

# Cardio-Oncology: What Survivors Need to Know



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TJUH-SKMC

Cancer Nation Survivorship Conference

# 2022 Cardio-Oncology Guidelines—ESC

JOURNAL ARTICLE GUIDELINES

## 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): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC) FREE

Alexander R Lyon ✉, Teresa López-Fernández ✉, Liam S Couch, Riccardo Asteggiano, Marianne C Aznar, Jutta Bergler-Klein, Giuseppe Boriani, Daniela Cardinale, Raul Cordoba, Bernard Cosyns ... [Show more](#)

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*European Heart Journal*, Volume 43, Issue 41, 1 November 2022, Pages 4229–4361,  
<https://doi.org/10.1093/eurheartj/ehac244>

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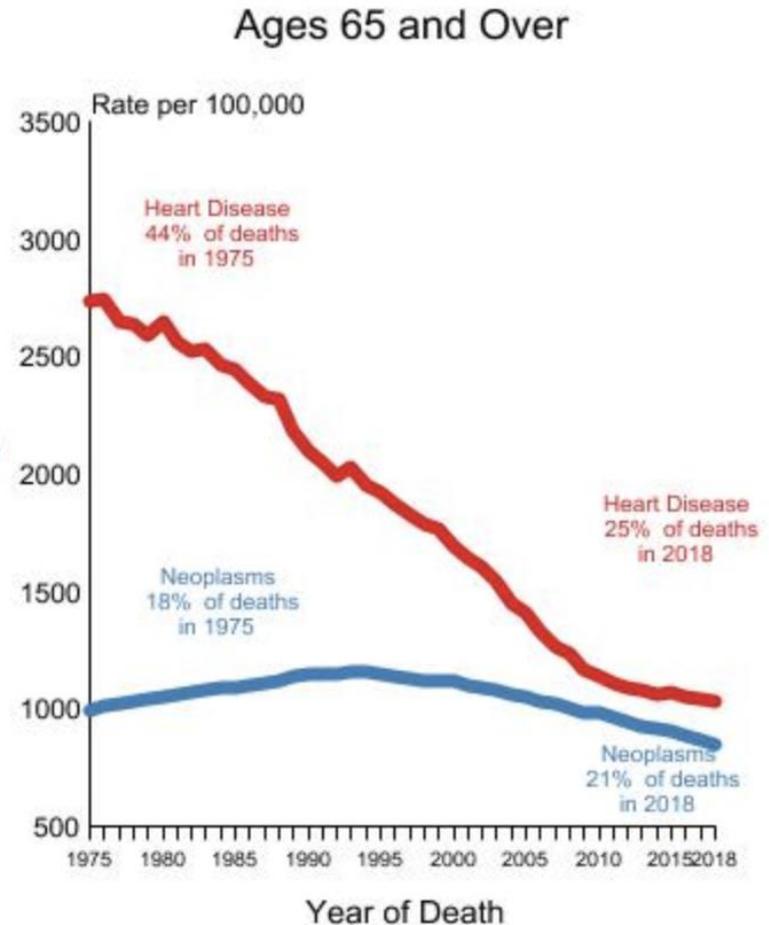
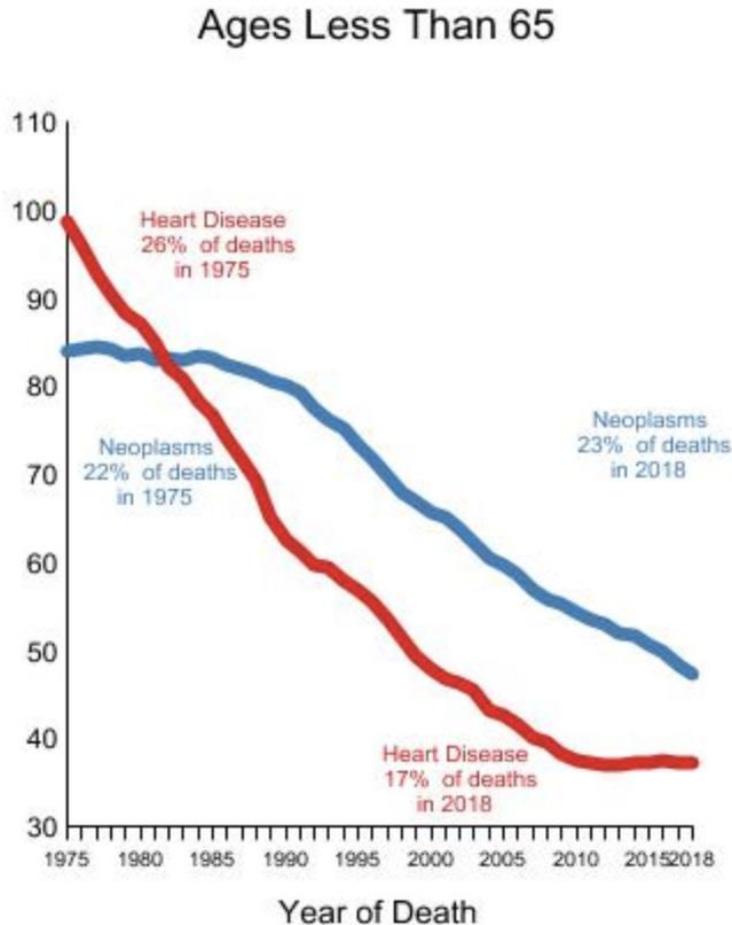
# Outline

- Facts about Cancer
- Heart and the Cardiovascular System
- Epidemiology
- Offending Agents
- Management

# Facts About Cancer

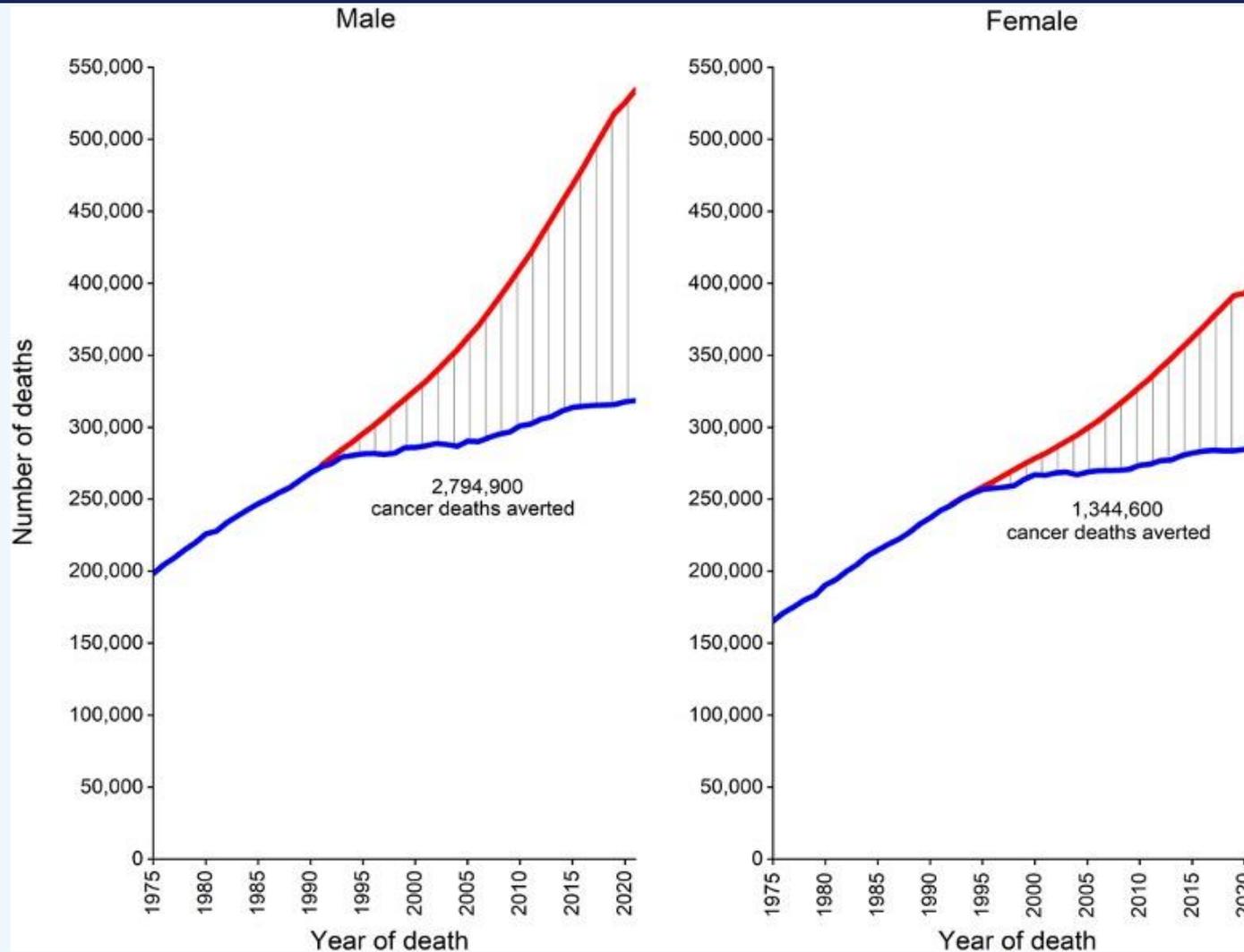
- Approximately 39.5% of men and women will be diagnosed with cancer at some point during their lifetimes (based on 2015–2017 data).
- In 2020, approximately 16,850 children and adolescents ages 0 to 19 were diagnosed with cancer and roughly 1,730 died of the disease.
- As of January 2019, there were an estimated 16.9 million cancer survivors in the United States. The number of cancer survivors is projected to increase to 22.2 million by 2030.

