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PREDICTIVE VALUE OF AGE AND SERIAL ANTI-MÜLLERIAN HORMONE LEVELS FOR OVARIAN RECOVERY FOLLOWING CHEMOTHERAPY IN HORMONE RECEPTOR–NEGATIVE BREAST CANCER: A LONGITUDINAL STUDY

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ABSTRACT

Objective: To investigate the association between menstrual status at 12 months after completion of chemotherapy and serial serum AMH levels, evaluated both as absolute concentrations and as relative changes from baseline, in a homogeneous cohort of young women with hormone receptor-negative breast cancer.
Methods: A prospective longitudinal study was conducted from January 2024 to December 2025. Women aged 18–45 years with regular menstrual cycles and histologically confirmed with newly diagnosed HR-negative breast cancer planned for chemotherapy were enrolled. Venous blood samples were collected for AMH measurement at baseline (bAMH), immediately post-chemotherapy (AMH0), and at 3 (AMH3) and 6 (AMH6) months post-treatment. AMH recovery at 3 months (rAMH3) and 6 months (rAMH6) was calculated as the percentage change from baseline. Chemotherapy-induced-amenorrhea (CIA) was defined as absence of menstruation for at least 12 consecutive months following completion of chemotherapy.
Results: Among 79 participants, women aged 40-45 years accounted for 55.7% of the cohort and 84.8% received an Antracycline-Cyclophosphamid (AC) protocol for chemotherapy. The CIA rate was 39.2%. bAMH, AMH6, rAMH6, and age demonstrated strong predictive capability for CIA at 12 months, yielding AUCs of 0.83 (95%CI: 0.74-0.93), 0.84 (95%CI: 0.75-0.93), 0.81 (95%CI: 0.71-0.91), and 0.82 (95%CI: 0.72-0.91), respectively. Multivariable analysis confirmed that age >42.5 years (OR = 0.823; 95% CI: 0.699–0.969) and bAMH <0.937 ng/mL (OR = 1.133; 95% CI: 1.027–1.250) are independent predictors of CIA.
Conclusion: Although 6-month AMH monitoring offers valuable confirmation, this study indicates that chronological age and pre-treatment AMH may serve as useful baseline predictors for CIA. This risk stratification could help identify patients at highest risk of CIA, thereby supporting individualized counseling on ovarian protection strategies, including the consideration of GnRH agonists prior to chemotherapy.

KEYWORDS: Anti-Müllerian hormone; Breast cancer; Chemotherapy-induced amenorrhea; Ovarian reserve; Hormone receptor-negative.

INTRODUCTION

Breast cancer is the most prevalent malignancy and a leading cause of morbidity among women worldwide. Advances in public awareness and the widespread implementation of effective screening programs have markedly increased the detection of breast cancer at earlier stages. As a result, 5-year overall survival rates for non-metastatic breast cancer in young women now exceed 80% in most regions [1]. With increasing life expectancy, preservation of quality of life has emerged as a major clinical priority [2]. Premature menopause remains one of the most significant long-term concerns for premenopausal women with breast cancer, who account for approximately one fifth of all breast cancer diagnoses [3]. Despite substantial advances in targeted therapies, chemotherapy remains a cornerstone of systemic treatment for breast cancer [4]. However, many chemotherapeutic agents—particularly alkylating agents—are gonadotoxic [5].
Anti-Müllerian hormone (AMH) has emerged as a reliable biomarker of ovarian reserve. Baseline AMH levels and patient age have consistently proven superior to other markers (FSH, LH, estradiol, and AFC) in predicting post-treatment ovarian activity) [6]. Additionally, recent data suggest that post-chemotherapy AMH dynamics

may offer further prognostic accuracy regarding functional recovery [7–9]. However, the clinical utility of AMH measurement and AMH recovery after chemotherapy remains uncertain, largely due to heterogeneity in study designs, patient populations, and outcome definitions.

