Original Article

Correlation between Age and Prognostic Factors in Thai Breast Cancer Women: A Single Institute Analysis

Chaichana Chantharakhit MD[1]

[1] Division of Medical Oncology, Department of Internal Medicine, Buddhasothorn Hospital, Chachoengsao, Thailand

Background: Breast cancer is the most common cancer in females, especially for those in their middle age between 40 to 60 years. There are prognostic factors of breast cancer such as an intrinsic subtype called triple-negative breast cancer (TNBC), HER2 overexpression, poorly differentiated, large tumor size, axillary lymph node status, and staging. Age at diagnosis is usually associated with aggressive cancer and poorer outcomes.

Objective: To explore the age and prognostic factors for breast cancer in Thailand.

Materials and Methods: The data were collected from pathological data collection and medical records of Buddhasothorn Hospital, Chachoengsao, Thailand, between 2015 and 2018. All data were collected for studying the relationship between age at diagnosis and prognostic factors.

Results: Three hundred three cases were collected. It was found that the age between 35 to 69 years had breast cancer the most (83.83%). The intrinsic subtypes found were Hormonal receptor-positive (HR+) 67.33%, TNBC 22.11%, and HER2 overexpression 10.56%. Age under 35 years had a risk of poor prognostic factors such as poorly differentiated (OR 1.528, 95% CI 0.306 to 7.627, p=0.605), large tumor size greater than 5 cm (OR 2.145, 95% CI 0.560 to 8.221, p=0.266), and axillary lymph node metastasis (OR 1.409, 95% CI 0.345 to 5.762, p=0.633). Age of 70 years and over had more favorable prognostic factors such as well-differentiated (OR 1.691, 95% CI 0.645 to 4.436, p=0.286), no axillary lymph node metastasis (OR 1.734, 95% CI 0.886 to 3.393, p=0.108), and the HR+ subtype (OR 2.158, 95% CI 0.954 to 4.882, p=0.065). Nonetheless, the present study data did show statistical significance.

Conclusion: The evidence of breast cancer in Thailand found that the different age ranges affected the prognostic factors differently. Specifically, young age breast cancer had a higher risk of poor prognostic factors, whereas the elderly breast cancer was associated with more favorable prognostic factors. However, a larger number of patient data to the confirm relationship between age and prognostic factors is required.

Keywords: Breast cancer; Age-related; Prognostic factors

Received 22 February 2021 | Revised 1 June 2021 | Accepted 1 June 2021

J Med Assoc Thai 2021;104(7):1153-8

Website: http://www.jmatonline.com

According to the data from the National Cancer Institute of Thailand, it was found that breast cancer is the most common type of cancer in the Thai female population. The most common age at diagnosis is between 40 to 60 years[1]. According to the data from previous studies, it was found that breast cancer showed different clinical symptoms and prognosis due to biological complexity[2-5]. The key prognostic factors are histologic grade, tumor size, axillary lymph node status, and disease staging. Another key prognostic factor is an intrinsic molecular subtype that helps classifying breast cancer into subtypes based on its intrinsic molecular, consisting of Luminal A, Luminal B, HER2 overexpression, and triple-negative (Basal-like). Each group contains different progression and prognosis, so different treatments are required for each subtype. Breast cancer classification based on intrinsic molecular subtypes has several testing methods to test gene expression. The most accurate and reliable methods for research and studies are molecular tests, or gene expression test. However, medical practice in Thailand still mostly relies on formalin-fixed and paraffin-embedded (FFPE), and special dye by immunohistochemistry to find the surrogates of intrinsic molecular subtypes[6,7].

Previous studies have tried to find the relationship between age and breast cancer prognosis[8-10]. It was mostly found that the young breast cancer usually had more severe symptoms than the elderly breast cancer[11-13]. However, many studies are still different, because of different data due to races and population groups[14-16].

Correspondence to:

Chantharakhit C.

Division of Medical Oncology, Department of Internal Medicine, Buddhasothorn Hospital, Chachoengsao 24000, Thailand.

Phone: +66-81-7866945

Email: Chaichana.MD@gmail.com

How to cite this article:

Chantharakhit C. Correlation between Age and Prognostic Factors in Thai Breast Cancer Women: A Single Institute Analysis. J Med Assoc Thai 2021;104:1153-8.

doi.org/10.35755/jmedassocthai.2021.07.12508

The present research aimed to study the age and prognostic factors for breast cancer in Thai patients, to find the relationship for further clinical utilization.

