INTRO TO CARDIO - ONCOLOGY

Dr. Philip Owen MD FACC

Disclosures

None relevant to presentation

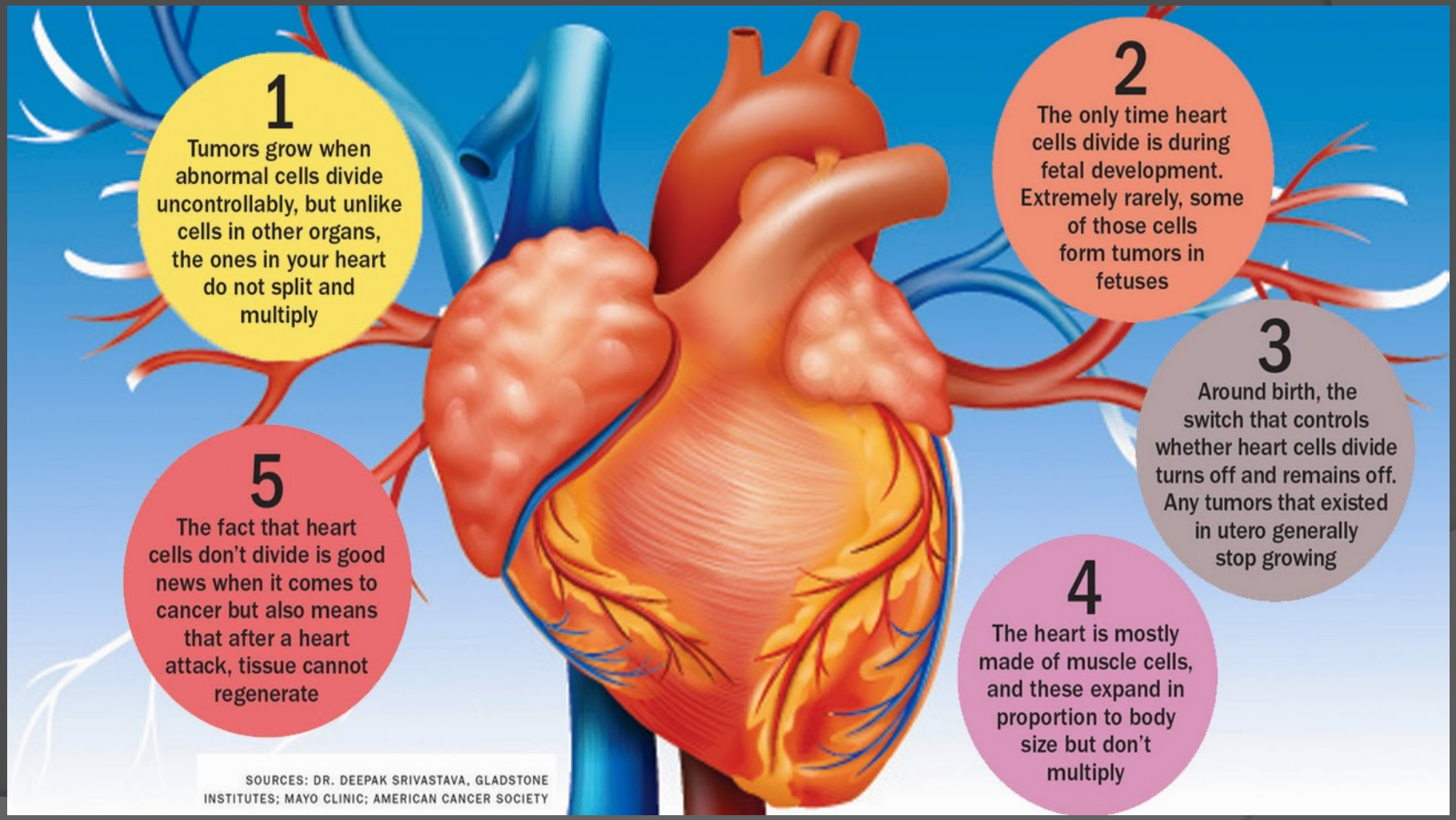
Why?

- Treatment of cancers is a medical team effort
- Cancer Rx needs a multidisciplinary approach

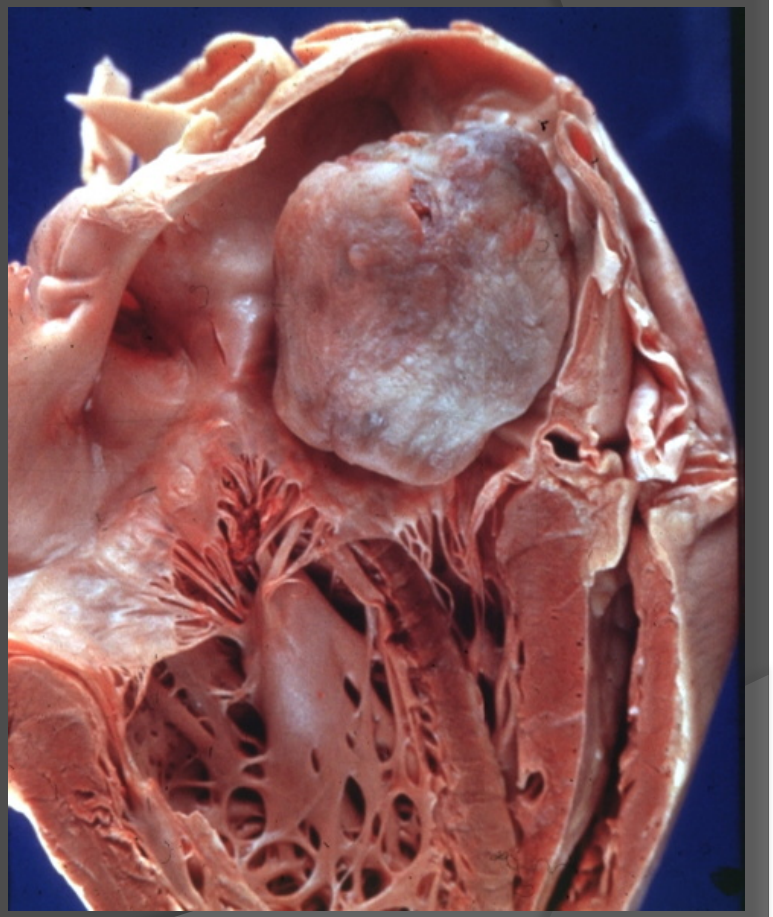
Cancer and the Heart Overview

- Primary vs Secondary
- Role of Cardio Oncology
- Impact of cancer
- Spectrum of toxicity
- Mechanisms
- Types of Cancer therapeutic related cardiotoxicity CTRCD
- Monitoring and Management

Primary Cancers /Rare

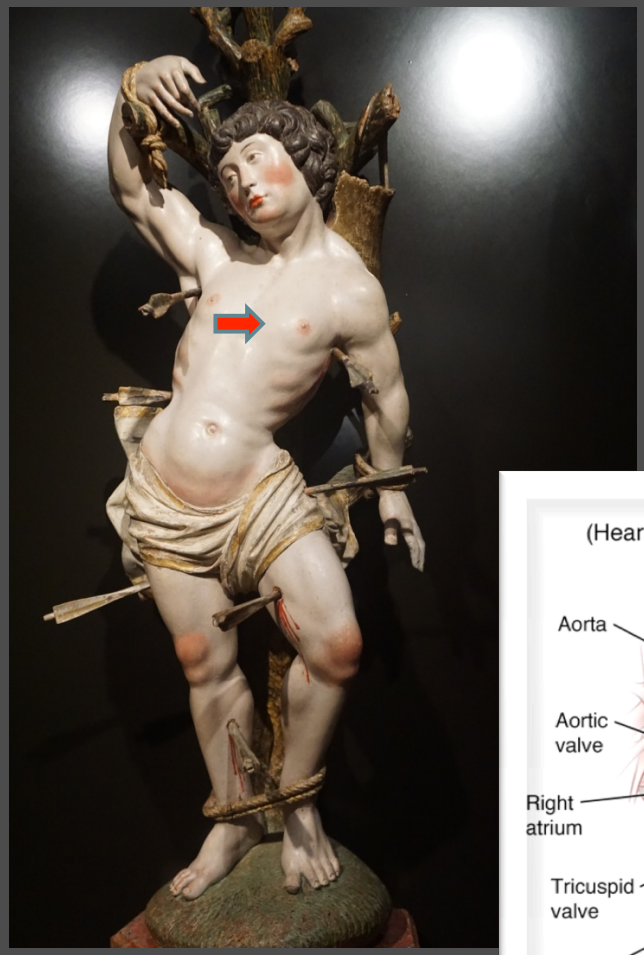


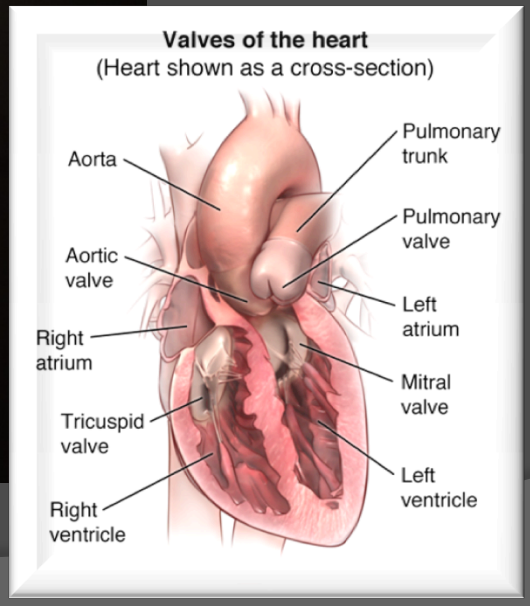
Primary Cardiac Cancers



Rare, < 0.1% cancer

Cancer / Multiorgan / Secondary





16 million cancer survivors
- Breast cancer
- Lymphoma
- Melanoma
- Lung cancer
- Renal
- Colon cancer

