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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

TEMPORAL DYNAMICS OF GLOBAL LONGITUDINAL STRAIN AND NT-PROBNP IN THE EARLY DETECTION OF ANTHRACYCLINE-INDUCED CARDIOTOXICITY: A 24-MONTH PROSPECTIVE STUDY IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER

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Abstract.

Background: As breast cancer survival improves, cardiovascular toxicity has emerged as a major determinant of long-term outcomes. Cancer therapy–related cardiac dysfunction is particularly prevalent among postmenopausal women with increased cardiovascular risk, highlighting the need for early cardiotoxicity detection and targeted cardio-oncology surveillance.

Objective: To assess correlations between longitudinal changes in Global longitudinal strain, conventional Left Ventricular systolic–diastolic echocardiographic parameters, and cardiac biomarkers for prediction and early detection of cancer therapy–related cardiac dysfunction.

Methods: A prospective 24-month single-center study (December 2019–March 2024) assessed 74 postmenopausal patients with primary breast cancer receiving anthracycline or anthracycline-trastuzumab. Left ventricular systolic and diastolic function and N-terminal pro–B-type natriuretic peptide was measured at baseline and seven follow-up visits. Cardiotoxicity was defined by Ejection Fraction and Global Longitudinal Strain changes. Outcomes were analyzed using multiple regression, paired t-tests, ANOVA, and survival analyses (Kaplan–Meier, Cox), with cardioprotective therapy administered to high-risk patients and those with worsening left ventricular systolic parameters; $p<0.05$.

Results: In 74 breast cancer patients receiving anthracycline-based therapy, CTRCD incidence increased from 13.5% to 36.5% over 24 months. GLS detected cardiotoxicity earlier and more frequently than EF. NT-proBNP >125 pg/mL was associated with early and moderate CTRCD, peaking at 3 months with high sensitivity (94.1%) and specificity (90.9%), whereas NT-proBNP >300 pg/mL identified a smaller subgroup with more severe biomarker elevation. Diastolic dysfunction progressed biphasically, with E/e′ >15 observed exclusively in high-risk CTRCD patients. Overall, NT-proBNP thresholds provided robust short-term biomarkers for early and severe CTRCD surveillance. ROC analysis demonstrated good diagnostic performance of NT-proBNP for CTRCD detection (AUC = 0.779; 95% CI 0.656–0.901; $p < 0.001$). Among the evaluated thresholds, 125 pg/mL demonstrated the most balanced diagnostic performance, achieving 100% specificity and 48.3% sensitivity.

Conclusion: In a 2-year study of postmenopausal breast cancer patients receiving anthracycline-containing regimens, GLS was the most sensitive and robust predictor of cardiotoxicity, outperforming EF. Early changes GLS predicted both early and late events, while diastolic indices showed temporal associations without independent predictive value; E/e′ increased mainly in high-risk patients, NT-proBNP demonstrated diagnostic utility but was not independently predictive.

Key words. NT pro-BNP, diastolic parameters, systolic parameters, cardiotoxicity, CTRCD.

Introduction.

Malignant neoplasms remain a major global health challenge and one of the primary causes of morbidity, mortality, and disability. Despite progress in diagnosis and therapy, the worldwide cancer burden continues to rise, ranking second only to cardiovascular diseases as a leading cause of death. Breast cancer is the most commonly diagnosed malignancy among women, accounting for roughly one-third of all new cancer cases [1-4]. Its incidence rises with age, with over 60% of cases occurring in women aged 50–70 years, predominantly postmenopausal, though it remains a leading cause of cancer-related mortality across all ages [2,5-8].

Cancer therapy–related cardiac dysfunction (CTRCD) is among the most serious complications, worsening prognosis and representing the leading cause of fatal non-cancer-related events during or after therapy [2,9-11].

As breast cancer survivorship grows, treatment-induced cardiotoxicity is increasingly observed, especially among postmenopausal women, due to age-related cardiovascular risk and pre-existing cardiac disease. These findings highlight the urgent need for early detection, prevention, and optimal management of cardiotoxicity in this high-risk population through effective screening and timely intervention.

Methods.

A 24-month prospective, single-center study was conducted at the Ultrasound Laboratory of the Medical Center, Ivane Javakhishvili Tbilisi State University (TSU). Between December 2019 and March 2024, 100 consecutive women with newly diagnosed breast cancer were screened for eligibility. Following the application of predefined inclusion and exclusion criteria, 79 eligible postmenopausal women were enrolled. During follow-up, three patients withdrew informed consent and two were excluded because of suboptimal echocardiographic image quality, resulting in a final longitudinal study cohort of 74 patients (mean age 62.3 ± 8.6 years; range 46–76 years). Inclusion criteria were primary breast cancer, indication for anti-cancer therapy with anthracycline- and trastuzumab-containing regimens, and postmenopausal status. Exclusion criteria included pregnancy, inability to provide informed consent, prior chemotherapy or radiotherapy, EF <50%, suboptimal imaging, or conditions affecting left ventricular function (e.g., severe valvular disease, atrial fibrillation/flutter, permanent pacemaker,

or primary cardiomyopathy). The study was approved by the TSU Ethics Committee (Protocol#1, 6/07/2019), and all patients provided written informed consent. All patients received doxorubicin, and HER2-positive patients (n=15) received sequential trastuzumab. At baseline, patients' demographics and cardiovascular risk factors were recorded according to the 2022 ESC Cardio-Oncology Guidelines [12]. All had at least one additional risk factor, including hypertension, diabetes, obesity, dyslipidemia, smoking, or cardiovascular disease. High-risk patients for cancer therapy–related cardiac dysfunction (CTRCD) or those with worsening systolic function (GLS or EF) received cardioprotective therapy [12].

Cardiotoxicity was defined as ≥10% EF reduction from baseline and/or EF <50%, and/or ≥15% GLS reduction from baseline and/or GLS<−16%. Serial assessments were performed at predefined intervals with close monitoring: prior to initiation of anti-cancer therapy (denoted as T0), and at 1 month(T1), 2 months(T2), 3 months(T3), 6 months(T4), 9 months(T5), 12months (T6), and 24 months(T7) after initiation of anthracycline therapy. For HER2-positive breast cancer patients, the T4 visit corresponded to three months after the first trastuzumab dose (the first follow-up post-trastuzumab).

All study participants underwent comprehensive assessment of cardiac structural and functional systolic and diastolic echocardiographic parameters. N-terminal pro–B-type natriuretic peptide (NT-proBNP)—were measured at each visit [12].

NT-proBNP levels were quantified using a commercially available Abbott electrochemiluminescence immunoassay, with <125 pg/mL considered normal. Levels >300 pg/mL were classified as exceeding the age-adjusted diagnostic threshold for heart failure ("gray zone") and considered clinically significant.

Statistical Analysis: Statistical analyses were performed using IBM SPSS v23.0 (IBM Corp., Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (SD). Between-group comparisons utilized independent t-tests and Fisher's exact tests. One-way ANOVA was applied where appropriate. Paired t-tests compared baseline and follow-up values. Categorical variables are expressed as percentages and compared using Chi-square or Fisher's exact tests. To assess the potential confounding effect of trastuzumab exposure, additional subgroup analyses comparing anthracycline-only and anthracycline-plus-trastuzumab patients were performed, and anti-HER2 therapy was included as a covariate in multivariable regression models.Because multiple paired comparisons between baseline and follow-up visits were performed, Bonferroni-adjusted significance thresholds were additionally applied. Given seven planned comparisons (T1–T7 versus baseline), statistical significance after correction was defined as $p < 0.007$ (0.05/7).

Multiple regression models assessed the combined effects of independent variables on dependent outcomes, predicting cardiotoxicity at T4(6months) and T7(24months). Independent variables included baseline characteristics: age, cardiotoxicity risk score, hypertension, type 2 diabetes mellitus, coronary artery disease, smoking, obesity, chemotherapy regimen, anti-HER2 therapy, radiotherapy, baseline EF(EF0), GLS(GLS0), S'(S'0), E/e'(E/e'0), E/A(E/A0), DT(D/T0), IVRT(IVRT0), NT-proBNP(NT-proBNP0), and segmental longitudinal strain at anterior, inferior, lateral, and septal basal, mid, and apical segments. Additionally, one-month changes (Δ) from baseline were included: ΔEF1, ΔGLS1, ΔE/e'1, ΔE/A1, ΔD/T1, ΔIVRT1, ΔS'1, and ΔNT-proBNP1.