Materials and Methods

The present study aimed to review the data of the examination results from the pathological specimens of 303 patients with breast cancer at the Department of Anatomical Pathology, Buddhasothorn Hospital, Chachoengsao, between July 2015 and November 2018, along with the data from the medical records. The data obtained included age at diagnosis, disease staging, pathological data related to prognostic factors consisting of tumor size, histologic grade, axillary lymph node status, and intrinsic molecular subtypes. In the present study, standard immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) were used to help classify the intrinsic subtypes into three groups, hormonal receptor-positive (ER+, PR+, HER2–), HER2 overexpression (ER–, PR–, HER2+), and triple-negative breast cancer (TNBC) (ER–, PR–, HER2–).

Next, the data obtained was brought to study the relationship between age and prognostic factors. The age ranges were divided into three groups, young age at less than 35 years, middle-aged at 35 to 69 years, and the elderly at 70 years and older. The present study main attention was to find the effects of the young age group and the elderly group on prognostic factors of breast cancer by multivariate logistic regression analyses. The significance level or alpha level is 0.05. The present study protocol was approved by the Institutional Review Board of Buddhasothorn Hospital BSH-IRB 010/2562.

Results

According to the data of 303 non-defected pathological specimens, it was found that the age of patients received breast cancer diagnosis was between 24 and 85 years. The age range of 35 to 69 years or middle age was found with the most breast cancer at 83.83%, while the young age group or the less than 35 years had 2.97%, and the elderly group or 70 years or older had 13.2% (Figure 1). Most of the patients (67.33%) were hormonal receptor-positive (HR+), followed by TNBC (22.11%), and HER2 overexpression (HER2+) (10.56%), respectively (Figure 2).

The age of patients with breast cancer was divided into three groups, young age at less than 35 years, middle-aged at 35 to 69 years, and the elderly at 70 years and older. Then, it was classified based on prognostic factors, as intrinsic subtypes, histologic grade, tumor size, axillary lymph node status, and disease staging, as shown in Table 1. After that, the effects of age in elderly group and young age group on prognostic factors were studied by multivariate logistic regression analysis compared with the middle-aged group, as shown in Table 2.

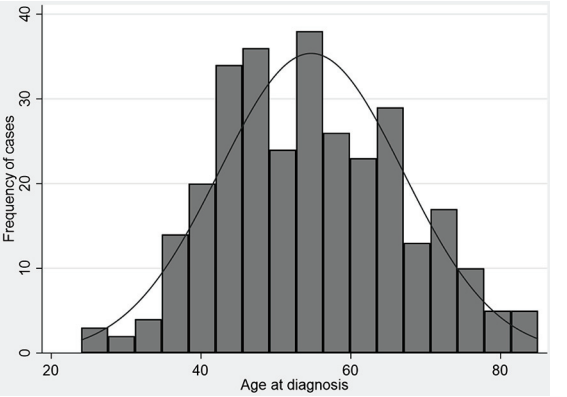

Figure 1. Distribution of age at diagnostic breast cancer.

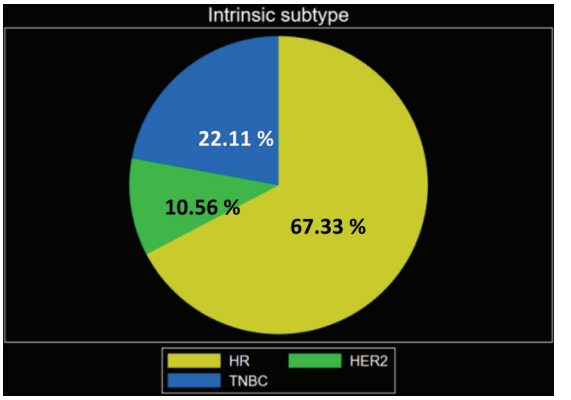

Figure 2. Intrinsic subtype breast cancer classification based on immunohistochemistry biomarkers.

Age-related associations with intrinsic subtypes

It was found that 80% of the elderly group had hormonal receptor-positive (HR+). This age group had a higher of HR+ than the middle-aged group (adjusted odds ratio 2.158, 95% CI 0.954 to 4.882, p=0.065). Likewise, young age had a higher of HR+ than the middle-aged group (adjusted odds ratio 1.888, 95% CI 0.384 to 9.280, p=0.434).

