How cancer treatment can impact the heart - role of the cardio-oncology service

Stuart D Rosen

Consultant Cardiologist, London NW & Royal Brompton Hospitals

Professor of Practice (Cardiology), Imperial College
and
Hon Adjunct Professor of Cardiovascular Medicine, King's College London, UK

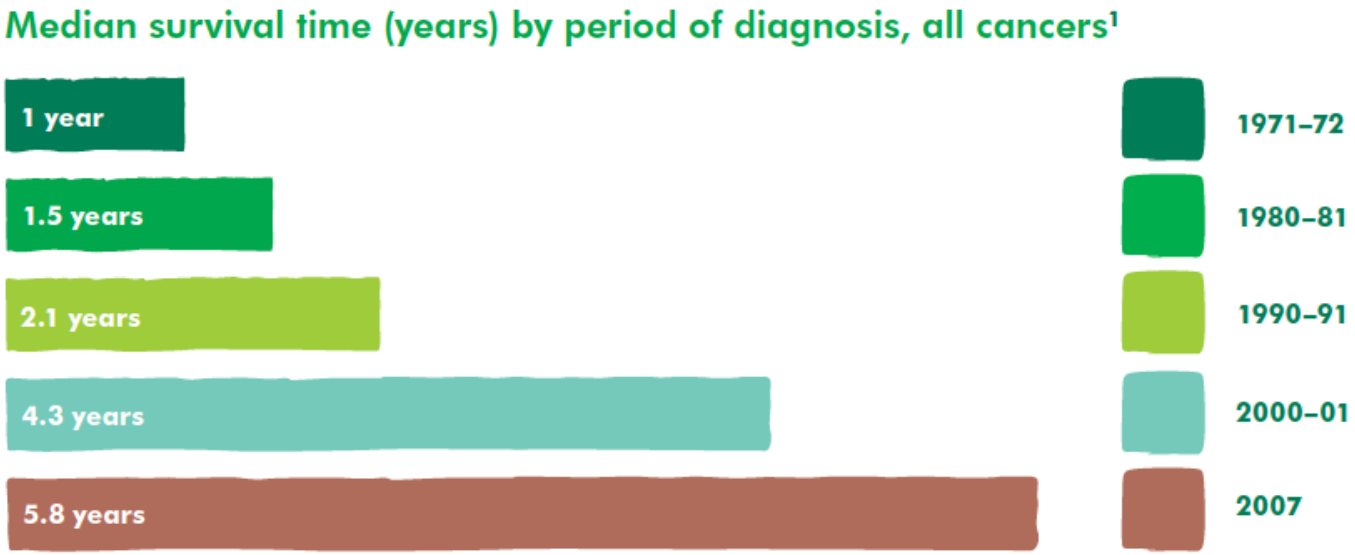
Nature of the problem

- Increasing survivorship
- Point at which treatment related illness exceeds mortality from cancer recurrence
- CVS side effects amongst the most clinically significant, affect mortality

