisposing risk factors, such as age, history of venous thromboembolism, and chronic illness, and any exposing risk factors, such as type and length of operation. The various risk factors are differentially weighted on the basis of historical incidence data from prior randomized trials. Tallying a patient’s set of predisposing and exposing risk factors yields an overall risk factor score and assignment to one of four venous thromboembolism risk categories (low, moderate, high, extreme).
moderate, high, and highest) as described by the American College of Chest Physicians.24

A number of risk factors with evidence-based weighting deserve special mention. Borow and Goldson reported a 20 percent incidence of deep vein thrombosis for procedures lasting 1 to 2 hours compared with a 62.5 percent rate of deep vein thrombosis in operations taking 3 or more hours.25 Given that the incidence of venous thromboembolism is proportional to surgical duration, operations are scored 1 to 5 depending on the length of surgery. The above scoring system is especially applicable in plastic surgery, where patients may undergo lengthy free tissue transfer procedures. Patients with a malignancy have up to a 6-fold increase in the incidence of venous thromboembolism as compared with those without a malignancy, with the risk of venous thromboembolism not disappearing with cancer cure or remission.21 These observations translate into a risk score of 3 for “present cancer” and 2 for a “previous malignancy,” which particularly relates to patients undergoing reconstructive operations for head and neck or breast cancer.

Women on hormonal contraception and replacement therapy also pose a higher venous thromboembolism risk. Overall observational data are consistent with a 3- to 6-fold increase in the risk of venous thromboembolism with oral contraceptive pill use and a 2- to 4-fold increase in risk with hormone replacement therapy.26 Oral contraceptive pills and hormone replacement therapy both contain estrogen, which lowers protein S levels and promotes thrombosis. The risk of venous thromboembolism is highest within the first month of starting hormonal medications and diminishes but does not disappear after the first year. In this risk assessment model, hormone replacement therapy or oral contraceptive pill use earns the patient a risk score of 1. Although definitive studies on the optimal time of hormonal medication discontinuation are lacking, we suggest discontinuation of hormonal medications at least 2 weeks before surgery.

**VENOUS THROMBOEMBOLISM PROPHYLAXIS**

Primary venous thromboprophylaxis is the most useful and cost-effective strategy for reducing the risk of venous thromboembolism in plastic surgery patients. Diagnostic tests for asymptomatic deep vein thrombosis screening remain expensive, impractical, and inaccurate, and waiting for symptoms to develop before taking action gambles with the patient's long-term health. Choice of thromboprophylaxis is based on the 2004 American College of Chest Physicians overall guidelines for each venous thromboembolism risk category24 (Fig. 3). Thromboprophylaxis begins with proper patient positioning on the operating table and early ambulation postoperatively. Flexion of the patient’s knees to approximately 5 degrees will maximize venous return through the popliteal vein. Proper patient positioning and early mobilization are sufficient for patients of low venous thromboembolism risk but must be supplemented with mechanical and/or pharmacologic prophylaxis for patients with more significant venous thromboembolism risk.

**Mechanical**

The 2004 American College of Chest Physicians overall recommendations for surgical patients include the option of mechanical thromboprophylaxis as stand-alone therapy in both moderate and high venous thromboembolism risk groups and as combination therapy with chemoprophylaxis in highest venous thromboembolism risk patients.24 Use of mechanical prophylaxis should begin before the induction of anesthesia, especially if general anesthesia is used, and continue into the postoperative period until the patient is fully mobile.5 Educating nurses about the importance of venous thromboembolism prophylaxis is critical to ensuring compliance with mechanical methods of prevention. Contraindications for mechanical prophylaxis include severe peripheral arterial disease, congestive heart failure, and acute superficial or deep vein thrombosis.

