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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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

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. Корректур авторам не высылаются, 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 computer-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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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 შედეგების 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 ფხიხლებში 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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EVALUATION OF LEFT VENTRICULAR SYSTOLIC FUNCTION IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER RECEIVING ADJUVANT ANTHRACYCLINE AND TRASTUZUMAB THERAPY: A 2-YEAR FOLLOW-UP STUDY

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Abstract.

Anti-cancer therapy with anthracyclines and trastuzumab has raised concerns regarding cancer therapy-related cardiac dysfunction (CTRCD) in breast cancer (BC) patients.

This study aimed to assess left ventricular (LV) ultrasound parameters in BC postmenopausal women during a 2-year follow-up period after starting anti-cancer therapy.

Methods: We studied 74 women with early-stage BC with, a mean age of 62.3 (SD-8.6), who underwent adjuvant doxorubicin or doxorubicin + trastuzumab therapy. Parameters such as LV ejection fraction (LVEF), global longitudinal strain (LVGLS), and mitral annulus systolic velocity(S') were evaluated. Serial evaluations were conducted at baseline(T0) and the first (T1), second (T2), third (T3), sixth (T4), ninth (T5), twelfth (T6), and twenty-fourth month (T7) following the initiation of the chemotherapy. Cardioprotective therapy (CPT) was administered to high-risk patients and those with worsening LV systolic parameters. A multiple regression model was employed to assess the combined effects of various factors and co-factors on the outcome variables. Cardiotoxicity was evaluated using the survival analysis tools (Kaplan-Meier curves and Cox proportional model).

Results: A total of 27 (36.5%) patients developed CTRCD, although no patients were presented with symptomatic heart failure. LVGLS started to decline one month after the first anthracycline dose (T1) in 13.5% of the cohort and 34.5% of patients with CTRCD ($p<0.000$). From the third month, 10.8 % of the patients showed a decrease in EF%, including 27.6% of patients with CTRCD ($P<0.000$).Throughout the study, S' remained within the normal range in patients without CTRCD, Only patients with CTRCD showed a decline in S'.

Conclusions: This prospective study revealed that:1) The dynamic assessment of GLS should be prioritized for the early detection of systolic dysfunction .2) S' possesses a high diagnostic value for identifying cardiotoxicity. 3) Implementing the optimal medical cardioprotective strategies and closely monitoring LV systolic function can prevent serious cardiac complications in patients undergoing highly cardiotoxic anti-cancer treatment.

Key words. Cardiotoxicity, breast cancer, global longitudinal strain, CTRCD, GLS, chemotherapy, EF, mitral annulus systolic velocity.

Introduction.

Globally, women are diagnosed with BC more often than any other cancer [1-3]. More than 60% of new cases occur in the 50–70 age group (postmenopausal women), where the incidence rises correspondingly with age [1,2]. The number of cancer survivors has increased recently due to significant advancements in treatment plans and early cancer detection

programs [1,3]. However, concurrent with these encouraging trends, a pressing issue has surfaced: cardiotoxicity or CTRCD, which significantly worsens prognosis [4,5]. Because of the increased risk of cardiovascular disease as well as the development of cancer, the frequency of short- and long-term side effects of cancer therapy increases proportionately with age [1,2,6]. It has been shown that the decrease in LVGLS is highly informative of CTRCD diagnostic [7-10]. GLS is analysis of myocardial deformation that preferentially reflects subendocardial longitudinally oriented fiber's function, which are most prone to subtle damage and wall stress. Compared to LVEF and other traditional echo parameters, LVGLS has a better predictive capacity [11]. A change in LVGLS occurs in asymptomatic patients when LVEF is still preserved, especially in intermediate- and high-risk individuals. Therefore, LVGLS is a more reliable marker of cardiotoxicity than LVEF [11,12]. According to several studies, LVGLS-guided CPT may be useful for preventing advanced forms of heart failure by potentially reducing the decline in LVEF that follows [13]. This could be achieved through optimizing the use of cardioprotective strategies. The prognostic value of LVGLS for CTRCD is supported by several meta-analyses [14-16]. Even with suboptimal visualization of the LV endocardium, mitral annular systolic velocity (S') can be measured and is informative in assessing left ventricular systolic function (LVSF). Although there are few studies on the usefulness of S' in cancer patients, currently available evidence points to S' advantages.

Materials and Methods.

A prospective single-center study within a 24-month follow-up was conducted at the ultrasound laboratory of Ivane Javakhishvili Tbilisi State University (TSU) Medical Center. The study included 100 consecutive female patients based on referral with newly diagnosed BC. The research data were collected from December 2019 to March 2024. The study was approved by the Ethical Committee of the Faculty of Medicine of TSU, all patients provided written informed consent. Inclusion criteria were primary BC, postmenopausal status, and an indication of anticancer therapy with anthracycline-trastuzumab-containing regimens. Furthermore, in addition to high CTRCD potential anticancer therapy patients had at least one risk factor for CTRCD development (Hypertension, Diabetes M. Obesity, Dyslipidemia, Smoking, and documented CVDs: CAD, Hypertensive heart disease). Exclusion criteria included: pregnancy, inability to provide informed consent, history of prior chemotherapy or radiotherapy, reduced LVEF<50%, suboptimal ultrasound views, severe valvular disease, patients with primary cardiomyopathy, medical history affecting LV function, atrial fibrillation, or implantation of permanent pacemakers. The two-year study's outcomes were

further examined in 74 women out of the 79 patients who were enrolled based on the aforementioned criteria. Five patients were dropped from the study due to personal reasons.

Cardiotoxicity was defined as a reduction in LVEF from the baseline of 10% and/or LVEF<50% and/or a decrease in LVGLS of 15% from baseline and/or a decrease in LVGLS below -16%.

The mean initial age of the study patients was 62.3 years (Standard Deviation (SD)-8.6), with a range of 46-76 years, and a median age of 64 years. At baseline a comprehensive medical history was obtained from each patient, including demographic information and CTRCD risk factors, the latter of which were selected by the 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC) [17]. Doxorubicin was administered to all patients (n-74), and human epidermal growth factor receptor 2 positive (HER2-positive) (n-15) patients received doxorubicin followed by trastuzumab. Data were analyzed in two age groups: < 65 years, 51.4% (n-38), and \geq 65 years, 48.6% (n-36). The research parameters and their dynamics were assessed based on CTRCD risk groups (high + medium (n-41) and low risk (n-33)), treatment regimen (anthracycline (n-59) and anthracycline + trastuzumab (n-15)), and doxorubicin doses (Dox1 \leq 250 mg/m² (n-44) and Dox2>250 mg/m² (n-30)) as well. If systolic parameters (GLS or EF) worsened or in any patient with a high risk of CTRCD, the attending cardiologist-initiated CPT (Beta blockers and angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB)). High-risk patients constituted 13 % (n-10) of the study population, medium-risk patients made up 41 % (n-31), and low-risk patients made up 44 % (n-33). A prospective serial evaluation was conducted at specified intervals, with all assessments performed before the commencement of anticancer therapy (denoted as T0) Subsequent assessments were performed following the commencement of anthracycline therapy at various time points: the first (T1), second (T2), third (T3), sixth (T4), ninth (T5), twelfth (T6), and twenty-fourth month (T7). Notably, for patients diagnosed with HER2-positive BC, the T4 evaluation coincided with the third month following the administration of the initial dose of trastuzumab.

