

# Chemoprophylaxis for Venous Thromboembolism Prevention: Concerns Regarding Efficacy and Ethics

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**Summary:** Chemoprophylaxis has been recommended for plastic surgery patients judged to be at increased risk for venous thromboembolism. Several investigators have encountered this complication in patients despite anticoagulation therapy. An increased rate of complications related to postoperative bleeding has been reported. This article examines the efficacy and safety of this intervention, along with ethical considerations, in an attempt to determine whether any benefits of chemoprophylaxis justify the additional risks. The statistical methods and conclusion of the Venous Thromboembolism Prevention Study are challenged. Other preventative measures that do not cause negative side effects are discussed as safer alternatives. (*PRS GO 2013;1:e23; doi:10.1097/GOX.0b013e318299fa26; Published online 20 June 2013.*)

Chemoprophylaxis for thromboembolism is a controversial topic in plastic surgery today. Surveys reveal a reluctance among plastic surgeons to adopt anticoagulation in their practices.<sup>1</sup> Proponents ask, which problem would you rather treat, a hematoma or a thromboembolism?<sup>2,3</sup>

Efforts to reduce the risk of venous thromboembolism are understandable. The seriousness of this complication is unquestioned. Why then the reluctance to incorporate chemoprophylaxis in one's practice? The issue is not just medical, but ethical. Despite the ethical principles at stake, there has been no discussion of them in our literature. We would do well to submit this issue to a critical analysis that includes ethical considerations.<sup>4</sup>

The dilemma is a classic example of the double-effect principle—the intervention is both good and bad. This ethical conundrum is hardly new or specific to plastic surgery. It was first considered by Thom-

as Aquinas.<sup>5</sup> The ethical criteria are summarized as follows<sup>6</sup>:

1. That the action in itself from its very object be good or at least indifferent.
2. That the good effect and not the evil effect be intended.
3. That the good effect be not produced by means of the evil effect.
4. That there be a proportionately grave reason for permitting the evil effect.

To be morally justified, these conditions must be met. An example is the use of vaccines. A vaccine would never be approved if as many people died from the side effects as were saved by prevention of the targeted disease.

## THAT THE ACTION IN ITSELF BE GOOD

First, the benefit must be clear. Perhaps surprisingly, this bar has not been met conclusively for plastic surgery outpatients. Guidelines provided by the American College of Chest Physicians cannot be reliably extrapolated to plastic surgery because of the differences in patient characteristics, presence of serious diseases, and types of surgery (W.H. Geerts, personal communication, April 16, 2013).<sup>7</sup> Plastic surgery pa-

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tients, particularly those undergoing elective cosmetic surgery, are predominantly healthy outpatients without disease processes or cancer diagnoses.

Not only are our patients different, but their anesthetic requirements are different too (or should be).<sup>8</sup> A laparoscopic cholecystectomy requires insufflation of the abdomen with carbon dioxide and positive pressure ventilation (mandating paralysis) using an endotracheal tube. This is not the case for elective plastic surgery outpatients. Even abdominoplasties may be performed under total intravenous anesthesia with spontaneous breathing and without muscle relaxation.<sup>8</sup>

A multicenter study funded by the Plastic Surgery Foundation compared the frequency of thromboembolism among 1458 inpatients undergoing primarily reconstructive surgery under general anesthesia who received postoperative enoxaparin with the frequency of thromboembolism among a control group of 1876 inpatients who did not receive this intervention. The findings were published in the journal *Plastic and Reconstructive Surgery* in 2011.<sup>9</sup> This study represents the only evaluation of anticoagulation and thromboembolism risk in a large number of plastic surgery patients, and it merits careful consideration. Pannucci et al. conclude that chemoprophylaxis reduces the incidence of this complication among patients deemed to be at higher risk according to their Caprini score, which assigns points based on risk factors for thromboembolism.<sup>10</sup> In patients with moderate scores, in the range of 3–6, there was no benefit from the intervention. In patients with risk scores of 7 or greater, the incidence of thromboembolism was lower in the treatment groups, but the differences were nonsignificant.

The finding that the differences were nonsignificant even in the higher risk categories is at odds with the study conclusion and title.<sup>9</sup> There were 42 cases of thromboembolism among all 3334 study patients. Surprisingly, the number of cases of thromboembolism in the treatment and control groups—arguably the two most important numbers in the study—are not to be found anywhere in the article or tables and must be calculated from the authors' Figures 2 and 3 by summing percentages. My calculations based on these percentages reveal that there were 18 cases of this complication among patients given enoxaparin and 24 among controls, yielding the same 1.2% incidence of thromboembolism in each group. How then do the authors determine a benefit from the intervention?

