Cardio-Oncology: A Historical Perspective
Past, Present and Future

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Disclosures

• Honararia – Pfizer, Novartis, Hoffman La Roche, Eli Lilly

• Advisory boards – Novartis, Hoffman La Roche, Eli Lilly, Pfizer
Objectives

• To discuss the historical evolution of cardio-oncology as a sub-specialty of medicine

• To discuss what we have learned and current knowledge gaps

• To discuss the importance of a multidisciplinary approach in the continued growth and development of cardio-oncology

• To discuss future research directions in cardio-oncology
How did we get started?
Risk of doxorubicin-associated congestive heart failure

Hazard ratio ( > 65: < = 65) = 2.25
95% C.I of ( > 65: < = 65) = (104.485)
Logrank P = value = 0.029
Wilcoxon P = value = 0.79

* = Patients at risk

Cumulative dose of doxorubicin (mg/m²)

≤ 65  458  431  345  206  103  50  20  6  4
> 65  172  161  119  92  28  12  3  1  1

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Chemotherapy-Induced CHF
Bad Prognosis

Who is responsible for patient care?

The cardiologist!
The patient developed cardiac disease!

The oncologist!
The patient has a cancer!

Oncologist
Cardiologist

Credit, Dr. Cardinale
Landscape is changing ......

Canadian Cardiac Oncology Network

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“The drug trastuzumab cuts the risk of tumours returning in women with early stage breast cancer by 50%...”
Evolution of Cancer Therapy

- Anthracyclines: 1970s
- Anti-VEGF Therapy: 2000’s
- Checkpoint inhibitors: 2010
- Trastuzumab: 1990’s
- Proteasome inhibitors: 2005

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Advances in Cancer Diagnosis, Treatment, and Survivorship

Cancer deaths per 100,000 persons

5-yr survival rate (%)


Deaths 5-yr survival

Cardiovascular Side Effects of Modern Cancer Therapy

- Arrhythmia
- Cardiac Dysfunction
  - Heart Failure
- AP / MI
- Hypertension
- Thromboembolism
The birth of Cardio-Oncology

A clinically based discipline focused on the cardiovascular health of cancer patients and cancer survivors

Optimize Cardiac Health

Best Cancer Care
The cardio-oncologist

Health care providers focused on the prevention, early detection, management and recovery of cardiovascular function potentially resulting from cancer therapies.
Cardiologia. 1996 Sep;41(9):887-91.

[A new frontier: cardio-oncology]

[Article in Italian]

Cardinale D.
Servizio di Cardiologia, Istituto Europeo di Oncologia, IRCCS, Milano.
PMID: 8983846 [PubMed - indexed for MEDLINE]
What have we learned?
Frequent coexistence of cardiac problems in cancer patients

Cardiac disease

Oncologic disease

Courtesy, Dr. Cardinale
Shared risk factors for cancer and cardiac disease

Modified from Farmakis D et al. Int J Cardiol 2016
Figure 1: Interaction Between Shared Risk Factors, Cardiac Disease & Cancer

- Shared Risk Factors:
  - Smoking
  - Obesity
  - Non-Prudent Diet
  - Physical Inactivity

- CANCER
  - Radiation
  - Targeted Therapy
  - Surgery
  - Chemotherapy

- CANCER Risk:
  - Less therapy offered due to LV dysfunction
  - Cardiotoxicity limits therapy

- Cancer Survivors:
  - High Long Term Risk

- Cardiac Risk:
  - Cardiotoxicity
  - Cancer therapy
  - Worsening risk factors

- Risk Factors Persist During Cancer Treatment
  - Risk Factors May Worsen During Cancer Treatment

- Clinical Cardiovascular Disease at Cancer Diagnosis
- Sub-Clinical Cardiovascular Disease at Cancer Diagnosis

Virani SA et al. Can J Cardiol 2016; 32:831-41
Cardiovascular Disease: Important cause of mortality in early breast cancer

What have we accomplished?
The Compelling Need for a Cardiology and Oncology Partnership and
the Birth of the International CardiOncology Society
Daniel J. Lenihan\textsuperscript{a}, Daniela Cardinale\textsuperscript{b}, Carlo M. Cipolla\textsuperscript{a,\textdagger}\textsuperscript{a,*}
We are growing quickly
First GCOS meeting in Nashville, 2015
In 2018.....

- 368 attendees
- 25 countries
Developing a Cardiology-Oncology Partnership
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)

Authors/Task Force Members: Jose Luis Zarzora* (Chairperson) (Spain), Patrizio Lancetti* (Co-Chairperson) (Belgium), Daniel Rodriguez Mullol (Spain), Victor Abonya (France), Riccardo Asteggiano (Italy), Maurizio Gallerani (Italy), Gilbert Haib (France), Daniel J. Leshin* (USA), Gregory Y. H. Lip (UK), Alexander K. Lyon (UK), Teresa Lopez Fernandez (Spain), Daniel Molty (France), Massimo F. Piepoli (Italy), Juan Tamargo (Spain), Adam Torbicki (Poland), and Thomas M. Suter (Switzerland)

Clinical practice guidelines

Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†

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Consensus Statement

Cardio-Oncology Training: A Proposal From the International Cardi-oncology Society and Canadian Cardiac Oncology Network for a New Multidisciplinary Specialty