# US Death Rate in Heart Disease vs Neoplasm between 1975-2018



Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

# Number of Cancer Deaths Averted between 1990-2021

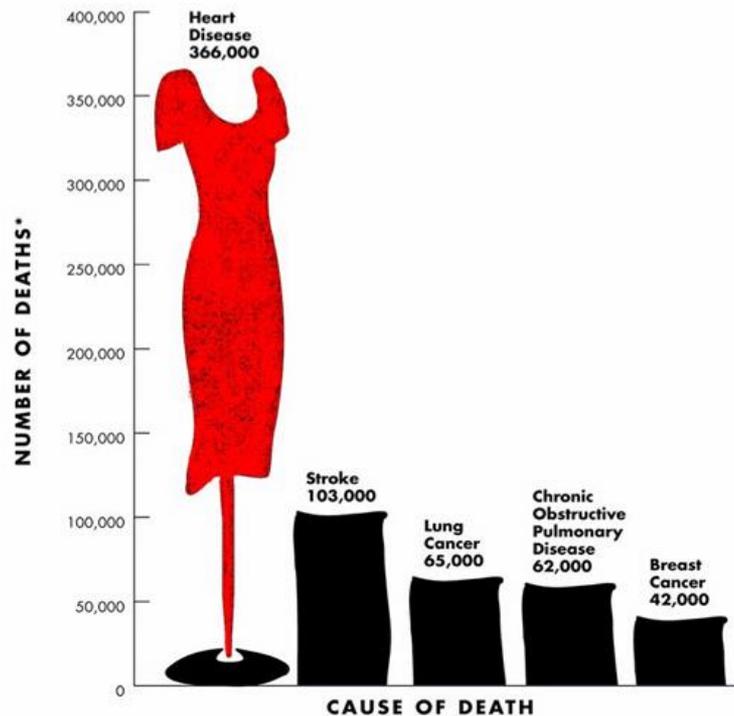


CA A Cancer J Clinicians, Volume: 74, Issue: 1, Pages: 12-49, First published: 17 January 2024, DOI: (10.3322/caac.21820)

# Leading Causes of Death in Women

## LEADING CAUSES OF DEATH FOR AMERICAN WOMEN (2000)

One in three women dies from heart disease. It's the #1 killer of women, regardless of race or ethnicity. It also strikes at younger ages than most people think, and the risk rises in middle age. And, two-thirds of women who have heart attacks never fully recover.



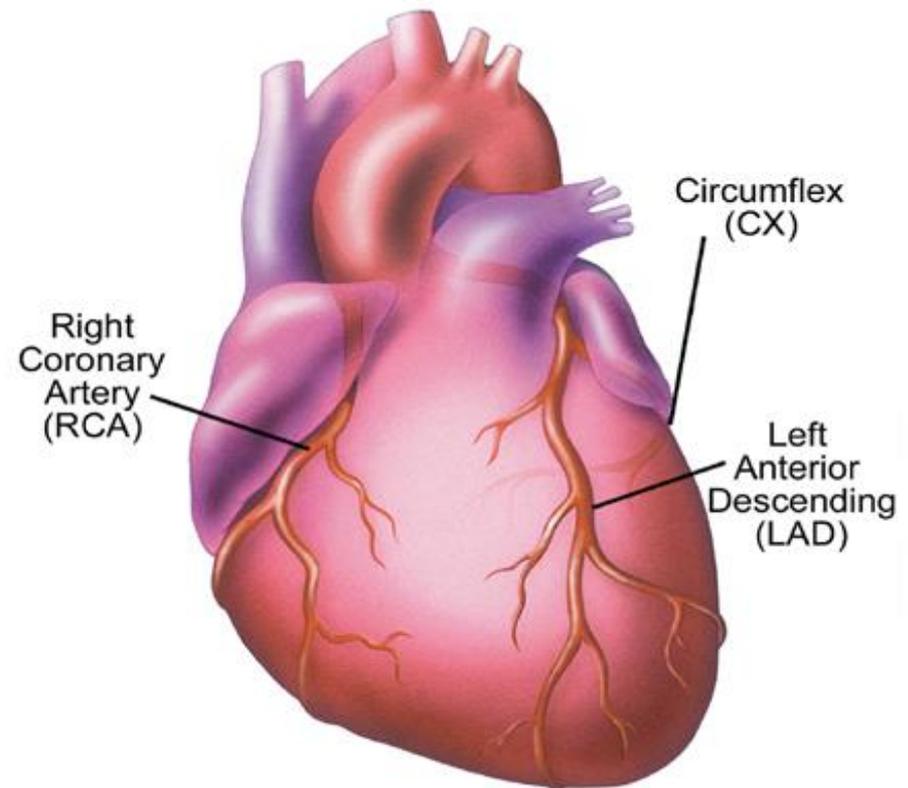
To learn more, visit [www.nhlbi.nih.gov/health/hearttruth](http://www.nhlbi.nih.gov/health/hearttruth)

Source: The Healthy Heart Handbook for Women, National Heart, Lung, and Blood Institute (2003).

\*Numbers of deaths are rounded to the nearest thousand.

