Title

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Journal

Breast Cancer Research and Treatment, 186(2)

ISSN

0167-6806

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Publication Date

2021-04-01

DOI

10.1007/s10549-021-06096-9

Peer reviewed

Breast Cancer Research and Treatment (2021) 186:295–303
https://doi.org/10.1007/s10549-021-06096-9

REVIEW

Heart failure prevention and monitoring strategies in HER2-positive breast cancer: a narrative review

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Received: 7 December 2020 / Accepted: 5 January 2021 / Published online: 22 January 2021

Abstract

Purpose Cardiotoxicity from anti-human epidermal growth factor receptor 2 (HER2) therapy carries a short- and long-term risk of incident heart failure and increased cardiovascular mortality in patients with breast cancer. Interruptions in anti-HER2 therapy due to cardiotoxicity can lead to suboptimal cancer treatment. The purpose of this narrative review is to outline opportunities to optimize cardiovascular care in patients with HER2-positive breast cancer to prevent interruptions in therapy.

Methods This case-based review presents the current literature on evidence-based strategies for personalized cardiotoxicity risk assessment, risk mitigation interventions, cardiac function surveillance tools, and management of asymptomatic left ventricular dysfunction in breast cancer patients receiving anti-HER2 therapy.

Results Pretreatment cardiac risk assessment incorporates both treatment-related risk factors and patient-related risk factors for the development of cardiac dysfunction. Prevention and monitoring strategies while on treatment utilize risk factor modification, imaging and biomarker surveillance. Management of asymptomatic left ventricular dysfunction due to anti-HER2 therapy is evolving. Permissive cardiotoxicity in asymptomatic patients while starting cardioprotective therapies requires close collaboration between oncology and cardiology, and referral to cardio-oncology if available.

Conclusions Patient-centered, multimodal strategies to prevent, detect, and manage cardiotoxicity from anti-HER2 therapy are necessary to improve outcomes in patients with HER2-positive breast cancer.

Keywords HER2-positive · Breast cancer · Cardiotoxicity · Trastuzumab

Introduction

Over 3.8 million breast cancer survivors are estimated to be living in the US [1]. In 2020, an estimated 276,480 new invasive breast cancer cases are expected in US women [2], and approximately 15% primary invasive breast cancers overexpress the human epidermal growth factor receptor 2 (HER2) protein [3]. Furthermore, cardiovascular disease (CVD) is highly prevalent and with significant contribution to morbidity and mortality in the US [4]. CVD-related mortality is higher in older woman who are breast cancer survivors than in women without a history of breast cancer [5, 6]. Moreover, older women who survive 5 years after the diagnosis of early-stage breast cancer are more likely to die from CVD than breast cancer [7]. Therefore, complications of breast cancer treatment on cardiovascular health are becoming increasingly important to understand and prevent.

Cancer therapy-related cardiotoxicity has a significant impact on a patient's ability to receive optimal cancer treatment. Anthracyclines, anti-human epidermal growth factor receptor 2 (HER2) agents (i.e., trastuzumab, pertuzumab), breast radiation, and hormonal therapies are all integral components of breast cancer treatment that carry both a short-term and long-term increased risk of heart failure [8–10]. Several newer treatments have been developed for breast cancer which carry additional arrhythmic, metabolic, and inflammatory toxicities, including CDK 4/6 inhibitors which cause QTc prolongation, PI3K inhibitors which cause hyperglycemia, and immunotherapies [8, 11]. Nearly 20% of patients on trastuzumab may experience an interruption in trastuzumab therapy due to cardiac toxicity [12]. However, interruption of trastuzumab therapy has been associated

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with poorer recurrence free survival in patients with HER2-positive breast cancer [13].

The current consensus guidelines from the American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), and European Society of Cardiology (ESC) recommend a comprehensive patient-centered approach for the prevention cardiac dysfunction in patients receiving cancer therapy. After first identifying patients at risk for cancer therapy-related cardiotoxicity, prevention and monitoring strategies should be implemented before, during, and after cancer therapy [14–16]. We present a case-based narrative review that highlights evidence-based strategies for risk assessment, prevention, monitoring, and treatment of new-onset heart failure from anti-HER2-based treatment.