British Cardiovascular Society

BRITISH CARDIO ONCOLOGY SOCIETY
www.BC-OS.org

Cancer Survivorship

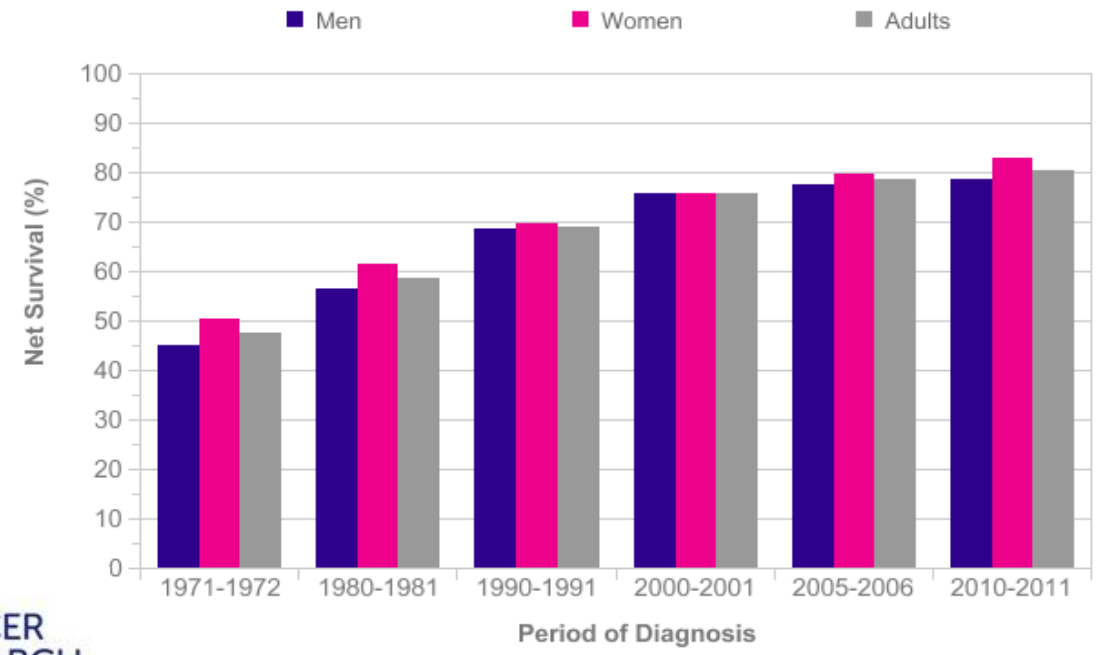


Macmillan Cancer Support 2009

18 million cancer survivors in USA

Age-Standardised Ten-Year Net Survival, England and Wales

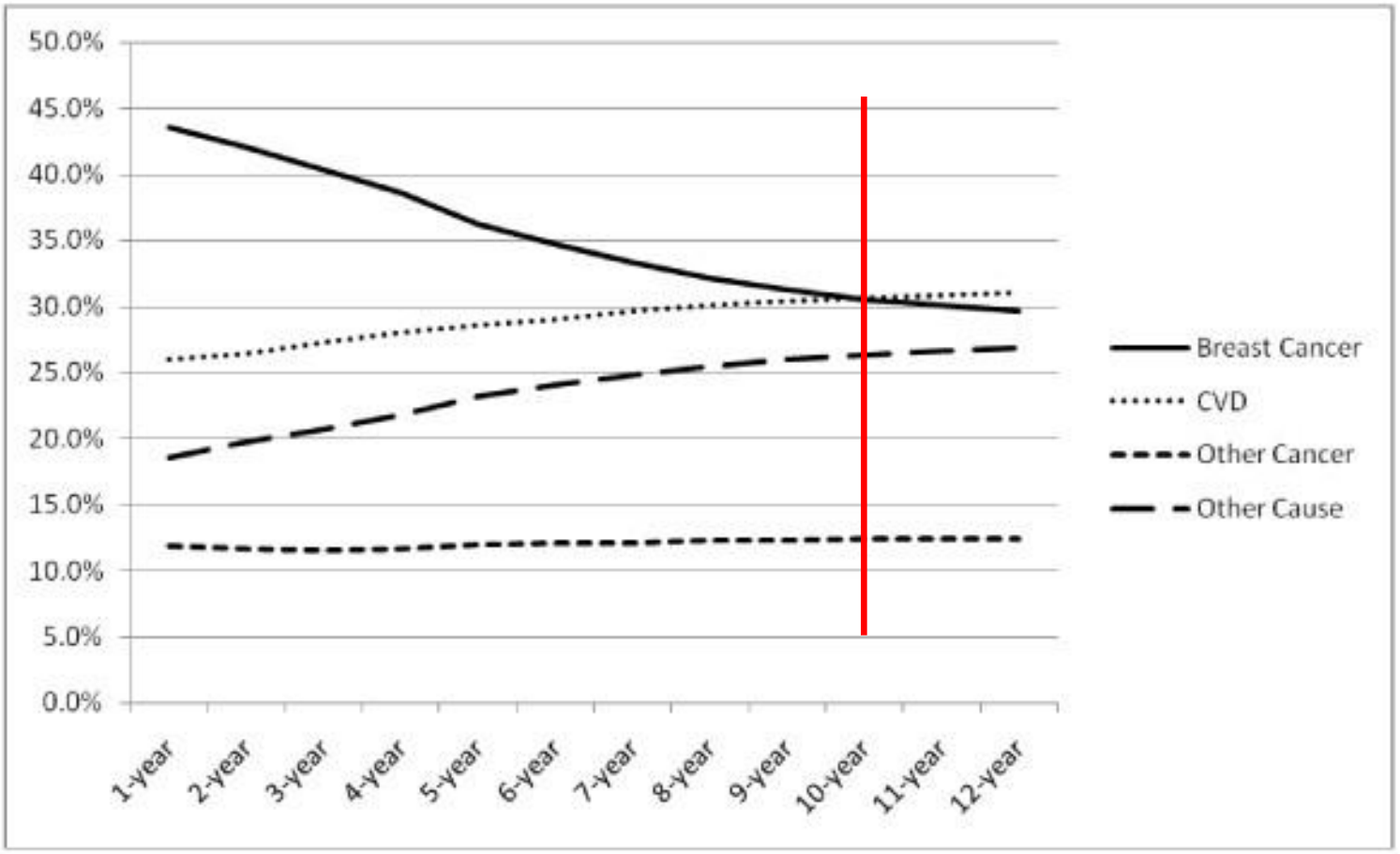
Hodgkin Lymphoma (C81): 1971-2011



CANCER RESEARCH UK

Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine. http://www.lshtm.ac.uk/eph/ncde/cancersurvival

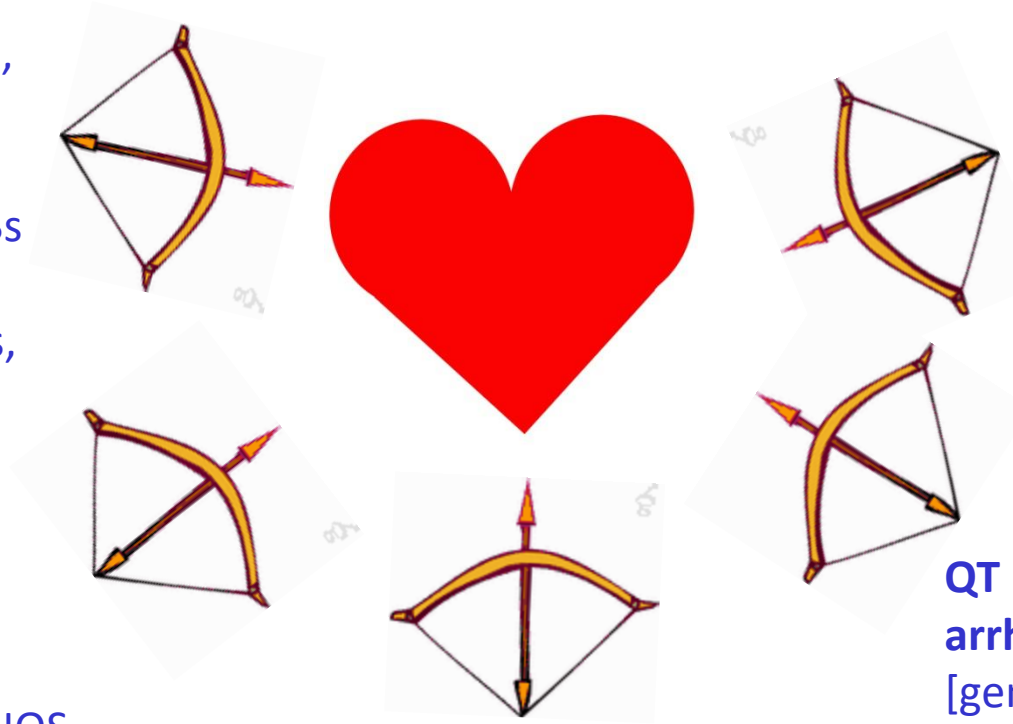
Proportional distribution of cumulative leading causes of death by time since breast cancer diagnosis - US SEER database (63,566 patients)



Patnaik et al Breast Cancer Res. 2011; 13(3): R64

What is good for the cancer is often bad for the heart.....

Cardiomyopathy
[cyclophsophamide, ifosphamide, **anthracyclines**, mitoxantrone, MABs inc traztuzumab, small molecule TKIs, taxanes]



Hypertension
[TKI – bevacizumab, sorafenib, sunitinib]

Ischaemia
[gemcitabine, ifosfamide, 5FU. eNOS and endothelium independent vasoconstriction]

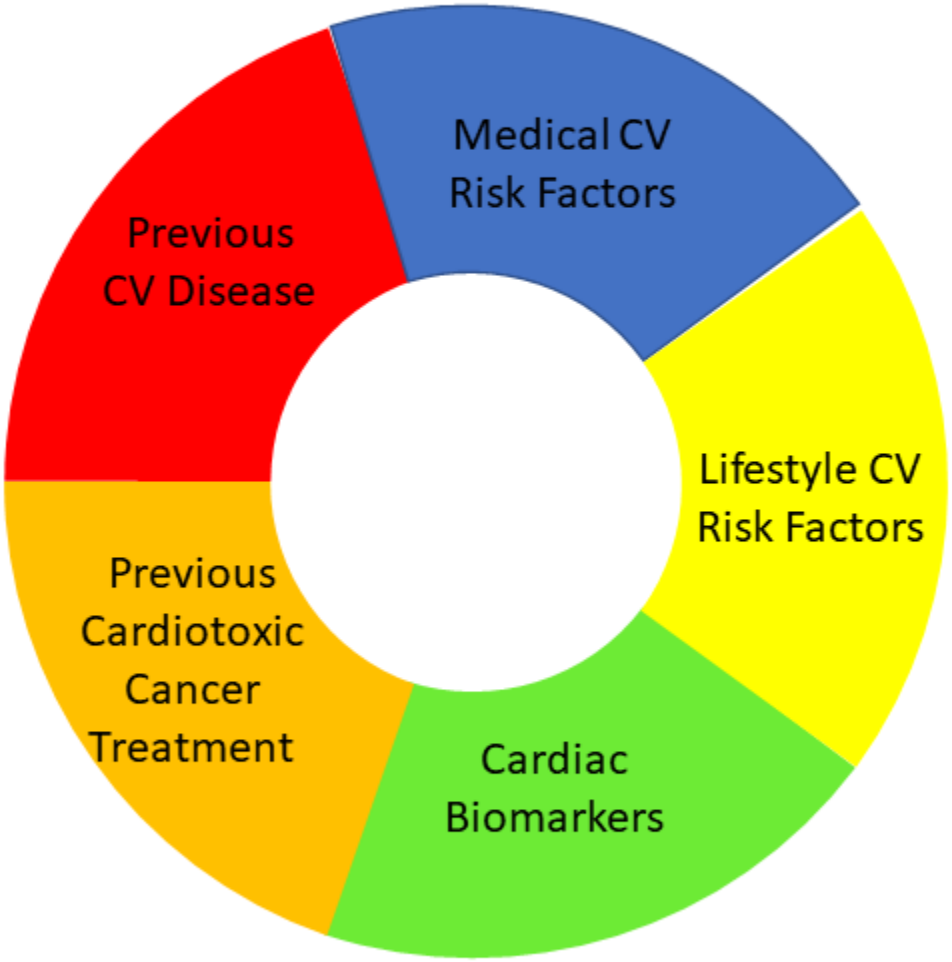
Thromboembolism
[esp alkylating agents, COX-2 inhibitors, anti-VEGF, cisPt]

QT prolongation and arrhythmias (esp AF)
[gemcitabine, ifosfamide, melphalan, 5FU, cisPt. IL2, VT – taxanes]

From: Yeh and Bickford JACC 2009;53:2231

What is the service for?

