

New Horizons of Cardio-Oncology

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Novos horizontes da Cardio-Oncologia

Nuevos Horizontes de Cardio-Oncología

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INTRODUCTION

Chronic non-communicable diseases (CNCD) were responsible for 71% of an estimated total of 57 million deaths in the world in 2016, 80% of them in low and medium income countries¹. Similar estimate occurred in Brazil and the CNCD responded for 74% of the deaths and predominance of cardiovascular diseases (CV) that correspond approximately to one third of the deaths followed by neoplasms, with nearly one sixth of the deaths, chronic obstructive diseases and diabetes². CNCDs share common risk factors and it is worth mentioning that the combined approach of CNCDs and its risk factors was considered a cost-effective package by the World Health Organization (WHO), requiring investments equivalent to US\$ 1 *per capita* of the low income countries, US\$ 1.5 of the low and medium income and US\$ 3 of the medium and high income³.

DEVELOPMENT

In the last decades, the CVs were the main causes of death in the world, being among the principal responsible of causes of lost years of life by premature death for both genders^{2,3}. During the last years, the standard rates of mortality for CVs reduced, however, there was a raise of standard rates for diabetes, chronic respiratory diseases and neoplasms that increased 1.7, 1.02 and 1.09 times, respectively, despite the relative stability of the last decade, even considering the ageing of the Brazilian population (Figure 1)².

The coexistence of cancer and CVs in the same patient is more common because of the ageing of the population and improvement of the efficacy of the chemotherapy drug. The rates of mortality per cancer, on the other hand, have greatly dropped in the last 30 years because of the strategies of early detection, improvement of the approach

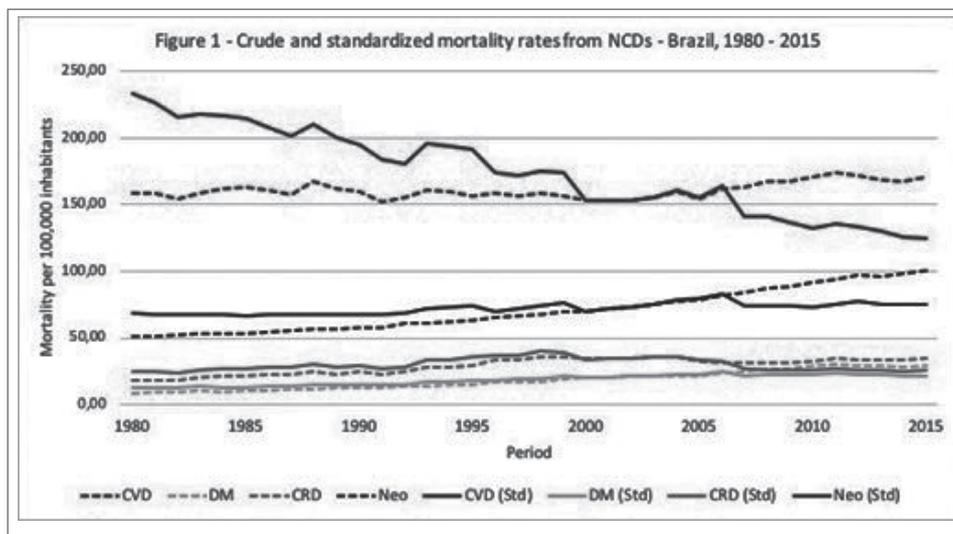


Figure 1. Raw and standard rates per chronic non-communicable diseases in Brazil, 1980-2015

Source: DATASUS (c2008)

Captions: CVD: cardiovascular diseases; DM: *diabetes mellitus*; CRD: chronic respiratory diseases; Neo: neoplasm.

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and progresses in cancer therapeutic. The improvement of survival may be associated to injuries in other organs, including the cardiovascular system. Currently, CV is the second main cause of morbidity and mortality in the long time among cancer survivals, standing out the relevance of the conjoint approach of the two main causes of CNCD⁴.

Proportionally to extended survival, morbidity increase because of the treatment adverse effects has also expanded⁵. The cardiovascular disorders are outstanding for this population resulting either from direct action of cancer treatment over the cardiac and/or vascular function and structure, but most of the times, for promoting the acceleration of the course of a subjacent cardiac disease or potentializing concomitant risk factors⁶.

