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J Clin Invest Surg. 2019; 4(1): 10-18 doi: 10.25083/2559.5555/4.1/10.18



Received for publication: August 9, 2018 Accepted: November 15, 2018

# Research article

## The incidence of haemorrhagic and thromboembolic events after breast cancer surgery in patients treated with pharmacological thromboprophylaxis

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#### Background. Hemorrhagic events and venous thromboembolic disease, including pulmonary Abstract embolism and deep venous thrombosis, are the most important complications after breast cancer surgery. Although hemorrhagic complications are not usually severe and do not have a high mortality risk, venous thromboembolic disease is often associated with high morbidity and mortality rates. Under such circumstances, it is highly important to evaluate the need for systemic antithrombotic prophylaxis as opposed to mechanical interventions and the optimal duration of chemoprophylaxis in patients undergoing breast cancer surgery. Methods. Using the database of the General Surgery Department of "Coltea" Clinical Hospital, we analyzed the data from 2015 to 2018. During this period, pharmacological prophylaxis was used in all patients undergoing breast cancer surgery. Mechanical prophylaxis (intermittent pneumatic compression or graduated compression) has also been recommended, but there was no record of patient compliance. The primary outcome was the occurrence of venous thromboembolic or hemorrhagic events within 30 days after surgery. *Results*. In our institution, the venous thromboembolic disease rate for breast cancer surgery was 4/540 (0.7%; 95% CI: 0.02-1.9%), being similar to that of other studies. Hemorrhagic events occurred in 29 (5.4%; 95% CI 3.6-7.6%) patients, most commonly as hematoma in 3.3% of the patients. The incidence of hematoma requiring operation was 1.1% (95% CI: 0.4-2.4%), while hematoma treated conservatively was 2.2% (95% CI:1.2-3.8%). Other forms of hemorrhagic events include hemorrhagic drainage and bleeding wound, occurring in 2.0% of the cases. Conclusions. The occurrence of venous thromboembolic events is reduced among patients undergoing primary breast cancer surgery. A current issue is decreasing venous thromboembolic disease rates without increasing the hemorrhagic event rate. Standard guidelines on the antithrombotic prophylaxis of these patients are not well established since studies show contradictory data. Further investigations are needed to determine exactly which type of thromboprophylaxis is more effective.

#### **Keywords**

- : breast cancer, venous thromboembolism, haemorrhagic complications, risk factors, epidemiology
- Highlights
- ✓ Venous thromboembolic disease is low among patients undergoing breast cancer surgeries, regardless of the thromboprophylactic methods being used.

**To cite this article**: Andrei CA, Scăunașu RV, Simionescu AA, Burcoș T, Lupușoru MD, Lica G. The incidence of haemorrhagic and thrombo-embolic events after breast cancer surgery in patients treated with pharmacological thrombo-prophylaxis. *J Clin Invest Surg.* 2019; 4(1): 10-18. DOI: 10.25083/2559.5555/4.1/10.18

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#### Introduction

The most significant complications occurring after breast cancer surgery are hemorrhagic events and venous thromboembolic (VTE) disease, including pulmonary embolism (PE) and deep venous thrombosis (DVT) (1-3).

It is well known that active malignancy is a risk factor for hypercoagulable states (4, 5). There are studies that prove the relationship between different diagnoses of cancer and VTE as a first manifestation of the disease, but not among the breast cancer population (6). An increased risk of VTE due to neoadjuvant treatment has been reported. Breast cancer patients receiving preoperative chemotherapy and/or hormonal treatment have a 9% risk of VTE after surgery (7, 8).

The incidence of VTE in breast cancer patients is low compared to other types of cancer. A 0.23% (95% CI: 0:19%-0,27%) incidence of VTE after 30 days was described in a study on 49,028 patients undergoing mastectomy, but this study did not specify what kind of antithrombotic prophylaxis had been used (9). In other studies, the incidence of VTE in breast cancer patients varies from 0.3% to 2.3% (8, 10-12).

VTE is a preventable disease associated with substantial morbidity and mortality, even though there are many prevention and treatment options. It has been proved that thromboprophylaxis reduces the incidence of DVT and PE (13-15).

There is not a worldwide accepted consensus regarding antithrombotic prophylaxis for patients undergoing breast cancer surgery. According to the American College of Chest Physicians (ACCP), surgeries for breast cancer are included in the "general surgery" category (14, 15). Adding risk factors such as active malignancy to this category results in the need of using pharmacological prophylaxis for all patients who undergo breast cancer surgery. On the other hand, the American Society of Breast Surgeons recommends mechanical prophylaxis for all patients undergoing breast surgery and personalised pharmacological prophylaxis, taking into account the duration and the type of surgery, the history of VTE or hypercoagulable disorders, or the multiple risk factors known for VTE and a Caprini score  $\geq 5$  (16).