- Multidisciplinary cardiovascular evaluation in all stages of the cancer process including prior to and during cancer therapy
- CV fitness for treatment (chemo and surgery)
- Helping recovery from the adverse effects of treatment
- Surveillance



Baseline CV Risk Assessment Checklist

Cardiac history
Cancer treatment history
CV risk factors

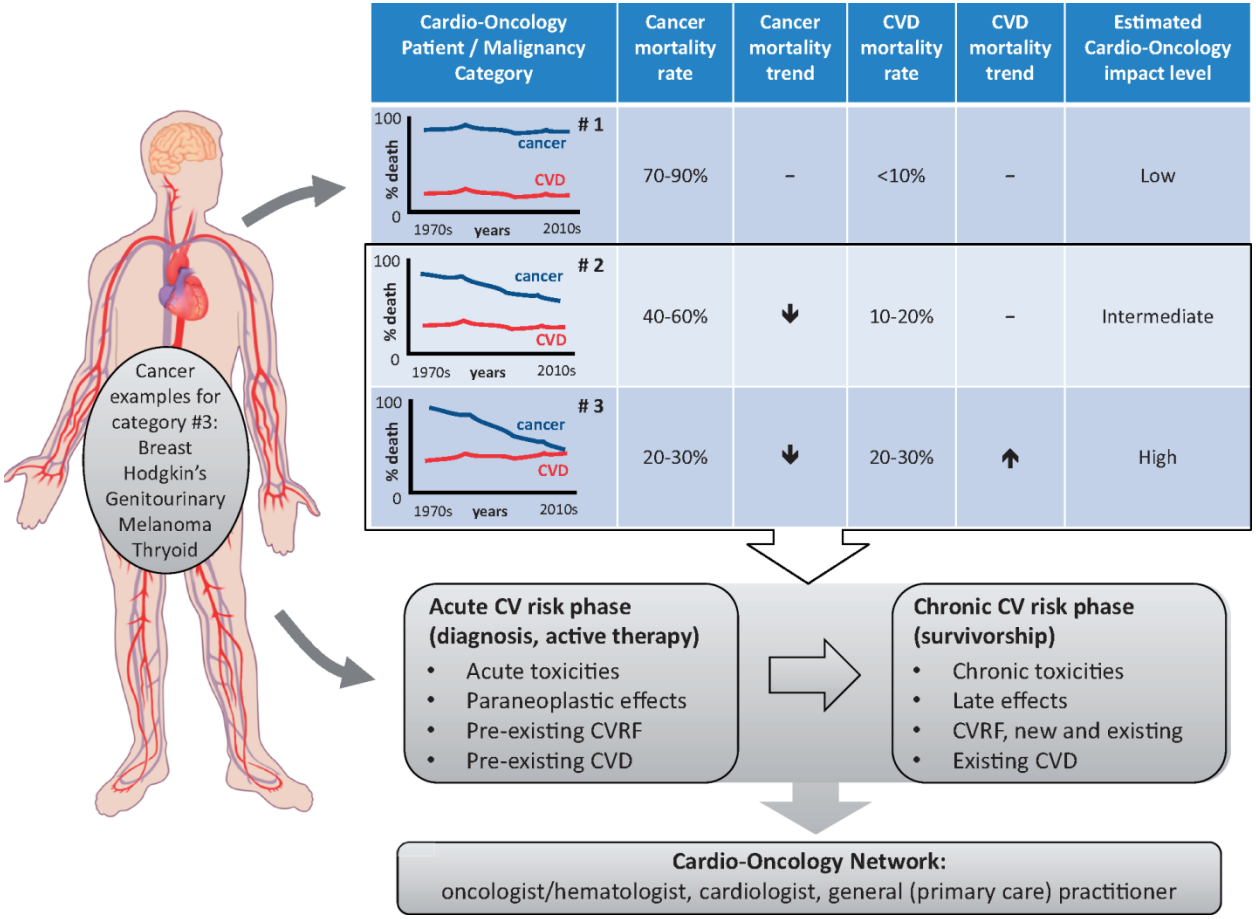
Blood pressure
HbA1c
Cholesterol profile

