ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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The Global Cardio-Oncology Registry

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H&O How did the field of cardio-oncology come about?

DS There are about 20 million cancer survivors in the United States. With significant improvements in immunotherapy, targeted therapies, chemotherapy, and personalized treatment approaches, more patients are surviving their cancer diagnosis. However, alongside these improvements in cancer treatment, there has been a significant increase in cardiovascular disease.

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The field of cardio-oncology emerged 10 to 15 years ago to meet the needs of this growing population of cancer survivors, with one of its main goals being to quickly detect, prevent, neutralize, or reverse the potential deleterious cardiovascular effects of certain cancer treatment modalities. By proactively addressing potential cardiovascular issues before and during cancer treatment, we can implement early detection and preventative strategies using imaging, biomarkers, and cardioprotective measures. These strategies allow patients to continue or even intensify cancer treatment while protecting cardiovascular health at the same time.

Cardio-oncology has grown significantly, with the establishment of dedicated journals and sections within leading organizations, including the American College of Cardiology (ACC), the American Heart Association (AHA), and the European Society of Cardiology (ESC). Additionally, it is gaining traction within oncology societies such as the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology. The main objective is to foster collaboration between cardiologists and oncologists, and we are achieving that. This collaboration is materialized with the emergence of the International Society of Cardio-Oncology, which a professional society co-led by cardiologists and oncologists, and is now the leading voice of cardio-oncology throughout the world.

H&O What is the Global Cardio-Oncology Registry, and why was it developed?

DS The Global Cardio-Oncology Registry (G-COR) is the first global collaboration to learn more about cardiovascular disease in real-world scenarios. Given that this field is relatively new, strong data from larger populations are lacking. Clinical trials in cardio-oncology have remained relatively small in scale, and emerging data have only started surfacing over the last decade or so. Furthermore, some oncology clinical trials exclude

patients with preexisting cardiovascular disease and some cardiology trials exclude patients with cancer, therefore potentially deepening the lack of data on patients with cancer and cardiovascular disease. Until recently, established guidelines did not exist. However, in August 2022, the ESC published the first comprehensive guidelines in cardio-oncology, involving all aspects of prevention, strategy, treatment, surveillance, post-cancer treatment, and methods for specific cardiotoxicities associated with anthracyclines, human epidermal growth factor receptor 2 therapies, tyrosine kinase inhibitors, immunotherapies, and radiation. It provides a comprehensive framework complete with algorithms for application and preventative strategies before, during, and after cancer treatment.

Because of the paucity of data in large populations, G-COR has emerged as a collaborative effort aimed at obtaining data from both academic centers and community hospitals to assess and validate existing data and cardio-oncology guidelines in real-world populations. This involves looking at the incidence and prevalence of cardiovascular disease among cancer patients in various scenarios, assessing adherence to the guidelines, and evaluating the utilization of imaging, biomarkers, and other methods across different locations. The registry also aims to facilitate the comparison of cancer treatments across different areas of the world to obtain data with actionable results that will help identify gaps in care and improve access to care for diverse populations.

H&O Could you describe the design of the pilot study?

DS As a part of this extensive collaboration, we initiated a pilot study in the United States (NCT05598879). Through surveys conducted at our sites, we identified 3 priority patient populations: those with breast cancer, those with hematologic malignancies, and those receiving immune checkpoint inhibitors (ICIs). Our study will first focus solely on breast cancer, as this was identified as the top priority for many cardio-oncology centers, and will subsequently include patients with hematologic malignancies and those treated with immune checkpoint inhibitors. We developed a platform integrating cardiovascular and oncologic data, including granular information on cancer staging and cancer treatments, cardiac history, cardiovascular risk factors, imaging, and cardiovascular therapeutic data, thus establishing a registry. We used a REDCap Cloud platform, which is housed by the Cleveland Clinic, to acquire and coordinate data. Currently, we have activated 21 centers and enrolled more than 500 patients in the United States. We will be presenting some of the baseline demographic data at the upcoming national ACC meeting, with our methodology published

a few months ago. We look forward to having further data in the next year or so.

