

Assessment of Alterations in Coagulation Parameters and Associated Factors in Breast Cancer Patients at Da Nang Oncology Hospital

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ABSTRACT

Background: Breast cancer is associated with coagulation abnormalities, increasing thrombotic risk and influencing disease progression. Understanding changes in coagulation parameters and their correlates is critical for patient management. **Methods:** A cross-sectional study was conducted from December 2023 to April 2024 at Da Nang Oncology Hospital, involving 105 female breast cancer patients. Platelet count (PLT), prothrombin time (PT), and activated partial thromboplastin time (APTT) were measured. Associations with age, disease stage (TNM classification), and metastasis status were analyzed using SPSS 20.0, with $p < 0.05$ considered significant. **Results:** PLT abnormalities occurred in 5.7% of patients, APTT in 1%, and PT showed no changes. Mean PLT was $254.4 \pm 76.9 \times 10^9/L$ (range: $58-458 \times 10^9/L$), APTT 24.2 ± 2.4 s, and PT 10.6 ± 0.7 s. PLT was significantly associated with age ($p < 0.05$), with a cutoff of $>240 \times 10^9/L$ (AUC 0.67, sensitivity 68.2%, specificity 62.9%). No significant associations were found with disease stage or metastasis ($p > 0.05$). **Conclusion:** PLT decreases with increasing age in breast cancer patients, with a cutoff of $240 \times 10^9/L$. Coagulation parameters remain largely within normal ranges, suggesting compensated hemostatic changes. Routine monitoring of PLT in older patients may aid risk stratification.

Keywords: Platelet Count, Prothrombin Time, Activated Partial Thromboplastin Time, Breast Cancer, Coagulation

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INTRODUCTION

Breast cancer is the most common malignancy among women globally, with over 2.2 million new cases and 680,000 deaths annually, according to GLOBOCAN 2020 [1]. In Vietnam, it accounts for 25.8% of female cancers, with 21,555 new cases and 9,345 deaths in 2020 [1]. Beyond its oncologic burden, breast cancer is associated with hemostatic dysregulation, increasing the risk of thrombotic events and contributing to disease progression [2].

Cancer cells activate coagulation through the release of tissue factor, cytokines, and procoagulant microparticles, promoting platelet activation, microthrombus formation, and metastasis [3].

Platelet count (PLT), prothrombin time (PT), and activated partial thromboplastin time (APTT) are key coagulation parameters. Platelets facilitate tumor cell extravasation, immune evasion, and angiogenesis, while PT and APTT reflect extrinsic and intrinsic coagulation pathways, respectively [4]. Abnormalities in these parameters may

indicate disseminated intravascular coagulation (DIC) or paraneoplastic syndromes, influencing prognosis [5]. In Vietnam, limited data exist on coagulation changes in breast cancer, despite the rising incidence. This study aims to evaluate PLT, PT, and APTT changes in breast cancer patients at Da Nang Oncology Hospital, identify associated factors (age, disease stage, metastasis), and establish a PLT cut-off for age-related risk stratification.

MATERIALS AND METHODS

Study Design

A cross-sectional study was conducted from December 1, 2023, to April 30, 2024, at Da Nang Oncology Hospital.

Participants

The study included 105 female patients diagnosed with breast cancer and undergoing medical treatment.

Inclusion criteria: Confirmed breast cancer diagnosis, complete medical records, and baseline PLT, PT, and APTT results at first admission.

Exclusion criteria: Use of anticoagulants, pregnancy, or age <18 years.

Patients were selected using convenience sampling, including all eligible cases during the study period.

Variables

Independent variables: Age (≤ 50 vs. 50 years), TNM stage (0, I, II, III, IV), metastasis status (present vs. absent).

Dependent variables:

- PLT: Normal $150 - 450 \times 10^9/L$, decreased $< 150 \times 10^9/L$, increased $> 450 \times 10^9/L$.

- APTT: Normal 20 – 35s, decreased $< 20s$, increased $> 35s$.

- PT: Normal 11 – 13s, decreased $< 11s$, increased $> 13s$.

Data Collection

Blood samples were collected at admission for complete blood count (PLT) and coagulation tests (PT, APTT) using automated analyzers (Sysmex XN-1000 for PLT, Stago STA Compact for PT/APTT). Clinical data (age, TNM stage, metastasis) were extracted from medical records.