On the other hand, resumption of menstruation has traditionally been considered a clinical marker of ovarian recovery [8]. Nevertheless, most studies evaluating the relationship between chemotherapy and ovarian activity have included heterogeneous populations of breast cancer patients, encompassing both hormone receptor-positive and hormone receptor-negative tumors [6]. In patients with hormone receptor-positive disease, adjuvant endocrine therapy—particularly tamoxifen—can significantly influence menstrual patterns, potentially confounding the assessment of ovarian recovery and biasing the interpretation of AMH as a predictor of post-chemotherapy menstrual status [4].

Therefore, the present study aimed to investigate the association between menstrual status at 12 months after completion of chemotherapy and serial serum AMH levels, evaluated both as absolute concentrations and as relative changes from baseline, in a homogeneous cohort of young women with hormone receptor-negative breast cancer. By minimizing the confounding effects of endocrine therapy, this study seeks to clarify the predictive value of AMH dynamics for ovarian function recovery in this specific population.

MATERIALS AND METHOD

Study design and setting

This prospective longitudinal observation study was conducted at K Hospital and Hanoi Obstetrics and Gynecology Hospital from January 2024 to December 2025.

Participants

Women aged 18–45 years with regular menstrual cycles and histologically confirmed, newly diagnosed localized hormone receptor–negative breast cancer were eligible for inclusion if neoadjuvant or adjuvant chemotherapy was planned. Chemotherapy regimens consisted of either an anthracycline-based protocol (AC: anthracycline/cyclophosphamide for 4 cycles followed by taxane for 4 cycles) or a non-anthracycline protocol (Non-AC: carboplatin plus taxane for 6–12 cycles), in accordance with current ESMO guidelines[4]. Exclusion criteria were irregular menstruation within 3 months prior to chemotherapy initiation, presence of chronic medical diseases, history of other malignancies, breast cancer progression or recurrence during study period, modification or prolongation of chemotherapy protocol, and pregnancy during the study period. All patients were enrolled in the study before initiating chemotherapy after receiving full disclosure from the investigators regarding the study. Baseline demographic and clinical characteristics were collected prior to the initiation of chemotherapy.

Study procedures

Venous blood samples for baseline anti-Müllerian hormone (bAMH) measurement were collected within 3 months prior to the initiation of chemotherapy. Patients were scheduled for follow-up visits with blood collection immediately after completion of chemotherapy (AMH0), at 3 (AMH3) and 6 (AMH6) months post-chemotherapy. At each specified time point, 2 mL of peripheral venous blood was drawn into serum-separating tubes. For patients recruited at K Hospital, samples were transported to the central laboratory at Hanoi Obstetrics and Gynecology Hospital in strict compliance with safety regulations, with the cold chain maintained at 2–8°C throughout transportation. Upon arrival, samples were centrifuged to separate serum at the Laboratory of Hanoi Obstetrics and Gynecology Hospital and subsequently stored at −80°C until analysis to ensure sample stability. Serum AMH concentrations were measured using an electrochemiluminescence immunoassay (ECLIA) on the fully automated Cobas e602 system (Roche Diagnostics, Mannheim, Germany). The assay had a limit of detection of 0.01 ng/mL; values below this threshold were recorded as 0.01 ng/mL for statistical analysis. All costs related to AMH measurement, including blood sample collection, transportation, storage, and laboratory testing, were covered by Hanoi Obstetrics and Gynecology Hospital.

The **acute change in AMH** was defined as the relative change from baseline and was calculated as the difference between the immediately post-chemotherapy AMH level and the baseline AMH level, divided by the baseline AMH value. **AMH recovery** at 3 months (rAMH3) and 6 months (rAMH6) were expressed as the percentage change from baseline and calculated as: $rAMH3 = (AMH3 - AMH0)/bAMH \times 100\%$ and $rAMH6 = (AMH6 - AMH0)/bAMH \times 100\%$.

