

Original Research

Comparative Study on Clinicopathological Characteristics of Breast Cancer in Vietnam and Italy

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Abstract

Background: In Vietnam and Italy, breast cancer (BC) occurs in women more frequently than any other cancer. Vietnam has a substantially lower incidence of breast cancer than Italy, but a higher mortality rate. Most Vietnamese patients present to the hospital with severe tumors at the late stages of diagnosis. The purpose of this study was to compare clinicopathologic features, biomarkers, and subtypes of BC between Vietnamese women and Italian ones. **Methods:** The sample was collected from all Vietnamese patients undergoing surgery with the diagnosis of primary invasive breast carcinoma in Hue Central Hospital as well as Hue University Hospital in Vietnam during 1 year from April 2016 to April 2017, and from the same category of women in Sassari University Hospital, Italy during the year 2016. The study parameters in both groups consisted of age at diagnosis, tumor size, histologic grade, histologic type, axillary node status, stages of diagnosis, biomarkers (Estrogen Receptor - ER, Progesterone Receptor - PR, Ki-67 cell proliferation marker - Ki-67, Human epidermal growth factor receptor 2 - HER2), and molecular subtypes of BC. **Results:** 323 patients were collected in total (235 from Sassari, Italy, and 88 from Thua Thien - Hue province, Vietnam). Vietnamese patients were diagnosed at a younger age than Italian patients, at just 52.5 on average, while the figure for Italian was 62. The Vietnamese BC patients also had a bigger tumor in size, higher grade, more axillary node positivity as well as a later stage of disease in comparison with Italian ones. The proportion of ER-positive was higher in the Italian group than that in Vietnam (88.1 vs 55.7%). The high Ki-67 expression prevalence was significantly higher in Vietnamese patients compared with Italian (81.8 vs 45.1%). The HER2-positive rate in Vietnam was 33%, higher than that in Italy (8.1%). Histologic grade and cell proliferation index Ki-67 were significantly correlated with HER2 positivity in both groups. **Conclusions:** Vietnamese patients demonstrated more aggressive tumor features and worse prognostic biomarkers than Italian patients. The prevalence of HER2 positive and high Ki-67 expression in Vietnamese patients was considerably higher than in Italian patients. The remarkable differences in clinicopathological characteristics between the two populations suggest the diversity of biological tumor, ethnicity, and environment as well as the effectiveness of the screening program.

Keywords: comparative; clinicopathological; characteristics; breast cancer; Vietnam; Italy

1. Introduction

Breast cancer is a frequent type of cancer and the first cause of cancer mortality in women, with an expected incidence of 2.3 million cases globally in 2020. Breast cancer incidence and mortality rates varied greatly among communities and nations due to variances in lifestyles, living environments, and races [1,2]. In Asia, the breast cancer incidence rate is lower compared to that of Western countries, however, it has been rising faster in the last decades [3,4]. Furthermore, recent investigations revealed that there are disparities between these two women groups with breast cancer regarding the clinical features and the biological profiles [5,6].

In Vietnam, a developing country in Southeast Asia, breast cancer happens most frequently, with 21,555 new

cases and 9345 cancer deaths in women in 2020 [1]. It is likewise the most prevalent type of cancer in Italy, a Southern Europe nation, with 55,133 new cases and 12,633 deaths in 2020 [1,7,8]. Breast cancer (BC) is the primary cause of mortality for women both in Vietnam and Italy. The majority of BC patients in Italy occurred in women aged 50 to 69, with a low proportion of metastases at first diagnosis [9].

In general, when compared to Western countries, Vietnam has younger breast cancer onset ages [6]. Vietnam has a greater mortality rate than Italy while having a significantly lower incidence rate of BC. Most Vietnamese BC patients present to the hospital at a young age having aggressive tumors at the late stages of diagnosis [10]. Furthermore, Vietnamese tumors have a high rate of human epidermal growth factor receptor (HER2)-positive and some mod-



ern techniques to evaluate the amplification of *HER2* gene, such as fluorescence *in situ* hybridization (FISH), have not been commonly used yet. As a result, many patients are not properly diagnosed, classified, and treated [6,10,11]. To identify BC patients who might be beneficial from targeted *HER2* therapy, it is essential to accurately assess *HER2* status [12].

