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Reconsidering the Role of Routine Anticoagulation for Venous Thromboembolism Prevention in Plastic Surgery

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Today, many plastic surgeons prescribe routine anticoagulation ("chemoprophylaxis") in an effort to reduce venous thromboembolism (VTE) risk in plastic surgery patients.[1–4] Anticoagulation has an appeal because it seems to make sense. However, its efficacy and safety have been challenged.[5–10]

New oral factor Xa inhibitors such as rivaroxaban (Xarelto; Janssen Pharmaceuticals, Titusville, NJ) and apixaban (Eliquis; Bristol-Myers Squibb, New York, NY) are often prescribed because they do not require injections.[2,3] However, oral anticoagulants have not been shown to be effective in reducing VTE risk in plastic surgery patients.[9] Dini et al[11] terminated their prospective randomized study of chemoprophylaxis because of an alarming rate of hematomas in abdominoplasty patients who received rivaroxaban. Patronella[12] discontinued using rivaroxaban after experiencing a 2.8% hematoma rate. Hunstad et al[3] reported 3 hematomas requiring evacuation among 132 patients (2.3%), excluding 2 hematomas that were evacuated before the patients received rivaroxaban. By contrast, in my own study of 167 consecutive abdominoplasties treated with no chemoprophylaxis, there were no hematomas.[13] Both the series reported by Hunstad et al[3] and my own identified 1 known VTE (0.76% and 0.60%, respectively).[3,13] Although its use is approved in patients undergoing knee or hip replacement, rivaroxaban is not approved by the US Food and Drug Administration (FDA) for deep venous thrombosis prophylaxis in plastic surgery.[14]

In a recently published study, Sarhaddi et al[4] conclude that fondaparinux reduces the risk of VTE without increasing the risk of bleeding. In a retrospective chart review, the authors compared 2 historical groups of abdominoplasty patients. The first group treated between 2008 and 2011 (n = 233) did not receive chemoprophylaxis. The second group treated between 2011 and 2014 (n = 259) were prescribed fondaparinux. There were 5 VTEs in the untreated group and zero in the treated group. A χ^2 test determined a significant difference ($P = 0.02$).[4] However, the study is limited by a small study population. Group sizes of just over 200 patients are small when examining a complication that typically occurs at a rate of less than 1%.[15]

A limitation of a retrospective study design is that it allows the investigator to choose the time periods for the study, inviting selection bias. Moreover, a traditional χ^2 test loses reliability when the cell sizes are fewer than 5.[16] Some statisticians use a Yates correction when the expected frequency is fewer than 10.[17,18] (In the study by Sarhaddi et al,[4] 2 of the 4 group sizes were 0 and 5.) This correction is recommended to reduce the risk of a type I statistical error (ie, concluding that a real difference exists when it does not).[16–18] When a Yates correction is used, the *P* value becomes 0.055.[16] The Yates correction is not universally accepted, and some statisticians believe it may be too rigorous,[18] but this issue underscores the weakness of the comparison.

In the study by Sarhaddi et al,[4] several of the VTEs were diagnosed at time points well beyond the 1-week period of anticoagulation. It is not clear that anticoagulation that stops 1 week after surgery will prevent VTEs that develop later. A therapeutic benefit is unlikely. Deep venous thromboses that develop after plastic surgery take 5 weeks on average to resolve with treatment.[19] Another limitation of this study is the fact that the true rate of deep venous thromboses is unknown because Doppler ultrasound screening was not done. Clinical signs of VTE are notoriously unreliable.[19]

Shaikh et al[20] were surprised to find that none of their 36 "highest risk" patients with Caprini scores of greater than 10 developed a VTE. A 2016 meta-analysis by Pannucci et al[21] found that chemoprophylaxis did not significantly reduce VTEs in plastic surgery patients with Caprini scores of greater than 8.[21] Moreover, the bleeding risk was increased. Pannucci et al[21] recommend against adding routine chemoprophylaxis to intermittent pneumatic compression for VTE prophylaxis in non–risk-stratified plastic surgery patients.

