Original Article

A retrospective analysis of clinicopathological characteristics and risk factors for recurrence in young patients with breast cancer

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Background: Younger and older patients with breast cancer often present with different clinicopathological characteristics and exhibit different risk factors for recurrence. This study sought to evaluate the biological characteristics and identify the recurrence risk factors in patients with operable breast cancer who were ≤40 years of age.

Methods: This retrospective study investigated the biological characteristics and clinical outcomes of young patients (aged ≤40 years) with operable breast cancer who had been admitted to the Second Affiliated Hospital of Soochow University for treatment from January 2015 to December 2019. Clinicopathological and follow-up data were collected and statistically analyzed using IBM SPSS 27.0 software. The disease-free survival (DFS) rates were evaluated, and regression analyses were conducted to identify risk factors associated with adverse outcomes.

Results: A total of 154 young patients (aged ≤40 years) with operable breast cancer were included in this study, of whom 68 (44.2%) were aged ≤35 years. In terms of breast cancer subtypes, there were 19 (12.3%) patients with luminal A-like disease, 74 (48.1%) patients with luminal B-like disease, 17 (11.0%) patients with human epidermal growth factor receptor 2 (HER2)-positive (non-luminal) disease, and 44 (28.6%) patients with triple-negative breast cancer (TNBC). The 5-year DFS rate of all the patients was 88%; among those with TNBC, the rate was slightly lower at 76%. According to the results of the log-rank test, tumor (T) stage, node (N) status (N0 or N+), the biological subtype, and the Ki-67 index (with a 14% cut-off value between high and low expression levels) were risk factors for recurrence. The Cox regression analysis showed that the biological subtype was the only risk factor for recurrence. The multiple linear regression analysis demonstrated that the pathological type, tumor grade, estrogen receptor (ER) labeling intensity, and progesterone receptor (PR) expression level significantly affected the level of Ki-67 expression.

Conclusions: This retrospective study showed that biological subtype was the most important risk factor for recurrence in operable breast cancer patients ≤40 years. The Ki-67 index is influenced by the pathological type, primary tumor grade, ER labeling intensity, and PR expression level. Fourteen percent is recommended as the cut-off value for the high and low expression of Ki-67 in clinical practice.

Keywords: Young; breast cancer; risk factor; recurrence

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Introduction

Breast cancer is the most commonly diagnosed cancer in women, with an estimated 2.3 million new cases reported in 2022, 15.5% of which were diagnosed in China (1). The age of onset of breast cancer in China is 45–55 years, which is significantly lower than that in Europe and the United States of America (USA) (1-3).

Approximately 15.0% of patients with breast cancer who received treatment at the Fudan University Shanghai Cancer Center were aged ≤40 years; this proportion was almost three times higher than the rate of 5.3% reported in the population-based Surveillance, Epidemiology, and End Results (SEER) registry (4).

Young breast cancer (YBC) patients often present with more aggressive pathological characteristics, such as a higher tumor grade and a greater degree of vascular invasion (5,6). The Helping Ourselves, Helping Others (HOHO) study and the Prospective study of Outcomes in Sporadic versus Hereditary breast cancer (POSH) conducted in Europe and the USA, respectively, reported higher early recurrence rates among YBC patients with luminal B and estrogen receptor (ER)-negative subtypes (7,8). A young age appears to be a negative predictor of cancer-specific survival outcomes and a higher rate of local recurrence (9).

Highlight box

Key findings

- The study showed that the biological subtype was the most important risk factor for recurrence in young operable breast cancer patients. Triple-negative breast cancer (TNBC) had the lowest 5-year disease free survival rate.
- Ki-67 index was influenced by the pathological type, primary tumor grade, estrogen receptor labeling intensity, and progestogen receptor expression level in this study. Fourteen percent is recommended as the cut-off value of Ki-67 in clinical practice.

What is known and what is new?