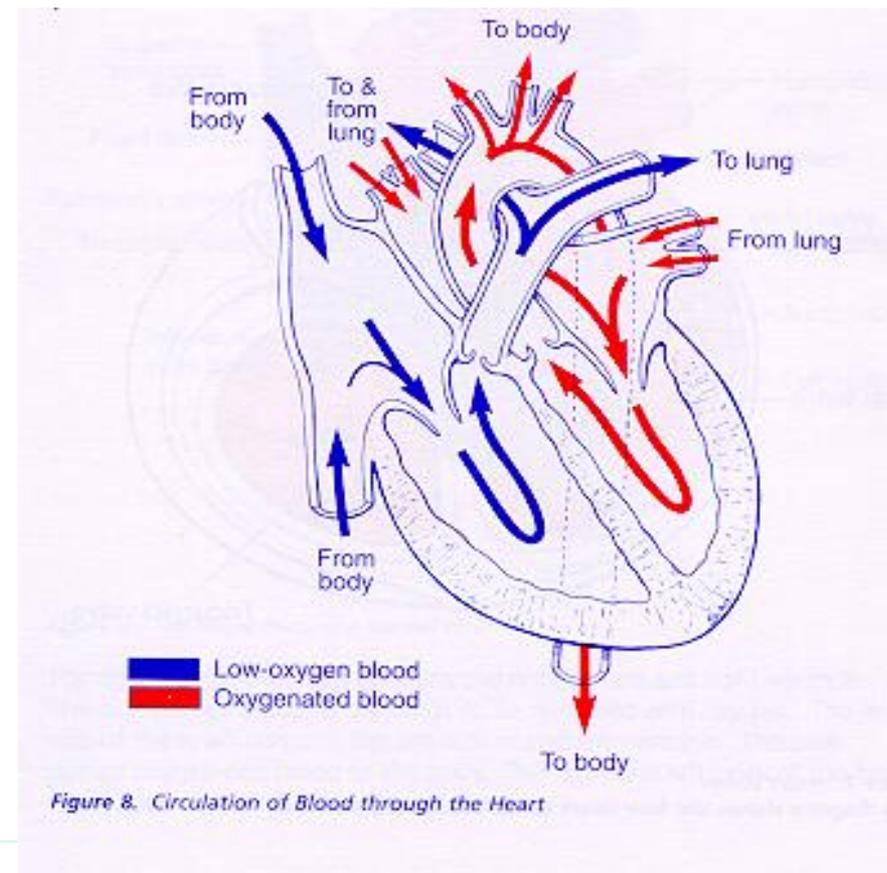
# The Cardiovascular System—The Heart

- Four chambered pump
  - Right atrium/right ventricle
  - Left atrium/left ventricle
- Right side and left side do NOT communicate.
- Like all pumps it needs energy
  - It gets its energy from the oxygen and glucose (sugar) in the blood
- Has its own blood supply:
  - Left Main-> LAD/LCx
  - Right Coronary Artery (RCA) .



# The Cardiovascular System—The Blood Vessels

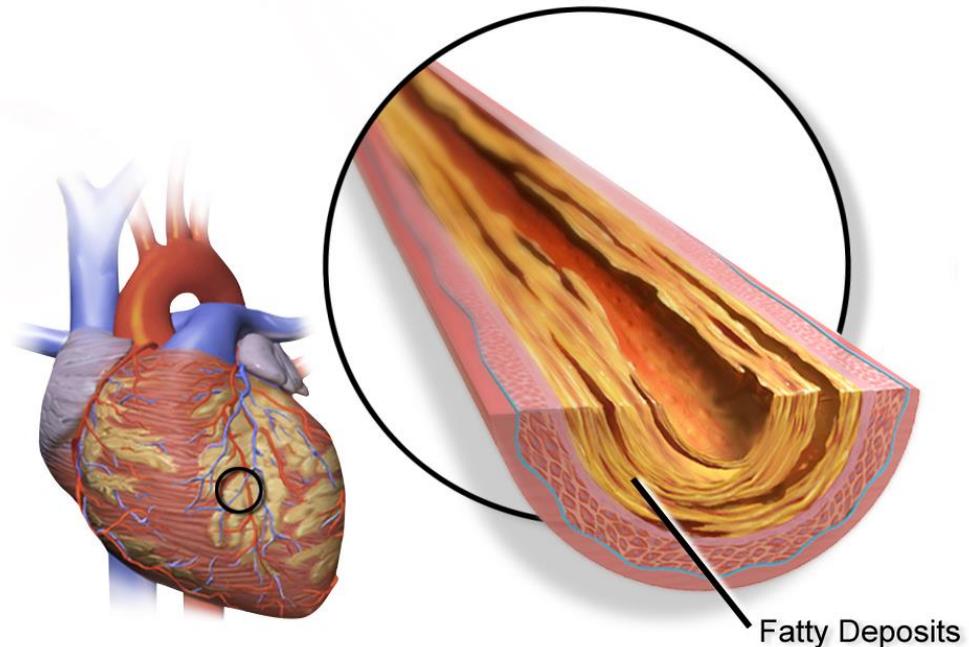
- -Arteries carry oxygen-rich blood from the heart to all the cells in the body
- -Veins carry oxygen-poor blood that has given up oxygen to the cells back to the heart
- -The right side of the heart pumps venous blood to the lungs to pick up oxygen and remove carbon dioxide
- -The left side of the heart pumps arterial blood around the body



# Cardiovascular Disease is disease of the heart or blood vessels

**Coronary Artery Disease** is disease (arteriosclerosis) of the inner lining of the arteries that supply blood to the heart.

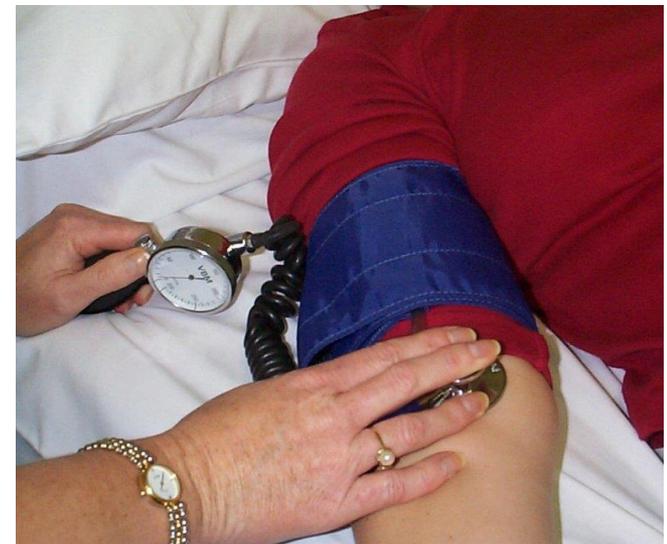
**CAD** is a major cause of illness and death.



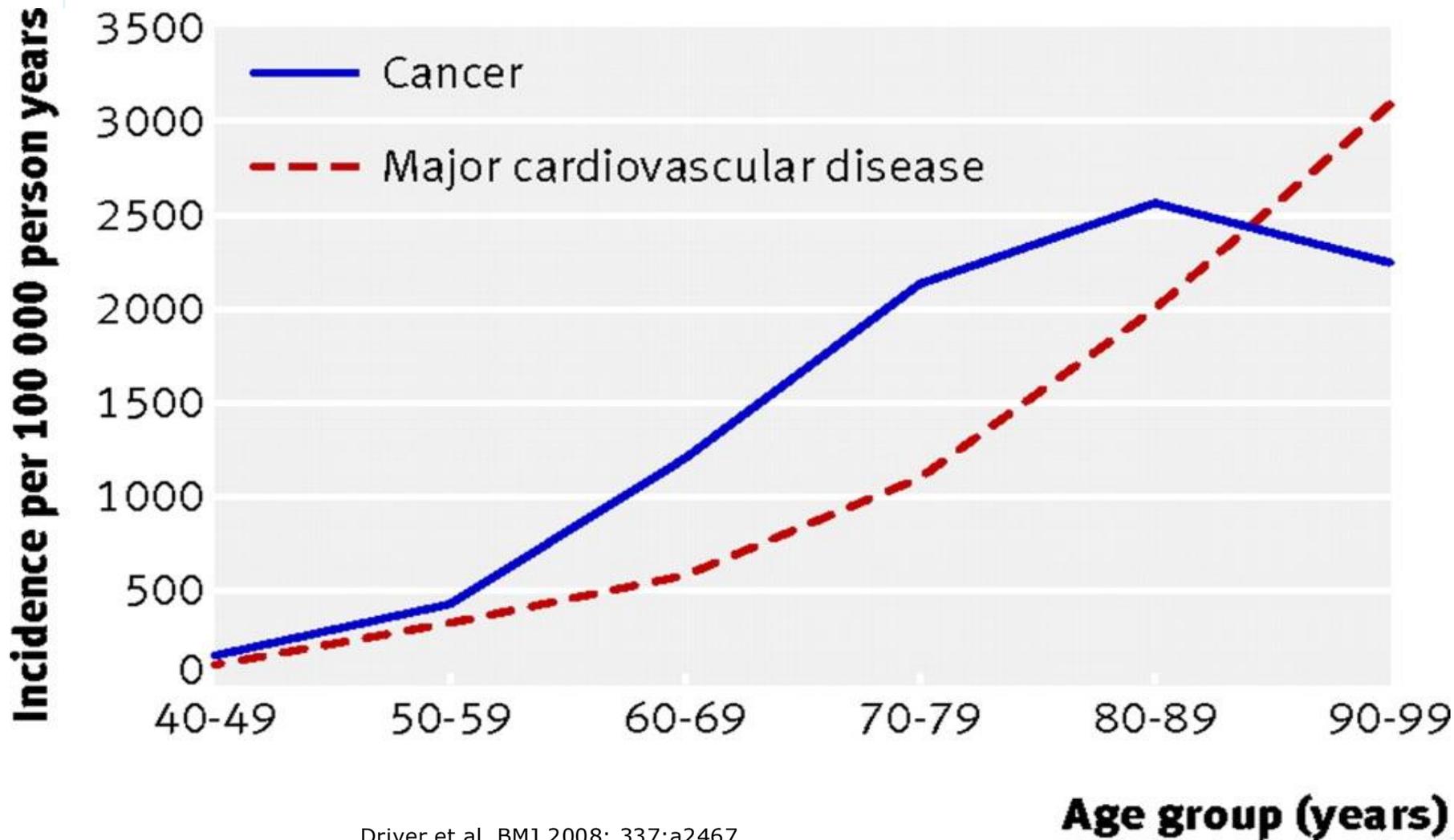
By BruceBlaus. When using this image in external sources it can be cited as: Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436. - Own work, CC BY 3.0, <https://commons.wikimedia.org/w/index.php?curid=29738538>

