CASE STUDY

Multimodal Safeguards Against Oncological Relapse and Therapy-Induced Cardiotoxicity:

A case study

Vivian Girotto[1]

Keywords: Cardiotoxicity, Breast Cancer, Lung Cancer, Radiotherapy, Cardioprotection

ABSTRACT

Background: A 65-year-old woman had been cured of breast cancer 15 years earlier (2010) with a regimen that included doxorubicin, and despite prolonged survival, cardiac evaluation revealed preexisting subclinical myocardial dysfunction. The central challenge arose with the diagnosis of locally advanced non-small cell lung cancer in 2024, requiring thoracic radiotherapy, which presented a significant risk of worsening her previous cardiac impairment.

Objectives: The aim of this case study is to report the clinical journey of a survivor of three distinct primary neoplasms (ovary, lung and thyroid) who achieved a successful natural conception and delivery, demonstrating the viability and safety of reproductive health through rigorous multidisciplinary management.

Methods: The investigation of the patient's new condition began with respiratory symptoms, and the diagnosis of NSCLC was confirmed by chest X-ray, contrast-enhanced computed tomography, and CT-guided lung biopsy with pathological examination and immunohistochemistry. A whole-body PET/CT scan was used for staging, revealing no distant metastases. A detailed cardiac evaluation before treatment revealed borderline left ventricular ejection fraction and decreased global longitudinal strain, confirming preexisting type I cardiotoxicity. The article followed the CARE protocol for Case Studies.

Results: Given the diagnosis of NSCLC, a multidisciplinary treatment plan focused on cardio-protection was defined, with early introduction of an angiotensin-converting enzyme inhibitor and a beta-blocker before starting radiotherapy.

Conclusion: The patient completed radiotherapy for NSCLC without experiencing severe acute cardiac toxicity during treatment. The lung tumour demonstrated a good therapeutic response.

Main Contribution to Evidence-Based Practice: The main contribution of this article to evidence-based practice is the demonstration that survival of multiple primary malignancies does not preclude natural conception, establishing a multidisciplinary management model that prioritizes oncological remission, correction of infertility factors, and rigorous

International Healthcare Review (online)
●
eISSN: 2795-5567
●
How to Cite
Girotto, V. (2026). Multimodal Safeguards Against Oncological Relapse and Therapy-Induced Cardiotoxicity: A Case Study. International Healthcare Review (online). https://doi.org/10.56226/139
●
Published online: 24/February/2026
●

Corresponding Author:

Vivian Giroto
São Leopoldo Mandic College, Campinas, Brazil
vgirotto.rodrigues@gmail.com

Authors' Affiliations:
[1] São Leopoldo Mandic College, Campinas, Brazil

What do we already know about this topic?
The integration of advanced technologies (AI and biomarkers) and preventive protocols allows for early monitoring of cardiotoxicity, ensuring that the success of cancer treatment is not compromised by cardiac damage, thus promoting survival with greater quality of life and overall health..

What is the main contribution to Evidence-Based Practice from this article?
The study proposes a unified care model that uses Artificial Intelligence and continuous monitoring to simultaneously prevent cancer recurrence and heart damage, transforming theoretical guidelines into a practical and personalized protocol to improve long-term survival and quality of life.

What are this research's implications towards health policy?
The article proposes a paradigm shift by integrating oncology and cardiology into a precision medicine model. It advocates the use of advanced technologies and interdisciplinary protocols to treat cancer without compromising the heart, guiding health policies that prioritize survival with quality of life and proactive monitoring.

Authors' Contributions Statement:
Girotto, is the.main and sole author.

Introduction

Cardiotoxicity is defined as any damage to the heart or cardiovascular system that arises as a direct or indirect consequence of cancer treatments (Siegel, Giaquinto, & Jemal, 2024; Cohn, Stewart, Fajardo, & Hancock, 1967). This condition represents a significant complication that can impact patients' quality of life (QOL) and survival, especially given the increasing cure rates and longevity of cancer survivors (Walls et al., 2025).

Cardiotoxicity can manifest in various ways, affecting different cardiac structures and functions (García-Pardo et al., 2023). The mechanisms by which anticancer agents induce heart damage vary widely, with the best-known ones identified in Table 1.

