Echocardiography

WILEY

Echocardiography

COMMENTARY OPEN ACCESS

Are We Ready to Monitor the Atrium? From Ventricular-Centric to Chamber-Integrated Cardiotoxicity Surveillance: The Emerging Role of Left Atrial Strain

Cristina Madaudo[1] | Daniela Di Lisi[2] | Giuseppina Novo[1,2]

[1]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (ProMISE), University of Palermo, Palermo, Italy | [2]Department of ProMISE, Division of Cardiology, University Hospital P. Giaccone, University of Palermo, Palermo, Italy

Correspondence: Cristina Madaudo (cristina.madaudo@gmail.com)

Received: 14 December 2025 | **Accepted:** 22 December 2025

Keywords: cancer therapy–related cardiac | cardio-oncology | diastolic dysfunction | dysfunction | left atrial strain | speckle-tracking echocardiography

Patients with diffuse large B-cell lymphoma (DLBCL) treated with the R-CHOP chemotherapy regimen represent a population at substantial risk of cancer therapy–related cardiac dysfunction (CTRCD) [1, 2]. Nearly 29% of patients developed a reduction in left ventricular systolic function during active treatment, highlighting cardiotoxicity as an early and clinically relevant complication of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) therapy [3]. Traditionally, left ventricular ejection fraction (LVEF) has served as the sole echocardiographic criterion for diagnosing CTRCD [4]. More recently, the 2022 ESC Cardio-Oncology Guidelines introduced left ventricular global longitudinal strain (LV-GLS) as an additional primary diagnostic parameter, acknowledging the limitations of LVEF in detecting early myocardial injury [1]. However, both indices primarily focus on ventricular systolic mechanics and may overlook early diastolic and left atrial (LA) involvement. This observation provides a strong rationale for refining cardiovascular monitoring strategies beyond conventional parameters. Most of the available evidence on LA function during cardiotoxic treatments originates from studies in breast cancer populations, resulting in heterogeneous conclusions [5, 6].

In this context, the study by Wang provides timely and clinically relevant insights into the role of LA function assessed by speckle-tracking echocardiography (STE) in patients with DLBCL treated with R-CHOP chemotherapy, shifting attention toward a chamber that plays a central role in cardiovascular hemodynamics and disease progression [7].

1 | Left Atrial Phasic Function and Diastolic Vulnerability

Assessment of LA phasic function has the potential to improve both the diagnostic accuracy and prognostic relevance of diastolic dysfunction and heart failure (HF), particularly heart failure with preserved ejection fraction (HFpEF) [8]. Left ventricular diastolic dysfunction generally precedes systolic dysfunction across a wide range of clinical settings and has been consistently established as an independent predictor of all-cause mortality with a 3.53-fold increased risk of cardiovascular events or death [9]. Within this framework, LA strain, especially reservoir strain (LASr), acts as an integrated marker of chronic filling pressure elevation, myocardial stiffness, and impaired ventricular–atrial coupling [10].

The authors demonstrate a significant deterioration of LA strain parameters following R-CHOP therapy, even in patients without overt systolic impairment. This finding reinforces the concept that atrial dysfunction may represent one of the earliest manifestations of CTRCD, preceding changes in LVEF and potentially even LV-GLS [7]. Notably, the authors provide robust validation of this approach by demonstrating that an LASr >35% cut-off showed substantial agreement with the 2016 ASE/EACVI diastolic dysfunction algorithm, with a kappa value of 0.765 ($p < 0.05$) [11]. This level of concordance supports the clinical reliability of LA strain as a surrogate marker of diastolic function and strengthens the translational value of the findings.

