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Venous thromboembolism prophylaxis in plastic surgery: state of the art and our approach

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Abstract. – OBJECTIVE: The issue of prevention of thromboembolism in plastic surgery is a rather controversial subject. The actual frequency of VTE among plastic surgery patients is probably higher than we know. Although several studies have shown that chemoprophylaxis likely increases rates of re-operative hematoma by less than one percent, surgeons are strongly resistant to adopting chemoprophylaxis due to the fear of increased bleeding and its complications.

MATERIALS AND METHODS: A literature review was conducted. The 2012 ACCP guidelines suggest the use of the 2005 Caprini score as the most widely used and well-validated individualized risk-stratification tool. We propose a modified 2005 Caprini score, with specific changes pertaining to plastic surgery, in which we combine a patient risk stratification model and a procedure-driven approach explicitly indicating what procedures have to be considered at high or low risk.

RESULTS: The risk of venous thromboembolism in plastic surgery cannot be disregarded. However, the plastic surgery literature still lacks high-level evidence for appropriate means of VTE prophylaxis, although an increasing amount of attention has been paid to the topic. We suggest the development of an international guideline, based on plastic surgical data, using a validated risk assessment model, which combines the surgical risk with the patient related risk.

CONCLUSIONS: Determining the proper venous thromboembolism prophylaxis is a clinical decision that should be made on a patient-to-patient basis. The algorithm presented in this article is meant to simplify this complex problem and to help expedite and clarify the decision-making process.

Key Words:
VTE, Thromboembolism, Plastic surgery, Prophylaxis, Guideline, Venous thromboembolism, Chemoprevention, Risk assessment.

Introduction

Deep venous thrombosis (DVT) is a preventable disease, and if not prevented or treated correctly, it can give rise to a deadly condition known as pulmonary embolism (PE).

Even though DVT is a well-known post-operative complication, few scientific articles evaluate its incidence in plastic surgery. Plastic surgery may stand to benefit from well-formulated guidelines to prevent venous thromboembolism (VTE)[1-4].

Currently, plastic surgeons are reluctant to use prophylaxis for DVT since it is believed to increase the rate of bleeding and its complications[5].

Despite the availability of evidence-based guidelines, there are still some gap areas that need to be filled and evaluated. The present literature review aims to propose a modified 2005 Caprini Score, in which a patient risk stratification model is combined with a procedure-driven approach, explicitly indicating which procedures have to be considered at high or low risk.

Materials and Methods

Primarily we performed a literature review using PubMed, MEDLINE, and Scopus. Search criteria were limited to articles published in English and year of publication from 2003 to 2019. Keywords used to search for the articles were as follows: "thromboembolism prophylaxis", "plastic surgery", and "thromboembolism risk". Qualitative and quantitative studies were used, and all the duplicate articles were removed. After the initial search, titles and abstracts of the articles were thoroughly eval-

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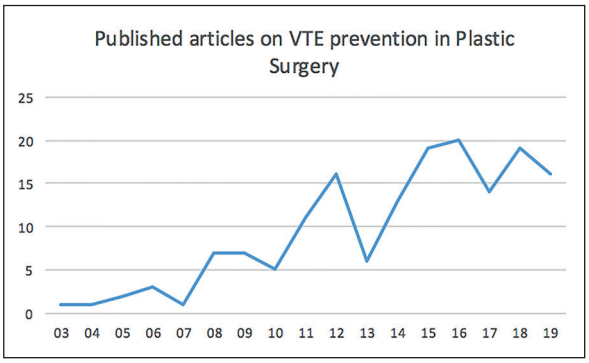

Figure 1. . Trend of the number of published articles in VTE prevention in Plastic Surgery from 2003 to 2019.

uated. As the main field of study was in plastic surgery, all studies that were not focused in this area were removed.

The study was conducted in accordance with the Helsinki Declaration of 1964 (revised 2008).

Results

We found a total of 161 studies that were related to the topic of VTE prevention in Plastic Surgery. Our protocol is illustrated in Tables I-XI.

Discussion

As described in Figure 1, plastic surgeons started to concern about the topic of VTE prevention only in recent years and a specific literature has consequently risen.

In 2012, the American College of Chest Physicians (ACCP) published the updated evidence-based clinical practical Guidelines regarding the prevention of thrombosis. The crucial change that has been implemented in the latest Guidelines as compared to the old ones published in 2008 is the presence of an additional paragraph regarding the VTE prevention in Plastic and Reconstructive Surgery's patients.