All ultrasound examination were conducted under conditions of normal blood pressure (BP) and heart rate (HR). Echo images were acquired using PHILIPS EPIQ 7G with X5-1 transducer, with optimal ECG signal control and minimal heart rate variability over four equal cardiac cycles. Two-dimensional Conventional (TTE) and speckle tracking echocardiography (STE) were performed in full compliance with the recommendations of the American Society of Echocardiography and the practical guidelines for performing of the British Society of Echocardiography minimum dataset [18-20]. All standard views were consistently selected correctly, including 3 apical views (A4C; A2C; A3C). A complete echocardiographic examination of LV structural and functional

systolic/diastolic parameters (including LVEF, GLS and S') was performed in the research groups.

To maximize reliability and reproducibility in STE, imaging was optimized by focusing directly on the region of interest (ROI), patients were excluded from the study when two or more segments *could not be adequately visualized/ tracked*. In order to avoid artifacts, the signal was obtained with optimal gain settings at the moment of breath holding at the end of exhalation. The frequency of frames between 60-90 seconds was considered valid. A semi-automatic tracing mechanism was used for speckle tracking. The endocardium was accurately traced. in the A4C, A3C and A2C views the ROI was defined in full compliance with the recommendations of the practical guideline of the British Society of Echocardiography and the American Society of Echocardiography for the minimum dataset [18-20]. GLS was calculated as the average of the peak systolic longitudinal strain values were from all LV segments in A4C, A3C, and A2C views. The bull's eye was finally obtained by integration; LV was divided into 18 segments, The bull's eye displays inferior, anterior, infero-septal, antero-septal, infero-lateral, antero-lateral segments of LV, each of which has apical, mid and basal regions. Longitudinal strain values was calculated for each segment (segmental strain) and as the average value of all segmental strains (global strain). LVEF was calculated using the modified Simpson biplane method. S' as well as e' were obtained in the A4C view by Pulsed Wave Tissue Doppler (PW TDI) by placing a sample volume in the septal and lateral annular sites during end-systole, after which S' mean and e' mean were calculated (average mean of septal and lateral). Age ranges were taken into account. The view was oriented parallel to the interposition of the annular motion and the ultrasound beam. It was obtained during breath holding at the end of exhalation. Mean E/e' was calculated by dividing the early (E) trans-mitral velocity wave by early annular diastolic velocity (mean e') using TDI imaging to compute the E/e' ratio. Mitral valve (MV) peak E- and A-wave velocities (cm/s) as well as DT were assessed using pulse wave (PW) doppler in A4C by the placement of the sample volume directly between the tips of the mitral valve leaflets, 1 to 3 mm from their ends. IVRT was measured from the apical five-chamber views (A5C) using PW doppler. The sample volume was placed between the aortic and the mitral valves.

Statistics: The SPSSv program was used to analyze the obtained results statistically. IBM SPSS, Chicago, IL, USA; 23.0. Quantitative variables as Mean \pm Standard Deviation (SD) are presented. Independent t-tests and Fisher's exact tests were used to compare the groups. One-way ANOVA was applied in certain instances. Paired t-tests were used to analyze baseline and follow-up data. Percentages are used to represent categorical variables. We used the Chi2-test and Fisher's exact test to compare the groups. A multiple regression model was used to examine the joint impact of various factors and co-factors (independent variables) on the outcome variables (dependent variables). The dependent variable, Y (outcome), is the presence of CTRCD at Stages 4 (six months after chemotherapy initiation) and 7 (24 months after chemotherapy initiation). Independent

variables: a) Baseline variables: including age, cardiotoxicity risk (score), hypertension (HT), diabetes mellitus type 2 (DM2), coronary artery disease (CAD), smoking (SM), obesity (OB), chemotherapy regimen, anti-HER2-therapy, radiotherapy, ejection fraction (EF0), global longitudinal strain (GLS0), and mitral annular systolic velocity (S'0). b) Change of following parameters from baseline value after one month: including EF(Delta_EF1), GLS (Delta_GLS1), S' (Delta_S'1). CTRCD was evaluated using the survival analysis tools (Kaplan-Meier curves and Cox proportional model). The Hazard Ratio (HR) was calculated alongside 95% confidence intervals (95% CI) to quantify the strength of the association between the variables of interest and the risk of cardiotoxicity. To determine the significance of the observed associations, a p-value threshold of <0.05 was established to reject the null hypothesis.

Results.

In our study, we conducted a comprehensive analysis of LV systolic parameters within our cohort over a two-year follow-up period. Study findings reveal that 36.5% (n=27) of participants developed CTRCD during this timeframe. Consequently, the survival rate free from CTRCD within the entire study population was determined to be 63.5%. We closely monitored the temporal dynamics associated with the onset of CTRCD throughout the 24-month follow-up. Notably, CTRCD manifested in the first month (T1) following the initiation of chemotherapy in 13.5% (n=10) of the cohort. The incidence reached its peak at the 24-month mark (T7), with a cumulative rate of 36.5% (n=27) (see Figure 1).

In our study, we stratified participants into two distinct age subgroups to assess the rates of survival from CTRCD. Group 1 included individuals aged 65 years or older (n=36), while Group 2 comprised those younger than 65 years (n=38). The survival rate for Group 1 was found to be 52.8%, in contrast to a notably higher survival rate of 73.7% in Group 2. Utilizing the Cox proportional hazards model for analysis, we calculated a hazard

ratio indicating that the risk of developing CTRCD in individuals aged 65 years and older was statistically significantly elevated, with an HR of 2.37 (95% confidence interval [CI]: 1.10-5.08, $p=0.026$), compared to their younger counterparts (see Figure 2). Furthermore, we examined the incidence of CTRCD based on treatment regimens, specifically differentiating between patients receiving anti-HER2 therapy (n=15) and those not receiving this specific treatment (n=59). The survival rate among patients undergoing anti-HER2 therapy was 26.7%, starkly lower than the 72.9% survival rate observed in the cohort not receiving anti-HER2 therapy. The hazard ratio derived from the Cox proportional hazards model revealed that the risk of CTRCD was significantly higher for patients on anti-HER2 therapy, with an HR of 4.45 (95% CI: 1.47-13.46, $p<0.001$) compared to those not on this therapy (see Figure 3).

Figure 4 presents the Kaplan-Meier survival curves stratified by doxorubicin dosage, delineating two distinct subgroups: Dox1, which includes patients administered doxorubicin at a dosage of ≤ 250 mg/m² (n=44), and Dox2, characterized by those receiving dosages exceeding 250 mg/m² (n=30). The application of the Cox proportional hazards model yielded a significant hazard ratio indicating that patients undergoing high-dose anthracycline therapy face a 2.42-fold increase in the risk of cardiotoxicity related to CTRCD compared to those receiving low-dose treatment (HR=2.42, 95% Confidence Interval [CI] = 1.11-5.28, $p=0.020$).