Participants self-monitored their menstrual status until 12 months after completion of chemotherapy. Ongoing menstruation referred to the maintenance of regular menses without a ≥3-month interruption during chemotherapy or the subsequent 12 months. Resumption of menstruation was defined as recovery of menstrual function, evidenced by at least one menstrual episode within 12 months after chemotherapy, following amenorrhea (≥3 consecutive months) during study period. Chemotherapy-induced-amenorrhea (CIA) was defined as absence of menstruation for at least 12 consecutive months following completion of chemotherapy. Non-Chemotherapy-induced-amenorrhea (Non-CIA) included ongoing and resumption of menstruation.

Outcomes

The primary outcome was the association between menstrual status at 12 months after completion of

chemotherapy and serial serum anti-Müllerian hormone (AMH) concentrations measured before and after chemotherapy, including both absolute and relative changes in AMH levels. The secondary outcome was the development of a multivariable predictive model for chemotherapy-induced amenorrhea at 12 months after completion of chemotherapy.

Statistical analysis

This study used a consecutive sampling method. A total of 79 participants were enrolled and evaluated at 12 months after completion of chemotherapy. Statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) or median (minimum–maximum), as appropriate. Categorical variables are expressed as number and percentage, with 95% confidence intervals (CIs) when applicable. Comparisons between groups were performed using the independent *t*-test for normally distributed continuous variables; non-parametric tests were applied when data were not normally distributed. A p-value < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was used to assess the ability of AMH levels and AMH recovery to predict chemotherapy-induced amenorrhea at 12 months after completion of chemotherapy. The DeLong test was applied to compare the areas under the ROC curves (AUCs) of different AMH-based predictive models. Multivariable logistic regression analysis was performed to construct a predictive model for chemotherapy-induced amenorrhea at 12 months following completion of chemotherapy.

RESULTS

Among the 79 included patients, 39.2% developed chemotherapy-induced amenorrhea (CIA) at 12 months after chemotherapy, whereas 60.8% maintained or recovered ovarian function. The mean age of the cohort was 39.0 ± 5.2 years, with the majority of patients aged 40–45 years (55.7%). Most patients had stage I–II disease (73.4%), invasive carcinoma of no special type (96.2%), and grade 3 histology (60.8%). HER2-positive and triple-negative subtypes accounted for 54.4% and 45.6% of cases, respectively. Anthracycline/cyclophosphamide-based chemotherapy was administered in 84.8% of patients, and 34.2% received anti-HER2 therapy. The median baseline AMH level of the overall cohort was 0.680 ng/mL (range: 0.020–9.710). (Table 1)

Table 1: Baseline Characteristics related to menstrual status by 12 months (n=79)

Clinical and Paraclinical Characteristics	**CIA (n=31)**	**Non-CIA (n=48)**	**p**
	n (%)	**n (%)**	
Age (years) **Mean ± SD** **Median (Min – Max)**	42.1 ± 3.2 43 (33-45)	36.9 ± 5.0 37 (26-45)	<0.001
< 35	2 (6.4%)	15(31.3%)	<0.001
35 - 39	3 (9.7%)	15 (31.3%)	
40 - 45	26 (83.9%)	18 (37.5%)	
Stage			
I	12 (38.7%)	17 (35.4%)	0.876
II	12 (38.7%)	17 (35.4%)	
III	7 (22.6%)	14 (29.2%)	
Histopathology			
Histological Type			
Invasive Carcinoma NOS	30 (96.8%)	46 (95.8%)	
Invasive Lobular Carcinoma	0	1 (2.1%)	
Invasive Medullary Carcinoma	0	1 (2.1%)	
Other Invasive Carcinomas	1 (3.2%)	0	
Histological Grade			0.693
Grade 2	13 (41.9%)	18 (37.5%)	
Grade 3	18 (58.1%)	30 (62.5%)	
Molecular Subtype			0.686
HER2 Positive	16 (51.6%)	27 (56.3%)	
Triple Negative	15 (48.4%)	21 (43.8%)	
Treatment Methods			
Surgical Method			
NSM/SSM	10 (32.3%)	16 (33.3%)	1.000
MRM	21 (67.7%)	32 (66.7%)	
Chemotherapy			0.874
Neoadjuvant	13 (41.9%)	21 (43.8%)	
Adjuvant	18 (58.1%)	27 (56.3%)	
Chemotherapy Regimen			1.000