However, in the current Guidelines, only indirect evidence[6] about relative risks from trials in general and mixed surgical patients have been applied to make ongoing recommendations.

At the moment, the 2005 Caprini Score is the most widely used and well-validated individualized risk-stratification tool for VTE[7]. In 2010, a

Table I. Minor surgical procedures.

Minor surgical procedures (1 point each)
Interventions on cutaneous and subcutaneous tissue
Otoplasty
Syndactily
Lipomas
Fat grafting (in one area)
Superficial lymphadenectomy
Lipoaspiration under local anaesthesia
Replacement of breast tissue expander with prosthesis
Lumpectomy
Quadrantectomy without axillary lymph nodes
Dermoepidermal grafts
Local flaps in head and neck
Pilonidal cyst

Surgery lasting < 60 minutes is generally considered as low-risk surgery. The following list is therefore to be considered purely indicative. Each case will be considered individually based on the experience of surgical teams. The following list is applicable to hospitalized patients only.

Table II. Major surgical procedures.

Major surgical procedures (2-3 points each)
Lipoaspiration under general anaesthesia
Modified total mastectomy followed by reconstruction
Reduction mammoplasty
Lymphadenectomy
Rhinoseptoplasty
Face Lift
Mastopexy
Breast augmentation with prosthesis
Gynaecomastia

Surgeries lasting > 60 minutes (2 points) and surgeries lasting > 2 hours (3 points) are generally considered as high-risk surgery. General anesthesia is an additional factor of thrombotic risk. The following list is therefore to be considered purely indicative. Each case will be considered individually based on the experience of surgical teams.

Table III. Major surgical procedures.

Surgery-related risk factors (5 points each)
Body contouring in postbariatric patients
Abdominoplasty
Complex mammary reconstruction (e.g., TRAM, LD)
Complex reconstruction of the limbs
Head/neck cancer procedures
Microsurgical flap°
Combined procedures
Surgery lasting > 6 hours

The following list is to be considered purely indicative. Each case will be considered individually based on the experience of surgical teams. *Low-Molecular-Weight Heparin. °For this type of procedure, a specific protocol is used.

Table IV. Patient-related risk factors (Low risk).

Patient-related risk factors Low risk factors: 1 point each
Age 41-60 years
Swollen legs (current)
Varicose veins
Obesity (BMI > 25)
Sepsis (< 1 month)
History of prior major surgery (< 1 month)
Minor surgery planned
Serious lung disease incl. pneumonia (< 1 month)
Abnormal pulmonary function (COPD)
Acute myocardial infarction
Congestive heart failure (<1 month)
Medical patient currently at bed rest
History of inflammatory bowel disease
History of chemotherapy
Smoking habit

new Caprini risk assessment model was created and owned some crucial innovations.

Changes brought in the 2010 Caprini Score, led to less rigorous risk stratification due to the overestimation of the patient's perceived risk score[8]. For this reason, the ACCP's Guidelines expressly advocate the use of the 2005 version of the Caprini Score[9,10].

Some issues have been raised concerning the Caprini Score[11,12]. While some of the factors are overrated, some others, which are also important, are not taking a significant role or are even absent in the stratification of the risk score assessment. These factors may include chemotherapy, smoking habit, long periods of travel (especially immediately after surgery), as well as the type of anaesthesia delivered[2,13-15].

As we know, many plastic surgical procedures might include traveling more than any other surgical procedures[2]. We need more evidence to understand the role of this factor.

The Ivo Pitanguy Hospital Protocol for VTE prevention entails the attribution of 1 point for travels between 4 hours and three days before surgery[16]. This protocol also gives 1 point for smoking habit and other scholars[17] suggest considering smoking as a high-risk factor for peri-operative thrombotic events.

Table V. Patient-related risk factors (Low risk).

Patient-related risk factors Low risk factors for women only: 1 point each
Oral contraceptives or hormone replacement therapy (e.g., Tamoxifen)
Pregnancy or postpartum (< 1 month)
History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant

Table VI. Patient-related risk factors (Moderate risk).