Clinical presentation part 1: baseline risk assessment

A 74-year-old Caucasian women is diagnosed with estrogen receptor-positive and HER2-positive left-sided invasive ductal carcinoma. She underwent a left segmental mastectomy and sentinel lymph node biopsy. Her oncology treatment is to begin adjuvant TH (docetaxel [Taxotere], trastuzumab [Herceptin]) and radiotherapy. She has a history of hypertension, dyslipidemia, and non-obstructive coronary artery disease. She is currently taking aspirin 81 mg daily, lisinopril 20 mg daily, and hydrochlorothiazide 25 mg daily. The patient declined statin therapy in the past. She has a 10 pack-year history of smoking and has a family history of heart failure. Due to concern about the long-term cardiac complications of her anticancer therapy, the patient presented for cardiac evaluation prior to initiation of treatment.

What is this patient's risk of trastuzumab-related cardiac dysfunction?

When approaching a baseline risk assessment for cardiotoxicity from trastuzumab therapy, it is important to consider both treatment-related risk factors and patient-related risk factors for the development of cardiac dysfunction. Treatment-related risk factors include consideration of drug selection (anthracycline vs. non-anthracycline-based regimen), prior remote anthracycline and/or chest radiation exposure, and prior trastuzumab cardiotoxicity. Patient-related factors include demographic factors (i.e., age), lifestyle factors, pre-existing cardiovascular disease risk factors, and prior anticancer therapy exposure [17, 18]. Common treatment- and patient-related risk factors for cardiotoxicity with anti-HER2 therapies are listed in Table 1.

Chemotherapy regimen selection and dose exposure

Trastuzumab is a humanized monoclonal antibody that binds to the extracellular domain of the human epidermal growth factor 2 (HER2) receptor and inhibits the proliferation of HER2-positive cancer cells. The biologic agent has been shown to reduce recurrence rates and improve survival in HER2-positive breast cancer patients in both early and late-stage disease.{Romond, 2005 #1} [19–21] Trastuzumab, on the other hand, produces myocardial dysfunction in a manner that is generally reversible and not related to cumulative dose [22]. The mechanism of trastuzumab-mediated cardiotoxicity is thought to be due to disruption of the ErbB2 signaling that is responsible for cell growth and repair, which promotes LV dysfunction [23]. Changes in ErbB signaling also lead to LV remodeling and the development of a dilated cardiomyopathy [24]. Cardiotoxicity is manifested as asymptomatic or symptomatic left ventricular (LV) dysfunction [25, 26]. Initial trials of trastuzumab reported an incidence of trastuzumab-related cardiac dysfunction up to 27% in the setting of concurrent administration of anthracycline and trastuzumab [27]. Subsequent clinical trials of sequential administration (trastuzumab given after anthracycline) reported an incidence of symptomatic trastuzumab-related cardiac dysfunction of approximately 4% [28, 29]. However, other studies suggest that at 1 year of trastuzumab therapy, an estimated

Table 1 Risk factors for cardiotoxicity on trastuzumab therapy [15, 17, 18]

Patient-related	Treatment-related
Age (> 65 years	Prior/serial anthracycline-based treatment
Obesity (BMI > 30 kg/m2)	Prior high-dose chest radiotherapy
Smoking (current/prior)	Prior trastuzumab cardiotoxicity
Hypertension	
Hyperlipidemia	
Diabetes Mellitus	
Coronary Artery Disease/Prior MI	
Low Baseline/post-anthracycline LVEF	
Severe valvular disease	

LVEF Left Ventricular Ejection Fraction, *MI* Myocardial Infarction

25% of patients with prior anthracycline exposure and 10% of patients without prior anthracycline exposure will develop LV dysfunction [15]. In a prospective study of 222 patients with early-stage HER2-positive breast cancer receiving adjuvant anthracyclines followed trastuzumab, independent predictors of trastuzumab-related cardiotoxicity include a lower baseline (pre-anthracycline) left ventricular ejection fraction (LVEF) and a greater interval decline in LVEF from pre- to post-anthracycline therapy [30]. Therefore, the decision of whether to recommend an anthracycline versus non-anthracycline-based treatment regimen has a significant impact on a patient's risk of trastuzumab-related cardiotoxicity. Cumulative dose of exposure may have an impact on risk of cardiotoxicity, as some studies suggest longer duration of treatment with trastuzumab is associated higher rates of cardiac toxicity [31]. In contrast to early-stage breast cancer, in which trastuzumab is typically administered in the adjuvant setting for 12 months, patients with metastatic breast cancer often require years of trastuzumab therapy. This longer exposure can partially explain the higher risk of cardiotoxicity seen in trastuzumab trials of patients with metastatic disease in comparison to adjuvant trials [15]. Newer anti-HER2 monoclonal antibody therapies (pertuzumab, margetuximab), antibody–drug conjugates (ado-trastuzumab, fam-trastuzumab) and the oral tyrosine kinase inhibitors (lapatinib, neratinib, tucatinib) do not appear to have as high a risk of cardiotoxicity as trastuzumab (Table 2) [15, 32–43].