Other investigators have reported VTEs despite anticoagulation.[22,23] Hatef et al[22] reported a 5% incidence of VTE after abdominoplasty despite administering enoxaparin in high-risk patients, plus an increased risk of bleeding. Jeong et al[23] reported 19 VTEs among 574 plastic surgery patients who received chemoprophylaxis (3.3%) versus only 5 VTEs among 1024 patients who did not receive chemoprophylaxis (0.5%). This difference, favoring the *untreated* patients, is highly significant ($P < 0.00001$).[19]

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Hematomas are not inconsequential.[11] Blood transfusions should rarely be needed for cosmetic surgery patients. In the study reported by Sarhaddi et al,[4] blood transfusions were required for 2 anticoagulated patients versus none in the untreated group. One patient's hemoglobin dropped to 4.4 g/dL, and she required a transfusion of 4 units of packed red blood cells in the emergency department.[4] This close call serves as a red flag, quite literally. The loss of a single life from bleeding is unacceptable if the patient was unlikely to develop a VTE in the first place, the efficacy of chemoprophylaxis is questionable, a reversal agent is unavailable, and safe alternative VTE risk reduction methods exist.[6,19,24]

Fondaparinux is a particularly questionable choice because it requires injection, unlike rivaroxaban and apixaban, and does not have an antidote.[1] The lack of a reversal agent is an important difference from other anticoagulants such as heparin, enoxaparin, warfarin, and (recently) rivaroxaban and apixaban that do have antidotes (protamine sulfate, vitamin K, and andexanet alfa, respectively). Similar to other anticoagulants, this medication is not approved by the FDA for VTE prophylaxis in plastic surgery patients. Fondaparinux is approved for VTE prophylaxis only in orthopedic and general surgery patients judged to be at high risk of VTE.[25] The use of anticoagulants in plastic surgery to prevent VTEs is therefore off-label. Unlike other factor Xa inhibitors such as enoxaparin, rivaroxaban, and apixaban, fondaparinux is not indicated for the treatment of acute deep venous thrombosis or pulmonary embolism unless accompanied by warfarin.[25] Plastic surgeons need to be aware of the specific indications and regulatory status of these anticoagulants and the potential for liability in patients who develop bleeding. Plaintiff attorneys are actively soliciting patients who have experienced bleeding complications.[26] A Google search is sobering.

A problem with using Caprini scores in a retrospective study[1,4] is that it is unlikely that the charts contain the information for all 40 factors. Therefore, such studies underestimate the actual Caprini scores.[27] Keyes et al[15] found Caprini scores unhelpful because 67.5% of VTEs after outpatient abdominoplasties occurred in patients with Caprini scores of 5 or less. Pannucci[28] recently concluded that the vast majority of aesthetic surgery patients do not require chemoprophylaxis.

Some plastic surgeons believe that flexing the operating table, rectus fascia plication, Scarpa fascia repair, skin closure, and applying an abdominal binder increase VTE risk.[4] A large study using ultrasound screening in abdominoplasty patients treated with fascial plication and hip flexion in surgery suggests otherwise.[19] Only 1 of 188 consecutive abdominoplasty patients (0.5%) was found to have a deep venous thrombosis on an ultrasound scan performed the day after surgery. In this patient, a congenital vascular anomaly causing compression of the left common iliac vein was discovered. A unique controlled study by Huang et al,[29] comparing intra-abdominal (actually intravesicular) pressures between abdominoplasty patients and breast reduction control patients, found no significant difference in pressures at all time points studied before, during, and after surgery. There is no evidence that Scarpa fascia repair, skin closure, or the garment increases VTE risk.