The authors find an overall treatment benefit by adjusting their data for Caprini score and length of hospitalization, which the authors determined to

be an independent risk factor for venous thromboembolism.<sup>9</sup> The authors contend that patients with longer hospitalizations are likely to be sicker. This premise may be true, although these patients would have also benefitted from a longer period of prophylaxis because the enoxaparin was continued for the duration of hospitalization. From a statistical perspective, it is not clear that the very small number of patients in the hospital stay subgroups justify this conclusion. Length of hospitalization is not one of the risk factors recognized by the Caprini model. In fact, Caprini points out that patients may remain recumbent at home after discharge from hospital.<sup>10</sup> Regardless, even accepting the authors' adjustments of their data, the overall *P* value was a modest 0.042, just within the bounds of a 0.05 level of significance, a level that would not have been reached without these adjustments. Despite the data adjustment, the differences for the higher risk patient subgroups remain nonsignificant (*P* = 0.182 and 0.230).

The authors' Figure 3 is the crux of their article. This bar graph shows a much higher bar for the highest Caprini > 8 control group than for the intervention group.<sup>9</sup> At first glance, this bar graph seems to indicate a greater rate of thromboembolism among untreated highest risk patients. However, when one considers actual numbers rather than percentages, the difference is much less impressive. Converting percentages to numbers reveals that there were 6.41 control patients with this complication vs 4.75 patients who developed thromboembolism despite anticoagulation (data adjustment evidently accounts for the non-whole numbers).

The authors use an  $\alpha$  level of 0.05, without correcting for multiple statistical comparisons. In this situation, many investigators prefer an  $\alpha$  level of 0.01. It is well known that repeating *t* tests without such a correction is liable to turn up false positives, creating type I errors. When the revised 2010 Caprini scoring values<sup>11</sup> are substituted for the 2005 values,<sup>10</sup> additional patients are added to the higher risk categories and the difference in complication rates among highest risk patients (already nonsignificant using the 2005 scores) is reduced. The authors do not question the basis for these changes, which they acknowledge as improvements.<sup>12</sup> Regardless, the same study and the same data, using either the 2005 or 2010 Caprini Risk Assessment Models, support a conclusion that chemoprophylaxis is ineffective in preventing thromboembolism even among hospitalized high-risk patients.

According to Dr. William Geerts (personal communication, April 16, 2013), who chaired the Prevention of Venous Thromboembolism section of the American College of Chest Physicians Consen-

sus Group on Antithrombotic Therapy and was the lead author of the widely referenced 2004 and 2008 American College of Chest Physicians guidelines, the study by Pannucci et al. “cannot be recommended as a general set of guidelines for plastic surgery outpatients.” Geerts adds, “although there is some evidence about risk factors across the board (age, cancer, immobility), the weight of each risk factor depends on the clinical context.” Geerts recommends no chemoprophylaxis for this group of outpatients having elective plastic surgery, regardless of their Caprini score, which he cautions is only partially validated. He does not find the Caprini score clinically useful and does not support individual risk stratification. Caprini<sup>10,11</sup> concedes that the basis for his scoring system includes nonscientific factors such as intuition, logic, emotion, and experience.

Clinical experience reveals a lack of efficacy. Hatef et al.<sup>13</sup> report a 5% incidence of venous thromboembolism after abdominoplasty despite the use of enoxaparin (including preoperatively) in high-risk patients. Another study reports 3 cases of thromboembolism, all occurring in patients receiving chemoprophylaxis.<sup>14</sup> The appropriate timing and duration of such prophylactic treatment in plastic surgery patients are not clear either.<sup>9</sup> It makes sense that such an intervention would be ineffective if venous clots originate after the period of anticoagulation.

### THAT THE GOOD EFFECT AND NOT THE EVIL EFFECT BE INTENDED

How well does prophylactic anticoagulation satisfy this criterion? Pannucci et al.<sup>15</sup> separately report a hematoma rate of 3.38% among treated patients vs 2.65% for controls and find no significant difference ( $P = 0.169$ ). This nonsignificant  $P$  value was in fact lower than the  $P$  values used by the same authors to determine a reduction in thromboembolism risk.<sup>9</sup> Their conclusion that “the absolute differences in reoperative hematoma rates when stratified by receipt of postoperative enoxaparin are small and likely irrelevant to everyday clinical practice”<sup>15</sup> could just as easily be applied to their study of thromboembolism rates with or without enoxaparin.