Regression results were reported according to American Psychological Association style. Kaplan–Meier survival curves were generated to assess cardiotoxicity-free survival, and Cox proportional hazards models calculated hazard ratios (HR) with 95% confidence intervals (CI) to quantify the association between covariates and cardiotoxicity risk. Statistical significance was defined as $p< 0.05$

Longitudinal biomarker analysis: Continuous biomarker levels (Table 1) are presented as mean ± SD and median values. Changes from baseline at each follow-up time point (n = 74) were assessed using paired t-tests. Normality of paired differences was evaluated; due to right-skewed distributions, median values are additionally reported. Sensitivity analyses using the Wilcoxon signed-rank test confirmed the robustness of results. Mean changes from baseline are presented with 95% confidence intervals.

Results.

Among 74 (mean age 62.3 ± 8.6 years) breast cancer patients monitored over 24 months after anthracycline-based chemotherapy, the cumulative incidence of CTRCD progressively increased over time, from 13.5% at 1 month to 36.5% at 24 months. representing a 2.7-fold rise over the observation period. The majority of new CTRCD cases emerged within the first 12 months, with a slower increase thereafter. Parallel changes were observed in NT-proBNP concentrations (See Figure 1).

In our study, EF-based cardiotoxicity was detected at the end of chemotherapy (T3) (10.8%, n-8), while GLS showed a change and reached the cardiotoxicity criterion already at the first dose of anthracycline exposure (T1) (13.5%,n-10). The number of CTRCD cases identified by GLS at T3 (23.0%, n-17) was 2 times higher than the number of cases identified by EF at the same visit. The frequency of CTRCD identified by GLS exceeded that identified by EF at all study visits (Figure 1).

NT-proBNP concentrations increased significantly from baseline across all measured timepoints. Baseline values were low (mean 44.9±15.5pg/mL; median 42.15pg/mL). At 1 month, NT-proBNP nearly doubled (mean 85.1±47.6 pg/mL; median 79.20 pg/mL; $p<0.001$), corresponding to a mean change of +40.2pg/mL (+89.5% relative mean increase; +87.9% median increase; $p<0.001$). Levels rose further at 2 months (mean 104.6±70.7pg/mL; median 87.90pg/mL; $p<0.001$), representing a mean increase approximately 2.3-fold from baseline +59.7pg/mL (+133.0% mean; +108.5% median; $p<0.001$) (Table 1).

A peak was observed at 3 months, with NT-proBNP reaching its highest values (mean 151.9±167.5pg/mL; median 112.00pg/mL; $p<0.001$), 3.4-fold increase from baseline exceeding baseline mean by +107.0 pg/mL (+238.3% mean; +165.8% median; $p<0.001$) with a 95% CI for the mean change of 69.1–144.9 ($p<0.001$) (Table 1).

Following the 3-month peak, NT-proBNP declined progressively but remained significantly elevated relative to

baseline. At 6 months, concentrations were still markedly higher (mean 141.4±151.8pg/mL; median 100.30pg/mL; p<0.001), a mean difference of +96.5pg/mL (+214.8% mean; +138% median; p<0.001). At 9 months, levels decreased but remained above baseline (mean 112.1±90.7pg/mL; median 84.45pg/mL p<0.001), with a mean change of +67.2 pg/mL (+149.8% mean; +100.4% median; p<0.01) (Table 1).

By 12 months, downward trajectories continued (mean 82.3±40.1pg/mL; median 71.70 pg/mL; p<0.001), corresponding to +37.37pg/mL relative to baseline (+83.3% mean; +70.1% median; p<0.001). At 24 months, NT-proBNP values approached near-baseline levels but remained mildly increased (mean 64.2±25.0pg/mL; median 54.50pg/mL), with a residual elevation of +19.3pg/Ml (+43.0% mean; +29.3% median; p<0.001) (Table 1).

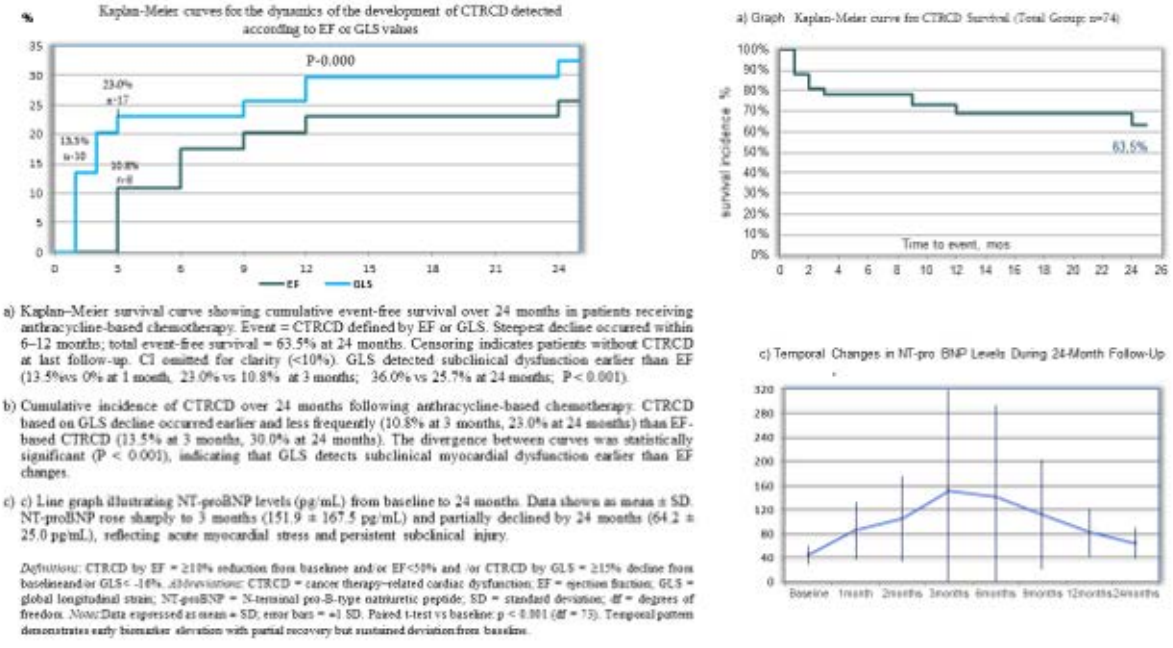
NT-proBNP dynamics with values >125pg/mL and >300pg/mL were assessed over 24 months. Elevated values were detected in 9.5% of total population (n-7) at 1 month, peaking at 28.4% (n-21) at 3 months, and declining thereafter to 1.4% at 24 months. This biphasic response pattern is shown in Table 2.

During the 2-year follow-up, by Cross-tabulation analysis NT-proBNP>125 pg/mL demonstrated a distinct diagnostic temporal pattern for the detection of cancer therapy–related cardiac dysfunction (CTRCD, n=7). This Association with the occurrence of CTRCD (n=27) at nearly all follow-up points (χ=21.4-41.8, p < 0.01 for T1–T6), with a nonsignificant association at 24 months (T7, χ^2=0.8, p=0.392). 100% of elevated cases at 1 months belonging to the CTRCD group, representing 70.0% of the CTRCD group at visit and 25.9% all CTRCD cases (T1,χ^2=29.6,p<0.001). At the pick (T3) from 21 patients 76.2% (n-16) was CTRCD patient, represented 94.1% of CTRCD cases at visit and 59.3% CTRCD all cases (T3, χ^2=41.8, p<0.001). NT-proBNP>125 pg/mL was consistently more prevalent in CTRCD than non-CTRCD patients (χ^2=21.4-41.8, all p<0.003) (Table 2).

Elevations in non-CTRCD patients were rare or absent (0-5 patients across visits) only 0-6.7% of non-CTRCD patients from all cohort exhibited such elevations (Table 2).

Marked elevations (>300pg/mL) were rare, occurring only during mid-treatment, observed in 12.2% at 6 months, all within the CTRCD subgroup and presenting 33.3 % of CTRCD patients (see Table 2).