Mechanical methods of thromboprophylaxis, either “passive” or “active,” have been shown to reduce the risk of deep vein thrombosis in a number of patient groups. “Passive” mechanical thromboprophylaxis includes graduated compression stockings, which prevent deep vein thromboses by improving valve function, reducing distention of the vein wall, and increasing venous flow velocity through cross-sectional area reduction. In some reports, use of graduated compression stockings reduced the rate of deep vein thrombosis by approximately 50 to 64 percent in general surgery patients.27 “Active” mechanical methods of thromboprophylaxis include intermittent pneumatic compression devices and venous foot pumps. Deep vein thrombosis prevention is achieved by relieving venous stasis through increased motion of blood and by stimulating fibrinolytic activity through reduction of plasminogen activator-1.28 In a study of face-lift patients, intermittent pneu-
matic compression devices led to a significant decrease in the rate of venous thromboembolism as compared with no thromboprophylaxis (59.2 percent versus 4.1 percent, respectively). In patients with contraindications to lower extremity compression devices, mechanical prophylaxis can be applied to the arm, with adequate reduction in the incidence of venous thromboembolism as reported by Knight and Dawson. The site of active mechanical prophylaxis is not critical, with studies demonstrating a decreased incidence of venous thromboembolism with thigh-high, knee-high, or plantar compression devices.

**Chemoprophylaxis**

The 2004 American College of Chest Physicians overall guidelines provide the option of chemoprophylaxis as stand-alone therapy in moderate, high, and highest venous thromboembolism risk groups or as combination therapy with mechanical prophylaxis in highest venous thromboembolism risk patients. Chemoprophylaxis agents include low-dose unfractionated heparin, low-molecular-weight heparin, fondaparinux, and vitamin K antagonists. Contraindications to chemoprophylaxis include active bleeding, heparin-induced thrombocytopenia, worsening renal insufficiency, coagulopathy, recent

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**Fig. 3.** Venous thromboembolism prophylaxis guidelines. Reprinted from Geerts et al., “Prevention of venous thromboembolism: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy,” *Chest* 126 (3 Suppl.): 338s, 2004, with permission from Elsevier.
intracranial surgery, and lumbar tap or epidural anesthesia within the past 24 hours.

Subcutaneous heparin, in the form of low-dose unfractionated heparin or low-molecular-weight heparin, remains the most-widely used form of chemoprophylaxis. Low-dose unfractionated heparin binds to antithrombin III, leading to inactivation of factors Xa and IIa (thrombin) and disruption of the coagulation cascade. Because of its high affinity for circulating plasma proteins and resultant poor bioavailability, low-dose unfractionated heparin requires more than once-daily dosing. The frequency of low-dose unfractionated heparin administration is affected by the level of venous thromboembolism risk, with low-dose unfractionated heparin dosed at 5000 units twice daily in moderate-risk patients and at 5000 units three times daily in high- and highest-risk patients.

Low-molecular-weight heparin, available as enoxaparin and dalteparin, has become the preferred form of subcutaneous heparin in venous thromboembolism prophylaxis among surgeons. Similar to low-dose unfractionated heparin, low-molecular-weight heparin mediates its effects through binding with antithrombin III; however, it inhibits thrombin to a lesser degree and factor Xa to a greater degree than low-dose unfractionated heparin. Advantages of low-molecular-weight heparin in comparison with low-dose unfractionated heparin include increased bioavailability (90 percent versus 30 to 40 percent, respectively) leading to once-daily dosing, superior efficacy in venous thromboembolism prevention, less bleeding if used at lower but equally efficacious dosages, and decreased frequency of heparin-induced thrombocytopenia (0 percent versus 2.7 percent, respectively). Dosage of low-molecular-weight heparin is affected by the level of venous thromboembolism risk. Low-molecular-weight heparin should be dosed at less than 3400 units once daily for moderate-risk patients and at greater than 3400 units once daily for high- and highest-risk patients.