Pannucci et al[30] believe that patients experiencing VTEs despite chemoprophylaxis represent "breakthrough" cases caused by inadequate anticoagulation. This conclusion is undermined by a flawed study design.[31] One cannot compare 90-day VTE risk by anti–factor Xa levels while simultaneously giving extra enoxaparin to patients with low levels. Higher doses for these individuals would theoretically remedy the low anti–factor Xa blood levels. Two studies would be needed, one to compare VTE risk by anti–factor Xa level and another to evaluate whether extra doses reduce risk. Otherwise, one could just as reasonably conclude that higher enoxaparin doses, not lower anti–factor Xa levels, increase the VTE risk. Moreover, the findings do not support the efficacy of additional dosing: all 5 VTEs (5/49, 10.2%) occurred in the group that received higher doses of enoxaparin.[30]

Importantly, 3 of the 5 VTEs in the study by Pannucci et al[30] supporting extra enoxaparin doses were upper-extremity thromboses in patients with central catheters. These secondary thromboses have a different etiology (foreign body and intimal trauma) related to the catheter,[32] as opposed to venous stasis and valvular hypoxia.[33] The VTE literature typically evaluates primary VTEs that originate in the lower extremities.[34,35] Excluding the upper-extremity thromboses, the 2.1% frequency (2/94) of VTE is similar to the 1.2% incidence (same for control and anticoagulated patients) among 3334 plastic surgery inpatients previously reported in the VTE Prevention study.[1] A small sample size (n = 94) precludes any meaningful comparisons. Confounding variables include diagnosis (particularly cancer), procedure, anesthesia method, body mass index, central catheters, immobilization, length of hospitalization, and duration of enoxaparin administration (range, 1–40 days).[30]

The FDA approves enoxaparin for VTE prophylaxis only in high-risk general surgery and joint replacement patients.[36] The recommended daily dose is 30 or 40 mg.[37] A dosing schedule of 40 mg twice a day, double the usual prophylactic dose, produces an alarming 6.8% rate of clinically relevant bleeding.[38] Thirty percent of patients receiving 40 mg of enoxaparin twice daily are overanticoagulated, as indicated by anti–factor Xa levels, and these patients are likely to suffer more bleeding, returns to the operating room, blood transfusions, and death.[39]

Testing for anti–factor Xa levels requires additional expense and inconvenience[30] but provides no diagnostic information regarding VTEs.[31] Pannucci et al[30] dismiss ultrasound screening, referencing the 2012 American College of Chest Physicians guidelines.[34] This low-grade (2C) recommendation was made for general and abdominal-pelvic surgery patients.[34] A grade 2C recommendation is considered a "weak recommendation, low- or very-low-quality evidence."[40] A grade 2C recommendation means that "other alternatives may be equally reasonable, and higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate."[40] That new evidence, obtained from ultrasound scans in 1000 consecutive plastic surgery outpatients, is now available.[19] This level II evidence replaces a weak recommendation with a strong (grade 1C) one.[19]

Ultrasound technology is quickly finding new applications in plastic surgery.[41] A point-of-care diagnosis expedites patient management.[41] Reliance on limb swelling is dangerous. Ten percent of symptomatic pulmonary embolisms present with sudden death.[35] Ultrasound surveillance removes the guesswork inherent in any risk prediction model by accurately detecting thromboses after surgery.[19,24,41,42] Patient surveys show that 93% of patients prefer ultrasound surveillance to anticoagulation.[41] The rate of hematomas among 188 abdominoplasty patients in a recent study of outpatients who did not receive chemoprophylaxis was zero.[19] These patients received total intravenous anesthesia without muscle paralysis and were monitored with ultrasound scans.[19] By contrast, published hematoma rates in anticoagulated abdominoplasty patients can be much higher.[11,12,22,43] One recent study reported 64 hematomas among 1128 anticoagulated abdominoplasty patients (5.7%).[43] Hematomas should not be considered an acceptable trade for a VTE, particularly if a VTE can be identified early in its development, when it is not dangerous, and managed with minimal disruption to the patient's activities and recovery.[10,19] Hematomas are distressing to patients and surgeons.[11]

The ideal solution would be a method to detect deep venous thromboses reliably before they propagate and potentially cause a fatal pulmonary embolism, obviating the need for a risk prediction model and eliminating unnecessary bleeding caused by routine anticoagulation. Such a solution is already available.[19,24,41,42] This technology has been shown to be effective, safe, and feasible for plastic surgeons.[19,24,41,42]

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