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CARDIO-ONCOLOGY (SA FRANCIS AND RB MORGAN, SECTION EDITORS)

A Cardio-Oncology Data Commons: Lessons from Pediatric Oncology

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Abstract

Purpose of Review To describe the role of big data in cardio-oncology.

Recent Findings There is a trend towards developing cloud-based, integrated registries to improve data collection, access, and analysis.

Summary Using a template from pediatric oncology, a cardio-oncology data commons is a novel opportunity to integrate data elements into a cloud-based platform. A cloud-based registry provides advantages of multi-institutional collaboration, rapid data access, a virtual visualization, and analytic tools to reduce infrastructure redundancy. The data commons would include integrated clinical data, blood samples, and genomic data to streamline discovery and analysis for researchers. A cardio-oncology data commons would be a large step forward in bringing cardio-oncology to the forefront of big data.

Keywords Cardio-oncology · Big data · Data commons · Pediatric oncology

Introduction

Cardio-oncology is an important field that has developed at the intersection of cancer and cardiac care [1, 2•]. Although survival after cancer has improved, an emerging side effect of cancer therapy is cardiac dysfunction [1, 2•, 3]. Cardiac dysfunction can occur in two forms: (1) direct toxicity in the form of cancer therapy damaging the heart muscle or (2) indirect toxicity by cancer therapy negatively impacting cardiac risk factors [1]. In addition to toxicity, survivorship has increased the burden of cardiovascular disease as there is a growing number of cancer survivors who are living longer and reaching an age where cardiac disease becomes more prevalent [2•, 4•, 5].

To address these issues, specialized multidisciplinary teams of cardiologists and oncologists have developed to manage the cardiac health of cancer patients [1, 6]. As a relatively young field, cardio-oncology lacks a large body of literature [6]. As a result, several consensus documents and clinical practice guidelines have been developed to assist in management of this growing population [1, 2•, 3, 6, 7, 8•]. In this review, we explore the role of big data and registries to inform and improve care in cardio-oncology and use initiatives in pediatric oncology as a template for cardio-oncology.

Big Data

Big data comprises three features that separate it from conventional data [9]. First, big data is data that is more complete and collected in significantly larger amounts than conventional data. Second, big data is analyzed using more advanced methods, like neural networks or clustering analysis, rather than traditional statistical tools like *t* tests. For example, neural

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networks are a statistical method where a computer algorithm can be trained to recognize outputs based on labeled inputs [10]. They have been used to assist in medical image analysis and to illustrate complex co-morbid interactions from large inputs of data [11, 12]. Lastly, conventional data is typically used to answer a defined question. Conversely, big data can be used to both answer questions as well as develop new hypotheses.

There is potential in cardio-oncology to leverage big data and registries. Prior examples of big data in cardio-oncology are projects from the Surveillance, Epidemiology, and End Result-Medicare to better understand incidence rates of cardiac toxicity [13] as well as develop risk prediction models [14] A. separate group of researchers at the University of California-Los Angeles used administrative data from the Healthcare Cost and Utilization Project to demonstrate that patients with cancer and heart failure were associated with worse outcomes [15]. There are also attempts to develop multi-institutional collaborations among cardio-oncology centers to better understand rare events like immune checkpoint inhibitor myocarditis [16]. However, often with a low event rate of cardiac toxicity, for instance an approximately 0.1–1% of immune checkpoint inhibitor myocarditis [17], the need for aggregation of large amounts of data in a collaborative manner is apparent.

Lessons from Pediatric Oncology

One big-data framework to learn from is that of childhood cancer. Similar to cardio-toxicity, pediatric cancer is not a common occurrence and it can be difficult for researchers due to a low sample size at a single institution [18]. As a result, the pediatric community has a strong track-record of collaboration to improve care. One such example is the Childhood Cancer Survivor Study, a registry-based collaborative retrospective cohort of over 30,000 survivors of childhood cancer with data starting in 1970 [19]. Data from this registry has yielded several insights into the cardiac care of pediatric cancer survivors. Researchers have shown the importance of modifiable cardiac risk factors in childhood cancer survivors. [20] In addition, Mulrooney and colleagues have used the Childhood Cancer Survivor Study to show the dose-response effect of anthracyclines and radiation on cardiac outcomes in survivors of childhood cancer [21].