Cardiac troponin
BNP or NT-proBNP

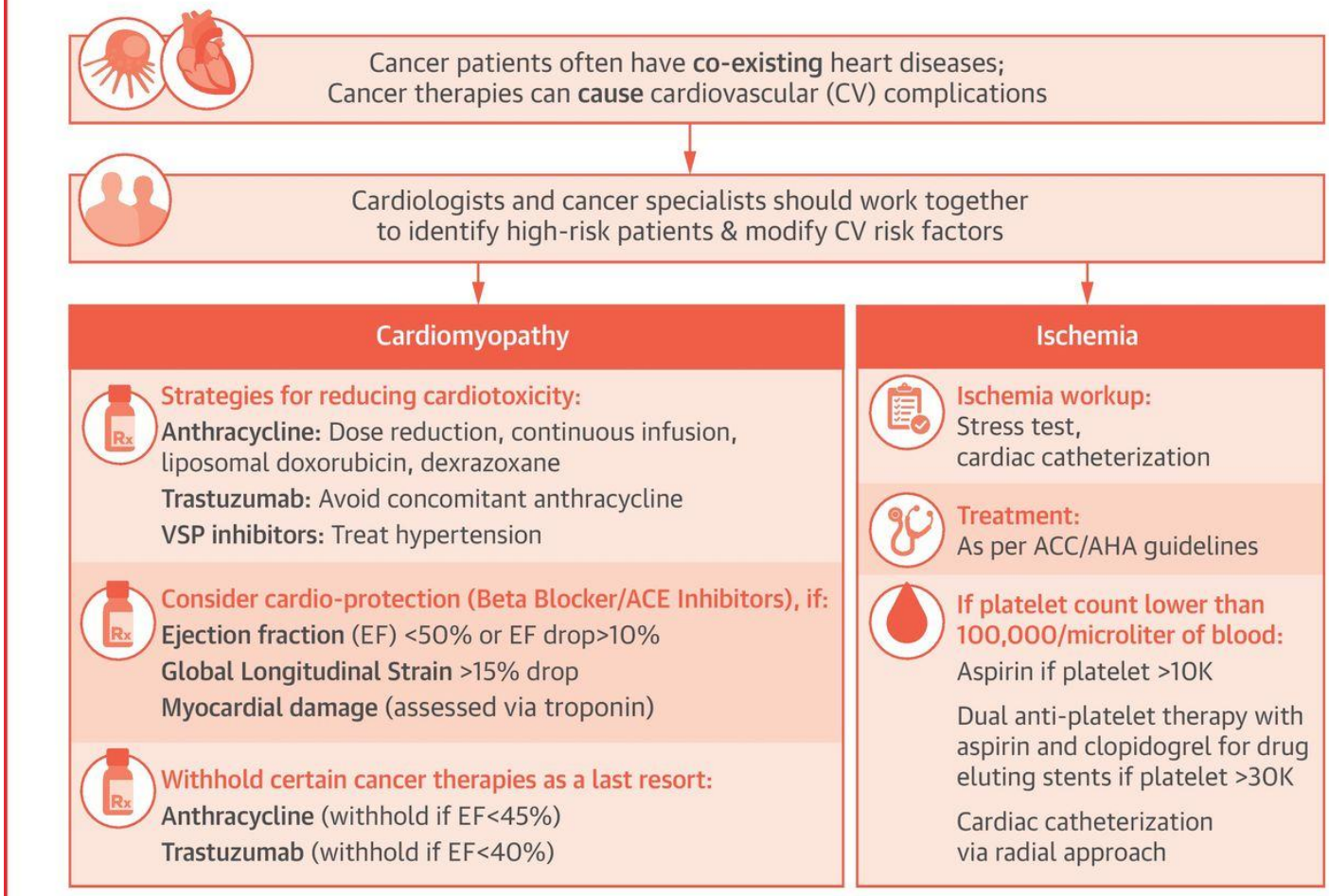
ECG

Echocardiogram

Figure 1 Illustration of the three groups of cancer patients that can be categorized based on the dynamics in cancer ...



CENTRAL ILLUSTRATION: Management of Cancer Therapy-Induced Cardiovascular Complications



Chang, H.-M. et al. J Am Coll Cardiol. 2017;70(20):2536-51.

JACC

CENTRAL ILLUSTRATION: Management of Cancer Therapy-Induced Cardiovascular Complications

Management of cancer or cancer-therapy associated cardiovascular (CV) complications

Hypertension

- Blood pressure (BP) goal <140/90 mm Hg
- Monitor weekly in first cycle
- Monitor every 2-3 weeks during therapy
- Initiate treatment when diastolic BP increases by 20 mm Hg

Radiation sequelae

- Identify, modify and treat CV risk factors
- **CV Monitoring:** Yearly: ECG, Echo if indicated
- 5 years after radiation: ECG, Echo
- 10 years after radiation: ECG, Echo, stress test, or coronary CT

Thromboembolism

- VSP and angiogenesis inhibitors increase risk
- Deep venous thrombosis or pulmonary embolism diagnostics
- Anti-coagulate as necessary
- Direct oral anticoagulant (limited data)
- Take bleeding precautions

QT prolongation

- Diagnosis with Tangent method & Fridericia correction
- Correct low potassium or magnesium
- Remove QT-prolonging medications

Chang, H.-M. et al. J Am Coll Cardiol. 2017;70(20):2552-65.

JACC

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 1756–1763
doi:10.1093/eurheartj/ehy453

SPECIAL ARTICLE
Disease management

Cardio-Oncology Services: rationale, organization, and implementation

A report from the ESC Cardio-Oncology council

Patrizio Lancellotti[1,2]*, Thomas M. Suter[3], Teresa López-Fernández[4], Maurizio Galderisi[5], Alexander R. Lyon[6], Peter Van der Meer[7], Alain Cohen Solal[8], Jose-Luis Zamorano[9], Guy Jerusalem[10], Marie Moonen[1], Victor Aboyans[11], Jeroen J. Bax[12], and Riccardo Asteggiano[13]

[1]Department of Cardiology, GIGA Cardiovascular Sciences, University of Liège Hospital, CHU Sart Tilman, Avenue de L'Hôpital 1, 4000 Liège, Belgium; [2]Gruppo Villa Maria Care and Research, Anthea Hospital, VIA C. ROSALBA, 35/37 70124 BARI (BA) - Puglia, Italy; [3]Department of Cardiology, Inselspital, Bern University Hospital, University of Bern; [4]Department of Cardiology, La Paz University Hospital, IdiPAZ, CiberCV, Madrid, Spain; [5]Department of Advanced Biomedical Sciences, Federico II University Hospital, Naples, Italy; [6]Royal Brompton Hospital and Imperial College, Dovehouse Street, London, SW3 6LY, UK; [7]Department of Cardiology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9713 GZ, The Netherlands; [8]UMR INSERM U-942 "BIOmarkers in CArdioNeuroVAScular diseases" Université Paris VII—Denis Diderot Assistance Publique—Hôpitaux de Paris Service de Cardiologie, Hôpital Lariboisière, 2 rue Ambroise-Paré, 75010 Paris, France; [9]University Alcala, Hospital Ramón y Cajal, Ciber CV, 28034 Madrid, Spain; [10]University of Liège Hospital, Medical Oncology, CHU Sart Tilman, Avenue de L'Hôpital 1, 4000 Liège, Belgium; [11]Department of Cardiology, Dupuytren University Hospital, Limoges, France; [12]Department of Cardiology, Leiden University Medical Center, The Netherlands; and [13]Cardiologist in Practice, Corso Venezia 10, 10155 Turin, Italy

Received 5 March 2018; revised 2 May 2018; editorial decision 9 July 2018; accepted 9 July 2018; online publish-ahead-of-print 6 August 2018