Table 1. Mechanisms causing heart damage

Mechanism	Damage
Type I (Direct and Irreversible Damage)	Caused primarily by anthracyclines, they cause cardiomyocyte death through oxidative stress, DNA damage, and mitochondrial dysfunction. The damage is cumulative and often irreversible, potentially leading to cardiomyopathy and congestive heart failure (CHF).
Type II (Reversible Dysfunction)	Associated with targeted therapies such as anti-HER2 agents. Although they can cause left ventricular (LV) contractile dysfunction, there is usually no direct and widespread damage to cardiomyocytes, and the dysfunction tends to be reversible after discontinuation of the drug.
Othe Mechanisms	Agents such as tyrosine kinase inhibitors, anti-angiogenics, immunotherapeutics (checkpoint inhibitors), antimetabolites and thoracic radiotherapy (RT) can induce coronary dysfunction, pericarditis (PE), arrhythmias, hypertension (HTN) and myocardial fibrosis

Source: The author

The diagnosis of cardiotoxicity is based on clinical evaluation and additional tests, with an emphasis on regular monitoring. In the baseline assessment, it is important to detail the clinical history, physical examination, electrocardiogram (ECG), and echocardiogram (ECHO) to assess left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS), the latter capable of detecting subclinical dysfunction early. Biomarkers such as troponins (TnI or TnT) and B-type natriuretic peptide (NT-proBNP) are also useful for assessing myocardial stress and cellular damage. Periodic monitoring, with regular follow-up and frequent testing according to the risk and type of therapy used, is essential. In some cases, specific tests are necessary, such as cardiac magnetic resonance imaging (CMRI) for a more detailed assessment of ventricular function, inflammation, and fibrosis; myocardial scintigraphy (MUGA) as an alternative to ECHO (Dess et al., 2017). The incidence and prevalence of cardiotoxicity vary widely depending on the chemotherapy agent, cumulative dose, duration of treatment, patient age, comorbidities, and radiation history. Anthracyclines can cause subclinical left ventricular dysfunction can ranging from 5 to 20%, while clinical CHF can occur in 1 to 5% of patients, increasing with cumulative dose (Kimenai et al., 2022). Trastuzumab can cause left ventricular dysfunction in approximately 15 to 30% of patients, but it is usually reversible, and the incidence of severe CHF is lower, at approximately 2 to 4%. Thoracic RT may carry a risk of radiation-induced heart disease (including coronary artery disease (CAD), PE, cardiomyopathy) that can range from 10% to 30% over 10 to 20 years, depending on the dose and irradiation field (Nygård et al., 2018).

The treatment of cardiotoxicity involves strategies for prevention, mitigation, and management of established cardiac dysfunction. Dose adjustments, administration via prolonged infusions, the use of liposomal formulations, or the use of cardioprotective agents such as dexrazoxane in specific situations should be frequently considered. Techniques such as intensity-modulated radiation therapy (IMRT) or deep inspiration breath-holding (DIBH) can reduce the radiation dose to the heart. In high-risk patients or those with detected subclinical dysfunction, the early use of angiotensin-converting enzyme inhibitors (ACEI) or beta-blockers can prevent or mitigate damage and should be considered (Wang et al., 2017).

Cardiotoxicity from breast cancer treatment is a significant and growing complication, given the high prevalence of the disease and the therapeutic success that has led to improved patient survival. It refers to any type of damage to the heart or cardiovascular system that occurs as a

side effect of therapies used to combat breast cancer. The main risk factors for cardiotoxicity are the cumulative dose of chemotherapy (QT), age, preexisting cardiovascular conditions, the combination of therapies, and genetic factors (Patz et al., 2014)

Methodology

A 65-year-old retired woman was diagnosed with breast cancer 15 years ago, in May 2010. At that time, she underwent surgery (quadrantectomy) followed by chemotherapy (including doxorubicin, a chemotherapeutic agent known for its cardiotoxicity) and adjuvant RT. The treatment was successful, and the patient was considered cured of the disease. However, her LVEF was monitored and remained stable, albeit at the lower limit of normal. The purpose of LVEF monitoring was not only to assess cardiac function during treatment but also to detect any signs of subclinical cardiac damage that could lead to long-term problems, such as HF. Early detection of a decline in LVEF would allow treatment adjustments or the initiation of cardioprotective therapies.

The patient's cardiotoxicity is a preexisting subclinical myocardial dysfunction directly attributed to exposure to doxorubicin 15 years ago. This is called type I cardiotoxicity, characterised by direct and often irreversible damage to the heart's muscle cells (myocytes).