Patient-related risk factors Moderate risk factors: 2 points each
Age 61-74 years
Malignancy (present or previous)
Patients confined to bed (> 72 hours)
Central venous access (e.g., port-a-cath)
Immobilizing plaster cast (< 1 month)
Obesity (BMI > 40)

The administration of chemotherapy for cancer treatment is another variable that further increases the risk[18]. In the first risk assessment Score by Caprini, in 2005, chemotherapy was not even mentioned as a risk factor. In the 2010 revision, it was inserted, together with the presence of cancer, for a 3-point value.

Furthermore, the Caprini model lacks the inclusion of independent risk factors, such as ethnicity, which could be a contributing factor to a hypercoagulable state (e.g., Caucasian females)[18,19].

In 2013, a new version of the Caprini RAM was presented. This new version includes some additional risk factors to the 2005 version that were not tested in validation studies but have been strongly associated with thrombosis in the literature. These factors include smoking, insulin-dependent diabetes, blood transfusion, BMI >40, chemotherapy and duration of surgery >2 hours[20]. Even if it has not been validated for plastic surgery yet, but only for arthroplasty patients, we embraced the addition of these risk factors, in particular, regarding smoking, chemotherapy, and BMI >40.

Table VII. Patient-related risk factors (High risk).

Patient-related risk factors High risk factors: 3 points each
Age > 75 years
History of DVT/PE
Family history of thrombosis
Heparin-induced thrombocytopenia (HIT)
Elevated anticardiolipin antibodies
Positive Factor V Leiden
Positive Prothrombin 20210A
Elevated serum homocysteine (> 50 µmol/L)
Positive Lupus Anticoagulant
Other congenital or acquired thrombophilia (e.g., Antithrombin deficiency, protein C or S deficiency)

Table VIII. Patient-related risk factors (Very High risk).

Patient-related risk factors Very High-risk factors: 5 points each
Stroke (< 1 month) Hip, pelvis or leg fracture (< 1 month) Multiple trauma (< 1 month) Acute spinal cord injury (paralysis) (< 1 month)

An international consensus is missing about the use of mechanical or chemoprophylaxis, as well as prophylaxis type, timing and duration in plastic surgery[21].

While the ACCP's Guidelines and American Society of Plastic Surgeons suggest considering the use of chemoprophylaxis with LMWH or LDUH for patients at high risk for VTE carrying a 2005 Caprini Score more or equal to 3 and with no risk for major bleeding events[6,10], Pannucci et a[9]. advocate the administration of Enoxaparin to patients who own a Caprini Score ≥7 but considering it on a case-by-case basis.

In our protocol, drug prophylaxis can be considered in patients classified as moderate risk (score 7-8) starting 12 hours after the procedure especially when no Intermittent Pneumatic Compression is available. For high-risk patients (score 9 or more), post-operative drug prophylaxis administration is mandatory, and it should begin 6-8 hours after the surgery.

Table IX. Prophylaxis safety considerations (Anticoagulants).

Prophylaxis safety considerations Check box if the answer is 'YES' Anticoagulants: Factors Associated with Increased Bleeding
• Is patient experiencing any active bleeding? • Does patient have (or has had history of) heparin-induced thrombocytopenia? • Is patient's platelet count < 100.000/mm^3? • Is patient taking oral anticoagulants, platelet inhibitors (e.g. NSAIDS, Clopidogrel, Salicylates)? • Is patient's creatinine clearance abnormal? If yes, please indicate value • Does patient have uncontrolled systolic hypertension (≥ 230/120 mmHg)? • Does patient undergo neuraxial anaesthesia in the form of an epidural and/or spinal block?*

If any of the above boxes are checked, the patient may not be a candidate for anticoagulant therapy and should consider alternative prophylactic measures. *In these patients particular caution need to be observed because of the risk of spinal/epidural haematoma. Spinal and epidural anesthesia should occur 10 to 12 hours after the last dose of LMWH. Remove the catheter a minimum of 10-12 hours after a dose of LMWH. Administer the next dose of LMWH no sooner than 2 hours after catheter removal.

Table X. Prophylaxis safety considerations (Intermittent Pneumatic Compression).

Prophylaxis safety considerations Check box if the answer is 'YES' Intermittent Pneumatic Compression (IPC)
• Does patient have severe peripheral arterial disease? • Does patient have congestive heart failure? • Does patient have an acute superficial/deep vein thrombosis?

If any of the above boxes are checked, the patient may not be a candidate for intermittent compression therapy and should consider alternative prophylactic measures.