Clinical and Paraclinical Characteristics	CIA (n=31)	Non-CIA (n=48)	p
	n (%)	n (%)	
AC	26 (83.9%)	41 (85.4%)	
Non-AC	5 (16.1%)	7 (14.6%)	
Anti Her-2 therapy			0.438
Yes	9 (29.0%)	18 (37.5%)	
No	22 (71.0%)	30 (62.5%)	

At 12 months, 39.2% (31/79) of patients remained amenorrheic (CIA group), while 60.8% (48/79) resumed menstruation. Baseline AMH levels were significantly higher in the non-CIA group compared with the CIA group (mean: 1.747 ± 1.751 vs. 0.467 ± 0.574 ng/mL; p<0.001). Immediately after chemotherapy, AMH levels declined markedly in both groups and approached near-undetectable values, although the non-CIA group still demonstrated slightly higher concentrations than the CIA group (0.033 ± 0.082 vs. 0.010 ± 0.002 ng/mL; p=0.005). At 3 and 6 months after treatment, AMH levels remained significantly higher among patients with ovarian function recovery, with the greatest separation observed at 6 months (0.240 ± 0.347 vs. 0.021 ± 0.023 ng/mL; p<0.001). Similarly, AMH recovery rates at both 3 and 6 months were significantly greater in the non-CIA group, indicating more substantial ovarian reserve recovery following chemotherapy. (Table 2 and Figure 1).

Table 2. Serial AMH Levels and AMH Recovery According to Ovarian Function Recovery Status at 12 Months After Chemotherapy (n=79)

Time Point	Non-CIA (n=48)	CIA (n=31)	p
Baseline AMH (bAMH), ng/mL			<0.001
Mean ± SD	1.747 ± 1.751	0.467 ± 0.574	
Median (Min–Max)	1.170 (0.024–9.710)	0.258 (0.020–2.280)	
Immediately post-chemotherapy (AMH0), ng/mL			0.005
Mean ± SD	0.033 ± 0.082	0.010 ± 0.002	
Median (Min–Max)	0.010 (0.010–0.416)	0.010 (0.010–0.020)	
3 months post-treatment (AMH3), ng/mL			<0.001
Mean ± SD	0.125 ± 0.259	0.015 ± 0.015	
Median (Min–Max)	0.015 (0.010–1.420)	0.010 (0.010–0.076)	
6 months post-treatment (AMH6), ng/mL			<0.001
Mean ± SD	0.240 ± 0.347	0.021 ± 0.023	
Median (Min–Max)	0.079 (0.010–1.740)	0.010 (0.010–0.090)	
AMH recovery rate at 3 months, %			0.001
Mean ± SD	5.8 ± 14.1	1.7 ± 7.9	
Median (Min–Max)	3.0 (0–85.0)	0 (0–44.0)	
AMH recovery rate at 6 months, %			<0.001
Mean ± SD	14.5 ± 20.6	2.8 ± 9.6	
Median (Min–Max)	7.2 (0–106.2)	0 (0–53.3)	