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Nashville, Tennessee; Tampa, Florida; Chicago, Illinois; Minneapolis, Minnesota; Indianapolis, Indiana; London, United Kingdom; Cleveland, Ohio; Houston, Texas; Richmond, Virginia; Tel Aviv, Israel; Palo Alto, California; Milan, Italy; Louisville, Kentucky; Lisbon, Portugal; St Louis, Missouri; Kansas City, Kansas; Atlanta, Georgia; Ottawa, Canada; Durham, North Carolina; and Philadelphia, Pennsylvania

ABSTRACT

There is an increasing awareness and clinical interest in cardiac safety during cancer therapy as well as in optimally addressing cardiac issues in cancer survivors. Although there is an emerging expertise in this area, known as cardio-oncology, there is a lack of organization in the essential components of contemporary training. This proposal, an international consensus statement organized by the International Cardi-oncology Society and the Canadian Cardiac Oncology Network, attempts to marshal the important ongoing efforts for training the next generation of cardio-oncologists. The necessary elements are outlined, including the expectations for exposure necessary to develop adequate training. There should also be a commitment to local, regional, and international education and research in cardio-oncology as a requirement for advancement in the field. (J Cardiac Fail 2016;22:465–471)

Key Words: Cardio-oncology, training, cardiotoxicity, survivorship.
**Aims and scope**

The editorial mission of *Cardio-Oncology* is to advance the science and practice of this emerging field to find a balance between oncologic efficacy and reducing adverse cardiovascular effects through timely publication and dissemination of peer-reviewed research. As an open access, online journal *Cardio-Oncology* provides a high visibility platform for the publication of original research and expert reviews on the cardiovascular effects of cancer treatment.

The journal welcomes submissions to the following sections:
- Adult Oncology - Giuseppe Curigliano and Susan Dent
- Clinical Cardiology - Daniela Cardinale and Daniel Lenihan
- Clinical Trials - Michael S Ewer and Thomas Suter
- Geriatric Oncology - Dawn L Hershman
- Imaging - Steven Colan
- Nursing - Anecita Fadol and Mary McCabe
- Pediatric Oncology - Gregory Armstrong and Stephen E Sallan
- Radiation Oncology - Louis Constine
- Translational Cardiology - Bonnie Ky and Ed TH Yeh

**Cardiooncologyjournal.biomedcentral.com**

cardiaconcology.ca
The Evolution of Cardio-Oncology

Reports of anthracycline-induced cardiotoxicity

1966

Understanding that anthracycline-induced cardiotoxicity depends on the cumulative dose

1977

Reports of hypertension, heart failure, and vascular occlusion with TKIs

1998

Reports of trastuzumab-induced cardiotoxicity

90 PubMed citations in “cardio oncology”

2007

ESMO Clinical Practice Guideline published

2012

European Society of Cardiology Position Paper published

2014

812 PubMed citations in “cardio oncology”

2016

37 cardio-oncology clinics in the US

2017

ASCO Clinical Practice Guideline published

Education

- National Organization (Canadian Cardiac Oncology Network) in 2011 (www.cardiaconcology.ca)
- ICOS (www.icosna.org)
- GCOS – Annual meeting
- ACC – Cardio-Oncology Section (www.acc.org)
- ECOG-ACRIN cardiotoxicity working group
The Connection Between Cancer Treatment and Cardiac Problems

As more people survive cancer, doctors are discovering the long-term side-effects of their treatments.

Learn About Asthma
Get More Information on Asthma Symptoms, Diagnosis and Treatment
www.brookhrginfo.com

Minimizing Heart Damage After Cancer Treatment

There are steps both patients and primary care physicians should take.
The Future of Cardio-Oncology
International Collaboration

- Argentina
- Poland
- China
- India
- Italy
- Mexico
- Japan
- Australia
- Brazil
- Spain
- Switzerland
- Israel

UNDER CONSTRUCTION
Challenges

• Better understanding of the mechanisms of cardiotoxicity
• Early identification of cardiac risk
  – e.g cardiac imaging, biomarker
• Strategies to prevent cardiotoxicity
  – Primary and secondary prevention
• Optimal cardiovascular drugs to manage cardiotoxicity
• Surveillance and monitoring
  – Imaging, frequency and duration
• Lifestyle modification
Optimization of cardiac monitoring; survivorship

- Risk prediction of cardiotoxicity
- Biomarkers + imaging

Cardio-oncology registry (SURVIVE)

Cardiac protection during cancer treatment

Early detection of cardiotoxicity using markers of apoptosis

198 registered CT on diagnosis and treatment of cardiotoxicity clinicaltrials.gov
Goals of Cardio-Oncology

• Improve access to effective multidisciplinary care
• To educate HCP’s and the public
• Improve the application of guideline based diagnosis and treatment
• Commit to collective research in this field
• Share our experiences with our colleagues
Key Messages

• Improvement in cancer therapies has resulted in long term survivors who may be at risk of cardiotoxicity.
• Individuals with heart disease may develop cancer and require potentially cardiotoxic cancer therapy.
• Close collaboration among HCP’s is needed in order to provide the best cancer care while optimizing cardiovascular health.
• The establishment of cardio-oncology clinics/programs provides the framework for optimizing clinical care delivery, education and research.
Thank-you!