Table 2 Cardiotoxicity of anti-HER2 therapies in adjuvant breast cancer treatment

	LVD	CHF	References
Monoclonal antibodies			
Trastuzumab (Herceptin)	5–10%	0.4–4%	[15, 34, 35]
Trastuzumab and hyaluronidase injection (Herceptin Hylecta)		0.4–3.2%	[36]
Pertuzumab (Perjeta)	4.4%	1%	[37]
Margetuximab (Margenza)	1.9%	–	[38]
Antibody–drug conjugates			
Ado-trastuzumab (Kadcyla)	0.4–1.8%	–	[39]
Fam-trastuzumab (Enhertu)	–	–	[40]
Tyrosine kinase inhibitors			
Lapatinib (Tykerb)	0.01–0.04%	0.005–0.009%	[41]
Neratinib (Nerlynx)	–	–	[42]
Tucatinib (Tukysa)	–	–	[43]

LVD Left Ventricular Dysfunction, *CHF* Congestive Heart Failure

Cardiovascular risk factor profile

Cardiovascular risk factors that increase the likelihood of developing trastuzumab-induced cardiotoxicity include older age, low baseline ejection fraction, hypertension (HTN), smoking, diabetes mellitus (DM), and hyperlipidemia (HL) [14, 27]. Therefore, thorough screening for existing cardiovascular risk factors is essential to inform a baseline risk assessment for treatment-related cardiotoxicity. Furthermore, a baseline echocardiogram is recommended to assess baseline LV function [14–16].

Risk prediction models

There is early work in developing risk prediction models in breast cancer patients to aid clinicians in performing a baseline cardiovascular risk assessment. Ezaz et al. developed a 7-factor model from a cohort of 1664 older women (mean age 73 years) with stage 1–3 breast cancer who received adjuvant trastuzumab to predict the 3 years of heart failure or cardiomyopathy. Factors included age, adjuvant chemotherapy, coronary artery disease, atrial fibrillation or flutter, DM, HTN, and renal failure. The models are classified by strata into low, medium, and high 3 years for heart failure/cardiomyopathy with rates of 16.2%, 26%, and 39.5%, respectively [44]. Abdel-Qadir et al. developed a score to predict the 5-year and 10-year risk of major adverse cardiovascular events (MACE) using registry data of 90, 104 women with early-stage breast cancer in Canada. Factors incorporated in the score include age, HTN, DM, ischemia heart disease, atrial fibrillation, heart failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, and chronic kidney disease [45]. The 10-year risk of MACE was great than 40-fold higher in the highest score decile in comparison to the lower. However, major limitations to these risk scores are the lack of quality external validation and the lack of generalizability to racial minorities, as the patient population used to develop them were predominantly white patients.

Risk summary statement *This patient's old age and several pre-existing cardiovascular risk factors (HTN, HL, prior tobacco) put her at higher risk to develop trastuzumab-related cardiac dysfunction. If accessible, this patient should be referred to cardio-oncology for optimal management.*

Clinical presentation part 2: risk mitigation Strategies & monitoring

Her body mass index is 26.5 kg/m2. Her blood pressure is 148/84 mmHg and the patient reports home blood pressure readings ranging 140–160/80 mmHg. Her examination of

cardiovascular and pulmonary is normal. Her lipid panel is as follows: total cholesterol 209 mg/dl; triglycerides 161 mg/dl, high-density lipoprotein 52 mg/dl; low-density lipoprotein 125 mg/dl. Her hemoglobin A1c is 5.9%. She has a baseline left ventricular ejection fraction (LVEF) of 63% and GLS -19.4%.

What prevention and monitoring strategies should be used for this patient?

