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BIOMARKER SPOTLIGHT

Cardiac biomarkers in the field of cardio-oncology

Daniela Cardinale [1]*, Nicholas L. Mills[2,3], and Christian Mueller [4]; on behalf of the Study Group on Biomarkers of the ESC Association for Acute CardioVascular Care

[1]Cardio-Oncology Unit, European Institute of Oncology, I.R.C.C.S., Via Ripamonti 435, 20141 Milan, Italy; [2]BHF Centre for Cardiovascular Sciences, University of Edinburgh, SU.226 Chancellor's Building, Royal Infirmary of Edinburgh, 49 Little France Crescent, Edinburgh EH16 4SU, UK; [3]Usher Institute, University of Edinburgh, 9 Little France Road, Edinburgh BioQuarter, Edinburgh EH16 4UX, UK; and [4]Department of Cardiology and Cardiovascular Research Institute Basel, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland

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The term 'Cardio-oncology' was coined at European Institute of Oncology in 1995 and made official in 1996 with the first publication on this topic.[1] Cardio-oncology is a new interdisciplinary medical field, based on a global approach, created for the management of all cardiovascular problems in oncologic patients. Over the last 20 years, the survival rate of cancer patients has significantly increased due to the terrific advances of modern cancer therapy. To achieve these results, however, a considerable price had been paid in terms of a rise in side effects associated with intensive anticancer treatment.[2] Cardiotoxicity is a serious adverse effect of anticancer therapy, impacting on the quality of life and overall survival of cancer patients.

The main goal of cardio-oncology is to allow oncologic patients to receive the best possible treatments safely, minimizing cardiotoxicity across the whole pathway of cancer care. In this view, early detection is crucial for applying preventive and supportive therapeutic strategies. Cardiotoxicity is probably a continuous phenomenon starting with myocardial cell injury, changes in myocardial deformation, followed by asymptomatic left ventricular dysfunction, which, if

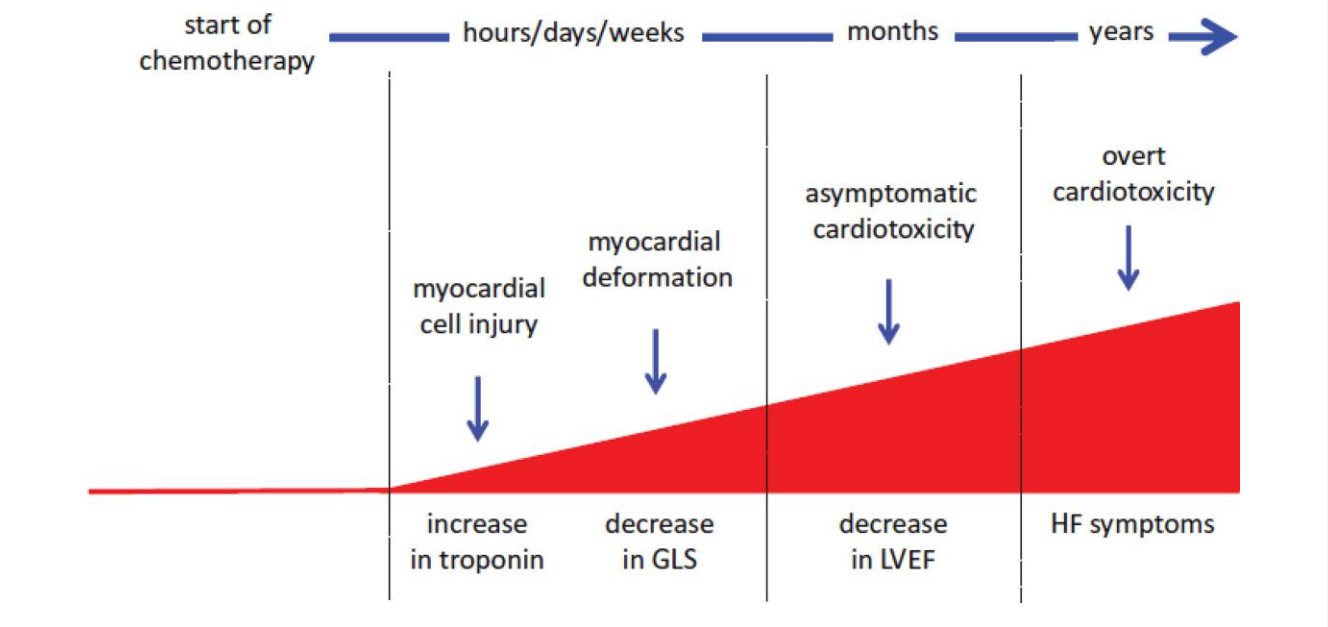

Figure 1 Schematic representation of cardiotoxicity progression: the continuum phenomenon hypothesis. GLS = global longitudinal strain, LVEF = left ventricular ejection fraction, LVD = left ventricular dysfunction, HF = heart failure. Modified from Cardinale *et al*. *Curr Cardiol Rep* 2016.