Furthermore, the incidence rates of CTRCD were analyzed across the study's temporal framework, differentiating between low risk (n=33) and high plus moderate risk groups (n=41). The analysis revealed that the hazard ratio for cardiotoxicity in the high plus moderate risk group is statistically significant, being 9.24 times greater than that of the low-risk group (HR = 9.24, 95% CI = 6.55-13.06, $p=0.001$), as illustrated in Figure 5.

Additionally, Figure 6 delineates the progression of CTRCD as assessed by echocardiographic parameters, specifically ejection fraction (EF) and global longitudinal strain (GLS), throughout the study period.

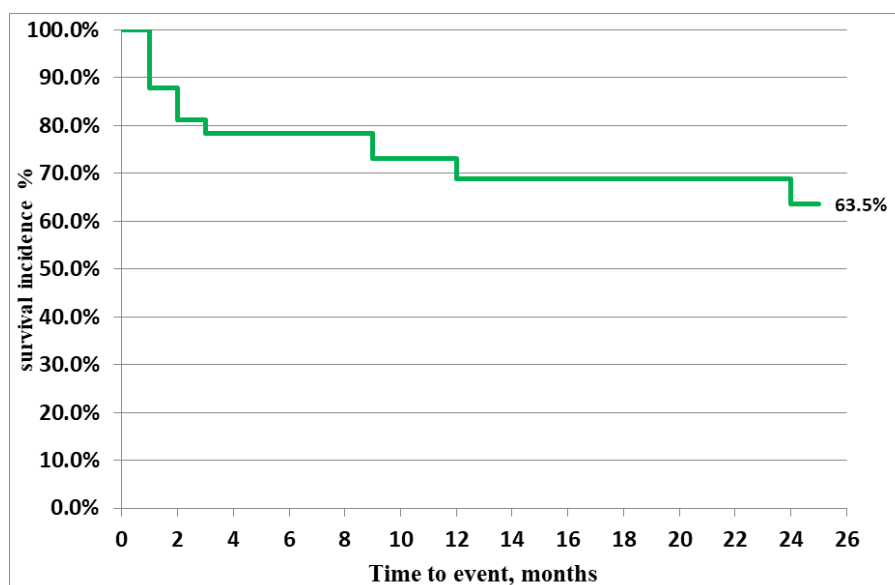
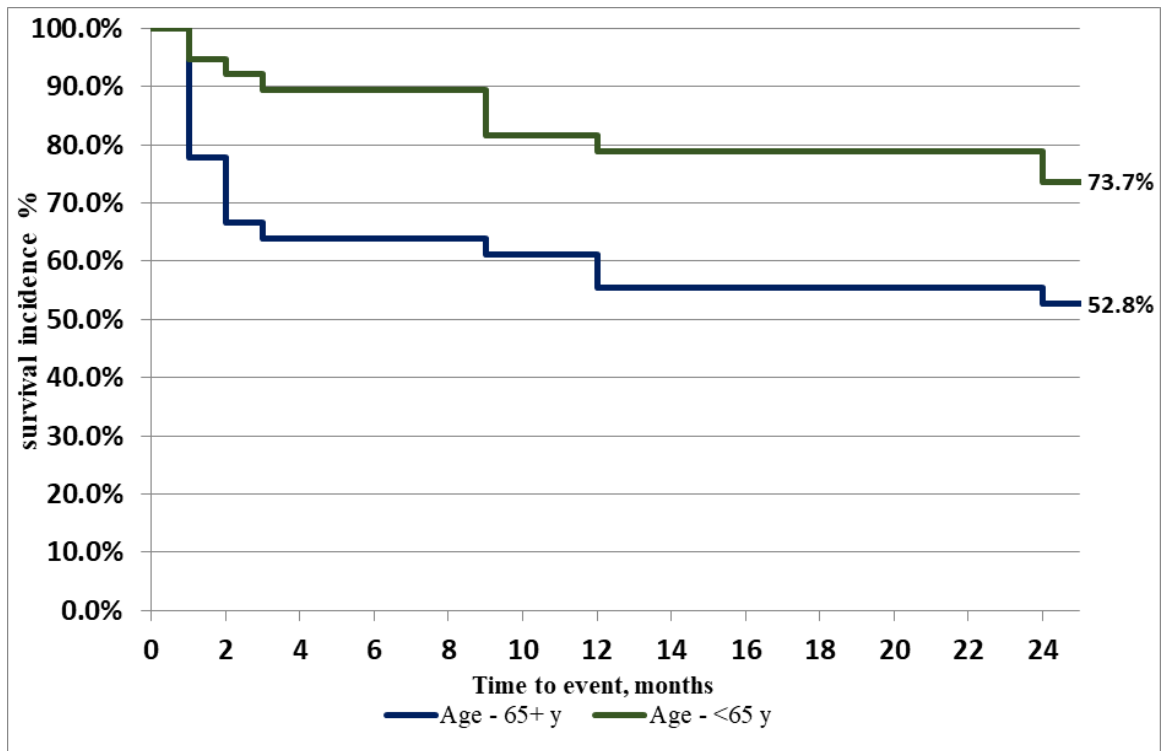
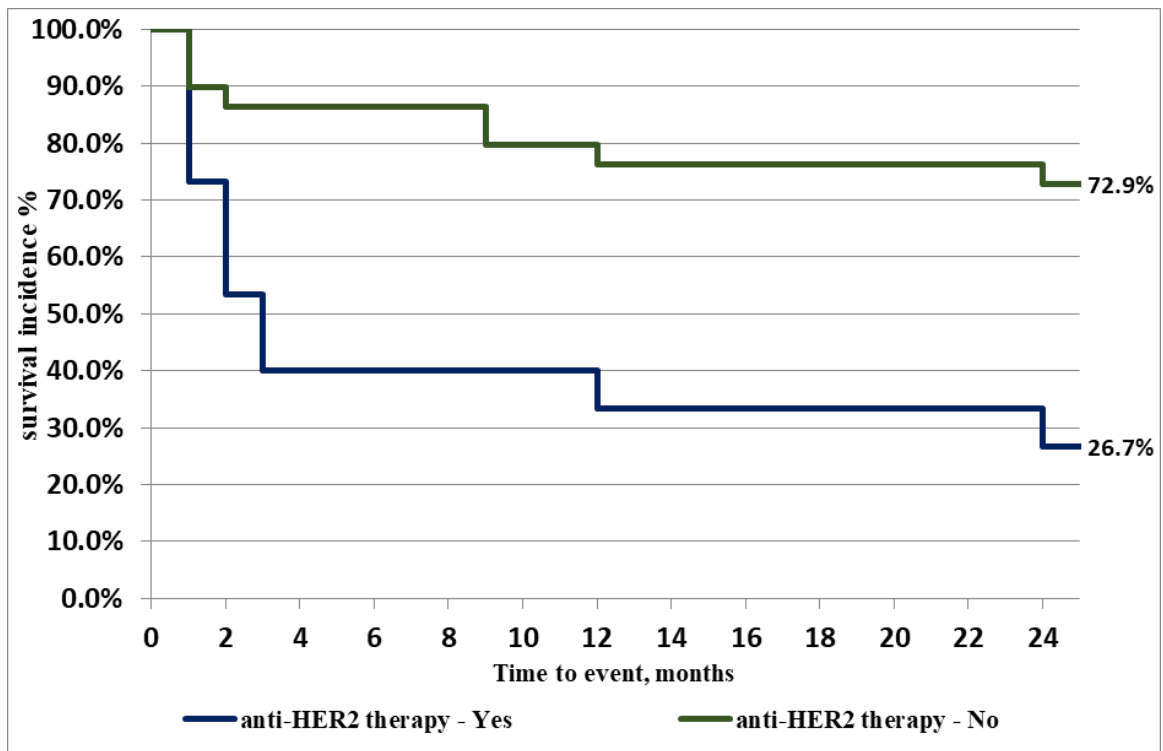