Goals of cardio-oncology team

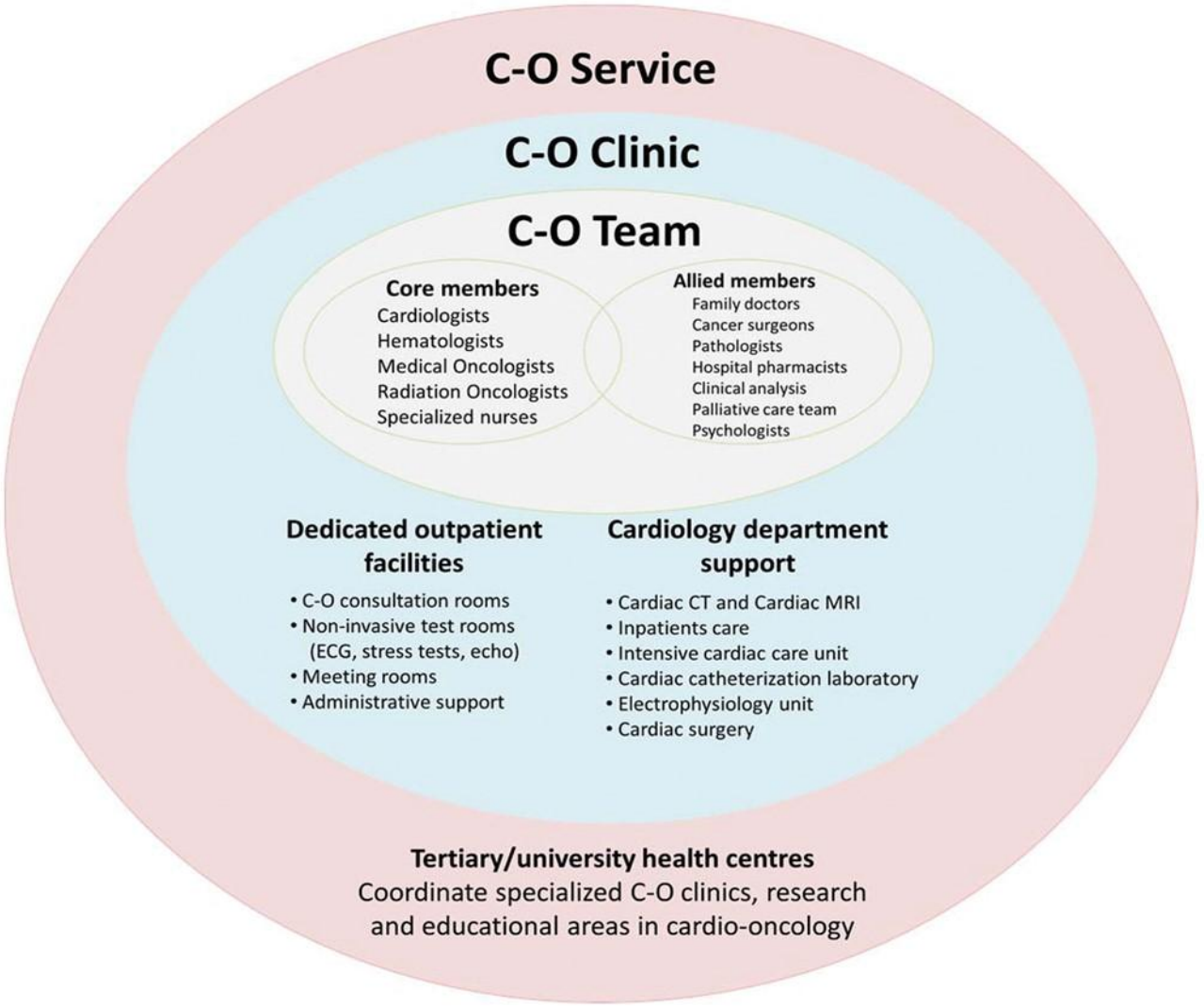
- Unification of the cancer care process
- Effective communication and coordination among professionals involved in cancer patients care to minimize unnecessary costs
- Development and adherence to local clinical protocols to reduce individual decisions
- Optimize acute and long-term cardiovascular health for patients who need potentially cardiotoxic drugs
- Prevention, early diagnosis, and treatment of cancer therapy-related cardiovascular complications
- Reduce interruptions of anticancer drugs
- Coordination of continuous medical education, medical training, and clinical research in cardio-oncology
- Health care quality control for clinical and research practice

From: Lancellotti et al. **Cardio-Oncology Services: rationale, organization, and implementation: A report from the ESC Cardio-Oncology council**

Eur Heart J. 2019, 40: 1756–1763, https://doi.org/10.1093/eurheartj/ehy453

- Staff/skill mix
- Patient selection
- Resources - cardiac imaging
    - Echo, CMR, CTCA, PET
    - Biomarkers
    - Procedural (cardiac catheterisation, electrophysiology, cardiac surgery, and cardiac devices)
    - Cardiac rehabilitation

Organisation of services - Models of care delivery



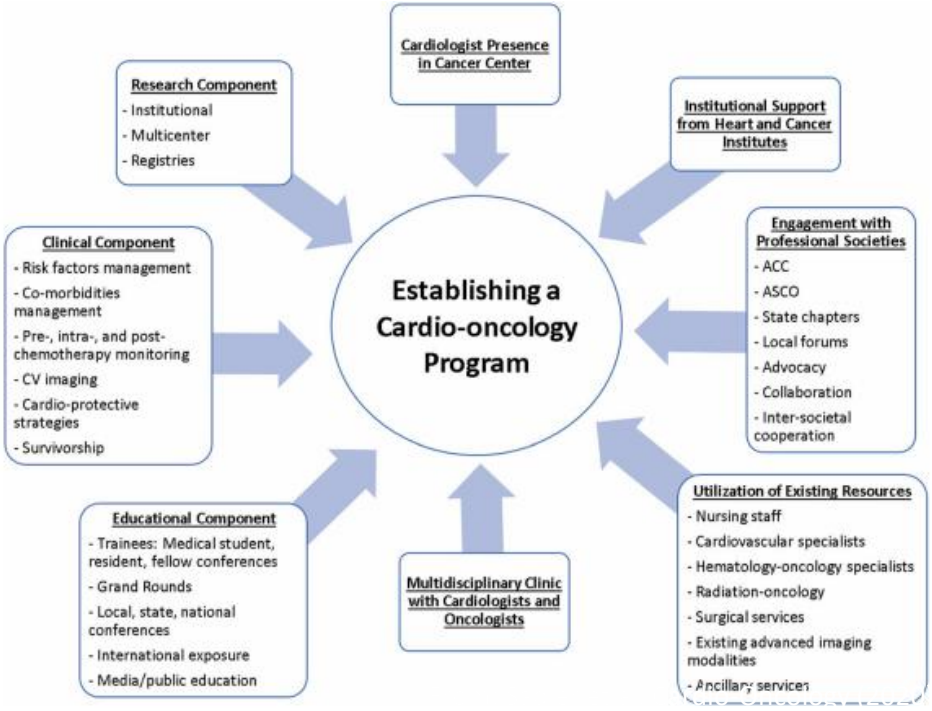
Requirements	General/district hospitals	Tertiary hospitals	Additional at selected centres
Patients	<10 patients /week [a]	> 10 patients/week [a]	> 20 patients/week [a]
Structures of the hospital	• Cardiology section/department • Oncology section/department • General intensive care unit	• Cardiology department • Radiation and medical oncology department • Haematology department	• Tertiary hospital facilities • Intensive cardiac care unit • Cardiac transplant program
Multidisciplinary teams			
• **Organization**	Basic Cardio-Oncology Team (core members) or a dedicated consultant cardiologist In Oncology Centres: “in house” basic cardiology services Connected with primary care physicians	Cardio-Oncology Team (core members + allied members) Connected with primary care physicians and general/district hospitals	Cardio-Oncology Team (core members + allied members) •Cardiac rehab centre •HF centre •Valvular heart centre •Facilities for research protocols •Connected 1° care DGH and 3° care

Technical resources			
Cardiac Imaging			
• **Standard Echo** • **Advanced Echo** • **CMR, cardiac CT, PET-CT**	• Yes • Not mandatory • Not mandatory • Yes	• Yes • Yes • Yes • Yes	• Yes • Yes • Yes • + New biomarkers/ • genetics
Cardiac biomarkers			
Procedures available: Cardiac catheterization; electrophysiology, cardiac surgery, cardiac devices	Smaller services to be connected to larger regional cardio-oncology services for interventional procedures and complex cases	Available	+ Cardiac transplantation
Data review			
• **Internal audit processes** • **Databases and research programs**	• Available • Not mandatory	• Available • Strongly recommended	• Available • Lead cardio-oncology research programs

• Dedicated outpatient C-O clinic	• Recommended	• Available	• Available (+ e-cardio-oncology consult)
• 24/7 h	• Recommended	• Available for acute inpatient problems	• Available for acute inpatient problems
• Structured clinical protocols	• Available	• Available	• Available
• Cancer survivorship programs		• Available	• Available
• Structured training programs		• Health care professionals training programs	• Health care professionals training programs + Educational patients programs

