A RETROSPECTIVE STUDY ON PATIENTS WITH BREAST CANCER CURATIVELY TREATED AT HUE UNIVERSITY HOSPITAL FROM 2013-2016

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ABSTRACT

Introduction: *Breast cancer is the most frequently diagnosed cancer and also the leading cause of cancer death in women all over the world. This makes breast cancer a global burden to women health including Vietnam. For decades, a considerable amount of effort has been made to improve the quality of screening, diagnosis, and treatment of breast cancer. Although the current methods for managing breast cancer are available in Vietnam, the application of all necessary multimodalities is not always feasible locally. Due to lacking of database about breast cancer treatment in Vietnam, especially in the central of Vietnam, we conducted this study to describe the characteristics of breast cancer, the treatment features and the outcome of the treatment.*

Patients and methods: *A retrospective study was conducted in a cohort of 182 women diagnosed with invasive breast cancer and treated with curative intention at the Hue University Hospital from 01/01/2013 to 31/12/2016. The clinical, histopathological characteristics, immunohistochemical findings and the progression of the disease were collected from medical records and telephone interviews with the patients. Patients with lacking needed information were excluded. Statistical analysis was performed in Microsoft Excel 2010 and R program.*

Results: *Median age at the diagnosis was 50 (range 29-79). Only 1 male in the cohort of study (0.55%). Patients with stage I-II accounted for 72.52% and that proportion of stage III was 27.47%. Predominant histopathological subtype was ductal carcinoma (80%) and grade 2 was 69.81%. Mean tumor size was 3.3±1.6cm. Hormone receptor was positive in 60.44% of cases. Regarding immunohistochemistry, the Her-2 of 3+ was found in 66.48% patients and strong positive Ki67 over 14% were dominant (70%). The treatment was carried out by a multimodality approach. In which, modified radical mastectomy was predominantly performed in 96.15%; 99.45% received chemotherapy mostly with AC4-T4 (62.64%). 99.72% of patients with hormone receptor positive received hormonotherapy. Although high rate of Her-2 amplification was found, only one patient got trastuzumab. Disease-free survival at 4 years was 82.4%.*

Conclusion: *Characteristics of breast cancer in our study are relatively identical to other reports in Vietnam. However, patients with Her-2 of 3+ and high Ki67 were found with high proportion in our study. Modified radical mastectomy, chemotherapy with AC4-T4 regimen, radiotherapy and endocrine therapy were still the mainstay of treatment . Trastuzumab was rarely applied here. The disease- free survival rate at two, three and four years were 95.6%; 86.5%; 82.4% respectively.*

Keywords: *breast cancer,curative treatment, retrospective study*

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I. INTRODUCTION

Breast cancer is the most frequently cancer diagnosed among malignancy tumors and the leading cause of death in women globally. Worldwide, about 1.7 million women were diagnosed with breast cancer and more than 522,000 patients died from this disease in 2012[1]. Therefore breast cancer was recognized as a global burden to women health. Nowadays, advancements in medical equipments and treatment modalities have improved the outcome of screening, diagnosis, and treatment of breast cancer. Treatment of breast cancer is a multimodality approach through multidisciplinary team with combination of surgery, radiation, chemotherapy, hormonotherapy and recently targeted therapy are majorly applied in most countries. The combination of these modalities depend on many factors especially the disease stages and immunohistochemitry profiles. The former radical mastectomy is a devastating surgery with all breast tissue, axillary lymph nodes, and pectoralis muscles removed[2]. It induced many debilitating side effects such as severe disfigurement, weakened arm function and lymphedema[3]. It drove the invention of less-extensive operations i.e modified radical mastectomy, simple mastectomy, skin-sparring/ nipple sparring mastectomy etc[4]. The application of radiation and chemotherapy made it feasible for performing breast-conserving surgery with good cosmetic and oncologic outcomes[5]. Intensity-modulated radiation therapy (IMRT) is a new, advanced technique in comparison with conventional radiotherapy, which delivers precise radiation doses to the tumor and minimizes radiation beam to normal surrounding areas and also has a lower incidence of toxicity[6,7]. After the success of traditional endocrine therapy, the advent of trastuzumab (Herceptin) in 1998, a monoclonal antibody targeting HER-2 receptor, started the new era of targeted therapy for breast cancer. Herceptin showed its magnificent influence in improvement of disease-free and overall survival among HER-2 (+) patients.[8]