The issue of the time of administration of prophylaxis is not even mentioned in the current ACCP Guideline. This might be explained by the mean of inadequate data in plastic surgery about the best time to use chemoprophylaxis[9,22-25].

Based on the available data, the American College of Chest Physicians concluded that the first dose of low-molecular-weight heparin may be given either before or after surgery[6].

Little is known about the duration of chemoprophylaxis; frequently, LMWH administration is extended until 5 to 10 days postoperatively, but the length of the treatment depends on the particular patient's risk factors[26-28].

Prolongation of chemoprophylaxis is described in the literature for abdominal and pelvic cancer patients. Randomized controlled trials demonstrated that extending the duration of chemoprophylaxis up to 35 days significantly reduces VTE incidence in high risk patients[9,29,30]. Extended LMWH prophylaxis in patients with cancer beyond the first post-operative week reduces the rate of VTE and we think it should also be extended in plastic surgery patients with cancer or undergoing chemotherapy[30].

In any case, therapy should be continued until the patient is fully ambulatory and a hematology consultation can be aided in cases when chemoprophylaxis duration cannot be easily fixed.

Concerning the type of chemoprophylaxis for VTE, heparin is the most commonly adopted drug due to its efficacy[19]. Among the two types of heparins, that is LMWH and LDUH, the first one is the preferred medication due to several factors. On the one hand, it is administered less frequently than LDUH as a result of its longer plasma-life and its slower rate of elimination[31-33]. Further-

Table XI. VTE Risk Assessment Score and recommended interventions.

Recommended interventions				
Score	**Vte risk category**	**Recommended intervention**		**Duration**
0 - 2	Very low	No specific pharmacologic or mechanical prophylaxis. Early ambulation.		
3 - 6	Low	Mechanical prophylaxis (ES* or IPC**)		Until discharge or 7 days in case of prolonged immobility and/or complications.
7 - 8	Moderate	Mechanical prophylaxis (ES* or IPC**) or LMWH*** (< 3400 U Anti-Xa, e.g. Enoxaparin 4000 IU) every 24h	1st dose: 12 hours post-op Subsequent doses: Every 24h	Until discharge or 7 days To be evaluated in case of prolonged immobility and/or complications (recommended at least 15 days). Prolonged prophylaxis for up to 4 weeks may be considered in cancer patients.
> 8	High	LMWH*** (< 3400 U Anti-Xa, e.g. Enoxaparin 4000 IU) every 24h + Mechanical prophylaxis (ES* or IPC**)	1st dose: 6-8 hours post-op Subsequent doses: Every 24h	Minimum 7 days To be evaluated in case of prolonged immobility and/or complications (recommended at least 15 days). Prolonged prophylaxis for up to 4 weeks may be considered in cancer patients.

*Elastic Stockings;**Intermittent Pneumatic Compression, ***Low-Molecular-Weight Heparin.

more, LMWH administered dose is smaller than LDUH's[19], and it is correlated to a lower appearance of heparin-induced thrombocytopenia (HIT)[34]. On the other hand, it has been observed that LMWH is associated with a significantly lower occurrence of asymptomatic DVT[33].

Fondaparinux was approved by the US Food and Drug Administration (FDA) in 2004 for VTE prophylaxis in orthopedic surgery. Soon after that, it was approved for general use as a VTE treatment. In late 2005, the FDA approved fondaparinux for prophylaxis in abdominal surgery[35].

It has been demonstrated that when the first dose of fondaparinux is given fewer than 6 hours after surgery, more bleeding occurs than with Enoxaparin. Diversely, bleeding rates are comparable when the first dose is administered between 6 and 8 hours after surgery[35]. We advocate the use of Fondaparinux as a safe alternative to LMWH in case the latter is not available or the patient reports heparin intolerance.

With respect to the risk of bleeding after administration of antithrombotic drugs, there is a significant discrepancy among the current studies: some of them[35] report lower bleeding complications when administering LMWH, while others declare the opposite[34]. A valid explanation that may be given for this disparity regards LMWH dose and timing of administration[19].

Plastic surgeons are generally reluctant to use antithrombotic agents because of the fear that these drugs may increase the risk of bruising, hematoma or the need for blood transfusion. However, multiple meta-analyses and placebo-controlled, blinded, and randomized clinical trials

have found little or no increase in the frequency of clinically significant bleeding when LMWH or fondaparinux are used appropriately[36,37].