Therefore, there is not a well-established method to classify the risk of VTE in patients with breast cancer.

Another complication occuring after breast cancer surgery is hemorrhage, but after the introduction of the electrocautery, the incidence of hemorrhagic events has significantly decreased. However, it may still develop in 2% to 10% of cases (17). Hemorrhaging may occur as hemorrhagic drainage through the suction catheters, hematoma or bleeding from the wound. A large hematoma carries a high morbidity rate, causing pain by its rapid expansion in a closed surgical wound. In these cases, reintervention should be reconsidered. Low volume hematomata determine extensive ecchymosis and can be treated conservatively. Hemorrhagic events requiring reintervention occur in 4% of the patients undergoing breast cancer surgery (18). The risk of postoperative hemorrhagic events may increase depending on the primary type of surgery, the age of the patient and the use of certain chronic treatments (19, 20). The patients who have been reoperated on for hematoma are more likely to have undergone radical surgery (69.3%) for breast cancer compared to those treated with conservative surgery (57.9%) (21).

In a study on 522 patients undergoing mastectomy with or without reconstruction, using the Caprini risk Assessment Model, the overall rate of hemorrhagic events was 3.4% (18/522, 95% CI 2.2-5.4%), the reoperation for hematoma occuring in 2.7% (14/522, 95% CI 1.6-4.5%) of the cases. The rate of VTE in this population was 0.2%.

Hemorrhagic complications in patients who underwent surgery for breast cancer are not severe and do not carry a mortality risk, whereas VTE is a disease with high morbidity and mortality rates.

The use of thromboembolic pharmacological prophylaxis may lead to a higher risk of hemorrhagic events. The use of pharmacological prophylaxis in patients who are not at risk for VTE may increase the risk of bleeding.

A current issue concerns the need for systemic antithrombotic prophylaxis as opposed to mechanical interventions and the optimal duration of chemoprophylaxis in patients with breast cancer surgery.

## **Materials and Methods**

In this article, we evaluate the rate of VTE events and the rate of hemorrhagic events in patients undergoing breast cancer surgery, within 30 days after surgery. All the patients were trained on the importance of immediate postoperative ambulation. They also received preoperative subcutaneous pharmacological prophylaxis consisting in a dose of low molecular weight heparin (LMWH, enoxaparin or dalteparin), continuing therapy until discharge. Although mechanical prophylaxis was recommended to all patients, unfortunately our clinic could not provide it.

The IT database of the hospital was used to collect data about age, sex, diagnosis, body mass index (BMI), the type of procedure undergone, the stage of breast cancer, neoadjuvant therapy, chronic diseases, chronic treatments with antiplatelet drugs or oral anticoagulants, the overall and after surgery length of hospital stay (LOS). VTE is defined as pulmonary embolism (PE) and deep venous thrombosis (DVT) diagnosed within 30 days after discharge. Hemorrhagic events were defined as a) the presence of hematoma which may or may not require reintervention; b) hemorrhagic drainage >200ml on the drain tube; c) bleeding wound.

The incidence of VTE and hemorrhagic events after primary breast cancer surgery in "Colţea" Clinical Hospital were evaluated with descriptive statistics using IBM SPSS Statistics Data Editor. For categorical variables, The Pearson's Chi-square test or 2-sided Fisher's exact test was used wherever applicable. Student's t-test was used for continuous variables. p<0.05 was defined as having statistical significance.

<b>Table 1:</b> Characteristics of 540 patbreast cancer surgery in General SuColțea Clinical Hospital	
Age, years [mean; median (range)	60,47; 62 (30-86)
Sex	
М	534 (98.9%)
F	6 (1.1%)
BMI	
Underweight [<18.5]	5 (0.9%)
Normal [18.5-25]	323 (59.8%)
Overweight [>25-30]	96 (17.8%)
Obesity, class I [>30-35]	73 (13.5%)
Obesity, class II [>35-40]	36 (6.7%)
Obesity, class III [>40]	7 (1.3%)
Phatological stage	
Not applicable	8 (1.5%)
0 (DCIS, LCIS, Paget)	22 (4.1%)
I	119 (22%)
П	240 (44,4%)
III	119 (22%)
IV	32 (5.8%)
Neoadjuvant therapy	
No	329 (60.9%)
Yes	211 (39.1%)
Procedure	
Type of surgery	
Lumpectomy	130 (24.1%)
Mastectomy	39 (7,2%)
MRM	367 (68%)
MRM + expander/implant	
reconstruction	4 (0.7%)
Axillary surgery	
Axillary dissection	500 (92.6%)
No surgery	40 (7.4%)
Hospital LOS after surgery, days [median (range)]	8 (2-31)