Pretreatment cardiovascular risk status is an important prognostic indicator for future cardiac toxicity [14]. Therefore, it is paramount to optimize and closely monitor comorbid cardiovascular risk factors prior and during treatment in effort to prevent cardiotoxicity, including blood pressure, lipid levels, and blood glucose levels. However, there is a paucity of research on prevention interventions, both pharmacologic and lifestyle strategies, in this patient population, underlying an area of significant need for future research.

Blood pressure management

For pre-existing HTN, blood pressure treatment target should follow the current ACC/AHA guidelines of less than 130/80 mmHg [46]. The optimal blood pressure medication for patients with pre-existing HTN on trastuzumab is not well established. However, there are limited data in patients on trastuzumab treated with angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), and selected beta blockers (BBs), suggesting a benefit in preventing cardiotoxicity. MANTICORE-101 Breast (Multidisciplinary Approach to Novel Therapies in Cardiology Oncology Research), a randomized primary prevention study of perindopril, bisoprolol, or placebo in 94 patients receiving trastuzumab found that both perindopril and bisoprolol groups had less cancer therapy-related cardiac dysfunction (CTRCD) and less interruptions in therapy compared to placebo. However, the primary outcome of trastuzumab-mediated LV remodeling was not prevented by these pharmacotherapies [47]. The most recent largest randomized study by Guglin et al. to evaluate primary prevention in breast cancer evaluated lisinopril, carvedilol, or placebo in 468 women receiving 12 months of trastuzumab with and without anthracycline use. While lisinopril and carvedilol prevented cardiotoxicity in the group receiving trastuzumab with serial anthracycline use, a benefit of lisinopril or carvedilol in the trastuzumab-only group was not observed [48]. Larger randomized trials powered to detect a treatment effect are needed [49].

Lipid management

Regarding lipid management, current ACC/AHA guidelines should be applied to guide management for those with clinical atherosclerotic cardiovascular disease (ASCVD) or at increased risk for ASCVD as determined by the pooled-cohort equation (PCE) [50]. However, the PCE does not take into account the multiplicative impact of cardiovascular risk factors in the setting of cardiotoxic medications, therefore personalized risk assessment is needed when considering statin therapy in those receiving cardiotoxic medications [51]. There are data to suggest that statin therapy may be beneficial to prevent cardiotoxicity in patients with breast cancer receiving anthracyclines [15, 52, 53], and a prospective randomized trial to assess if atorvastatin is protective during anthracycline-based treatment for breast cancer is currently underway (PREVENT study, NCT01988571) [54]. However, data on the efficacy of statin use to prevent cardiotoxicity prior, during, or after treatment in patients with breast cancer receiving trastuzumab are lacking.

Lifestyle management

Patients should be counseled on a heart-healthy lifestyle, including diet and exercise. The American Cancer Society recommends 150 min of moderate intensity or 75 min of vigorous intensity exercise per week for adult cancer patients. A large, prospective, observational study of women with nonmetastatic breast cancer found that adherence to guideline-recommend exercise ($\geq$ 9 MET-h/week) was associated with an adjusted 23% reduction in the risk CV events, including in older patients and those with pre-existing CV risk factors [55]. Side effects of cancer treatment, including fatigue and nausea, may impact a patient's ability to adhere a heart-healthy lifestyle during active treatment. The AHA recommends the development of multimodal cardio-oncology rehabilitation programs in order to provide a structured approach to exercise and lifestyle interventions in cancer patients [56].

Imaging-based surveillance for cardiotoxicity

Surveillance imaging of cardiac function is recommended in patients at risk for therapy-related cardiotoxicity [14–16]. In patients receiving trastuzumab therapy, assessment of LVEF is currently recommended at a minimum of every 3 months. However, this is based on clinical trial design and it is unclear if this is the optimal frequency for patients. Modification of cardiac surveillance frequency has been proposed by pretreatment risk [57] and by symptoms during the COVID-19 pandemic, with delay or lengthened intervals for echocardiograms in asymptomatic breast cancer patients in stable condition [58].