Overall diagnostic performance was moderate, with accuracy ranging from 90.5% (T1, T2, T5) to 93.2% at 6 months(T4) (≈90–93%). The highest overall accuracy was at 6 month (T4)-93.2%. The sensitivity of NT-proBNP peaked at 3 months (94.1%) with diagnostic specificity of 90.9% (χ^2 =41.8, p<0.001), achieving the high accuracy (91.9%) and a positive likelihood ratio (+LR) of 10.3. specificity remained excellent throughout follow-up (90.9–100%). Positive likelihood ratios exceeded 10-fold during the 2–4-month interval (T2–T3), indicating strong rule-in value, whereas negative likelihood ratios remained below 0.42 during the 6 months (T1–T4), reflecting moderate rule-out capacity. At 1 month, sensitivity was 70.0% with perfect specificity (100%, p<0.001), and between 6 and 12 months, specificity remained 100% while sensitivity progressively declined from 68.4% to 29.2%, consistent with normalization of NT-proBNP despite persistent subclinical ventricular dysfunction. By 24 months, discriminatory performance diminished markedly, with sensitivity of only 3.7% despite 100% specificity (p=0.392), reflecting limited late predictive value despite a cumulative CTRCD incidence of 36.5%. NT-proBNP >300 pg/mL identified a smaller subset of patients with perfect specificity (100%) but low sensitivity (0–47.4%), providing high positive predictive value but limited rule-out capacity. By 24 months, both thresholds showed minimal sensitivity (3.7% for >125 pg/mL;0% for >300pg/mL), reflecting normalization of NT-proBNP in most patients despite a cumulative CTRCD incidence of 36.5%. Collectively, these findings support NT-proBNP >125 pg/mL as a highly sensitive and specific early biomarker



a) Kaplan–Meier survival curve showing cumulative event-free survival over 24 months in patients receiving anthracycline-based chemotherapy. Event = CTRCD defined by EF or GLS. Steepest decline occurred within 6–12 months; total event-free survival = 63.5% at 24 months. Censoring indicates patients without CTRCD at last follow-up. CI omitted for clarity (<10%). GLS detected subclinical dysfunction earlier than EF (13.5%vs 0% at 1 month, 23.0% vs 10.8% at 3 months; 36.0% vs 25.7% at 24 months; P < 0.001).

b) Cumulative incidence of CTRCD over 24 months following anthracycline-based chemotherapy. CTRCD based on GLS decline occurred earlier and less frequently (10.8% at 3 months, 23.0% at 24 months) than EF-based CTRCD (13.5% at 3 months, 30.0% at 24 months). The divergence between curves was statistically significant (P < 0.001), indicating that GLS detects subclinical myocardial dysfunction earlier than EF changes.

c) c) Line graph illustrating NT-proBNP levels (pg/mL) from baseline to 24 months. Data shown as mean ± SD. NT-proBNP rose sharply to 3 months (151.9 ± 167.5 pg/mL) and partially declined by 24 months (64.2 ± 25.0 pg/mL), reflecting acute myocardial stress and persistent subclinical injury.

Definitions: CTRCD by EF = ≥10% reduction from baseline and/or EF<50% and /or CTRCD by GLS = ≥15% decline from baselineand/or GLS< -16%. *Abbreviations:* CTRCD = cancer therapy–related cardiac dysfunction; EF = ejection fraction; GLS = global longitudinal strain; NT-proBNP = N-terminal pro-B-type natriuretic peptide; SD = standard deviation; df = degrees of freedom. *Note:* Data expressed as mean ± SD; error bars = ±1 SD. Paired t-test vs baseline: p < 0.001 (df = 73). Temporal pattern demonstrates early biomarker elevation with partial recovery but sustained deviation from baseline.

Figure 1. *Dynamics of Cancer Therapy–Related Cardiac Dysfunction (CTRCD) and NT-proBNP Levels Over 24 Months in Postmenopausal Breast Cancer Patients Receiving Anthracycline-Based Chemotherapy.*

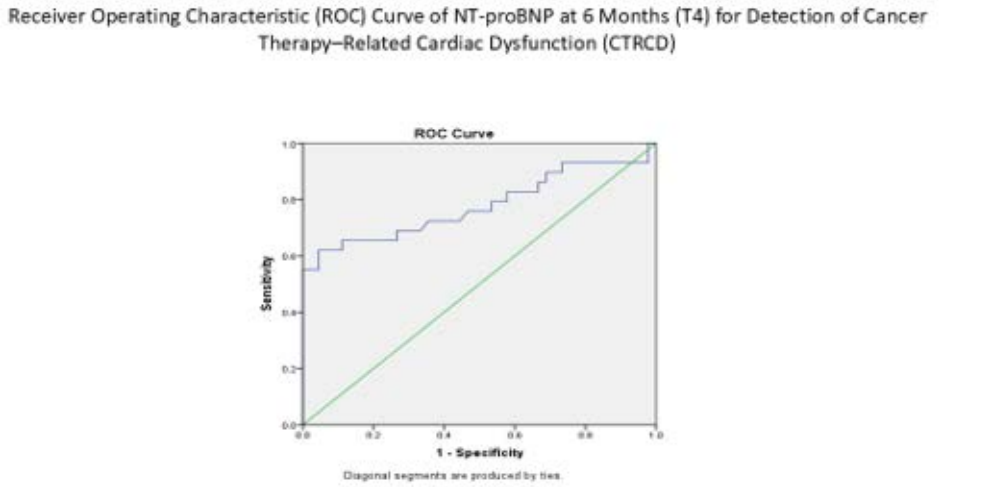


Figure 2. *ROC Curve of NT-proBNP (T4) for Prediction of CTRCD.*

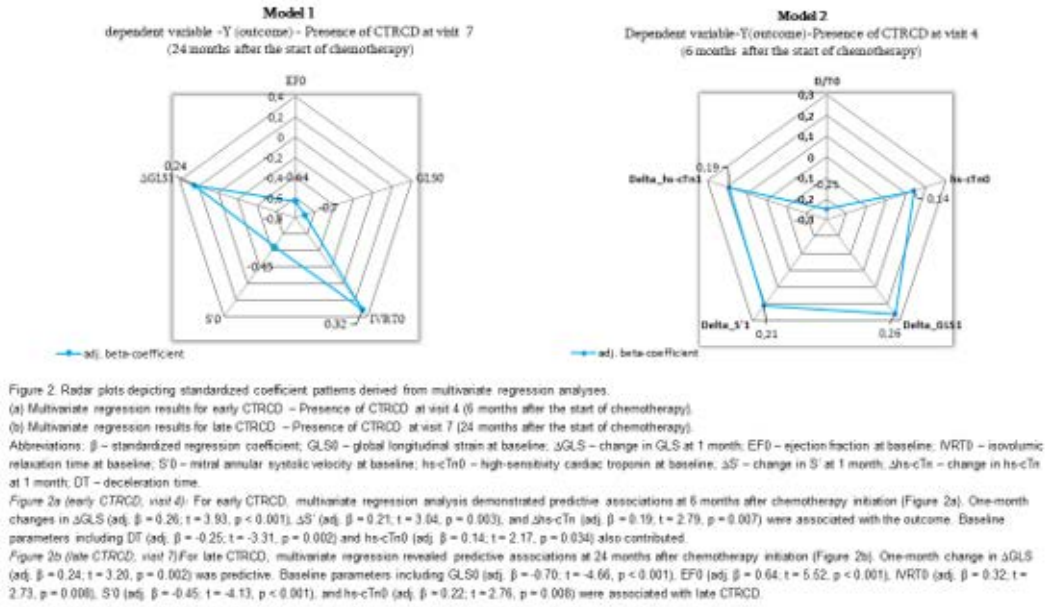


Figure 3. *Radar Plots of Standardized Coefficient Patterns from Multivariate Regression Analyses Predicting Early and Late CTRCD.*

Table 1. *Longitudinal NT-proBNP Trajectories Over 24 Months and Paired Comparisons with Baseline Values.*

Timepoint	Mean (absolute), pg/mL	SD	Median, pg/mL	Min, pg/mL	Max, pg/mL	Difference from baseline, pg/mL (mean ± 95% CI)	Paired t-test	df	P value
Baseline	44.9	15.5	42.15	19.5	92.3	–	–	–	–
1 month	85.1	47.6	79.20	34.6	280.3	40.18 (30.04–50.31)	7.90	73	<0.001
2 months	104.6	70.7	87.90	37.6	424.4	59.67 (43.96–75.38)	7.57	73	<0.001
3 months	151.9	167.5	112.00	44.5	897.9	106.99(69.06–144.92)	5.62	73	<0.001
6 months	141.4	151.8	100.30	42.7	803.8	96.53 (62.01–131.05)	5.57	73	<0.001
9 months	112.1	90.7	84.45	40.5	441.2	67.18 (46.64–87.71)	6.52	73	<0.001
12 months	82.3	40.1	71.70	39.9	273.2	37.37 (28.78–45.96)	8.67	73	<0.001
24 months	64.2	25.0	54.50	31.2	156.8	19.30 (14.55–24.05)	8.09	73	<0.001

Note: *NT-proBNP concentrations are expressed in pg/mL. Values are presented as mean ± SD, median, minimum, and maximum. Mean change from baseline is shown with 95% confidence intervals (CI). Comparisons with baseline were performed using paired t-tests (n = 74).*
Abbreviations: NT-proBNP = N-terminal pro–B-type natriuretic peptide; SD = standard deviation; CI = confidence interval; df = degrees of freedom.

