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## Stratification of the risk of chemotherapy-induced cardiotoxicity: Reply

### *Estratificación del riesgo de cardiotoxicidad inducida por quimioterapia: Respuesta*

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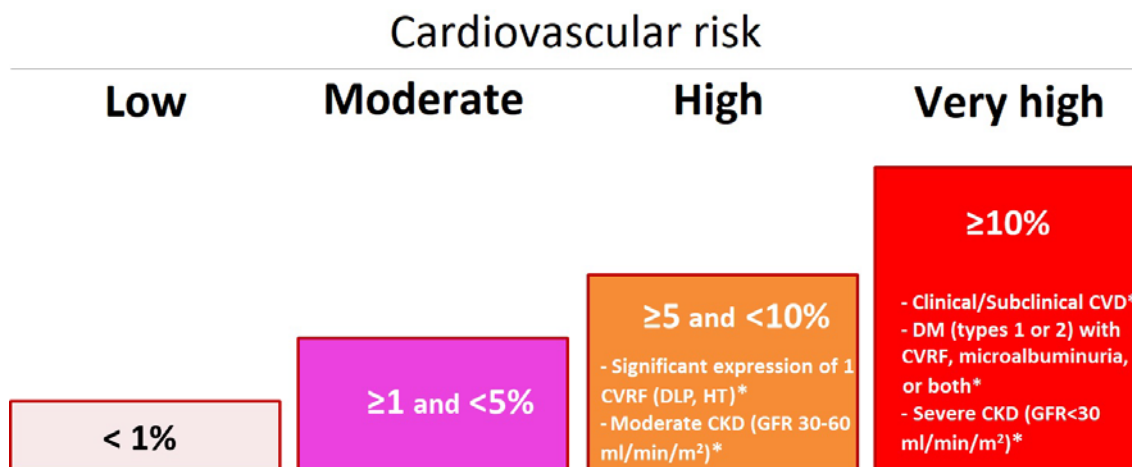
### To the Editor,

We agree with Rodríguez Ramos<sup>1</sup> that adequate prophylaxis and early diagnosis of chemotherapy-induced cardiotoxicity (CIC) will be critically important to reduce or delay the onset of ventricular dysfunction and clinical heart failure in a large part of the population affected by tumor diseases.

The improved survival in cancer patients, in general, and in advanced disease; the development of personalized medicine, the incidence of second neoplasms in cancer survivors, therapeutics with long-term medications, the possibility of using new lines of treatment –locations with more than 4 lines–, the development of radiotherapy techniques that allow re-irradiation, the advances in rescue surgery, among other reasons that show the transition of the disease towards chronicity, grant urgency to develop adequate strategies of prevention and treatment of the patient to avoid or delay the damage or myocardial affection generated by the exposure to chemotherapeutic agents.

As we mentioned in the review article<sup>2</sup>, in order for cardiotoxicity to occur due to a drug, factors specific to the agent and the patient must interact. With regard to the drug, the type of agent, the dose applied during each session and the cumulative dose, as well as frequency, route of administration and other combined agents, are factors that affect the form and time of presentation of CIC. Age (children and over 65 years), any previous cardiovascular disease, prior radiotherapy, mainly mediastinal, metabolic alterations and hypersensitivity to different drugs are considered among the factors related to the patient<sup>2,3</sup>.

Chemotherapy-induced cardiotoxicity may appear at any age; however, the probability of presenting complications increases with age. Women have a higher risk of presenting cardiovascular events with the use of chemotherapy, despite the fact that men are more likely to develop atherosclerosis, which should be taken into account by oncologists, cardiologists or doctors who assist these patients. In turn, the higher the cumulative dose, the greater the risk



**Figure.** Stratification of cardiovascular risk. Taken and modified from López Fernández et al. *Rev Esp Cardiol.* 2017; 70(6):474-86<sup>3</sup>. CKD, chronic kidney disease; CVD, cardiovascular disease; CVRF, cardiovascular risk factor; DLP, dyslipidemia; DM, diabetes mellitus; GFR, glomerular filtration rate; HT, hypertension.

\* Regardless of the calculated SCORE (%), the presence of these factors is associated with a high or very high cardiovascular risk.

of developing CIC. A clear example of this is the use of anthracyclines, such as doxorubicin, where the risk of heart failure associated with the cumulative dose is 0.2% at a dose of 150 mg/m<sup>2</sup>, de 1.6% with 300 mg/m<sup>2</sup>, 3.3% with 450 mg/m<sup>2</sup> and 8.7% with 600 mg/m<sup>2</sup><sup>2,4</sup>.

At present there are no prospective scales that jointly assess cardiovascular risk and cardiotoxicity, and traditional scales underestimate the risk associated with cancer treatment. Despite this limitation, it is recommended to stratify cardiovascular risk according to the joint recommendations of the *Sociedades Españolas de Cardiología, Oncología y Radioterapia, y Hematología* (Spanish Societies of Cardiology, Oncology and Radiotherapy, and Hematology); and the European guidelines for the prevention of cardiovascular disease (**Figure**)<sup>3,5</sup> before initiating antitumor treatment and evaluating the presence of those factors detected in retrospective studies and registries, which increase the risk of cardiovascular events during antitumor treatment (**Table**)<sup>3,6</sup>.