# What, treat blood pressure? But I have cancer.

- High Blood Pressure—Hypertension:
  - Causes the heart to work harder
  - Causes the heart to enlarge
  - Causes the heart to fail
  - Accelerates arteriosclerosis
  - Causes strokes
  - Causes kidney damage and failure



## Incidence of Cancer and Heart Disease Increase with Age and May Occur Concurrently: Physicians Health Study



Driver et al, BMJ 2008; 337:a2467

# Oncologic Treatments Associated With Cardiovascular Toxicities



# Oncologic Treatments Associated with Cardiovascular Toxicities

Radiation

Anthracyclines

Anti-metabolites (5FU)

VEGF Inhibitors

Her2 Targeted Therapies

Cancer Immunotherapies (Immune Checkpoint Inhibitors): **Myocarditis**

Immunomodulators (IMiDs):

Proteasome inhibitors

MEK/RAF TKI

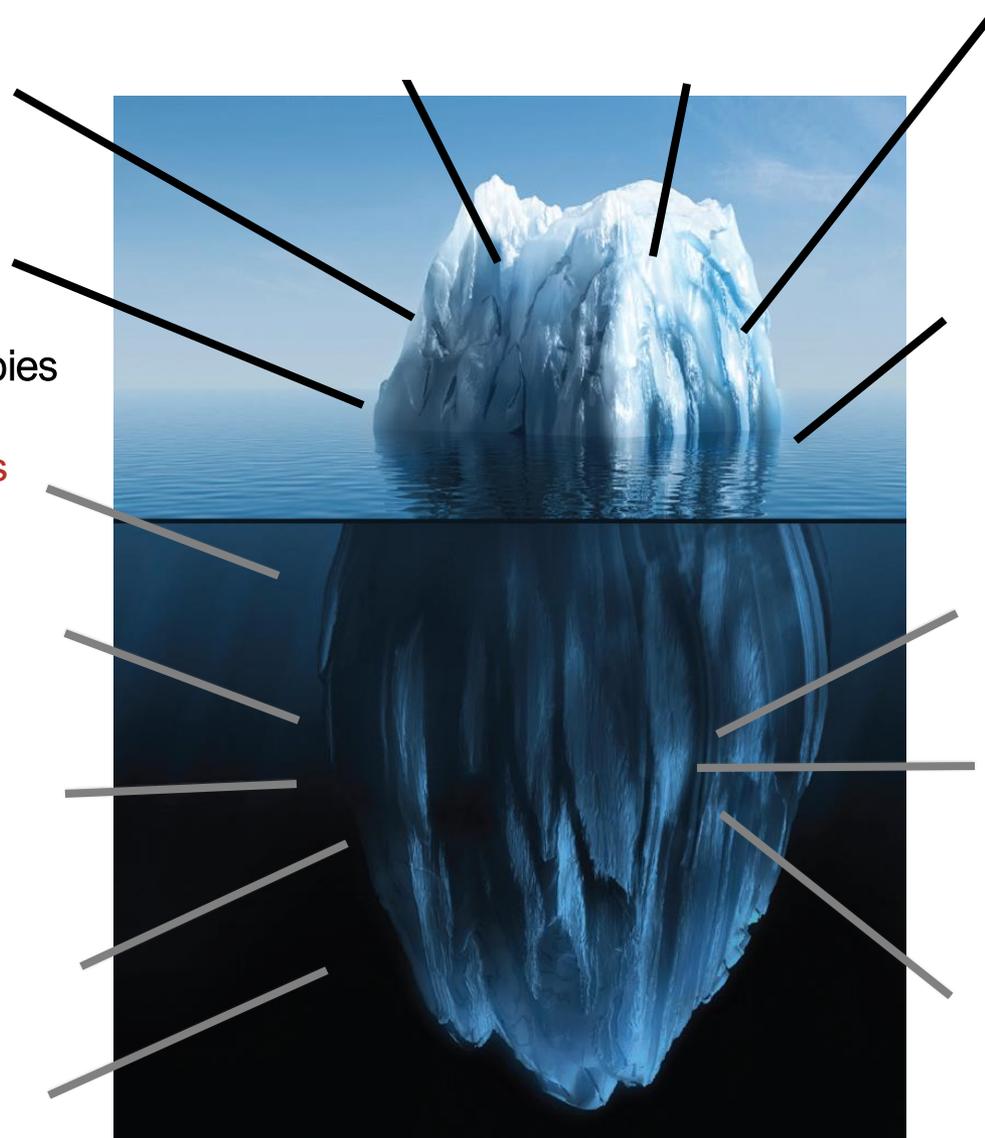
Cancer Survivorship

CML TKIs

CDK4/6 inhibitors

PI3K Inhibitors

BTK Inhibitors



Adapted from Moslehi, Cheng. *Science Translational Medicine*, 2013. Moslehi, *NEJM*. 2016.

# Oncologic Treatments Associated with Cardiovascular Toxicities

Radiation

**Pericarditis, CAD  
Valvular Stenosis**

Anthracyclines

**Cardiomyopathy  
Heart Failure**

Anti-metabolites (5FU)

**Ischemia  
Vasospasm**

VEGF Inhibitors

**Hypertension  
Heart Failure  
Thrombosis**

Her2 Targeted  
Therapies

**Cardiomyopathy**

Cancer  
Immunotherapies  
(Immune Checkpoint  
Inhibitors):

**Myocarditis**

Immunomodulators  
(IMiDs):

**thrombosis**

Proteasome inhibitors

**?vascular**

MEK/RAF TKI

**Cardiomyopathy**

**Cancer Survivorship**

CML TKIs

Imatinib: ?protective  
Dasatinib/Nilotinib/  
Bosutinib/Ponatinib:  
**PAH/Vascular/  
Atherosclerosis**