Imaging modalities without radiation are preferred to multigated acquisition (MUGA) scan, including echocardiography and cardiac magnetic resonance imaging [15]. An additional benefit of echocardiography is the ability to obtain myocardial deformation imaging to detect subclinical cardiac dysfunction. In patient on trastuzumab therapy, trending change in global longitudinal strain (GLS) is superior for predicting future cardiotoxicity than changes in LVEF, especially in those on serial therapy with anthracycline followed by trastuzumab. Abnormal GLS typically predates reductions in LVEF in this patient cohort and may provide an important window to implement cardioprotective medication to prevent LV dysfunction and interruption of trastuzumab therapy [15, 59–61]. In the SUCCOUR trial, 331 anthracycline-treated breast cancer patients were assigned to a strain-guided vs. EF-guided strategy for the development of CTRCD (symptomatic EF reduction > 5% or > 10% asymptomatic to < 55%) [62]. Although there was no difference in LVEF between arms at 1 year, fewer patients in the GLS-guided arm met criteria for CTRCD (5.8% vs. 13.7%, p = 0.02), and thus supporting the use of GLS for surveillance of CTRD [63].

Biomarker-based surveillance for cardiotoxicity

Cardiac biomarkers, including troponin and natriuretic peptides, in patients on trastuzumab have shown variable association with cardiotoxicity and have primarily been studied in patients also receiving anthracyclines. Elevations of Troponin I and T measured before and after administration of trastuzumab have been shown to identify those who are at higher risk for cardiotoxicity and less likely to recover cardiac dysfunction [64, 65]. Fewer studies have looked at the use of BNP or NT-proBNP in patients on trastuzumab, and demonstrate mixed results. Therefore, there is no recommendation for baseline cardiac biomarker assessment in patients on trastuzumab by major oncology societies [14, 15].

Prevention and monitoring summary statement *The patient was given a blood pressure goal of < 130/80 mmHg. Initially her lisinopril was increased to 40 mg daily, and subsequently carvedilol was added due to suboptimal blood pressure control. The patient was advised to start statin therapy, but she declined due to personal preference. The patient was given diet and exercise counseling. Her cardiac function monitoring plan was serial echocardiography with GLS every 3 months while on trastuzumab.*

Clinical presentation part 3: asymptomatic left ventricular dysfunction management

The patient was monitored with serial echocardiography with GLS, and after 3 months of trastuzumab therapy her left ventricular ejection fraction fell from 63 to 52% with corresponding reduction in GLS from -19.4% to -17.8%. The patient denied symptoms of heart failure including dyspnea, orthopnea, or lower extremity edema. Her examination of cardiovascular and pulmonary was normal without evidence of volume overload.

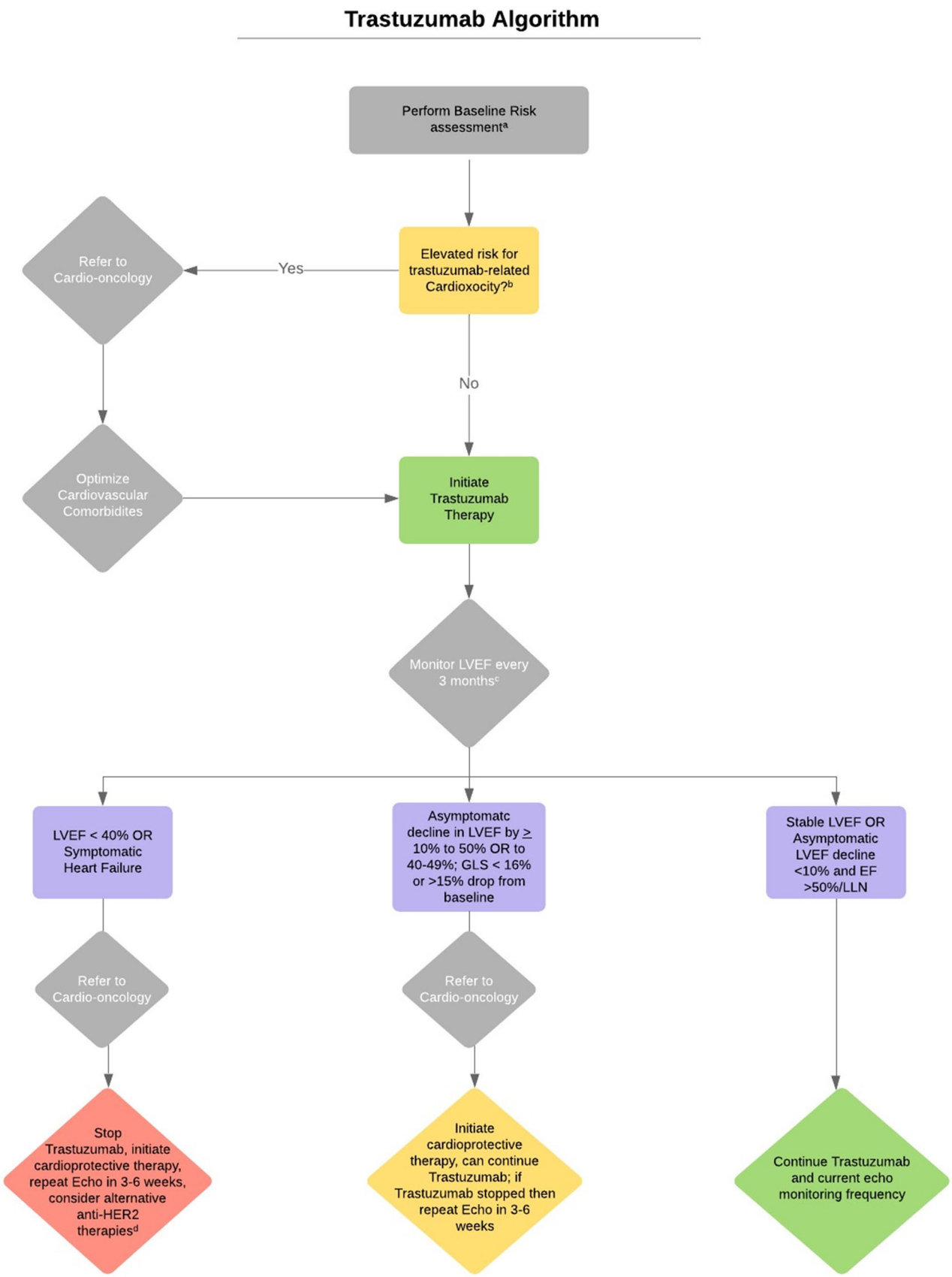
Does this patient have CTRCD? can she continue trastuzumab therapy?