In Vietnam, breast cancer is the most common malignancy and the third leading cause of cancer death in women in 2012[1]. Evidence has shown that a large number of females in Vietnam are diagnosed at younger age, more aggressive tumor and the increasing incidence exceeds that of the Western world[9]. All of the advancements of treatment in the world is currently available in Vietnam, but the accessibility varies and depends on regions, development of local health service, economic status etc. Due to lacking data about breast cancer in central Vietnam, especially in Thua Thien Hue province, we conduct this study with aims:

- To describe the clinical, histopathological and immunohistochemical characteristics of patients with breast cancer in the study cohort.
- To depict the features of the definitive treatment.
- To estimate the disease-free survival.

II. PATIENTS AND METHODS

Study design: A retrospective study was conducted in a cohort of 182 women diagnosed with invasive breast cancer and treated with curative treatment at Hue University Hospital from 01/01/2013 to 31/12/2016. The clinical, histopathological characteristics, immunohistochemical findings and the progression of the disease were collected from medical records and telephone interviews with the patients. Patients with lacking needed information were excluded.

Statistical analysis was performed in Microsoft Excel 2010 and R program.

III. RESULTS

3.1. Descriptions of the cohort are summarised in Table 1.

Table 1: Clinical and pathological characteristics of breast cancer patients

		n	%			n	%
Gender	Female	181	99.45	Tumor size (cm)	≤2	44	24.18
	Male	1	0.55		>2-5	112	61.54
Age	29-36	12	6.6		>5	26	14.28
	36-43	29	15.93	Tumor grade	G1	18	12.16
	43-50	56	30.77		G2	90	69.81
	50-57	44	24.16		G3	40	27.03
	57-64	25	13.74	Histology	Ductal	145	79.67
	>64	16	8.8		Lobular	34	18.68
Stage	IA	34	18.68		Other	3	1.65
	IIA	44	24.18	Nodal status	Negative	76	41.76
	IIB	54	29.67		1-3 positive	64	35.16
	IIIA	36	19.78		>3 positive	42	23.08
	IIIB	1	0.55				
	IIIC	13	7.14				

Median age at the diagnosis was 50 (range 29-79). There was 1 male (0.55%) in the cohort of study. Of 182 patients at their first diagnosis, 72.52% patients were diagnosed at stage I-II; only 27.47% were at stage III. Ductal carcinoma was the most common histologic subtype (about 80%). Histology grade 2 was observed in 69.81% cases. Tumour size varied from 0.7- 8.0 cm with a mean size of 3.3cm. In term of nodal status, patients with axillary node positive were found in more than 58% cases.

Table 2: Immunohistochemical (IHC) markers in the primary tumor

		n	%			n	%
ER	Positive	89	48.9	HER-2	3+	121	66.48
	Negative	93	51.1		2+	33	18.13
PR	Positive	90	49.45		-/ 1+	28	15.39
	Negative	92	50.55	Ki67	≤14%	55	30.22
HR	Positive	110	60.44		>14%	127	69.78

Hormone receptor (HR) was positive in 60.44% of cases. The immunohistochemical HER-2 of 3+ were 66.48%. 18.13% cases with Her-2 of 2+ need FISH confirmation and 15.39% were HER-2 negative. The rate of high Ki67 (>14%) were found at the high level (70%).

3.2. Description of BC treatment

Table 3: Treatment characteristics

Treatment		n	%
Surgery	Modified radical mastectomy	175	96.15
	Breast-conserving surgery	6	3.30
Chemotherapy	AC4-T4	114	62.64
	AP8	54	29.76
	Other	12	6.59
Radiotherapy		38	20.88

Up to 96.15% surgery were modified radical mastectomy. AC4-T4 is the most commonly used chemotherapy (62.64%) followed by AP8 (29.76%). Also, radiotherapy was performed in 20.88% patients. 97.72% patients (107 over 110 cases) with HR (+) received endocrine therapy. Moreover, among 121 HER-2 positive patients, only 1 of them got Trastuzumab in the course of treatment.

