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DIASTOLIC DYSFUNCTION AS AN EARLY INDICATOR OF ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN BREAST CANCER PATIENTS: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Breast cancer is one of the most common malignancies worldwide, and anthracyclines remain a cornerstone of its treatment. However, their use is associated with the risk of cardiotoxicity, which may lead to subclinical myocardial injury, progressive ventricular dysfunction, and heart failure. Although left ventricular ejection fraction is still widely used in routine surveillance, it often decreases relatively late. Therefore, increasing attention has been directed toward diastolic dysfunction as a possible earlier marker of anthracycline-induced cardiac injury.
Methods: A systematic review was conducted using the PubMed database. The search strategy included the terms “breast cancer” OR “breast neoplasms,” “anthracycline” OR “doxorubicin” OR “epirubicin,” and “diastolic dysfunction” OR “diastolic function.” The search was limited to studies published between 2010 and 2026, written in English, and conducted in humans. A total of 43 records were identified. After title and abstract screening, 15 full-text articles were assessed for eligibility. Fourteen studies met the inclusion criteria and were included in the final qualitative synthesis.
Results: The reviewed studies showed that anthracycline therapy was associated with worsening of conventional and tissue Doppler indices of diastolic function, including E/A ratio, deceleration time, e′ velocity, and E/e′ ratio, often despite preserved left ventricular ejection fraction. Several studies also demonstrated abnormalities in more advanced echocardiographic markers, such as diastolic strain rate, diastolic strain time, left atrial strain, and intrinsic wave velocity propagation. In longitudinal analyses, early diastolic dysfunction was associated with later worsening of global longitudinal strain, decline in left ventricular ejection fraction, or subsequent cancer therapy-related cardiac dysfunction.
Conclusions: Diastolic dysfunction appears to be a clinically relevant and potentially early marker of anthracycline-induced cardiotoxicity in breast cancer patients. Its earlier recognition may support closer cardio-oncology surveillance, improve risk stratification, and help identify patients who may benefit from earlier specialist evaluation and consideration of cardioprotective strategies before overt systolic dysfunction develops. Further prospective studies are needed to determine which diastolic parameters are the most sensitive and clinically useful in routine practice.

KEYWORDS

Breast Cancer; Anthracycline Cardiotoxicity; Diastolic Dysfunction; Echocardiography; Cardio-Oncology; Early Detection

CITATION

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Introduction

Breast cancer remains one of the most important global health challenges and continues to impose a substantial clinical, social, and economic burden worldwide. According to the most recent GLOBOCAN estimates, breast cancer is among the most frequently diagnosed malignancies globally, with approximately 2.3 million new cases reported in 2022, making it one of the leading causes of cancer-related morbidity in women (Bray et al., 2024). The World Health Organization likewise identifies breast cancer as the most common cancer in women in the majority of countries and a major cause of cancer-related mortality, underlining its continued relevance as a public health priority (World Health Organization, 2025). Improvements in screening, earlier diagnosis, and more effective systemic therapies have substantially improved survival, resulting in a growing population of long-term breast cancer survivors (Bray et al., 2024; World Health Organization, 2025). As survival improves, however, greater attention must be paid not only to oncologic outcomes but also to treatment-related complications that may adversely affect long-term prognosis and quality of life.

Among these complications, cardiovascular toxicity has emerged as one of the most clinically relevant non-oncologic consequences of anticancer treatment. The development of cardio-oncology reflects the growing need to balance effective cancer therapy with preservation of cardiovascular health, particularly in patients exposed to agents with known cardiotoxic potential (Lyon et al., 2022). The 2022 ESC Guidelines on cardio-oncology emphasize that cancer therapy-related cardiovascular toxicity has become an increasingly important clinical issue as advances in oncology have prolonged survival and shifted attention toward long-term adverse effects of treatment (Lyon et al., 2022). Anthracyclines remain a cornerstone of breast cancer therapy because of their established antineoplastic efficacy, yet they are also among the treatments most strongly associated with cancer therapy-related cardiac dysfunction (CTRCD) (Lyon et al., 2022). In clinical practice, anthracycline-induced cardiotoxicity may manifest across a broad spectrum, ranging from asymptomatic myocardial injury and subclinical ventricular dysfunction to overt heart failure and late cardiovascular morbidity (Lyon et al., 2022; Plana et al., 2014).

Traditionally, surveillance of cardiotoxicity has focused primarily on left ventricular ejection fraction (LVEF). Although LVEF remains widely used in routine clinical practice, it has important limitations, particularly in the detection of early or subclinical myocardial injury (Plana et al., 2014). A measurable decline in LVEF often reflects a relatively advanced stage of myocardial dysfunction, potentially occurring after structural and functional abnormalities have already developed (Lyon et al., 2022; Plana et al., 2014). For this reason, increasing attention has been directed toward more sensitive imaging markers capable of identifying cardiotoxicity at an earlier stage, before irreversible myocardial damage becomes clinically apparent. Expert recommendations on multimodality imaging in patients undergoing cancer therapy identify echocardiography as the first-line imaging modality for cardiac surveillance because of its availability, safety, repeatability, and comprehensive functional assessment (Plana et al., 2014). Over time, echocardiographic monitoring has evolved beyond conventional two-dimensional measures to include tissue Doppler imaging, myocardial deformation imaging, left atrial functional assessment, and other advanced techniques intended to improve sensitivity in detecting subtle myocardial abnormalities (Nagueh et al., 2009; Plana et al., 2014).

Within this context, diastolic dysfunction has attracted growing interest as a potentially important marker of anthracycline-related myocardial injury. Diastolic abnormalities may reflect impaired ventricular relaxation, altered compliance, and increased filling pressures, all of which can develop before overt systolic dysfunction becomes clinically evident (Nagueh et al., 2009). Echocardiographic evaluation of diastolic function includes parameters such as transmitral inflow velocities, E/A ratio, deceleration time, tissue Doppler e′ velocity, E/e′ ratio, and left atrial structural and functional indices (Nagueh et al., 2009). These measurements provide insight into left ventricular filling dynamics and may capture early functional disturbances that are not apparent on standard LVEF assessment alone. In principle, this makes diastolic function an attractive area of

investigation in cardio-oncology, particularly in breast cancer patients receiving anthracycline-based chemotherapy.