CDK4/6 inhibitors

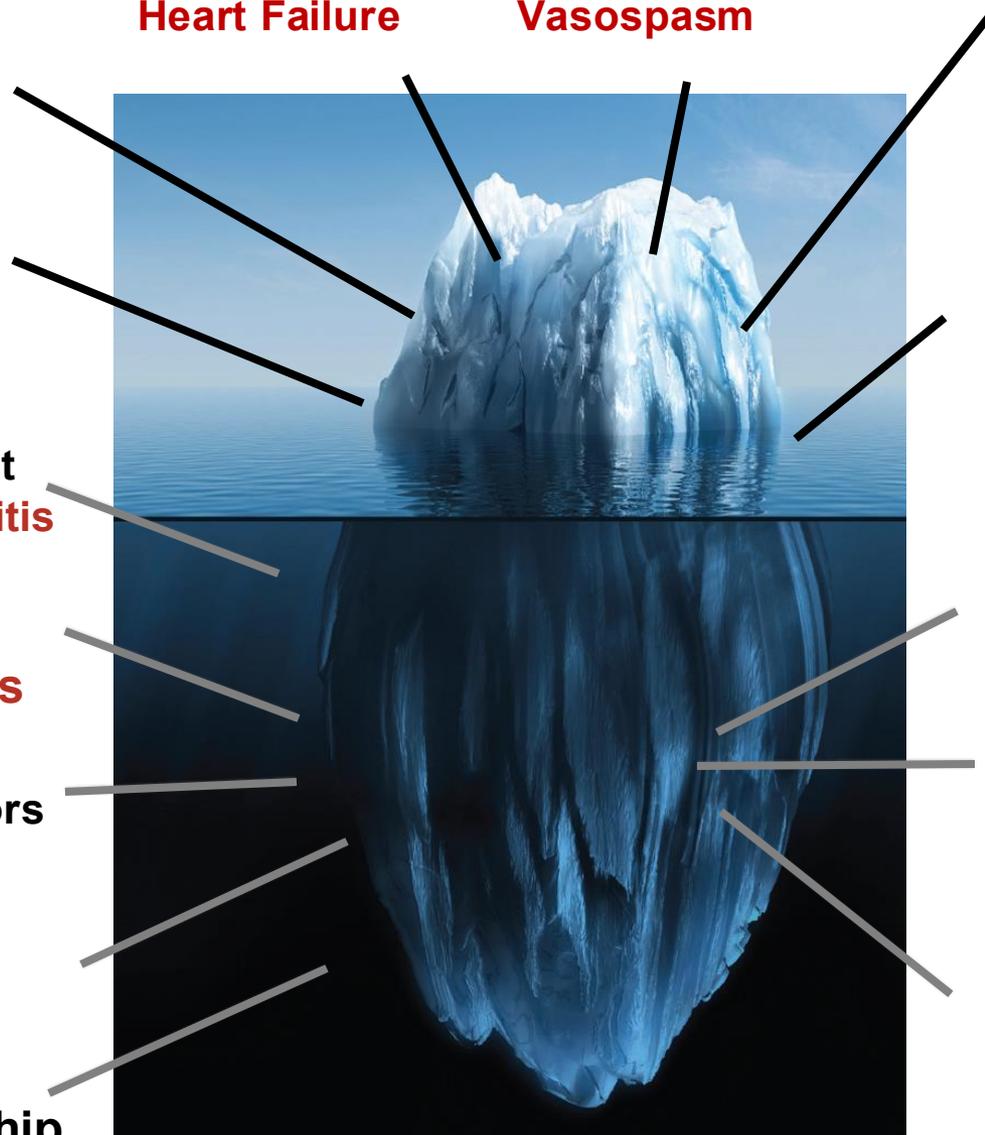
**?Arrhythmia**

PI3K Inhibitors

**Hyperglycemia  
Metabolic  
?Myocardial/  
Arrhythmia**

BTK Inhibitors

**Arrhythmias**



# Oncologic Treatments Associated with Cardiovascular Toxicities

Radiation  
Pericarditis, CAD  
Valvular Stenosis

Anthracyclines  
Cardiomyopathy  
Heart Failure

Anti-metabolites (5FU)  
Ischemia  
Vasospasm

VEGF Inhibitors  
Hypertension  
Heart Failure  
Thrombosis

Her2 Targeted  
Therapies  
Cardiomyopathy

CML TKIs  
Imatinib: ?protective  
Dasatinib/Nilotinib/  
Bosutinib/Ponatinib:  
PAH/Vascular/  
Atherosclerosis