- Young breast cancer patients often present with more aggressive pathological characteristics. However, more aggressive treatments given solely based on the age was not suitable.
- The biological subtype was the most important risk factor except for tumor node metastasis (TNM) stage for recurrence in patients ≤40 years. TNBC had the worst prognosis.

What is the implication, and what should change now?

- The treatment decision should be made on the biological subtype and TNM stage for the patients ≤40 years and 14% is recommended as the cut-off value of Ki-67 in clinical practice.

More specifically, an age ≤40 years has been shown to be associated with a significant increase in the risk of breast cancer-related death among women with luminal A and luminal B disease (10). However, YBC patients often face a variety of other concerns, such as fertility issues, sexual dysfunction, and impaired social and vocational functioning. If more aggressive treatments are administered solely based on the age of the patients, there is a risk of overtreatment, and patients' quality of life may also be negatively affected (11,12). Therefore, it is necessary to more accurately determine the clinicopathological characteristics of YBC patients.

At present, no international standardized cut-off value exists to define the age of a "young" patient; for example, some studies have defined those aged ≤35 years as "young", while other studies have used 40 years as the cut-off value. Considering the importance of fertility protection and the poor cancer-specific survival rate among patients aged ≤40 years old, the Breast Cancer in Young Women (BCY) guidelines and the expert consensus on the diagnosis and treatment of young breast cancer in China have defined "young" as an age ≤40 years (13,14).

Also in recent studies, Ki-67 is considered an indicator of active cellular proliferation in tumors (15-17). However, the standard threshold to indicate high and low expression is not clear.

This study aimed to retrospectively analyze the pathological characteristics and clinical outcomes following standard adjuvant treatment among patients with operable breast cancer who were aged ≤40 years to elucidate the risk factors for recurrence and provide further insights to guide clinical decision making in this patient population. We present this article in accordance with the STROBE reporting checklist available at https://gs.amegroups.com/article/view/10.21037/gs-24-193/rc).

Methods

Study design

A retrospective, single-center cohort study was conducted to evaluate the pathological characteristics and risk factors for recurrence among YBC patients. Operable YBC patients who had been admitted to the Second Affiliated Hospital of Soochow University between January 2015 and December 2019 were enrolled in the study. Information related to clinical and pathological variables including age, tumor size and stage, lymph node stage, pathological type, tumor

grade, biological subtype, HER-2 expression level, and complication were collected from the hospital's electronic case reporting system, and the patients' follow-up data were collected by telephone and from the imaging system. The inclusion criteria were as follows: a diagnosis of operable breast cancer; an age ≤40 years; and the absence of distant metastasis. Patients who could not receive or who refused to receive standard adjuvant treatment were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (No. JD-HG-2023-56). Informed consent for this retrospective analysis was waived.

Definitions

Immunohistochemistry (IHC) was performed to evaluate the ER and progesterone receptor (PR) expression levels; values below 1% were considered negative. Qualitative labeling intensity and the percentage of positively labeled cells were reported for positive specimens. Human epidermal growth factor receptor 2 (HER2)-positivity was defined as IHC 3+ or as IHC 2+ with positive fluorescence in situ hybridization (FISH) detection of *HER2* gene amplification (18). Low HER2 expression was defined as IHC 1+ or as IHC 2+ without FISH amplification (19). Ki-67 is a nuclear antigen that is solely expressed in proliferating cells. According to the ER, PR, and HER2 status, and the Ki-67 expression level, the patients were classified into the following four biological subtypes: luminal A-like (ER-positive and PR-positive, HER2-negative, and Ki-67 labeling 14%); luminal B-like (HER2+ or HER2–) (ER-positive and/or PR-positive and HER2-positive; or ER-positive and/or PR-positive and HER2-negative and Ki-67 >14%); HER2-positive (non-luminal) (ER-negative, PR-negative, and HER2-positive); and triple-negative (ER-negative, PR-negative, and HER2-negative) breast cancer (TNBC) (20,21).