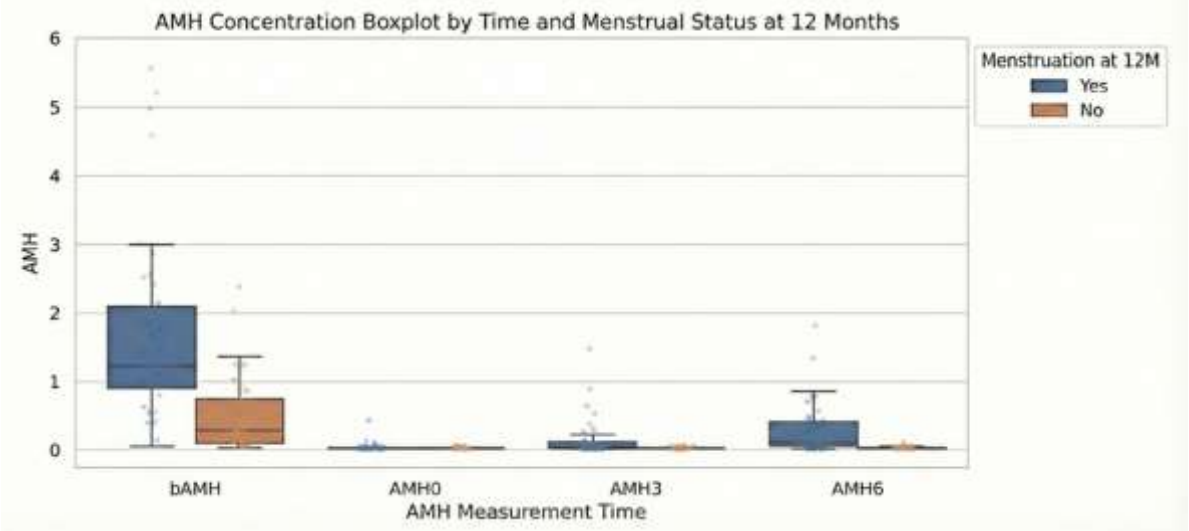

Figure 1. AMH concentration boxplot by time and menstruation status at 12 months post-chemotherapy (n=79).

ROC curve analysis demonstrated that AMH concentration at 6 months after chemotherapy (AMH6) showed the highest predictive performance for ovarian function recovery at 12 months, with an AUC of 0.840 (95% CI: 0.753–0.927), followed closely by baseline AMH concentration (AUC: 0.834; 95% CI: 0.742–0.926) and age (AUC: 0.815; 95% CI: 0.720–0.911). A baseline AMH cut-off value of 0.937 ng/mL provided 72.9% sensitivity and 83.9% specificity, while an AMH6 cut-off of 0.022 ng/mL yielded 77.1% sensitivity and 80.6% specificity. AMH recovery rate at 6 months also demonstrated good predictive ability (AUC: 0.806), whereas predictive performance of AMH measured immediately after chemotherapy was limited and did not reach statistical significance (AUC: 0.630; p=0.051). Overall, 6-month AMH-related indices showed superior predictive performance compared with 3-month measurements. (Table 3 and Figure 2).

Table 3. Predictive Performance of Age and AMH-Related Indices for Ovarian Function Recovery at 12 Months After Chemotherapy (n=79)

Predictor	N	AUC (95% CI)	p	Optimal Cut-off	Sensitivity	Specificity
Baseline AMH concentration (bAMH), ng/mL	79	0.834 (0.742–0.926)	<0.001	0.937	72.9%	83.9%
AMH concentration at 6 months (AMH6), ng/mL	79	0.840 (0.753–0.927)	<0.001	0.022	77.1%	80.6%
AMH recovery rate at 6 months, %	79	0.806 (0.706–0.905)	<0.001	16.5	87.5%	64.5%
AMH concentration at 3 months (AMH3), ng/mL	79	0.712 (0.600–0.825)	0.002	0.013	56.3%	83.9%
AMH recovery rate at 3 months, %	79	0.698 (0.581–0.814)	0.003	4.5	58.3%	80.6%
Immediately post-chemotherapy AMH (AMH0), ng/mL	79	0.630 (0.509–0.752)	0.051	—	—	—
Age, years	79	0.815 (0.720–0.911)	<0.001	42.5	87.5%	64.5%

