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Research Article

Association between immunohistochemistry of core needle biopsy additional to gross tumor pathology and 3 years disease free survival in invasive breast cancer patients

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ABSTRACT

Background: Immunohistochemistry markers are often used to guide treatment decisions, classify subtypes that are biologically distinct or behave differently, and serve as both prognostic and predictive factors. Most of the time, immunohistochemistry are done only in gross tumor pathology. Many studies found the discordance rate of immunohistochemistry between core needle biopsy and gross tumor pathology to be about 7 – 22 %, which may affect treatment decisions and prognosis of breast cancer patients. We conduct the study to examine additional benefit of immunohistochemistry from core needle biopsy in adjuvant breast cancer treatment. This study aims to examine the 3 years disease-free survival of breast cancer patients with immunohistochemistry in core needle biopsy samples additional to gross tumor pathology versus patients with immunohistochemistry in gross tumor pathology alone.

Methods: A retrospective analysis was done using the medical records of patients who underwent surgery for stage I – III breast cancer, with an exclusion of patients who received neoadjuvant therapy, from January 2014 to December 2018 at Bangkok Metropolitan Administration General Hospital.

Results: There were 140 patients in the gross tumor group and 26 patients in the core needle biopsy additional to gross tumor group. We found no statistically significant difference in baseline characteristics, underlying diseases and tumor staging. There were no statistically significant difference of 3 years disease free survival (87.9% vs 84.6% ; p = 0.747), local recurrence rate (5.7% vs 0.0% ; p = 0.359), metastatic rate (6.4% vs 15.4% ; p = 0.125) and mortality rate (5.0% vs 7.7% ; p = 0.633) of both groups. Six out of twenty-six patients (23.1%) whose core needle biopsy produced a different immunohistochemistry result from its gross tumor pathology counterpart.

Conclusions: Immunohistochemistry from core needle biopsy additional to gross tumor pathology did not improve 3 years disease free survival of breast cancer patient.

Keywords: breast cancer, immunohistochemistry, retrospective study

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INTRODUCTION

Breast cancer is the world's second most common cancer found with the number of new patients around two million in 2018. Moreover, there were 627,000 fatalities who had passed away because of breast cancer in 2018[1].

For operable instances, surgery is currently the primary treatment for breast cancer. Chemotherapy, radiotherapy, hormonal therapy, and targeted therapy were used for adjuvant treatments.

Immunohistochemistry was used to categorize intracellular proteins of various tissues in the body for breast cancer, and it was used to classify each patient's subtype of breast cancer. This leads to an evaluation of prognosis, treatment planning, and the response by using adjuvant treatments such as chemotherapy, hormonal therapy, and targeted therapy.

Nonetheless, examination findings interpretation discrepancies in immunohistochemistry can occur at several phases, beginning with tissue preservation and affecting quality. Due to the color staining nature of immunohistochemistry, translating staining findings into subjective data may result in errors between interpreters or interpersonal variability which may result in disparities in therapy selection, particularly adjuvant treatment.

Immunohistochemistry that is currently dyed includes ER, PR, HER-2, and Ki-67, however research by the EQA UK project discovered false negative ER ranging from 10% to 60%, and the proportion of Ki-67 index was also recorded. The varied indexes could not be compared among institutions, as both the human eye estimate and the image analysis value diverged[2].

In 2013, the study conducted by Chen discovered that immunohistochemistry from the whole piece of tissue obtained from surgery and the biopsies obtained from the core needle biopsy were not significantly different[3]. However, when considered in detail, it was found that there were reports of discrepancies in the results of immunohistochemistry in individuals at the rate of 7-22%, and the effect on treatment choice was not studied or oncologic outcome in cases where there was a discrepancy in reporting such outcomes[4].

Suppose there are disparities in immunohistochemistry results, it may be affected to consider adjuvant treatment. For example, ER and PR are positive in core needle biopsy, but negative in gross pathology; either from tissue preservation or from the reader's perception of the results. Changes in complementary therapy may occur. By taking into account the outcomes, immunohistochemistry from gross pathology may not require adjuvant therapy with hormonal therapy, while adjuvant therapy with hormonal therapy is required based on core needle biopsy immunohistochemistry.