Statistical analysis

All the statistical analyses were conducted using IBM SPSS Statistics, version 27.0 software (IBM Corp., Armonk, NY, USA). The demographic data, risk factors, pathological variables, and follow-up results were analyzed descriptively. The continuous numerical variables are presented as the mean and standard deviation, the discrete variables are presented as the median, and the categorical variables are expressed as the percentage. The disease-free survival (DFS) and cumulative recurrence-free survival rates were calculated using the life table method. The log-rank test and Kaplan-Meier survival curves were used for the univariate analysis of factors affecting recurrence risk, and Cox regression was used for the multivariate analysis of recurrence risk. A multivariate linear regression analysis was conducted to assess the influence of biological breast cancer parameters (such as ER and PR positivity) on the Ki-67 level, and a P value ≤0.05 was considered statistically significant.

Results

Patient characteristics

A total of 928 patients with breast cancer who received radical/modified radical/breast-conserving surgery were identified, of whom 158 (17.0%) were aged ≤40 years. Among these 158 patients, four were excluded for the following reasons: three refused to undergo any adjuvant treatment, and one patient returned to her hometown, and her adjuvant treatment data were unavailable. Thus, 154 patients were enrolled in the study and included in the data analysis.

There were 68 (44.2%) patients aged ≤35 years. The mean age of the patients was 35.4 years, and the minimum age at diagnosis was 23 years. The primary tumor size was obtained from pathology report and for the patients with neoadjuvant chemotherapy, the size was obtained from ultrasound report. The average size was 2.7±1.5 cm (minimum: 0.5 cm; maximum: 10 cm). In terms of tumor (T) staging, 73 (47.4%) patients were classified as T1, 74 (48.1%) as T2, and 7 (4.5%) as T3. In terms of lymph node (N) staging, 88 (57.1%) patients exhibited no lymph node metastasis (N0), 40 (26.0%) had 1–3 lymph node metastasis (N1), 20 (13.0%) had 4–6 lymph node metastasis (N2), and 6 (3.9%) had >6 lymph node metastasis (N3). In term of TNM stage, 52 (33.8%) patients had stage I disease, 77 (50%) had stage II disease, and 25 (16.2%) had stage III disease. Thirty-six (23.4%) patients exhibited evidence of lympho-vascular invasion.

In terms of the pathological types, invasive ductal carcinoma was diagnosed in 94.8% of cases; much lower proportions of patients were diagnosed with mucinous adenocarcinoma (2.6%), invasive lobular carcinoma (1.3%), and mixed carcinoma (1.3%). There were 13 (8.4%) patients with grade one (G1) tumors, 110 (71.4%) with grade 2 (G2) tumors, and 31 (20.1%) with grade 3 (G3) tumors. In relation

Table 1 Demographic and clinical features of the patients

Variable	Value (N=154)
Age (years)	35.4±4.0 [23–40]
≤35	68 (44.2)
>35–40	86 (55.8)
Primary tumor size (cm)	2.65±1.50 [0.5–10]
Primary tumor stage	
T1	73 (47.4)
T2	74 (48.1)
T3	7 (4.5)
Lymph node stage	
N0	88 (57.1)
N1	40 (26.0)
N2	20 (13.0)
N3	6 (3.9)
TNM stage	
I	52 (33.8)
II	77 (50.0)
III	25 (16.2)
Pathological type	
Invasive ductal carcinoma	146 (94.8)
Adenocarcinoma	4 (2.6)
Invasive lobular carcinoma	2 (1.3)
Mixed carcinoma	2 (1.3)
Lympho-vascular invasion	
Yes	36 (23.4)
No	118 (76.6)
Tumor grade	
G1	13 (8.4)
G2	110 (71.4)
G3	31 (20.1)
Ki-67 level	
≤14%	30 (19.5)
>14%	124 (80.5)
Biological subtype	
Luminal A-like	19(12.3)
Luminal B-like	74 (48.1)
HER2-positive (non-luminal)	17 (11.0)
TNBC	44 (28.6)
HER2 expression level	
Negative	39 (25.3)
Low (IHC 1+ or 2+ and FISH negative)	78 (50.6)
Positive	37 (24.0)
Medical comorbidities	
Pregnancy	1 (0.6)
Contralateral breast cancer	2 (1.3)
Rheumatic heart disease	1 (0.6)
Thyroid adenoma	1 (0.6)
Hypertension	1 (0.6)