Statistical Analysis

Data were analyzed using Microsoft Excel and SPSS 20.0. Means \pm standard deviations (SD) were reported for continuous variables. Chi-square tests assessed associations between coagulation parameters and categorical variables. Receiver Operating Characteristic (ROC) analysis determined the PLT cut-off for age. Significance was set at $p < 0.05$.

Ethical issues

The study was approved by the Biomedical Ethics Committee of Da Nang University of Medical Technology and Pharmacy (No. 870/BB-HĐĐĐ, November 2023). Informed consent was obtained from all participants, and data were anonymized.

RESULTS

Coagulation Parameter Characteristics

Mean PLT was $254.4 \pm 76.9 \times 10^9/L$ (range: $58 - 458 \times 10^9/L$), APTT 24.2 ± 2.4 s (range: 12.6–29.8 s), and PT 10.6 ± 0.7 s (range: 9.5–12.6 s) (Table 1). PLT and APTT were within normal ranges, while PT was slightly below the reference range (11–13 s).

Table 1. Mean Values of Coagulation Parameters

Parameter	Mean \pm SD	Reference Range	Min	Max
PLT ($\times 10^9/L$)	254.4 ± 76.9	150–450	58	458

APTT (s)	24.2 ± 2.4	20–35	12.6	29.8
PT (s)	10.6 ± 0.7	11–13	9.5	12.6

Prevalence of Coagulation Abnormalities

PLT abnormalities occurred in 5.7% (6/105) of patients, APTT in 1% (1/105), and PT showed no abnormalities (Table 2).

Table 2. Prevalence of Coagulation Abnormalities

Parameter	Abnormal, n (%)	Normal, number (percentage)	Total
PLT	6 (5.7)	99 (94.3)	105
APTT	1 (1.0)	104 (99.0)	105
PT	0 (0.0)	105 (100.0)	105

Factors Associated with Coagulation Changes

Age

PLT was significantly lower in patients >50 years ($239.4 \pm 81.1 \times 10^9/L$) compared to ≤ 50 years ($278.8 \pm 6.1 \times 10^9/L$, $p < 0.05$). No significant differences were found for APTT or PT ($p > 0.05$, Table 3). ROC analysis identified a PLT cutoff of $>240 \times 10^9/L$ for age differentiation (AUC 0.67, sensitivity 68.2%, specificity 62.9%, Figure 1).

Table 3. Coagulation Parameters by Age

Parameter	≤ 50 years old	> 50 years old	p-value
PLT ($\times 10^9/L$)	278.8 ± 6.1	239.4 ± 81.1	< 0.05
APTT (s)	24.4 ± 2.3	24.0 ± 2.5	ns
PT (s)	10.7 ± 0.8	10.6 ± 0.6	ns

ns: not significant

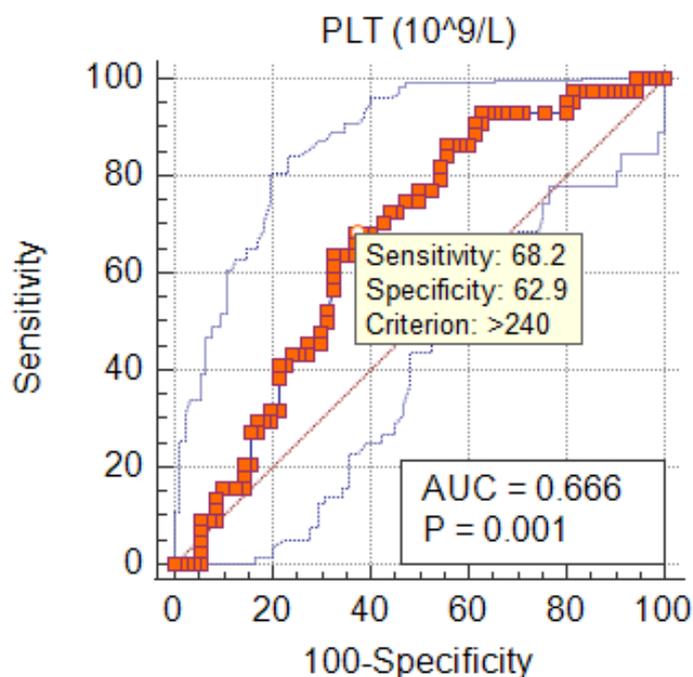


Figure 1. ROC Curve for PLT Cutoff by Age

PLT cutoff of $>240 \times 10^9/L$ distinguishes patients ≤ 50 vs. >50 years old (AUC 0.67, sensitivity 68.2%, specificity 62.9%).