With regards to mechanical prophylaxis, three primary methods are available: elastic stockings, Intermittent Pneumatic Compression (IPC) and venous foot pump (VFP).

Pannucci et al[25] recommend using either IPC or elastic compression stockings (Grade IB), pointing out that the first method is more efficient than the last one. However, these recommendations do not have any direct meta-analysis performed in plastic surgery.

Same findings are encountered in the current ACCP's Guidelines, where the use of mechanical prophylaxis is recommended for several categories of patients and in most of these categories the use of IPC is the preferred method over elastic stockings[6,34].

We propose a modified 2005 Caprini score, with specific changes pertaining to plastic surgery.

Regarding the risk related with operation time, 2005-Caprini Score identifies 45 minutes as a cut-off for risk assessment, giving a score of 1 when the surgical procedure was lasting 0-44 minutes and a score of 2 points ≥45 minutes. Davidson-Caprini Score instead sets the cut-off at 60 minutes. The 2010 Caprini Score further divides the operative time into 0-59 minutes, 60-119 minutes, 120-179 minutes and ≥180 minutes, conferring a score of 1,2,3,5 points, respectively. NICE guidelines, on the other hand, establishes the cut-off for surgical time as 90 minutes, comprehensive of anesthetic and surgical time. In our protocol, we gave 2 points for surgeries lasting more than 60 minutes and 3 points for surgeries lasting more than 2 hours. This further distinction was deemed to be relevant even in the subset of cosmetic surgery patients, for instance when they undergo combined aesthetic surgery procedures.

We believe that the Caprini Score should include indicative examples of both minor and major surgeries to more easily assess patients' risk for VTE with more clarity.

Examples of minor plastic surgery procedures are listed in Table I; it is fundamental to highlight that each surgery duration is highly operator dependent, so this list is to be considered purely indicative.

With respect to major surgeries (Table II), we consider high risk procedures the following, when performed under general anesthesia, lasting more than one hour (Table III): abdominoplasty, post-bariatric surgery (dermolipectomy of the thighs and the arms), complex mammary reconstruction (e.g., TRAM, LD), complex reconstruction of the limbs, complex reconstruction of the head and neck, combined procedures and operations lasting >6 hours. This way the surgeon is urged to consider chemoprophylaxis for those procedures that according to the literature bear the highest risk of VTE.

According to the ASPS VTE task force, LMWH for the above-mentioned procedures should be practically always considered[10]. We added to this list microsurgical flaps. As a matter of fact, regarding free flaps we use a separate protocol that consists in giving an intraoperative bolus heparin (50 to 100 IU of heparin per kilogram) at the time of the anastomosis during microsurgical procedures, followed by a continuous intravenous heparin infusion (50 to 100 IU of heparin per kilogram) 2 ml/h over 24 hours for 5 days that are then replaced by 4000 IU subcutaneous up to 30 days[38,39]. General anesthesia is a known risk factor for venous stasis due to the elimination of the calf muscle pump action[9]. Swanson et al recently demonstrated that patients avoiding endotracheal anesthesia were reported to have low rates of VTE, even when mechanical prophylaxis was not used[40].

We decided to include any prothrombotic hormone therapy (e.g., Tamoxifen), in the Score (1 point). The reason for this inclusion is that these sex hormones are known to increase VTE's risk further (Tables IV, V).

In contrast with the 2005 Caprini Score, we also prefer to consider chemotherapy as an independent risk factor and give it a 1-point value, that can be added to the risk factor of present or previous cancer. As suggested by Caprini himself in the 2013 RAM Score version, we included factors as smoking habit, chemotherapy, and BMI >40 as additional 1 point score risk factors. These elements were not tested in validation studies, because they have been strongly associated with thrombosis in the literature[17,20] (Tables VI-VIII).

We believe it is crucial to better investigate if an algorithm to stop peri-operative Tamoxifen to decrease VTE risk is necessary and appropriate. The one proposed by Sweetland et al[41] could be a suitable option.

With regards to the preventive measures, we consider that dose, duration, and interval of LMWH should be used for patients with moderate risk (score 7-8) <3400 IU every 24 hours, with the

first dose 12 hours postoperatively (e.g., Enoxaparin 2000 IU). For patients carrying a high risk for VTE (score >8), we believe that the administration of LMWH <3400 IU (e.g., Enoxaparin 4000 IU) should be every 24 hours, with the first dose 6-8 hours postoperatively. This therapy should be considered to be prolonged up to 4 weeks postoperatively in oncological or prolonged immobility patients[20].