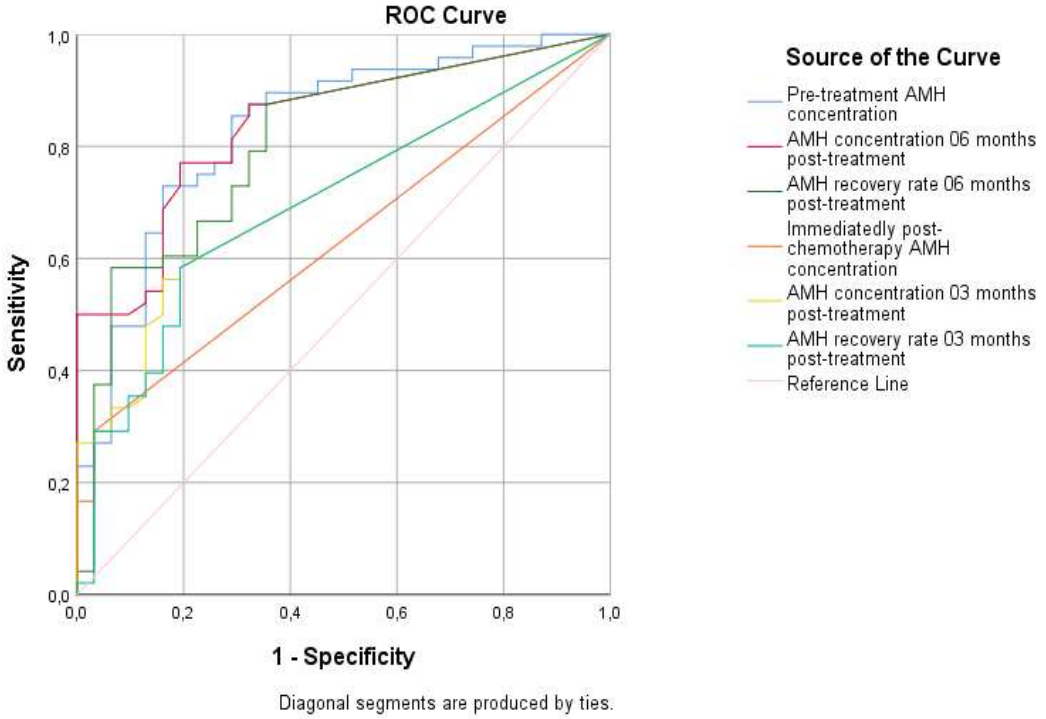

Figure 2. AMH concentration in predicting the probability of menstruation return within 12 months post-chemotherapy (n=79).

DeLong test analysis demonstrated no significant difference in predictive performance between baseline AMH and AMH concentration at 6 months (p=0.905) or between baseline AMH and the 6-month AMH recovery rate (p=0.644). In contrast, baseline AMH showed significantly better predictive ability than both AMH concentration at 3 months (p=0.027) and the 3-month AMH recovery rate (p=0.022). Additionally, AMH concentration at 6

months demonstrated significantly superior predictive performance compared with AMH concentration at 3 months ($p<0.001$), indicating that later post-treatment AMH assessment provides more accurate prediction of ovarian function recovery after chemotherapy. (Table 4)

Table 4. Comparison of Predictive Performance Between AMH-Related Indices for Ovarian Function Recovery at 12 Months After Chemotherapy Using the DeLong Test (n=79)

Comparison	N	Difference in AUC (95% CI)	Z	p
bAMH vs. AMH6	79	−0.006 (−0.099 to 0.088)	−0.120	0.905
bAMH vs. rAMH6	79	0.028 (−0.091 to 0.148)	0.462	0.644
bAMH vs. AMH3	79	0.122 (0.014 to 0.230)	2.206	0.027
bAMH vs. rAMH3	79	0.136 (0.020 to 0.253)	2.290	0.022
AMH6 vs. AMH3	79	0.127 (0.061 to 0.194)	3.765	<0.001

Multivariable logistic regression analysis demonstrated that both age and baseline AMH level were independent predictors of ovarian function recovery at 12 months after chemotherapy. The probability of ovarian function recovery was estimated using the following logistic regression equation:

$$P = \frac{1}{1 + e^{-Z}}$$

$$Z = 7.134 - (0.195 \times \text{Age}) + (0.125 \times \text{AMH})$$

Where:

- P: probability of ovarian function recovery at 12 months after chemotherapy
- e: base of the natural logarithm
- Age: patient age in years
- AMH: baseline AMH level expressed per 0.1 ng/mL increase

Increasing age was associated with a lower likelihood of menstrual recovery (OR: 0.823; 95% CI: 0.699–0.969; p=0.019), indicating that each 1-year increase in age reduced the odds of ovarian recovery by approximately 17.7%. In contrast, higher baseline AMH levels were significantly associated with improved ovarian recovery (OR: 1.133; 95% CI: 1.027–1.250; p=0.013). Specifically, each 0.1 ng/mL increase in baseline AMH was associated with a 13.3% increase in the odds of menstrual recovery after chemotherapy. (Table 5)

Table 5. Multivariable logistic regression analysis for prediction of ovarian function recovery at 12 months after chemotherapy (n=79)

Predictor	B coefficient	OR	95% CI	p
Age (years)	−0.195	0.823	0.699–0.969	0.019
Baseline AMH (per 0.1 ng/mL increase)	0.125	1.133	1.027–1.250	0.013
Constant	7.134	—	—	0.044

DISCUSSION

Our findings confirm that the pre-treatment ovarian reserve is a critical determinant of post-treatment function. A robust primordial follicle pool can absorb the cytotoxic effect and still retain a critical mass of follicles sufficient to restart the HPO axis. The destruction of the growing cohort triggers a compensatory, accelerated recruitment of dormant primordial follicles, leading to premature exhaustion of the reserve [10]. Patients with a larger initial pool (high bAMH) are better equipped to withstand this accelerated loss without depleting their reserve below the threshold of menopause.

A clinically actionable finding of this study Is the redundancy of AMH measurement immediately after chemotherapy (AMH0). We observed that AMH levels collapsed to near-undetectable limits in both recovered and amenorrheic groups. Consequently, AMH0 demonstrated poor prognostic value, failing to reach statistical significance. This phenomenon aligns with the hypothesis proposed by Ben-Aharon et al., suggesting that immediate ovarian dysfunction is driven by acute stromal compromise and a temporary shutdown of follicular recruitment rather than solely by reserve depletion [10]. Therefore, AMH0 reflects acute toxicity rather than long-term potential. Our data suggests that a latency period of at least 6 months is required for the ovary to recover from this acute insult and recruit a new cohort of AMH-secreting follicles. This 6-month landmark (AMH6) proved to be a far superior predictor (AUC 0.840), confirming that delayed assessment is necessary for accurate prognostication.

As our data demonstrated, even among patients who resumed menstruation, the AMH levels at 6 months remained profoundly diminished compared to their baseline (recovering only 14.5%). This suggests a state of compensated but significantly reduced ovarian reserve, highlighting that while endocrine function may partially return, true reproductive potential likely remains compromised.

A distinctive feature of our analysis was the lack of correlation between tumor-related characteristics and ovarian outcomes. In this cohort, tumor-related characteristics were not significantly associated with ovarian outcomes. Ovarian recovery appeared to be driven primarily by the patient's baseline physiological reserve (age and pre-treatment AMH) rather than the tumor's biological behavior.

Although the significant imbalance between AC and non-AC regimens in our cohort precludes a comparison of differential toxicity, ovarian recovery appeared to be primarily driven by age and baseline reserve. This suggests that for young breast cancer patients, the decision to undergo chemotherapy is the critical risk event, rather than the specific nuance between standard anthracycline or platinum-based protocols. Furthermore, the addition of anti-HER2 therapy (Trastuzumab) did not alter the risk of amenorrhea. This aligns with recent consensus that monoclonal antibodies, while potentially carrying cardiac risks, do not exert the direct follicular cytotoxicity seen with cytotoxic chemotherapy [11].