#### Results

As seen in Table 1, the final group comprises 540 patients treated surgically for breast cancer. The mean age of our population was 60.47 years at the time of surgery. 61.9% of the patients have one or more medical comorbidities and 39.4% of the patients have a body mass index >25. An early stage (0, I and II) of breast cancer was diagnosed in 70.5% of patients, advanced stages of breast cancer being encountered only in 32 (5.8%) patients. Neoadjuvant therapy was used in 211 (39.1%) patients.

The most common means of treating patients with breast cancer in our clinic was modified radical mastectomy (MRM) in 68% (367) of the cases, followed by lumpectomy in 24.1% (130) of them. Mastectomy includes simple mastectomy, "skin sparing" and "nipple sparing" techniques in 39 (7.2%) cases. The surgical treatment of the axilla was performed in 500 (92.6%) patients with a mean figure of 16.77 surgically excised lymph nodes. The median length of hospital stay after surgery was 8 days (range 2-31).

#### VTE events

In our institution, the VTE rate for breast cancer surgery was 4/540 (0.7%; 95% CI: 0.02-1.9%) and none of these events were fatal or needed admission to the intensive care unit (ICU). None of these patients had previous history of VTE. Out of the 4 patients who developed VTE after surgery, 2 had PE and 2 had DVT. Both patients with PE and one patient with DVT underwent modified radical mastectomy and lymph node dissection (LND), while the other patient with DVT underwent lumpectomy and LND. Neoadjuvant chemotherapy was used in both patients with PE. The BMI was >25 for all the patients who developed VTE. Out of these patients, one had undergone previous surgery for contralateral breast cancer. Varicose veins in the lower limbs were present in 1 out of 2 patients with DVT.

Table 2: The incidence of VTE and bleeding events in 540 patients undergoing breast cancer surgery N(%) 95% CI VTE DVT/PE 4(0.7%)0.02-1.9% Hemorrhagic events 29 (5.4%) Overall 3.6-7,6% Operative hematoma 6 (1.1%) 0.4-2.4% Non operative hematoma 12 (2.2%) 1.2-3.8% Hemorrhagic drainage 5 (0.9%) 0.3-2.1% Bleeding wound 6(1,1%)0.4-2.4% Transfusion 12 (2.2%) 1.2-3.8%

	VTI	E events	Hematoma			
	N (%)	95% CI	p-value <sup>a</sup>	N (%)	95% CI	p-value <sup>b</sup>
Our Clinic (n=540)	4 - 0.7%	0.02-1.9%	-	18 (3.3%)	2.0-5.2%	-
J. K. Lovely et al. <sup>1</sup> ( $n=752$ )	4 - 0.5%	0.2-1.4%	0,63	15 (2.0%)	1.1-3.3%	0,11
A. Laws et al. <sup>2</sup> ( $n=522$ )	1 - 0.2% 114 -	0.03-1.1%	0,19	18 (3.4%)	2.2-5.4%	0,91
B.H. Tran et al. <sup>9</sup> (n=49,028)	0.23% 395 -	0.19-0.27%	0,016			
A. Momeni et al. <sup>3</sup> (n=52,547)	0.75%	0.68-0.83%	0,97			

Table 3: VTE and hematoma rates in breast cancer in Colțea Clinical Hospital compared with other similar studies

<sup>*a*</sup> *p* value compares the VTE rate to the VTE rate in our institution

<sup>b</sup> p value compares the hematoma rate to the hematoma rate in our institution

Table 4: Comparison of clinical characteristics between patients with or without hemorrhagic events

