CLINICAL AND SUBCLINICAL CHARACTERISTICS OF BREAST CANCER PATIENTS UNDERGOING TRASTUZUMAB TREATMENT

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ABSTRACT

Objective: Describing the clinical and subclinical characteristics of the breast cancer patient treated with Trastuzumab at Thong Nhat hospital.

Subjects and methods: A retrospective study on 48 patients with breast cancer were treated with Trastuzumab at Thong Nhat hospital.

Results: Mean age: 48.4 ± 3.4 years old. The 45-60 age group accounted for the largest proportion with 47.92%. Functional symptoms: the proportion of patients who self-examined the tumor accounted for the highest rate with 64.58%. There were 12.50% of patients with pain symptoms, 10.42% of patients with nipple discharge. Physical symptoms: tumor in the upper-external quadrant accounted for the largest percentage with 58.33%. The average size of the tumors was 2.78 ± 1.32 (cm). The main type of lesions was detected on ultrasound was local lesion with over 77.08% with an unknown boundary feature (66.67%) and invasive, accounting for 43.75%. Histopathological type accounted for the highest proportion was the invasive tubular carcinoma (79.92%). Histological degree accounted for the highest percentage was degree 2 with 45.83%. Stage II accounted for the highest rate with 39.58%, stage VI had the lowest rate with 10.42%.

Conclusion: Common age of breast cancer patients was 45 - 60 years old, mainly the self-examined tumor, common breast tumors were found in the upper-external quadrant. On ultrasound, mainly the local lesion, the boundary was not clear. The histopathological type was the invasive tubular carcinoma.

Keywords: Breast cancer, trastuzumab, clinical and subclinical features.

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1. INTRODUCTION

According to GLOBOCAN 2018, an estimated 2.1 million new cases of female breast cancer (BC) were diagnosed globally, accounting for 1/4 of all cancers in women. BC also causes the death of more than 600,000 patients, accounting for 6.6% of all cancer cases [1]. In Vietnam, BC is the most common cancer overall in 2012. The incidence rates increase between 30-34 years old and the highest rates are around 55-59 years old [2]. Most BC are carcinomas. Lesions are primary malignant neoplasms located in any portion of the mammary gland. A biopsy is the only definitive way to make a diagnosis of BC; however, when this test is available, it is usually not an early stage cancer. Therefore, screening and early detection of BC should be based on a number of clinical and subclinical features. Therefore, we conducted this study with the aim of describing the clinical and subclinical characteristics of the breast cancer patient treated with Trastuzumab at Thong Nhat hospital".

2. RESEARCH SUBJECTS AND METHODS

2.1. Patient population

48 breast cancer patients received trastuzumab therapy at Thong Nhat hospital.

* Inclusion criteria

- Breast cancer patients received at least onedose of trastuzumab.

- Patients with breast cancer had received least one echocardiogram prior to treatment with trastuzumab (LVEF >53%).

* Exclusion criteria

- Patients with other types of cancer.

- The patient refused to participate in the study.

- Incomplete medical records.

- Patients taking other medications that have been shown to affect myocardial function.

- Patients with significant cardiovascular history such as recent myocardial infarction, CHF, angina, significant arrhythmias or conduction disorders, uncontrolled hypertension, LV hypertrophy, or valvular disease significant heart.

2.2. Research methods

Study design: Retrospective study.

Sample size: Choosing the whole sample, including all patients who met the inclusion criteria during the study period, the total number of patients was 48.

Research variables:

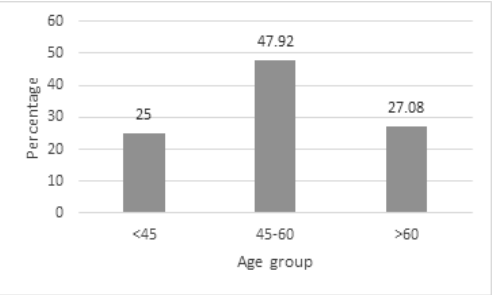
Clinical characteristics: Age (year) and age groups (<45 years; 45-60 years; >60 years). Menopausal status when diagnosed with BC (menopause, non-menopause). Pain (Yes/no). Tumor features (location, size, nipple discharge).