Several studies have explored whether diastolic abnormalities occur during or shortly after anthracycline therapy in breast cancer patients. Early reports suggested that conventional Doppler and tissue Doppler indices may reveal subtle changes even in the setting of preserved systolic function (Appel et al., 2011; Mizia-Stec et al., 2013). Other studies demonstrated that anthracycline therapy may impair both systolic and diastolic myocardial performance shortly after treatment, supporting the concept that cardiotoxicity develops as a continuum rather than as an isolated decline in LVEF (Boyd et al., 2017; Stoodley et al., 2013). Prospective and longitudinal data in breast cancer cohorts have shown that diastolic dysfunction may be frequent after anthracycline exposure and, in some patients, may persist during follow-up (Serrano et al., 2015, 2023; Upshaw et al., 2020). Importantly, some investigations suggest that early worsening of diastolic parameters may be associated with subsequent deterioration in systolic indices such as global longitudinal strain (GLS) or LVEF, raising the possibility that diastolic dysfunction may serve as an early warning sign of future CTRCD (Hochstadt et al., 2020; Serrano et al., 2023; Upshaw et al., 2020).

At the same time, the available evidence remains heterogeneous. Some studies reported measurable early changes in diastolic indices or left atrial mechanics after anthracycline exposure (Emerson et al., 2024; Yaylali et al., 2016), whereas others found only modest abnormalities or limited short-term sensitivity of conventional diastolic parameters (Appel et al., 2011). More recent work has expanded the field beyond traditional Doppler measurements by incorporating newer imaging techniques such as left atrial strain, diastolic strain time, three-dimensional echocardiographic mechanics, and novel indices of myocardial stiffness, including intrinsic wave velocity propagation (Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Zhang et al., 2018). These developments reflect a broader trend in cardio-oncology toward more refined imaging-based phenotyping of myocardial dysfunction. Contemporary studies indicate that diastolic dysfunction may coexist with or even precede other manifestations of myocardial injury in selected patients, although its exact role relative to GLS and other established surveillance markers remains incompletely defined (Hochstadt et al., 2020; Huang, Rankin, et al., 2025; Upshaw et al., 2020).

Given the growing number of breast cancer survivors and the clinical importance of minimizing long-term cardiovascular complications, better characterization of early imaging markers of anthracycline-induced cardiotoxicity is of considerable relevance. In particular, clarifying the diagnostic and prognostic value of diastolic dysfunction may improve risk stratification, optimize surveillance strategies, and support earlier intervention in patients at increased risk of treatment-related cardiac injury. Therefore, the aim of this systematic review is to evaluate the available evidence regarding diastolic dysfunction as an early indicator of anthracycline-induced cardiotoxicity in breast cancer patients, with particular emphasis on echocardiographic parameters and emerging imaging techniques used in contemporary cardio-oncology practice.

Materials and Methods

This systematic review was conducted to evaluate the available evidence on diastolic dysfunction as an early indicator of anthracycline-induced cardiotoxicity in breast cancer patients. The review focused on original human studies assessing left ventricular diastolic function in women with breast cancer treated with anthracycline-based chemotherapy.

Literature search strategy

A structured literature search was performed in the PubMed database using the following search strategy: (“breast cancer” OR “breast neoplasms”) AND (anthracycline OR doxorubicin OR epirubicin) AND (“diastolic dysfunction” OR “diastolic function”). The search was limited to studies published between 2010 and 2026, written in English, and conducted in humans. This search yielded 43 records, which were initially screened based on title and abstract.

Eligibility criteria and study selection

Studies were considered eligible if they met the following criteria:

(1) original clinical investigation, (2) population including breast cancer patients, (3) exposure to anthracycline-containing therapy, and (4) assessment of diastolic dysfunction, diastolic echocardiographic parameters, or related diastolic imaging markers.

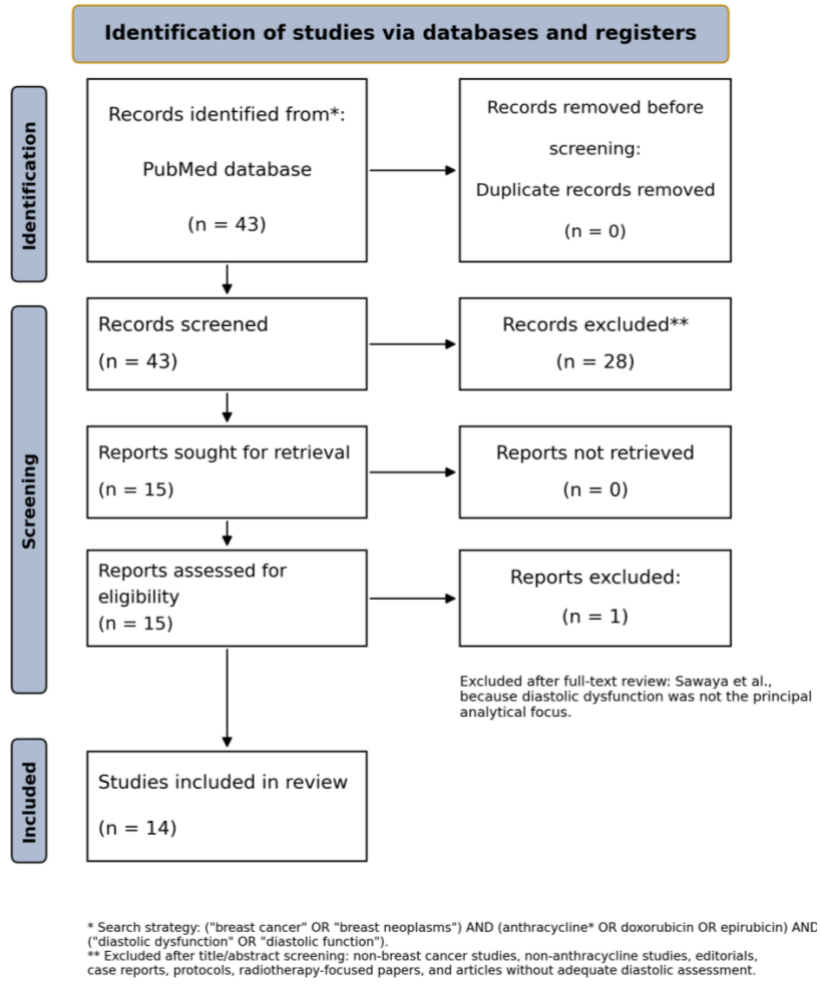
Studies were excluded if they were editorials, commentaries, case reports, study protocols, prevention or intervention trials without a clear focus on diastolic assessment, biomarker-led studies without sufficient echocardiographic diastolic analysis, radiotherapy-only studies, trastuzumab-only studies, or papers primarily focused on non-diastolic endpoints. Examples of records excluded at the title and abstract screening stage included editorial or commentary papers, such as the JACC commentary by Thavendiranathan and Calvillo-Argüelles; a protocol paper by Antunes et al.; a case report by Framarino-dei-Malatesta et al.; radiotherapy-focused studies such as those by Clasen et al. and Cao et al.; and papers centered mainly on trastuzumab-related dysfunction or non-diastolic outcomes.