N=540	Hemorrhagic events			
	Yes (n=29)	No (n=511)	<i>p</i> -value	
BMI				
<30	24/424 (5.7%)	400/424 (94.3%)	0.81	
<u>≥30</u>	5/116 (4.3%)	111/116 (95.7%)		
Гуреs of surgery				
Mastectomy / MRM $\pm$ breast reconstruction	26/410 (6.3%)	384/412 (93.7%)	0.075	
Lumpectomy	3/130 (2.3%)	127/128 (97.7%)		
Neoadjuvant therapy				
Yes	16/211 (7.6%)	195/211 (92.4%)	0.068	
No	13/329 (4%)	316/329 (96%)		
Axillary surgery				
Yes	26/500 (5.2%)	474/500 (94.8%)	0.46	
No	3/40 (7.5%)	37/40 (92.5%)	0.46	
Number of disected lymph nodes: Mean $\pm$ STD				
(n=540)	$16.24\pm9.16$	$15.58 \pm 7.90$	0.70	
Number of disected lymph nodes: Mean $\pm$ STD (excludig patients without axillary surgery			0.32	
(n=500)	$18.12 \pm 7,67$	16,73±7,9	0.32	
$\leq 10$ lymph nodes	2/83 (2.4%)	81/83 (97,6%)	0,28	
>10 lymp nodes	24/417 (5.8%)	393/417 (94.2%)		
Hospital LOS after breast surgery: Mean $\pm$ STD	$10.48\pm4.22$	$8.81 \pm 4.098$	0.034	
Chronic treatment with oral anticoagulants or				
antiplatelet drugs				
Yes	4/90 (4.4%)	86/90 (95.6%)	0.80	
No	25/450 (5.6%)	425/450 (94.4%)		
Stage (without patients who have not been assigne	0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,			
0-I-II	14/381 (3.7%)	367/381 (96.3%)	0.004	
III-IV	15/151 (9.9%)	136/151 (90.1%)		

VTE events in patients undergoing breast cancer surgery varies widely from 0.3% to 2.3% (8, 10-12). Our results correspond to previous reports regarding this question. Moreover, the incidence of hematomata after surgery is similar to other studies (1, 2).

The only statistically significant difference was found between the VTE incidence in our group and in B.H. Tran's et al. study group, 0.7% (95%CI: 0.02-1.9%) and 0.23% (95% CI: 0.19-0.27%, p=0.016), respectively. However, the authors do not specify the type of antithrombotic prophylaxis in this study.

#### Hemorrhagic events

Hemorrhagic events occurred in 29 (5.4%; 95% CI 3.6-7.6%) patients. The most common form was hematoma, in 3.3% of the patients. The incidence of hematoma requiring surgery was 1.1% (95% CI: 0.4-2.4%), while hematoma treated conservatively was 2.2% (95% CI:1.2-3.8%). The mean hospital LOS after breast cancer surgery in patients with hematoma that needed reintervention was  $10.62 \pm$ 3.96 days compared to those treated conservatively,  $8.5 \pm$ 1.17 (p=0.018). Other forms of hemorrhagic events are hemorrhagic drainage and bleeding wound, occurring in 2.0% of cases.

We divided the group of patients who underwent surgery for breast cancer according to the presence or absence of hemorrhagic events (Table 4). We intended to determine whether there were any variables that influence the bleeding accidents. Bleeding events occurred in 6.3% of the patients who underwent radical breast surgery compared to 2.3% of those who underwent lumpectomy (p=0.075). Neoadjuvant therapy also has a higher rate of hemorrhagic events (7.6%) in contrast with those untreated before surgery (4%, p=0.068). Even though these variables could influence the incidence of postoperative hemorrhage, the values are not statistically significant for our population.

The mean LOS was  $10.48 \pm 4.22$  days in patients with a bleeding event, compared to the mean LOS of  $8.81 \pm 4.098$  days in the other group (p=0.034). Strong statistical significance (p=0.004) resulted from a comparison of hemorrhagic events between different stages of cancer. Most bleeding events occurred in 9.9% of the patients with stages III or IV of breast cancer.

## Discussions

There are many studies that assess the risk of VTE in different types of malignancies, but the incidence of VTE in breast cancer patients was little approached, despite being the second most prevalent type of cancer in women. This analysis reveals that our VTE rate following pharmacological prophylaxis in patients undergoing breast surgery is low (0.7%, 95% CI: 0.02-1.9%) and similar to other retrospective studies, although the values vary depending on the type of surgical procedure and prophylaxis regimen used and whether immediate reconstruction was done or not. The American College of Surgeons from the National Surgical Quality Improvement Program (NSQIP) conducted a study on 68,285 patients which revealed that the 30-day VTE incidence is different by procedure: 0.13% in the lumpectomy group, 0.29% in the mastectomy group and 0.52% in the mastectomy with reconstruction group (p<0.0001) (22).