Figure 1. Kaplan-Meier curve for CTRCD Survival (Total Group; n=74).



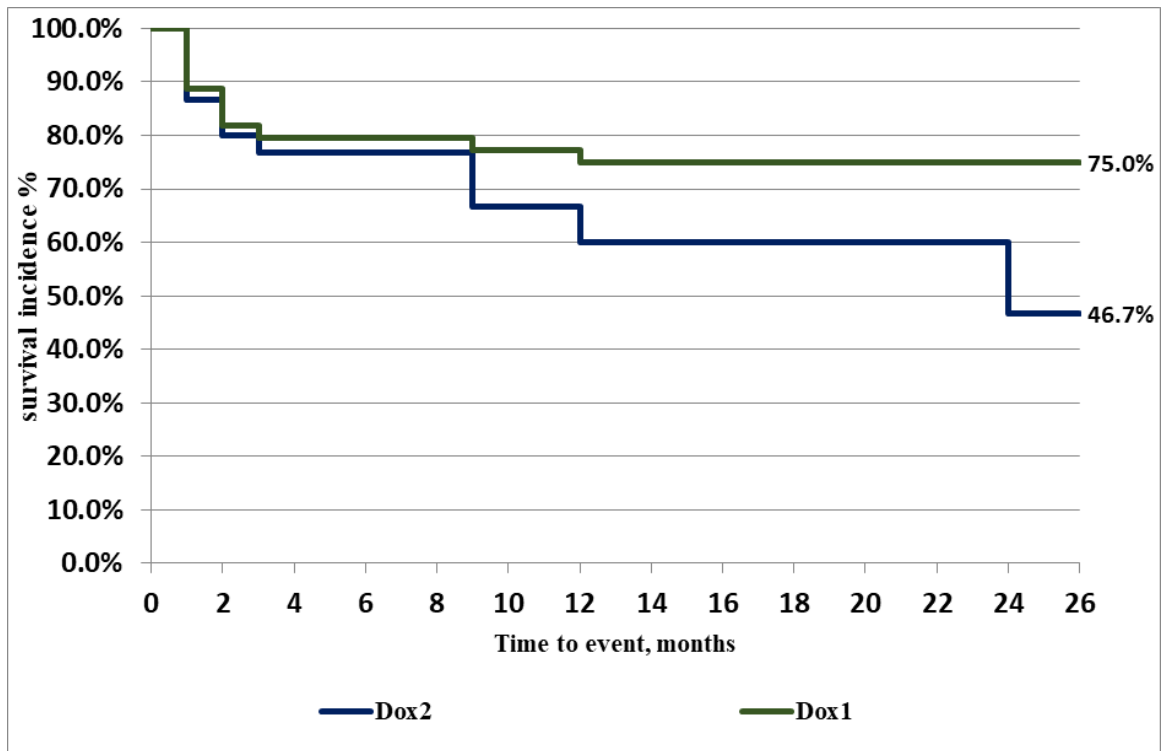
(HR=2.37, p=0.026)

Figure 2. Kaplan-Meier curves for CTRCD Survival for the groups divided by age: the group 1 (Age ≥ 65; n=36) vs. the group 2 (Age < 65; n=38).



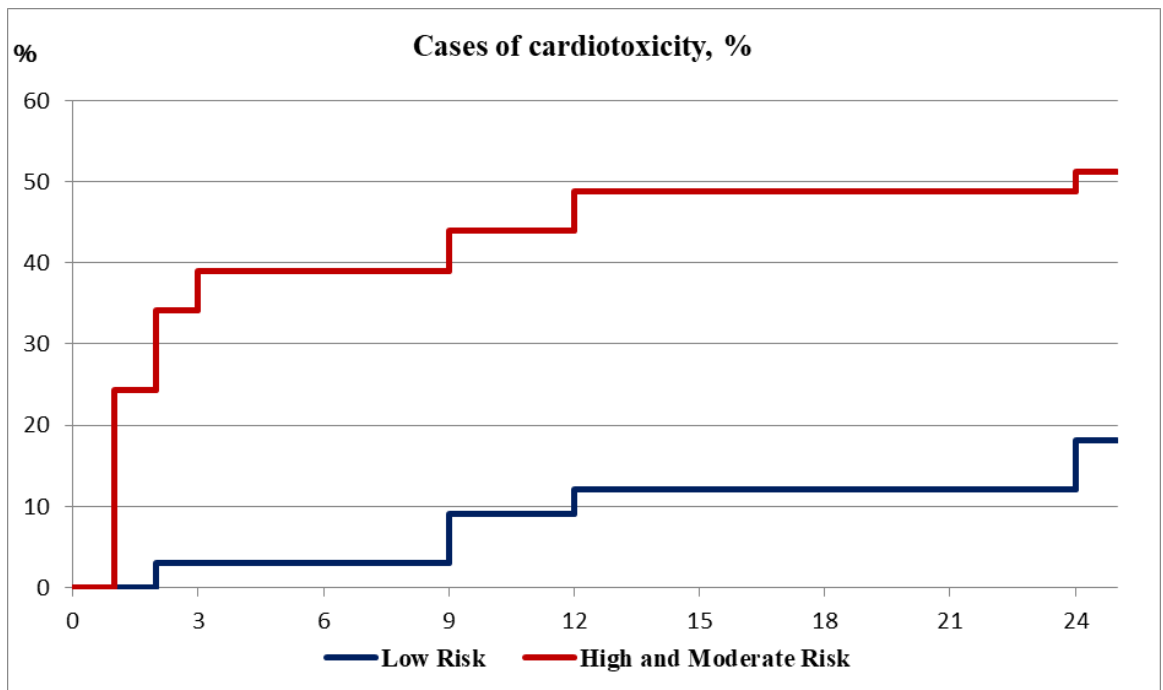
(HR=4.45, p<0.001)

Figure 3. Kaplan-Meier curves for CTRCD Survival for the groups divided by the presence of anti-HER2 therapy: the group 1 (anti-HER2 therapy - Yes; n=15) vs. the group 2 (anti-HER2 therapy - No; n=59).