After title and abstract screening, 15 full-text articles were selected for detailed eligibility assessment. Full-text review was performed to determine whether the studies specifically examined diastolic dysfunction, diastolic echocardiographic parameters, or related diastolic deformation markers in breast cancer patients receiving anthracycline-containing therapy.

Of the 15 full-text articles assessed, 14 studies were finally included in the qualitative synthesis, and 1 study was excluded after full-text review. The excluded study was the article by Sawaya et al., which was highly relevant to early cardiotoxicity detection in breast cancer patients treated with anthracyclines and trastuzumab, but was primarily focused on longitudinal strain and cardiac biomarkers as predictors of cardiotoxicity. Although diastolic parameters were reported, they were not the principal analytical focus and were not shown to predict cardiotoxicity in that study. Therefore, this paper was excluded from the final review sample and considered only as contextual background.

Ultimately, the final qualitative synthesis included 14 original studies investigating diastolic dysfunction or diastolic imaging abnormalities in breast cancer patients treated with anthracycline-based regimens (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018).

The study selection process is presented in Figure 1.



Data extraction

From each included study, the following data were extracted: publication year, study design, sample size, treatment regimen, timing of echocardiographic assessment, methods used to evaluate diastolic function, definition of cardiotoxicity, and the principal findings related to diastolic abnormalities. Because the included studies differed substantially in design, follow-up duration, imaging methodology, and definitions of abnormal diastolic function, a narrative synthesis rather than a pooled quantitative analysis was performed.

Assessment of diastolic dysfunction

A major aim of this review was to analyze how diastolic dysfunction was assessed across the included studies. Most studies used transthoracic echocardiography as the principal imaging modality, usually performed before anthracycline exposure and repeated at predefined time points during or after treatment. Conventional Doppler echocardiography and tissue Doppler imaging formed the methodological basis of diastolic assessment in the majority of studies (Appel et al., 2011; Boyd et al., 2017; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016).

The most frequently reported conventional parameters included transmitral inflow velocities in early and late diastole (E and A waves), the E/A ratio, deceleration time (DT), and isovolumetric relaxation time (IVRT). Tissue Doppler imaging was commonly used to measure early and late diastolic mitral annular velocities (e′ and a′, or E′ and A′), and derived ratios such as E/e′ were used as surrogate markers of left ventricular filling pressure. In some studies, left atrial size or function was also incorporated into the evaluation of diastolic abnormalities (Nagueh et al., 2009; Serrano et al., 2015; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016).

Several studies formally graded diastolic dysfunction using combinations of conventional Doppler and tissue Doppler parameters, allowing differentiation between normal filling, impaired relaxation, pseudonormal filling, and restrictive filling patterns. This approach was used, among others, in the studies by Serrano et al. and Boyd et al., which assessed the incidence and progression of diastolic dysfunction during follow-up (Boyd et al., 2017; Serrano et al., 2015, 2023).

In addition to conventional methods, several studies applied more advanced echocardiographic techniques. Speckle-tracking echocardiography was used to assess myocardial deformation, including early and late diastolic strain rate. Stoodley et al. and Boyd et al. used two-dimensional speckle-tracking to evaluate longitudinal diastolic strain and diastolic strain rate, thereby identifying subtle post-treatment changes in myocardial relaxation (Boyd et al., 2017; Stoodley et al., 2013).

More recent studies explored novel diastolic markers. Hochstadt et al. evaluated diastolic strain time (Dst) as a potential predictor of later systolic dysfunction (Hochstadt et al., 2020). Emerson et al. assessed left atrial phasic strain, including reservoir and conduit strain, as markers of early diastolic impairment (Emerson et al., 2024). Huang et al. introduced intrinsic wave velocity propagation (IVP) as a novel parameter reflecting myocardial stiffness and early diastolic dysfunction (Huang, Fan, et al., 2023). The 2025 study by Huang et al. further expanded this framework by assessing diastolic dysfunction both with conventional grading and with a modified approach incorporating left atrial reservoir strain (LARS) (Huang, Rankin, et al., 2025).

Overall, substantial methodological heterogeneity was identified in the evaluation of diastolic dysfunction. While conventional Doppler and tissue Doppler indices remained the core tools in most studies, newer investigations increasingly incorporated deformation imaging, left atrial strain, diastolic strain time, and stiffness-related parameters (Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Stoodley et al., 2013; Zhang et al., 2018). This heterogeneity was clinically relevant, because some studies suggested that advanced diastolic markers may detect subtle anthracycline-related myocardial changes earlier than routine parameters, whereas traditional indices alone were not consistently sensitive in early follow-up (Appel et al., 2011; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023).