The diagnosis of cardiotoxicity was made not only by clinical history but also by objective findings, such as an LVEF at the lower limit of normal, which indicates that, although the heart was still functioning, its reserve capacity was already compromised, making it less resilient to future stressors; a decrease in global longitudinal strain, one of the most important signs, as strain measurement is a much more sensitive echocardiographic indicator than LVEF. It detects subtle changes in heart muscle deformation. The fact that the patient's strain was already decreased indicates early myocardial damage, even without a drastic drop in LVEF, and an elevation in NT-proBNP, a biomarker released by the heart in response to increased stress or stretching. Its elevation confirmed that the heart was under stress, even without symptoms of severe HF.

In April 2024, the patient sought medical attention due to a persistent cough that did not improve with conventional treatments and mild dyspnea on exertion. These symptoms, initially attributed to ageing or a respiratory infection, progressively worsened over the following month.

At the time of the consultation, several tests were ordered, including a chest X-ray, which revealed the presence of a solid mass in the lower portion of the left lung, a finding that raised the suspicion of a lung neoplasm. A chest computed

tomography (CT) scan with contrast for a more detailed evaluation confirmed the presence of a solid nodule, approximately 3.5 cm in diameter, located in the left lower lobe of the lung. The examination also revealed slightly enlarged mediastinal lymph nodes (lymphadenopathy), suggesting possible regional lymph node involvement.

A CT-guided lung biopsy was performed to obtain a definitive diagnosis. Pathological examination and immunohistochemistry were crucial in identifying Non-Small Cell Lung Carcinoma (NSCLC) (adenocarcinoma type). The immunohistochemical profile, which was negative for breast cancer markers (such as estrogen receptors, progesterone receptors, and HER2), confirmed that this was a new primary tumour and not a recurrence of breast cancer. A whole-body PET/CT scan was ordered to determine whether the cancer had spread to other parts of the body. The PET/CT confirmed high metabolic activity in the lung mass and mediastinal lymph nodes, but showed no evidence of distant metastases (in bones, liver, or brain). Laboratory tests were requested, which identified: Hemoglobin: 11.8 g/dL (slightly below normal, suggesting mild anemia, common in cancer patients), Leukocytes: 6,500/mm³ (within the normal range, with no signs of infection or significant bone marrow alteration, Platelets: 240,000/mm³ (within the normal range), Fasting Glucose: 98 mg/dL (normal), Creatine: 0.9 mg/dL (normal, indicating good renal function), Liver Function (AST/ALT/Bilirubin): All results within the normal range, with no evidence of hepatic impairment, Lactate Dehydrogenase (LDH): 280 U/L (slightly elevated, a nonspecific finding that may be associated with tumor activity), Carcinoembryonic Antigen (CEA): 8.5 ng/mL (value above the (normal, a common finding in some types of lung cancer. Although not used for diagnosis, it can serve as a marker for monitoring response to treatment), TnI: Undetectable level (normal result, ruling out acute myocardial injury at this time), NT-proBNP: 550 pg/mL (elevated value, a sensitive marker for stress or heart failure).

Results

Based on the results, the final diagnosis was NSCLC (stage III, locally advanced). The patient's case was brought to a tumour board meeting for discussion with other oncology departments to determine the best course of treatment for her. RT was recommended as part of the curative treatment, aiming for local control of the disease and avoiding more invasive surgery, due to the tumour location and associated risks. Indication of RT for the lung tumour presented a critical challenge, as the irradiation field would cover a significant portion of the heart, an organ that already had limited functional reserve due to anthracycline treatment 15 years

ago.

The challenge The problem presented was not only technical but also ethical and clinical, requiring in-depth deliberation by the medical team. The indication for RT for lung carcinoma in the left lower lobe, despite being the standard of care for the disease, posed a critical dilemma. Based on the patient's clinical history and overall clinical presentation, a treatment plan was defined. The patient underwent a second echocardiogram. The exam confirmed a borderline LVEF and revealed a decrease in global longitudinal strain, an early sign of subclinical myocardial damage. ACEI inhibitors and a beta-blocker were administered to protect the myocardium before and during RT. IMRT and, in addition, the DIBH technique were used. The patient was instructed to hold her breath during radiation, which moved the heart away from the radiation field, minimising cardiac dose. The plan was optimised to maintain the mean dose to the heart, the maximum dose to critical structures of the heart (such as the left ventricle and coronary arteries), and the volume of the heart that would receive a high dose. As low as possible without compromising tumour dose. During and after RT, the patient was closely monitored. She was regularly monitored for any symptoms of worsening HF. RT was indicated with extreme caution after the introduction of ACEI inhibitors and beta-blockers.