Age-related association with histologic grade

The present study revealed that 15% of the elderly group had well-differentiated tumor grade

Table 1. Age group status by intrinsic subtype, tumor grade, size, axillary lymph node status, and stage

	Age <35 years; n (%)	Age 35 to 69 years; n (%)	Age ≥70 years; n (%)	p-value
Intrinsic subtype				
HR+	7 (77.8)	165 (65.0)	32 (80.0)	0.048
HER2+	0 (0.0)	32 (12.6)	0 (0.0)	0.011
TNBC	2 (22.2)	57 (22.4)	8 (20.0)	0.735
Histologic grade				
Well differentiate	1 (11.1)	24 (9.45)	6 (15.0)	0.283
Moderate differentiate	6 (66.7)	190 (74.80)	30 (75.0)	0.941
Poorly differentiate	2 (22.2)	40 (15.75)	4 (10.0)	0.414
Tumor size				
Small (<2 cm)	2 (22.2)	48 (18.9)	8 (20.0)	0.838
Medium (>2 to 5 cm)	3 (33.3)	137 (53.9)	23 (57.5)	0.851
Large (>5 cm)	4 (44.5)	69 (27.2)	9 (22.5)	0.695
Axillary lymph node status				
No metastasis	3 (33.3)	105 (41.3)	22 (55.0)	0.137
Metastasis	6 (66.7)	149 (58.7)	18 (45.0)	0.137
Stage				
Stage 1	2 (22.2)	34 (13.4)	7 (17.5)	0.420
Stage 2	3 (33.3)	114 (44.9)	22 (55.0)	0.301
Stage 3	3 (33.3)	81 (31.9)	7 (17.5)	0.076
Stage 4	1 (11.2)	25 (9.8)	4 (10.0)	0.958

TNBC=triple-negative breast cancer

Table 2. Logistic regression analysis evaluated risk between age-related compared with the middle-aged group in prognostic factors

	Young age breast cancer (<35 years)		Elderly breast cancer (≥70 years)	
	Adjusted odds ratio (95% CI)	p-value	Adjusted odds ratio (95%CI)	p-value
Intrinsic subtype				
HR+	1.888 (0.384 to 9.280)	0.434	2.158 (0.954 to 4.882)	0.065
HER2+	-	-	-	-
TNBC	0.987 (0.200 to 4.885)	0.988	0.864 (0.377 to 1.979)	0.730
Histologic grade				
Well differentiate	1.198 (0.144 to 9.989)	0.867	1.691 (0.645 to 4.436)	0.286
Moderate differentiate	0.674 (0.164 to 2.772)	0.584	1.010 (0.468 to 2.182)	0.979
Poorly differentiate	1.528 (0.306 to 7.627)	0.605	0.594 (0.200 to 1.762)	0.348
Tumor size				
Small (<2 cm)	1.226 (0.247 to 6.089)	0.803	1.073 (0.465 to 2.475)	0.869
Medium (>2 to 5 cm)	0.427 (0.104 to 1.745)	0.236	1.155 (0.589 to 2.266)	0.674
Large (>5 cm)	2.145 (0.560 to 8.221)	0.266	0.778 (0.352 to 1.718)	0.535
Axillary LN status				
No metastasis	0.710 (0.174 to 2.901)	0.633	1.734 (0.886 to 3.393)	0.108
Metastasis	1.409 (0.345 to 5.762)	0.633	0.576 (0.295 to 1.128)	0.108
Stage				
Stage 1	1.849 (0.369 to 9.271)	0.455	1.372 (0.562 to 3.349)	0.487
Stage 2	0.614 (0.150 to 2.510)	0.497	1.501 (0.768 to 2.934)	0.235
Stage 3	1.068 (0.260 to 4.378)	0.927	0.453 (0.192 to 1.068)	0.070
Stage 4	1.145 (0.138 to 9.534)	0.900	1.018 (0.335 to 3.096)	0.975

TNBC=triple-negative breast cancer; CI= confidence interval

higher than in the middle-aged group (adjusted odds ratio 1.691, 95% CI 0.645 to 4.436, p=0.286). Besides, it was also found that young age group had higher poorly differentiated breast cancer cells than the middle-aged group (adjusted odds ratio 1.528, 95% CI 0.306 to 7.627, p=0.605).

Age-related association with tumor size

It was found that 44.5% of the young age group had tumor grade over 5 cm. When compared with the middle-aged group, there was more of the large size over 2.145 times (adjusted odds ratio 2.145, 95% CI 0.560 to 8.221, p=0.266).