Outcomes of interest

The primary outcome of interest was the occurrence of diastolic dysfunction or worsening of diastolic parameters following anthracycline exposure. The secondary outcome was the relationship between early diastolic abnormalities and subsequent evidence of systolic dysfunction or cardiotoxicity, including deterioration in global longitudinal strain or decline in left ventricular ejection fraction. Several included studies specifically examined whether early diastolic impairment preceded, accompanied, or predicted later cancer therapy-related cardiac dysfunction (Boyd et al., 2017; Hochstadt et al., 2020; Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020).

Data synthesis

Because of the heterogeneity of study populations, chemotherapy regimens, echocardiographic protocols, and definitions of abnormal diastolic function, meta-analysis was not performed. Instead, the findings were synthesized qualitatively, with emphasis on:

(1) the timing of diastolic abnormalities relative to anthracycline exposure,

(2) the echocardiographic techniques used to detect these abnormalities, and

(3) the extent to which diastolic dysfunction functioned as an early or complementary marker of anthracycline-induced cardiotoxicity.

Results

Study selection and general characteristics

The PubMed search identified 43 records. After title and abstract screening, 28 records were excluded. Fifteen full-text articles were assessed for eligibility. One study was excluded after full-text review because diastolic dysfunction was not the principal analytical focus of the analysis. Ultimately, 14 studies were included in the qualitative synthesis (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018).

The included studies were published between 2011 and 2025 and were predominantly prospective observational cohorts. Sample sizes ranged from 35 to 362 participants. Most studies enrolled women with breast cancer treated with anthracycline-based regimens, usually doxorubicin or epirubicin, although in some cohorts a subgroup also received trastuzumab. Timing of cardiac assessment varied from immediate post-treatment imaging to long-term follow-up extending beyond 4 years (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018).

Conventional Doppler and tissue Doppler evidence of diastolic dysfunction

A recurrent finding across the included studies was that anthracycline exposure was associated with deterioration in conventional and tissue Doppler markers of diastolic function, often despite preserved left ventricular ejection fraction (Appel et al., 2011; Boyd et al., 2017; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016).

In the 2015 study by Serrano et al. (2015), 100 breast cancer patients underwent serial echocardiographic evaluation at baseline, at the end of anthracycline-based chemotherapy, and at 3 and 9 months. Fifteen patients had baseline diastolic dysfunction and were excluded from the main incidence analysis. Among the remaining patients, 49 developed diastolic dysfunction during follow-up, corresponding to 57.6% of the evaluable cohort. Diastolic dysfunction persisted in 36 of those 49 patients and reversed in 13. During follow-up, significant deterioration was observed in the main diastolic parameters, including a decrease in septal and lateral E′ velocities, an increase in E/E′ ratio, prolongation of deceleration time and isovolumetric relaxation time, a decrease in E/A ratio, and a reduction in mitral inflow propagation velocity. Importantly, all three patients who later developed systolic dysfunction had previously developed diastolic dysfunction (Serrano et al., 2015).

The long-term follow-up of the same cohort, reported by Serrano et al. (2023), confirmed the persistence and prognostic significance of these findings. In that study, mean baseline LVEF was 67.1% and baseline GLS was −18.9%. Fifteen patients had baseline diastolic dysfunction and 49 developed diastolic dysfunction within the first year, including 46 with grade I and 3 with grade II dysfunction. The incidence of diastolic dysfunction was similar in patients receiving anthracyclines alone and those receiving anthracyclines plus trastuzumab (57% vs 60%). Again, significant worsening was observed in tissue Doppler parameters, especially a decrease

in E′ at the septal and lateral mitral annulus and an increase in E/E′ ratio. Early diastolic dysfunction was independently associated with later anthracycline-related cardiotoxicity (Serrano et al., 2023).

Boyd et al. (2017) assessed 140 patients before and within 7 days after anthracycline treatment. Although LVEF remained within the normal range, it declined slightly from 60 ±3% to 59 ±3% ($p = 0.04$), while triplane GLS worsened from −20.0 ±1.6% to −19.1 ±1.8% ($p < 0.001$). Diastolic dysfunction grade increased significantly from 46% before treatment to 57% after treatment ($p < 0.001$). Moreover, diastolic dysfunction was more common in patients with reduced systolic GLS than in those without relevant GLS change (30% vs 11%; $p = 0.04$). The percentage change in early diastolic strain rate and transmitral E velocity independently predicted a >11% reduction in GLS (Boyd et al., 2017).

Mizia-Stec et al. (2013) evaluated 35 women before and 6 months after standard-dose anthracycline chemotherapy. Global systolic function remained preserved, but left ventricular end-diastolic diameter increased from 46 ±3.5 mm to 48 ±4 mm ($p = 0.004$) and left ventricular end-diastolic volume increased from 101 ±25 mL to 112 ±26 mL ($p = 0.01$). Regarding diastolic function, the Tei index increased from 0.49 ±0.09 to 0.54 ±0.10 ($p = 0.04$), E′ decreased ($p = 0.049$), A′ decreased ($p = 0.02$), and the lateral E/E′ ratio increased significantly ($p < 0.0001$). These changes indicated impaired relaxation and higher filling pressure despite preserved LVEF (Mizia-Stec et al., 2013).

Yaylali et al. (2016) focused on atrial function and left ventricular filling approximately 11 ±7 months after anthracycline-containing chemotherapy in 53 patients compared with 42 healthy controls. Several classic diastolic parameters were significantly altered: mitral A velocity was higher in treated patients (0.8 ±0.2 vs 0.6 ±0.2, $p = 0.0001$), deceleration time was prolonged (201.2 ±35.6 ms vs 163.7 ±21.8 ms, $p = 0.0001$), E/A ratio was lower (1.0 ±0.3 vs 1.3 ±0.3, $p = 0.0001$), mitral Em was lower (0.09 ±0.03 vs 0.11 ±0.03, $p = 0.001$), and E/Em was higher (8.8 ±3.2 vs 7.6 ±2.6, $p = 0.017$). These data supported the presence of impaired relaxation and altered filling characteristics after anthracycline therapy (Yaylali et al., 2016).