Models of care delivery

- MD Anderson – cardiologists in cancer hospital
- Milan – Parallel teams, oncology and cardiology
- RBH – Separate tertiary hospitals, integrated service
- Mayo Clinic (Haematology with Cardiology)
- Cleveland Clinic (Comprehensive)



https://doi.org/10.1186/s40959-020-00063-x

Current Oncology Reports (2021) 23: 64
https://doi.org/10.1007/s11912-021-01059-1

CARDIO-ONCOLOGY (EH YANG, SECTION EDITOR)

Reaching Across the Aisle: Cardio-Oncology Advocacy and Program Building

Diego Sadler[1] · Anita Arnold[2] · Joerg Herrmann[3] · Andres Daniele[4] · Carolina Maria Pinto Domingues Carvalho Silva[5] · Arjun K Ghosh[6] · Sebastian Szmit[7] · Roohi Ismail Khan[8] · Luis Raez[9] · Anne Blaes[10] · Sherry-Ann Brown[11]

Accepted: 11 March 2021 / Published online: 14 April 2021

Abstract

Purpose of Review This study aims to assess the current state of cardio-oncology in reference to advocacy efforts, access to care, and perspective of stakeholders in their ability to provide patient care as well as development of "across the aisle" synergy among cardiologists and oncologists and academic and non-academic centers in various worldwide locations.

Recent Findings During the last decade, there has been a significant and diverse growth in cardio-oncology. We reviewed the experience from cardiologists and oncologists across different healthcare systems, the global trends, the role of collaborative networks, and the importance of advocacy efforts.

Summary Cardio-oncology will continue to grow, but there is an unmet need to increase awareness, improve education, and expand access to care to larger segments of the cancer population in order to have a more significant impact on their health. The growing collaboration through professional societies and collaborative networks provides an opportunity to advance the cardiovascular care of cancer patients to meet the projected needs in a growing and more diverse population.

Keywords Cardio-oncology · Advocacy · Healthcare

Attributes of success

- Communication
- Value every member of the team
- Holistic approach
- Prize education
- Continuous learning
- Self criticism and analysis
- Research as driver to improving service (service delivery vs clinical vs translational)

External functions and relations (I) Registries

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 1720–1729
doi:10.1093/eurheartj/ehaa006

CLINICAL RESEARCH
Heart failure/cardiomyopathy

Classification, prevalence, and outcomes of anticancer therapy-induced cardiotoxicity: the CARDIOTOX registry

José López-Sendón [1]*, Carlos Álvarez-Ortega [1], Pilar Zamora Auñon[1], Antonio Buño Soto [1], Alexander R. Lyon [2], Dimitrios Farmakis[3,4], Daniela Cardinale[5], Miguel Canales Albendea[1], Jaime Feliu Batlle[1], Isabel Rodríguez Rodríguez[1], Olaia Rodríguez Fraga [1], Ainara Albaladejo[1], Guiomar Mediavilla[1], Jose Ramón González-Juanatey[6], Amparo Martínez Monzonis[6], Pilar Gómez Prieto[1], José González-Costello [7], José María Serrano Antolín[8], Rosalía Cadenas Chamorro[9], and Teresa López Fernández[1]*; on behalf of the CARDIOTOX Registry Investigators

External functions and relations (II)

- Networks
- Communities
- National and international guidelines
- Advocacy – curricula, reimbursement (eg non-imbursed: biomarkers during chemotherapy treatment, strain imaging and CMR used for early detection of cardiac effects of cancer-related therapies)
- Shared knowledge of the specialist subject, interface between two major disciplines

Shared research interest (common factors etc – HF and cancer)

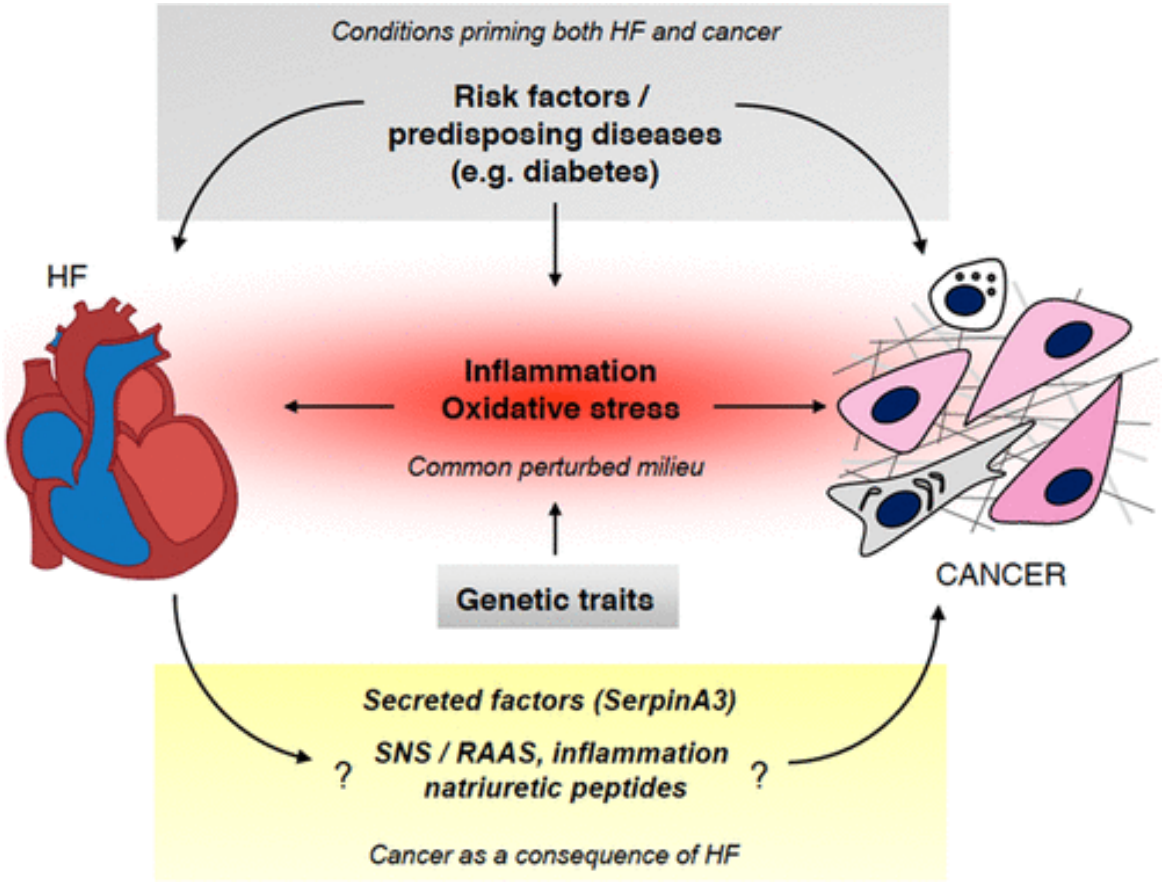
ESC European Society of Cardiology

European Journal of Heart Failure (2020) 22, 2272–2289
doi:10.1002/ejhf.2029

POSITION PAPER

Common mechanistic pathways in cancer and heart failure. A scientific roadmap on behalf of the Translational Research Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