The data are expressed as number (percentage of patients), mean ± SD, or [min–max]. T, tumor; N, lymph node; M, metastasis; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; SD, standard deviation.

to the subtypes, there were 19 (12.3%) patients with luminal A-like disease, 74 (48.1%) with luminal B-like disease, 17 (11.0%) with HER2-positive disease, and 44 (28.6%) with TNBC. According to the IHC and FISH results, the level of HER2 expression was classified as negative in 39 cases (25.3%), equivocal in 78 cases (50.6%), and positive in 37 cases (24.0%). In addition, 66 patients were classified as HER2 IHC 2+ based on qualitative IHC scores, of whom nine (13.6%) were confirmed to be HER2-positive based on the FISH results. There were 30 (19.5%) patients had Ki-67 level ≤14% and 124 (80.5%) >14%.

One patient, who was diagnosed with breast cancer at 32 weeks of pregnancy, had a mass in her left breast that significantly increased in size during pregnancy. After giving birth, the patient received neoadjuvant chemotherapy and underwent modified radical mastectomy. Two patients had a history of contralateral breast cancer, one patient had a history of rheumatic heart disease, one patient had thyroid adenoma, and one patient had hypertension (*Table 1*).

In terms of treatment, 10 (6.5%) patients received neoadjuvant chemotherapy, and 51 (33.1%) underwent breast-conserving surgery. Based on the postoperative pathological staging and biological subtype, the patients received proper adjuvant treatment according to the National Comprehensive Cancer Network (NCCN) guidelines at that time.

Table 2 Data on recurrence and log-rank analysis of risk factors for recurrence

Variable	Value
Follow-up time (months), median [min–max]	51.5 [6–101]
Local recurrence, n (%)	3 (1.9)
Distant metastasis, n (%)	19 (12.3)
Risk factors for recurrence (P value)	
Age (≤35 *vs.* >35–40 years)	0.43
Pathological type	0.82
Tumor grade	0.58
Vascular invasion	0.08
T stage	0.02*
N status (N0 or N+)	0.01*
Biological subtype	0.02*
Ki-67 index	
≤10% *vs.* >10%	0.11
≤14% *vs.* >14%	0.050*
≤20% *vs.* >20%	0.74
≤30% *vs.* >30%	0.54
HER2 expression level	0.95

*, a P value ≤0.05 indicates a statistically significant effect. HER2, human epidermal growth factor receptor 2.

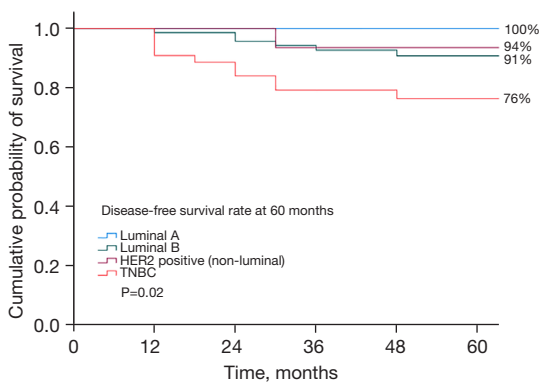

Figure 1 Disease-free survival rate curves according to the molecular subtype of breast cancer. HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