Serious side effects have been reported by other investigators, including study participants.<sup>13,16</sup> Bleeding, hematomas, operating times, and blood transfusions are all significantly increased by enoxaparin.<sup>13,16</sup> One recent randomized study had to be stopped before it could be completed because of a startling number of hematomas and wound dehiscences after abdominoplasty, all occurring in the anticoagulated patients.<sup>16</sup> Such occurrences are not surprising. Side effects of enoxaparin include

wound hematomas (11%) and drug-induced thrombocytopenia (1.5%).<sup>17</sup> Clearly, chemoprophylaxis is not without serious risk as once thought.<sup>3</sup> Safety concerns are justified. Plastic surgeons’ reluctance to adopt this intervention should not be deemed inadequate or mistaken for a lack of clinical understanding.<sup>9</sup>

It is one thing for a natural adverse event to take place; it is quite another to substitute it with one that is iatrogenic. Venous thromboembolism is a known risk even without surgery. A pulmonary embolus may be viewed as an act of God, impossible to reliably predict or to completely avoid. On the other hand, bleeding from anticoagulation may be attributed to a specific intervention ordered by the surgeon to paradoxically impair a normal coagulation system in a patient who is going to need it. Moreover, many patients are at home when bleeding from anticoagulation develops.<sup>16</sup> Is it safe to leave a postsurgical patient at risk for sudden bleeding in such an unmonitored setting?

The indications for anticoagulation will always be relative and experts will disagree. There is an emerging opinion that anticoagulation in plastic surgery is part of the standard of care. It is not difficult to imagine a plastic surgeon having to defend *not using* chemoprophylaxis in a patient who develops thromboembolism or, on the other hand, defending *using* anticoagulation in a patient who suffers the consequences of excessive bleeding. The medicolegal climate is difficult enough without adding this intervention (and a perceived failure to intervene) to our liability risk.

### THAT THE GOOD EFFECT BE NOT PRODUCED BY MEANS OF THE EVIL EFFECT

Anticoagulation does not fully satisfy the third criterion for ethical care in that the good effect (theoretically dissolving blood clots forming in the thigh veins) relies on an evil effect (indiscriminately dissolving blood clots, including in the operative field). This situation is different from a vaccine, in which the beneficial effect does not rely upon the negative effect.

Chemoprophylaxis does not target Virchow’s triad of factors that are linked to the formation of a deep venous thrombosis.<sup>18</sup> Enoxaparin dissolves existing clots or clots that are forming and the hope is that it will do so in the thigh veins, not just the operative field. In this sense, it is a therapeutic measure (and a nonselective one), not a strictly prophylactic measure.

## THAT THERE BE A PROPORTIONATELY GRAVE REASON FOR PERMITTING THE EVIL EFFECT

Although proponents suggest that bleeding is the lesser of two evils,<sup>2,3</sup> the trade-off in risks is far from assuredly favorable. Chemoprophylaxis invites new problems for patients that were never going to suffer a deep venous thrombosis anyway, challenging the basic rule of *primum non nocere*. The consequences of postoperative bleeding and hematomas should not be discounted. These are major problems that can drastically alter the surgical outcome and the patient–physician relationship. Hematomas do not contribute to a successful elective plastic surgery practice. Of course, bleeding can represent more than a temporary nuisance; it can be life-threatening. Blood transfusions should rarely be necessary for cosmetic surgery patients. Postoperative anemia is a common cause of morbidity. Our objective should be to reduce this problem,<sup>8</sup> not to exacerbate it.

## SAFE PREVENTION OF THROMBOEMBOLISM

The conscientious plastic surgeon may ask, if we do not give chemoprophylaxis, what can we do to minimize risk? Fortunately, there are much safer ways to reduce the risk of this complication,<sup>7,8,19–25</sup> and ones that are aimed at the root of the problem—venous stasis. Perhaps surprisingly, the effectiveness of sequential compression devices is controversial. A meta-analysis supports their use,<sup>26</sup> although the reliability of the data is open to question (W.H. Geerts, personal communication, April 16, 2013). However, this widely used measure poses no serious risks.

Notably, many investigators using total intravenous anesthesia, including myself, report very low rates of thromboembolism<sup>8,19–21</sup>; some surgeons report no cases at all in very large (ie, 4000 to over 30,000 cases) series of patients that include abdominoplasties and face lifts.<sup>22–25</sup> One German survey of serious complications found that all 8 liposuction fatalities from pulmonary emboli occurred in patients administered general anesthesia.<sup>27</sup> There may be a physical basis for these findings. Avoidance of muscle relaxation may reduce blood pooling in the lower extremities.<sup>24,25</sup> This is a physiologic argument that has not been clinically proven (W.H. Geerts, personal communication, April 16, 2013). However, such large patient series with exceptionally low rates of thromboembolism<sup>19–25</sup> constitute empirical evidence pointing to additional risk from traditional general endotracheal anesthesia and should not be dismissed (W.H. Geerts, personal communication, April 16, 2013).