Subclinical characteristics: Features on ultrasound include: morphology, orientation, margins, internal structure, echogenicity and invasiveness of the tumor. Hormone receptor status (positive/negative). Pathological features: type of cancer; histological grade (grade 1, grade 2, grade 3 and unclassified) and TNM staging for BC.

2.3. Statistical analysis: Data were entered and analyzed using IBM SPSS software.

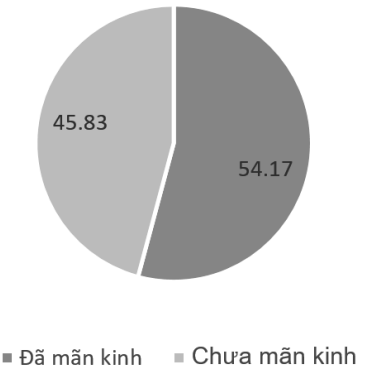
3. RESULTS

Figure 1. Age characteristics of participants



Age group 45-60 accounted for the largest proportion with (47.92%). Age group < 45 accounted for the lowest proportion (25%). Ages ranged from 28 to 75 years old. Mean age was 48.4 years.

Figure 2. Menopausal status when diagnosed with breast cancer



The proportion of menopausal patients (54.17%) is higher than the that of non-menopausal patients (45.83%).

Table 1. Clinical symptoms

Reason for admission	Number of patients	Percentage
Breast pain	6	12.50
Nipple discharge	5	10.42
Self-detected breast mass	31	64.58
Other breast changes	3	6.25
Accidental discovery	6	12.50

Among the reasons for admission, the highest rate was self-detected breast mass (64.58%). 12.50% of patients had breast pain. 10.42% of patients had nipple discharge. Other breast changes accounted for 6.25%.

Table 2. Clinical signs

Clinical signs	**Number of patients**	**Percentage**
Tumor location		
Upper inner quadrant	8	16.67
Upper outer quadrant	28	58.33
Lower inner quadrant	1	2.08
Lower outer quadrant	6	12.50
Other location	5	10.42
Size (cm)		
X ± SD	2.78 ± 1.32	
Min	1.33	
Max	7.65	

Tumors in the upper outer quadrant are the most frequent site of tumor location (58.33%). Tumors in the lower inner quadrant are the least frequent site of tumor location (2.08%). The mean tumor size was 2.78 ± 1.32 (cm). The largest size was 7.65 cm

Table 3. Ultrasound characteristics of breast lesions

Ultrasound characteristics		Number of patients	Percentage
Type of lesions	Localized	37	77.08
	Diffuse	11	22.92
Margin	Well-defined	16	33.33
	Ill-defined	32	66.67
Echogenicity	Hypoechoic	46	95.83
	Isoechoic	2	4.17
Echotexture	Solid	45	93.75
	Heterogeneous	3	6.25
Invasion	No	27	56.25
	Yes	21	43.75

The lesions are mainly localized (77.08%) with ill-defined margin (66.67%), invasive (43.75%), hypoechoic (95.83%) and solid echo texture (93.75%).

Table 4. Histopathologic characteristics

Histological grade	Number of patients	Percentage
Grade 1	4	8.33
Grade 2	22	45.83
Grade 3	14	29.17
Unclassified	8	16.67
Total	48	100.00

According to histological grade, grade 2 accounted for the highest proportion (45.83%). Grade 1 accounted for the lowest proportion (8.33%). 16.67% of patients were not graded histologically.

Table 5. Histological types of breast cancer

Histological types	Number of patients	Percentage
Invasive ductal carcinoma	35	72.92
Lobular carcinoma	6	12.50
Mixed ductal and lobular carcinoma	4	8.33
Medullary carcinoma	3	6.25
Mucinous carcinoma	0	0.00
Total	48	100.00

Invasive ductal carcinoma accounted for the highest percentage (79.92%). Medullary and mucinous carcinomas accounted for the lowest percentage with 6.25% and 0%.

Table 6. Hormone receptor status

Hormone receptor	Number of patients	Percentage
Positive	12	25.00
Negative	36	75.00
Total	48	100.00

The proportion of patients with hormone receptor-negative cancers (ER-/PR-) was high, accounting for 75.00%. There were 8 patients with ER+/PR+ cancers, 2 patients with ER+/PR- cancers, 2 patients with ER-/PR+.