This study aimed to make a comparison of the clinical and pathological features of BC between Vietnamese and Italian women as well as to correlate *HER2* with prognostic factors to find out whether there are significant disparities in the biological profiles of tumors in both countries. The findings of this research will also contribute to improving the Vietnamese breast cancer screening program.

2. Methods

2.1 Study Settings

This comparative retrospective study investigated the clinicopathological features of women diagnosed with primary invasive breast carcinoma in two communities from Thua Thien - Hue, Vietnam, and Sassari, Italy.

2.2 Data Collection

2.2.1 Vietnamese Group

Paraffin tissue was blocked of 88 Vietnamese female patients consecutively diagnosed with primary invasive breast carcinoma for 1 year, from April 2016 to April 2017 at Hue University of Medicine and Pharmacy Hospital and Hue Center Hospital, Vietnam. The blocks were re-examined regarding histopathology, immunohistochemistry (IHC), and fluorescence *in situ* hybridization (FISH) at the Anatomical pathology institute of Sassari University hospital, Italy.

2.2.2 Italian Group

The retrospective data included 235 consecutive invasive breast carcinomas diagnosed during the year 2016 at the Anatomical pathology institute of Sassari University hospital. The IHC results for biomarkers such as Estrogen Receptor (ER), Progesterone Receptor (PR), Ki-67 cell proliferation marker (Ki-67), *HER2* and the FISH to detect *HER2* gene amplification were extracted from an established information system data of the Anatomical Pathology Institute of Sassari University Hospital.

In both groups, the tissue specimens were re-embedded when necessary. The IHC assays were conducted on all formalin-fixed, paraffin-embedded breast cancer tissue. The FISH tests were performed on all cases with *HER2* score (2+) in IHC. The results were analyzed by the same pathologists in the Anatomical Pathological Institute of Sassari University Hospital.

2.3 Histology and Immunohistochemistry

All tissue specimens were formalin-fixed paraffin-embedded and stained with hematoxylin and eosin for histopathological examination, according to WHO Classification [13]. Histological grading was evaluated based on the Elston-Ellis criteria [14].

The IHC assays were performed on 3 μ m thicknesses of tissue sections on the Ventana Benchmark Ultra automatic staining system, using antibodies such as anti-Estrogen receptors (SP1), anti-Progesterone Receptor (1E2), anti-Ki-67 (30-9) and anti-*HER2/neu* (4B5). The ER, and PR staining results were scored $\geq 1\%$ of tumor cell nuclei staining as positive. Cell proliferation index Ki-67 was assessed based on the percentage of positively stained cells among the total number of invasive tumor cells and using a cut-off point of 14% to classify [15].

HER2 protein expressions were scored from 0 to 3+, based on the intensity of cell membrane immunostaining and the percentage of membrane-positive cells, according to ASCO/CAP 2013 guidelines update. *HER2* scores 0 and 1+ in IHC were classified as negative. The cases of IHC 2+ and 3+ were equivocal and positive, respectively [16].

2.4 Fluorescence in Situ Hybridization

The FISH was applied to the cases of *HER2* (2+) to detect the gene amplification at the Anatomical pathology institute of Sassari University hospital, Italy, using the PathVysion *HER2* DNA probe kit (Vysis Abbott Molecular Inc), following the protocol of the manufacturer's instructions. The evaluation is based on recommendations of ASCO/CAP guideline update 2013 for *HER2* testing, using the ratio: total LSI *HER2/neu* signals (red)/total CEP 17 signals (green) to analyze the result. *HER2/neu* gene amplification was identified if the LSI *HER2/neu* to CEP17 ratio is ≥ 2 or if this ratio was < 2.0 but the average *HER2* copy number ≥ 6.0 signals/cell. *HER2/neu* gene is not amplified if the average *HER2* copy number < 4.0 signals/cell. A score of equivocal was given in the case of the average *HER2* copy number ≥ 4.0 signals/cell and < 6.0 signals/cell [16].