(HR=2.42, p<0.020)

Figure 4. Kaplan-Meier curves for CTRCD Survival for the groups divided by the dose of Doxorubicin: the group 1 (Dox 1 - Doxorubicin ≤ 250 mg/m²; n=44) vs. the group 2 (Dox2 -Doxorubicin >250 mg/m²; n=30).



(HR=9.24, p<0.001)

Figure 5. Kaplan-Meier curves for Cardiotoxicity onset for the groups divided by risk: the group 1 (low risk; n=33) vs. the group 2 (high +moderate risk; n=41).

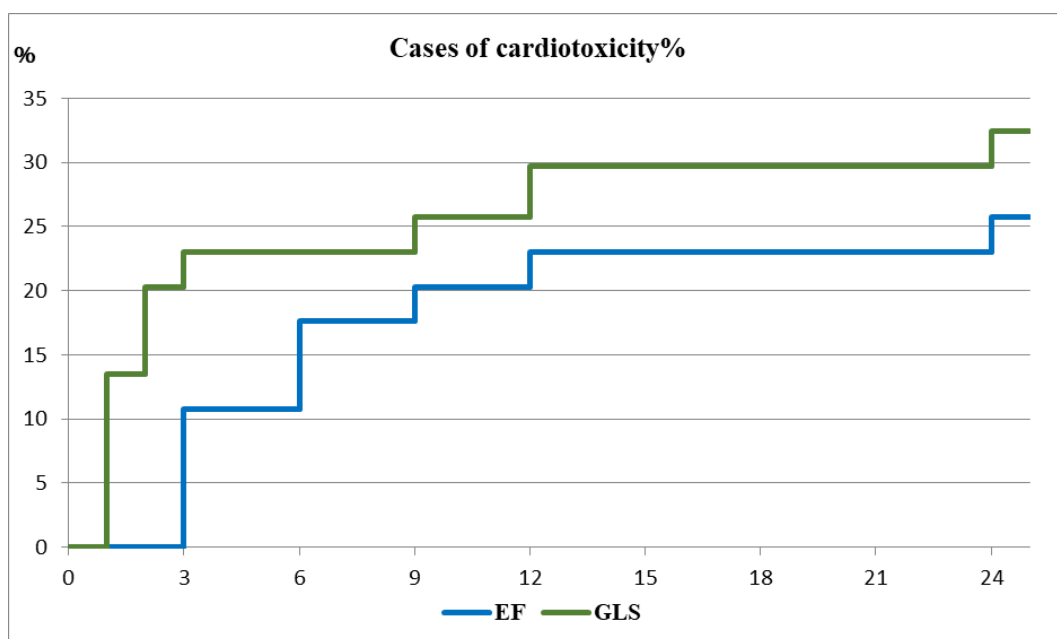


Figure 6. Kaplan-Meier curves for the dynamics of the development of cardiotoxicity detected according to LVEF or LVGLS values.

Table 1. Changes in GLS from the baseline at all stages of the study.

GLS, %	Baseline	1month	2months	3months	6months	9months	12months	24months
Mean	-21.4	-20.2	-19.6	-19.0	-18.5	-18.4	-18.4	-18.0
SD	2.7	3.0	3.3	3.5	3.8	3.3	2.9	2.6
Median	21.3	19.9	19.7	19.1	18.8	18.4	18.4	17.6
Min	15.2	10.2	8.9	9.5	7.8	8.0	10.6	11.9
Max	25.9	24.9	24.5	24.0	23.8	23.9	23.8	22.7
Comparison with Baseline Value								
Difference		1.21	1.76	2.40	2.92	2.93	2.95	3.34
95%CI Lower		0.94	1.39	1.94	2.33	2.48	2.60	2.98
95%CI Upper		1.48	2.14	2.85	3.50	3.39	3.30	3.70
Paired t-test		8.99	9.38	10.53	9.91	12.76	16.87	18.54
df		73	73	73	73	73	73	73
Sig (2-tailed)		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 2. Values in EF at all stages of the study.

EF, %	Baseline	1month	2months	3months	6months	9months	12months	24months
Mean	61.9	61.5	61.0	60.0	58.7	58.1	57.8	56.8
SD	3.8	3.8	3.7	4.1	5.1	4.9	4.6	4.2
Median	61.6	61.0	60.3	59.7	59.0	58.2	57.3	56.1
Min	55.7	55.4	55.0	49.2	41.8	44.8	47.3	45.3
Max	68.9	68.8	68.3	67.9	67.6	67.1	67.0	66.5
Comparison with Baseline Value								
Difference		0.4	0.83	1.91	3.13	3.77	4.05	5.05
95%CI Lower		0.27	0.65	1.41	2.25	2.85	3.22	4.14
95%CI Upper		0.44	1.01	2.41	4.01	4.69	4.89	5.96
Paired t-test		8.13	9.06	7.60	7.08	8.19	9.70	11.10
df		73	73	73	73	73	73	73
Sig (2-tailed)		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Our investigation scrutinized the longitudinal dynamics of systolic function indicators—namely LVGLS, LVEF, and S'—across the comprehensive cohort over a two-year observational timeframe. Our findings indicate a progressive decline in GLS throughout the study duration, as illustrated in Table 1.

Notably, LVGLS began to decrease one month following the administration of the first dose of anthracycline (T1), with a decline observed in 34.5% of CTRCD patients ($p < 0.000$). In comparison, this decline was noted in only 13.5% of the entire cohort, as depicted in Figure 6.

Table 3. Values in S' at all stages of the study in groups divided by CTRCD (CTRCD group (n=10) vs. without CTRCD group (n=64)).

Stage	Cardiotoxicity - Yes	Cardiotoxicity - No	Levene's test for equality of variances F-test	p	Independent t-test	p
	Mean (SD) n	Mean (SD) n				
Stage 1 (after 1 month)	10.35 (1.93) n=10	12.63 (2.63) n=64	10.53	.002	2.63	.011
Stage 2 (after 2 months)	9.91 (1.29) n=15	12.63 (2.55) n=59	29.95	.000	3.70	.000
Stage 3 (after 3 months)	8.69 (1.79) n=17	12.21 (2.51) n=57	12.78	.001	5.39	.000
Stage 4 (after 6 months)	7.67 (1.69) n=17	11.96 (2.39) n=57	8.49	.005	6.89	.000
Stage 5 (after 9 months)	8.38 (2.17) n=21	11.89 (2.42) n=53	4.11	.046	5.79	.000
Stage 6 (after 12 months)	8.61 (1.69) n=24	11.86 (2.34) n=50	10.58	.002	6.08	.003
Stage 7 (after 24 months)	9.14 (1.74) n=27	11.71 (2.33) n=47	9.20	.003	4.98	.000

After the 24-month follow-up period, the overall study population exhibited a significant reduction in LVEF from baseline, with an average decrease of 5.05%, resulting in a mean EF of 56.8% (SD=4.2), as shown in Table 2. When assessing changes in EF, defined as EF <50% and Δ EF \geq 10%, the emergence of CTRCD was first documented at three months (T3), affecting 27.6% of the CTRCD cohort (P < 0.000) and 10.8% of the total population. The highest incidence of CTRCD was recorded at T7, as illustrated in Figure 6.