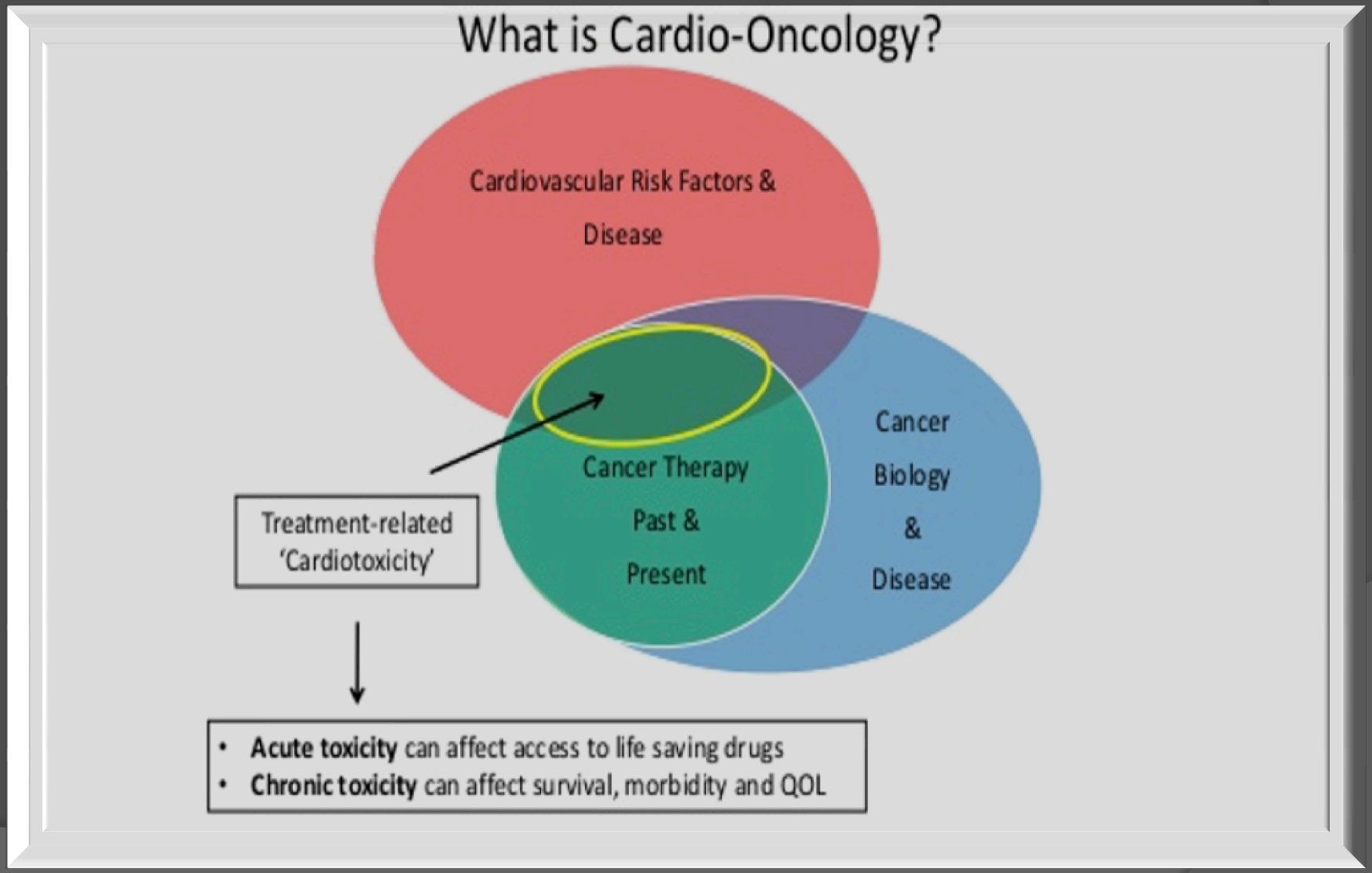
METS 40 x more likely than cardiac primaries

15 % of cancer patients have cardiac involvement

Cancer - Risks to the Heart

- Metastatic disease – valvular, cavitary, pericardial, conducting system
- Treatment related risks - Radiation , chemotherapy, surgical
- Existing cardiac conditions affected
- Stress related
- Thromboembolic vascular risks
- Interference with existing Rx

Basis for Cardio - Oncology

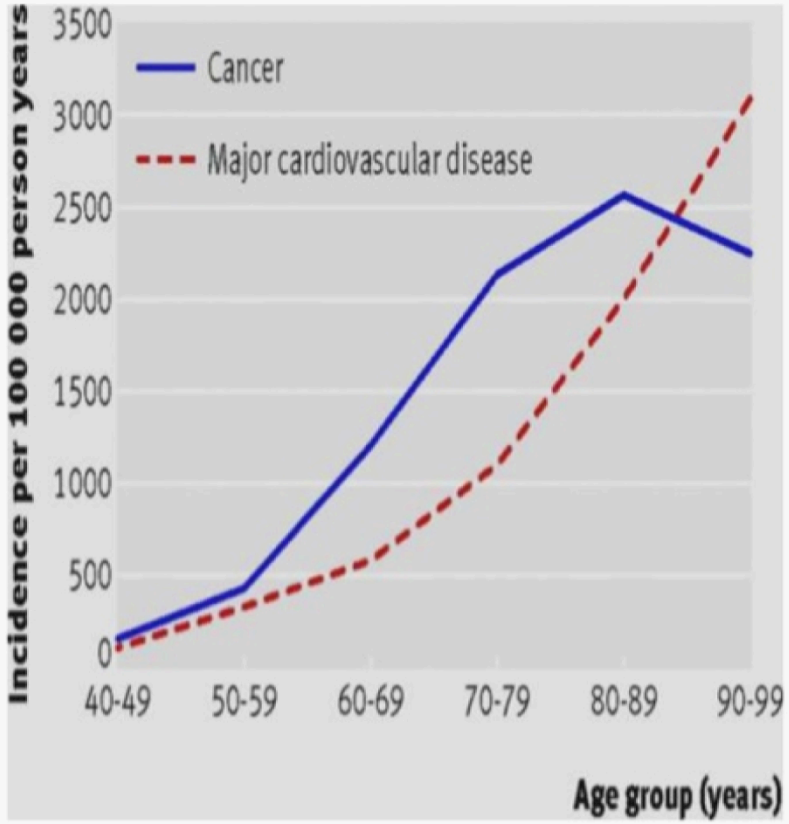


What Does Cardio-Onc Entail?

- Defining and monitoring Cancer Rx effects on the heart
- Using state of the art cardiac testing to identify and minimize cardiac risks
- Optimizing cardiac and cancer Rx outcomes as issues arise
- Positioning cardiac w/ups to not interfere with effective cancer Rx

Basis for Cardio - Oncology

Why Cardio-Oncology?