HER2 positive includes the *HER2* (3+) score in immunohistochemistry and the *HER2* gene amplification in FISH.

2.5 Statistical Analysis

Utilizing the SPSS version 16.0 statistical program (IBM Corp, Chicago, IL, USA) and the Chi-Square test to compare clinicopathological characteristics between the Vietnamese and Italian women. *p* values less or equivalent to 0.05 were considered significant.

Table 1. Characteristics of breast cancer patients in Vietnam and Italy.

Parameters	Vietnam (n = 88)	Italy (n = 235)	p-value
	n (%)	n (%)	
Age			
Range	29–91	27–99	
Median \pm SD	52.5 \pm 12.8	62 \pm 13.2	$p < 0.001$
<30	2 (2.3)	1 (0.4)	
30–<40	8 (9.3)	8 (3.4)	
40–<50	19 (21.6)	36 (15.3)	
50–<60	35 (39.8)	52 (22.1)	$p < 0.001$
60–<70	14 (15.9)	60 (25.6)	
≥ 70	10 (11.4)	78 (33.2)	
Tumor size			
≤ 2 cm	24 (27.3)	154 (65.5)	
> 2 – ≤ 5 cm	48 (54.6)	71 (30.2)	
> 5 cm	16 (18.2)	6 (2.6)	$p < 0.001$
Unknown	0 (0)	4 (1.7)	
Histological type			
Ductal	82 (93.2)	199 (84.7)	
Others	6 (6.8)	36 (15.3)	$p = 0.043$
Histological grade			
I	5 (5.7)	32 (13.6)	
II	38 (43.2)	133 (56.6)	
III	39 (44.3)	34 (14.5)	$p < 0.001$
Unknown	6 (6.8)	36 (15.3)	
Axillary node			
No metastasis	38 (43.2)	135 (57.4)	
Metastasis	48 (54.6)	78 (33.2)	$p < 0.001$
Unknown	2 (2.3)	22 (9.4)	
Stage of disease			
I	13 (14.8)	102 (43.4)	
II	47 (53.4)	57 (24.2)	
III	26 (29.5)	6 (2.6)	$p < 0.001$
IV	0 (0)	47 (20)	
Unknown	2 (2.3)	23 (9.8)	

3. Results

3.1 Characteristics of Breast Cancer Patients in Vietnam and Italy

323 women who have invasive breast carcinoma in total (88 from Thua Thien - Hue province, Vietnam, and 235 from Sassari, Italy) were included in this cohort study. The clinicopathologic characteristics of both groups were shown in Table 1.

Between the two groups being studied, there was a significant difference in the age of the patients at diagnosis ($p < 0.001$). The Vietnamese women were diagnosed approximately 10 years on average earlier than Italian women (52.5 vs 62). The highest-proportion group of Vietnamese patients in the study was the 50 to 60-year-old group, while breast cancer in Italy increased with age and peaked at the age above 70. Vietnamese women had a considerably greater rate of BC than Italian patients in the group of people under 50 years old (33% vs 19.2%).

Invasive carcinoma of no special type was the most prevalent histological type of cancer among Vietnamese and Italian women. Vietnamese patients rarely had invasive lobular carcinoma. Most Italian women presented with an earlier stage of disease than Vietnamese women (43.4 vs 14.8% in stage I). In contrast, the vast number of Vietnamese patients (72.7%) had a tumor size of ≥ 2 cm compared to 30.6% of the Italian group with the same size range. Vietnamese women presented with poorly differentiated tumors compared to Italian women (30.2 vs 25.0% in grades III and IV). Comparatively to Italian women, Vietnamese women obtained a higher percentage of axillary lymph node-positive disease (33.2% vs 54.6%). Breast cancers in Italy were diagnosed at an early stage, which was significantly higher than that in Vietnam (48.1 vs 15.1%). Inversely, most of the Vietnamese tumors were at late stages, with a percentage of approximately 85% in stage II and stage III.