Timóteo et al. (2019) retrospectively evaluated 100 women during one year of breast cancer treatment, including 74% exposed to anthracyclines. New or worsening diastolic dysfunction developed in 20% of patients, and age was the only independent predictor. The study also showed impairment in left atrial contractile function in 20.8% of patients. Although treatment exposure was mixed, this work supported the concept that diastolic abnormalities are common during contemporary breast cancer therapy (Timóteo et al., 2019).

By contrast, Appel et al. (2011) reported largely negative short-term findings after low-dose epirubicin. In 80 women examined before and after three treatment series, only a marginal reduction in E/A ratio was observed, while conventional Doppler and tissue Doppler indices of systolic and diastolic function showed no clinically relevant short-term changes. This study suggests that conventional diastolic measures may have limited sensitivity in low-dose, short-interval settings (Appel et al., 2011).

Deformation imaging and advanced diastolic markers

Several studies suggested that advanced echocardiographic techniques may detect subtler diastolic abnormalities than conventional Doppler indices alone (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Stoodley et al., 2013; Zhang et al., 2018).

Stoodley et al. (2013) prospectively assessed 52 women 1 week before and 1 week after anthracycline therapy using conventional Doppler, tissue velocity imaging, and two-dimensional speckle-tracking echocardiography. The study demonstrated altered left ventricular diastolic function immediately after chemotherapy, including changes in early diastolic strain rate (E-Sr), and showed that post-treatment systolic strain was the strongest independent predictor of impaired E-Sr ($p = 0.001$). These findings supported a close early relationship between systolic and diastolic myocardial impairment (Stoodley et al., 2013).

Hochstadt et al. (2020) introduced diastolic strain time (Dst) as a novel parameter in 69 breast cancer patients undergoing doxorubicin therapy. Significant GLS reduction at the end of treatment was observed in 10 patients (20%). The change in basal diastolic strain time from baseline to interim assessment was significantly associated with subsequent GLS reduction in both univariate and multivariate analyses ($p < 0.04$). This finding suggests that dynamic changes in diastolic deformation may precede or accompany later systolic decline (Hochstadt et al., 2020).

Huang, Fan, et al. (2023) evaluated 68 newly diagnosed breast cancer patients treated with anthracycline-based chemotherapy and measured intrinsic wave velocity propagation (IVP), GLS, longitudinal systolic strain rate, early diastolic strain rate (LSRe), late diastolic strain rate, and E/LSRe ratio across serial

treatment cycles. IVP increased significantly already after the first chemotherapy cycle (T1), whereas GLS, LSRs, and LSRe did not change significantly until the second cycle (T2). The E/LSRe ratio increased significantly from the third cycle (T3). Baseline IVP showed good predictive value for later subclinical dysfunction, with an area under the curve of 0.752 ($p < 0.001$). These results support IVP as a potentially sensitive early marker of diastolic impairment (Huang, Fan, et al., 2023).

Emerson et al. (2024) assessed 128 HER2-negative breast cancer patients before and immediately after anthracycline exposure. Although all patients retained normal post-treatment LVEF, LV GLS declined significantly. Traditional diastolic parameters also worsened, with reductions in peak E velocity and e′ velocity. In parallel, left atrial reservoir strain decreased from 34.8% to 31.5% ($p < 0.001$), and left atrial conduit strain decreased from 17.2% to 14.4% ($p < 0.001$). A >15% reduction in LASRES was observed in 32% of patients, compared with a >15% reduction in LV GLS in 23%. Reduced LASRES was observed in 74% of patients with indeterminate diastolic function post-treatment, indicating that left atrial strain may identify subclinical dysfunction not fully captured by standard grading (Emerson et al., 2024).

Zhang et al. (2018) used three-dimensional speckle-tracking echocardiography in 142 women receiving doxorubicin with or without trastuzumab. Three-dimensional LVEF, global circumferential strain, GLS, and principal strain all worsened significantly after anthracycline treatment ($p < 0.001$), and several 3D parameters were associated with concurrent E/e′, supporting the concept that three-dimensional mechanics capture abnormalities linked to diastolic dysfunction (Zhang et al., 2018).

Longitudinal studies linking diastolic dysfunction with subsequent cardiotoxicity

The largest longitudinal study was that of Upshaw et al. (2020), which included 362 breast cancer patients treated with doxorubicin, doxorubicin followed by trastuzumab, or trastuzumab alone. Over a median follow-up of 2.1 years, patients treated with doxorubicin-containing regimens showed persistent worsening in E/A ratio, septal and lateral e′ velocities, and E/e′ ratio (all $p < 0.01$). Incident abnormal diastolic function grade occurred in 60% at 1 year, 70% by 2 years, and 80% by 3 years. Abnormal diastolic function grade was associated with a subsequent decrease in LVEF of −2.1% (95% CI: −3.1 to −1.2; $p < 0.001$) and worsening longitudinal strain of 0.6% (95% CI: 0.1 to 1.1; $p = 0.013$). Changes in E/e′ ratio were also modestly associated with worsening strain (0.1%; 95% CI: 0.0 to 0.2; $p = 0.022$) (Upshaw et al., 2020).

The 2025 study by Huang, Rankin, et al. (2025) further strengthened the prognostic role of diastolic abnormalities. In 136 women with early-stage HER2-positive breast cancer, CMR-defined CTRCD developed in 27%, worsening GLS in 42%, and incident diastolic dysfunction in 19.4% using conventional grading and 14.4% using modified grading incorporating left atrial reservoir strain. Patients who first transitioned to diastolic dysfunction had a higher rate of later CTRCD than those who first transitioned to worsening GLS (63% vs 18%). Worsening diastolic dysfunction was associated with markedly higher odds of subsequent CTRCD (OR 20.9; 95% CI: 3.4–129.5), compared with worsening GLS (OR 4.9; 95% CI: 2.6–9.4) (Huang, Rankin, et al., 2025).

Overall synthesis of findings

Taken together, the included studies show that anthracycline therapy in breast cancer patients is associated with measurable deterioration in diastolic function across multiple echocardiographic domains (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018). Conventional parameters such as E/A ratio, DT, IVRT, E′, and E/E′ frequently worsened during follow-up, while advanced markers—including early diastolic strain rate, diastolic strain time, left atrial strain, and IVP—appeared to detect subtle abnormalities at very early stages (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Stoodley et al., 2013). The most consistent longitudinal signal was that early diastolic dysfunction was not only common but also associated with subsequent systolic deterioration or later cardiotoxicity in several cohorts (Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020).