The transition to total intravenous anesthesia need not represent a major change in practice. An unconscious anesthetic still requires the attendance of an anesthesiologist or certified nurse anesthetist.<sup>8</sup> Avoidance of prone positioning, which eliminates pelvic pressure that might impair venous return<sup>13</sup> and intraoperative movement of the lower extremities, may also be helpful in reducing risk.<sup>7,8</sup> Circumferential liposuction may be performed just as effectively from lateral positions.<sup>8</sup> Massive weight loss patients are likely to need a second operation anyway, so that staging belt lipectomies, a procedure known to increase risk,<sup>13</sup> is not a major impediment for patients and is likely to reduce morbidity from postoperative anemia.

Proponents of chemoprophylaxis may ask for controlled studies demonstrating the benefits of total intravenous anesthesia.<sup>2</sup> Admittedly, none is available. Such a study would be (1) impractical because of the large number of patients needed (especially with complication rates of <1%) and reluctance of surgeons to vary their surgical and anesthetic methods (using different surgeons would involve too many confounding variables) and (2) possibly unethical because of the other known safety advantages of total intravenous anesthesia. For example, it may be difficult to justify the use of a muscle relaxant triggering a case of malignant hyperthermia if a safe alternative is available.

Of course, we are told that treatment is to be individualized,<sup>11,28</sup> but such a recommendation may be difficult to reconcile with an algorithm or scoring system that is meant to group patients together in categories with a view to assigning a treatment.<sup>28,29</sup> Many cases of thromboembolism occur in patients with moderate risk scores.<sup>9,14,21</sup> Notably, the 2012 guidelines of the American College of Chest Physicians have been downgraded to include aspirin as an alternative to low-molecular-weight heparin prophylaxis in orthopedic surgery.<sup>30</sup> When asked whether one would prefer to treat a thromboembolism or a hematoma,<sup>2,3</sup> the well-informed plastic surgeon will respond, “neither.”

After encountering a series of complications from anticoagulation, Dini et al.<sup>16</sup> conclude that the only alternative may be to recommend against surgery in some patients. As plastic surgeons, it is hoped that we can provide a safer surgical option, with full involvement of the patient who is properly informed regarding risks and the precautions that are taken to reduce them. Patients are aware of blood clots and they respond well to such frank discussions. A decision to use anticoagulants may still be justified in selected cases. Patients appreciate the surgeon’s candor and concern, and the discussion only builds their confidence in their surgeon.



## CONCLUSIONS

The evidence speaks against a recommendation of chemoprophylaxis among plastic surgery patients based on a risk scoring system. There are substantial risks in using prophylactic anticoagulation. Plastic surgeons should not feel compelled to recommend anticoagulation based solely on a Caprini score. Other preventative measures are logical, consistent with our understanding of the pathophysiology of thromboembolism, ethical, and, most importantly, invite no new risk. *Safely* reducing the number of patients who suffer venous thromboembolism is clearly in our patients' interest and in ours.