Multiple definitions of CTRCD have been proposed, with a unifying element of decline in cardiac function, with different definition criteria [8]. Criteria proposed by the American Society of Echocardiography (ASE) included a decrease of LVEF of > 10 percentage points to a value of < 53%, which is generally comparable to previous definitions [15, 66].

Management of asymptomatic trastuzumab-related cardiotoxicity

Management of asymptomatic trastuzumab-related cardiotoxicity is summarized in Fig. 1. After identification of CTRCD, in asymptomatic patients with significant reductions in LVEF, it is important to recognize they have stage B HF and should be treated with HF-specific medications per the ACC/AHA guidelines [15, 67, 68].

Original guidelines recommended stopping trastuzumab if LVEF falls ≥ 10% below baseline and below the lower limit of normal (LLN) or LVEF drop ≥ 16% from baseline [19]. A retrospective, observational analysis of patients on trastuzumab therapy with asymptomatic decline in LVEF to < 50% (median LVEF nadir of 43%) found no difference in final LVEF (median follow-up 633 days) between groups in whom trastuzumab was continued and in those it was interrupted [69] Furthermore, SCHOLAR, a recent Phase 1 prospective trial of 20 patients with mild trastuzumab-related cardiotoxicity (asymptomatic drop in LVEF between 40% and the LLN or ≥ 15% from baseline) treated with ACE-I and/or BB therapy found 90% participants were able to complete all planned trastuzumab doses without developing cardiac dose-limiting toxicity (defined as cardiovascular death, LVEF < 40% with any heart failure symptoms, or LVEF < 35%) [70]. Also, the SAFE-HEaRt Study, a prospective trial of 31 patients with an LVEF between 40 and 49% on HER2-targeted therapies and cardioprotective medications (BB, ACE-I, ARB therapy), found that 90% of patients completed the planned HER2-targeted therapy


Trastuzumab Algorithm
Perform Baseline Risk assessment[a]
Elevated risk for trastuzumab-related Cardioxocity?[b]
Yes
Refer to Cardio-oncology
No
Optimize Cardiovascular Comorbidites
Initiate Trastuzumab Therapy
Monitor LVEF every 3 months[c]
LVEF < 40% OR Symptomatic Heart Failure
Asymptomatc decline in LVEF by ≥ 10% to 50% OR to 40-49%; GLS < 16% or >15% drop from baseline
Stable LVEF OR Asymptomatic LVEF decline <10% and EF >50%/LLN
Refer to Cardio-oncology
Refer to Cardio-oncology
Stop Trastuzumab, initiate cardioprotective therapy, repeat Echo in 3-6 weeks, consider alternative anti-HER2 therapies[d]
Initiate cardioprotective therapy, can continue Trastuzumab; if Trastuzumab stopped then repeat Echo in 3-6 weeks
Continue Trastuzumab and current echo monitoring frequency