Immune Checkpoint  
Inhibitors: Myocarditis

CDK4/6 inhibitors  
Arrhythmia

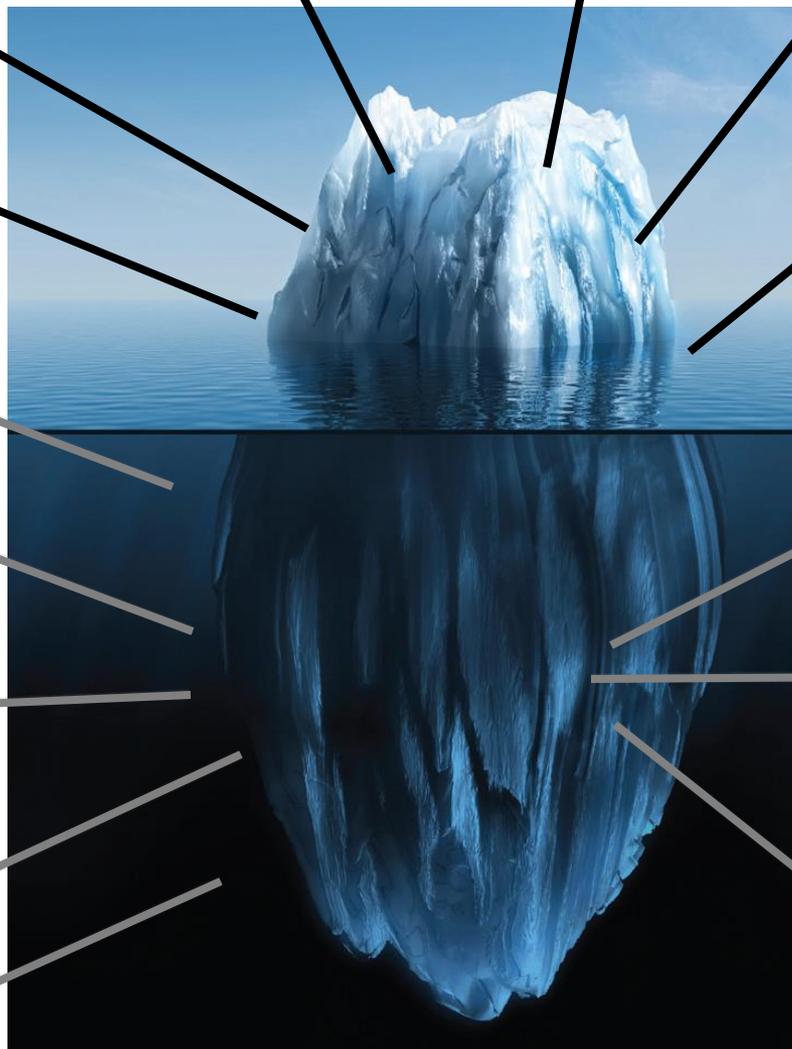
Immunomodulators  
(IMiDs): thrombosis

PI3K Inhibitors:  
Hyperglycemia  
Metabolic  
?Myocardial/  
Arrhythmia

Proteasome inhibitors  
?vascular

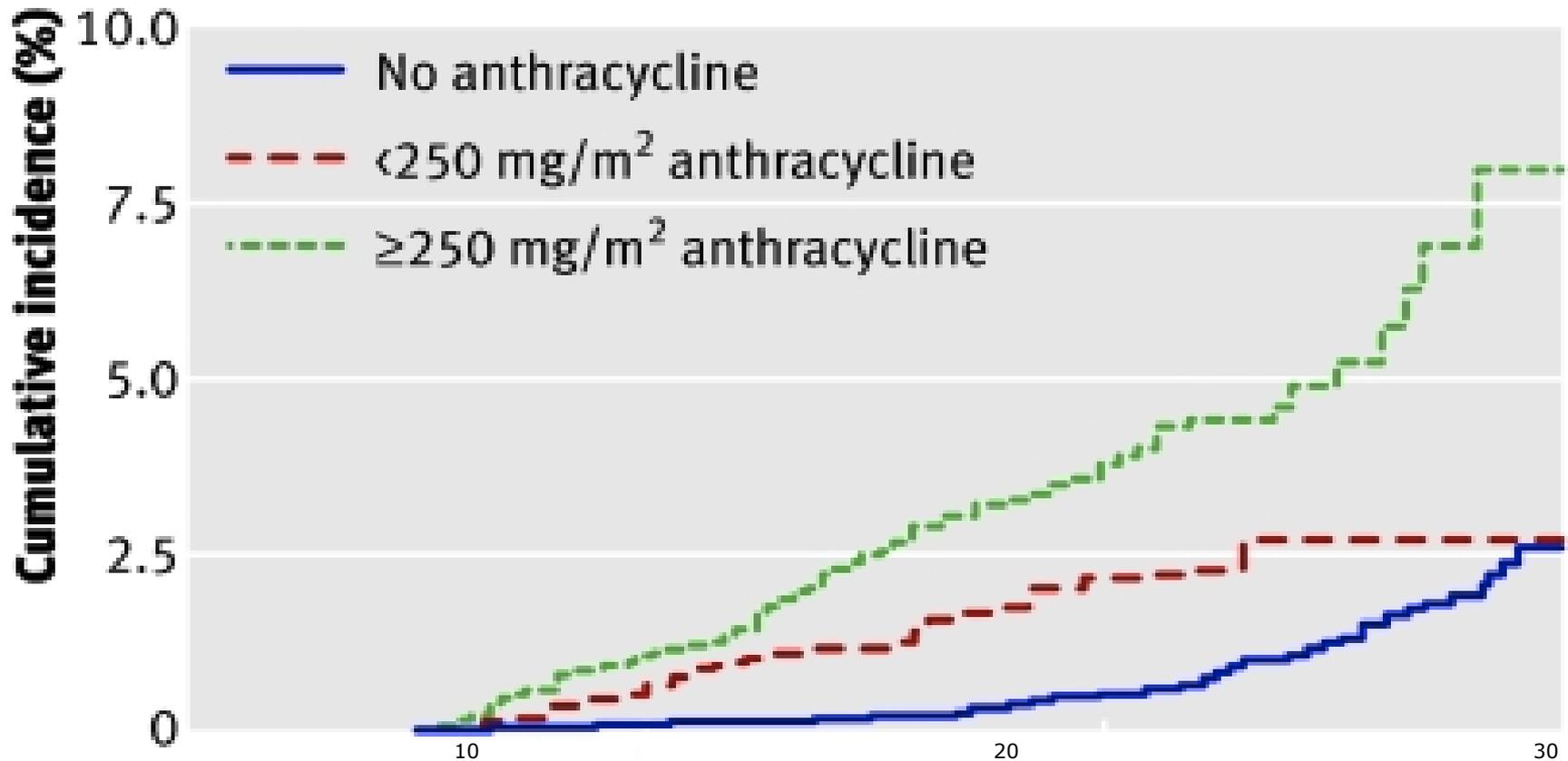
MEK/RAF TKI  
Cardiomyopathy

BTK Inhibitors  
Arrhythmias



**Cancer Survivorship**

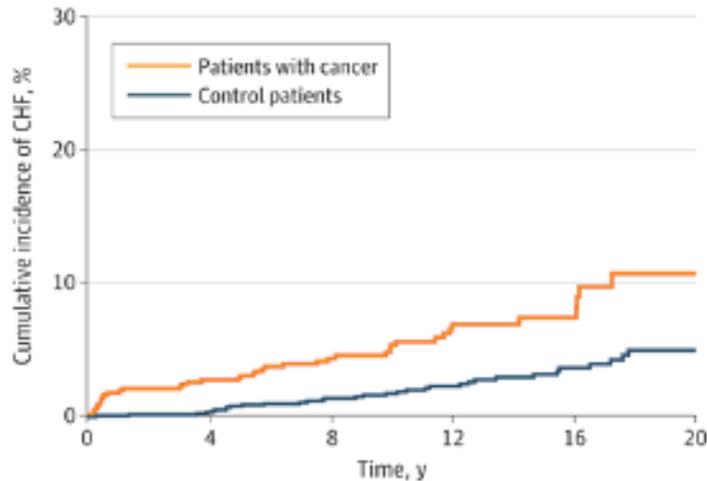
# Cumulative Incidence of Congestive Heart Failure Among Childhood Cancer Survivors by Anthracycline Dose



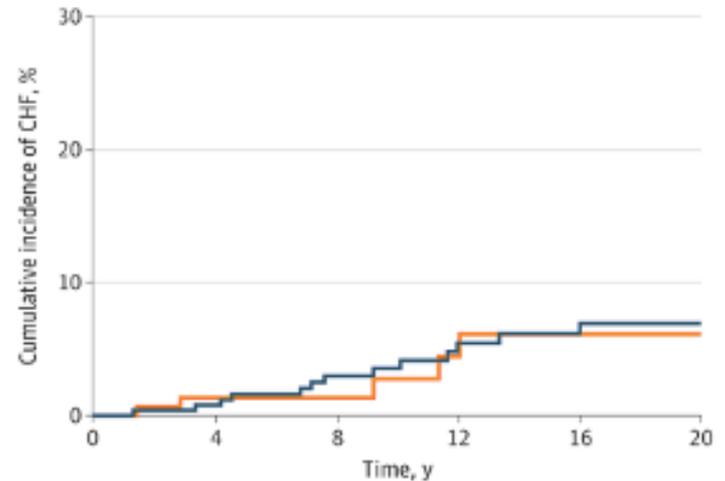
Adapted from Mulrooney et al, BMJ 2009; 339:b4606

# Cumulative Incidence of Congestive Heart Failure In Adults Over Time Treated with Anthracycline

**A** Patients with cancer treated with anthracycline



**B** Patients with cancer not treated with anthracycline



No. at risk	0	4	8	12	16	20
Patients with cancer	662	487	268	108	32	
Control patients	1132	1108	757	403	150	

No. at risk	0	4	8	12	16	20
Patients with cancer	150	89	33	20	14	
Control patients	251	240	142	100	75	

In this case-control study among 2196 individuals, including 812 participants with cancer and 1384 control participants, the cumulative incidence of HF in participants with cancer treated with anthracycline was 7.4% over 15 years, more than 2 times higher than in matched controls, and was not significant for a subgroup of participants with cancer not treated with anthracycline compared with controls

From: **Association of Anthracycline With Heart Failure in Patients Treated for Breast Cancer or Lymphoma, 1985-2010**

JAMA Netw Open. 2023;6(2):e2254669. doi:10.1001/jamanetworkopen.2022.54669

# Risk Factors for Developing Anthracycline Cardiotoxicity and CHF

- Chemo dose and schedule dependent
- Mode of administration
- Sex--Women >> Men
- Underlying cardiac risk factors (age, hypertension, hyperlipidemia, family history, diabetes, tobacco history)
- Underlying cardiac disease
- mediastinal radiation
- concurrent or sequential Herceptin use or other cardiotoxic agent use such as paclitaxel.
- increased length of time since anthracycline completion.
- lack of exercise/sedentary lifestyle.