Disease Stage

No significant associations were found between PLT, APTT, or PT and TNM stage ($p > 0.05$, Table 4). PLT was lowest in stage I ($239.0 \pm 72.4 \times 10^9/L$) and highest in stage 0 ($299.1 \pm 94.4 \times 10^9/L$).

Table 4. Coagulation Parameters by TNM Stage

Parameter	Stage 0	Stage I	Stage II	Stage III	Stage IV	p-value
PLT ($\times 10^9/L$)	299.1 ± 94.4	239.0 ± 72.4	249.3 ± 77.5	262.9 ± 66.5	279.0 ± 80.9	ns
APTT (s)	24.1 ± 2.0	24.4 ± 1.6	24.2 ± 2.9	23.7 ± 2.0	24.3 ± 3.6	ns
PT (s)	10.3 ± 0.7	10.6 ± 0.6	10.7 ± 0.7	10.6 ± 0.8	11.2 ± 0.8	ns

ns: not significant

Metastasis

No significant differences were observed in PLT, APTT, or PT between patients with and without metastasis ($p > 0.05$, Table 5).

Table 5. Coagulation Parameters by Metastasis Status

Parameter	No Metastasis	Metastasis	p-value
PLT ($\times 10^9/L$)	259.3 ± 79.8	246.4 ± 72.1	ns
APTT (s)	24.2 ± 2.7	24.1 ± 2.0	ns
PT (s)	10.6 ± 0.7	10.8 ± 0.7	ns

ns: not significant

DISCUSSIONS

This study found a low prevalence of coagulation abnormalities in breast cancer patients at Da Nang Oncology Hospital, with PLT and APTT changes in 5.7% and 1% of cases, respectively, and no PT abnormalities. Mean PLT ($254.4 \times 10^9/L$), APTT (24.2 s), and PT (10.6 s) were largely within or near normal ranges, suggesting compensated hemostatic changes. A significant association was observed between PLT and age ($p < 0.05$), with a cut-off of $> 240 \times 10^9/L$, but no associations were found with TNM stage or metastasis. These findings

align with prior studies while highlighting unique aspects of the Vietnamese context.

Coagulation Parameter Changes

The mean PLT of $254.4 \times 10^9/L$ is consistent with Toaiz et al. (2014), who reported $256.1 \times 10^9/L$ in breast cancer patients [6], and slightly lower than Faruk et al. (2014)'s $318 \times 10^9/L$ [7]. The 5.7% prevalence of PLT abnormalities (primarily thrombocytopenia) is lower than Liu et al. (2022)'s 7.9% in Chinese breast cancer patients [8], possibly reflecting differences in patient populations, treatment regimens, or disease severity. Thrombocytopenia in breast cancer may result from bone marrow suppression due to chemotherapy or tumor infiltration, while

thrombocytosis, observed in some cases, is linked to paraneoplastic syndromes driven by cytokines like interleukin-6 [9]. The low prevalence of APTT (1%) and PT (0%) abnormalities aligns with Toaiz et al. (2014), who found normal PT and APTT but elevated fibrinogen and PLT compared to controls [6]. This suggests that breast cancer induces a hypercoagulable state with compensated coagulation pathways, preventing overt DIC in most patients [10]. The slightly shortened mean PT (10.6 s vs. reference 11–13 s) contrasts with Faruk et al. (2014)'s prolonged PT (14.8 s) [7]. This discrepancy may stem from differences in assay methodologies, patient treatment status (e.g., chemotherapy-induced liver dysfunction), or population-specific factors, such as nutritional status in Vietnamese patients affecting vitamin K-dependent factors [11]. APTT's normal range (24.2 s) is consistent with international studies, indicating intact intrinsic pathway function despite cancer-related procoagulant activity [12]. The low rate of abnormalities suggests effective hemostatic compensation, possibly due to early-stage disease or pre-treatment sampling in our cohort.