Table 2. *Association Between NT-proBNP Thresholds and Cancer Therapy–Related Cardiac Dysfunction (CTRCD) Over 24-Month Follow-Up.*

Parameter	T1 (1 mo)	T2 (2 mo)	T3 (3 mo)	T4 (6 mo)	T5 (9 mo)	T6 (12 mo)	T7 (24 mo)
CTRCD cases at visit (n, % of 74)	10 (13.5%)	15 (20.3%)	17 (23.0%)	19 (25.6%)	21 (28.4%)	24 (32.4%)	27 (36.5%)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
NT-proBNP >125 pg/mL (n, % of 74)	7 (9.5%)	11 (14.9%)	21 (28.4%)	13 (17.6%)	10 (13.5%)	7 (9.5%)	1 (1.4%)
CTRCD cases from >125 pg/mL (n, %)	7 (100%)	9 (81.8%)	16 (76.2%)	13 (100%)	10 (100%)	7 (100%)	1 (100%)
Non-CTRCD cases from >125 pg/mL (n, %)	0 (0%)	2 (18.2%)	5 (23.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
NT-proBNP >125 pg/mL in whole CTRCD (n, % of 27)	7 (25.9%)	9 (33.3%)	16 (59.3%)	13 (48.1%)	10 (37.0%)	7 (25.9%)	1 (3.7%)
NT-proBNP >125 pg/mL in CTRCD at visit (n, %)	7 (70.0%)	9 (60.0%)	16 (94.1%)	13 (68.4%)	10 (47.6%)	7 (29.2%)	1 (3.7%)
χ^2 (p)	29.6 (<0.001)	22.1 (<0.003)	41.8 (<0.001)	36.2 (<0.001)	30.1 (<0.001)	21.4 (<0.001)	0.8 (0.392*)
Sensitivity (%)	70.0	60.0	94.1	68.4	47.6	29.2	3.7
Specificity (%)	100.0	96.4	90.9	100.0	100.0	100.0	100.0
Accuracy (%)	90.5	90.5	91.9	93.2	90.5	86.5	73.0
+LR	∞	16.7	10.3	∞	∞	∞	∞
–LR	0.30	0.42	0.06	0.32	0.52	0.71	0.96
Whole cohort NT-proBNP >300 pg/mL (n, %)	0 (0.0%)	3 (4.1%)	7 (9.5%)	9 (12.2%)	9 (12.2%)	0 (0.0%)	0 (0.0%)
CTRCD cases from >300 pg/mL (n, %)	0 (0.0%)	3 (100%)	7 (100%)	9 (100%)	9 (100%)	0 (0.0%)	0 (0.0%)
NT-proBNP >300 pg/mL in CTRCD group (n = 27)	0 (0.0%)	3 (11.1%)	7 (25.9%)	9 (33.3%)	9 (33.3%)	0 (0.0%)	0 (0.0%)
χ^2 (p)	0 (0.1)	2.6 (0.11*)	15.4 (<0.01)	20.3 (<0.001)	17.2 (<0.001)	0 (0.1*)	0 (0.1*)
Sensitivity (%)	0.0	20.0	41.2	47.4	42.9	0.0	0.0
Specificity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Accuracy (%)	86.5	90.5	91.9	93.2	91.9	86.5	73.0
+LR	–	∞	∞	∞	∞	–	–
–LR	1.00	0.80	0.59	0.53	0.57	1.00	1.00

This table summarizes the temporal relationship between elevated NT-proBNP levels (>125 pg/mL and >300 pg/mL) and the incidence of CTRCD across serial follow-up time points. Diagnostic performance indices (sensitivity, specificity, accuracy, likelihood ratios) are presented for each time point relative to CTRCD status. Note: Time points: T1 = 1 month, T2 = 2 months, T3 = 3 months, T4 = 6 months, T5 = 9 months, T6 = 12 months, T7 = 24 months. CTRCD defined as cancer therapy–related cardiac dysfunction. NT-proBNP thresholds (>125 pg/mL and >300 pg/mL) correspond to standard clinical cut-offs for mild and significant ventricular dysfunction, respectively. Diagnostic performance indices (sensitivity, specificity, accuracy, +LR, –LR) were calculated for each follow-up point relative to CTRCD status. χ^2 (p) refers to chi-square test for association between NT-proBNP elevation and CTRCD occurrence. $p < 0.05$ considered statistically significant; "" denotes non-significant comparisons. Abbreviations: CTRCD = cancer therapy–related cardiac dysfunction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; +LR = positive likelihood ratio; –LR = negative likelihood ratio; SD = standard deviation.*

Table 3. *Correlation Between NT pro-BNP and Echocardiographic Systolic Parameters During 2-years Follow-Up.*

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Pearson r Time Point	**NT pro-BNP vs EF**	**NT pro-BNP vs. GLS**	**NT pro-BNP vs. S'**
Baseline	−0.27 (0.021) *	−0.31 (0.008) *	−0.33 (0.005) *
T1 (1 month)	−0.10 (0.419)	−0.29 (0.012) *	−0.22 (0.061)
T2 (2 months)	−0.16 (0.187)	−0.43 (<0.001) **	−0.26 (0.027) *
T3 (3 months)	−0.40 (<0.001) **	−0.55 (<0.001) **	−0.48 (<0.001) **
T4 (6 months)	−0.51 (<0.001) **	−0.58 (<0.001) **	−0.53 (<0.001) **
T5 (9 months)	−0.51 (<0.001) **	−0.53 (<0.001) **	−0.54 (<0.001) **
T6 (12months)	−0.45 (<0.001) **	−0.34 (0.003) **	−0.49 (<0.001) **
T7 (24months)	−0.46 (<0.001) **	−0.34 (0.003) **	−0.47 (<0.001) **

Notes: *Pearson correlation coefficient (r) with 2-tailed p-values is shown. *p < 0.05, **p < 0.01. Negative r values indicate inverse relationships: higher NT-proBNP corresponds to lower EF, less negative GLS, and reduced S'. Abbreviations: NT-proBNP = N-terminal pro-B-type natriuretic peptide; EF = ejection fraction; GLS = global longitudinal strain; S′ = mitral annular systolic velocity.*

Table 4. *E/e' values and proportion of elevated cases (>15) in CTRCD vs Non-CTRCD patients.*

Parameter	T0	T1	T2	T3	T4	T5	T6	T7
CTRCD-Yes, n=27								
Mean	6.448	6.779	7.028	7.910	9.845	11.128	10.631	9.686
Median	6.900	6.800	7.400	7.800	8.000	8.700	8.900	9.900
CTRCD-No, n=64								
Mean	6.304	6.553	6.778	7.016	7.313	7.489	7.653	7.613
Median	6.000	6.700	6.800	7.000	7.400	7.500	7.700	7.700
Elevated E/e′ >15, CTRCD cases	0	0	0	3	8	4	1	-
%	0.0	0.0	0.0	4.1	10.8	5.4	1.4	-
Elevated E/e′ >15, Non-CTRCD cases	0	0	0	0	0	0	0	-
%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-
p-value	-	-	-	0.056	0.000	0.021	0.392	-

Notes: *CTRCD = cancer therapy–related cardiac dysfunction. Elevated E/e' defined as >15. Mean and median are shown for each group at each time point. p-values reflect comparison between CTRCD and Non-CTRCD groups.*

for short-term CTRCD surveillance, achieving peak diagnostic accuracy in the late post-chemotherapy period: at 6 months and strongest early rule-in capacity during the 2–4-month interval, supporting its role as a short-term surveillance biomarker. while NT-proBNP >300 pg/mL provides robust confirmatory evidence of true cardiac dysfunction (Table 2).

We performed a correlation analysis between NT-proBNP and echocardiographic parameters-EF, GLS, and S'-at all study visits. All significant correlations were negative, indicating that higher NT-proBNP levels were associated with lower EF, GLS, and S' values. Correlations were generally weak at baseline, strengthened from 3 to 9 months, and remained moderate at later follow-up (12–24 months). Baseline: EF (r=−0.27, p=0.021), GLS (r=−0.31, p=0.008), S' (r=−0.33, p=0.005). 1 month (T1): GLS (r=−0.29, p=0.012); EF and S' not significant. 2 months (T2): GLS (r = −0.43, p < 0.001), S' (r = −0.26, p = 0.027); EF not significant. 3 months (T3): EF (r=−0.40, p<0.001), GLS (r=−0.55, p<0.001), S' (r=−0.48, p<0.001). 6–9 months (T4–T5): EF (r=−0.51, p<0.001), GLS (r=−0.58 to −0.53, p<0.001), S' (r=−0.53 to −0.54, p<0.001). 12–24 months (T6–T7): EF (r=−0.45 to −0.46, p<0.001), GLS (r =−0.34, p= 0.003), S' (r=−0.49 to −0.47, p<0.001) (Table 3).