The 5-year DFS and recurrence risk analysis

The median follow-up time for all the patients was 51.5 months (minimum: 6 months; maximum: 103 months). During the follow-up period, 3 (1.9%) patients experienced local recurrence, and 19 (12.3%) patients developed distant metastasis. The log-rank test was used to analyze the influence of various factors on recurrence, including the patients' age (≤35 *vs.* >35–40 years old), pathological type, tumor grade, vascular invasion status, T stage, N status (N0 or N+), biological subtype, Ki-67 level (≤14% *vs.* >14%), and HER2 expression level. T stage, N status (N0 or N+), the biological subtype, and the Ki-67 level had a statistically significant effect on tumor recurrence, but a younger age (≤35 years old) did not. As an independent factor, the Ki-67 index with a cut-off value of 14% had a significant effect on recurrence (P=0.050). We also tested the cut-off value of 10%, 20% and 30%, no significant effect was observed at 10% (P=0.11), 20% (P=0.74) and 30% (P=0.54) (*Table 2*). According to the Cox multivariate regression analysis, the biological subtype (P=0.007) was the only factor with a significant effect on recurrence.

The life table revealed that the 5-year DFS rates were 88% for all patients, 100% for those with luminal A disease, 91% for those with luminal B disease, 94% for those with HER2-positive disease, and 76% for those with TNBC (P=0.02). The subgroup analysis demonstrated that the 5-year DFS rate of patients with TNBC was significantly lower than that of patients with either the luminal A-like (P=0.02) or luminal B-like (P=0.02) disease subtypes, and there was no statistically significant difference between those with TNBC and HER2-positive breast cancer (P=0.12) (*Figure 1*).

The relevant factor analysis of Ki-67

In the present study, when a cut-off value of 14% was selected, the log-rank test showed the DFS rate differed significantly between the groups with values above and below that cut-off value (*Figure 2*). Further the multivariate linear regression analysis showed that the pathological type (P=0.001), primary tumor grade (P<0.001), ER labeling intensity (P=0.02), and PR expression level (P=0.04) had a significant effect on the Ki-67 index (*Table 3*).

Discussion

This study retrospectively analyzed the biological characteristics of 154 young patients (aged ≤40 years) with operable breast cancer, and the risk factors for recurrence after undergoing standard treatment. Considering the prognostic influence of the Ki-67 index on early breast

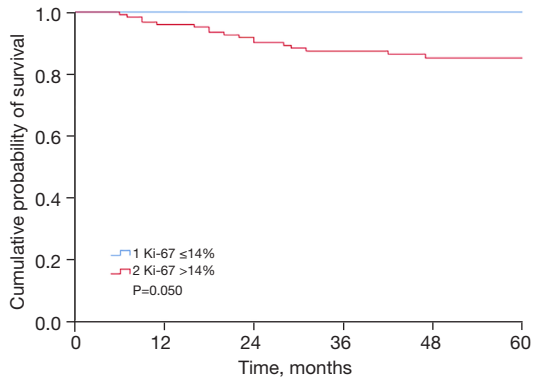

Figure 2 Disease-free survival rate curves according to Ki-67 expression level (cut-off value 14%).

Table 3 Multivariate linear regression analysis of factors associated with Ki-67 expression

Factors associated with Ki-67 expression	B (95% CI)	P value
Age	−0.16 (−0.94, 0.63)	0.70
Pathological type	−6.01 (−9.58, −2.44)	0.001*
Primary tumor grade	14.87 (8.24, 21.51)	<0.001*
ER expression level	0.07 (−0.11, 0.25)	0.46
ER labeling intensity	−9.48 (−17.56, −1.39)	0.02*
PR expression level	−0.17 (−0.33, −0.12)	0.04*
PR labeling intensity	−1.29 (−8.27, 5.69)	0.72
HER2 expression level	3.12 (−1.29, 7.52)	0.17

*, P≤0.05. CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

cancer outcomes, the factors influencing Ki-67 expression were also analyzed. The results showed that the 5-year DFS rate was 88% among all the YBC patients following standard adjuvant treatment, with a lower rate of 76% among those with TNBC. The Cox regression analysis revealed that the biological subtype of breast cancer was the most important risk factor for recurrence in this patient population, and a younger age (≤35 years) had no further effect on the risk of recurrence. Ultimately, the multivariate linear regression analysis demonstrated that the pathological type, tumor grade, ER labeling intensity, and PR expression level significantly associated with the expression of the prognostic marker Ki-67.