Discussion

The findings of this review suggest that diastolic dysfunction may represent a clinically meaningful component of anthracycline-induced cardiotoxicity in breast cancer patients and, in some settings, may be detectable before overt systolic impairment becomes apparent. Across the included studies, deterioration in diastolic indices was observed both in conventional Doppler and tissue Doppler parameters and in more advanced echocardiographic markers, including diastolic strain rate, diastolic strain time, left atrial strain, and intrinsic wave velocity propagation (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018). Importantly, several studies showed that these abnormalities occurred despite preserved left ventricular ejection fraction, supporting the concept that anthracycline-related myocardial injury may begin at a subclinical stage not captured by conventional systolic assessment alone (Boyd et al., 2017; Emerson et al., 2024; Mizia-Stec et al., 2013; Serrano et al., 2015; Stoodley et al., 2013; Yaylali et al., 2016).

A key observation emerging from the reviewed literature is that diastolic dysfunction appears to have potential value not only as a descriptive echocardiographic abnormality but also as a marker of future risk. In the study by Serrano et al. (2015), diastolic dysfunction developed in a substantial proportion of patients during follow-up, and in the later long-term analysis early diastolic dysfunction was independently associated with subsequent anthracycline-related cardiotoxicity (Serrano et al., 2023). Similarly, Upshaw et al. (2020) demonstrated that abnormal diastolic function grade and worsening diastolic parameters were associated with later deterioration in both LVEF and longitudinal strain. The 2025 study by Huang, Rankin, et al. (2025) further reinforced this observation by showing that patients who first transitioned to diastolic dysfunction had a higher probability of developing later CTRCD than those who first showed worsening GLS. Together, these findings suggest that diastolic impairment may have prognostic relevance and may help identify patients at increased risk of subsequent myocardial dysfunction (Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020).

From a clinical perspective, this has important implications. In routine practice, cardiotoxicity surveillance is still frequently centered on LVEF, yet the studies included in this review consistently indicate that LVEF may remain normal even when measurable diastolic abnormalities are already present (Boyd et al., 2017; Emerson et al., 2024; Mizia-Stec et al., 2013; Serrano et al., 2015; Stoodley et al., 2013; Yaylali et al., 2016). This creates a clinically relevant diagnostic gap. If diastolic dysfunction is recognized earlier than overt systolic decline, it may offer an opportunity to intensify monitoring before irreversible myocardial damage develops. In other words, early changes in diastolic function may help identify a subgroup of breast cancer patients who require closer cardio-oncology surveillance, more frequent echocardiographic follow-up, and more aggressive management of cardiovascular risk factors (Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020).

One of the most practically relevant aspects of this review is the possibility that earlier identification of subclinical diastolic dysfunction could support earlier implementation of cardioprotective strategies. Although the reviewed studies do not prove that every diastolic abnormality should automatically trigger pharmacologic treatment, they strongly suggest that such findings should not be regarded as incidental. In selected patients, early worsening of E/e′, reduction in e′ velocity, progressive diastolic dysfunction grade, or abnormal deformation-based diastolic markers may justify earlier referral to cardio-oncology, reassessment of cumulative anthracycline exposure, optimization of blood pressure and metabolic risk factors, and consideration of cardioprotective therapy before a clinically significant fall in LVEF occurs (Hochstadt et al., 2020; Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020). In this sense, diastolic dysfunction may function as an early warning signal that enables a more proactive rather than reactive clinical approach.

The review also highlights that not all diastolic markers appear equally useful. Conventional parameters such as E/A ratio, deceleration time, and IVRT were informative in many studies, but their sensitivity in very early follow-up was not consistent (Appel et al., 2011; Boyd et al., 2017; Mizia-Stec et al., 2013; Serrano et al., 2015; Stoodley et al., 2013; Yaylali et al., 2016). Appel et al. (2011), for example, found only a marginal short-term reduction in E/A ratio and no clinically relevant early changes in other conventional or tissue Doppler indices after low-dose epirubicin. By contrast, newer parameters seemed more promising in detecting subtle subclinical dysfunction. Early diastolic strain rate in Boyd et al. (2017), diastolic strain time in Hochstadt et al. (2020), left atrial strain in Emerson et al. (2024), and IVP in Huang, Fan, et al. (2023) all appeared capable of identifying early abnormalities that might not be fully appreciated using routine indices alone. This suggests

that the future clinical role of diastolic assessment in cardio-oncology may depend not only on whether diastolic dysfunction occurs, but also on which specific imaging marker is used (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023).

At the same time, the available evidence does not support the conclusion that diastolic dysfunction should replace GLS or other established surveillance markers. A more balanced interpretation is that diastolic dysfunction should be considered a complementary and potentially early marker of anthracycline-induced myocardial injury. In some patients it may precede overt systolic abnormalities; in others it may accompany them or provide additional phenotypic information about the pattern of myocardial dysfunction. This interpretation is better supported by the literature than the stronger claim that diastolic dysfunction is universally earlier or superior to GLS (Boyd et al., 2017; Huang, Rankin, et al., 2025; Serrano et al., 2023; Upshaw et al., 2020). Indeed, the heterogeneity of results across studies suggests that the most effective surveillance strategy may ultimately involve integration of systolic and diastolic measures rather than reliance on a single parameter (Huang, Rankin, et al., 2025; Upshaw et al., 2020; Zhang et al., 2018).