MATERIAL AND METHOD

The study was carried out as a retrospective study to analyze a database containing information about patients who underwent breast surgery for stage I–III breast cancer from January 2014 to December 2018 at Bangkok Metropolitan Administration General Hospital. The patients performed immunohistochemistry in gross tumor pathology and both core needle biopsy additional to gross tumor pathology. The patient data were extracted from medical record database of the hospital.

ELIGIBILITY CRITERIA AND STUDY SELECTION

The inclusion criteria were all patients who had pathological diagnosis of invasive breast cancer stage I – III and underwent surgery from January 2014 to December 2018; patient age is greater than or equal to 18 years, did not receive neoadjuvant therapy or previous invasive malignancy that received chemotherapy or radiation.

The exclusion criteria were advanced-stage breast cancer patients, breast patients who do not have ductal or lobular subtypes, and the patients who had concomitant malignancy.

The biologic subtypes of breast cancer were classified based on European Society for Medical Oncology (ESMO) Clinical Practice Guidelines for diagnosis, treatment and follow up[5]. Tumor staging was classified by the 8th edition of American Joint Committee on Cancer (AJCC) manual[6].

STATISTICAL ANALYSIS

All calculations were performed using SPSS software. According to the immunohistochemistry study, patients were divided into gross tumor group and core needle biopsy additional to the gross tumor group. Categorical data were presented as frequencies and percentages and compared by the chi-squared test. Parametric and nonparametric continuous data were presented as mean and median, and evaluated by Student's t-test and Mann–Whitney U test, respectively. Comparisons between the two groups were made on an intention-to-treat basis. P-value less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

One hundred sixty-six patients were enrolled and analyzed during the study period, 140 were in the gross tumor group, and 26 were in the core needle biopsy additional to the gross tumor group.

The patient demographic characteristics are described in Table 1. Baseline characteristics, including weight, height, underlying disease, clinical staging, and pathological staging, were no statistically significant differences between the two groups.

A similar weight of patients in the gross tumor group and core needle biopsy additional to gross tumor group were found at 58.69 kg and 59.19 kg, respectively, (p=0.84). As same heights of both groups were found at 155.41 cm and 153.31 cm (p=0.09). Most patients in both groups have underlying disease, hypertension (HT) 38.6% in the gross tumor group and 50.0% in the core needle biopsy additional to gross tumor group but no significant difference between the two groups (p=0.29). Furthermore, no statistically significant difference in other underlying disease, including diabetes mellitus (DM) (p=0.43), liver disease (p=0.60), and chronic kidney disease (CKD) (p=0.56).

The majority of the patients in this study is early breast cancer in clinical staging, 43.6% of gross tumor group were stage 1A, and 37.1% were stage 2A. In the core needle biopsy addition to the gross tumor group, most patients were stage 2A (42.3%) followed by stage 1A (34.6%). But no statistically significant difference in clinical staging between both groups (p=0.704).

Table I Generalized Characteristic

	Gross tumor (n=140)	CNBx +Gross tumor (n=26)	P-value
Weight (Mean(SD))	58.69(12.51)	59.19(11.58)	0.843
Height (Mean(SD))	155.41(5.74)	153.31(6.30)	0.093
Underlying disease			
DM	27(19.3%)	7(26.9%)	0.428
HT	54(38.6%)	13(50.0%)	0.285
Liver disease	3(2.1%)	1(3.8%)	0.604
CKD	1(0.7%)	0(0.0%)	0.559
Other	36(25.7%)	7(26.9%)	0.898
Clinical staging			0.704
1A	61(43.6%)	9(34.6%)	
2A	52(37.1%)	11(42.3%)	
3A	21(15.0%)	4(15.4%)	
4A	6(4.3%)	2(7.7%)	
Pathological staging			0.356
1A	34(24.3%)	5(19.2%)	
2A	62(44.3%)	9(34.6%)	
2B	21(15.0%)	4(15.4%)	
3A	16(11.4%)	7(26.9%)	
3C	7(5.0%)	1(3.8%)	
Treatment			
Adjuvant CMT	105(75.0%)	17(65.4%)	0.337
Radiation	39(27.9%)	9(34.6%)	0.487
Hormonal therapy	90(64.3%)	20(76.9%)	0.262
Targeted therapy	8(5.7%)	2(7.7%)	n/a
Type of surgery			
Total mastectomy	126(90.0%)	24(92.3%)	0.752
Wide excision	14(10.0%)	2(7.7%)	0.752
Margin free	140(100.0%)	26(100.0%)	n/a