Rudolf A. de Boer[1]*, Jean-Sébastien Hulot[2,3], Carlo Gabriele Tocchetti[4], Joseph Pierre Aboumsallem[1], Pietro Ameri[5,6], Stefan D. Anker[7], Johann Bauersachs[8], Edoardo Bertero[9], Andrew J.S. Coats[10], Jelena Čelutkienė[11], Ovidiu Chioncel[12], Pierre Dodion[13], Thomas Eschenhagen[14,15], Dimitrios Farmakis[16,17], Antoni Bayes-Genis[18,19,20], Dirk Jäger[21], Ewa A. Jankowska[22], Richard N. Kitsis[23], Suma H. Konety[24], James Larkin[25], Lorenz Lehmann[26,27,28], Daniel J. Lenihan[29], Christoph Maack[9], Javid J. Moslehi[30], Oliver J. Müller[31,32], Patrycja Nowak-Sliwinska[33,34], Massimo Francesco Piepoli[35], Piotr Ponikowski[22], Radek Pudil[36], Peter P. Rainer[37], Frank Ruschitzka[38], Douglas Sawyer[39], Petar M. Seferovic[40], Thomas Suter[41], Thomas Thum[42], Peter van der Meer[1], Linda W. Van Laake[43], Stephan von Haehling[44,45], Stephane Heymans[46,47], Alexander R. Lyon[48], and Johannes Backs[49,50]



Edoardo Bertero. Linking Heart Failure to Cancer, Circulation 2018; 138: 735-742 DOI: (10.1161/CIRCULATIONAHA.118.033603)

Challenges (I)

- In patient vs out patient problems
- Need for urgent imaging and quality
- Racial and ethnic disparities – *first requirement is awareness*
  - lower household income and food insecurity
  - lack of medical literacy
  - lack of insurance
  - inability to gain access to health care providers
  - disparities in CVD and CVD risk factors likely contribute to inequities in cardiotoxicity from cancer therapies

Challenges (II)

- lack of reimbursement/funding
- consensus building between oncologists and cardiologists
- lack of professional training on multidisciplinary team work
- absence of service standards for cardio-oncology services

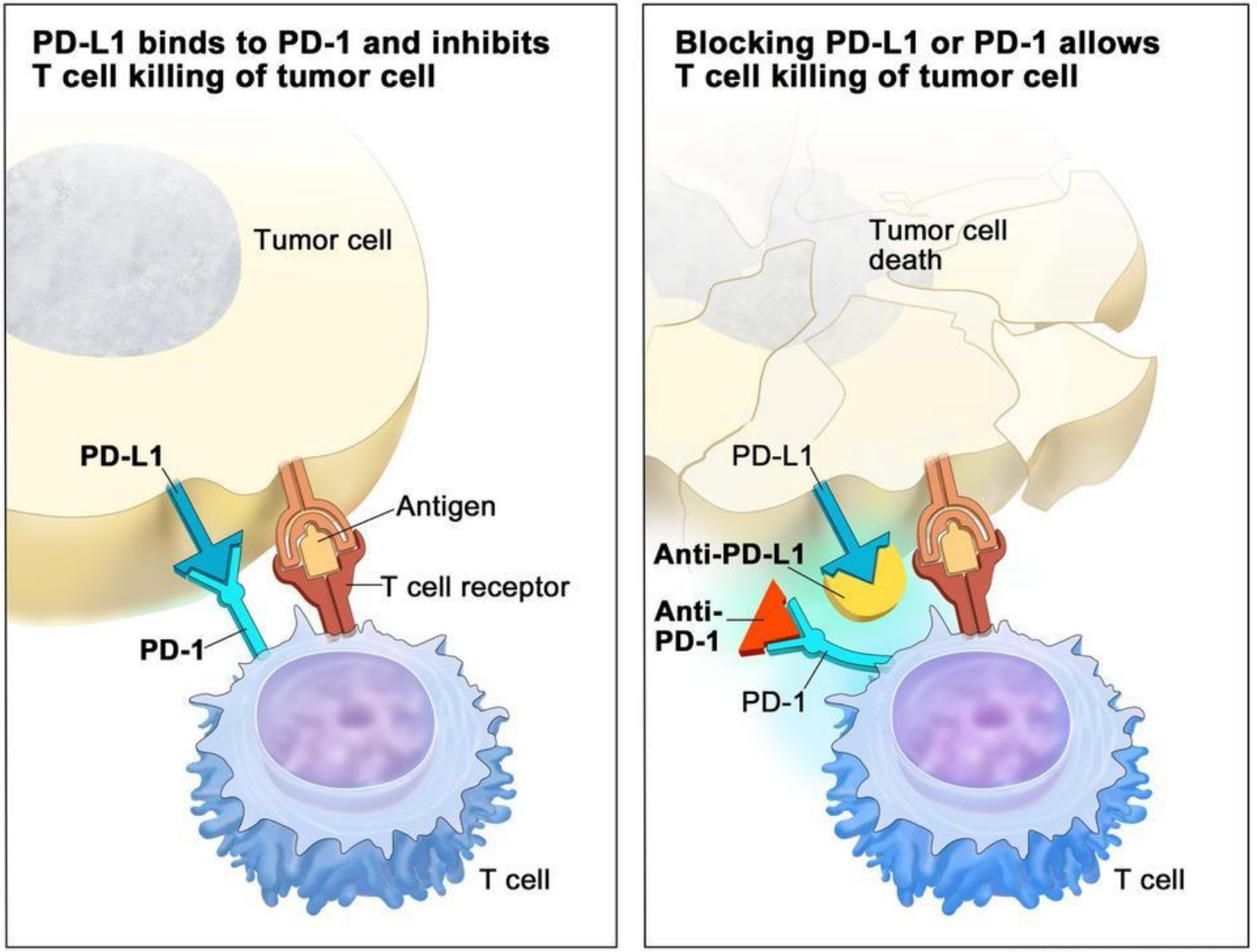
Horizon scanning – New and emerging clinical problems (I)

ICI - Increasing use of immune checkpoint inhibition; context Danish study - Immune checkpoint inhibitor (ICI) therapy is associated with a 2- to 4-fold increased risk of cardiac events including myocarditis, arrhythmias, and heart failure.

The 1-year absolute risk of cardiac events in patients with ICI ranged between 7-10%.

Identifying risk factors and underlying mechanisms for ICI-related cardiac events is necessary to mitigate the expected increase in cardiac morbidity related to expansion of ICI use

Lili Zhang et al. J Am Coll Cardiol CardioOnc. 2021 ;3: 35–47



Credit: US National Cancer Institu

Horizon scanning – New and emerging clinical problems (II)