3.2 Comparison of Biomarkers among the Vietnamese and Italian Patients

All breast tissue sections that were formalin-fixed and paraffin-embedded underwent IHC. Biomarkers detection in breast cancer tissue specimens was presented in Fig. 1. Biomarker differences between the two investigated groups were highly significant (Table 2). The proportion of ER-positive and PR-positive BC was higher in the Italian group than that in Vietnam. On the other hand, the tumor breast cancers from Vietnam presented a higher level of Ki-67 than that from Italy.

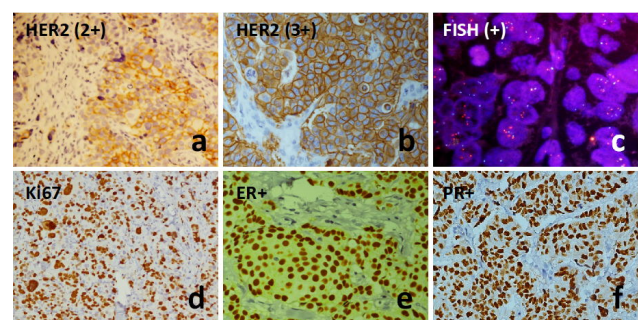


Fig. 1. Biomarkers detection in breast cancer tissue specimens. (a,b) HER2 expression by immunohistochemistry (200 \times magnification). (c) HER2 gene amplification by FISH. Red signals represent HER2 gene, green signals represent CEP17 ($\times 600$). (d) Ki-67 expression by immunohistochemistry (200 \times magnification). (e) ER expression by immunohistochemistry (200 \times magnification). (f) PR expression by immunohistochemistry (200 \times magnification).

Regarding HER2, the FISH tests were applied to all HER2 equivocal (2+) cases in immunohistochemistry to identify the gene amplification. HER2 positivity was defined as either a HER2 score (3+) in IHC or amplification

Table 2. Comparison of biomarkers among the Vietnamese and Italian patients.

Parameters	Vietnam (n = 88) n (%)	Italy (n = 235) n (%)	p-value
ER status			
Negative	39 (44.3)	28 (11.9)	$p < 0.001$
Positive	49 (55.7)	207 (88.1)	
PR status			
Negative	52 (59.1)	63 (26.8)	$p < 0.001$
Positive	36 (40.9)	172 (73.2)	
HER2 status			
Negative	59 (67.1)	216 (91.9)	$p < 0.001$
Positive	29 (32.9)	19 (8.1)	
Ki-67			
<14	16 (18.2)	129 (54.9)	$p < 0.001$
≥14	72 (81.8)	106 (45.1)	

of the *HER2* gene in FISH (Fig. 1c). The rate of HER2 positive was higher in Vietnamese patients than in Italian patients, at 32.9% vs 8.1%, respectively. These differences were considered significant with $p < 0.001$.

The correlation between HER2 status and prognostic factors in patients from Vietnamese and Italian patients was demonstrated in Table 3. The histological grade and the cell proliferation index Ki-67 significantly correlated with HER2 status in both groups. Additionally, HER2-positive, and ER-negative were closely correlated in Vietnamese patients ($p < 0.001$). The tumor size, axillary lymph node metastasis as well as stage of disease were not significantly associated with HER2 status. However, tumors with large size, metastasis and late stage were more frequently associated with HER2 positive. On the contrary, the HER2 status was strongly related with tumor size and stage of disease in Italian patients. However, we found that HER2 was not related to ER status in this group.

3.3 Comparison of Molecular Subtypes among Vietnamese and Italian Patients

Our results showed significant differences between the two studied groups in the distribution of molecular subtypes of BC (Table 4). Italian women were more likely to develop luminal A than more aggressive kinds of BC (HER2 and TNBCs). Approximately 54.1% of Italian women and 18.2% of Vietnamese women had Luminal A subtype, however, Italian women had fewer HER2-enriched (0.9%) than Vietnamese women (22.7%). Comparing the Vietnamese to the Italian group, the proportion of triple-negative subtypes was greater in the Vietnamese group (21.6 vs 10.7%).