Another important practical implication concerns the expanding role of modern echocardiographic techniques. The reviewed studies indicate a shift from a purely LVEF-based model of surveillance toward a broader and more sensitive imaging framework that includes myocardial deformation, atrial mechanics, and indices of myocardial stiffness (Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Stoodley et al., 2013; Zhang et al., 2018). This evolution is particularly relevant in breast cancer survivors, in whom long-term cardiovascular risk is increasingly recognized (Bray et al., 2024; Lyon et al., 2022; World Health Organization, 2025). If future studies confirm the prognostic value of newer diastolic markers, these methods may become useful for refining risk stratification and tailoring follow-up intensity according to the degree of subclinical myocardial injury. Such an approach would be particularly valuable in patients exposed to cumulative anthracycline doses, combination regimens, or additional cardiovascular risk factors (Huang, Rankin, et al., 2025; Lyon et al., 2022; Upshaw et al., 2020).

This review has several limitations. First, the included studies were heterogeneous with respect to sample size, chemotherapy regimen, timing of echocardiography, and definitions of abnormal diastolic function (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018). Second, some studies focused primarily on conventional parameters, whereas others used advanced deformation-based techniques, which limits direct comparability (Appel et al., 2011; Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Stoodley et al., 2013; Zhang et al., 2018). Third, not all studies used the same definitions of cardiotoxicity or the same relationship between diastolic endpoints and clinical outcomes (Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Upshaw et al., 2020). Finally, several cohorts included mixed exposure patterns, particularly anthracyclines combined with trastuzumab, which may complicate attribution of observed abnormalities to anthracyclines alone (Huang, Rankin, et al., 2025; Timóteo et al., 2019; Upshaw et al., 2020; Zhang et al., 2018). These methodological differences precluded quantitative synthesis and require cautious interpretation of the findings.

Despite these limitations, the overall pattern of evidence supports the clinical relevance of diastolic assessment in anthracycline-treated breast cancer patients (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Huang, Rankin, et al., 2025; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018). Earlier recognition of subclinical diastolic abnormalities may have practical value by prompting intensified surveillance, earlier specialist evaluation, and consideration of cardioprotective measures before overt systolic dysfunction develops. Therefore, diastolic dysfunction should not be viewed merely as a secondary echocardiographic observation, but rather as a potentially useful component of contemporary cardio-oncology monitoring. Future prospective studies should determine which diastolic parameters are the most reproducible, which are the earliest to change, and whether acting on such abnormalities improves long-term cardiac outcomes (Huang, Rankin, et al., 2025; Lyon et al., 2022; Upshaw et al., 2020).

Conclusions

The available evidence suggests that diastolic dysfunction is a relevant and potentially early manifestation of anthracycline-induced cardiotoxicity in breast cancer patients. Across the reviewed studies, abnormalities in conventional Doppler and tissue Doppler parameters, as well as in newer imaging markers such as diastolic strain rate, diastolic strain time, left atrial strain, and intrinsic wave velocity propagation, were observed even when left ventricular ejection fraction remained preserved (Boyd et al., 2017; Emerson et al., 2024; Hochstadt et al., 2020; Huang, Fan, et al., 2023; Mizia-Stec et al., 2013; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020; Yaylali et al., 2016; Zhang et al., 2018). These findings indicate that diastolic impairment may help identify subclinical myocardial injury at a stage earlier than overt systolic dysfunction (Boyd et al., 2017; Emerson et al., 2024; Huang, Rankin, et al., 2025; Serrano et al., 2015, 2023; Stoodley et al., 2013; Timóteo et al., 2019; Upshaw et al., 2020).

From a practical clinical perspective, this may be highly important. Earlier recognition of diastolic abnormalities may support closer cardio-oncology surveillance, improve risk stratification, and help identify patients who could benefit from earlier specialist evaluation, optimization of cardiovascular risk factors, and consideration of cardioprotective therapy before a clinically significant decline in LVEF occurs (Huang, Rankin, et al., 2025; Lyon et al., 2022; Serrano et al., 2015, 2023; Upshaw et al., 2020). At the same time, the current evidence supports viewing diastolic dysfunction not as a replacement for established surveillance markers such as GLS, but rather as a complementary and potentially early marker that may strengthen contemporary echocardiographic monitoring strategies (Huang, Rankin, et al., 2025; Lyon et al., 2022; Upshaw et al., 2020). Further prospective studies are needed to determine which diastolic parameters are the most sensitive, reproducible, and clinically actionable, and whether earlier intervention based on these abnormalities improves long-term cardiac outcomes in breast cancer survivors (Bray et al., 2024; Lyon et al., 2022; World Health Organization, 2025).

REFERENCES

1. Appel, J. M., Sogaard, P., Mortensen, C. E., Skagen, K., & Nielsen, D. L. (2011). Tissue-Doppler assessment of cardiac left ventricular function during short-term adjuvant epirubicin therapy for breast cancer. *Journal of the American Society of Echocardiography, 24*(2), 200–206. https://doi.org/10.1016/j.echo.2010.12.004
2. Boyd, A., Stoodley, P., Richards, D., Hui, R., Harnett, P., Vo, K., Marwick, T., & Thomas, L. (2017). Anthracyclines induce early changes in left ventricular systolic and diastolic function: A single centre study. *PLOS ONE, 12*(4), e0175544. https://doi.org/10.1371/journal.pone.0175544
3. Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians, 74*(3), 229–263. https://doi.org/10.3322/caac.21834
4. Emerson, P., Stefani, L., Boyd, A., Richards, D., Hui, R., Altman, M., & Thomas, L. (2024). Alterations in left atrial strain in breast cancer patients immediately post anthracycline exposure. *Heart, Lung and Circulation, 33*(5), 684–692. https://doi.org/10.1016/j.hlc.2023.06.864
5. Hochstadt, A., Arnold, J., Rosen, R., Sherez, C., Sherez, J., Mor, L., Derakhshesh, M., Moshkovits, Y., Merdler, I., Arbel, Y., Kapusta, L., Rozenbaum, Z., Topilsky, Y., & Laufer-Perl, M. (2020). Diastolic strain time as predictor for systolic dysfunction among patients with active breast cancer. *Echocardiography, 37*(11), 1890–1896. https://doi.org/10.1111/echo.14791
6. Huang, F., Rankin, K., Sooriyakanthan, M., Signorile, M., Fan, C.-P. S., Thampinathan, B., Marwick, T. H., Osataphan, N., Yu, C., Koch, C. A., Amir, E., Hanneman, K., Abdel-Qadir, H., Wintersperger, B. J., & Thavendiranathan, P. (2025). Phenotypes of myocardial dysfunction on serial echocardiography and CMR in women with early-stage breast cancer. *JACC: Cardiovascular Imaging, 18*(5), 540–553. https://doi.org/10.1016/j.jcmg.2024.12.010
7. Huang, X., Fan, X.-Y., Cheng, Q., Zhang, J., Sun, J., Tang, Q.-Y., Deng, Y.-B., & Bi, X.-J. (2023). Intrinsic wave velocity propagation: A novel parameter for assessing the effect of anthracycline chemotherapy agents on cardiac diastolic function in breast cancer patients. *Current Medical Science, 43*(6), 1229–1237. https://doi.org/10.1007/s11596-023-2807-5
8. Lyon, A. R., López-Fernández, T., Couch, L. S., Asteggiano, R., Aznar, M., Bergler-Klein, J., Boriani, G., Cardinale, D., Castiglione, M., Čelutkienė, J., Cottin, Y., Dent, S., Dilaveris, P. E., Farmakis, D., López-Sendón, J. L., Ky, B., Lambrinou, E., Lenneman, C., Maack, C., . . . ESC Scientific Document Group. (2022). 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). *European Heart Journal, 43*(41), 4229–4361. https://doi.org/10.1093/eurheartj/ehac244