According to the American College of Chest Physicians (ACCP), both pharmacological and mechanical prophylaxis are recommended for all general surgery patients, except for low-risk patients, those who are going to have minor surgery procedures and those at increased risk of hemorrhagic events (14, 15). Breast surgical procedures are classified as being part of the general surgery procedures. Low incidence of VTE in retrospective studies for breast cancer surgery, even though no pharmacological prophylaxis was used, determined the American Society of Breast Surgeons (ASBrS) to recommend an individualized path based on the Caprine score in patients that do not undergo mastectomy with or without immediate reconstruction (13, 16). Although this score has been validated in multiple procedures, all patients >40 years undergoing breast cancer surgery would be included in the "high risk" category.

Brian H. Tran et al. evaluated 49,028 patients undergoing mastectomy to determine the risk factors associated with VTE in this group. The study found 114 (0.23%, 95% CI: 0.19-0.27%) patients with VTE. The authors identified some independent risk factors for VTE: obesity, inpatient status, central venous catheterization and operative time >3h. The immediate reconstruction after mastectomy, as well as neoadjuvant therapy, were not identified as independent risk factors for VTE after the previously mentioned risk factors were adjusted. The authors do not specify the regimen of antithrombotic prophylaxis used (9).

Momeni et al. evaluated 52,547 patients undergoing breast cancer surgery and identified 395 (0.75%, 95% CI:0.68%-0.83%) VTE events. Out of those events, 67.1% were identified within 90 days after discharge. 74.4% of VTE were identified during the first 7 weeks postdischarge. The authors identified that patients who had respiratory diseases, a LOS > 5 days, previous VTE and mastectomy with autologous reconstruction are more likely to develop postdischarge VTE. The authors concluded that VTE prophylaxis should not be limited to the initial hospitalization (3).

In the Andtbacka et al. study published in 2006 on 4,416 patients undergoing breast cancer surgery, the incidence of VTE was 0.16% using only mechanical prophylaxis such as knee-length antiembolism elastic compression stockings and calf-length intermittent pneumatic compression devices, applied immediately after anesthesia is induced. and early ambulation postoperatively. The authors' conclusions based on these results are that the use of systemic prophylaxis is not necessary after breast cancer surgery (23). The comparison between our findings, 0.7% VTE rate, with those of Adtbacka's et al., indicates a significantly statistic result (p=0.006). Having these findings, it is plausible that the only use of mechanical prophylaxis could be more efective than pharmacological prophylaxis.

In the EORTC 10,854 patient trial, VTE prophylaxis was left to the physician's clinical judgment. The VTE rate was lower in those patients who had received perioperative prophylactic subcutaneous heparin (0.6% vs 2.0%). Other methods of prophylaxis were not reported (10).

In a trial consisting of 752 patients, Lovely et al. reported an overall incidence of 0.5% (95%CI: 0.2-1.4%) of VTE events within 30 days after surgery. The antithrombotic prophylaxis regimen used was mechanical prophylaxis (such as sequential compression devices preoperatively, intraoperatively and postoperatively while the patient is resting in bed, associated with early ambulation) with selective pharmacological prophylaxis based on the surgeon's clinical judgment. 19.5% (147/752) received phramacological prophylaxis. The VTE rate in the group that received PCP was 0.7% (1/147) (95% CI: 0.0-3.8%) and 0.5% (3/605) (95% CI: 0.1-1.4%, p=0.58) in the group that did not receive PCP. All of the VTE complications occured in patients undergoing mastectomy (4/522, 0.8%). The reoperation rate for hematoma was 2% (3/147) (95% CI: 1.1-3.3%) in the group that used pharmacological prophylaxis (PCP) and 2% (95% CI: 12/605) in the group that did not receive pharmacological prophylaxis (p=1.0). The author concluded that pharmacological prophylaxis should be used alongside mechanical prophylaxis in patients undergoing mastectomy  $\pm$  reconstruction, but taking into account the reduced number of thromboembolic events in this study group, recommendations on selective pharmacological prophylaxis could not be formulated (1). Comparing our VTE rate (4/540) and also the hematoma overall rate (18/540) in our study group to the non-pharmacological-prophylaxis group of J.K. Lovely et al. study (3/605, 12/605) we did not find a statistically significant result, with p=0.59 and p=0.15, respectively.