Fondaparinux, a short-acting synthetic pentasaccharide, is a recently approved chemoprophylaxis agent that indirectly inhibits factor Xa. It is usually dosed at 2.5 mg subcutaneously once daily. In comparing fondaparinux with low-molecular-weight heparin, studies have found mixed results. Meta-analysis of three major orthopedic studies showed a 55.2 percent reduction in venous thromboembolism with a similar rate of bleeding when comparing fondaparinux to low-molecular-weight heparin (enoxaparin). In contrast, rates of venous thromboembolism and bleeding were equivalent for abdominal surgery patients on postoperative fondaparinux versus perioperative low-molecular-weight heparin (dalteparin).

Oral vitamin K antagonists, such as warfarin, are recommended for highest risk patients and are titrated to an international normalized ratio goal of 2 to 3. Through inhibition of vitamin K–dependent clotting factor (II, VII, IX, X) synthesis, vitamin K antagonists disrupt the coagulation cascade. Given the delayed onset of action, daily monitoring, drug-drug interactions, and significantly lower efficacy in venous thromboembolism prevention in comparison with low-molecular-weight heparin, vitamin K antagonists are not considered a first-line agent in thromboprophylaxis.

If long-term (3 months of longer) thromboprophylaxis is necessary, however, patients may be transitioned from other regimens of chemoprophylaxis to oral vitamin K antagonists.

Optimal timing of chemoprophylaxis remains controversial. Aggregate evidence from clinical research on low-molecular-weight heparin supports the concept that administering the first dose 12 hours preoperatively is too early, that giving the first dose 12 or more hours postoperatively is probably too late for optimal effectiveness, and that administering the first dose 2 hours postoperatively results in increased bleeding without improved efficacy as compared with giving the first dose 6 hours postoperatively. Additional studies are needed to compare different times of postoperative low-molecular-weight heparin initiation to definitively determine the optimal timing of the first dose. Regarding fondaparinux, a recent study on its use in thromboprophylaxis reported an increased rate of bleeding with equivalent efficacy in orthopedic patients receiving a first dose 6 to 8 hours postoperatively versus patients receiving a first dose 24 hours postoperatively. In response, some have advocated starting fondaparinux the morning after surgery.

Duration of chemoprophylaxis is a function of a patient’s venous thromboembolism risk category and ambulatory status. In general, thromboprophylaxis should continue until the risk of an acute postoperative venous thromboembolism has been mitigated and then until the patient is fully ambulatory. The most common practice is to continue thromboprophylaxis for 5 to 10 days after surgery. Some studies have stressed a month-long duration of thromboprophylaxis for highest venous thromboembolism risk patients. In a study of orthopedic hip fracture patients, extended-duration (30 to 35 days) low-molecular-weight heparin chemoprophylaxis was more effective in ve-
nous thromboembolism prevention than a 7- to 10-day course. These findings are not unexpected, considering that the risk of venous thromboembolism is highest within the first 2 weeks after surgery. Additional studies are needed to compare the efficacy of various durations of thromboprophylaxis within different venous thromboembolism risk categories.

CONCLUSIONS

Given the devastating morbidity and mortality associated with venous thromboembolism and the inaccuracy and expense of screening modalities, venous thromboembolism prevention should be the goal in plastic surgery patients. We recommend an individualized assessment of thrombotic risk, based on a patient’s set of predisposing and exposing risk factors. Patients are stratified into low, moderate, high, or highest venous thromboembolism risk, depending on the total risk factor score. Based on the 2004 American College of Chest Physicians overall guidelines for surgical patients, a thromboprophylaxis regimen is selected for the appropriate venous thromboembolism risk category. Proper patient positioning and early ambulation are recommended for low venous thromboembolism risk patients. Either mechanical prophylaxis or chemoprophylaxis may be used in moderate or high venous thromboembolism risk patients. Chemoprophylaxis is necessary as stand-alone or as combination therapy with mechanical prophylaxis in highest venous thromboembolism risk patients. Optimal timing and duration of chemoprophylaxis is controversial and warrants further clinical trials.

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