Cardio-oncology has stemmed from the necessity of treating the effects of the antineoplastic therapy in the cardiovascular system and represents today a blooming area of development. In 2009, the International Cardio-Oncology Society was founded to gather the specialties Cardiology and Oncology in the promotion of the appropriate care to the oncologic patient⁷. In 2011, the Brazilian Society of Cardiology (*Sociedade Brasileira de Cardiologia* – SBC), supported by the Brazilian Society of Clinical Oncology published the First Brazilian Guideline of Cardio-Oncology (“*I Diretriz Brasileira de Cardio-Oncologia*”) of SBC in the Brazilian Archives of Cardiology, preceding the guidelines and later international positions about the theme^{6,8,9}. In 2013, as pioneers, the same entities gathered for the publication of the First Guideline of Pediatric Cardio-Oncology (*I Diretriz de Cardio-Oncologia Pediátrica*) of SBC¹⁰.

Today, the cardiovascular complications of the cancer therapy are well established and embrace new main categories: myocardial dysfunction and cardiac insufficiency; coronary arterial disease, heart valve disease; arrhythmia, especially those induced by drugs that prolong the interval QT; arterial hypertension; thromboembolic disease; vascular disease involving the encephalic stroke and peripheral arteriopathy; pulmonary hypertension and pericardial complications⁶.

Until very recently there were no evidences that the cardiovascular therapy was able to induce the appearance of neoplasms. There are, however, recent indications of the increase of risk of the non-melanoma skin cancer using hydrochlorothiazide^{11,12}, of lung cancer with inhibitors of the enzyme of conversion¹³, in addition to the identification of carcinogenic nitrosamines in impurities of generic formulations of some blockers of the angiotensin receptor¹⁴, among other possible post-carcinogenic effects of drugs used in cardiology.

Cancer and cardiovascular disease share common risk factors where inflammation can be the core

link, responsible for the beginning, progression and complication of both diseases¹⁵. Evidences that the clonal hematopoiesis is able to cause leukemia or atherosclerotic disease represents one more common point between these two apparently disparate diseases¹⁶. 27-hydroxycholesterol, a cholesterol metabolite can act as a direct receptor of estrogen, stimulating the growth and metastatic dissemination of breast cancer¹⁷. The modulation of the inflammatory pathways has shown to be transformative while crossing the threshold of the clinical reality in cancer treatment, reducing also the risk of cardiovascular outcomes^{18,19}.

CONCLUSION

Cardio-oncology represents an area of endless horizons and exponential development all over the world, much beyond the care of the complications of oncologic treatment and the assets of the specialties of cardiology and oncology as supposed ten years ago when the International Cardio-Oncology Society was created.

CONTRIBUTIONS

Both authors participated of all the stages of the manuscript and approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There are no conflict of interests to declare.

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REFERENCES

1. Institute for Health Metrics and Evaluation. GBD results toll [Internet]. Seattle, WA: IHME; 2017. [cited 2019 Ago 12]. Available from: <http://ghdx.healthdata.org/gbd-results-tool>
2. Ministério da Saúde (BR), Secretaria Executiva. DATASUS: informações de saúde (TABNET) [Internet]. Brasília, DF: DATASUS; c2008. [acesso 2019 ago. 22]. Disponível em: <http://www2.datasus.gov.br/DATASUS/index.php?area=02>
3. World Health Organization. Scaling up action against noncommunicable diseases: how much will it cost? [Internet]. Geneva: WHO; 2011. [cited 2019 Ago. 22]. Available from: http://apps.who.int/iris/bitstream/10665/44706/1/9789241502313_eng.pdf
4. Dent S, Liu P, Brezden-Masley C, et al. Cancer and cardiovascular disease: the complex labyrinth.