According to data from five randomized controlled trials, comprising a total of 4,105 patients (International Breast Cancer Study Group Trials I to V), the 5-year recurrence rate of patients with operable breast cancer was approximately 10.4% (22). A retrospective analysis based on data from China and the SEER database showed that the 5-year DFS rate of patients with breast cancer who were aged ≤40 years was 85.5% (4). Several studies investigating the outcomes of adjuvant endocrine therapy for patients with hormone receptor (HR)-positive premenopausal breast cancer have reported 5-year DFS rates of 85% to 93% following standard adjuvant therapy (23-25). The 5-year DFS rate of 88% in patients aged ≤40 years reported in the present study is consistent with the rates previously reported.

YBC patients often present with a more aggressive tumor biology; for example, a study involving 2,956 operable YBC patients reported that 58.9% had Grade 3 tumors, and 50.2% had positive lymph nodes (8). Similarly, Collins *et al.* reported that among 399 YBC patients, 55% had Grade 3 tumors, and 34% exhibited evidence of vascular invasion (26). An epidemiological study involving nearly 15,000 YBC patients showed that young patients often presented with large masses, positive lymph nodes, poor differentiation, and HR negativity (27). The results of a study of 5,227 Chinese patients from Fudan University showed that 44.5% of young patients had tumors >2 cm in size, 36.25% had positive lymph nodes, and 15.22% had Grade 3 disease (4). In the present study, the clinical characteristics of the patients were less severe than those reported in studies from the United Kingdom and USA but were similar to the results of the study from Fudan University, indicating that the biology of breast cancer in young patients may differ according to race.

It is important to note that the distribution of molecular subtypes among YBC patients also differs from that of older breast cancer patients. For example, Sabiani *et al.* reported that TNBC was diagnosed in 22.2% of patients aged ≤35 years; this percentage decreased with respect to age to 19.1% in those aged 35–40 years, 14.3% in those aged 40–45 years, and 10.4% in those aged 45–50 years. The opposite trend was observed in terms of the proportion of patients with luminal A disease, with rates of 39.8% in those aged ≤35 years, 51.7% in those aged 35–40 years, 62.5% in those aged 40–45 years, and 71.7% in those aged 45–50 years, suggesting a higher proportion of young patients with TNBC and a lower proportion with luminal A disease (28). Another study showed that among patients aged ≤40 years, 33% had luminal A disease, 35% had

luminal B disease, 11% had HER2-positive breast cancer, and 21% had TNBC (26). However, another study from the Republic of Türkiye reported that among YBC patients, 16.8% had luminal A disease, 38.7% had luminal B disease, 30.5% had HER2-positive breast cancer, and 15.3% had TNBC, and these rates were quite different from those reported in other studies (29). Among the 154 patients in the present study, 28.6% were triple-negative, 11.0% were HER2-positive, only 12.3% were luminal A-like type, and 48.1% were luminal B-like type. The findings of both the present study and the previously reported studies suggest that the distribution of the biological subtypes of breast cancer can vary by race; however, the biological subtypes associated with a poorer prognosis, such as TNBC or luminal B-like, are often encountered in higher proportions in younger patients.

Several studies have explored the risk factors for recurrence among YBC patients. For example, Sabiani *et al.* reported that an age ≤35 years, a mass >50 mm, and a tumor grade of 3 were risk factors for recurrence, and the HER2-positive and luminal B (non-HER2-positive) subtypes were associated with a worse prognosis in patients aged ≤35 years (28). Partridge *et al.* reported that the prognosis of patients with luminal A and B disease was worse in those aged ≤40 years than those aged >40 years, which was not the case for those with HER2-positive breast cancer and TNBC (10). In the present study, the T stage, N status (N0 or not) molecular subtype, and Ki-67 index were all identified as risk factors for disease recurrence, and the Cox regression analysis showed that among them, the molecular subtype was the most important risk factor for recurrence.