Additional subgroup analyses were performed comparing patients treated with anthracycline alone (n = 59) and those receiving anthracycline followed by trastuzumab (n = 15). No statistically significant differences were observed in the incidence of early CTRCD (T4; Fisher's exact test, p = 0.245) or late CTRCD (T7; Fisher's exact test, p = 0.564) between treatment groups. Furthermore, trastuzumab exposure was not identified as an independent predictor of cardiotoxicity in multivariable regression analyses.

Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic performance of NT-proBNP for the identification of cancer therapy–related cardiac dysfunction (CTRCD). NT-proBNP measured at 6 months (T4) demonstrated good discriminatory ability, with an area under the curve (AUC) of 0.779 (95% CI 0.656–0.901; p < 0.001). Among the evaluated thresholds (100, 125, 200, and 300 pg/mL), the 125 pg/mL cutoff demonstrated the most balanced diagnostic performance. A threshold of 100 pg/mL yielded higher sensitivity but substantially lower specificity, whereas thresholds of 200 pg/mL and 300 pg/mL maintained excellent specificity at the expense of markedly reduced sensitivity. The 125 pg/mL threshold achieved 100% specificity while maintaining 48.3% sensitivity, supporting its selection as the clinically optimal cutoff in this cohort. Although NT-proBNP >300 pg/mL (the conventional heart failure "gray zone") also demonstrated excellent specificity, its substantially lower sensitivity limited its utility for early CTRCD detection. These findings suggest that lower NT-proBNP thresholds may be more appropriate for surveillance and early risk stratification in cardio-oncology populations (Figure 2).

Figure 2 Receiver Operating Characteristic (ROC) Curve of NT-proBNP at 6 Months (T4) for the Detection of Cancer Therapy–Related Cardiac Dysfunction (CTRCD). The area under the curve (AUC) was 0.779 (95% CI 0.656–0.901; p < 0.001), indicating good discriminatory performance. The 125 pg/mL threshold demonstrated 100% specificity and 48.3% sensitivity and was selected as the clinically optimal cutoff.

Multiple regression analysis did not confirm the prognostic role of NT-proBNP (Figure 3).

We also analyzed diastolic parameters during the 2-year study. Across the study population (n = 74), longitudinal analysis revealed a consistent pattern of progressive deterioration in diastolic function parameters over time. Patients who subsequently developed CTRCD demonstrated more pronounced changes in all diastolic indices compared with those who did not. During the 24-month follow-up, diastolic function exhibited a biphasic trend with mid-term perturbation and partial recovery. Mean IVRT declined from 105.3±21.2ms at baseline to 61.0±31.0 ms at T3 (−42% from T2), followed by partial recovery to 81.0±32.1 ms at T7 (+32% from nadir). Deceleration time shortened from 231.1 ± 43.7 ms to 179.1 ± 55.9 ms at T4 (−22.5%) and partially rebounded to 201.4 ± 52.8 ms (+12.4%). The E/A ratio increased from 1.0 ± 0.5 at baseline to 1.5 ± 0.4 at T4 (+50%) before slightly declining to 1.3 ± 0.5 at T7 (−13%). The largest interval changes occurred between T2–T3 for IVRT and DT, and T1–T2 for E/A, highlighting mid-follow-up as the phase of greatest diastolic alteration in this cohort. The steepest changes for IVRT and DT occurred between T1–T4 and T2–T4, respectively, while the E/A ratio showed maximal slope between T2–T4, indicating that mid-

follow-up represented the phase of most dynamic diastolic adjustment in this cohort

The mean E/e′ ratio increased over time but remained within the normal range. The increase was more pronounced among patients who developed CTRCD compared with those who did not. Notably, E/e′ values exceeding 15—indicative of elevated left ventricular filling pressures—were observed exclusively in the CTRCD subgroup, predominantly among patients classified as high risk. No significant increase in E/e′ >15 was detected in patients without CTRCD during chemotherapy (Table 4).

In our study, E/e'>15 was first detected in the anthracycline-trastuzumab regimen at the first follow-up visit (T4) after exposure to the first dose of trastuzumab (4.1%, n=3, p=0.056), all three patients were in the high-risk group. The peak was observed at T5 (10.8%, n=8, p=0.000), of which 6 patients were in the high-risk group. At 1 year (T6), the number of cases was halved (5.4%, n=4, P=0.02), all four remaining patients were in the high-risk group. The statistically significant increase in E/e' continued up to 1 year (Table 4).

The prognostic value of E/e' could not be confirmed. DT0- was significantly associated with early CTRCD (β=-0.25; t=-3.31, p=0.002), while IVRT0- was significantly associated with late CTRCD (β=0.32; t=2.73, p=0.008).

Discussion.

We provided a detailed longitudinal evaluation of NT-proBNP and echo parameters dynamics and their diagnostic and prognostic performance for the detection of CTRCD across a 24-month longitudinal study of 74 high-risk, postmenopausal breast cancer woman (mean age 62.3 ± 8.6 years) receiving anthracycline-based regimen and 20% of them subsequent trastuzumab.

This study provides a unified temporal framework of cardiotoxicity, demonstrating that biochemical stress, subclinical myocardial deformation, and overt functional decline occur in a sequential and time-dependent manner rather than as isolated phenomena.

The cumulative incidence of CTRCD increased from 13.5% at 1 month to 36.5% at 24 months (2.7-fold increase), with no cases of overt heart failure. CTRCD developed predominantly within the first year (32%), followed by minimal additional accrual thereafter (4.1% by 24 months), indicating a time-dependent but front-loaded pattern of cardiotoxicity in this population. These findings support the presence of a critical early vulnerability window after anthracycline initiation and emphasize the importance of early, structured biomarker- and imaging-based surveillance. Detection of subclinical dysfunction during this phase may allow “timely intervention before irreversible myocardial injury, with implications for optimizing anthracycline safety and tailoring cardioprotective strategies.

Similarly, in the 24-month prospective multicenter CARDIOTOX Registry, López-Sendón et al. [13]. reported late CTRCD in 37.5% of patients (31.6% mild, 2.8% moderate, and 3.1% severe), broadly consistent with our findings. Similarly, Lu et al. [14] reported that most CTRCD events 21% occurred at 1 year (95%CI 12–32%), rising marginally to 25% by year 3 (95% CI 15–35%). Over half of affected patients required treatment interruption. Similarly, Bouwer et al. [15] observed annual cardiotoxicity rates of 11.7% and 9.1% in the first and second years, respectively, followed by a decline.

In our cohort, the cumulative incidence of CTRCD was modestly higher than reported in prior studies, likely reflecting a higher baseline cardiovascular risk profile (older age, postmenopausal status) and the application of more sensitive diagnostic criteria. Earlier detection of CTRCD may therefore be attributable to the superior sensitivity of GLS over LVEF for identifying subclinical myocardial dysfunction. namely, GLS-defined CTRCD emerged after the first anthracycline cycle, whereas EF-based cardiotoxicity became apparent only at treatment completion. Although cardiotoxicity is generally thought to occur predominantly within the first year, longer-term prospective data suggest a progressive increase over time. In the 4.5-year study by Caballero et al. [16], incidence rose from 1% at one year to 16.5% at study completion, while Serrano et al. [17] reported rates of 4% at one year and 18% at four years. Notably, GLS was not included in these studies, likely contributing to inter-study variability and supporting the notion that reliance on LVEF alone may underestimate early cardiotoxic injury.

Compared with prior studies limited to 3–6 month intervals, our findings reveal a biphasic NT-proBNP pattern: an early post-treatment rise followed by gradual decline to near-baseline by 24 months, reflecting early subclinical myocardial stress and incomplete biochemical recovery, suggesting cumulative myocardial remodeling or persistent neurohormonal activation. In our study, baseline NT-proBNP concentrations were low (mean 44.9 ± 15.5 pg/mL; median 42.2 pg/mL) but demonstrated a pronounced and prolonged increase, rising by 89.5% at 1 month (85.1 pg/mL) and peaking at 3 months with a marked 3.4-fold increase (151.9 pg/mL; mean change +107.0 pg/mL; +238.3%, $p < 0.001$). By 6 months, levels began to decline (mean 141.4 ± 151.8 pg/mL) but remained markedly elevated relative to baseline (mean change +96.5 pg/mL; +214.8%, $p < 0.001$), indicating only partial normalization. Despite further decline, NT-proBNP levels remained persistently elevated through 24 months (64.2 pg/mL; +29% from baseline). The steeper rise and higher peak observed likely reflect the older, exclusively female, comorbidity-enriched population. This pattern—rapid, higher-amplitude peak at 3 months followed by an incomplete decline at 6 months—suggests an initial phase of acute myocardial stress with subsequent transition to a subacute or evolving hemodynamic load.