- J Oncol. 2015;2015:516450. doi: <https://doi.org/10.1155/2015/516450>
5. Ferlay J, Soerjomataram I, Ervik M, et al., editors GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012 v1.0. Lyon, France: International Agency for Research on Cancer; 2013 [cited 2018 Mar 15]. (IARC CancerBase n. 11).
 6. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. 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). *Eur Heart J*. 2016 Sep 21;37(36):2768-2801. Erratum in: *Eur Heart J*. 2016 Dec 24. doi: <https://doi.org/10.1093/eurheartj/ehw211>
 7. Kalil Filho R, Hajjar LA, Bacal F, et al. I Diretriz brasileira de cardio-oncologia da Sociedade Brasileira de Cardiologia. *Arq Bras Cardiol*. 2011;96(2 supl.1):1-52.
 8. Campia L, Moslehi JJ, Amiri-Kordestani L, et al. Cardio-oncology: vascular and metabolic perspectives: a scientific statement from the American Heart Association. *Circulation*. 2019 Mar 26;139(13):e579-e602. Erratum in: *Circulation*. 2019 Apr 9;139(15):e838-e839.
 9. Virani SA, Dent S, Brezden-Masley C, et al. Canadian cardiovascular Society Guidelines for Evaluation and Management of cardiovascular complications of cancer Therapy. *Can J Cardiol*. 2016 Jul;32(7):831-41. doi: <https://doi.org/10.1016/j.cjca.2016.02.078>
 10. Seber A, Miachon AS, Tanaka AC, et al. [First guidelines on pediatric cardio-oncology from the Brazilian Society of Cardiology]. *Arq Bras Cardiol*. 2013 May;100(5 Suppl 1):1-68. doi: <http://dx.doi.org/10.5935/abc.2013S005>
 11. Bendinelli B, Masala G, Garamella G, et al. Do thiazide diuretics increase the risk of skin cancer? a critical review of the scientific evidence and updated meta-analysis. *Curr Cardiol Rep*. 2019 Jul 27;21(9):92. doi: <https://doi.org/10.1007/s11886-019-1183-z>
 12. Gandini S, Palli D, Spadola G, et al. Anti-hypertensive drugs and skin cancer risk: a review of the literature and meta-analysis. *Crit Rev Oncol Hematol*. 2018 Feb;122:1-9. doi: <https://doi.org/10.1016/j.critrevonc.2017.12.003>
 13. Hicks BM, Filion KB, Yin H, et al. Angiotensin converting enzyme inhibitors and risk of lung cancer: population based cohort study. *BMJ*. 2018 Oct 24;363:k4209. doi: <https://doi.org/10.1136/bmj.k4209>
 14. Byrd JB, Chertow GM, Bhalla V. Hypertension hot potato - Anatomy of the angiotensin-receptor blocker recalls. *N Engl J Med*. 2019 Apr 25;380(17):1589-91. doi: <https://doi.org/10.1056/NEJMp1901657>
 15. Libby P, Kobold S. Inflammation: a common contributor to cancer, aging, and cardiovascular diseases-expanding the concept of cardio-oncology. *Cardiovasc Res*. 2019 Apr 15;115(5):824-29. doi: <https://doi.org/10.1093/cvr/cvz058>
 16. Libby P, Sidlow R, Lin AE, et al. Clonal hematopoiesis: crossroads of aging, cardiovascular disease, and cancer: JACC review topic of the week. *J Am Coll Cardiol*. 2019 Jul 30;74(4):567-77. doi: <https://doi.org/10.1016/j.jacc.2019.06.007>
 17. Nelson ER, Chang CY, McDonnell DP. Cholesterol and breast cancer pathophysiology. *Trends Endocrinol Metab*. 2014 Dec;25(12):649-55. doi: <https://doi.org/10.1016/j.tem.2014.10.001>
 18. Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med*. 2017 Sep 21;377(12):1119-31. doi: <https://doi.org/10.1056/NEJMoa1707914>
 19. Ridker PM, MacFadyen JG, Thuren T, et al. Effect of interleukin-1 β inhibition with canakinumab on incident lung cancer in patients with atherosclerosis: exploratory results from a randomised, double-blind, placebo-controlled trial. *Lancet*. 2017 Oct 21;390(10105):1833-42. doi: [https://doi.org/10.1016/S0140-6736\(17\)32247-X](https://doi.org/10.1016/S0140-6736(17)32247-X)

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