As technology improved, big data in pediatric cancer also advanced. The International Neuroblastoma Risk Group (INRG) was a consortium of international pediatric cancer centers contributing data on neuroblastoma [18] Unfortunately, the INRG database was difficult to access and analyze as data was fragmented among various sources. In 2012, the University of Chicago took the lead in integrating these data sources and created a novel cloud-based platform to streamline the process. Currently, the Neuroblastoma Data Commons has data on over 18,000 pediatric neuroblastoma patients. The cloud-based commons is accessible to researchers after a formal request. Importantly, it is an integrated platform of clinical, biospecimen, and genomic data, it reduces time from request to data access, and includes cloud-based tools to facilitate analysis [18].

Building on the push towards cloud-based data, St. Jude has launched the St. Jude Cloud, a cloud-based platform with the goal to advance pediatric cancer research by making genomic data available to researchers. At its introduction in 2018, the St. Jude Cloud had genomic data on over 5000 pediatric cancer patients with an anticipated growth to 10,000 patients by 2019. The St. Jude Cloud was created by an academic-private collaboration between St. Jude Children's Hospital, DNAnexus, and Microsoft. Similar to the INRG Data Commons, it is an integrated platform, it reduces data access times, and includes cloud based tools, such as enhanced data visualization features and statistical packages [22, 23]. Using the background of pediatric cancer's need for collaboration and the prior successes of data integration, the National Cancer Institute (NCI) recently introduced the Childhood Cancer Data Initiative (CCDI), a large-scale proposal to integrate pediatric cancer data. With a budget of $500 million dollars over 10 years, the goal of the project is to improve the collection, access, and analysis of pediatric cancer data [24, 25].

Faced with similar limitations of low event rates of cardiotoxicity and fragmented data sources, cardio-oncology can learn valuable lessons from the pediatric cancer community in creating a big-data infrastructure. First, it appears that a cloud-based research platform is essential in modern day research. It facilitates data entry, data access, data querying, and data analysis [18]. Second, big data projects require multi-institutional collaborations with a governance structure for data collection, storage, security, access, and analysis [18]. Lastly, success in big data initiatives will be most successful with public-academic-private partnerships, as suggested in the initial vision for the CCDI [25] as well as was the case of the St. Jude Cloud [23].

Cardio-oncology Data Commons

With this template, we propose the concept of a cardio-oncology data commons (Fig. 1), a multi-institutional consortium with the goal to collect and analyze toxicity from cancer therapy. We envision a joint venture between the National Cancer Institute and the National Heart, Lung, and Blood Institute (NHLBI) with representatives from academic centers, community centers, cooperative oncology groups, the Food and Drug Administration, and pharmaceutical companies. It would contain granular data on patients who are high