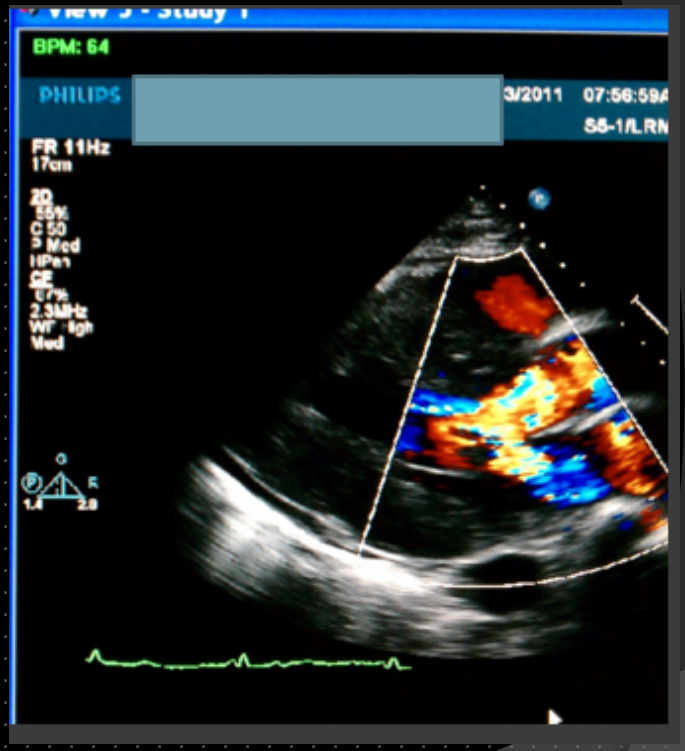
Driver, et al. *BMJ*, 2008

I. Survival gains in cancer and CV disease in recent decades

II. Cancer and CV disease pose competing risks:
   i. Cancer survivors remain at risk for CV disease
   ii. CV disease survivors remain at risk for malignancy

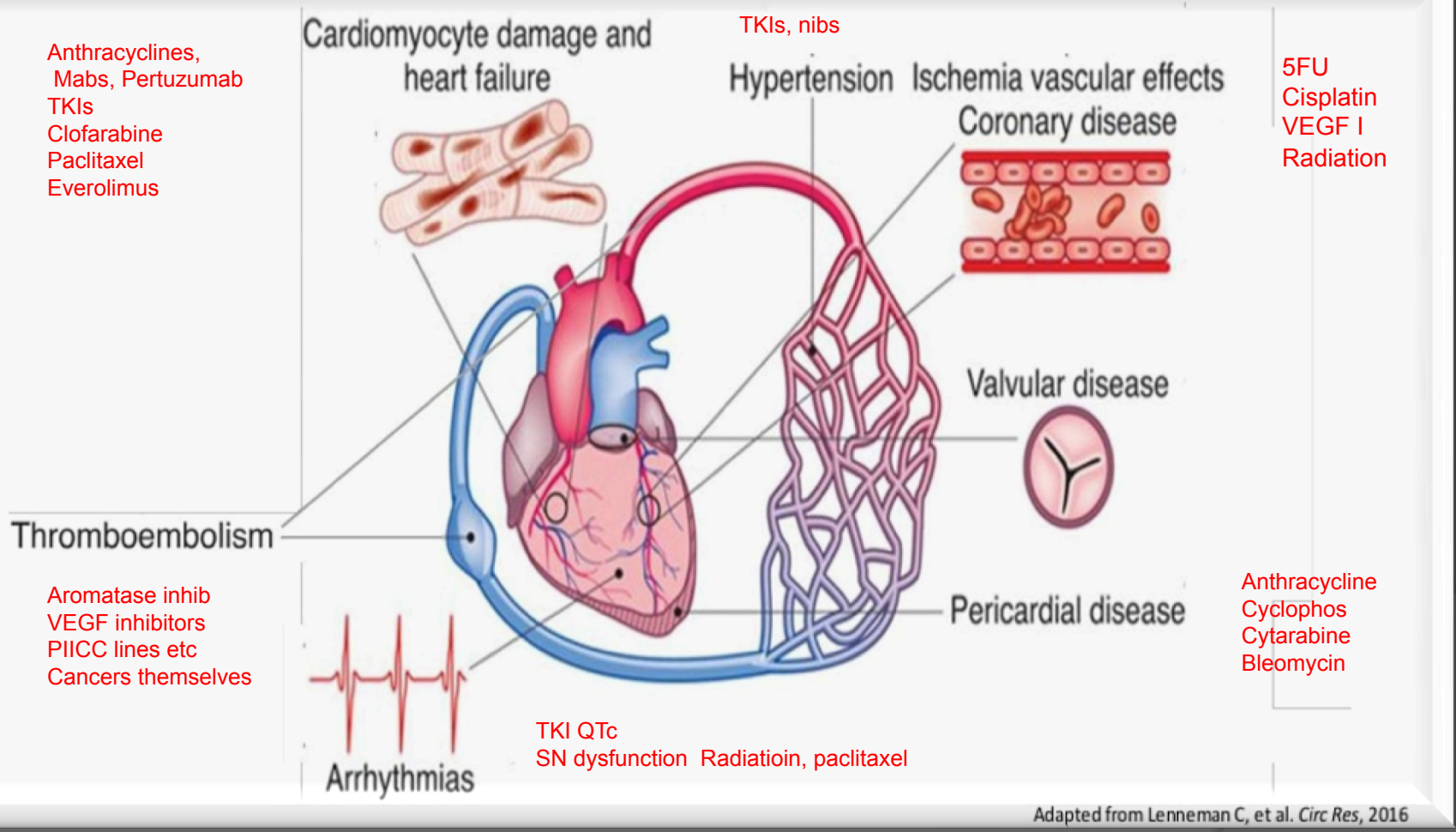
III. Cancer therapies can increase CV risk
   I. Toxicities of conventional cancer treatments remain
   II. New 'targeted' therapies are being developed rapidly, many of which have recognized or unrecognized cardiovascular toxicities

