# Cardio-Oncology: To Enable Cancer Treatment while Minimizing Cardiovascular Toxicity

## Cardio-Oncologia: Tratar o Cancro Minimizando a Toxicidade Cardiovascular

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## Introduction

Although cardiotoxicity induced by anthracyclines has been known since the 70´s, Cardio-Oncology as an organized discipline is a relatively new concept. It emerged from the growing need to provide specific cardiovascular care to cancer patients throughout their cancer treatment journey. In fact, due to dramatic improvements in cancer therapy and prevention strategies, we have an increasing number of cancer survivors. This leads to greater awareness for potential sequelae of treatments that can negatively impact long term prognosis. Additionally, in some non-curable cancers there has been a paradigm shift of sorts - patients now can live many years with chronic treatment, most of the times with sequential lines of therapy that can have multiple cardiac side effects, with an earlier presentation. Thus, dedicated professionals who can offer a specific approach to these patients are key.

## Cardio-Oncology in the World

The field of Cardio-Oncology (CO) has experienced an exponential growth worldwide. It is increasingly represented at international cardiology and oncology meetings and there are two dedicated CO journals, including the JACC Cardio-Oncology that was launched in 2020 which has driven much-needed research in this area. CO councils in both European Society of Cardiology (ESC) and American College of Cardiology were created, and the International Cardio-Oncology Society (ICOS) has gained more relevance as the number of international chapters and members grows. ICOS brings together Cardiologists and Oncologists from all over the world, promotes regular training and issues consensus papers in partnership with other societies, as the recent ESC/ICOS joint CO Guidelines.[1] It is also the only entity with a certification process in this area, for both physicians and centers of excellence.

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## Cardio-Oncology in Portugal

Portugal has been no exception to this growing interest and awareness in CO.

The Cardio-Oncology Study Group (GECO) of the Portuguese Society of Cardiology was created in 2019 with the mission of promoting the development of CO in our country, stimulating collaboration between national centers, postgraduate training and research.

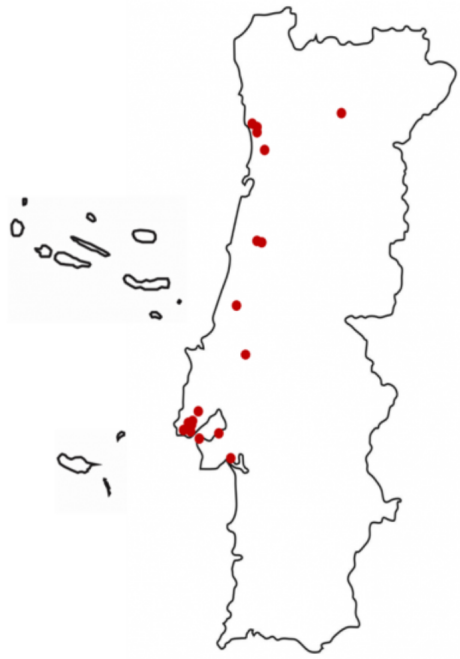
To fulfill the gap on the recommendations, GECO partnered with the Portuguese Association of Cardiovascular Intervention (APIC) to issue a joint position paper regarding interventional cardiology in cancer patients.[2] This is an important contribution in a very challenging field.

GECO also aims to promote international cooperation and has recently established the Portuguese Chapter of the International Cardio-Oncology Society.

An important landmark in CO education in Portugal is the Postgraduate Course in Cardio-Oncology that is organized by the Faculty of Medicine of the Lisbon University and Santa Maria University Hospital. It started in 2018 with collaboration from a multidisciplinary faculty – Cardiologists, Oncologists, Hematologists, Radiation Oncologists, Pediatric Cardiologists, Physical Medicine and Rehabilitation physicians, nurses and basic researchers - from all over the country and from 2021 onwards, the course has also had major contributions from international renowned experts.

Since the creation of the first CO unit in 2016 at Santa Maria University Hospital, the number of national centers providing CO care has been growing. A survey held by GECO in 2021 has shown that there are 17 centers in 12 cities with adult CO units (including Lusíadas group) and one offering a specific pediatric CO consultation (Fig.1). The dimension and structure of these units are not homogeneous. In 10 hospitals there is just one dedicated physician and 3 in just two centers. Most of these cardiologists are heart failure or imaging subspecialists, but in 3 centers there were also interventional cardiologists. Eight centers had nurses and cardiopulmonary technicians as members of the team. There are two national centers with ICOS certification– Santa Maria University Hospital distinguished with Gold center of excellence and Santarém Hospital with Silver.