Age-related association with axillary lymph node status

It was 66.7% or the maximum of the young age group had axillary lymph node metastasis, higher than the middle-aged group (adjusted odds ratio 1.409, 95% CI 0.345 to 5.762, p=0.633). Besides, it was found that 45%, or most of the elderly group, had axillary lymph node metastasis. When compared with the middle-aged group, there might be a protective factor against the axillary lymph node metastasis (adjusted odds ratio 0.576, 95% CI 0.295 to 1.128, p=0.108).

Age-related association with stage

It was found that 11.2% of the young age group was at stage 4, higher than the middle-aged group (adjusted odds ratio 1.145, 95% CI 0.138 to 9.534, p=0.900). In addition, 10% of the elderly group were at stage 4, higher than the middle-aged group (adjusted odds ratio 1.018, 95% CI 0.335 to 3.096, p=0.975).

Discussion

According to the present study, it was found that the effects of age and prognostic factors had relationship directions, to be described as follows. Hormonal receptor-positive subtype, poorly differentiated, large tumor size, and axillary lymph node metastasis had a higher chance to be found in the young age breast cancer. For elderly breast cancer, it was found to have a hormonal receptor-positive subtype as well as differentiation grading. A higher chance of axillary lymph node metastasis was not found when comparing with the middle-aged group as a common population group.

The results were different from several previous studies, in which the incidence of the intrinsic subtypes called TNBC and HER2 positive were mostly found in the young age breast cancer[17,18], while high incidence of hormonal receptor-positive was found in the elderly breast cancer[8,19,20].

The study of Shitalmala et al[21] found poor prognostic factors were usually found in young age breast cancer or less than 40 years, with more aggressive cancer and poorer outcomes when compared with the elderly group. Similar forms of cancer were also found in the present study. To clarify, poor prognostic factors in the present study were related to young age group, with poor differentiation, large tumor size, and axillary lymph node metastasis, except for the young age breast cancer, in which increasing hormonal receptor-positive was found. In contrast, the study of Jasmine et al[9] found that the young age group or less than 40 years did not have more axillary lymph node metastasis than other age groups.

In the aspect of intrinsic subtypes, the study of Lakshmaiah et al[22] found that the young age group usually had TNBC and that TNBC was the group with aggressive cancer, high grade or poorly differentiated, and poor prognosis. However, it was found that the young age breast cancer frequently had an intrinsic subtype of hormonal positive in the present study, possibly because this was a single-institute study with limited data. Thus, further studies should be conducted in the Thai population.

When comparing between the young age group and the elderly group, it was found that the elderly group had more favorable prognostic factors with well-differentiated, no axillary lymph node metastasis, and hormonal receptor-positive. The results in this point conformed to the study of Emily et al[23], which found a significant increase of favorable intrinsic subtypes such as Luminal A, Luminal B, and Luminal A+B, in the higher age ranges (p<0.0001).

In the Thai population[24], there were data revealing poor prognostic factors affecting the survival of the patients with breast cancer as axillary lymph node metastasis and tumor sizes over 2 cm. In the present study, there was higher risk of axillary lymph node metastasis by 1.409 times when compared with the middle-aged group, which was likely to have the most incidence of breast cancer.

The present research aimed to study the effects of age on the prognostic factors for breast cancer in Thailand. The initial point found that the young age breast cancer had a higher risk of poor prognostic factors than the elderly group. Simultaneously, the elderly group or older than 70 years, had a higher risk of favorable prognostic factors. Even so, the

study of the effects of age on prognostic factors for breast cancer in Thailand contained limited data. In other words, this is only a single-institute study with a small number of patients. Consequently, the statistical data obtained did not show statistical significance. Nonetheless, an associated relationship direction between age and prognostic factors was found. Thus, further studies in a larger Thai population must be conducted.

What is already known on this topic?

Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients. However, many studies are still different because of different data due to races and population groups.

What this study adds?

The aim of this study was to explore the correlation between age and prognostic factors in Thai breast cancer women. The study found that young age has a trend of more risk of poor prognostic factors than in the elderly group.

Acknowledgement

The author would like to thank Dr. Ulan Suankwan from the Department of Anatomical Pathology, Buddhasothorn Hospital for providing pathological information.

Conflicts of interest

The author confirms that there were no relevant financial or non-financial competing interests to report and no conflicts of interest to declare.