* Corresponding author. Email: daniela.cardinale@ieo.it

disregarded and not treated, progressively may lead—after months, after years—to overt heart failure.[3] We can identify cardiotoxicity at each of these different phases depending on the diagnostic tools we use (*Figure 1*). According to the current standard for monitoring cardiac function, cardiotoxicity is usually detected only when a functional impairment has already occurred, precluding any chance of preventing its development. Over the last two decades, however, a new approach, based on the use of cardiac biomarkers, has emerged and has proven to be an effective alternative strategy for early detection of subclinical cardiac injury. Very recently, the use of biomarkers in the field of cardio-oncology was included and recommended in the guidelines.[4,5] Measurement of serum biomarkers represents a feasible and promising opportunity to help in baseline risk stratification, diagnosis of early cardiotoxicity during and following treatment, identification of cancer patients who may benefit from cardioprotective treatment while continuing oncologic treatment, and of patients who may deserve long-term follow-up, excluding low risk patient from an prolonged expensive monitoring programme.

Cardiac troponins and natriuretic peptides [B-type natriuretic peptide (BNP), NT-terminal-pro-hormone BNP (NT-proBNP)] are complimentary and could help identify patients at risk of cardiotoxicity to guide the use of imaging. Repeated measurements of cardiac troponin and early treatment with angiotensin-converting enzyme inhibitors, in patients showing increased cardiac troponin concentrations indicating cardiomyocyte injury, has shown promise in preventing cancer therapy-induced cardiac dysfunction and related cardiac events in an impressive pilot study.[6] Further prospective studies are needed to clarify whether combined assessment with cardiac troponin and natriuretic peptides permit better stratification of the cardiac risk for patients treated with cancer-therapies.

Data availability

No new data were generated or analysed in support of this research.

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Other members of the Study Group on Biomarkers of the ESC Association for Acute Cardiovascular Care include:

Allan Jaffe, MD[1]; Evangelos Giannitsis, MD[2]; Lori Daniels, MD[3]; Kurt Huber, MD[4]; Johannes Mair, MD[5]; Louise Cullen, MD, PhD[6]; Ola Hammarsten, MD, PhD[7]; Martin Möckel, MD[8]; Konstantin Krychtiuk, MD[9]; Kristian Thygesen, MD[10]; Matthias Thielmann, MD[11]

[1]Departments of Cardiology and Laboratory Medicine and Pathology, Mayo Clinic, Rochester Minnesota, U.S.A.;
[2]Department of Cardiology, University Heidelberg, Germany;
[3]Department of Medicine, Sulpizio Cardiovascular Center, University of California, San Diego; La Jolla, CA, SA;
[4]Department of Medicine, Cardiology and Intensive Care Medicine, Wilhelminenhospital, and Sigmund Freud University, Medical School, Vienna, Austria;
[5]Department of Internal Medicine III—Cardiology and Angiology, Medical University Innsbruck, Austria;
[6]Emergency and Trauma Centre, Royal Brisbane and Women`s Hospital, University of Queensland, Australia;
[7]Department of Clinical Chemistry and Transfusion Medicine, University of Gothenburg, Gothenburg, Sweden;
[8]Division of Emergency Medicine, Charité-Universitätsmedizin Berlin, Germany;
[9]Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Austria;
[10]Department of Cardiology, Aarhus University Hospital, Denmark; and
[11]Klinik für Thorax- und Kardiovaskuläre Chirurgie, Westdeutsches Herz- und Gefäßzentrum Essen, University of Duisburg-Essen, Germany

References

1. Cardinale D. Una nuova frontiera: la cardioncologia. *Cardiologia* 1996;**41**:887–891.
2. Curigliano G, Cardinale D, Dent S, Criscitiello C, Aseyev O, Lenihan D, Cipolla CM. Cardiotoxicity of anticancer treatments: epidemiology, detection, and management. *CA Cancer J Clin* 2016;**66**:309–325.
3. Cardinale D, Biasillo G, Salvatici M, Sandri MT, Cipolla CM. Using biomarkers to predict and to prevent cardiotoxicity of cancer therapy. *Expert Rev Mol Diagn* 2017;**17**:245–256.
4. Pudil R, Mueller C, Čelutkienė J, Henriksen PA, Lenihan D, Dent S, Barac A, Stanway S, Moslehi J, Suter TM, Ky B, Štěrba M, Cardinale D, Cohen-Solal A, Tocchetti CG, Farmakis D, Bergler-Klein J, Anker MS, Von Haehling S, Belenkov Y, Iakobishvili Z, Maack C, Ciardiello F, Ruschitzka F, Coats AJS, Seferovic P, Lainscak M, Piepoli MF, Chioncel O, Bax J, Hulot JS, Skouri H, Hägler-Laube ES, Asteggiano R, Fernandez TL, de Boer RA, Lyon AR. Role of serum biomarkers in cancer patients receiving cardiotoxic cancer therapies: a position statement from the cardio-oncology study group of the heart failure association and the cardio-oncology council of the European Society of Cardiology. *Eur J Heart Fail* 2020;**22**:1966–1983.
5. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, Boriani G, Cardinale D, Cordoba R, Cosyns B, Cutter DJ, de Azambuja E, de Boer RA, Dent SF, Farmakis D, Gevaert SA, Gorog DA, Herrmann J, Lenihan D, Moslehi J, Moura B, Salinger SS, Stephens R, Suter TM, Szmit S, Tamargo J, Thavendiranathan P, Tocchetti CG, van der Meer P, van der Pal HJH; ESC Scientific Document Group. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J* 2022;**43**:4229–4361.
6. Cardinale D, Colombo A, Sandri MT, Lamantia G, Colombo N, Civelli M, Martinelli G, Veglia F, Fiorentini C, Cipolla CM. Prevention of high-dose chemotherapy-induced cardiotoxicity in high-risk patients by angiotensin-converting enzyme inhibition. *Circulation* 2006;**114**:2474–2481.