The Impact of Cancer on the Heart

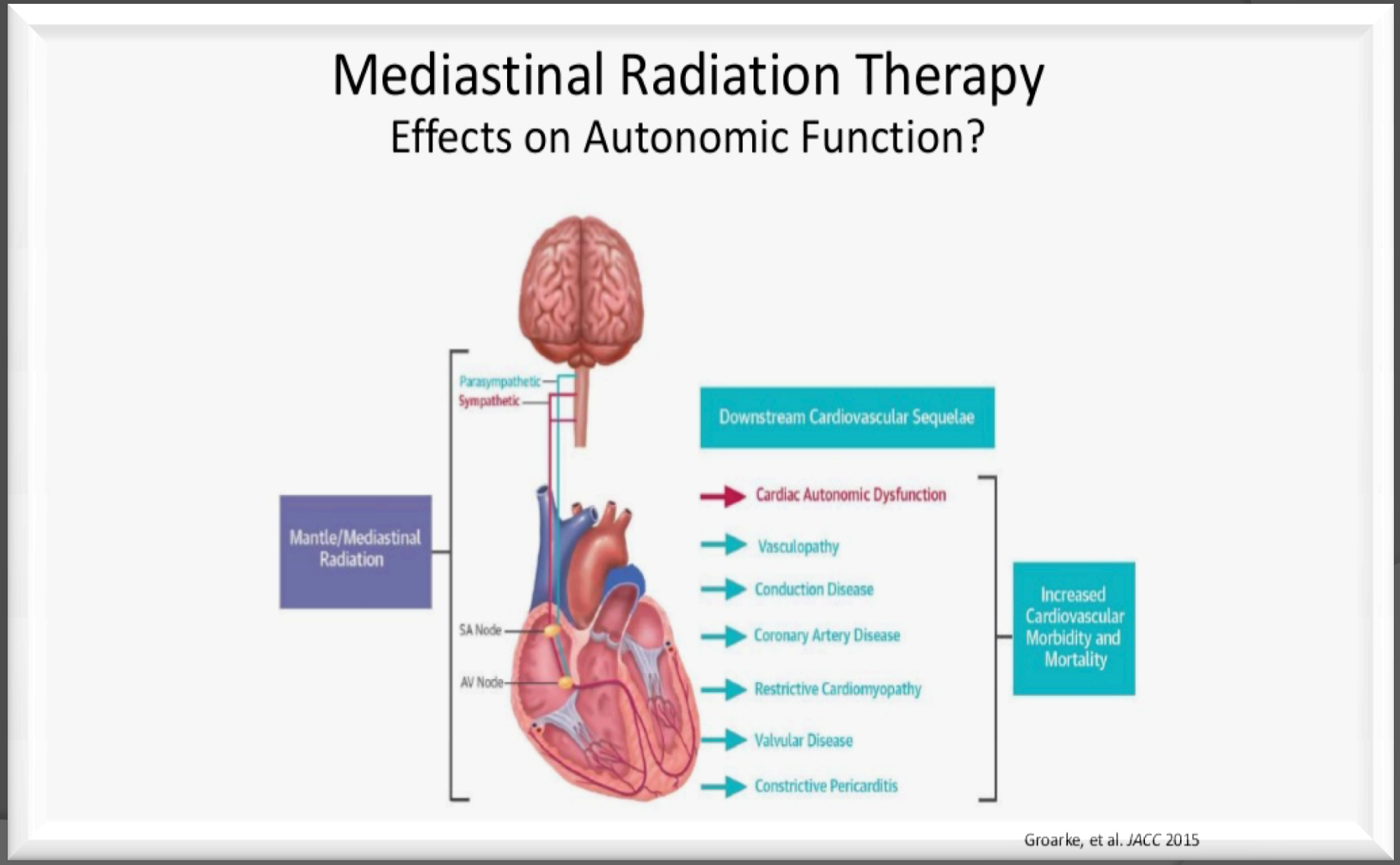


Echocardiography

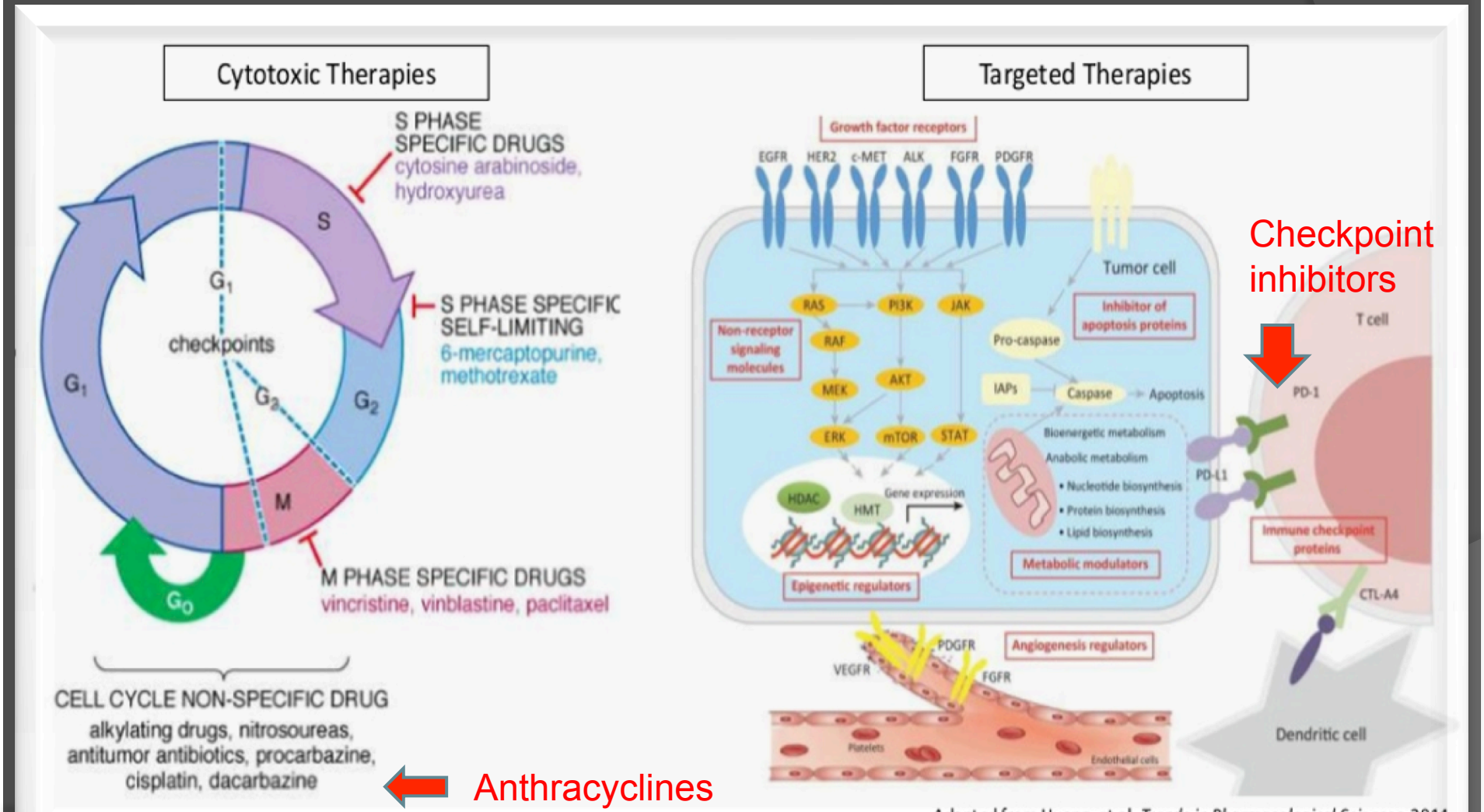
Spectrum of Cardiotoxicity



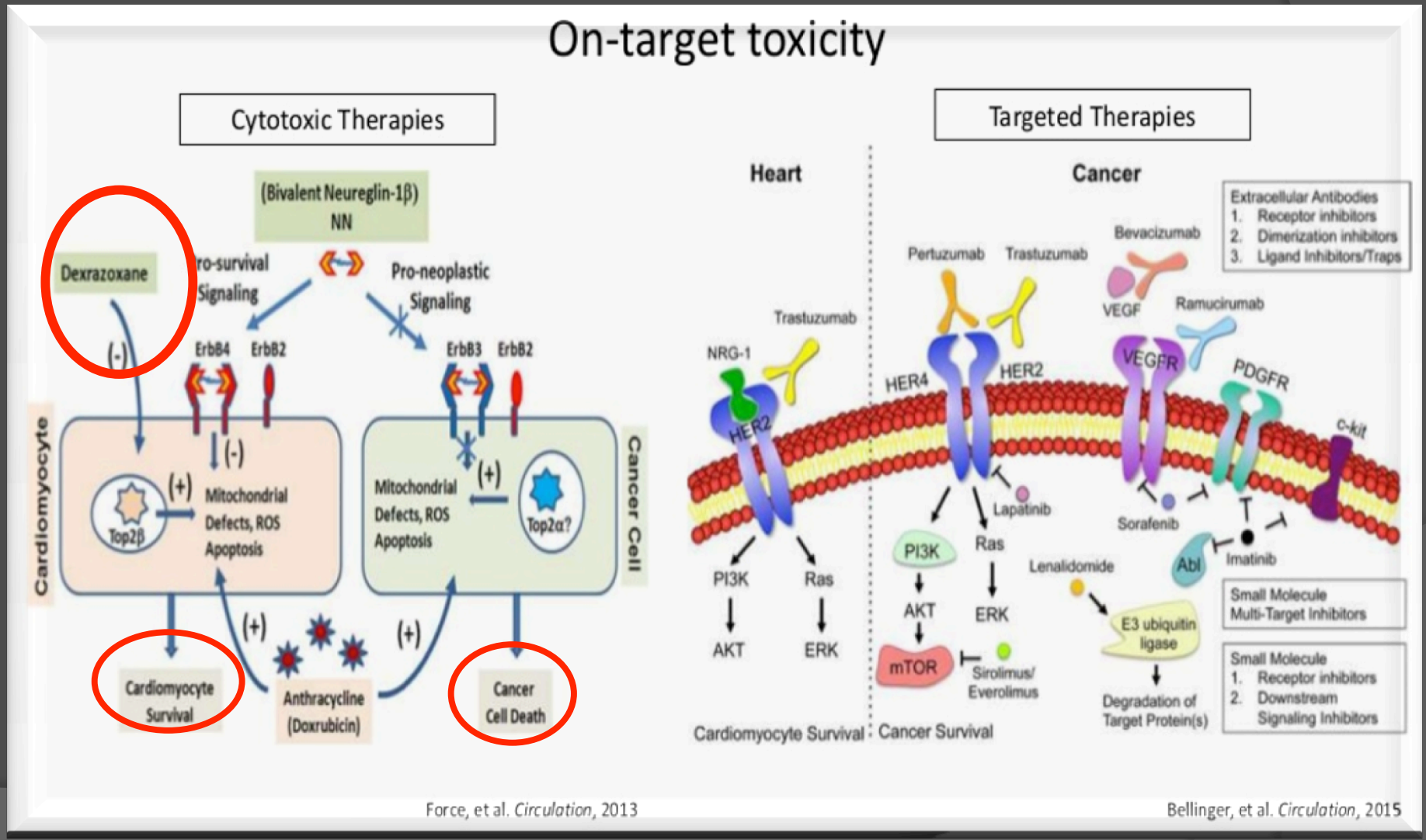
Non Cardiomyopathic Rx Effects



Cancer Therapies



Mechanisms of Cardiotoxicity



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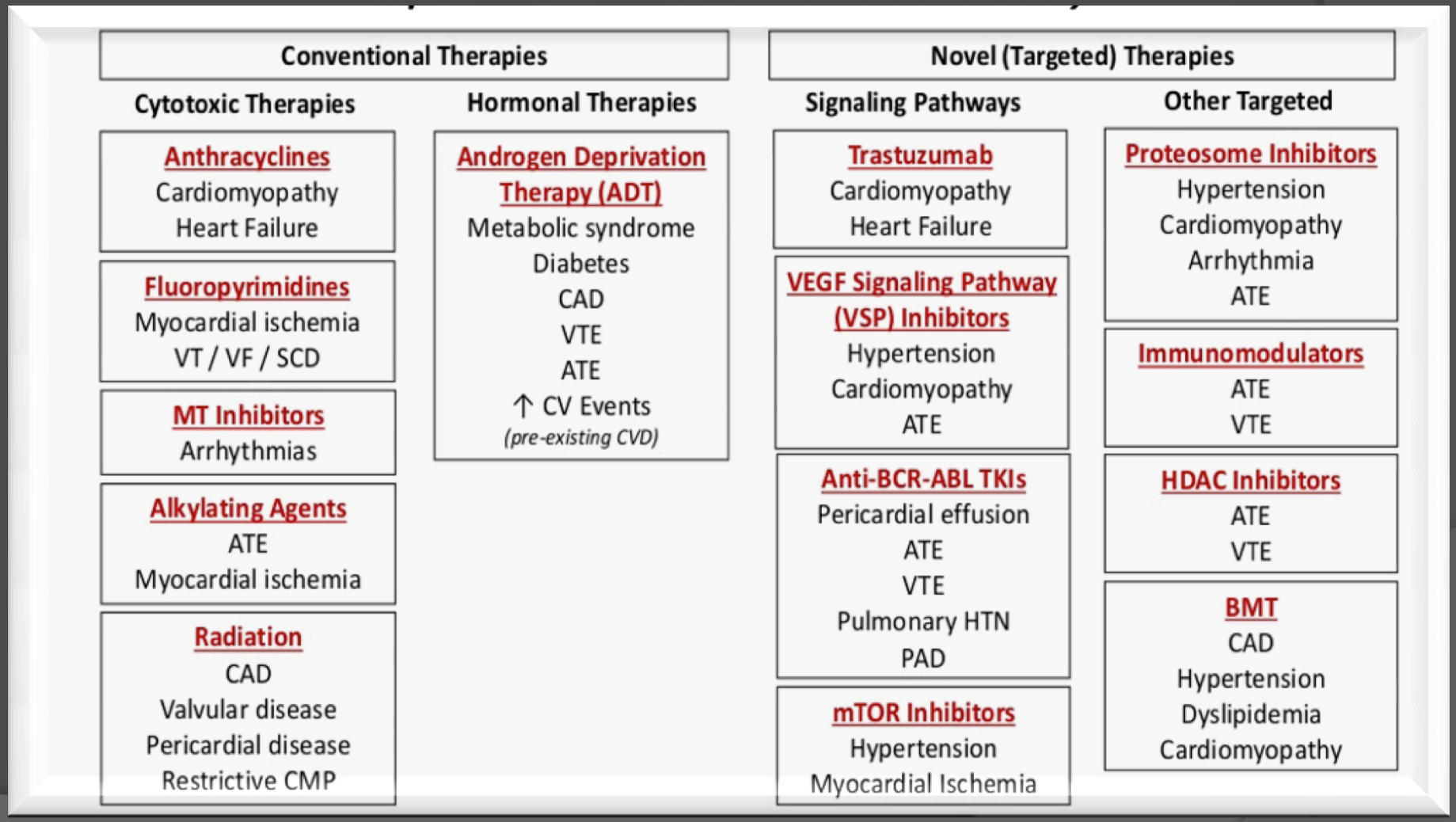


CTRCD

Cancer therapeutics-related cardiac dysfunction