◂**Fig. 1** Trastuzumab Algorithm. Incorporating a baseline risk assessment to every breast cancer patient undergoing anti-HER2 therapy is part of optimal management. Cardiac surveillance resulting in overt heart failure or permissive cardiotoxicity requires to be referred to a cardio-oncology clinic. **a** Baseline risk assessment includes a baseline assessment of LV function, traditional cardiovascular risk factors and concomitant cardiotoxicity chemotherapy, radiotherapy or other anticancer therapies. b Elevated risk for cardiotoxicity in non-anthracycline trastuzumab-based regimens includes the addition to ≥ 2 cardiovascular risk factors (smoking, HTN, DM, HL, obesity), older age (≥ 60 years) and structural heart disease at baseline (low EF, prior MI, moderate-to-severe valve disease) to trastuzumab therapy; or serial administration of trastuzumab following anthracycline. **c** The frequency of LVEF surveillance is currently recommended at a minimum of every 3 months. However, it is unclear if this is the optimal frequency for all patients. **d** Ongoing cancer-directed treatment with less cardiotoxic anti-HER2 therapies should be considered, including monoclonal antibodies against HER2 (pertuzumab, margetuximab), antibody–drug conjugates (ado-trastuzumab, fam-trastuzumab), and the oral tyrosine kinase inhibitors (lapatinib, neratinib, tucatinib)

without developing a cardiac event (HF, myocardial infarction, arrhythmia, cardiac death) or asymptomatic worsening of cardiac function (decline in LVEF > 10% from baseline or to ≤ 35%) [71]. Further randomized studies with larger cohorts and longer follow-up are needed to better understand the risk of continuing trastuzumab in the setting of asymptomatic, mild trastuzumab-related cardiotoxicity.

In asymptomatic patients on trastuzumab with an LVEF decrease to > 10% from baseline or a drop ≥ 40% but < 50%, the ESMO recommends initiation of cardioprotective medications (ACE-I, ARBs, BB) and advises if it is possible to continue trastuzumab. If trastuzumab is stopped, a repeat LVEF assessment should be completed in 3–6 weeks and re-challenge trastuzumab if LVEF returns to > 50% [15]. Given the complexity and individualized decision making required for asymptomatic reductions in LVEF, it is important to have interdisciplinary approach with cardiology and oncology involvement.

Management summary statement *The patient was identified as having CTCRD. However, she was asymptomatic and was continued on trastuzumab therapy. Her carvedilol and lisinopril doses were maximized and given ongoing elevated blood pressure readings, spironolactone replaced hydrochlorothiazide for the mineralocorticoid benefits in HF. Her EF remained stable for the duration of treatment and the echocardiogram at completion of one year of trastuzumab therapy demonstrated an ejection fraction of 69%.*

Conclusions

With the growing body of evidence for HF prevention in patients receiving anti-HER2 therapies, clinicians are able to more effectively implement HF risk mitigation strategies in patients with breast cancer. A personalized baseline HF risk assessment should be performed in patients with breast cancer prior to the initiation of anti-HER2 therapies, and those at higher risk of CTCRD should be referred to cardio-oncology if available. Risk mitigation strategies include in optimization of pre-existing cardiovascular comorbidities, counseling on a heart-healthy lifestyle, and consideration of cardioprotective medications. HF surveillance tools include cardiac imaging and biomarkers. Management of asymptomatic anti-HER2-related cardiotoxicity is rapidly evolving. Effective management of patients to prevent and treat the development cancer therapy-related cardiac dysfunction requires a close collaborative approach between cardiologists, oncologists, primary care physicians, pharmacists, dieticians, and physiotherapists, and referral to cardio-oncology if available.

Acknowledgements Drs. Jafari and Akhter have no conflict of interest to disclose.

Funding None.

Data availability Not applicable.

Code availability Not applicable.

Compliance with ethical standards

Ethical approval Not applicable.

Informed consent Not applicable.

Consent to publication Not applicable.

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