4. Discussion

Our research revealed that clinical profile and tumor characteristics varied significantly between breast cancer patients in Italy and Vietnam. The variations in presenta-

tion, clinicopathological profiles, biomarkers, and molecular subtypes might be attributed to the differences in race, lifestyle, living environment, and late diagnosis expression [3,17,18]. Our findings from this study are roughly in accord with those reported in Vietnam and Italy, respectively [6,9,18–21].

Vietnam is advantageously exposed to more light and sunshine because of its southern location compared to Italy. Exposure to light and sunshine promotes cellular glucose absorption while upregulating all hormonal processes, increasing estrogen and thyroxin signals and vitamin D production. In southern populations, all of these characteristics contribute to lower cancer incidence, including lower breast cancer incidence [22].

Compared to Italian women, Vietnamese ones had an earlier onset of breast cancer, in our study. While the average age at diagnosis of Italian women was 62, that figure for Vietnamese was just 52.5. The highest-proportion group of Vietnamese patients in the study was the 50 to 60-year-old group, while breast cancer in Italy increased with age and peaked at the age above 70. Our result was consistent with studies carried out by other Vietnamese and Asian authors. For example, Thanh Huong Tran [23] and Dung X. Pham [4] reported a mean age at diagnosis of approximately 50. The mean age of our findings was comparable to earlier reports from Asian nations [5]. A similar result was also seen in studies on the Italian population as Cossu and Tagliabue [9,24] documented a figure of 60.4 and 61 years old, respectively. The consistency in results so far ultimately proved that Asian women tend to have breast cancer at a younger age than Western ones [4,6]. This suggests that the Vietnamese screening program should be frequently implemented in women 45 to 60 years of age and widely applied in the general population.

When it comes to tumor size, while most Vietnamese patients had larger-than-2 cm tumors (72.2%), in Italy, the highest percentage belonged to small tumors which were less than 2 cm in size (65.5%). Similarly, compared to Italian patients, a much lower percentage of Vietnamese ones with breast cancer had been diagnosed early (15.1% vs 48.1%). Most Vietnamese patients were diagnosed with an advanced diagnosis, with about 85% in stages II and III. Our study showed that Vietnamese patients hospitalized with big tumors had been developing diseases for a long time and had metastasis. Moreover, most of them were in high grade. Specifically, the percentage of tumors in grade III was significantly higher than that in Italian patients (47.6% vs 17.1%).

Similar characteristics of Vietnamese breast cancer patients were also reported in other recent studies [18,25]. For instance, a study by Vu Hong Thang also compared those features among Vietnamese and Swedish patients with breast cancer [19,26]. Furthermore, similar to our findings, a study by Giovanna Tagliabue showed that Italian patients had smaller tumors and were diagnosed at an early

Table 3. Correlation between HER2 status and prognostic factors in Vietnamese and Italian patients.

Parameters	Vietnam			Italy		
	HER2 negative	HER2 positive	<i>p</i> value	HER2 negative	HER2 positive	<i>p</i> value
	n (%)	n (%)		n (%)	n (%)	
Age						
<50	17 (28.8)	12 (41.4)	0.238	41 (19)	4 (21)	0.766
≥50	42 (71.2)	17 (58.6)		175 (81)	15 (79)	
Tumor size						
≤2 cm	19 (32.2)	5 (17.2)	0.061	147 (69.3)	7 (36.8)	0.016
>2–≤5 cm	33 (55.9)	15 (51.7)		60 (28.3)	11 (57.9)	
>5 cm	7 (11.9)	9 (31.1)		5 (2.4)	1 (5.3)	
Stage of disease						
I	12 (21.1)	1 (3.4)	0.057	98 (50.7)	4 (21.1)	0.005
II	31 (54.4)	16 (55.2)		47 (24.4)	10 (52.6)	
III	14 (24.5)	12 (41.4)		4 (2.1)	2 (10.5)	
IV	0 (0)	0 (0)		44 (22.8)	3 (15.8)	
Histological type						
Ductal	53 (89.8)	29 (100)	0.172	180 (83.3)	19 (100)	0.088
Others	6 (10.2)	0 (0.0)		36 (16.7)	0 (0)	
Histological grade						
I	5 (9.4)	0 (0.0)	<0.001	32 (17.8)	0 (0)	0.0035
II	32 (60.4)	6 (20.7)		122 (67.8)	11 (57.9)	
III	16 (30.2)	23 (79.3)		26 (14.4)	8 (42.1)	
Axillary node status						
No metastasis	29 (50.9)	9 (31.1)	0.08	125 (64.4)	10 (52.6)	0.31
Metastasis	28 (49.1)	20 (68.9)		69 (35.6)	9 (47.4)	
ER status						
Negative	19 (32.8)	20 (69.0)	<0.001	26 (12)	2 (10.5)	0.845
Positive	40 (67.2)	9 (31.0)		190 (87)	17 (89.5)	
PR status						
Negative	32 (54.2)	20 (69.0)	0.187	58 (26.9)	5 (26.3)	0.96
Positive	27 (45.8)	9 (31.0)		158 (73.1)	14 (73.7)	
Ki-67						
<14	16 (27.1)	0 (0.0)	0.002	128 (59.3)	1 (5.3)	<0.001
≥14	43 (72.9)	29 (100.0)		88 (40.7)	18 (94.7)	