Additionally, we monitored the dynamics of S' indicators across both CTRCD and non-CTRCD groups throughout the 24-month follow-up period. The data presented in Table 3 demonstrates that at each study stage, the S' indicators exhibited statistically significant differences between the two groups (p<0.05).

Discussion.

In a two-year prospective follow-up study, we investigated the dynamics of left ventricular systolic function (LVSF) parameters and the incidence of CTRCD at various stages following the initiation of anticancer therapy in postmenopausal women diagnosed with primary BC who were receiving anthracycline-trastuzumab-containing regimens. Throughout the study period, a total of 27 (36,5%) patients developed CTRCD. This incidence is relatively higher than that reported in similar studies, which documented lower rates [21,22]. The higher incidence may be attributed to the relatively high-risk profile of our cohort, including postmenopausal status, advanced age, and increased cardiovascular risk. Detection of CTRCD commenced within one month following the first administration of doxorubicin, with an initial incidence of 13.5% (n=10), and subsequently peaked at the 24-month mark with an incidence of 36.5% (n=27). Consequently, the survival rate from CTRCD in our cohort was 63.5%. In HER2-positive patients (n=15), the initiation of targeted therapy was associated with a subsequent increase in CTRCD rate (73.3% vs 27.1%). Patients in our study underwent targeted therapy. All participants received anthracyclines, followed by trastuzumab in certain patients. We assume that

the greater incidence of CTRCD associated within trastuzumab subgroup is due to both trastuzumab and the cumulative effects of anthracycline. The combination of these therapies may lead to cardiotoxicity with a higher frequency than anthracycline alone. Early CTRCD (within 1 year) associated with anthracyclines is reported to range from 1-25% in various studies [8,16,21,23,24]. At the end of a 12-week prospective study, Hager Allam et al. found CTRCD in 12.5%, though their cohort was relatively young and only 68.8% were female [23]. Na Kim et al. And Wanzhu Zhang et al. reported CTRCD rates of 19% and 23.5%, respectively, at 6 months after anthracycline use, which is close to our finding of 22% at the same time point [8,25]. By the end of 1 year, the frequency of CTRCD in our study was 32%, increased by only 4.1% over the subsequent year, likely due to optimal CPT. Numerous studies have documented the incidence of cardiotoxicity associated with anthracycline-containing regimens, revealing a significant variability in outcomes by the end of a 12-month treatment period. A 1-year prospective cohort study by Maryam Esmailzadeh et al. found CTRCD rates of 42% by GLS, 23% by 2D LVEF, 22% by 3D LVEF, and 27% by cardiac magnetic resonance (CMR) respectively [26]. Our study showed a higher CTRCD rate detected by GLS (32%) as compared to EF% (20%). Naoko Ichikawa et al. (n=279) identified a prevalence of CTRCD at 22% (n=55), which is notably lower than the findings presented in our current study [21]. This discrepancy may be attributed to the older age of our study population, in our investigation, the hazard ratios derived from the Cox proportional hazards model indicated that patients aged over 65 years exhibit a statistically significant increased risk of developing CTRCD, quantified at 2.37 times higher than their younger counterparts under 65 years of age. Furthermore, the incidence of CTRCD reported by Florian Posch et al. was even lower at 10%, noting that cardiotoxicity was assessed solely based on LVEF [22]. In the study of late CTRCD José López-Sendón et al in a 24-month prospective multicenter study, the "CARDIOTOX Registry", similar to our study CTRCD was detected in 37.5%, although they obtained 31.6% mild, 2.8% moderate, and 3.1% severe CTRCD [27]. In contrast

in our study, symptomatic heart failure was not detected, which is probably due to optimal CPT. In a prospective 4.5-year study by Rebeca Mata Caballero et al. [24], CTRCD peaked at the end of the study, similar to our study, but in contrast to our results, the CTRCD incidence at 1 year was only 1%, and at the end of follow-up was 16.5%. Notably, they had a different CTRCD criterion (GLS was not considered) and the mean age was younger compared to our study group. In addition, the rigorous follow-up protocols implemented in our study facilitated early detection and management of CTRCD through the application of optimal CPT, which may explain the differences between studies.

The findings presented in our study reveal significant insights into the relationship between anthracycline dosage and the incidence of cardiotoxicity, as well as differences in CTRCD rate among various patient risk groups. Utilizing the Cox proportional hazards model, we observed that higher doses of anthracycline are associated with a statistically significant increase in the risk of developing cardiotoxicity. Specifically, patients receiving high doses exhibited a hazard ratio of 2.42 (HR=2.42, $p=0.020$), exhibiting more than double the risk compared to lower dosages. Furthermore, within the high and moderate risk patient cohort, this risk escalated dramatically to 9.24 times that of their low-risk counterparts (HR=9.24, $p<0.001$).

Throughout the two-year duration of the study, the mean LVGLS showed a gradual decline, culminating in a peak decrease at the end of the observation period; however, it remained within the normal range. The most significant pathological reduction in the minimum LVGLS value was recorded at T4, reaching -7.8%. Following this nadir, a positive trend was observed, potentially linked to the administration of CPT, although the minimum LVGLS value still fell short of the normative threshold, registering at -11.9%. In contrast to previous research, we specifically examined the incidence of chemotherapy-induced LV dysfunction utilizing both the criteria of $\Delta\text{GLS}\geq 15\%$ and $\text{GLS}<16\%$ at each time point in the study. Our results indicated that alterations in GLS were detectable following the initial dose of chemotherapy (T1), with measurements falling into the CTRCD category at 13.5% (n=10). This observation aligns with prior studies, including that of Astri Astuti et al. [12], which identified a notable decline in LVGLS earlier than in LVEF. Specifically, their research demonstrated a significant reduction in LVGLS as early as three weeks post-chemotherapy, while LVEF remained unchanged after the first chemotherapy cycle, reinforcing our findings of the sensitivity of LVGLS as an early marker for CTRCD in patients receiving anthracycline treatment.

D. van der Linde et al. [9] and Maryam Esmaeilzadeh et al. [26] and Christian P. Houbois et al. [28] with long-term observation (1-1.5 years), and Laila Sulaiman et al. with a 6-week study [29] showed that LV GLS is a more reliable early prognostic indicator of LV subclinical dysfunction as compared with 2D and 3D LVEF.

In the study by Wei Liu et al. [30], in the anthracycline group, LVGLS showed a decrease at the second cycle of chemotherapy ($P < 0.05$) and in the trastuzumab group at T4 ($P < 0.05$). Ahmed

A Fawzy et al. [31], Mi-Na Kim et al. [8] and Italian Society of Cardiology multicenter [32] studies showed that LVGLS change at 3 months was the strongest, most sensitive parameter to detect CTRCD. The period given for all four studies corresponded to the first echocardiographic control after the initial examination. In our investigation, multiple regression analyses revealed that the change in LVGLS after one month serves as a significant prognostic indicator for both early ($p=0.001$) and late (two years) CTRCD ($p=0.002$).