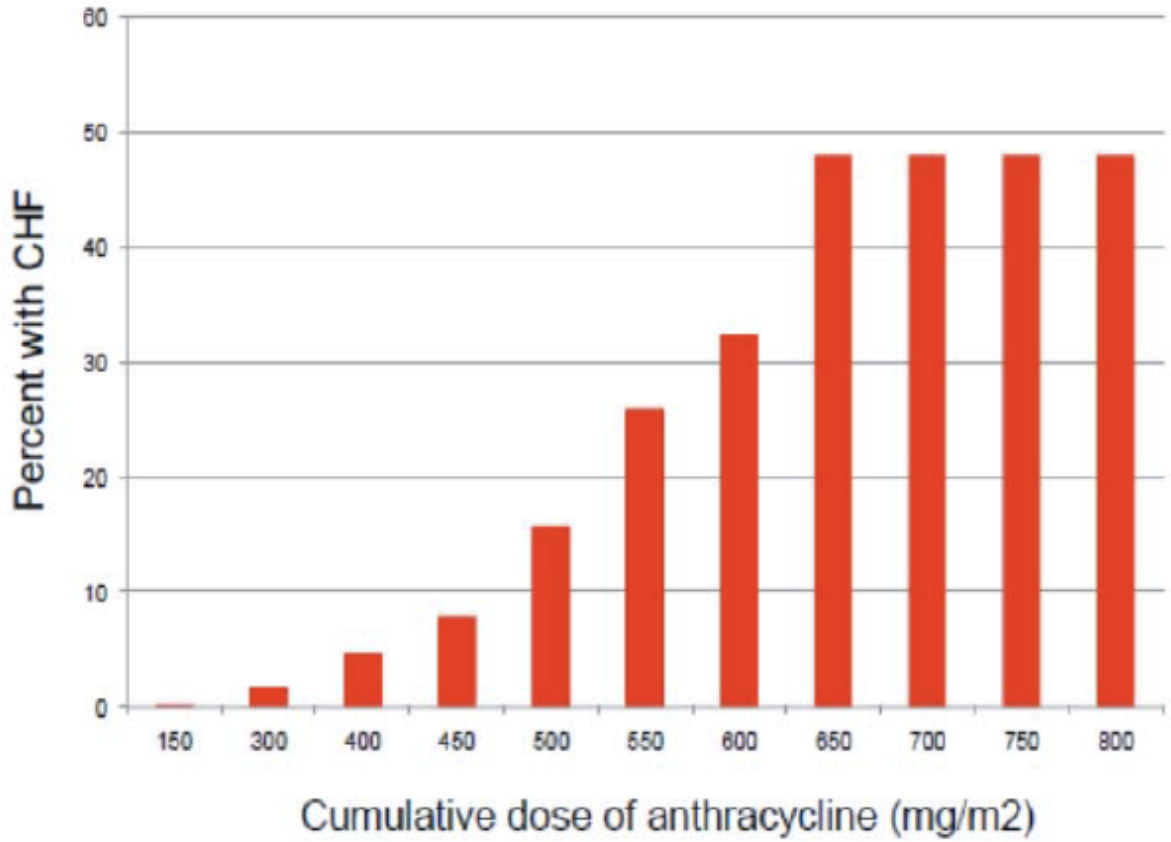
(CTRCD) is defined as a drop in LV EF of ≥5% ⬇ in symptomatic patients

or

a drop in LV EF of ≥10% ⬇ to an EF of <55% in asymptomatic patients

EXAMPLE Patients who have received a cumulative dose of >250–300 mg/m^2 of doxorubicin or its equivalent are considered to be at high risk of developing CTRCD; however, there is individual variability with some patients developing cardiotoxicity at lower cumulative doses