*Don't be evil.*

—Google

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## REFERENCES

- Clavijo-Alvarez JA, Pannucci CJ, Oppenheimer AJ, et al. Prevention of venous thromboembolism in body contouring surgery: a national survey of 596 ASPS surgeons. *Ann Plast Surg.* 2011;66:228–232.
- Pannucci CJ. Reply: reducing venous thromboembolism risk without chemoprophylaxis. *Plast Reconstr Surg.* 2013;131:451e–452e.
- Young VL, Watson ME. The need for venous thromboembolism (VTE) prophylaxis in plastic surgery. *Aesthet Surg J.* 2006;26:157–175.
- Chung KC, Pushman AG, Bellfi LT. A systematic review of ethical principles in the plastic surgery literature. *Plast Reconstr Surg.* 2009;124:1711–1718.
- Doctrine of double effect. Available at: <http://plato.stanford.edu/entries/double-effect>. Accessed March 5, 2013.
- Mangan JT. An historical analysis of the principle of double effect. *Theol Stud.* 1949;10:40–61.
- Swanson E. Reducing venous thromboembolism risk without chemoprophylaxis. *Plast Reconstr Surg.* 2013;131:450e–451e.
- Swanson E. Prospective study of lidocaine, bupivacaine, and epinephrine levels and blood loss in patients undergoing liposuction and abdominoplasty. *Plast Reconstr Surg.* 2012;130:702–722; discussion 723–725.
- Pannucci CJ, Dreszer G, Wachtman CF, et al. Postoperative enoxaparin prevents symptomatic venous thromboembolism in high-risk plastic surgery patients. *Plast Reconstr Surg.* 2011;128:1093–1103.
- Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon.* 2005;51:70–78.
- Caprini JA. Risk assessment as a guide to thrombosis prophylaxis. *Curr Opin Pulm Med.* 2010;16:448–452.
- Pannucci CJ, Barta RJ, Portschy PR, et al. Assessment of postoperative venous thromboembolism risk in plastic surgery patients using the 2005 and 2010 Caprini Risk score. *Plast Reconstr Surg.* 2012;130:343–353.
- Hatef DA, Kenkel JM, Nguyen MQ, et al. Thromboembolic risk assessment and the efficacy of enoxaparin prophylaxis in excisional body contouring surgery. *Plast Reconstr Surg.* 2008;122:269–279.
- Murphy RX Jr, Peterson EA, Adkinson JM, et al. Plastic surgeon compliance with national safety initiatives: clinical outcomes and “never events”. *Plast Reconstr Surg.* 2010;126:653–656.
- Pannucci CJ, Wachtman CF, Dreszer G, et al. The effect of postoperative enoxaparin on risk for reoperative hematoma. *Plast Reconstr Surg.* 2012;129:160–168.
- Dini GM, Ferreira MC, Albuquerque LG, et al. How safe is thromboprophylaxis in abdominoplasty? *Plast Reconstr Surg.* 2012;130:851e–857e.
- Enoxaparin Side Effects. Available at: <http://www.drugs.com/sfx/enoxaparin-side-effects.html>. Accessed April 17, 2013.
- Lowe GD. Virchow's triad revisited: abnormal flow. *Pathophysiol Haemost Thromb.* 2003;33:455–457.
- Reinisch JF, Bresnick SD, Walker JW, et al. Deep venous thrombosis and pulmonary embolus after face lift: a study of incidence and prophylaxis. *Plast Reconstr Surg.* 2001;107:1570–1575; discussion 1576–1577.
- Friedberg BL. Lethal pulmonary embolisms are avoidable. *Plast Reconstr Surg.* 2009;123:768.
- Somogyi RB, Ahmad J, Shih JG, et al. Venous thromboembolism in abdominoplasty: a comprehensive approach to lower procedural risk. *Aesthet Surg J.* 2012;32:322–329.
- Stuzin JM, Baker TJ, Baker TM. Deep venous thrombosis and pulmonary embolus after face lift: a study of incidence and prophylaxis (Discussion). *Plast Reconstr Surg.* 2001;107:1576–1577.
- Bitar G, Mullis W, Jacobs W, et al. Safety and efficacy of office-based surgery with monitored anesthesia care/sedation in 4778 consecutive plastic surgery procedures. *Plast Reconstr Surg.* 2003;111:150–156; discussion 157–158.
- Ersek RA. Dissociative anesthesia for safety's sake: ketamine and diazepam—a 35-year personal experience. *Plast Reconstr Surg.* 2004;113:1955–1959.
- Mustoe TA, Buck DW II, Lalonde DH. The safe management of anesthesia, sedation, and pain in plastic surgery. *Plast Reconstr Surg.* 2010;126:165e–176e.
- Urbankova J, Quiroz R, Kucher N, et al. Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients. *Thromb Haemost.* 2005;94:1181–1185.
- Lehnhardt M, Homann HH, Daigeler A, et al. Major and lethal complications of liposuction: a review of 72 cases in Germany between 1998 and 2002. *Plast Reconstr Surg.* 2008;121:396e–403e.
- Davison SP, Venturi ML, Attinger CE, et al. Prevention of venous thromboembolism in the plastic surgery patient. *Plast Reconstr Surg.* 2004;114:43E–51E.
- Murphy RX Jr, Alderman A, Gutowski K, et al. Evidence-based practices for thromboembolism prevention: summary of the ASPS Venous Thromboembolism Task Force Report. *Plast Reconstr Surg.* 2012;130:168e–175e.
- American College of Chest Physicians Antithrombotic Guidelines, 9th ed. Available at: <http://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/Antithrombotic-Guidelines-9th-Ed>. Accessed April 17, 2013.