Table II Primary outcome

	Gross tumor (n=140)	CNBx +Gross tumor (n=26)	P-value
At three years			
3 years disease free	123(87.9%)	22(84.6%)	0.747
Local recurrence	8(5.7%)	0(0.0%)	0.359
Metastasis	9(6.4%)	4(15.4%)	0.125
Death	7(5.0%)	2(7.7%)	0.633

The majority of patients in both groups performed a total mastectomy, 90.0% in the gross tumor group and 92.3% in core needle biopsy additional to the gross tumor group. There were no statistically significant differences between the two groups (p=0.75). Resection margins were similar in both groups, and none of them was found to be positive.

Most patients in the two groups received adjuvant chemotherapy and hormonal therapy for adjuvant treatment. In the gross tumor group, 105 (75.0%) patients received adjuvant chemotherapy, 90 (64.3%) patients received hormonal therapy and only 8 (5.7%) patients received targeted therapy. In a core needle biopsy additional to the gross tumor group, 17 (65.4%) patients received adjuvant chemotherapy, 20 (76.9%) patients received hormonal therapy and only 2 (7.7%) patients received targeted therapy. There were no statically significant difference between two group with regard to adjuvant chemotherapy (p=0.34), radiation (p=0.49), hormonal therapy (p=0.26) and targeted therapy (p=N/A).

Comparing the gross tumor group with the core needle biopsy additional to gross tumor group, there were no statistically significant difference of 3 years disease free survival rate (87.9% vs 84.6%; p = 0.747), local recurrence rate (5.7% vs 0.0%; p = 0.359), metastatic rate (6.4% vs 15.4%; p = 0.125) and mortality rate (5.0% vs 7.7% ; p = 0.633) as shown in Table 2.

DISCUSSION

This comparative study analyzed data on breast cancer patients who received immunohistochemistry study from only gross tumor pathology alone and core needle biopsy additional to gross tumor pathology. Our results showed no significant difference in 3 years disease free survival, local recurrence rate, and metastatic rate between the two groups.

From the result of my study, most patients of the study are luminal-subtyped breast cancer. The 3 years survival is 87.9% in the gross tumor group 84.6% in the core needle biopsy additional to gross tumor group. Hence, it is the same result as the previous study[7].

However, it was observed that as many as 6 of the 26 samples collected in the core needle biopsy additional gross tumor pathology group were discordant with their gross pathology results, most notably of HER-2 marker. With all of the discordancy of HER-2 marker, we found that HER-2 marker from gross tumor pathology was negative, but positive in core needle biopsy. Because of the smaller core needle biopsy specimen, the preservative solution can diffuse into tissue better than a large specimen of the gross tumor specimen. Further studies can take into consideration this fact as it could one day alter our approach to targeted therapy. This result could also lead to future studies on the discordancy of HER-2 markers in immunohistochemistry and steps towards improving the accuracy of such tests.

Limitation of the treatment by trastuzumab in some patients may affect the outcomes of this study. In this study, HER-2 marker positive was 13.1% in the gross tumor group and 11.5% in the core needle additional to gross tumor group. However, not all patients received targeted therapy due to financial problems. That may be affected 3 years disease free survival of the patients.

As a result of immunohistochemistry in core needle biopsy samples being an uncommon trend during the studied years, we were only able to collect 26 samples. This may have interfered with

and caused the indifference in the 3 years disease free survival between the two groups. In the future, if we can collect more information of patients and follow up the results of patients more than 3 years. We may find the difference.

CONCLUSION

Immunohistochemistry from core needle biopsy additional to gross tumor pathology did not improve 3 years disease free survival of breast cancer patient.

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