In a study on 522 patients undergoing mastectomy  $\pm$ reconstruction, the Caprini score was used to assess the VTE risk, to choose perioperative antithrombotic prophylaxis regimen. The VTE rate reported was 0.2% (1/522, 95% CI: 0.03-1.1%). Hematomata occurred in 3.4% (18/522, 95% CI: 2.2-5.4%) of the patients, 2.7% (14/522, 95% CI: 1.6-4.5%) requiring reoperation and 0.8% (4/522, 95% CI: 0.3-2.0%) having non-operative hematomata. Each of all 18 patients had Caprini scores ≥5 and received preoperative heparin. 6/18 received postoperative pharmacological prophylaxis as per protocol, 4/18 received a single dose postoperatively and 8/18 did not receive postoperative heparin. Out of the 19 patients with a Caprini score  $\geq 8$  that received pharmacological prophylaxis (LMWH) after discharge, bleeding events had occured in 2/19 (10.5%) patients (2).

In our institution, our VTE rate of 0.7% is slightly higher than that of other studies, but not statistically significant. This might be explained by the patients' high risk characteristics such as high rates of multiple comorbidities, obesity, types of surgery, but also the lack of use of mechanical antithrombotic prophylaxis, except for early ambulation.

There are few studies that have tracked the effect of using pharmacological antithrombotic prophylaxis on the occurrence of bleeding complications after breast cancer surgery. There is a retrospective study on 425 surgeries for breast cancer in which the authors deduced that the use of low weight mollecular heparin was an independent risk factor for postoperative hematoma compared to a group that only used mechanical prophylaxis (OR 3.0, 95% CI 1.38-7.13) (24). On the other hand, as presented before, Alisson et al. concluded that there is no difference in hematoma formation between the group of patients who received pharmacological prophylaxis and those who did not (p=1.0) (2).

Hemorrhagic events occured in 5.4% (29/540, 95% CI 3.6-7.6%) of the patients, the results being similar to other reported rates (0.4-13%) (1, 19, 25-29). Out of the 29 patients, 6 (1.1%, 95% CI:0.4-2.4%) developed hematomata that required reintervention, 12 (2.2%, 95%

CI: 1.2-3.8%) had non-operative hematomata with an overall hematoma rate of 3.3% (95% CI: 2.0-5.2%). The 12 remaining patients experienced hemorrhagic drainages and bleeding wounds. The patients with advanced stages of breast cancer (III-IV) had a higher rate of hemorrhagic events (9.9%) compared to early stages of breast cancer (0-I-II) (3.7%, p=0.004). LOS in hospital was prolonged in the hemorrhagic events group by approximately 2 days (p=0.034).

The lack of guidelines on antithrombotic prophylaxis for breast cancer surgeries is not a new issue, having been in continuous research for the past years. The real incidence of DVT and PE is not well established in patients undergoing breast cancer surgery without the use of perioperative thromboprophylaxis. The efficacy of pharmacological prophylaxis is not questionable, and the use of LMWH as well as low dose heparin have shown a similar decrease in the risk of VTE. However, the use of pharmacological methods increases the risk of postoperative hematoma development (24). Intermittent pneumatic compression devices, elastic compression stockings or both used for thromboprophylaxis have shown similar efficacy without increasing the hemorrhagic complications (30-33).

## Conclusions

In our clinic, we have found that the VTE rate is low among patients undergoing breast cancer surgeries and similar to other studies regardless of the thromboprophylactic methods being used. The rate of hemorrhagic events was also similar to the published data.

The goal of this article is not to determine which method of thromboprophylaxis is better. We could not recommend what to use after this study, as we lacked a control group to compare our results to, but using other control groups we found contradictory results between the methods of prophylaxis used that were not statistically significant. We also believe that reducing the possibility of VTE events should be balanced with the increased risk of hemorrhagic events, as reintervention is often needed, the hospitalization length is prolonged and a new general anesthetic is required, thus putting the patients' lives at undue risk.

Further investigations should be made to compare the thromboembolic risk and the rate of hemorrhagic events in populations who may or may not receive pharmacological prophylaxis. Moreover, it should be taken into account that VTE is often asymptomatic and the actual prevalence of DVT and PE might be higher (30).

## Acronyms and abbreviations:

VTE – Venous thromboembolic disease PE - Pulmonary embolism DVT - Deep venous thrombosis ACCP - American College of Chest Physicians CI - Confidence Interval LMWH - Low molecular weight heparin BMI - Body mass index LOS – Length of stay DCIS - Ductal carcinoma in situ LCIS - Lobular carcinoma in situ LND - Lymph node dissection MRM - Modified radical mastectomy STD - Standard deviation NSQIP - National Surgical Quality Improvement Program ASBrS - The American Society of Breast Surgeons

## **Conflict of interest disclosure**

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

## Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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