Risk of Toxicity

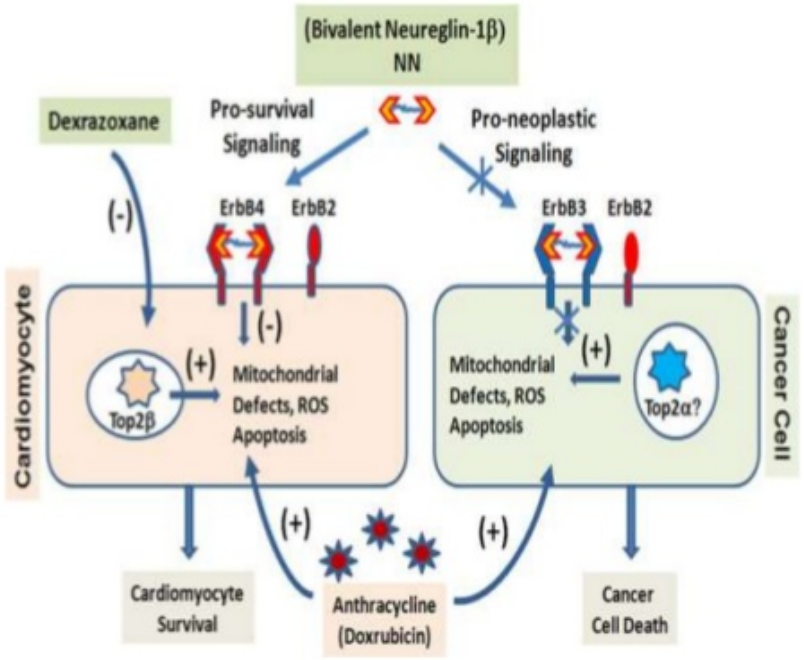


Swain et al. Cancer. 2003;97:2869-79

Mechanisms of Cardiotoxicity

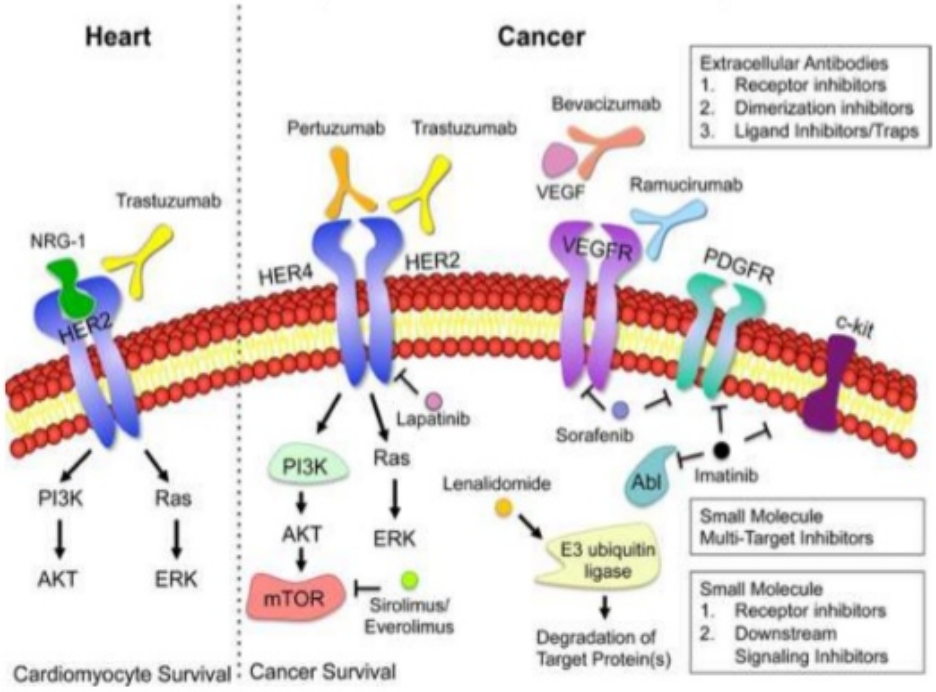
On-target toxicity

Cytotoxic Therapies



Force, et al. *Circulation*, 2013

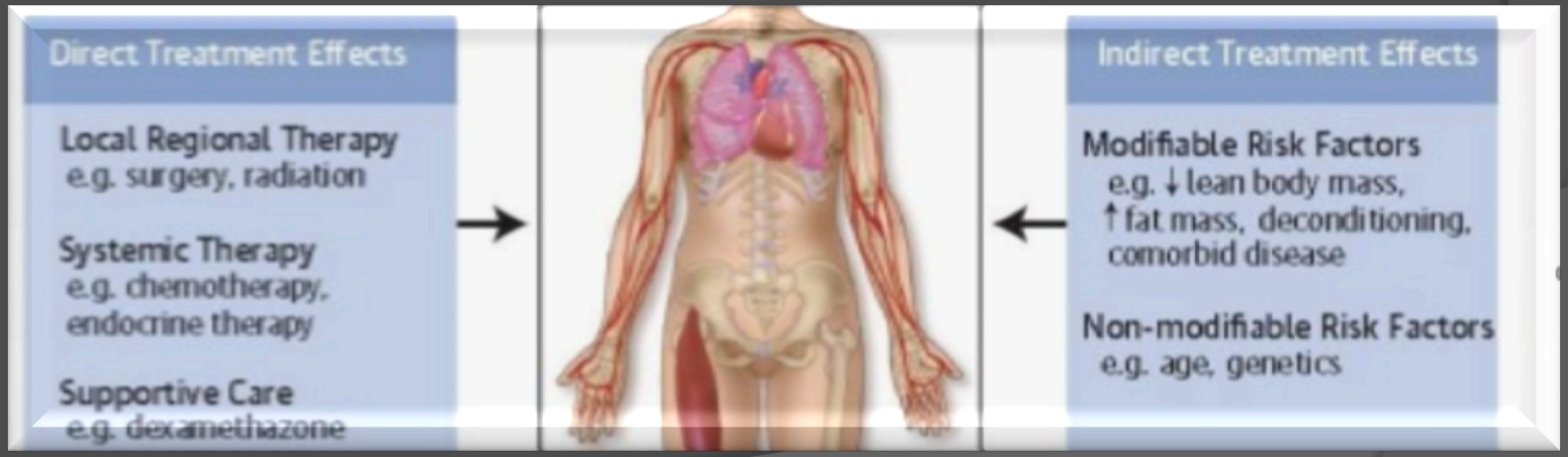
Targeted Therapies



Bellinger, et al. *Circulation*, 2015

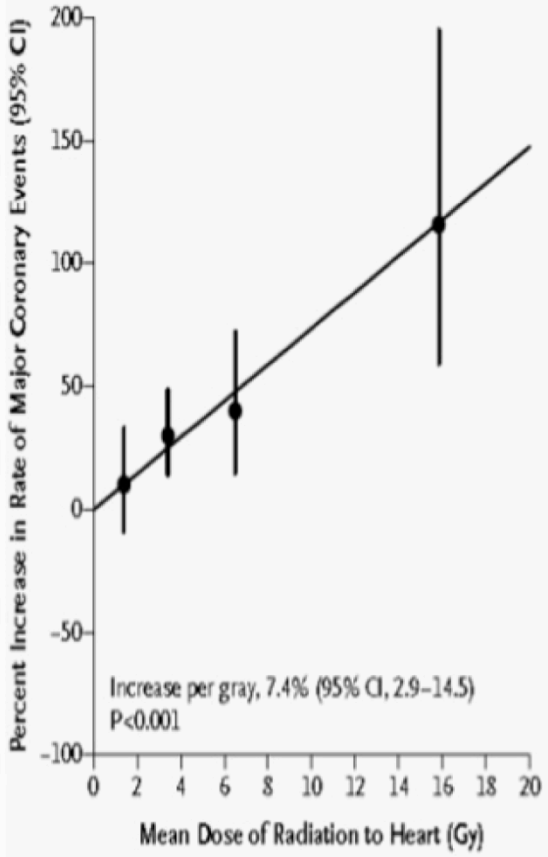
Multi – Hit Hypothesis

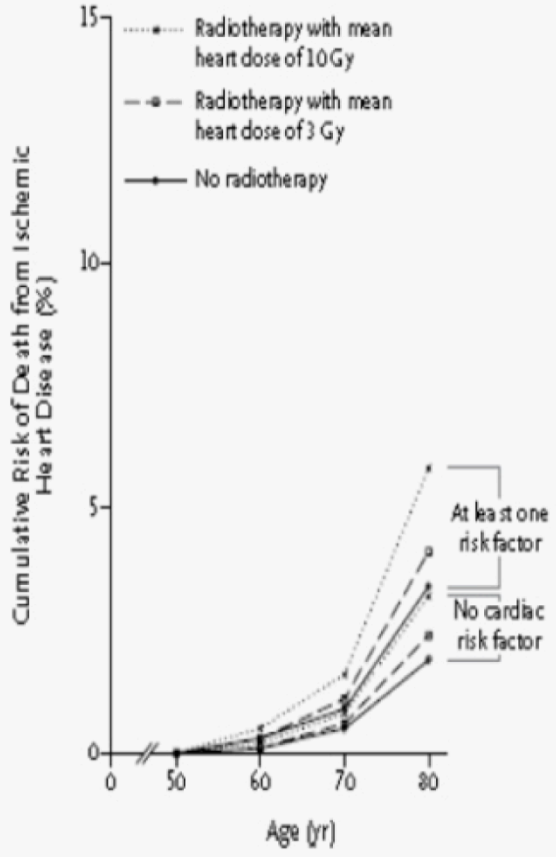
A multi-hit hypothesis has been proposed to explain CTRCD. By this hypothesis, multiple insults to the myocardium increase the risk of developing cardiotoxicity. These insults to the myocardium can be in the form of pre-existing cardiovascular disease (coronary artery disease, heart failure and arrhythmias) or cardiovascular risk factors (age, hypertension, diabetes mellitus and hyperlipidemia