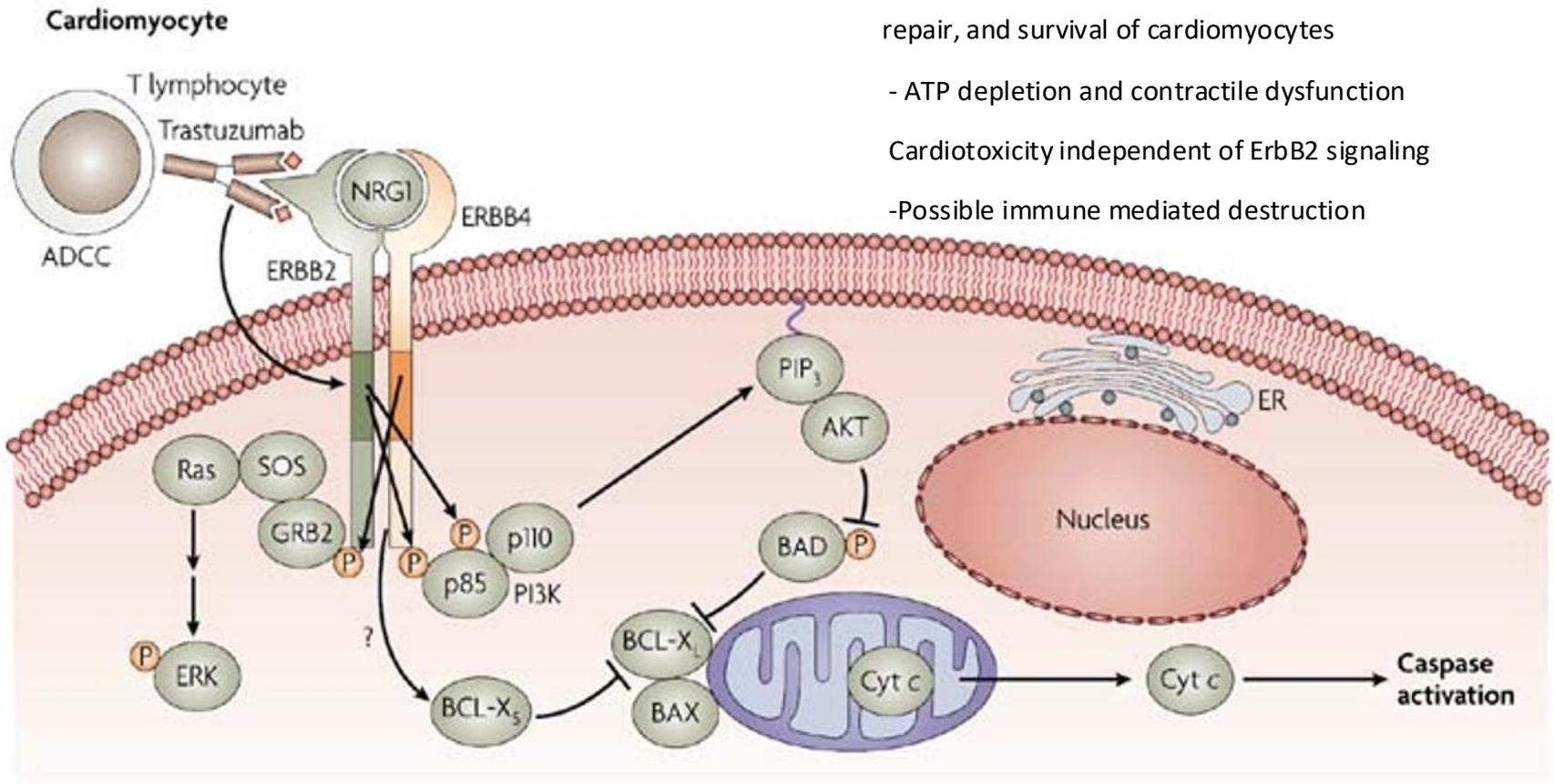
# Mechanisms of Trastuzumab Cardiotoxicity

Inhibition of ErbB2 in cardiomyocytes: interferes with growth, repair, and survival of cardiomyocytes

- ATP depletion and contractile dysfunction

Cardiotoxicity independent of ErbB2 signaling

-Possible immune mediated destruction



Nature Reviews | Cancer

# Risk Factors for Developing Trastuzumab Toxicity

- Standard risk factors for developing structural heart disease.
- Previous doxorubicin exposure
- Previous chest wall irradiation
- Obesity

## **Reversibility—**

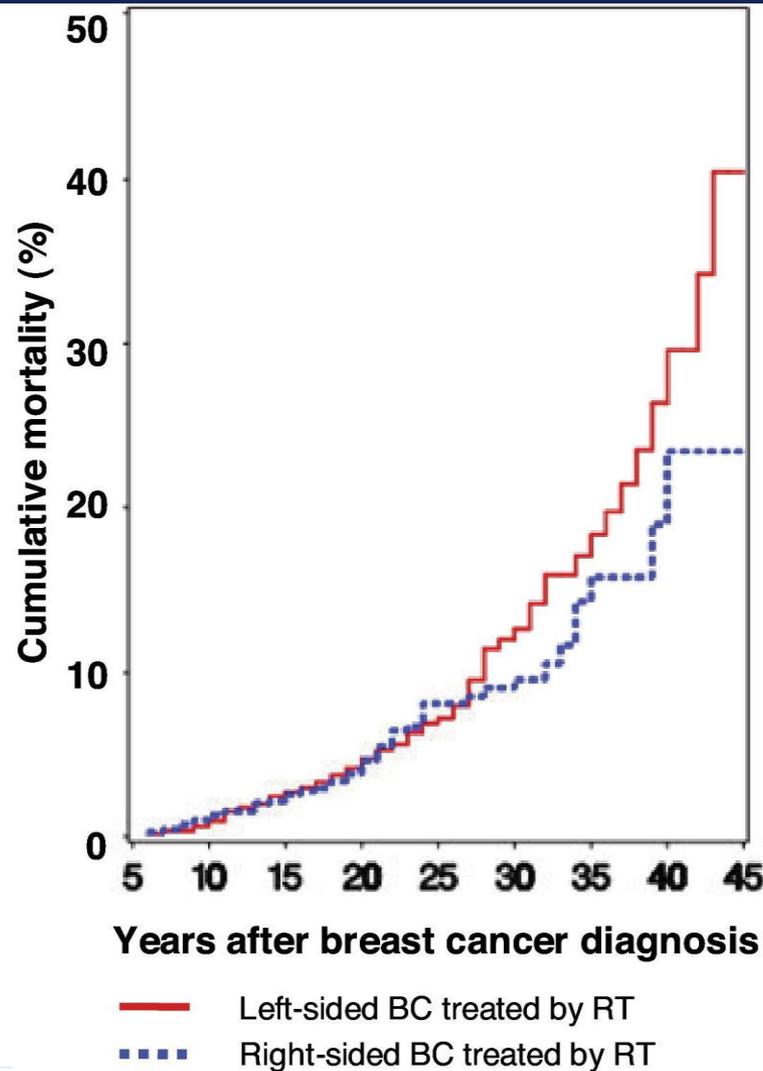
- largely possible but not necessarily 100%

## **Prevention—**

- treatment of underlying risk factors prior to initiating Trastuzumab.