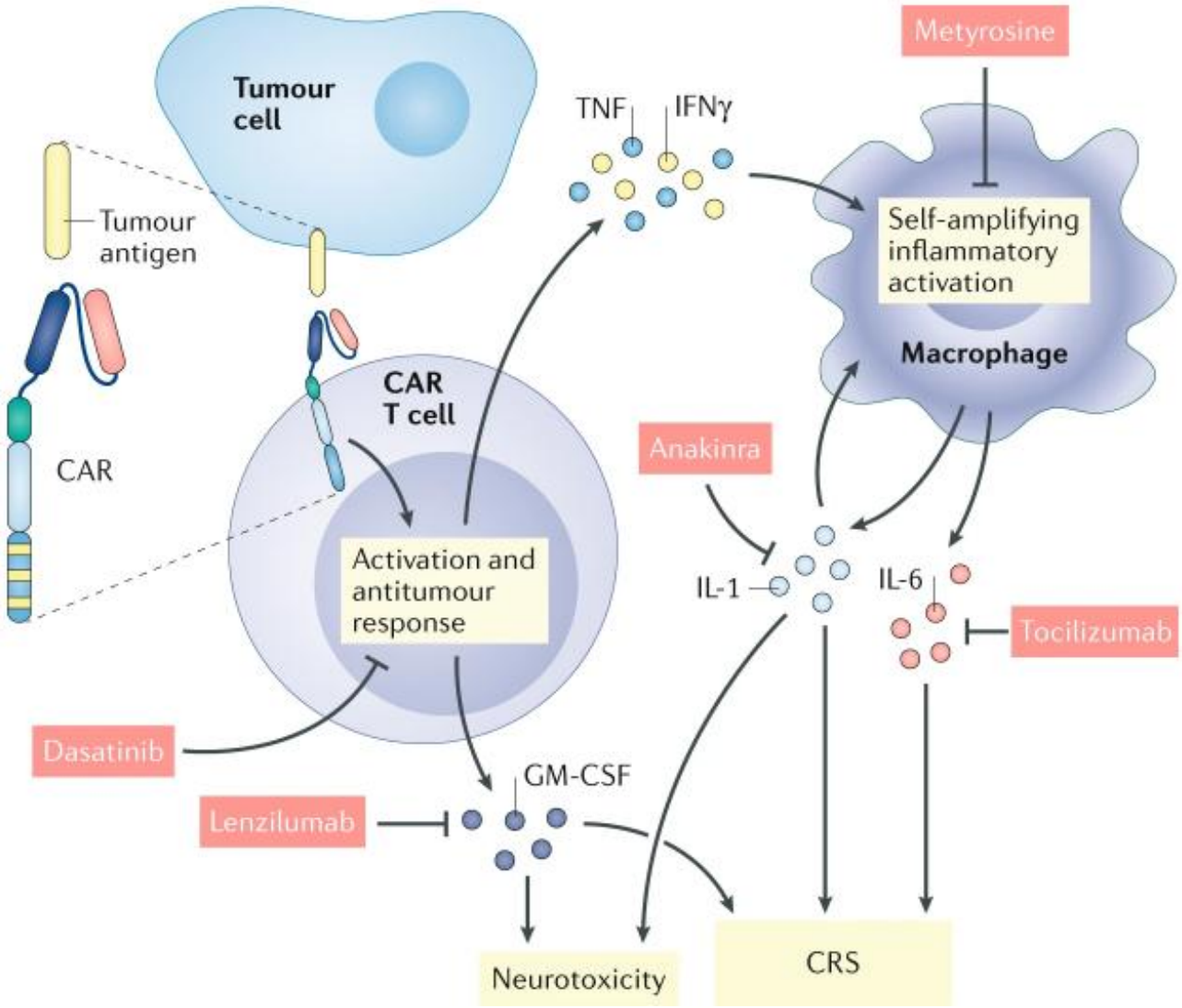
Chimeric Antigen Receptor (CAR) T-cell immunotherapy is a cancer therapy designed to redirect T-cell specificity to tumor-associated antigens

Cytokine release syndrome (CRS) related major adverse cardiac events (MACE) include arrhythmias, cardiomyopathy, heart failure (HF), and death.

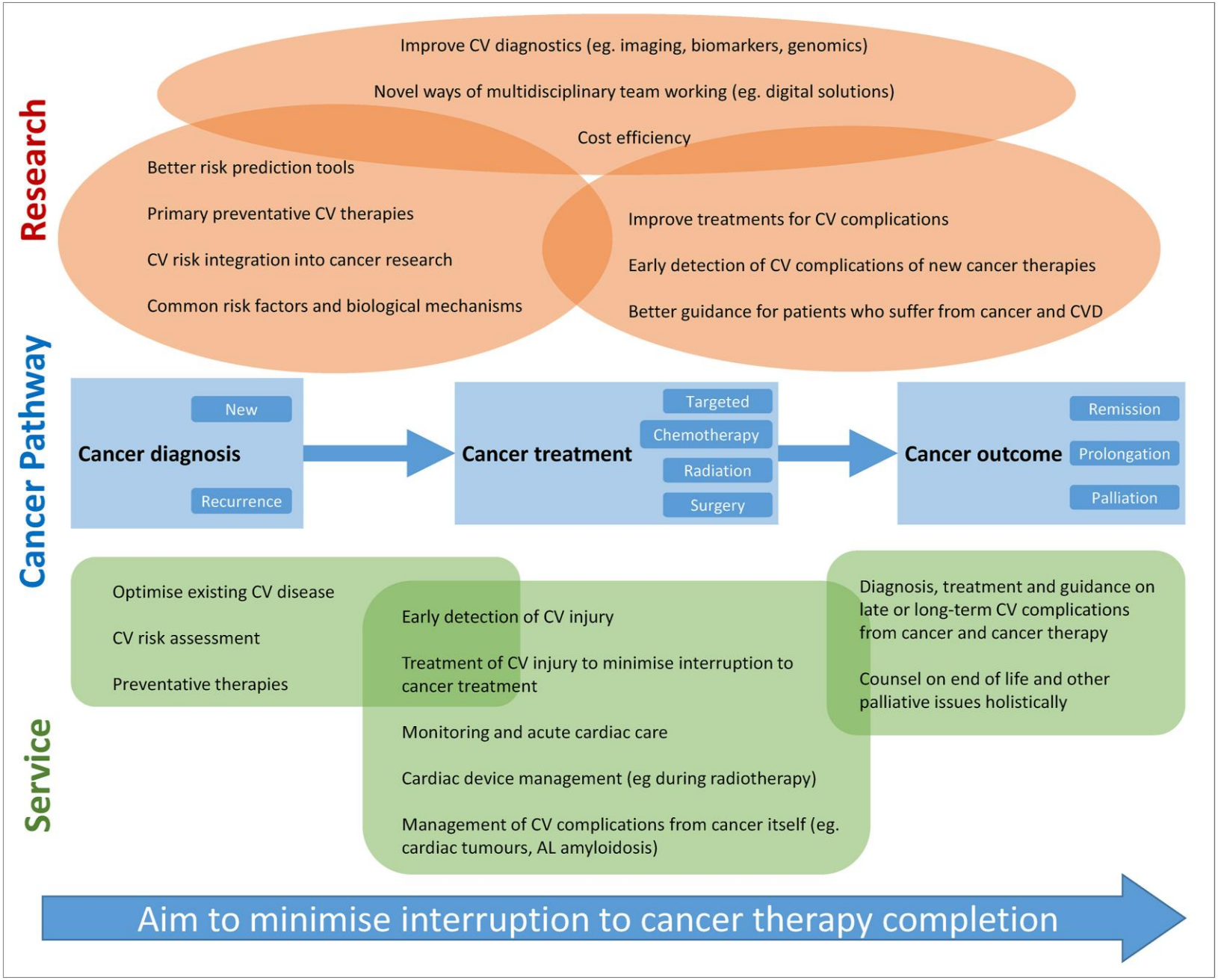
Myocardial injury (evidenced by ↑ troponin is common and associated with adverse CV events

Signs and symptoms of high-grade CRS should trigger further cardiac evaluation with ECG, troponin, BNP and echo

Early administration of tocilizumab after the onset of CRS may be associated with lower rate of CV events.



Larson Rc and Maus MV *Nature Reviews Cancer* **volume 21**, pages145–161 (2021)



Potential benefits of cardio-oncology along the stages of the (simplified) cancer care pathway.
Andres M et al Clin Onc 2021; 33: 483-493. https://doi.org/10.1016/j.clon.2021.03.012