Radiation Therapy

Coronary Events in Breast Cancer





1958 - 2001

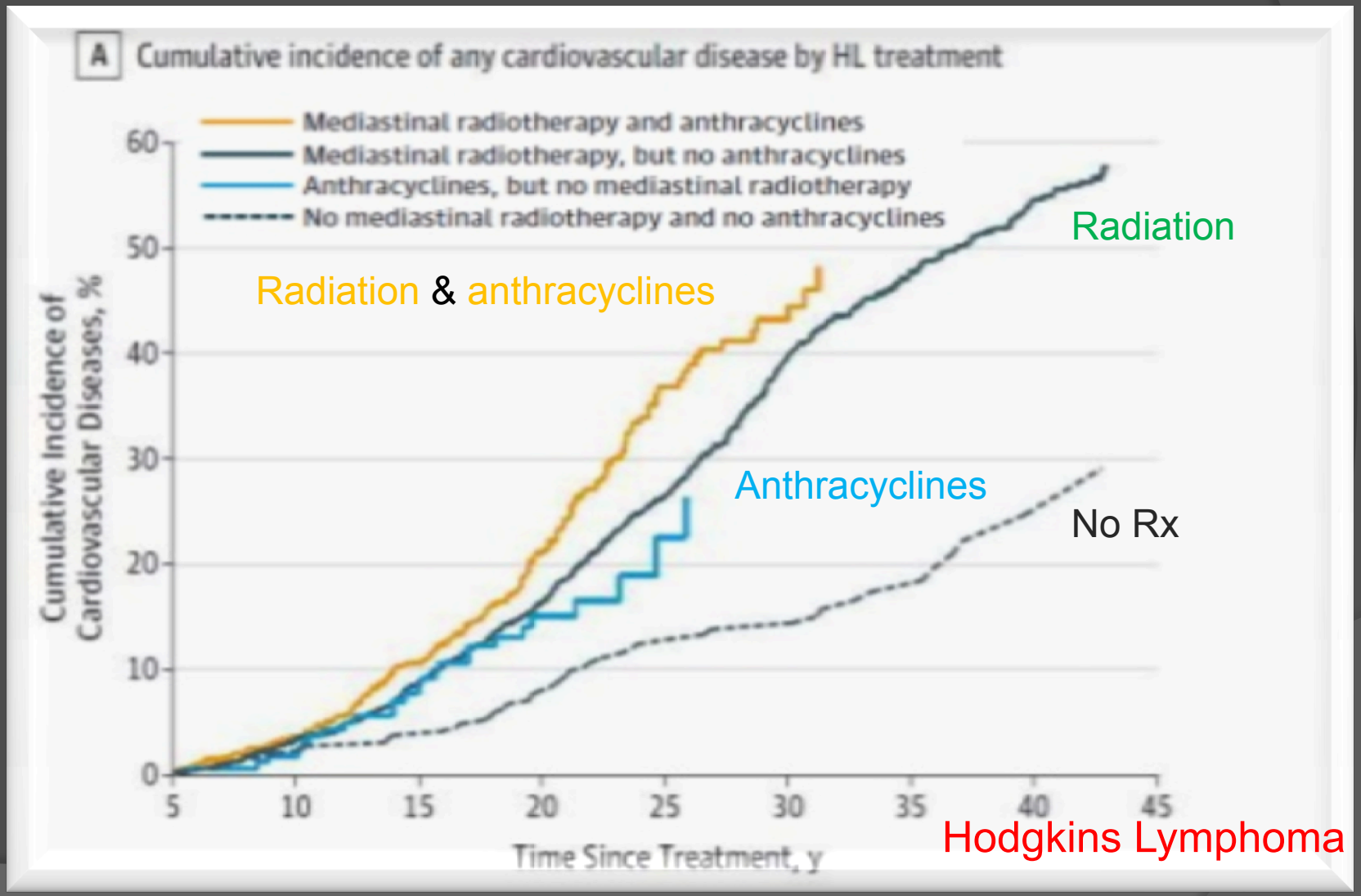
50 year old
300 cGy mean dose

No risk factors
Death from IHD by age 80
AR: 1.9% increased to 2.4%

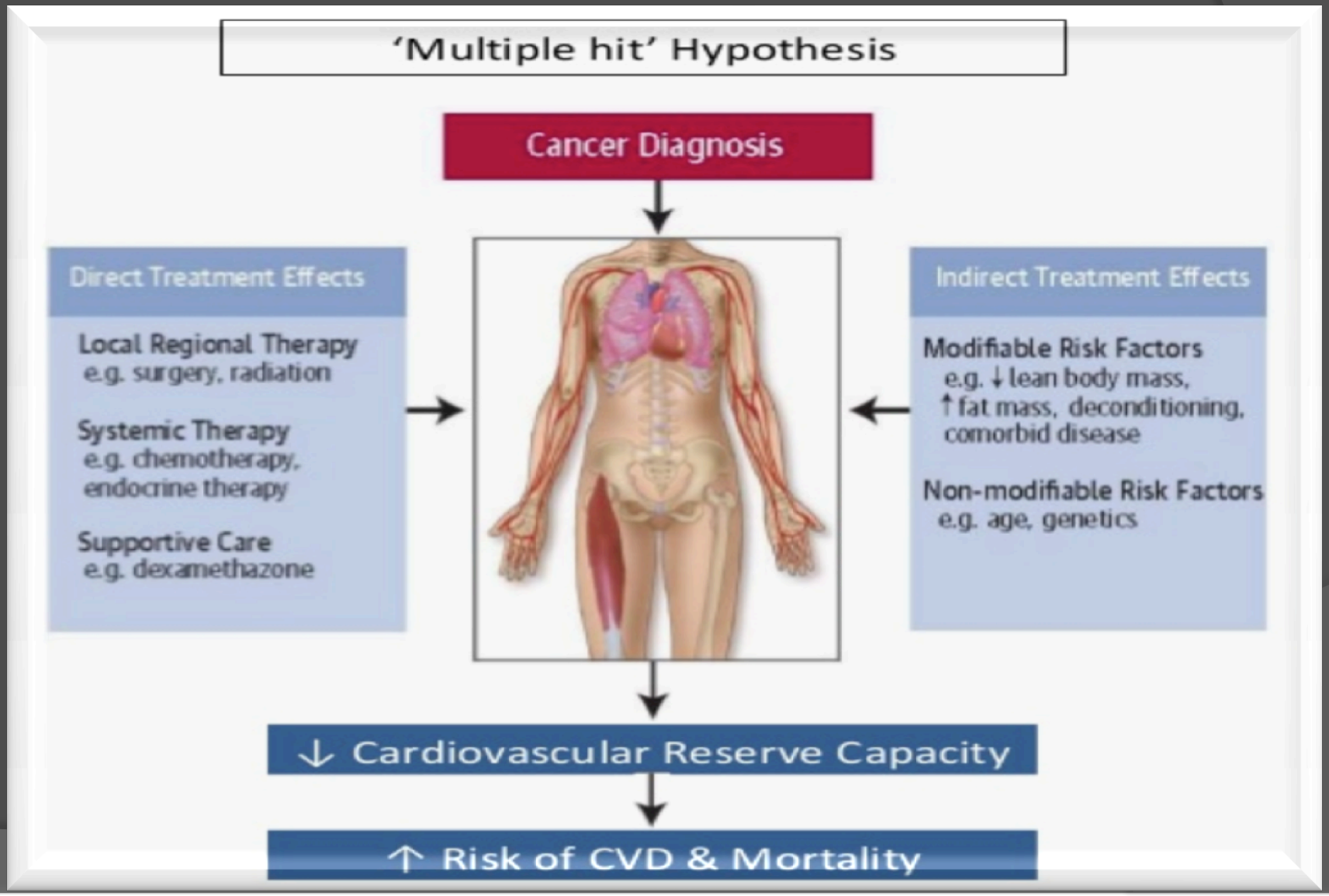
1 or more risk factors
Death from IHD by age 80
AR: 3.4% increased to 4.1%

Darby, et al. *NEJM* 2013

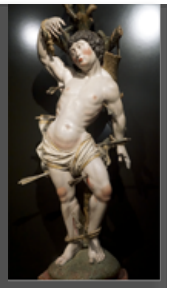
Incidence of CV Disease



Interaction with the Heart



...CTRCD



Two types of CTRCD have been described. Type 1 is an irreversible, dose-dependent toxicity that results from ultra-structural changes in the myocardium.
Example:
anthracycline cardiotoxicity

CTRCD Type 2 is largely reversible, not dose dependent, and does not cause ultra-structural changes in the myocardium. It is typified by trastuzumab cardiotoxicity.