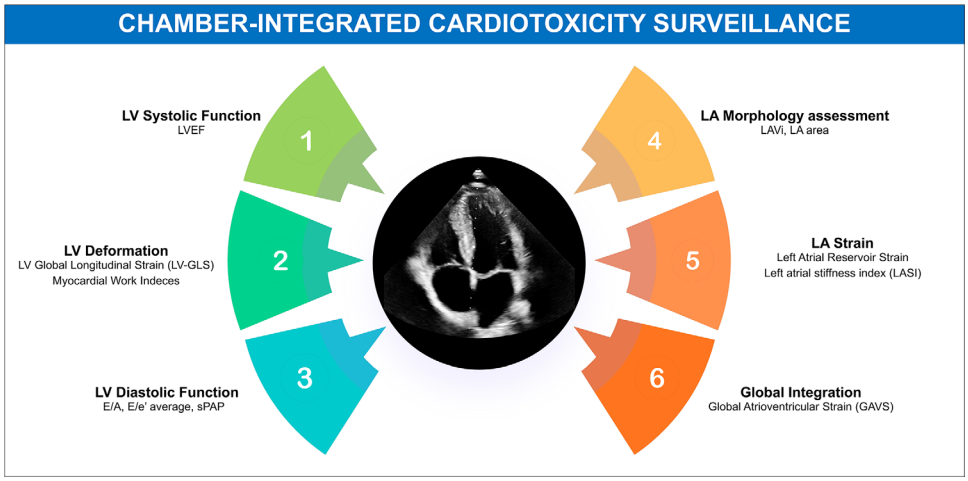

FIGURE 1 | Chamber-integrated cardiotoxicity surveillance. A conceptual framework illustrating a comprehensive echocardiographic approach to cancer therapy–related cardiac dysfunction. Beyond conventional assessment of left ventricular systolic function, a chamber-integrated strategy incorporates diastolic function, left atrial morphology and deformation, and global atrioventricular mechanics. E/A, ratio of early to late diastolic transmitral flow velocities; E/e′, ratio of early diastolic transmitral flow velocity to early diastolic mitral annular velocity; GAVS, global atrioventricular strain; LA, left atrium; LASI, left atrial stiffness index; LAVi, left atrial volume index; LV, left ventricle; LV-GLS, left ventricular global longitudinal strain; LVEF, left ventricular ejection fraction; PALS, peak atrial longitudinal strain; sPAP, systolic pulmonary artery pressure.

1.1 | Pathophysiological Considerations: Atrial Myocardium as a Direct Target

The mechanisms underlying CTRCD remain incompletely understood, but growing evidence suggests a central role for oxidative stress, driven by an imbalance between reactive oxygen species (ROS) and antioxidant defenses [12]. This process leads to cardiomyocyte injury, mitochondrial dysfunction, and progressive myocardial remodeling [12]. In DLBCL patients treated with R-CHOP, LA dysfunction may arise through two complementary mechanisms: elevated filling pressures secondary to impaired ventricular relaxation and direct cytotoxic effects of chemotherapy on the atrial myocardium itself. Importantly, cardiomyocyte injury should be viewed as a global myocardial phenomenon, affecting not only the ventricle but also the atrial myocardium. The observed impairment in LA strain in the absence of significant changes in LA volume supports this hypothesis and highlights the vulnerability of atrial tissue to early toxic injury [12].

1.2 | Beyond Left Atrial Volume: Sensitivity of Deformation Imaging

LA enlargement is a well-established marker of adverse cardiovascular outcomes; however, it reflects a chronic and relatively late remodeling process that develops after prolonged exposure to pressure or volume overload. Consequently, left atrial volume index (LAVi) lacks sensitivity for detecting subtle or early functional alterations [10]. Consistent with previous studies, the authors report no significant changes in LAVi after completion of chemotherapy, despite clear impairment in LA strain [7]. This dissociation underscores the superiority of deformation imaging over volumetric assessment in the early phases of cardiotoxicity and supports the routine inclusion of LA strain in cardio-oncology echocardiographic protocols [13].

Nevertheless, the interpretation of the LA strain requires careful clinical contextualization. Age-related atrial stiffening, systemic hypertension, and common cardiovascular comorbidities may all influence baseline atrial mechanics, potentially reducing the discriminative value of fixed LASr cut-offs. Moreover, conditions such as atrial fibrillation or frequent atrial ectopy not only act as major confounders but may also preclude reliable strain acquisition altogether, limiting the applicability of this technique in a substantial proportion of real-world oncology patients. In such patients, an LASr value below conventional thresholds may reflect pre-existing atrial remodeling rather than chemotherapy-induced injury [14].

Additional methodological considerations further complicate interpretation. Variability across vendors and software platforms remains an unresolved issue, and the choice of the electrocardiographic reference point for strain analysis continues to be debated. While P-wave–based timing may better reflect atrial electromechanical coupling, QRS-based gating offers greater feasibility and reproducibility in routine practice, particularly in oncologic populations where ECG quality, rhythm stability, and heart rate variability may be suboptimal.

Taken together, these factors highlight the need for larger, multicenter registries and studies conducted across diverse clinical settings to establish age-adjusted and context-specific reference values, refine acquisition protocols, and improve risk stratification in heterogeneous cardio-oncology populations. Only through such efforts can LA strain be fully integrated into personalized surveillance strategies while avoiding overinterpretation in patients with competing sources of atrial dysfunction.

2 | Future Directions and Conclusions

The study by Wang and colleagues supports a paradigm shift toward a more comprehensive, chamber-integrated approach to

cardiotoxicity surveillance, in which the left heart is no longer viewed as two distinct anatomical units but rather as a single, functionally interconnected system. In this context, LA strain should not be considered merely an ancillary parameter, but part of a broader assessment of global left heart mechanics. The emerging concept of global atrioventricular strain (GAVS), by integrating atrial and ventricular deformation, may further refine early detection of myocardial involvement, effectively bridging subclinical diastolic dysfunction and the development of overt HF [15].

In patients with DLBCL undergoing R-CHOP therapy, LA dysfunction detected by STE represents an early and clinically meaningful signal of chemotherapy-related cardiac involvement. By demonstrating strong agreement between LASr and established diastolic dysfunction algorithms, and by highlighting atrial vulnerability beyond volumetric changes, the present study contributes substantially to the evolving landscape of cardio-oncology imaging. Incorporating LA strain into routine practice may enhance early detection, refine risk stratification, and ultimately improve cardiovascular outcomes in this high-risk population (Figure 1).

Acknowledgments

Open access publishing facilitated by Universita degli Studi di Palermo, as part of the Wiley - CRUI-CARE agreement.