A broadly consistent pattern of early proportional NT-proBNP elevation has been reported in anthracycline- and trastuzumab-based acute phase investigations despite substantial inter-cohort variability in baseline values and absolute concentrations. Allam et al. [18] and Muckienė et al. [19] reported higher baseline mean NT-proBNP levels than in our cohort, yet demonstrated similar relative increases (≈60%), closely paralleling our observed trajectory. Specifically, NT-proBNP rose from 75.6±20.2pg/mL to 124.4±40.0pg/mL at three weeks (+61.4%) and from 94.8pg/mL to 154.1pg/mL after two cycles (+62%). Collectively, these data confirm early NT-proBNP elevation as a sensitive marker of acute anthracycline-related myocardial stress, independent of absolute values, while the higher peak in our study suggests a

more intense acute phase driven by cumulative risk factors and preceding overt functional impairment.

Intermediate-duration, anthracycline-only, younger cohorts show reproducible NT-proBNP kinetics up to 3 months, diverging thereafter, reflecting a transition from acute injury to evolving myocardial stress. Sulaiman et al. [20], (n=51) and Bhagat et al. [21], (n=43) reported similar baseline levels (61 and 57 pg/mL), mid-therapy rises to 98 (+60%) and 92 pg/mL (+61%), and 6-month peaks of 146 (+139%) and 128 pg/mL (+124%). Dong et al. [22] (n=90) confirmed stepwise increases from 60 to 85 (+42%) after 2 cycles, 112 (+87%) after 4 cycles, 125 (+108%) at 3 months, and 131 (+118%) at 6 months. Our cohort showed median comparable early acceleration but higher magnitude (112 at 3 mo, +166%) with partial reversal at 6 months (100, +138%). The early parallel kinetics reflect the universal anthracycline NT-proBNP rise (peaking 3–6 months), while the attenuated 6-month peak and trajectory shift likely reflect cohort-specific factors (older age, higher baseline risk, cardiometabolic burden), and partial mitigation by our cardioprotective regimen.

Longer 12-month studies incorporating trastuzumab, with or without anthracyclines, showed progressive NT-proBNP increases sustained through late follow-up, contrasting with our cohort. Bouwer et al. [23] (n=135) reported median NT-proBNP rising from 68 to 152 pg/mL at 6 months (+124%) and 170 pg/mL at 12 months (+150%). The SUCCOUR biomarker sub-analysis (n=323) [24] showed a slower rise from 58 at baseline to 72 (+24%) at 3 months, 84 (+45%) at 6 months, and 91 pg/mL (+57%) at 12 months. Díaz-Antón et al. [25] (n=118) demonstrated a similar sequence: 55 at baseline, 92 post-anthracycline (+67%), 118 (+114%) at 3 months, 124 (+125%) at 6 months, and 130 pg/mL (+136%) at 12 months. These consistent patterns highlight NT-proBNP as a robust biomarker of cumulative cardiotoxic stress, while the earlier, sharper elevations in our cohort likely reflect older age, higher baseline risk, and predominance of acute myocardial stress versus the progressive load under sustained trastuzumab exposure.

In marked contrast, Posch et al. [26] (n=185) reported higher baseline NT-proBNP (median 94 pg/mL) with no significant longitudinal change after baseline adjustment. This divergence likely reflects cohort-specific factors—elevated baseline risk, greater baseline variability, or treatment exposure-stage differences (adjuvant vs neoadjuvant). In such populations, baseline NT-proBNP may outweigh temporal changes in prognostic significance, underscoring context-dependent interpretation of NT-proBNP dynamics.

In our study baseline NT-proBNP did not discriminate patients who developed CTRCD from those who did not (49.1 ± 14.0 vs. 42.5 ± 15.9 pg/mL, $p < 0.05$), reinforcing that meaningful elevations primarily reflect treatment-induced myocardial stress rather than pre-existing vulnerability. This pattern aligns with multiple studies showing negligible baseline differences in NT-proBNP assessed by either mean or median. Consistent with our cohort, both Bhagat et al. [21] (60 ± 28 vs. 56 ± 33 pg/mL; $p = 0.54$, n=43) and Andersson et al. [27] (88 vs. 76 pg/mL; $p = 0.34$) reported no significant baseline median NT-proBNP differences in early-stage breast cancer patients scheduled for anthracycline therapy despite CTRCD status. By contrast Muckiene et al. [19] reported significantly higher baseline NT-proBNP in women with advanced non-metastatic cancer who progressed to cardiotoxicity (113.7 ± 37.2 vs. 87.3 ± 44.3 pg/mL, $p = 0.021$). Similarly, Allam et al. [18] observed higher baseline levels in those developing cardiotoxicity (109 ± 24.3 vs. 70.8 ± 14.3 pg/mL), though absence of tumour stage or metastasis data limits interpretation. Remarkable, cohort resembled ours with early-stage cancer, baseline NT-proBNP levels were low and similar to our data. By contrast, higher baseline NT-proBNP has been reported in patients who later developed cardiotoxicity, predominantly in cohorts enriched with metastatic or advanced-stage disease, likely reflecting underlying disease burden and comorbidity rather than by intrinsic biomarker sensitivity to early cardiotoxic injury. Shaaban et al. [28] further demonstrated that baseline NT-proBNP alone lacks robust discriminatory power; median levels were higher in patients with mild dysfunction (80.1 [62–105] pg/mL) than in those with moderate (57.95 [20–128.5]) or no dysfunction (52.5 [34–68]), without statistical significance ($p = 0.065$), indicating only subtle trends of limited clinical interpretability.

In contrast, dynamic NT-proBNP responses strongly and consistently differentiated CTRCD from non-CTRCD groups. In our study, CTRCD patients exhibited a 2.2-fold rise at 1 month (↑126.7% vs. ↑57.3%; $p < 0.001$), with substantially higher mean values (111.3 ± 63.0 vs. 70.0 ± 26.7 pg/mL). By 3 months, both mean (248.4 vs. 96.4 pg/mL) and median (151.6 vs. 99.2 pg/mL) values confirmed persistent divergence. This early and persistent temporal profile aligns with observations reported in previous studies [22-23,25,29] across heterogeneous populations and treatment regimens, although the magnitude of elevation varied according to comorbidity burden, regimen intensity, and metastatic status. These convergent findings underscore that serial NT-proBNP trajectories-rather than baseline levels-provide the earliest and most clinically actionable signal of anthracycline- and HER2-therapy–related cardiotoxicity, supporting serial assessment as central to surveillance.

Our prospective cohort demonstrated that NT-proBNP correlated inversely with EF, GLS, and S', strengthening from weak baseline associations to moderate relationships between 3 and 9 months and persisting through 24 months, reflecting evolving anthracycline-related myocardial stress. Deformation parameters (GLS, S') showed earlier and stronger associations than EF, confirming their superior sensitivity for subclinical dysfunction. ROC analysis identified 125 pg/mL as the only NT-proBNP threshold with stable diagnostic performance, whereas NT-proBNP was not independently predictive in multivariable models, highlighting its role primarily in early detection and risk stratification rather than long-term outcome prediction. Interestingly, although the conventional NT-proBNP heart failure "gray zone" threshold (>300 pg/mL) demonstrated perfect specificity for CTRCD, its sensitivity remained low throughout follow-up. This finding suggests that thresholds commonly used for overt heart failure may be insufficiently sensitive for the detection of early or subclinical cancer therapy–related cardiac dysfunction. In contrast, the lower 125 pg/mL threshold provided a more balanced diagnostic profile and may therefore be more suitable for surveillance purposes in cardio-oncology populations.