Table 7. TNM staging

Stage	Number of patients	Percentage
Stage 1	12	25.00
Stage 2	19	39.58
Stage 3	12	25.00
Stage 4	5	10.42
Total	48	100.00

Stage 2 breast cancer accounted for the highest percentage (39.58%). Stage 4 breast cancer accounted for the lowest percentage (10.42%).

4. DISCUSSION

Clinical characteristics

In many studies, breast cancer patients aged <40 years have a higher risk of recurrence and death than those aged over 40 years. The decision to offer adjuvant chemotherapy and endocrine therapy must take into account the factor of patient age (under 40 or under 35) [3]. Therefore, age is an important factor in breast cancer research, which may be an independent prognostic factor for breast cancer. In this study, the mean age was 48.4 years (range 28-75 years). This findings is quite similar to the domestic studies. 45-60 age group accounted for the largest proportion (47.92%). Under 45 age group accounted for the lowest proportion (25.00%). In the study of Phung Thi Huyen et al (2016), the 51-60 age group is the most common (46%) [4].

Obstetric history is one of the risk factors for breast cancer. Specifically, late-onset menopause is a risk factor for breast cancer. Risk increases by 1.03% for each year of delayed menopause, equivalent to the use of menopausal hormone therapy [5]. In addition, the risk of breast cancer is also higher in women with a late first pregnancy [6]. In this study, the proportion of menopausal patients (54.17%) was higher than the proportion of non-menopausal patients (45.83%). The results are consistent with results from the study of Somaira Nowsheen (2018) [7].

The most common reason for admission was self-detected breast mass (64.58%). Other reasons for admission included breast pain (12.50%), nipple discharge (10.42%), other breast changes (6.25%).

Regarding the clinical symptoms, breast pain is uncommon and often appears in the late stages of BC. In patients with BC, breast pain may be not related to the menstrual cycle, or breast pain in one side, or persistent pain. In this study, the percentage of patients with breast pain symptoms (12.5%) was quite similar to the percentage of patients with stage IV breast cancer (10.42%).

Regarding the clinical signs, tumors in breast cancer can be fixed or mobile. Tumor sizes vary with boundaries that can be difficult to define. On palpation, it may or may not be painful. Most palpable tumors are > 1 cm in diameter. The most common location is upper outer quadrant of the breast (about 44%).

Our study results are consistent with the medical literature. Specifically, tumors in the upper outer quadrant are the most frequent site of tumor location (58.33%); and tumors in the lower inner quadrant are the least frequent site of tumor location (2.08%). According to Le Hong Quang et al (2012), the proportion of left and right breast cancer are 52.4% and 47.6%, respectively. The tumor in upper outer quadrant accounted for the highest proportion (58.8%) [5]. Foreign authors also gave similar results. Umberto Veronesi et al. (2010) studied 516 patients and reported that in upper outer quadrant accounted for 72% [8].

The mean tumor size was 2.78 ± 1.32 (cm). The largest size was 7.65 cm. Our results are quite similar to the research results of Phung Thi Huyen et al (2016). In both our study and that of the above authors, the study subjects were mainly patients with stage 2 and 3 BC. Phung

Thi Huyen et al. reported that the mean tumor size was 2.99 cm; The smallest tumor was 1 cm in diameter but had metastasized axillary lymph nodes. The largest tumor size was 8 cm in diameter [4].

Regarding cancer staging, stage 2 breast cancer accounted for the highest proportion (39.58%). Stage 4 breast cancer accounted for the lowest proportion (10.42%). This result is quite similar to the study of Somaira Nowsheen et al (2018) [7].

Subclinical characteristics

On ultrasound, the lesion was mainly localized (77.08%), ill-defined margins (66.67%), invasive (43.75%), hypoechoic (95.83%) and solid (93.75%). According to Nguyen Van Thang et al. (2013), ultrasound features with high sensitivity include: solid lesion (98.9%), spiculated margins (93.5%), mật độ không đều (88%), hypoechoic (85.9%). Features with high predictive value of breast cancer include: depth–width ratio > 1 (96%), suspected malignancy of lymph nodes (95.5%), Calcified lesions (90.3%), ill-defined margins (88%), spiculated margins (82.7%) [9].