Concerning the factors associated with a high risk of bleeding, we believe that it is essential to consider as increased risk also those patients presenting with uncontrolled systolic blood pressure (230/120 mmHg or more). This parameter is not considered in the original Caprini Score, while it is examined in the NICE guidelines (Tables IX, X).

As previously mentioned, our paper aims to analyze and present the current status of VTE prophylaxis' recommendations in Plastic Surgery. Although there is still no consensus regarding all operations to implement in order to reduce VTE risk in all Plastic Surgery fields, many authors have proposed different risk assessment scores that have been used so far. For sure, the Caprini Score is the most used and studied one. In our experience, though, we found that our modifications may produce a more effective and easier score. In Table XI we present our Plastic Unit's VTE Risk Assessment Score, with the characteristics previously mentioned.

We applied the prophylaxis regimen suggested by Pannucci et al[25], and other recent studies and reviews[35,40-45].

Our protocol is applicable to hospitalized patients only. Little is known about the incidence of VTE requiring treatment after outpatient surgical procedures[46].

Our protocol brings minor changes to the extensively validated 2005 Caprini Score that may prove useful in plastic surgery everyday practice.

Based on the study by Keyes et al[47] the 95% of patients with VTE after abdominoplasty (responsible for 58% of all VTE after aesthetic surgery procedures), had a Caprini Score ≤6.

Giving 5 points to particularly high-risk procedures (Table III) was arbitrary but seemed reasonable to our team in view of the literature and our clinical experience[48,49]. This way the surgeon is urged to be cautious in front of specific surgeries but still, it does not necessarily mean that the patient is going to be subjected to antithrombotic chemoprophylaxis.

The proposed score has undergone no formal validation and is to be considered as an integration to 2005 Caprini Score and not in contrast to it.

We present some final general considerations that we recommend to all our patients together with some good clinical practices that are not included in the Score:

- all patients are prompted to walk on the day of surgery;
- in the first consultation, the patient should be instructed to discontinue any medications with thrombogenic potentials, such as oral contraceptives and hormone replacement therapy, including vaginal rings, one month before and up to 2 weeks after the surgery, when they are expected to be able to walk normally;
- patients who are active tobacco users are urged to stop smoking for one month before surgery;
- post-operatory hydration is pivotal. A low fluid volume state (i.e., dehydration) can lead to hemoconcentration and low venous flow;
- for patients at particularly high risk, surgeons may obtain pre-operative hematology consultation to understand their peri-operative VTE risk better;
- proper positioning on the operating table should be applied to all patients undergoing surgery regardless of their risk. The objective is to position the patient in such a way to obtain maximum venous flow through the legs and avoid external pressure. This is accomplished by slightly flexing the knee at 5 degrees. Placing a pillow under the knees will help achieve this. Proper positioning and early ambulation are recommended for all risk groups, regardless of additional therapeutic measures;
- avoid combination procedures in high-risk patients;
- when feasible, avoid general endotracheal anesthesia in high-risk patients;
- practitioners will notice that using our score, mechanical prophylaxis should be used in almost every case;
- to patients who will be traveling in the days before the surgery, several pre-operative instructions are given. For instance, they are advised not to drink alcohol 48 hours before surgery while they are urged to drink liquids during their trip, frequently moving their legs and walking every 2 hours when feasible and wearing elastic stockings for moderate compression if there are no contraindications;
- upon discharge, the guidelines including high liquid intake, frequent walking, and using elas-

tic stockings or LMWH for one week or more, when indicated, are carefully explained to the patient.

Conclusions

The risk of VTE in plastic surgery cannot be disregarded. However, the plastic surgery literature still lacks high-level evidence for appropriate VTE prophylaxis means, although an increasing amount of attention has been paid to the topic[43,44].

In conclusion, more randomized clinical trials are needed for VTE in plastic surgery. Determining the proper VTE prophylaxis is a clinical decision that should be made on a patient-to-patient basis. The algorithm presented in this article is meant to simplify this complex problem and to help expedite and clarify the decision-making process.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee of the Policlinico Umberto I, Rome, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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