

## INCIDENCE OF BREAST NEOPLASM ASSOCIATED WITH PULMONARY THROMBOEMBOLISM: A RETROSPECTIVE SINGLE CENTER STUDY

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**BREAST NEOPLASM IN PATIENTS WITH PULMONARY THROMBOEMBOLISM: A RETROSPECTIVE STUDY (Abstract):** This study **aims** to evaluate the incidence of pulmonary embolism among breast cancer patients, emphasizing its correlation with the histological types, cancer staging, and thrombus characteristics **Materials and methods:** We retrospectively analyzed 211 patients diagnosed with pulmonary thromboembolism (PTE) using contrast-enhanced chest computed tomography at “Sf. Spiridon” County Clinical Emergency Hospital, Iasi, from the 1<sup>st</sup> of January 2023 to 31<sup>st</sup> of November 2024. Patients with previous diagnosis of breast cancer were identified, and data including demographic details, breast cancer stage, histopathological findings, and thrombus localization were collected. **Results:** The incidence of breast cancer associated with PTE, found in our cohort was 4.73% (n=10), with a majority of postmenopausal women (80%), a median age of  $55 \pm 6.96$  years and an interquartile range (IQR) of 9.25 years. Incidence by cancer stage was as follows: stage I - 0.47% (n=1), stage II - 0.94% (n=2), stage III - 0.94% (n=2), stage IV - 2.36% (n=5). The incidence was higher among patients with stage IV cancer (2.47%) compared to stage I-III (0.5-1%). Histologically, 9 patients (4.26%) were diagnosed with invasive ductal carcinoma (IDC), while only 1 patient (0.47%) had invasive lobular carcinoma (ILC). Studying thrombus localization we found saddle thrombus in one case (0.47%), lobar artery thrombi in 2 cases (0.94%) and 7 patients (3.31%) with segmental and subsegmental arteries thrombosis. None of the patients had PTE preceding breast cancer diagnosis, all PTE occurred after treatment, with acute PTE being found in 2 cases - 0.94%, while the other 8 (3.79%) were diagnosed as chronic thrombosis **Conclusions:** Pulmonary thromboembolism was observed in 4.73% of breast cancer patients, with a majority of postmenopausal women, a higher prevalence in patients with advanced-stage disease, all PTE occurring after treatment, most of them being chronic thrombosis. The study’s limitations include a small study group and study duration. **Keywords:** PULMONARY THROMBOEMBOLISM, BREAST CANCER, COMPUTED TOMOGRAPHY, MALIGNANCY-ASSOCIATED THROMBOSIS.

# **Incidence of breast neoplasm associated with pulmonary thromboembolism: a retrospective single center study**

## **INTRODUCTION**

Breast cancer is the most frequently diagnosed malignancy in women worldwide and the leading cause of cancer-related mortality in females, according to World Health Organization (WHO) (1). Given its high prevalence, the correlation between breast cancer and thromboembolic events, such as PTE, has become a significant clinical concern (2).

PTE is a life-threatening complication and a major cause of morbidity and mortality, with an annual incidence of 39-115 cases per 100,000 individuals (3). PTE is frequently associated with malignancy, particularly due to cancer-induced hypercoagulability and cancer-related treatments, which increase thromboembolic risk by four to seven times compared to the general population (2, 4, 5).

Certain malignancies, such as pancreatic, ovarian, brain, stomach, gynecological, and hematological cancers, carry a high risk for thromboembolism, while lung and colorectal cancers pose an intermediate risk. Breast cancer is traditionally considered to have a lower risk of thromboembolism than these malignancies; however, literature on this topic remains limited (2, 6).

Imaging plays an important role in the evaluation and management of PTE and contrast-enhanced chest computed tomography remains the golden standard for diagnosis (7, 8).

## **MATERIALS AND METHODS**

We conducted a retrospective study using electronic medical records from "Sf. Spiridon" County Clinical Emergency Hospital from Iasi, database analysing patients from the 1st of January 2023 to 31st of November 2024, and selected a number of 211 patients diagnosed with PTE. Patients were

included in this study if they had histologically confirmed breast cancer and were diagnosed with PTE through contrast enhanced chest computed tomography. SPSS version 29.0 was the software for the statistical analysis. We used descriptive statistics to calculate mean, standard deviation, median, and interquartile range.

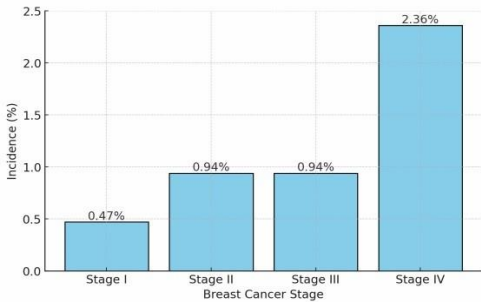
Computed tomography pulmonary angiography (CTPA) was performed with a Philips Incisive 64 detector CT with the following protocol: cranio-caudal thoracic scan from the chest aperture to the costophrenic angles, in post inspiratory apnea, beginning with a noncontrast enhanced scan; bolus tracking technique; up to 100 mL (1 mL/kg body weight) iodinated contrast medium (concentration of 370-400 mg iodine/mL) is injected intravenously with an automatic injector, with the speed of 3-4 mL/second (s), followed by 50 mL of saline chaser with the same speed. The delay for the arterial phase scan is 7s after the density in the pulmonary artery reaches 180 HU (Hounsfield Units) and the venous phase is performed at 20 s after the arterial phase (9).