ROC analyses from two prospective studies (6 months: Andersson et al. [27] n=42; 12 months: Blancas López-Barajas et al. [29] (n=66) identified early NT-proBNP thresholds predictive of cardiotoxicity. Andersson et al. [27] reported ΔNT-proBNP >100 pg/mL (AUC 0.89; sensitivity 89%, specificity 83%; p<0.001), while Blancas López-Barajas et al. [29] identified a 3-month NT-proBNP >200 pg/mL (AUC 0.88; sensitivity 83%, specificity 84%). In both studies, NT-proBNP remained independently predictive in multivariable models (OR 1.02 per pg/mL, p=0.004; OR 5.7, p=0.007), supporting the superiority of dynamic over absolute NT-proBNP changes for early detection of HER2-related myocardial injury. However, prior cohorts included advanced and metastatic disease, applied trastuzumab-only regimens, and defined cardiotoxicity solely by LVEF decline. In contrast, our models integrated comprehensive systolic–diastolic parameters, including GLS and its temporal change, which may have attenuated the independent predictive contribution of NT-proBNP. Moreover, the greater NT-proBNP elevations reported in advanced and metastatic disease—reflecting higher tumor burden, treatment intensity, and systemic stress—may partly account for the stronger predictive performance observed in earlier studies. Moreover, Demissei et al. [24] identified NT-proBNP as an independent predictor of anthracycline-related cardiac dysfunction at 12 months (≈2–3-fold risk per 1-log increase; p<0.01), with each doubling associated with a 0.7% LVEF decline (95% CI −1.2 to −0.2; p=0.004); findings were confirmed in Cox models and improved discrimination beyond clinical covariates. Divergent results may reflect methodological differences, including a younger, more heterogeneous cohort; generalized estimating equation based NT-proBNP analyses with multi-phase biomarker sampling; longer biomarker–LVEF intervals (median 2.1 months); EF-only cardiotoxicity definitions; differing assays and treatment regimens (shorter doxorubicin exposure, more frequent radiotherapy); the absence of systematic cardioprotection, whereas in our study cardioprotective therapy was initiated early in high-risk patients with broader pharmacologic coverage.

Conversely, several studies, including Bouwer et al. [23] and Kumar et al. [30], align with our findings, showing that NT-proBNP reflects early myocardial stress and is associated with cardiotoxicity in univariate or ROC analyses, but loses independent significance in multivariable models at different time-points. Collectively, these data indicate that NT-proBNP parallels subclinical strain-based impairment, yet its standalone prognostic value diminishes once advanced imaging metrics or cumulative clinical factors are incorporated. In a 12-month follow-up, Bouwer et al. [23] identified NT-proBNP >200 pg/mL at 6 months as the optimal cardiotoxicity threshold (AUC 0.83; sensitivity 79%, specificity 82%); using the Elecsys assay, baseline NT-proBNP independently predicted CTRCD (HR 1.04; p=0.003), and longitudinal increases correlated with LVEF decline. Nevertheless, the authors concluded that NT-proBNP lacked sufficient reliability for early, individual-level CTRCD detection, consistent with our results. Likewise, in the study by Sulaiman et al. [20], changes in NT-proBNP correlated strongly with GLS reduction (AUC ≈0.9), and a twofold increase identified >15% GLS decline with an AUC of 0.93. However, in multivariable regression analyses, only the Tei index remained independently associated with NT-proBNP, consistent with our observation that its predictive contribution diminishes once direct indices of systolic performance are included.

Several additional studies [19,21-22,25-26,31-33]—reported significant correlations or ROC-based discrimination for NT-proBNP, although most did not perform multivariable analyses, limiting confirmation of independence. In univariable logistic regression, Rüger et al. [32] in a univariable logistic regression showed that NT-proBNP levels at 6 weeks were significantly associated with cardiotoxicity (OR 1.03; 95%CI 1.008–1.055; p = 0.01). In ROC analysis by Muckienė et al. [19] (n=85; mean age 54.5 ± 9.3 years) at T2 showed a relative increase in NT proBNP of > 125 ng/L from baseline to T1 gave sensitivity 90.0 %, specificity 56.9 %, AUC 0.78 (p < 0.001). but their did not assessed multiple regression. In addition, Spearman correlation analyses by Bhagat et al. [21] identified baseline and post-therapy NT-proBNP as correlates of LVEF decline (ρ=−0.45 and −0.40), with ΔNT-proBNP >80 pg/mL at 6 months discriminating subclinical cardiotoxicity (AUC 0.86; sensitivity 82%; specificity 80%); notably, our study additionally incorporated a GLS <16% criterion. Díaz-Antón et al. [25] reported predictive value using univariate regression and ROC analyses over 14 months (p < 0.05). In the Essen Cardio-Oncology Registry, Hinrichs et al. [31] (n=116) demonstrated correlations between NT-proBNP and LVEF reduction (r=0.406; p<0.001) and diastolic dysfunction (OR 1.73; p=0.018), though no independent association after adjustment. Similarly, Wolf et al. [33] (n=156) found elevated NT-proBNP (>125 pg/mL) associated with impaired strain and diastolic abnormalities in long-term childhood cancer survivors (median of 10.1-year post-anthracycline follow-up), without independent predictive value in multivariable models.

In summary, NT-proBNP emerges as a sensitive marker of early myocardial stress that tracks cardiotoxic evolution over time; however, its independent prognostic value diminishes once comprehensive systolic–diastolic indices—particularly absolute GLS and early GLS change—are incorporated. Accordingly, NT-proBNP should be viewed as a complementary biomarker for early screening and longitudinal monitoring rather than a standalone predictor of CTRCD. Higher NT-proBNP levels reported in metastatic and advanced disease likely reflect greater tumor burden, intensified cardiotoxic therapy, and sustained systemic stress, resulting in more persistent biomarker release than in early-stage cohorts; these baseline physiological stress, stage- and treatment-related differences may partly explain the stronger predictive performance observed in prior studies compared with our findings.

Diastolic dysfunction is central to HFpEF diagnosis [34,35], yet data in anthracycline–trastuzumab–treated patients remain limited and inconsistent [36,37]. Some studies suggest early diastolic changes may predict subsequent systolic dysfunction, though findings are contradictory, and the superiority of GLS is not consistent.

In our 2-year follow-up, diastolic indices followed a biphasic pattern (IVRT, DT, E/A), showing transient and sustained myocardial effects. Consistent with prior longitudinal observations indicating gradual yet non-uniform worsening of diastolic indices [38], as well as early transient abnormalities

described in smaller prospective studies [39-40]. E/e′ increased progressively, largely within the normal range but more pronounced in patients developing CTRCD; E/e′ >15 occurred exclusively in this subgroup, mainly high-risk patients, supporting the relevance of newly acquired diastolic dysfunction. Our findings align with prior evidence indicating that diastolic dysfunction during cancer therapy is a dynamic and treatment-dependent process rather than a linear decline [21,38-42].

In contrast to studies suggesting an independent prognostic role for E/e′ [43], E/e′ did not independently predict CTRCD in our analysis. Instead, baseline relaxation indices demonstrated temporal specificity: DT_0 predicted early CTRCD, whereas $IVRT_0$ late CTRCD, indicating phase-specific pathophysiology, whereby early abnormalities in filling deceleration reflect acute relaxation impairment, while prolonged IVRT may capture delayed myocardial recovery and cumulative injury. Notably, In the first multicenter study of early diastolic dysfunction in chemotherapy (n-68, mean age 49) conducted by Calabrese et al. [39], grade I diastolic dysfunction was detected 1 week after chemotherapy according to E/A and DT data (n-14), but EF and E'/e remained within the normal range.

Early NT-proBNP elevation (1–3 months) in our study preceded E/e′ increases (6–12 months), supporting a staged model in which biochemical stress anticipates echocardiographic diastolic changes, consistent with prior studies [36,39-40]. These findings reinforce that diastolic parameters are adjunctive to systolic measures, with GLS providing earlier and stronger predictive value [43-45].

Principal Findings.

Introduces a time-dependent, staged framework of cardiotoxicity, integrating biomarker kinetics and echocardiographic dynamics across the treatment continuum.

Demonstrates a biphasic NT-proBNP trajectory, distinguishing acute treatment-related myocardial stress from subsequent structural remodeling.

Provides temporal mapping of echocardiographic parameters, showing phase-specific associations of systolic and diastolic indices rather than uniform predictive behavior.

Identifies a critical early vulnerability window within the first year of therapy, supporting time-sensitive surveillance strategies.

Advances a multiparametric risk stratification model, emphasizing dynamic integration of imaging and biomarkers rather than isolated parameter interpretation

Clinical implications.

Early, structured surveillance should prioritize the initial months following anthracycline exposure.

GLS should serve as the primary imaging modality for early detection of subclinical myocardial dysfunction.

NT-proBNP may be used as a complementary early-phase screening tool, particularly during acute treatment-related stress.

Diastolic parameters may provide phase-specific supportive information, but should not guide decision-making independently.

A multiparametric surveillance strategy is essential for optimal early detection and risk stratification.

Conclusion.