Our study identified a specific age cut-off of 42.5 years for recovery, This finding adds precise prognostic granularity, as current guidelines (e.g., ESMO, ASCO) broadly recommend ovarian protection for premenopausal women without defining a specific age threshold for predicting chemotherapy-induced amenorrhea risk [12,13] . In the context of Asian epidemiology, where the peak incidence of breast cancer occurs at a younger age (40–50 years) compared to Western populations, this finding is significant [1]. Similarly, our identified bAMH cut-off of 0.937 ng/mL differs from other major studies. While Anderson et al. identified pre-treatment AMH as a predictor, they focused on odds ratios rather than a binary clinical cut-off. Their study indicated that only AMH remained as a significant predictor of menses with odds ratio 13.0; 95% confidence interval (CI) 2.5– 66.7] [14]. Our cut-off is higher than the 0.7 ng/mL proposed by Su et al., suggesting that a higher reserve baseline is required to ensure recovery after standard anthracycline-taxane regimens in this population [15]. These findings must be interpreted in light of the recently published individual patient data meta-analysis by van Zwol-Janssens et al. Analyzing data from 1,029 premenopausal breast cancer patients, they confirmed that pre-chemotherapy AMH demonstrates good predictive ability for the resumption of ovarian function, yielding an AUC of 0.79–0.83[16]. This strongly aligns with our model's predictive performance (AUC 0.834). However, their comprehensive analysis also highlighted a critical limitation in current literature: the establishment of a universal, clinically reliable AMH cut-off remains elusive due to significant inter-assay variability, differences in follow-up duration, and patient age. Therefore, while our specific cut-off of 0.937 ng/mL provides a risk stratification within our defined cohort utilizing the fully automated Roche Cobas e602 system, we acknowledge that this threshold cannot be broadly generalized across different laboratory platforms without further assay standardization.

By utilizing our model to stratify risk prior to the first cytotoxic dose, clinicians could utilize this risk stratification to support discussions regarding ovarian protection strategies, including the potential use of GnRHa, in accordance with current clinical guidelines.. Crucially, the restoration of ovarian function serves a dual purpose: safeguarding fertility and maintaining vital endocrine health. Chemotherapy-induced menopause is associated with severe long-term sequelae, including accelerated bone mineral density loss, increased cardiovascular morbidity, and impaired sexual function, all of which significantly compromise the quality of life in young survivors [2,17]. This proactive approach aligns with findings from the landmark POEMS trial (Moore et al.), which demonstrated that in hormone receptor-negative breast cancer, GnRHa co-administration significantly reduced the risk of ovarian failure (OR = 0.30) and improved pregnancy rates [18]. Furthermore, Lambertini et al. have consistently advocated for the use of GnRHa not only as a fertility preservation strategy but also to reduce the prevalence of chemotherapy-induced premature ovarian insufficiency [19].
We fully acknowledge that the small number of younger patients is a limitation of our study. While the restriction to HR-negative patients is a methodological strength, it limited our sample size to 79 participants, precluding detailed subgroup analyses of different chemotherapy protocols. This was also a single-center cohort. Therefore, these findings should be considered exploratory, and larger, multi-center studies are required to validate the predictive accuracy of our multivariable model before widespread clinical implementation. Future research can integrate biochemical markers with transvaginal ultrasound (antral follicle count) to correlate functional recovery with anatomical reserve, providing a more holistic view of post-treatment ovarian health.

CONCLUSION

Although AMH monitoring at 6 months still provides valuable confirmation, this study indicates that chronological age and pre-treatment AMH may serve as useful baseline predictors for CIA in similar populations. This immediate risk stratification could help identify patients at highest risk of CIA, thereby supporting individualized counseling on ovarian protection strategies, including the consideration of GnRH agonists prior to chemotherapy. By preventing chemotherapy-induced premature menopause, we can safeguard patients from its debilitating long-term consequences, placing ovarian function recovery at the heart of comprehensive survivorship care.

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