Histologic grade was based on Scarff-Bloome-Richardson grading system (the degree of tubule/duct formation, nuclear size and pleomorphism, and mitotic rate). Grade 2 accounted for the highest percentage (50.18%). Grade 1 accounted for the lowest percentage (2.33%). Histologic grade has prognostic value in BC. According to Phung Thi Huyen et al. (2012), the percentage of histological grade 1, 2, 3 and unclassified were 5.8%, 64.2%, 12.6% and 17.4%, respectively [4].

Histological type of BC is also one of the factors affecting survival rate. Some histopathological types with good prognosis include mucinous, lobular, and papillary breast cancers. For these groups, it is usually diagnosed at an early stage, with positive hormone receptor and negative HER-2. However, these histological types are encountered with a small rate (about 3% of diagnosed BC). In our study, the histological type accounting for the highest percentage was invasive ductal carcinoma (79.07%). Medullary and mucinous carcinoma accounted for the lowest percentage (2.33% and 0%). According to Phung Thi Huyen et al (2016), invasive ductal carcinoma accounted for 81%, followed by invasive lobular, medullary (4.8%) [4]. The percentage of histological types has no difference compared with domestic and foreign studies. Invasive ductal carcinoma accounted for the highest percentage in most of the studies. Because mammary gland structure is mainly ductal and mammary gland tissue is deeply influenced by female hormones, cancer usually originates from ductal part.

5. CONCLUSION

- Mean age was 48.4 years. Age group 45-60 accounted for the largest proportion (47.92%). Age group < 45 accounted for the lowest proportion (25%).

- Among the reasons for admission, the highest rate was self-detected breast mass (64.58%). 12.50% of patients had breast pain. 10.42% of patients had nipple discharge. Other breast changes accounted for 6.25%.

- Clinical signs:

+ Tumors in the upper outer quadrant are the most frequent site of tumor location (58.33%). Tumors in the lower inner quadrant are the least frequent site of tumor location (2.08%).

+ Mean tumor size was 2.78 ± 1.32 (cm)..

- Subclinical characteristics:

+ On ultrasound, lesions are mainly localized (77.08%) with ill-defined margin (66.67%), invasive (43.75%), hypoechoic (95.83%) and solid echo texture (93.75%).

+ Invasive ductal carcinoma accounted for the highest percentage (79.92%). Medullary and mucinous carcinomas accounted for the lowest percentage with 6.25% and 0%.

+ Grade 2 BC accounted for the highest proportion (45.83%). Grade 1 BC accounted for the lowest proportion (8.33%)..

- Stage 2 breast cancer accounted for the highest percentage (39.58%). Stage 4 breast cancer accounted for the lowest percentage (10.42%).

REFERENCES

[1] Freddie Bray, Jacques Ferlay, Isabelle Soerjomataram et al., Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. Ca Cancer J Clin, 2018; 68: 394–424.

[2] Bui Dieu et al., Trends in breast cancer in Vietnam to 2020. Vietnam Medical Journal, 2012; 393(1): 127-131.

[3] Fredholm H, Eaker S, Frisell J et al., Breast cancer in young women: poor survival despite intensive treatment. PloS One, 2009; 4(11): e7695.

[4] Phung Thi Huyen, Evaluation of results of adjuvant chemotherapy regimens 4AC + 4T combined with trastuzumab on patients with breast cancer stage II, III with Her 2 neu positive, Doctor of Medicine thesis, Hanoi Medical University, 2016.

[5] Le Hong Quang, Application of imaging techniques and biopsy of portal nodes in assessing axillary lymph node metastasis in breast cancer patients, Doctor of Medicine Thesis, Hanoi Medical University, 2012.

[6] Khouri MG, Douglas PS, Mackey JR et al., Cancer therapyinduced cardiac toxicity in early breast cancer: Addressing the unresolved issues. Circulation research, 2012; 126: 2749–2763.

[7] Somaira Nowsheen, Aziz K, Park JY et al., Trastuzumab in Female Breast Cancer Patients With Reduced Left Ventricular Ejection Fraction. J Am Heart Assoc, 2018; Aug 7;7(15):e008637

[8] Veronesi U, Viale G, Paganelli G et al., Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. Ann Surg, 2010; 251: 595-600.

[9] Nguyen Van Thang, Study on the diagnostic value of mammogram x-ray combined with ultrasound of the breast. Journal of Practical Medicine, 2013; 4:22-29.