

## Cardio-Oncology in Iran: Cardio-toxicity Registry

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### ABSTRACT

Advances in cancer treatment have resulted in a growing number of cancer survivors. However, powerful treatments such as chemotherapy, radiation treatments, and some cancer drugs are not without risks, including the potential for serious, long-term damage to the heart. Cardiology and oncology specialists often collaborate to mitigate these risks when treating cancer patients. This joining is known as cardio-oncology. The main goals of cardio-oncology are to screen for and actively manage modifiable cardiovascular risk factors and diseases in cancer patients. Cardio-oncology plays an increasingly active role at every stage of cancer therapy, including baseline risk assessment pretreatment, surveillance and prevention during treatment, response to acute complications, and assessment of survivors' post-cardiotoxic treatments. Cancer treatment has been optimized through new treatment strategies. The first cardio-oncology clinic in Iran was instituted about 4 years ago (2017) at Shaheed Rajaei Cardiovascular Medical and Research Center in Tehran, which is the first cardio-oncology clinic in the Middle East. It provides care for cancer patients with a history of cardiovascular disease or risk for cardiotoxicity during cancer therapy. Also, all patients are enrolled in the multicenter cardio-oncology Toxicity Registry research database, and 13 other hospitals from different centers in the whole country are involved in the registry. The establishment of the cardio-oncology clinic with a focus on the patient registry is discussed in this article.

**Keywords:** Cancer, Cardiotoxicity, Cardio-Oncology, Registry

### INTRODUCTION:

Iran is a developing country in the Middle East that has experienced rapid development caused by industrialization and modernity. The new lifestyle and environmental changes in recent years, along with improvements in life expectancy and the growing elderly population are postulated to impact cancer prevalence and the epidemiologic patterns of various malignancies [1].

In Iran, cancer is the second large group of chronic non-communicable diseases and the third most common cause of death after heart disease and motor vehicle accidents [2]. The age-standardized incidence rates of cancers were 110 and 98 per 100,000 among male and female Iranians, respectively, and the estimated cancer mortality rates were 65 and 41.1 per 100,000, respectively [1]. The 5 most common cancers (other than skin cancer) were stomach, prostate, lung, colorectal, and bladder in male Iranians and breast, colorectal, stomach, lung, and thyroid in female Iranians [3].

The main purpose of cardio-oncology is to consider aspects of both cardiology and oncology in a patient, creating a bridge between the 2 fields to make the best decisions regarding the prevention, monitoring, and treatment of the diseases. So, it is crucial to establish a collaborative effort to achieve the best possible cancer and cardiovascular outcomes [4].

### Cardio-Oncology in Iran

The first cardio-oncology clinic in Iran was instituted about 4 years ago (2017) at Shaheed Rajaei Cardiovascular Medical and Research Center (the Cardiology Center of Iran University of Medical Sciences) in Tehran, which was the first cardiooncology clinic in the Middle East and functions as a center for visiting patients with cancer and who also have a history of cardiovascular disease or risk for cardiotoxicity during cancer therapy, as well as for patients affected by primary or metastatic tumors involving the heart.

A cardio-oncologist and professor of echocardiography is the founder and head of the team. Other team members include heart failure and cardiac imaging special-

ists, cardiovascular interventionalists and surgeons, hematologists, radiation oncologists, pathologists, nutritionists, primary care physicians, psychiatrists, palliative care specialists, and trained nurses at other centers. The team's most important aim is to gain a better understanding of cardiac complications of oncology treatments and to develop early detection and intervention strategies to optimize the cardiac health of cancer patients. This mission will be realized by clinical work and also research. The cardio-oncology research center was established in December 2019. All the patients' data are recorded in this center, and various clinical trials and research projects are advancing to promote our knowledge about this emerging field and propose the best therapeutic protocols and practical guidelines. The center has published numerous papers and books. Organizing numerous conferences, congresses, and biweekly webinars to introduce challenging cardio-oncology cases, with the active cooperation of cardiologists and oncologists as well as fellows and residents, are another steps toward introducing this field.

Furthermore, educating cardio-oncology fellows in an 18-month fellowship course to spread this knowledge throughout the country is actively going on with excellent acclaim of the cardiologists to be part of the field. Making pamphlets to educate general populations, constructing an up-to-date website, and televisits (especially in the COVID-19 era) are the other steps [5].