By Raquel Araujo-Gutierrez et al. After adjusting for cardiovascular and cancer therapy-related risk factors, similar to our study, baseline LVGLS or decreased baseline LVGLS were predictive of CTRCD development [10]. In the SUCCOUR multicenter prospective randomized controlled trial, in the first year of patients with CTRCD, the LVEF-managed arm had a greater reduction in LVEF at follow-up than in the GLS-managed arm [13]. Patients underwent CPT, however, 3-year SUCCOUR data showed no difference in EF% change between GLS- and EF-guided cardioprotection in patients on potentially cardiotoxic chemotherapy [33]. Notably, the SUCCOUR cohort is younger, 95% female, only 93% had BC, 84% were treated with anthracycline-trastuzumab-containing regimens, and a more lenient criterion of LVGLS $> 12\%$ was used.

In our study, we observed a significant discrepancy between the detection rates of CTRCD using different echocardiographic modalities. Specifically, the number of cases identified by LVGLS following the completion of chemotherapy (T3) was 23.0% (n=17), which is nearly twice as high as the 10.8% (n=8) detected by EF% at the same time point. This trend was consistent throughout all stages of the study, demonstrating that the frequency of CTRCD identified by GLS exceeded that of EF%. At the baseline, all participants exhibited normal LVEF. Interestingly, after the administration of the initial dose of doxorubicin (T1), we noted no significant alterations in the mean EF% compared to the baseline measurements. However, throughout the course of the study, there was a progressive decline in EF%, reaching its nadir at T7, although the mean EF% continued to fall within the normal limits. When assessing the minimum ejection fraction (EF% min), initial measurements indicated a normal range (EF% min =55.7%). By T3, at the conclusion of chemotherapy, we observed a pathological reduction in EF min, dropping to 49.2%. The most pronounced decline occurred at T4, approximately six months post-therapy, following the first dose of trastuzumab, where EF% min reached a critical low of 41.8%. Despite subsequent treatment interventions, a slight trend towards recovery was noted; however, the EF% min at T7 remained in the pathological range at 45.3% ($P=0.001$). Notably, CTRCD, as indicated by EF%, emerged only after chemotherapy (T3) with a prevalence of 10.8% (n=8), and subsequently progressed, peaking at two years post-treatment (T7) with an incidence of 25.7% (n=27). Our findings highlight the importance of utilizing LVGLS for the early detection of CTRCD, as it may provide a more sensitive measure than traditional EF assessment during and after chemotherapy.

In our investigation, we conducted a multiple regression analysis that identified a significant predictive relationship

between initial LVEF percentage and the subsequent development of CTRCD after a 24-month period. This finding aligns with the research conducted by Belén Díaz-Antón et al. and Florian Posch et al., which also indicated that baseline LVEF serves as a predictive marker for CTRCD [22,34]. However, in the study of the Italian Society of Cardiology, none of the patients developed cardiotoxicity according to the LVEF criterion, regardless of the type of chemotherapy [32].

To assess LVFS change, we analyzed S' during the 2-year follow-up. In the entire study group, there was a progressive decrease in mean S' from the basal value with a peak at 1 year. However, S' remained within the normal range at all stages of the study. However, when we compared the dynamics of S' values in the 2 subgroups divided by CTRCD (the groups were divided both by CTRCD at each visit and by CTRCD obtained at the final stage of the study), the dynamics of S' in the CTRCD and non-CTRCD groups differed. In non-cardiotoxic patients, S' showed a slight downward trend with a peak after 2 years but remained within the normal range. After the first course of chemotherapy (T1) in both groups, S' remained within the normal range, although it was lower in CTRCD patients, while at the end of chemotherapy only in the CTRCD group there was a pathological reduction of S'. The peak was noted at T4, with further small positive dynamics (which is probably related to the optimal CPT started on time), however, until the end of the study, S' remained below the normal range.

Multiple regression analysis showed that the change in S' after 1 month was an independent predictor for the development of CTRCD at the end of 6 months ($p=0.003$).

The measurement of S' is significant even in instances of suboptimal visualization of LV endocardium. Notably, while there is a limited number of studies investigating the predictive value of S' in cancer patients, existing literature, including our study, supports the utility of S' in forecasting CTRCD [21,25,35]. Additionally, research conducted by Naoko Ichikawa et al. highlights that S' demonstrates a superior diagnostic capability in identifying CTRCD when compared to LVGLS [21]. In the context of our findings, S' was found to be less effective than LVGLS; however, it proved to be more advantageous than LVEF in the assessment of cardiac function. This suggests that while S' may not be the most sensitive measure in this cohort, it retains clinical relevance in detecting changes associated with CTRCD.

Limitations of the study.

The primary limitation of the present study is the relatively small number of enrolled participants. Additionally, we did not separately analyze the various chemotherapy regimens separately, particularly those that consist of different combinations of chemotherapeutic agents, including those containing doxorubicin. Furthermore, the patients undergoing concurrent radiotherapy were not evaluated as a distinct group. These factors may impact the generalizability of our findings and warrant further investigation in future research.

Conclusion.

The prospective study of cardiotoxicity in postmenopausal women with early BC who underwent adjuvant therapy with anthracycline and trastuzumab revealed that: 1) The dynamic assessment of GLS should be prioritized for the early detection

of cardiac systolic dysfunction. 2) S' possesses high diagnostic value for identifying cardiotoxicity. 3) Close monitoring of LVFS and implementation of optimal medical cardioprotection strategies may mitigate the risks associated with highly cardiotoxic anti-cancer therapy and help prevent severe cardiac complications.