9. Mizia-Stec, K., Gościńska, A., Mizia, M., Haberka, M., Chmiel, A., Poborski, W., & Gąsior, Z. (2013). Anthracycline chemotherapy impairs the structure and diastolic function of the left ventricle and induces negative arterial remodelling. *Kardiologia Polska, 71*(7), 681–690. https://doi.org/10.5603/KP.2013.0154
10. Nagueh, S. F., Appleton, C. P., Gillebert, T. C., Marino, P. N., Oh, J. K., Smiseth, O. A., Waggoner, A. D., Flachskampf, F. A., Pellikka, P. A., & Evangelista, A. (2009). Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Journal of the American Society of Echocardiography, 22*(2), 107–133. https://doi.org/10.1016/j.echo.2008.11.023
11. Plana, J. C., Galderisi, M., Barac, A., Ewer, M. S., Ky, B., Scherrer-Crosbie, M., Ganame, J., Sebag, I. A., Agler, D. A., Badano, L. P., Banchs, J., Cardinale, D., Carver, J., Cerqueira, M., DeCara, J. M., Edvardsen, T., Flamm, S. D., Force, T., Griffin, B. P., . . . Lancellotti, P. (2014). Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: A report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography, 27*(9), 911–939. https://doi.org/10.1016/j.echo.2014.07.012
12. Serrano, J. M., González, I., Del Castillo, S., Muñiz, J., Morales, L. J., Moreno, F., Jiménez, R., Cristóbal, C., Graupner, C., Talavera, P., Curcio, A., Martínez, P., Guerra, J. A., & Alonso, J. J. (2015). Diastolic dysfunction following anthracycline-based chemotherapy in breast cancer patients: Incidence and predictors. *The Oncologist, 20*(8), 864–872. https://doi.org/10.1634/theoncologist.2014-0500
13. Serrano, J. M., Mata, R., González, I., Del Castillo, S., Muñiz, J., Morales, L. J., Espinosa, M. J., Moreno, F., Jiménez, R., Cristobal, C., Graupner, C., Talavera, P., Gutierrez Landaluce, C., Curcio, A., Alonso, J., Guerra, J. A., & Alonso, J. J. (2023). Early and late onset cardiotoxicity following anthracycline-based chemotherapy in breast cancer patients: Incidence and predictors. *International Journal of Cardiology, 382*, 52–59. https://doi.org/10.1016/j.ijcard.2023.04.026
14. Stoodley, P. W., Richards, D. A. B., Boyd, A., Hui, R., Harnett, P. R., Meikle, S. R., Clarke, J. L., & Thomas, L. (2013). Altered left ventricular longitudinal diastolic function correlates with reduced systolic function immediately after anthracycline chemotherapy. *European Heart Journal–Cardiovascular Imaging, 14*(3), 228–234. https://doi.org/10.1093/ehjci/jes139
15. Timóteo, A. T., Moura Branco, L., Filipe, F., Galrinho, A., Rio, P., Portugal, G., Oliveira, S., & Ferreira, R. C. (2019). Cardiotoxicity in breast cancer treatment: What about left ventricular diastolic function and left atrial function? *Echocardiography, 36*(10), 1806–1813. https://doi.org/10.1111/echo.14487
16. Upshaw, J. N., Finkelman, B., Hubbard, R. A., Smith, A. M., Narayan, H. K., Arndt, L., Domchek, S., DeMichele, A., Fox, K., Shah, P., Clark, A., Bradbury, A., Matro, J., Adusumalli, S., Carver, J. R., & Ky, B. (2020). Comprehensive assessment of changes in left ventricular diastolic function with contemporary breast cancer therapy. *JACC: Cardiovascular Imaging, 13*(1 Pt 2), 198–210. https://doi.org/10.1016/j.jcmg.2019.07.018
17. World Health Organization. (2025, August 14). *Breast cancer*. https://www.who.int/news-room/fact-sheets/detail/breast-cancer
18. Yaylali, Y. T., Saricopur, A., Yurtdas, M., Senol, H., & Gokoz-Dogu, G. (2016). Atrial function in patients with breast cancer after treatment with anthracyclines. *Arquivos Brasileiros de Cardiologia, 107*(5), 411–419. https://doi.org/10.5935/abc.20160146
19. Zhang, K. W., Finkelman, B. S., Gulati, G., Narayan, H. K., Upshaw, J., Narayan, V., Plappert, T., Englefield, V., Smith, A. M., Zhang, C., Hundley, W. G., & Ky, B. (2018). Abnormalities in 3-dimensional left ventricular mechanics with anthracycline chemotherapy are associated with systolic and diastolic dysfunction. *JACC: Cardiovascular Imaging, 11*(8), 1059–1068. https://doi.org/10.1016/j.jcmg.2018.01.015