Our 2-year prospective study of postmenopausal women with primary breast cancer receiving anthracycline–trastuzumab therapy, GLS emerged as the most sensitive and robust predictor of cardiotoxicity, outperforming conventional echocardiographic parameters. Early ΔGLS predicted both early and late cardiotoxicity, while baseline GLS and EF predicted late events only. Diastolic indices showed temporal associations (DT with early and IVRT with late cardiotoxicity) but lacked independent predictive value; E/e′ increased predominantly in cardiotoxic, high-risk patients without independent prognostic significance. NT-proBNP was not independently predictive. These findings underscore the primacy of GLS-based surveillance and the importance of early, comprehensive cardioprotective strategies to mitigate treatment-related cardiac risk.

Limitations.

The primary methodological limitations of the present study include the relatively small sample size and the single-center design. In addition, different treatment combinations were not analyzed as separate subgroups, and diastolic parameters and biomarkers were assessed as secondary outcomes. These factors may limit the generalizability of our findings and warrant confirmation in larger, multicenter studies. An additional limitation is the relatively small number of patients receiving trastuzumab (n = 15). Although subgroup and multivariable analyses did not identify anti-HER2 therapy as an independent predictor of cardiotoxicity, the study was not powered to detect small-to-moderate treatment-specific effects. Therefore, a potential influence of trastuzumab exposure cannot be completely excluded and should be evaluated in larger prospective studies specifically designed to compare anthracycline-only and anthracycline-plus-trastuzumab regimens.

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Competing Interests.

Author has declared that no competing interests exist.

List of abbreviations.

EF: left ventricular ejection fraction

GLS: global longitudinal strain

S′: mitral annulus systolic velocity

NT-proBNP: (N-terminal pro-B-type natriuretic peptide)

ΔNT-proBNP: Changes in N-terminal pro-B-type natriuretic peptide from baseline

Δ1- NT-proBNP: Changes in N-terminal pro-B-type natriuretic peptide from baseline at one month

CTRCD: Cancer therapy -related cardiac dysfunction

BC: breast cancer

TSU: Ivane Javakhishvili Tbilisi State University

E/A: Ratio of early (E) to late (A) ventricular filling velocities

IVRT: Isovolumetric Relaxation Time

DT: Deceleration Time of the E wave

E/e': Ratio of mitral inflow E velocity to mitral annular early diastolic velocity (e')

Declarations.

Ethics approval and consent to participate.

The study was approved by the Ethics Committee of the TSU Faculty of Medicine (Protocol #1, 06/07/2019), Written informed consent was obtained from all participants prior to enrollment.

Consent for publication.

Not applicable.

Availability of data and materials.

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author on reasonable request

Competing interests.

The authors declare that they have no competing interests.

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Authors' contributions.

All authors contributed to the study conception, data analysis, and manuscript preparation. All authors read and approved the final manuscript.

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აბსტრაქტი.
შესავალი: ძუძუს კიბოს მქონე პაციენტების გადარჩენის მაჩვენებლის გაუმჯობესებასთან ერთად, კარდიოვასკულური ტოქსიკურობა გრძელვადიანი გამოსავლების ერთ-ერთ მნიშვნელოვან განმსაზღვრელ ფაქტორად იქცა. კიბოს თერაპიასთან ასოცირებული გულის დისფუნქცია (Cancer Therapy–Related Cardiac Dysfunction, CTRCD) განსაკუთრებით ხშირია პოსტმენოპაუზურ ქალებში, რომელთაც მომატებული კარდიოვასკულური რისკი აქვთ, რაც ხაზს უსვამს კარდიოტოქსიურობის ადრეული გამოვლენისა და მიზნობრივი კარდიოონკოლოგიური მონიტორინგის აუცილებლობას.
მიზანი: გლობალური გრძივი დეფორმაციის (Global Longitudinal Strain, GLS), მარცხენა პარკუჭის სისტოლური და დიასტოლური ფუნქციის ტრადიციული ექოკარდიოგრაფიული პარამეტრებისა და კარდიული

ბიომარკერების დინამიკურ ცვლილებებს შორის კავშირის შეფასება კიბოს თერაპიასთან ასოცირებული გულის დისფუნქციის პროგნოზირებისა და ადრეული გამოვლენის მიზნით.

მასალა და მეთოდები: ჩატარდა 24-თვიანი ერთცენტრიანი პროსპექტული კვლევა (2019 წლის დეკემბერი–2024წლისმარტი),რომელშიცჩართულიიყო პირველადი ძუძუს კიბოს მქონე 74 პოსტმენოპაუზური პაციენტი, რომლებიც იღებდნენ ანტრაციკლინზე ან ანტრაციკლინ–ტრასტუზუმაბზე დაფუძნებულ თერაპიას. მარცხენა პარკუჭის სისტოლური და დიასტოლური ფუნქცია, ასევე N-ტერმინალური პრო-B ტიპის ნატრიურეზული პეპტიდის (NT-proBNP) დონე შეფასდა საწყის ეტაპზე და შემდგომი შვიდი ვიზიტის განმავლობაში. კარდიოტოქსიურობა განისაზღვრა განდევნის ფრაქციის (Ejection Fraction, EF) და გლობალური გრძივი დეფორმაციის (GLS) ცვლილებების საფუძველზე. შედეგები გაანალიზდა მრავალფაქტორული რეგრესიის, დაწყვილებული t-ტესტის, ANOVA-სა და გადარჩენის ანალიზის (Kaplan–Meier, Cox) გამოყენებით. მაღალი რისკის პაციენტებსა და მარცხენა პარკუჭის სისტოლური ფუნქციის გაუარესების მქონე პირებს უტარდებოდათ კარდიოპროტექტორული თერაპია. სტატისტიკური მნიშვნელობა განისაზღვრა $p<0.05$-ის შემთხვევაში.

შედეგები: ანტრაციკლინზე დაფუძნებული თერაპიის მიმღებ 74 პაციენტში CTRCD-ის სიხშირე 24-თვიანი დაკვირვებისპერიოდში13.5%-დან36.5%-მდეგაიზარდა. GLS-მა კარდიოტოქსიურობა უფრო ადრე და უფრო ხშირად გამოავლინა, ვიდრე EF-მა. NT-proBNP >125 პგ/მლ ასოცირებული იყო ადრეულ და საშუალო სიმძიმის CTRCD-თან და პიკურ მნიშვნელობას 3 თვეზე აღწევდა, მაღალი მგრძნობელობით (94.1%) და სპეციფიკურობით (90.9%), ხოლო NT-proBNP >300 პგ/მლ დაკავშირებული იყო უფრო გამოხატულ ბიომარკერულ მატებასთან და მძიმე შემთხვევების იდენტიფიკაციასთან. დიასტოლური დისფუნქცია ორფაზიანი (ბიფაზური) მიმდინარეობით ხასიათდებოდა, ხოლო E/e′ >15 აღინიშნებოდა მხოლოდ მაღალი რისკის CTRCD-ის მქონე პაციენტებში. მთლიანობაში, NT-proBNP-ის ზღვრული მნიშვნელობები ეფექტურ მოკლევადიან ბიომარკერებს წარმოადგენდა ადრეული და მძიმე CTRCD-ის მონიტორინგისთვის. ROC ანალიზმა NT-proBNP-ისკარგიდიაგნოსტიკურიშესაძლებლობააჩვენა CTRCD-ის გამოსავლენად (AUC=0.779; 95% CI: 0.656–0.901; $p<0.001$). შეფასებულ ზღვრულ მნიშვნელობებს შორის, 125 პგ/მლ-მა ყველაზე დაბალანსებული დიაგნოსტიკური მახასიათებლები აჩვენა — 100% სპეციფიკურობითა და 48.3% მგრძნობელობით.

დასკვნა: პოსტმენოპაუზურ ქალებში, რომლებიც ანტრაციკლინის შემცველ თერაპიულ სქემებს იღებდნენ, GLS აღმოჩნდა კარდიოტოქსიურობის ყველაზე მგრძნობიარე და საიმედო პროგნოზული მაჩვენებელი, რომელმაც EF-ს გადააჭარბა. GLS-ის ადრეული ცვლილებები როგორც ადრეულ, ისე გვიან კარდიოტოქსიკურ მოვლენებს პროგნოზირებდა. დიასტოლური პარამეტრები დროზე დამოკიდებულ ასოციაციებს ავლენდა, თუმცა დამოუკიდებელი პროგნოზული მნიშვნელობა არ გააჩნდა. E/e′ ძირითადად მაღალი რისკის მქონე პაციენტებში იზრდებოდა. მიუხედავად იმისა, რომ NT-proBNP-ს მნიშვნელოვანი დიაგნოსტიკური ღირებულება ჰქონდა, იგი მრავალფაქტორულ მოდელებში დამოუკიდებელ პროგნოზულ ფაქტორად არ დადასტურდა.