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REFERENCES

1. F. Bray, M. Laversanne, H. Sung, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74:229-263.
2. S Łukasiewicz, M Czezelewski, A Forma, et al. Breast Cancer-Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies-An Updated Review. *Cancers (Basel).* 2021;13:4287.
3. R L Siegel, AN Giaquinto, A Jemal. Cancer statistics, 2024. *CA Cancer J Clin.* 2024;74:12-49.
4. J Bergler-Klein, P Rainer, M Wallner, et al. Cardio-oncology in Austria: cardiotoxicity and surveillance of anti-cancer therapies: Position paper of the Heart Failure Working Group of the Austrian Society of Cardiology. *Wien Klin Wochenschr.* 2022;134:654-674.
5. D Valiyaveetil, D Joseph, M Malik. Cardiotoxicity in breast cancer treatment: Causes and mitigation. *Cancer Treat Res Commun.* 2023;37:100760.
6. D Ioffe, SC Bhatia-Patel, S Gandhi, et al. Cardiovascular Concerns, Cancer Treatment, and Biological and Chronological Aging in Cancer: JACC Family Series. *JACC CardioOncol.* 2024;6:143-158.
7. Li L, Jiang X, Xie Q. Prognostic value of left ventricular global longitudinal strain on speckle echocardiography for predicting chemotherapy-induced cardiotoxicity in breast cancer patients: A systematic review and meta-analysis. *Echocardiography.* 2023;40:306-317.
8. Mi-Na Kim, So-Ree Kim, Hee-Dong Kim, et al. Serial changes of layer-specific myocardial function according to chemotherapy regimen in patients with breast cancer. *Park Eur Heart J Open.* 2022;2:oeac008.
9. D van der Linde, I van Hagen, K Veen, et al. Global longitudinal strain: an early marker for cardiotoxicity in patients treated for breast cancer. *Neth Heart J.* 2023;31:103-108.
10. R Araujo-Gutierrez, KR Chitturi, J Xu, et al. Baseline global longitudinal strain predictive of anthracycline-induced cardiotoxicity. *Cardiooncology.* 2021;7:4.
11. W Chen, Z Jiao, W Li, et al. Two-dimensional speckle tracking echocardiography, a powerful method for the evaluation of anthracyclines induced left ventricular insufficiency. *Medicine (Baltimore).* 2022;101:e31084.
12. A Astuti, E Erwinanto, MR Akbar, et al. Global and Regional Longitudinal Strain Reduction in Breast Cancer Patients After First Chemotherapy Cycle With Fluorouracil, Adriamycin, and Cyclophosphamide Regimen. *Cardiol Res.* 2021;12:238-243.

13. P Thavendiranathan, T Negishi, E Somerset, et al. Strain-Guided Management of Potentially Cardiotoxic Cancer Therapy. *J Am Coll Cardiol*. 2021;77:392-401.
14. L Zhang, R Zhang, P Shuai, et al. A global case meta-analysis of three-dimensional speckle tracking for evaluating the cardiotoxicity of anthracycline chemotherapy in breast cancer. *Front Cardiovasc Med*. 2022;9:942620.
15. L D Cocco, A F Chiaparini, M A L Saffi, et al. Global Longitudinal Strain for the Early Detection of Chemotherapy-Induced Cardiotoxicity: A Systematic Review and Meta-analysis. *Clin Oncol (R Coll Radiol)*. 2022;34:514-525.
16. R Simões, L M Silva, A N de Oliveira, et al. Identification of Clinical and Laboratory Variables Associated with Cardiotoxicity Events Due to Doxorubicin in Breast Cancer Patients: A 1-Year Follow-Up Study . *Cardiovasc Toxicol*. 2021;21:106-114.
17. A R Lyon, T López-Fernández, L S Couch, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J*. 2022;43:4229-4361.
18. S Robinson, B Rana, D Oxborough, et al. A practical guideline for performing a comprehensive transthoracic echocardiogram in adults: the British Society of Echocardiography minimum dataset. *Echo Res Pract*. 2020;7:G59-G93.
19. R Dobson, A K Ghosh, B Ky, et al. British Society for Echocardiography and British Cardio-Oncology Society guideline for transthoracic echocardiographic assessment of adult cancer patients receiving anthracyclines and/or trastuzumab. *Echo Res Pract*. 2021;8:G1-G18.
20. C Mitchell, P S Rahko, L A Blauwet, et al. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2019;32:1-64.
21. N Ichikawa, Y Nishizaki, S Miyazaki, et al. Efficacy of mitral annular velocity as an alternative marker of left ventricular global longitudinal strain to detect the risk of cancer therapy-related cardiac disorders. *Echocardiography*. 2024;41:e15877.
22. F Posch, T Niedrist, T Glantschnig, et al. Left ventricular ejection fraction and cardiac biomarkers for dynamic prediction of cardiotoxicity in early breast cancer. *Front Cardiovasc Med*. 2022;9:933428.
23. H Allam, M Kamal, M Bendary, et al. The diagnostic value of global longitudinal strain combined with cardiac biomarkers on early detection of anthracycline-related cardiac dysfunction. *J Echocardiogr*. 2023;21:165-172.
24. R M Caballero, J M S Antolín, R M J Hernández, et al. Incidence of long-term cardiotoxicity and evolution of the systolic function in patients with breast cancer treated with anthracyclines. *Cardiol J*. 2022;29:228-234.
25. W Zhang, F Azibani, E Libhaber, et al. The role of conventional echocardiographic parameters on detecting subclinical anthracycline therapy related cardiac dysfunction-The SATRACD study. *Front Cardiovasc Med*. 2022;9:966230.
26. M Esmaeilzadeh, CMU Fresno, E Somerset, et al. A Combined Echocardiography Approach for the Diagnosis of Cancer Therapy-Related Cardiac Dysfunction in Women With Early-Stage Breast Cancer. *JAMA Cardiol*. 2022;7:330-340.
27. J López-Sendón, C Álvarez-Ortega, P Z Auñón, et al. Classification, prevalence, and outcomes of anticancer therapy-induced cardiotoxicity: the CARDIOTOX registry. *Eur Heart J*. 2020;41:1720-1729.
28. C P Houbois, M Nolan, E Somerset, et al. Serial Cardiovascular Magnetic Resonance Strain Measurements to Identify Cardiotoxicity in Breast Cancer: Comparison With Echocardiography. *JACC Cardiovasc Imaging*. 2021;14:962-974.
29. L Sulaiman, D Hesham, M A Hamid, et al. The combined role of NT- proBNP and LV-GLS in the detection of early subtle chemotherapy-induced cardiotoxicity in breast cancer female patients. *Egypt Heart J*. 2021;73:20.
30. W Liu, W Li, H Li, et al. Two-dimensional speckle tracking echocardiography helps identify breast cancer therapeutics-related cardiac dysfunction. *BMC Cardiovasc Disord*. 2022;22:548.
31. A A Fawzy, K A El- Menyawi, W M Sallam, et al. Two-dimensional speckle tracking echocardiography in chemotherapy-induced cardiotoxicity in females with breast cancer. *Cardiooncology*. 2024;10:13.
32. C Zito, R Manganaro, M C Piccione, et al. Anthracyclines and regional myocardial damage in breast cancer patients. A multicentre study from the Working Group on Drug Cardiotoxicity and Cardioprotection, Italian Society of Cardiology (SIC). *Eur Heart J Cardiovasc Imaging*. 2021;22:406-415.
33. T Negishi, P Thavendiranathan, M Penicka, et al. Cardioprotection Using Strain-Guided Management of Potentially Cardiotoxic Cancer Therapy: 3-Year Results of the SUCCOUR Trial. *JACC Cardiovasc Imaging*. 2023;16:269-278.
34. B Díaz-Antón, R Madurga, B Zorita, et al. Early detection of anthracycline- and trastuzumab-induced cardiotoxicity: value and optimal timing of serum biomarkers and echocardiographic parameters. *ESC Heart Fail*. 2022;9:1127-1137.
35. A Banke, M Schou, M Ewertz, et al. Immediate evaluation of global longitudinal strain at initiation of trastuzumab treatment in breast cancer patients. *Echocardiography*. 2021;38:1702-1710.