3.3. The outcome of the treatment

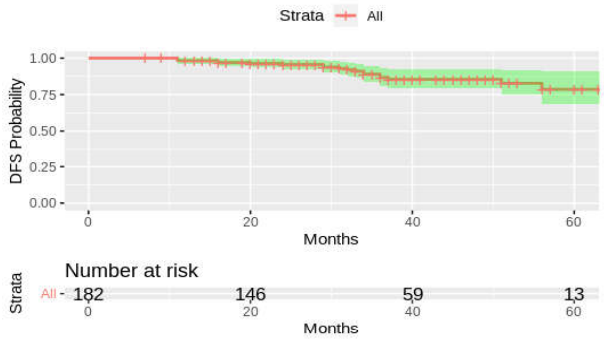

Figure 1: Disease- Free Survival

Disease-free survival of 182 patients were illustrated in Figure 1. Disease- free survival rates were 95.6% (CI 0.924- 0.989); 86.5% (CI 0.803- 0.931) and 82.4% (CI 0.743- 0.914) at 2-year, 3-year and 4-year interval, respectively.

IV. DISCUSSION

Of general clinicopathological characteristics, median age at the diagnosis with BC in our study was 50 years (highest in the group 43-50 years old); 1 male (0.55%) in the cohort of study. The most common histopathology was invasive ductal carcinoma (79.67%) with grade 2 of 69.81%. 61.54% patients were diagnosed with primary tumor >2-5cm. This is quite equivalent to other studies in Vietnam and other countries[10]. It also showed that 72.52% and 27.47% of patients were diagnosed at stage I-II and stage III respectively. This result is rather similar to the study of the author Nguyen Ba Duc with 75.9% at stage I-II; 27.6% at stage III-IV[11].

We also found that the rate of ER positive was approximately 50% and that of PR positive was also about the same. This is almost identical to the study of Nguyen Thanh Ha 2004 with ER-positive and PR-positive at 52.2% and 47.5% respectively. However, our ER result was slighty lower than the author Ta Van To in a study of 2207 patients (ER-positive: 59.1%). This could be due to the difference in the size of study cohort. In addition, we have to highlight that the percentage of HER2 positive tumor in our study is 66.48% (HER-2 of 2+ not included). This was much higher than the author Ta Van To in 2004 (35.1%). This reveals a potential of applying targeted therapy in treatment for HER-2 positive patients.

In the matter of the treatment, modified radical mastectomy was recognized as the most common surgical option and it may decrease the cases of radiation in the study. In addition, our study showed the favor of using AC4-T4 regimen over the others for adjuvant chemotherapy at Hue University Hospital. Furthermore, the data also showed that 97.72% patients with HR positive received endocrine therapy in the course of the treatment while only 1 per 121 Her-2 positive patient received trastuzumab (0.83%). Meanwhile, there was a study from 2009-2014 in Hanoi with a cohort of 63 patients treated with trastuzumab[12]. These clues revealed that the indication of trastuzumab was difficult because of the costly price. It is actually less feasible for low-income patients - the majority of population in Central Vietnam.

As regards the efficacy of the treatment, after 2-year, 3-year, 4-year follow up, disease-free survival was 95.6%; 86.5% and 82.4% respectively. The more indeep analysis is needed as we get more patients in the study and more years of follow up.

V. CONCLUSION

Characteristics of breast cancer in our study were almost identical to other studies in Vietnam. However, patients with Her-2 of 3+ and high rate

of ki67 (poor prognostic factor) were majorly found in our study. Modified radical mastectomy, chemotherapy with AC4 T4 regimen, radiotherapy and endocrine therapy were still the mainstay of the curative treatment at Hue University Hospital. Trastuzumab was rarely applied in here. The DFS at two, three and four years of follow up was 95.6%, 86.5% and 82.4% respectively.

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