The systematic coronary risk evaluation (SCORE) through SCORE tables<sup>5</sup> calculates the 10-year risk of a first fatal atherosclerotic episode. All the codes of the International Classification of Diseases that can reasonably be considered atherosclerotic, such as coronary heart disease, cerebrovascular accident and aneurysm of the abdominal aorta, have been included<sup>3</sup>. Most traditional systems calculated only

the risk of coronary heart disease. But recently, several risk calculation systems have been modified to calculate that of all cardiovascular diseases.

The risk stratification from Mayo Clinic<sup>7</sup> to which Rodríguez Ramos refers<sup>1</sup>, undoubtedly constitutes a useful tool for the evaluation of these patients, but we particularly prefer the use of cardiovascular risk assessment by López-Fernández *et al*<sup>3</sup> that we have commented on.

In addition to optimizing cardiovascular risk and considering primary prevention strategies, cardio-oncology teams must coordinate the monitoring of antitumor treatments to identify and treat early cardiovascular complications. It is recommended that patients with poor control of their risk factors and significant alterations in imaging studies or biomarkers be referred to a specialized cardiology consultation; this way it is possible to identify the possibilities of developing cardiac diseases during oncological treatment.

The development of strategies for prevention, monitoring, early diagnosis and treatment of CIC will continue to keep the scientific community busy at times when cancer and cardiovascular diseases are leading causes of death in Cuba and the world. The interdisciplinary approach to cancer patients by Cardiologists and Oncologists is, for this reason, a crucial tool to improve the cardiovascular health of cancer patients.

**Table.** Risk factors for ventricular dysfunction in patients treated with antitumor drugs and radiotherapy (if the volume of irradiation, totally or partially, includes the heart). Taken and modified from López Fernández *et al.* Rev Esp Cardiol 2017;70(6):474-86<sup>3</sup>.

Risk factors of VD-CTox	Anthracyclines	Anti-HER2*	Anti-VEGF <sup>‡</sup>	Thoracic radiotherapy
Genetic factors	x			
Accumulated dose	x			≥ 35 Gy or ≥ 2 Gy/day
Women	x			x
Less than 15 or greater than 65 years	x	x		x
Hypertension	x	x	x	
Ischemic heart disease	x	x	x	x
Normal/limit LVEF (50-55%) before treatment	x	x		
History of HF or VD-CTox	x	x	x	
Combined antitumoral therapy <sup>Ω</sup> and thoracic radiotherapy	x	x	x	x
Renal failure	x			
Obesity (BMI>30) and sedentary lifestyle		x		
Time elapsed since treatment				x

\* Drugs that block the human epidermal growth factor receptor 2

‡ Drugs that inhibit vascular endothelial growth factor

Ω High risk drugs: anthracyclines, cyclophosphamide, trastuzumab; moderate risk: docetaxel, pertuzumab, sunitinib, sorafenib; low risk: bevacizumab, dasatinib, imatinib and lapatinib.

BMI, body mass index; HF, heart failure; LVEF, left ventricular ejection fraction; VD-CTox, ventricular dysfunction secondary to cardiotoxics.

## CONFLICTS DE INTERESTS

None

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## CorSalud, the first Cuban scientific journal in the 2017 ranking of the Ibero-American Network of Innovation and Scientific Knowledge (REDIB)

### *CorSalud, primera revista científica cubana en el ranking de 2017 de la Red Iberoamericana de Innovación y Conocimiento Científico (REDIB)*

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### To the Editor,

Next 2019 we will celebrate the tenth anniversary of CorSalud and we are proud of the important achievements made in less than a decade. We said in the first issue: our biggest challenge (...) is to get it going<sup>1</sup>; and it has been like that, but we have made it<sup>2,4</sup>.

We have worked our way through difficulties and, though hard at the beginning, we are finally recognized nationwide. However, as the poet Antonio Machado (1875-1939) said: "...the path unfolds as we walk it..." and today CorSalud is highly regarded in the national and international arena<sup>5,8</sup>.

The premises of our results have been teamwork and giving our all at work. We would not have made it without the help of authors, mainly Cubans, to whom we have much to thank and recognize; as well as external reviewers, mostly foreigners, who help maintain and increase the quality of the published articles. We wish to express our most sincere

gratitude to all of you; as these achievements we are disclosing today are also yours.

Dear authors, readers, reviewers and members of the Editorial Board of this Journal: we are pleased to inform you that CorSalud has climbed to the first position among Cuban scientific journals (**Figure 1**) in the 2017 ranking of the Ibero-American Network of Innovation and Scientific Knowledge (REDIB), it ranks 30 in Health Sciences (**Figure 2**), and 301st among a total 2634 journals (**Figure 3**).

It is not only a great honor but a challenge to keep on pursuing excellence.

Gratitude is owed to all who collaborated with CorSalud and made this result possible.

### CONFLICT OF INTERESTS

The authors are members of the Editorial Board of CorSalud.