stage with low grades [9]. The differences in tumor characteristics between Vietnamese and Italian groups may be mainly due to delays in diagnosis and treatment in Vietnam. Lack of knowledge, being too busy, staying far from treatment facilities, bearing high treatment costs, and not receiving good quality healthcare service, ... might be some reasons leading to the delay in the treatment [10]. In addition, the participation rate in breast cancer screening programs in Vietnam and other Asian countries was lower compared to Western countries [3,18]. There is not enough information provided about screening processes and how screening services are integrated with other areas of the health system. Thus, several patients arrived at the hospital when their tumor had already become large in size and their disease stage was late with high grade and accompanying metastasis [18]. Delay in cancer diagnosis is also a major contributor to an increased risk of premature mortality, lower cancer survival rate, and a higher cancer burden. Therefore, it is necessary to launch a more positive screening strategy for the early diagnosis of cancer patients.

Regarding ER/PR status, our result recognized a lower percentage of ER- and PR-positive in Vietnamese tumors than that in Italian ones. Similar to our findings, ER-positive rates of breast cancer in Vietnamese patients were statistically significantly lower than in Swedish ones, as reported in another study [26]. Our results reconfirmed previous findings of a lower percentage of ER/PR positive in Asian women than in Western ones in the advanced publication [27].

Moving to cell proliferation index (Ki-67), this is a crucial biomarker that has been used in routine clinicopathological practice. This prognostic marker predicts whether endocrine therapy and chemotherapy will be effective or ineffective. Most Vietnamese patients with breast cancer were diagnosed at a late stage when their tumor had been developing for a long time. Thus, the percentage of the Ki-67 high (≥14%) in the Vietnamese patients was undoubtedly higher than that in the Italian ones (81.8% vs 45.1%). The mean Ki-67 of the Vietnamese group was substantially greater than that of the Italian ones (28.9% vs

Table 4. Distribution of molecular subtypes among Vietnamese and Italian patients.

Molecular subtypes	Vietnam	Italy	<i>p</i> -value
	n (%)	n (%)	
Luminal A (HER2 negative, Ki-67 low)	16 (18.2)	127 (54)	<i>p</i> < 0.001
Luminal B (HER2 negative, Ki-67 high)	24 (27.3)	64 (27.2)	
Luminal B (HER2 positive)	9 (10.2)	17 (7.2)	
HER2 enriched	20 (22.7)	2 (0.9)	
Triple-negative	19 (21.6)	25 (10.6)	
Total	88 (100)	235 (100)	

18.2%). Based on Elston-Ellis, tumor grading includes an analysis of mitotic numbers. It is not surprising to know that tumors of Vietnamese patients had high Ki-67 values, which were corresponding to grade III. Similar results have also been reported in another study on Vietnamese women in 2015 [19].