Trastuzumab is most commonly used in the treatment of breast cancer. Importantly, because type 2 toxicity is usually reversible, re-challenge with the offending drug is usually well tolerated after initiating cardiac protective therapy

Risk Evaluation

1. Risk assessment

Tests: TTE with strain, ECG, cTn

Medication-related risk

High (risk score 4):
Anthracyclines, cyclophosphamide, ifosfamide, clofarabine, herceptin

Intermediate (risk score 2):
Docetaxel, pertuzumab, sunitinib, sorafinib

Low (risk score 1):
Bevacizumab, dasatinib, imatinib, lapatinib

Rare (risk score 0):
For example, etoposide, rituximab, thalidomide

Patient-related risk factors

- Cardiomyopathy or heart failure
- CAD or equivalent (incl. PAD)
- HTN
- Diabetes mellitus
- Prior or concurrent anthracycline
- Prior or concurrent chest radiation
- Age <15 or> 65 years
- Female gender

Overall risk by cardiotoxicity risk score (CRS)

(risk categories by drug-related risk score plus number of patient-related risk factors: **CRS >6:** very high, **5-6:** high, **3–4:** intermediate, **1–2:** low, **0:** very low)

CTRCD Monitoring : Echo

2. Monitoring recommendations

Very high cardiotoxicity risk: TTE Echo before every (other) cycle, end, 3–6 months, and 1 year; optional ECG, cTn with TTE during chemotherapy

High cardiotoxicity risk: TTE Echo every 3 cycles, end, 3–6 months and 1 year after chemotherapy; optional ECG, cTn with TTE during chemotherapy

Intermediate cardiotoxicity risk: TTE Echo mid-term, end, and 3–6 months after chemotherapy; optional ECG, cTn mid-term of chemotherapy

Low cardiotoxicity risk: Optional TTE with strain and/or ECG, cTn at the end of chemotherapy

Very low cardiotoxicity risk: None

Mayo Clinic Proceedings, Volume 89(9)

Monitoring Tn I

Cardiac biomarkers may play a complementary role to cardiac imaging in monitoring patients for cardiotoxicity. Elevations in cardiac troponin I (TnI) either early (checked with each cycle of chemotherapy) or late (one month after completion of last cycle of chemotherapy) have been shown to be predictive of LV EF reduction and cardiac events .

The greatest value of TnI may be the high negative predictive value, such that patients who do not have an elevation in TnI have a very low cardiac event rate and perhaps need less-frequent surveillance imaging

CTRCD

Cancer therapeutic related cardiac dysfunction

3. Management recommendations

Very high cardiotoxicity risk: Initiate ACE-I /ARB, carvedilol, and statins, starting at lowest dose and start chemotherapy in 1 week from initiation to allow steady state, up-titrate as tolerated

High cardiotoxicity risk: Initiate ACE-I /ARB, carvedilol, and/or statins

Intermediate cardiotoxicity risk: Discuss risk and benefit of medications

Low cardiotoxicity risk: None, monitoring only

Very low cardiotoxicity risk: None, monitoring only

Radiation Therapy

Patients who have received radiation therapy are at risk of long-term cardiovascular toxicity including radiation-induced heart disease (valvular disease, pericardial disease, myocardial disease and coronary artery disease) and peripheral artery disease depending on the field of radiation.

Risk factors for radiation-induced heart disease include anterior or left chest radiation, cumulative radiation dose >30 Gy, radiation fraction dose >2 Gy/day,

Age <50 years, tumor in or near the heart, lack of shielding, concomitant chemotherapy particularly with an anthracycline, smoking and medical comorbidities (diabetes mellitus, hypertension, hyperlipidemia and obesity)

Radiation Followup

In asymptomatic patients, a transthoracic echocardiogram is recommended 5 years after exposure in high-risk individuals and 10 years after exposure in all others.

Subsequently, transthoracic echocardiograms are recommended for reassessment every 5 years.

Additionally, a cardiac stress test is recommended after 5 years in high-risk individuals, and after 10 years, in all others

Journal of the American Society of Echocardiography 26

Conclusions: Cardio-Oncology

Cardiovascular disease can cause significant morbidity in cancer survivors.

The goal is to decrease this morbidity by early risk factor modification, serial monitoring with imaging and/or biomarkers, cardioprotective medical therapy and optimal medical therapy for cardiotoxicity when it occurs.

Further study is ongoing and greatly needed to define the optimal methods to achieve these aims with regard to both surveillance methods and timing of surveillance as well as to optimal medical therapies for prevention and treatment of type I and type II CTRCD.

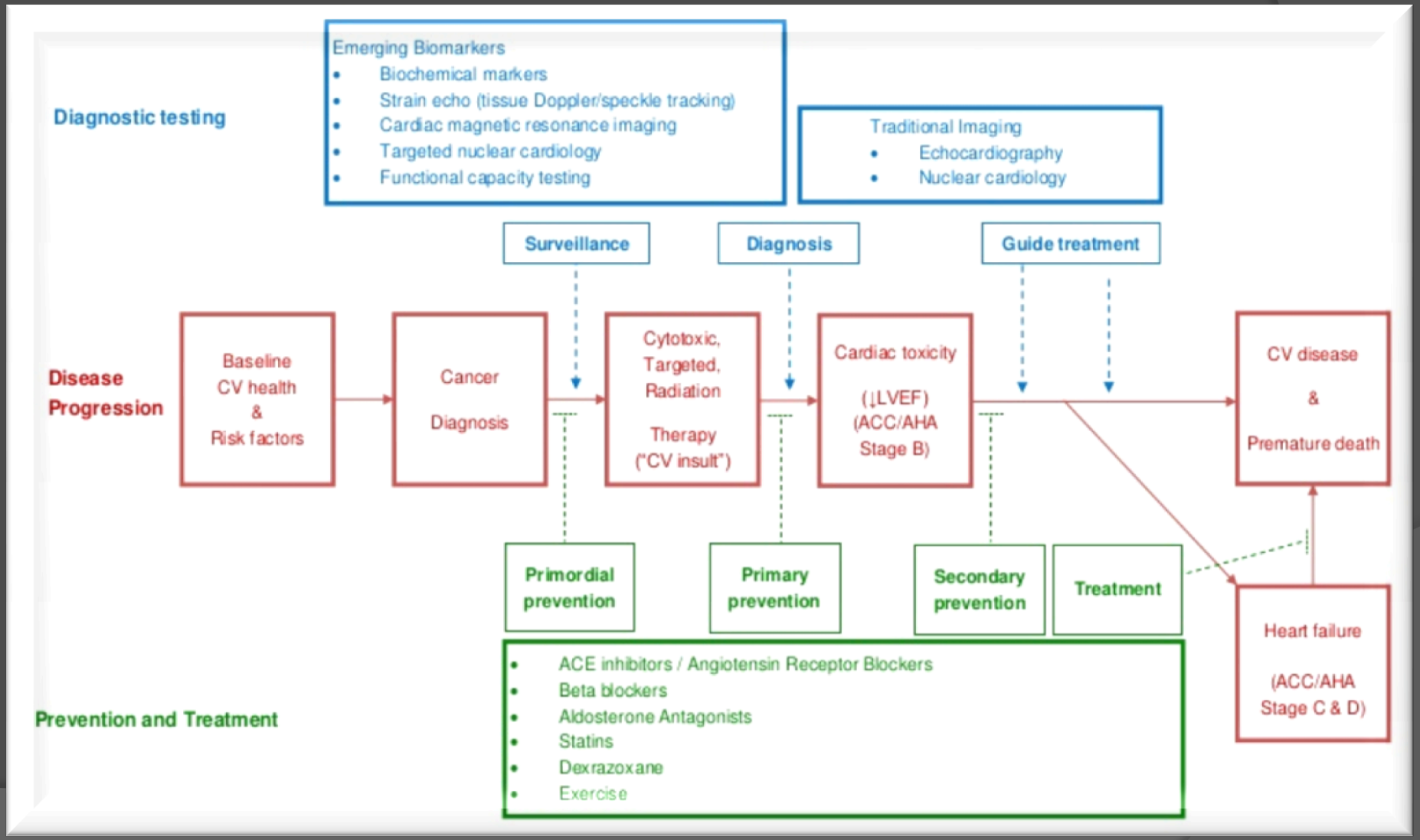
In Conclusion

- When your patient needs cancer treatments
- - consider risks of treatment and benefit
- - risk stratify
- - address risk factors

Future is cloudy but breakthroughs are possible

Venice: we would rather be here…

Progression of disease



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MRI


FEMALE LISTENING SKILLS
TONE, INFLECTION, POINT OF VIEW, DOUBLE MEANINGS, INNUENDO, HIDDEN MESSAGES...
MALE LISTENING SKILLS
MMM... PEPPERONI.