### Cardio-Oncology Registry

All of our patients are enrolled in the multicenter cardio-oncology toxicity registry research database with the collaboration of partners from 13 other centers. All new patients with cancer referred to active oncologists in the project are registered in this program. Verbal and written consent is obtained from patients who agree to be enrolled in the program.

Before starting therapeutic agents for cancer, all patients referred to this clinic undergo careful assessment, including demographic characteristics, complete history taking, and physical examination to determine baseline cardiovascular state and cardiovascular risk

factors. Also, all the oncology data like cancer and tumor type with staging and grading will be collected. Then, all records are registered, and patients undergo risk stratification according to the data gathered. After the initial intake, a treatment plan for the patient is proposed. The patient forms detailing the history and plan are then submitted, either manually or electronically. At this center, patients are visited by a physician and undergo advanced echocardiography (or any other multimodality imaging needed).

Fortunately, at the moment, we can benefit from advanced echocardiography modalities like 3D and speckle tracking echocardiography. We performed strain echocardiography for all the patients, evaluated twist and torsion, and evaluated left ventricular ejection fraction by 3D echocardiography and had interesting discoveries. If necessary, medication is prescribed, and physicians fill out the form with the final information. Primary prevention measures are prescribed as lifestyle modification or medication therapy for their underlying cardiovascular conditions if necessary. Potential cardiovascular complications of various treatment strategies are discussed with the oncologist, and the best strategy is chosen for each patient. Depending on the selected treatment plan, the frequency of follow-up visits, and the potential development of treatment complications, the cardio-oncology team decides to stop or modify the cancer treatment strategy. Furthermore, since the complications of cancer therapy may appear years after treatment, all enrolled patients undergo long-term follow-up at this center.

Currently, about 2,000 patients are represented in our center's registry. The main purpose of this registry is to collect data on the epidemiologic factors affecting the Iranian population in cancer and heart disease. Risk factors, patient response to therapy, relapse, and factors affecting cardiac complications are collected, along with demographic and racial information to compare with regional (i.e., the Middle East and Asia) and worldwide statistics. For example, we found in a preliminary analysis that circumferential strain will be affected by cardiotoxic drugs way sooner than longitudinal strain, which will be published in an article. We also represented dyssynchro-

ny as one of the first markers of cardiotoxicity, published as a letter to the editor and accepted by the cardiooncology society. Besides, we concluded that the right ventricle would be affected by cardiotoxicity before the left ventricle in about 75% of the patients. Also, cardiac valves with mild abnormalities (like mild regurgitation) and in physiologic amounts are more susceptible to chemotherapy and radiotherapy cardiotoxic effects. All the findings are going to be produced in multiple articles.

Recently, we are adding an important new line to the registry assigned to patients undergoing HSCT (hematopoietic stem cell transplantation). More than 70% of the transplantations are performed in Tehran, the capital city, but all the cities will be involved soon in the project. We believe that these data will benefit the development of national guidelines and improve patient care in cardio-oncology. The main cardiooncology center, the referral center, is located in Shaheed Rajaie Cardiovascular Medical & Research Center. Still, as mentioned earlier, 13 other hospitals from different centers in Tehran and other cities, which are oncology centers, are involved in the registry. Our perspective is to widen the registry from the country to the middle east region and also connect this registry to an established large cardio-oncology registry (CONFUCIUS) on ClinicalTrials.gov.

### Limitations

Financial and human resources limitations are the challenges, like every new foundation. Benefiting from charities like the Iranian Heart Charity in Shaheed Rajaie Cardiovascular Medical & Research Center, and grand cardiology associations like Iranian Heart Association and oncology associations, pharmaceutical companies, and companies involved in the health or food industry with massive financial resources and also financial institutions like banks, and syndicates like jewelers is planned to overcome this problem.

Gatherings and seminars to introduce the broad scope of cardio-oncology, create acceptance of it as a new field of research and clinical practice, and explain how effective it can be in decreasing patients' symptoms, optimizing their quality of life, decreasing their morbidity and

mortality, and increase their life expectancy have made cardio-oncology a well-appreciated field. With the education of a new generation of fellows, we hope that now that cardio-oncology has been approved as a fellowship course, human resources will also be supplied.

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