References

1. National Cancer Institute of Thailand. The most common top 10 cancer. In: Hospital-based cancer registry 2018. Bangkok: National Cancer Institute Department of Medical Services Ministry of Public Health Thailand; 2019. p. 19-20.
2. Yersal O, Barutca S. Biological subtypes of breast cancer: Prognostic and therapeutic implications. World J Clin Oncol 2014;5:412-24.
3. Parsa Y, Mirmalek SA, Kani FE, Aidun A, Salimi-Tabatabaee SA, Yadollah-Damavandi S, et al. A review of the clinical implications of breast cancer biology. Electron Physician 2016;8:2416-24.
4. Kimbung S, Loman N, Hedenfalk I. Clinical and molecular complexity of breast cancer metastases. Semin Cancer Biol 2015;35:85-95.
5. Sørlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci U S A 2001;98:10869-74.
6. Tang P, Tse GM. Immunohistochemical Surrogates for Molecular Classification of Breast Carcinoma: A 2015 Update. Arch Pathol Lab Med 2016;140:806-14.
7. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer (unabridged version). Arch Pathol Lab Med 2010;134:e48-72.
8. Kolečková M, Kolář Z, Ehrmann J, Kořínková G, Trojanec R. Age-associated prognostic and predictive biomarkers in patients with breast cancer. Oncol Lett 2017;13:4201-7.
9. Brandt J, Garne JP, Tengrup I, Manjer J. Age at diagnosis in relation to survival following breast cancer: a cohort study. World J Surg Oncol 2015;13:33.
10. Lian W, Fu F, Lin Y, Lu M, Chen B, Yang P, et al. The impact of young age for prognosis by subtype in women with early breast cancer. Sci Rep 2017;7:11625.
11. Anders CK, Hsu DS, Broadwater G, Acharya CR, Foekens JA, Zhang Y, et al. Young age at diagnosis correlates with worse prognosis and defines a subset of breast cancers with shared patterns of gene expression. J Clin Oncol 2008;26:3324-30.
12. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492-502.
13. Aryandono T, Harijadi, Soeripto. Breast cancer in young women: prognostic factors and clinicopathological features. Asian Pac J Cancer Prev 2006;7:451-4.
14. Rahmawati Y, Setyawati Y, Widodo I, Ghozali A, Purnomosari D. Molecular subtypes of Indonesian breast carcinomas - lack of association with patient age and tumor size. Asian Pac J Cancer Prev 2018;19:161-6.
15. Holm J, Eriksson L, Ploner A, Eriksson M, Rantalainen M, Li J, et al. Assessment of breast cancer risk factors reveals subtype heterogeneity. Cancer Res 2017;77:3708-17.
16. Sengal AT, Haj Mukhtar NS, Vetter M, Elhaj AM, Bedri S, Hauptmann S, et al. Comparison of receptor-defined breast cancer subtypes between german and sudanese women: A facility-based cohort study. J Glob Oncol 2018;4:1-12.
17. Park S, Koo JS, Kim MS, Park HS, Lee JS, Lee JS, et al. Characteristics and outcomes according to molecular subtypes of breast cancer as classified by a panel of four biomarkers using immunohistochemistry. Breast 2012;21:50-7.
18. Gulbahce HE, Bernard PS, Weltzien EK, Factor RE, Kushi LH, Caan BJ, et al. Differences in molecular features of triple-negative breast cancers based on the age at diagnosis. Cancer 2018;124:4676-84.
19. de Kruijf EM, Bastiaannet E, Rubertá F, de Craen AJ,

Kuppen PJ, Smit VT, et al. Comparison of frequencies and prognostic effect of molecular subtypes between young and elderly breast cancer patients. Mol Oncol 2014;8:1014-25.
20. Diab SG, Elledge RM, Clark GM. Tumor characteristics and clinical outcome of elderly women with breast cancer. J Natl Cancer Inst 2000;92:550-6.
21. Thangjam S, Laishram RS, Debnath K. Breast carcinoma in young females below the age of 40 years: A histopathological perspective. South Asian J Cancer 2014;3:97-100.
22. Lakshmaiah KC, Das U, Suresh TM, Lokanatha D, Babu GK, Jacob LA, et al. A study of triple negative breast cancer at a tertiary cancer care center in southern India. Ann Med Health Sci Res 2014;4:933-7.
23. Jenkins EO, Deal AM, Anders CK, Prat A, Perou CM, Carey LA, et al. Age-specific changes in intrinsic breast cancer subtypes: a focus on older women. Oncologist 2014;19:1076-83.
24. Laohavinij S, Ruikchuchit K, Maneechavakajorn J. Survival and prognostic factors of stage I-III breast cancer. J Med Assoc Thai 2013;96 Suppl 3:S23-34.