Data Availability Statement

The authors have nothing to report.

References

1. A. R. Lyon, T. López-Fernández, L. S. Couch, et al., "2022 ESC Guidelines on Cardio-Oncology Developed in Collaboration With the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)," *European Heart Journal* 43 (2022): 4229–4361, https://doi.org/10.1093/eurheartj/ehac244.

2. D. Di Lisi, C. Cadeddu Dessalvi, C. Zito, et al., "Management of Cancer Patients at High and Very-High Risk of Cardiotoxicity: Main Questions and Answers," *Current Problems in Cardiology* 49 (2024): 102229, https://doi.org/10.1016/j.cpcardiol.2023.102229.

3. P.-P. Xu, D. Fu, J.-Y. Li, et al., "Anthracycline Dose Optimisation in Patients With Diffuse Large B-Cell Lymphoma: A Multicentre, Phase 3, Randomised, Controlled Trial," *Lancet Haematology* 6 (2019): e328–37, https://doi.org/10.1016/S2352-3026(19)30051-1.

4. J. L. Zamorano, P. Lancellotti, and D. Rodriguez Muñoz, "2016 ESC Position Paper on Cancer Treatments and Cardiovascular Toxicity Developed Under the Auspices of the ESC Committee for Practice Guidelines: The Task Force for Cancer Treatments and Cardiovascular Toxicity of the European Society of Cardiology (ESC)," *European Journal of Heart Failure* 19 (2017): 9–42, https://doi.org/10.1002/ejhf.654.

5. D. Di Lisi, A. Moreo, G. Casavecchia, et al., "Atrial Strain Assessment for the Early Detection of Cancer Therapy-Related Cardiac Dysfunction in Breast Cancer Women (The STRANO STUDY: Atrial Strain in Cardio-Oncology)," *Journal of Clinical Medicine* 12 (2023): 7127, https://doi.org/10.3390/jcm12227127.

6. P. W. Stoodley, D. A. B. Richards, A. Boyd, et al., "Altered Left Ventricular Longitudinal Diastolic Function Correlates With Reduced Systolic Function Immediately After Anthracycline Chemotherapy," *European Heart Journal—Cardiovascular Imaging* 14 (2013): 228–234, https://doi.org/10.1093/ehjci/jes139.

7. B. Wang, X. Hao, Y. Yu, et al., "Left Atrial Function in Patients With Diffuse Large B-Cell Lymphoma Treated With R-CHOP Chemotherapy Regimen: A Speckle Tracking Echocardiographic Study," *Echocardiography* 42 (2025): e70339, https://doi.org/10.1111/echo.70339.

8. A. B. S. Santos, G. Q. Roca, B. Claggett, et al., "Prognostic Relevance of Left Atrial Dysfunction in Heart Failure With Preserved Ejection Fraction," *Circulation: Heart Failure* 9 (2016): e002763, https://doi.org/10.1161/CIRCHEARTFAILURE.115.002763.

9. R. Ladeiras-Lopes, M. Araújo, F. Sampaio, et al., "The Impact of Diastolic Dysfunction as a Predictor of Cardiovascular Events: A Systematic Review and Meta-Analysis," *Revista Portuguesa de Cardiologia* 38 (2019): 789–804, https://doi.org/10.1016/j.repc.2019.03.007.

10. T. Sugimoto, S. Robinet, R. Dulgheru, et al., "Echocardiographic Reference Ranges for Normal Left Atrial Function Parameters: Results From the EACVI NORRE Study," *European Heart Journal—Cardiovascular Imaging* 19 (2018): 630–638, https://doi.org/10.1093/ehjci/jey018.

11. S. F. Nagueh, O. A. Smiseth, C. P. Appleton, et al., "Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update From the American Society of Echocardiography and the European Association of Cardiovascular Imaging," *Journal of the American Society of Echocardiography* 29 (2016): 277–314, https://doi.org/10.1016/j.echo.2016.01.011.

12. M. Sousa-Pimenta, M. M. Estevinho, M. Sousa Dias, et al., "Oxidative Stress and Inflammation in B-Cell Lymphomas," *Antioxidants (Basel)* 12 (2023): 936, https://doi.org/10.3390/antiox12040936.

13. D. Di Lisi, C. Madaudo, F. Macaione, et al., "Cancer Survivors and Cardiovascular Diseases: From Preventive Strategies to Treatment," *Journal of Cardiovascular Medicine (Hagerstown)* 26 (2025): 8–17, https://doi.org/10.2459/JCM.0000000000001681.

14. M. J. Herzog, P. Müller, K. Lechner, et al., "Arterial Stiffness and Vascular Aging: Mechanisms, Prevention, and Therapy," *Signal Transduction and Targeted Therapy* 10 (2025): 282, https://doi.org/10.1038/s41392-025-02346-0.

15. D. Di Lisi, C. Madaudo, A. Ortello, et al., "Assessment of Cancer Therapy-Related Cardiac Dysfunction in Breast Cancer Women Using a New Speckle Tracking Echocardiography Index: The GAVS," *Echocardiography* 41 (2024): e15881, https://doi.org/10.1111/echo.15881.