Lusíadas Group started a CO consultation in 2019 with one dedicated cardiologist. Nowadays it has a robust team of cardiologists with training in CO, from different sub-specialties – imaging, clinical, arrhythmology and interventional cardiology – that can provide truly comprehensive care for cancer patients.



- Hospital de Vila Real, CHTMAD
- Hospital de Santa Maria da Feira, CHEDV
- Hospital de Vila Nova de Gaia, CHVNGE
- Hospital Pedro Hispano – Matosinhos
- Hospital de São João, CHUSJ
- Centro Hospitalar e Universitário de Coimbra – Cardiologia Pediátrica
- Instituto Português de Oncologia de Coimbra
- Centro Hospitalar de Leiria
- Hospital Distrital de Santarém
- Hospital de Santa Maria, CHULN
- Centro Hospitalar Lisboa Ocidental
- Hospital de Santa Marta, CHLC
- Hospital da Luz Lisboa
- Hospital dos Lusíadas Lisboa
- Hospital Beatriz Ângelo
- Hospital Garcia de Orta
- Hospital de Setúbal, CHS
- Centro Hospitalar Barreiro-Montijo

**Figure 1.** Cardio-Oncology centers in Portugal (with authorization from the Cardio-Oncology Study Group of the Portuguese Society of Cardiology)

## Scope of Cardio-Oncology

CO is a multidisciplinary field that requires a strict collaboration between cardiologists and oncologists/hematologists. The main goal of CO is to enable cancer treatment while minimizing cardiovascular side effects.

While a detailed description of the full spectrum of CO is beyond the scope of this paper, a few issues merit a succinct reference.

The most widely known form of cardiotoxicity is left ventricle dysfunction/heart failure and the one that has been the

subject of the majority of research. However, cardiotoxicity encompasses a spectrum of manifestations: arrhythmias, coronary artery disease, hypertension, venous thromboembolic disease, pulmonary hypertension or pericardial disease.[1]

International guidelines, both from Cardiology[1] and Oncology[3] societies, state that patients should be stratified before cancer treatment with drugs of potential cardiotoxicity. Cardiovascular risk factors control should be assessed, as well as the presence and stability of heart disease, in order to select high-risk patients that should be evaluated in CO consultation. For specific agents, like anthracyclines, anti-HER2 therapies, proteosome inhibitors and osimertinib, a baseline echocardiogram should be performed.[1]

During treatment, patients should be monitored to detect cardiotoxicity earlier, thus allowing an earlier cardiology intervention to minimize cancer therapy interruptions. The monitoring protocols depend on the potential cardiotoxicity of the drug used. The most established ones are for anthracyclines and anti-HER2 therapies, and include clinical and echocardiography assessment, although biomarkers like troponin can be of use too.[1]

Long term cardiovascular side effects are mainly an issue for patients submitted to anthracyclines or thoracic radiotherapy. Guidelines recommend screening with echocardiography every 5 years and every 2 years in high and very high-risk patients (high dose of anthracyclines, high dose of radiotherapy, cardiovascular risk factors or cardiotoxicity during treatment).[1,3]

Cardio-Oncology rehabilitation programs seem to be an important too, both during cancer therapy and in the survivorship setting. Studies showed that supervised exercise is safe, improves cardio-respiratory fitness, reduces cardiovascular risk factors and cardiovascular risk and improves quality of life.[1] So, structures programs should be developed in our country to fulfill this need.

## Future Perspectives

Cardiovascular disease and cancer continue to be the leading causes of death in our country. In addition to the cardiotoxicity of cancer treatment, these two diseases seem to be more intrinsically linked. Not only do cancer patients have a higher risk of developing cardiovascular disease, as the former is associated to an increased risk of cancer, especially atherosclerotic disease.[4] They not only share traditional risk factors, but also pathophysiological mechanisms. Clonal hematopoiesis of indetermined potential (presence of clonal expansion of hematopoietic stem that have acquired somatic mutations resulting in a survival and proliferative advantage), for example, is an area of intense research, since is associated with an increased risk of both hematologic cancer and coronary artery disease.[5] Unraveling these links could provide the development of therapies to address these two diseases.

Multicenter clinical trials to guide decision-making in many aspects of CO, such as risk stratification, are fundamental. Most of the recommendations of the ESC guidelines[1] are based on opinion of experts (208/272 recommendations are level of evidence C), highlighting the need of a major effort on building up evidence.

## Responsabilidades Éticas

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