## **RESULTS**

This study aims to provide an in-depth analysis of the correlation between breast cancer and pulmonary thromboembolism through a retrospective observational study. We conducted a retrospective study using electronic medical records from hospital database analyzing patients from the 1st of January 2023 to 31st of November 2024, and selected a number of 211 patients diagnosed with PTE; among them 34 have previously been diagnosed with malignancies, 19 with digestive malignant tumors, 10 with breast cancer and 5 with lung cancer. The incidence of breast cancer associated with PTE found in our study was

4.73% (n=10), less frequently associated with PTE compared to digestive cancers (n=19, 9%) and more frequently compared to lung cancer (2.36%). Among the patients diagnosed with breast cancer, 80% (n=7), were postmenopausal women, while premenopausal women were 20% (n=3). The mean age was 55, with standard deviation (SD) 6.96 years and an interquartile range (IQR) of 9.25 years.

The breast cancer stage analysis in our study group was as follows: stage I - 0.47% (n=1), stage II - 0.94% (n=2), stage III - 0.94% (n=2), stage IV - 2.36% (n=5). This data indicates a higher prevalence of pulmonary embolism among stage IV breast cancer patients (2.36%) compared to those in earlier stages (0.5-1%) (fig. 1).

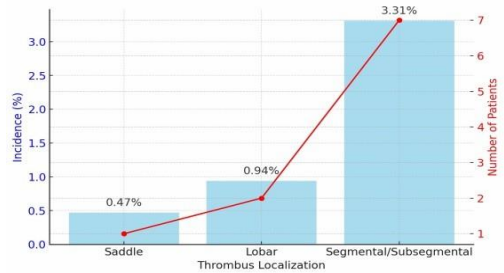


**Fig. 1.** Breast cancer associated with PTE - stage analysis

Among breast cancer cases, 9 patients (4.26%) were morpho pathologically diagnosed with IDC, while only 1 patient (0.47%) had ILC; these findings are probably related to the frequency of IDC versus ILC, not with the higher tendency of the first type of cancer to be related with PTE (10, 11).

From the perspective of thrombus localization, we found saddle thrombus in one case (0.47%), lobar artery thrombi in 2 cases (0.94%) and 7 patients (3.31%) with

segmental and subsegmental artery thrombosis (fig. 2).



**Fig. 2.** Breast cancer associated with PTE - thrombus localization

The most important comorbidities in the breast cancer study group were obesity (n=7, 3.31%), heart conditions including ischemic heart disease (n=5, 2.36%), diabetes (n=2, 0.94%) vasculitis and deep vein thrombosis in the lower limb (n=1, 0.47%) (12, 13).

None of the patients had PTE preceding breast cancer diagnosis, all cases of PTE occurred after treatment, acute PTE was found in 2 cases - 0.94% (the saddle thrombus and one of the lobar artery thrombosis), the other 8 (3.79%) being chronic thrombosis. Considering these two findings we can assume that the thromboembolic risk associated with breast cancer is not necessarily connected to cancer-induced hypercoagulability but rather with cardio-vascular risk factors and cancer-related treatments (14).

**DISCUSSION**

Our findings align with existing literature indicating that malignancy-associated thrombosis is a well-recognized complication (2, 5, 15). The observed 4.73% incidence of breast cancer patients associated with PTE falls within the range of reported data in the literature for malignancy-associated thrombosis (0.13%-8.65%) which

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is higher compared with the incidence of PTE in patients without malignancies (0.11%) (16, 17, 18). PTE incidence that we found is in the middle of the literature range probably because malignancy was found to be associated with PTE particularly in men (4, 19, 20, 21, 22, 23, 24) and our study was exclusively comprised of women.

Moreover, although breast cancer is the number one malignancy in women according to WHO, in our study, digestive cancers (n=19, 9%) were found to be more frequently associated with PTE compared to breast cancers (n=10, 4.73%) This could be attributed to factors such as delayed detection, aggressive tumor type, and distinct thrombotic mechanisms involved in gastrointestinal malignancies.

The most frequent comorbidity in this breast cancer study group was obesity (7 cases) associated in 2 cases with diabetes, both diseases being related to heart conditions and deep vein thrombosis which are associated with a high risk of PTE even without the presence of malignancy and cancer-related treatments (25).

This study is subject to certain limitations, including a relatively small number of breast cancer patients diagnosed with pulmonary embolism, from a single center point of view and a short study duration (two years), which may not fully capture

long-term trends and potential biases related to retrospective data collection.

While promising, further validation with a larger cohort and additional predictive variables is required to improve specificity and clinical applicability for PTE in breast cancer patients.

### **CONCLUSIONS**

This retrospective study highlights the notable incidence of 4.73% of PTE in breast cancer patients, with a majority of postmenopausal women, a higher prevalence in patients with advanced-stage disease, all PTE occurring after treatment, most of them being chronic thrombosis. The study's limitations include a small study group and study duration. While breast cancer remains a leading malignancy in women, its association with thromboembolic events needs further research and increased clinical awareness. Future studies with larger sample sizes and multi-institutional data may provide deeper insights into the pathophysiology, and management of breast cancer-associated PTE.

### **CONFLICT OF INTEREST AND FUNDING**

The authors declare no conflicts of interest. This research received no external funding.

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