Conclusion

The patient, after being diagnosed with locally advanced NSCLC and already undergoing treatment for cardiotoxicity, was recommended RT for the lung tumour, despite the significant risk of worsening her already compromised cardiac functional reserve. The patient's lung cancer treatment was successful, with a good tumour response and no severe acute cardiac toxicity, validating the strategy meticulously planned by the multidisciplinary team. The proactive introduction of ACEI and beta-blockers was essential. This pharmacological measure acted as a protective shield for an already vulnerable heart. The adoption of IMRT and DIBH techniques proved crucial. IMRT allowed precise dose conformation to the tumour, sparing adjacent cardiac structures as much as possible. DIBH, by moving the heart away from the irradiation field, further optimised protection, resulting in reduced mean and maximum doses to the left ventricle and coronary arteries. This combination of technologies and positioning strategies exemplifies the state-of-the-art in modern RT, seeking to cure cancer while preserving organ function as much as possible. Due to her history of anthracycline cardiotoxicity and additional exposure to thoracic RT, the patient remains at risk for developing late cardiotoxicity. Long-term monitoring, with

annual ECHOs and regular follow-up, is imperative for early detection of any signs of progressive cardiac dysfunction.

Abreviations

ACEI - Angiotensin-Converting Enzyme Inhibitors, **CAD -** Coronary Artery Disease, **CEA -** Carcinoembryonic Antigen, **CHF -** Congestive Heart Failure, **CMRI -** Cardiac Magnetic Resonance Imaging, **CT -** Computed Tomography, **DIBH -** Deep Inspiration Breath-Hold, **ECG -** Electrocardiogram, **ECHO -** Echocardiogram, **GLS -** Global Longitudinal Strain, **HF -** Heart Failure, **HTN –** Hypertension, **IMRT -** Intensity Modulated Radiation Therapy, **LDH -** Lactate Dehydrogenase, **LV -** Left Ventricle, **LVEF -** Left Ventricular Ejection Fraction, **MUGA -** Myocardial Scintigraphy, **NSCLC -** Non-Small Cell Lung Carcinoma, **NT-proBNP -** B-type Natriuretic Peptide, **PE -** Pericarditis, **QT -** Chemotherapy, **QOL -** Quality of Life, **RT -** Radiotherapy, **TnI –** Troponins.

CEP Approval Number

4.682.446

RECEIVED: 4/September/2025 ● ACCEPTED: 20/October/2025 ● TYPE: CASE STUDY ●FUNDING: There was no funding for the execution of this study project. ● DECLARATION OF CONFLICTING INTERESTS: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ● Availability of data and materials data is available from the corresponding author on reasonable request ● Ethics approval and consent to participate: The case study was approved by the Ethics Committee of the authors' organization with a GEP Approval number: CEP Approval Number 4.682.446. Approval file is available in the Journal's platform

References

Bradley, J. D., Hu, C., Komaki, R. R., Masters, G. A., Blumenschein, G. R., Schild, S. E., Bogart, J. A., Forster, K. M., Magliocco, A. M., Kavadi, V. S., Narayan, S., Iyengar, P., Robinson, C. G., Wynn, R. B., Koprowski, C. D., Olson, M. R., Meng, J., Paulus, R., Curran, W. J., Jr, & Choy, H. (2020). Long-Term Results of NRG Oncology RTOG 0617: Standard- Versus High-Dose Chemoradiotherapy With or Without Cetuximab for Unresectable Stage III Non-Small-Cell Lung Cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *38*(7), 706–714. https://doi.org/10.1200/JCO.19.01162

Cohn, K. E., Stewart, J. R., Fajardo, L. F., & Hancock, E. W. (1967). Heart disease following radiation. *Medicine*, *46*(3), 281–298. https://doi.org/10.1097/00005792-196705000-00003

Dess, R. T., Sun, Y., Matuszak, M. M., Sun, G., Soni, P. D., Bazzi, L., Murthy, V. L., Hearn, J. W. D., Kong, F. M., Kalemkerian, G. P., Hayman, J. A., Ten Haken, R. K., Lawrence, T. S., Schipper, M. J., & Jolly, S. (2017). Cardiac Events After Radiation Therapy: Combined Analysis of Prospective Multicenter Trials for Locally Advanced Non-Small-Cell Lung Cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *35*(13), 1395–1402. https://doi.org/10.1200/JCO.2016.71.6142