Targeted pharmacotherapies against HER2 have significantly improved the clinical prognosis of patients with HER2-positive breast cancer (30). For example, antibody-drug conjugate (ADC) therapies targeting HER2 have even improved the clinical outcomes of patients with low levels of HER2 expression; thus, there has been renewed clinical interest in low HER2 expression status (31). In the present study, which also analyzed the HER2 status of the YBC patients, 78 patients (50.6%) exhibited low HER2 expression, which was similar to the 45–55% rates reported in the literature (19,32). Several retrospective studies have investigated the prognosis of patients with a low HER2 expression status; however, the results have been inconsistent (33-35). In the present study, the log-rank test results failed to identify the HER2 expression level as an independent risk factor for recurrence; however, this variable may be an important prognostic factor in the coming ADC era.

The question of whether younger patients aged ≤35 years require more intensive treatment continues to be investigated. Avci *et al.* previously divided 137 YBC patients into two groups depending on whether they were aged ≤35 years old or were aged 35–40 years; in the younger group, the rate of recurrence was 31%, while in the older group, the rate was significantly lower at just 11% (29). In another study from the Republic of Türkiye, the patients were divided into the following three groups according to age: those aged ≤35 years; those aged >45 years; and those aged >35–45 years. In that study, the results failed to show that a younger age (≤35 years) was associated with a poorer prognosis (36). The results of the log-rank test in the present study also failed to show that age (≤35 *vs.* >35–40 years) affected the DFS rate. The international consensus recommendations for the management of breast cancer in young women also define "young" as an age ≤40 years, and they do not recommend a younger age be used as a prognostic indicator, or as a reason to administer more aggressive adjuvant treatment (13).

Ki-67 is an antigen expressed only in proliferating cells and is considered an indicator of active cellular proliferation in tumors (15). Some studies have reported that the Ki-67 index is higher in some molecular subtypes of breast cancer, such as TNBC (37), and a higher Ki-67 index is associated with some prognostic factors for adverse outcomes and a poor prognosis, especially for patients with luminal breast cancer (38-41). In the monarchE study, a high Ki-67 index was considered one condition for the use of cyclin-dependent kinase 4/6 intensive adjuvant treatment for patients with HR-positive breast cancer (42). Ki-67 plays an important role in HR+/HER2– breast cancer molecular subtyping; however, there is not yet any standardized threshold to indicate high or low expression levels, and previous studies have selected different Ki-67 cut-off values (e.g., 5%, 10%, 14%, 20%, and 30%) (41,43-48). A meta-analysis that included the data of 64,196 patients with early breast cancer found that the patients with Ki-67 levels >25% experienced significantly worse DFS and overall survival outcomes than those with Ki-67 levels <25% (49). In the present study, the log-rank test results did not show that Ki-67 had a significant effect on the DFS rate at a cut-off value of 30%; however, when a cut-off value of 14% was selected, the DFS rate differed significantly between the groups with values above and below that cut-off value. Therefore, we recommend 14% as the cut-off value for the high and low expression of Ki-67 in clinical practice.

Chidananda Murthy reported Ki-67 index had a positive correlation with pathological stage, grade, and molecular subtype and inversely associated with ER and PR status (50) which was consistent with this study. However, there were several limitations because of the retrospective study nature. The small sample size and confounding factors might interfere with the reliability of the conclusions.

Conclusions

Ultimately, this retrospective study showed that the 5-year DFS rate of operable YBC patients was 88% after adjuvant treatment, TNBC had the lowest 5-year DFS rate. Of the variables evaluated, T stage, N status (N0 or not), the biological subtype and Ki-67 were the risk factors of recurrence, and biological subtype was the most important factor. This study also showed that the Ki-67 index was influenced by the pathological type, tumor grade, and ER labeling intensity, and PR expression level of breast cancer, and 14% was identified as the recommended cut-off value for high and low expression levels of Ki-67. These findings could be used to guide clinical decision making in the future to improve prognostic outcomes in this patient population.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-193/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (No. JD-HG-2023-56). Informed consent for this retrospective analysis was waived.

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