In terms of HER2 results, our study revealed that Vietnamese patients had a considerably greater prevalence of HER2 positive than Italian patients did (32.9% vs 8.1%). Our findings in HER2-positive Italian patients matched those of a previous study by K.D. Awadelkarim [20] and a study by Pathmanathan were conducted in Southern Vietnam [6]. The prevalence of HER2-positive breast cancer diagnosed in Vietnam matched that in other Asian nations (Malaysia and Hong Kong), but it was generally higher than that in Western nations [6,20,28]. A study comparing Vietnamese and Swedish breast cancer patients has also discovered these differences [26]. These disparities could result from variations in population characteristics including biological profiles, ethnicities, geographical location, and environment [29]. Recent studies found a correlation between the HER2 status and clinicopathological features, as well as between the HER2 status and biomarkers in breast cancer [30,31]. We got similar findings in our study, showing that the status of HER2 in Vietnamese women was substantially correlated with histological grade and cell proliferation index Ki-67, but not with any other clinicopathological characteristics such as tumor size, axillary lymph node metastasis or stage of disease. On the other hand, tumors with big size, metastasis and advanced stage were more likely to have HER2-positive breast cancer. The prevalence of HER2 positive and high Ki-67 index was considerably higher in Vietnamese patients than in Italian ones. Therefore, Vietnamese breast cancer had a worse prognosis and higher mortality rate. In addition, most of the Vietnamese breast cancer were premenopausal cases that were associated with worse prognostic indicators such as low ER/PR positive, higher Ki-67, and HER2 enrichment. This leads to a high breast cancer mortality rate in Vietnam.

The Ki-67 index was added as a criterion by the 12th St. Gallen International Breast Cancer Conference to identify luminal A from luminal B [32]. In our study, 14% was chosen as an optimal cut-off point for Ki-67. This cut-off point has also been utilized by several authors in their re-

search [15,33]. Breast cancer subtypes in Italian and Vietnamese people differed in some aspects. Luminal A cancers were less prevalent (18.2%), whereas Luminal B, triple-negative, and HER2 enrichment tumors were commonly found. In contrast, Italian women were more likely to have luminal A than Vietnamese women (54.1% vs 18.2%). Italian women, on the other hand, had less HER2 enrichment than Vietnamese women (0.9% vs 22.7%). Our findings for subtypes matched those of another study on Italian women [9,21]. This study showed that the luminal A subtype had the highest percentage (66.2%), while the triple-negative occupied 8.5% [9]. Another study comparing the luminal A of Vietnamese and Swedish patients found that the luminal A of Sweden was higher than that of the Vietnamese. In contrast, HER2 enrichment in Vietnam was lower than in Sweden [19]. These differences among studies existed because of the heterogeneous nature of the breast cancer [34]. Furthermore, in this study, an increase in the percentage of high Ki-67 contributed to a decrease in the prevalence of luminal A. In addition, the variances in biological properties of tumors among countries may be explained by our baseline data being different from other studies. The environment, ethnicity and geographic location all also affect molecular subtypes' distribution [21,29].

5. Conclusions

In conclusion, Vietnamese patients demonstrated more severe tumor features and worse prognostic biomarkers than Italian patients. Most Vietnamese patients presented to the hospital with large tumor size at the advanced stage of disease with high histologic grade and metastasis. The HER2 positive, high-level Ki-67 and luminal B prevalence in Vietnamese women were considerably higher than in Italian ones. Histological grade and the cell proliferation index Ki-67 were significantly correlated with HER2 positivity in both groups. The remarkable differences in clinicopathological characteristics between two populations might be explained by the diversities in biological profiles, ethnicities, geographical location, living environment, and the effectiveness of the screening program as well. We recommend a screening program be implemented in the younger population, particularly in women with a family having a history of BC to detect breast cancer at an earlier stage.

Data Availability

The dataset used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization, methodology, and supervision—FT, VM, and TDC; data collection, formal analysis, statistical analysis—TTNP, FT, VM, TNT, HTA, TLV, and HTVT; the original draft, manuscript revision, review, and editing—TTNP, TNT, and TDC. All authors contributed to the interpretation of the data and approved the final manuscript.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The privacy of all patients enrolled in this study was protected. The study was approved by the Institutional ethics committee of Hue University of Medicine and Pharmacy (approval number: H2020/034).

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Conflict of Interest

The authors declare no conflict of interest.

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