Emami, B., Lyman, J., Brown, A., Coia, L., Goitein, M., Munzenrider, J. E., Shank, B., Solin, L. J., & Wesson, M. (1991). Tolerance of normal tissue to therapeutic irradiation. *International journal of radiation oncology, biology, physics*, *21*(1), 109–122. https://doi.org/10.1016/0360-3016(91)90171-y

García-Pardo, M., Chang, A., Schmid, S., Dong, M., Brown, M. C., Christiani, D., Tindel, H. A., Brennan, P., Chen, C., Zhang, J., Ryan, B. M., Zaridze, D., Schabath, M. B., Leal, L. F., Reis, R. M., Tardon, A., Fernández-Tardon, G., Shete, S. S., Andrew, A., Brenner, H., … Liu, G. (2023). Respiratory and Cardiometabolic Comorbidities and Stages I to III NSCLC Survival: A Pooled Analysis From the International Lung Cancer Consortium. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer*, *18*(3), 313–323. https://doi.org/10.1016/j.jtho.2022.10.020

Kimenai, D. M., Pirondini, L., Gregson, J., Prieto, D., Pocock, S. J., Perel, P., Hamilton, T., Welsh, P., Campbell, A., Porteous, D. J., Hayward, C., Sattar, N., Mills, N. L., & Shah, A. S. V. (2022). Socioeconomic Deprivation: An Important, Largely Unrecognized Risk Factor in Primary Prevention of Cardiovascular Disease. *Circulation*, *146*(3), 240–248. https://doi.org/10.1161/CIRCULATIONAHA.122.060042

Le Pechoux, C., Pourel, N., Barlesi, F., Lerouge, D., Antoni, D., Lamezec, B., Nestle, U., Boisselier, P., Dansin, E., Paumier, A., Peignaux, K., Thillays, F., Zalcman, G., Madelaine, J., Pichon, E., Larrouy, A., Lavole, A., Argo-Leignel, D., Derollez, M., Faivre-Finn, C., … Bardet, A. (2022). Postoperative radiotherapy versus no postoperative radiotherapy in patients with completely resected non-small-cell lung cancer and proven mediastinal N2 involvement (Lung ART): an open-label, randomised, phase 3 trial. *The Lancet. Oncology*, *23*(1), 104–114. https://doi.org/10.1016/S1470-2045(21)00606-9

Nygård, L., Vogelius, I. R., Fischer, B. M., Kjær, A., Langer, S. W., Aznar, M. C., Persson, G. F., & Bentzen, S. M. (2018). A Competing Risk Model of First Failure Site after Definitive Chemoradiation Therapy for Locally Advanced Non-Small Cell Lung Cancer. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer*, *13*(4), 559–567. https://doi.org/10.1016/j.jtho.2017.12.011

Patz, E. F., Jr, Pinsky, P., Gatsonis, C., Sicks, J. D., Kramer, B. S., Tammemägi, M. C., Chiles, C., Black, W. C., Aberle, D. R., & NLST Overdiagnosis Manuscript Writing Team (2014). Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA internal medicine*, *174*(2), 269–274. https://doi.org/10.1001/jamainternmed.2013.12738

Postoperative radiotherapy in non-small-cell lung cancer: systematic review and meta-analysis of individual patient data from nine randomised controlled trials. PORT Meta-analysis Trialists Group. (1998). *Lancet (London, England)*, *352*(9124), 257–263.

Siegel, R. L., Giaquinto, A. N., & Jemal, A. (2024). Cancer statistics, 2024. *CA: a cancer journal for clinicians*, *74*(1), 12–49. https://doi.org/10.3322/caac.21820

Walls, G. M., Bergom, C., Mitchell, J. D., Rentschler, S. L., Hugo, G. D., Samson, P. P., & Robinson, C. G. (2025). Cardiotoxicity following thoracic radiotherapy for lung cancer. *British journal of cancer*, *132*(4), 311–325. https://doi.org/10.1038/s41416-024-02888-0

Wang, K., Eblan, M. J., Deal, A. M., Lipner, M., Zagar, T. M., Wang, Y., Mavroidis, P., Lee, C. B., Jensen, B. C., Rosenman, J. G., Socinski, M. A., Stinchcombe, T. E., & Marks, L. B. (2017). Cardiac Toxicity After Radiotherapy for Stage III Non-Small-Cell Lung Cancer: Pooled Analysis of Dose-Escalation Trials Delivering 70 to 90 Gy. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *35*(13), 1387–1394. https://doi.org/10.1200/JCO.2016.70.0229