Age and Platelet Count

The significant association between PLT and age ($p < 0.05$), with lower PLT in patients >50 years (239.4 vs. $278.8 \times 10^9/L$), corroborates Santimone et al. (2011), who reported PLT of $258.5 \times 10^9/L$ in individuals ≤ 50 years and $241.7 \times 10^9/L$ in those >50 years [13]. The PLT cutoff of $>240 \times 10^9/L$ (AUC 0.67) is slightly higher than Shaoqing et al. (2020)'s $229.5 \times 10^9/L$ for poor prognosis prediction [14] but lower than Ronnau et al. (2023)'s $297 \times 10^9/L$ in Brazilian patients [15]. Age-related PLT decline may reflect reduced hematopoietic stem cell reserve or lower thrombopoietin

levels in older patients, as proposed by Biino et al. (2013) [16]. In breast cancer, older age may exacerbate thrombocytopenia due to cumulative treatment effects or comorbidities, such as liver dysfunction or malnutrition, common in Vietnam's aging population [17].

The moderate diagnostic performance of the PLT cutoff (sensitivity 68.2%, specificity 62.9%) suggests its utility in risk stratification, particularly for older patients. Low PLT in elderly patients may indicate increased thrombotic or bleeding risk, necessitating tailored monitoring [18]. In Vietnam, where breast cancer incidence is rising among older women due to improved screening and life expectancy [19], age-specific PLT thresholds could guide clinical decision-making, such as anticoagulant prophylaxis or chemotherapy adjustments.

Disease Stage and Metastasis

The lack of association between coagulation parameters and TNM stage ($p > 0.05$) contrasts with Caine et al. (2003), who reported progressive coagulation abnormalities with advanced stages [20]. Our findings align with Giannakeas et al. (2022), who found no consistent PLT changes across stages [21]. The lowest PLT in stage I ($239.0 \times 10^9/L$) and highest in stage 0 ($299.1 \times 10^9/L$) may reflect sampling variability or early compensatory thrombopoiesis in non-invasive disease. Similarly, no association with metastasis ($p > 0.05$) differs from Liu et al. (2022), who linked thrombocytopenia to metastatic disease [8]. This discrepancy may be due to our cohort's limited metastatic cases or pre-treatment sampling, which may not capture advanced disease's procoagulant effects [22].

Breast cancer's hypercoagulable state, driven by tissue factor and thrombin,

promotes metastasis by facilitating tumor cell adhesion and angiogenesis [23]. The absence of significant PT/APTT changes across stages suggests that these parameters are less sensitive to disease progression than biomarkers like D-dimer or fibrinogen, which were not measured here [24]. In Vietnam, late-stage diagnosis is common due to limited screening access in rural areas [25], yet our cohort's normal coagulation parameters may indicate early intervention or selection bias toward treated patients.

Clinical Implications in Vietnam

The low prevalence of coagulation abnormalities suggests that routine PLT, PT, and APTT monitoring may suffice for most breast cancer patients in Vietnam, with additional tests (e.g., D-dimer) reserved for high-risk cases. The age-PLT association highlights the need for age-stratified management, particularly in older patients prone to thrombocytopenia-related complications [26]. Vietnam's healthcare system, with constrained resources, could benefit from integrating PLT cutoffs into clinical guidelines to optimize thromboprophylaxis and reduce bleeding risks during chemotherapy [27]. Future research should explore longitudinal coagulation changes post-treatment and include biomarkers like fibrinogen and D-dimer to better predict thrombotic risk.

The study's small sample size ($n = 105$) and single-center design limit generalizability to Vietnam's diverse population. Convenience sampling may introduce bias, and the lack of post-treatment data restricts insights into therapy-induced coagulation changes. D-dimer, fibrinogen, or thrombopoietin levels were not measured, potentially missing subtle hemostatic alterations. Larger, multi-center studies with longitudinal designs are

needed to validate the PLT cut-off and explore stage/metastasis associations.

CONCLUSIONS

To conclude, breast cancer patients at Da Nang Oncology Hospital exhibit minimal coagulation abnormalities, with PLT and APTT changes in 5.7% and 1% of cases, respectively, and no PT changes. PLT is significantly associated with age, decreasing in patients >50 years, with a cutoff of $>240 \times 10^9/L$. No associations were found with disease stage or metastasis. Routine PLT monitoring, particularly in older patients, may aid risk stratification in resource-limited settings like Vietnam.

Supplementary Materials

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Author Contributions

Study concept and design: TTL; data acquisition: NTN; data analysis and interpretation: NTN; manuscript drafting: TTL; statistical analysis: TTMD.

Institutional Review Board Statement

The study was conducted according to the Declaration of Helsinki and approved by the Biomedical Ethics Committee of Da Nang University of Medical Technology and Pharmacy (No. 870/BB-HĐĐĐ, November 2023).

Informed Consent Statement

Informed consent was obtained from all participants.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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