H&O Could you explain the significance of the top 3 priorities of the G-COR—breast cancer, hematologic malignancies, and ICIs—and why they were selected as focal points for the registry?

DS When we developed this collaboration, we aimed to invite centers we were familiar with. Through our involvement in professional societies such as the ACC's Cardio-Oncology Leadership Council, the AHA, and the International Cardio-Oncology Society, we identified academic and community centers suitable for participation. Invitations were then extended to these centers, and the majority demonstrated sufficient patient volume and infrastructure to manage cardio-oncology cases.

As part of the demographic and survey process, we sought to figure out their priorities and the patient populations they most commonly encountered in the cardio-oncology domain. These discussions led to the identification of the top 3 priorities: breast cancer; hematologic malignancies, including patients with lymphomas, leukemias, and multiple myelomas; and patients treated with ICIs involving solid tumors and some hematologic malignancies. It is worth noting that internationally, we have received demographics from 150 hospitals across 35 countries, all of which are eagerly awaiting participation in the G-COR global phase.

H&O How will data be collected and managed within G-COR?

DS All data entered into the REDCap Cloud platform is thoroughly deidentified to ensure patient confidentiality. Each participating center and patient receives a unique identifier, so there is no personally identifiable health information in the G-COR registry. Furthermore, our research group is strict in terms of protected deidentified data. For instance, specific dates are not recorded; instead, data are categorized by quarters, such as date of encounters, cancer treatments, testing, surgeries, and radiation therapy. This rigorous deidentification process ensures patient privacy and confidentiality.

In terms of data collection and governance, we have a scientific committee with participants from various countries and geographic locations. We prioritize diversity among our academic and community centers, as well as our investigators, to ensure comprehensive representation across all ethnicities, backgrounds, academic institutions, and genders. This inclusive approach allows us to better reflect the populations we serve.

To manage data effectively on a large scale, we have designed a method where each country or region has its own data silo where they will have access to all electronic case report forms and platforms. This will facilitate efficient collaboration while maintaining control over data privacy and security. Ultimately, this will allow us to conduct global analyses using data collected from all different regions.

H&O Can you elaborate on the roles of the governing committees within G-COR?

DS The scientific committee plays a large role in the governance of G-COR. This committee consists of both cardiologists and oncologists from different academic and community centers across different geographic areas. For now, we are in the pilot phase, with plans to expand globally in the future. One of the main roles of the scientific committee and governance committee is to identify studies to be conducted by participants in the registry. We aim to encourage collaboration among participants, using this platform as a comprehensive database for research.

H&O What future goals will G-COR strive for after the initial launch of the registry?

DS With the G-COR registry already underway, our next objective is to launch the global phase later this year. Our primary aim is to validate the incidence of cardiotoxicity in populations exposed to different drugs and assess their safety. We also will investigate the long-term cardiovascular effects of these treatments and evaluate differences among patient groups and geographic areas.

An essential aspect of G-COR's mission is to assess social determinants of health and socioeconomic factors within the populations we serve to ensure equitable access to care for individuals from different backgrounds, ethnicities, and geographic regions in terms of diagnostic methods, cancer treatments, and cancer outcomes. The overarching goal is to conduct these assessments on a global scale, identifying disparities, addressing gaps in access to care, and finding opportunities for improvement.

Looking ahead, as we move into the digital era alongside the emergence of artificial intelligence, machine learning, and personalized therapies, we envision incorporating studies exploring these innovative approaches into our registry. However, for this initial phase, in order to have a broader representation of the cardio-oncology world in different areas, it is important that we start with basic information that can be collected from a diverse range of sites.

Disclosures
Dr Sadler has no conflicts of interest to disclose.

Suggested Readings

Lyon AR, López-Fernández T, Couch LS, et al; 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(41):4229-4361.

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