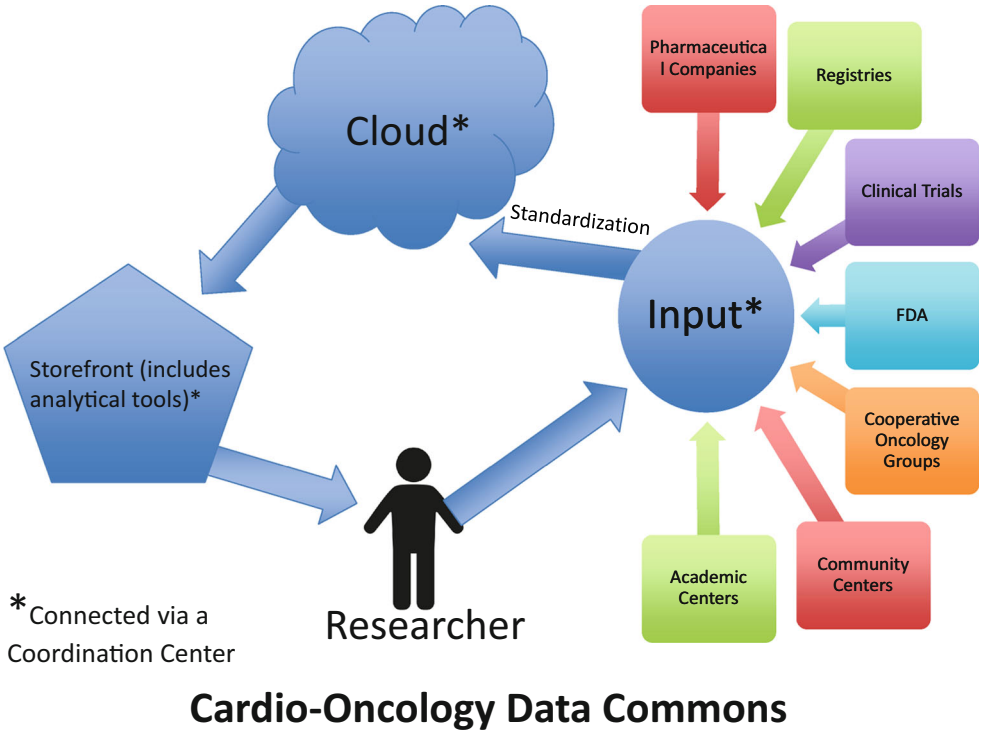

Fig. 1 Model for a cardio-oncology data commons

risk for developing cardiac toxicity from cancer therapy as well as those who develop acute cardiac toxicities from cancer therapy. De-identified clinical data, blood samples, and genomic data would be cataloged and integrated into a cloud-based platform. Similar to the INRG Data Commons and the St. Jude Cloud, data can be queried and analyzed using a virtual server, avoiding replication of informatics infrastructure at individual centers. We believe such a cardio-oncology data commons is essential for the field.

A cardio-oncology data commons will not be an easy task. Due to the multidisciplinary nature of cardio-oncology, the data elements collected in the data commons must be inclusive of both granular cardiac and oncologic information. For instance, for a breast cancer patient, data elements would need to include information on demographics, cardiac risk factors, cardiac diagnostics, labs, oncologic stage, pathology, and a detailed therapy plan. Unlike many other registries, this will require specialized input from personnel trained in cardiology and oncology working together. The alternative of using administrative data or data specific to one field will be limited in its ability to answer critical questions such as the toxicity of cumulative dosing or pre-clinical markers of toxicity. The second barrier is a common definition of cardiotoxicity. Cardiotoxicity has variable definitions depending on the consensus guideline. For instance, the America Society of Echo (ASE) defines heart failure from cardiotoxicity as a decrease in left ventricular ejection fraction (LVEF) by greater than 10% to an absolute ejection fraction of less than 53%. However, the Common Terminology Criteria for Adverse Events (CTCAE) provides a more subjective definition of heart failure than varies from grade 1 to grade 5 with a less specific focus on ejection fraction [26]. Further complicating the equation is literature suggesting that a 10% difference in LVEF may be within the error range for inter-reader variability [27]. Ultimately, for big data to be meaningful in cardio-oncology, the field needs to resolve taxonomy differences and adopt universal definitions for the spectrum of cardio-toxicity.

Conclusion

Cardio-oncology is an emerging field with tremendous opportunity to help cancer patients. However, there is a growing need for data. Unlike more established fields, cardio-oncology has the unique opportunity to develop its research framework from scratch and can use lessons from recent successes in big data like the Childhood Cancer Survivor Study, the INRG Data Commons, and the St. Jude Cloud. The path forward to aggregate data will be on display in the implementation of the CCDI. Although challenges exist, a cardio-oncology data commons, a cloud-based, integrated platform with virtual analytic tools, is the future of big data in cardio-oncology.

Compliance with Ethical Standards

Conflict of Interest Anant Mandawat, Logan Eberly, and William Border declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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