# Radiation Therapy

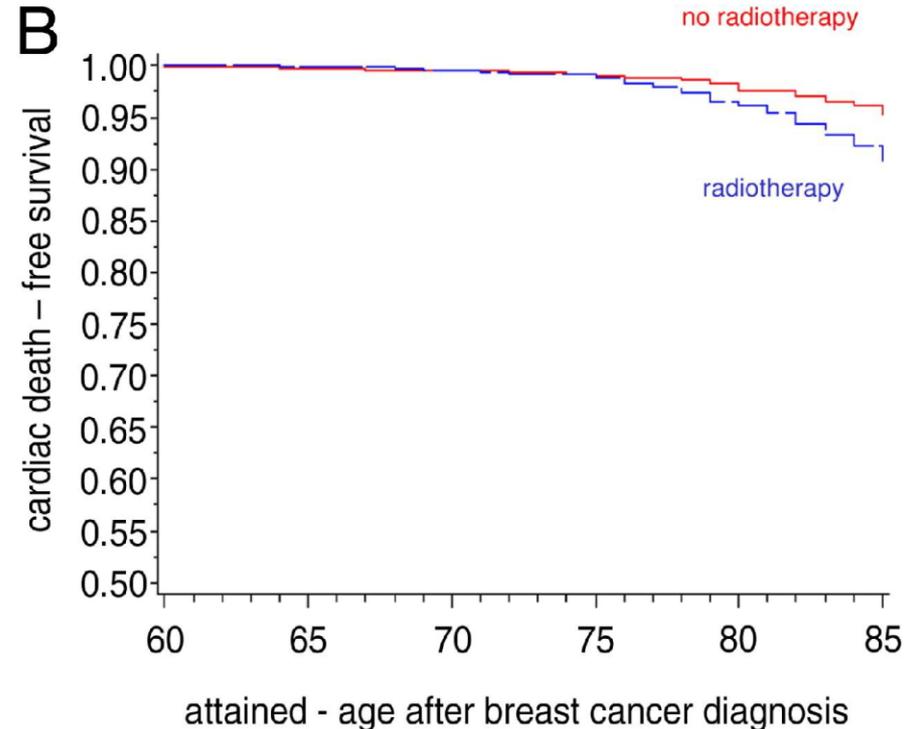
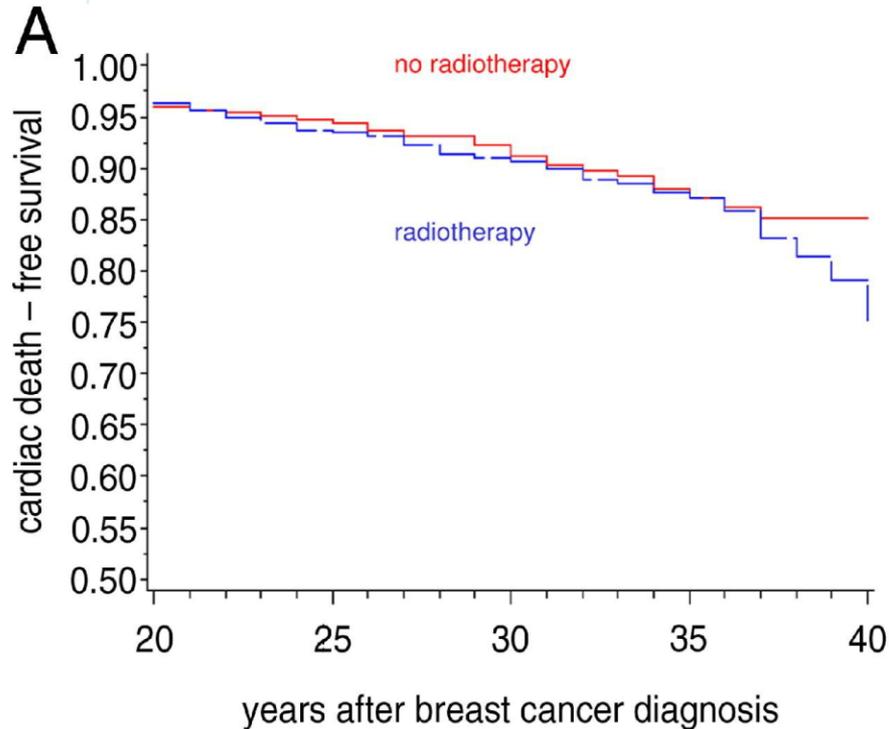
# Cumulative Mortality Due to Cardiac Disease According to Breast Cancer Laterality



4500 women—radiation of  
IMC at Institute Gustave  
Roussy, France

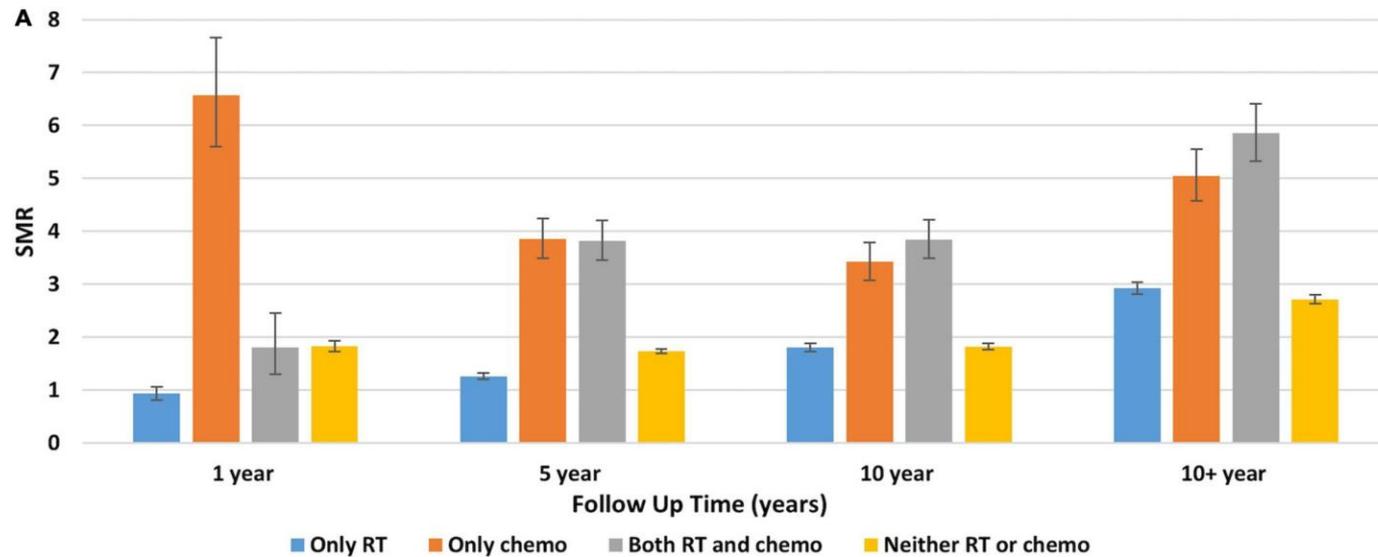
Bouillon, K., et al. *Journal of the American College of Cardiology*, (2011) Volume 57 (4); 445-452.

# Cardiac Death-Free Survival According to Radiotherapy Status

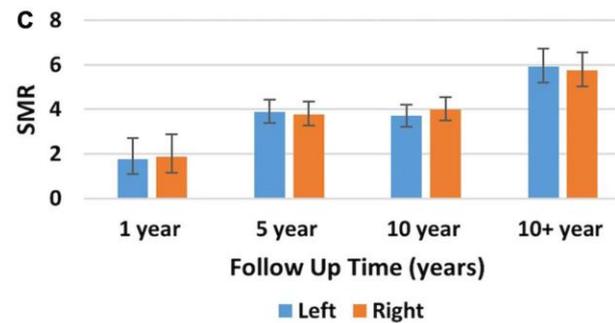
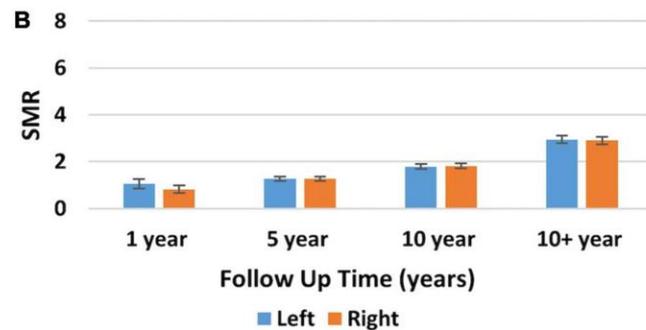


Bouillon, K., et al. *Journal of the American College of Cardiology*, (2011) Volume 57 (4); 445-452.

# Standard Mortality Ratios for Death from Heart Disease in Breast Cancer Patients Based on Treatment, Disease Laterality, and Era of Diagnosis



SEER Database:  
Woman  
diagnosed from 1992  
to 2014



Agha, A. et al. Front. Cardiovasc. Med., 13 April 2022

Sec. Cardio-Oncology

Volume 9 - 2022 | <https://doi.org/10.3389/fcvm.2022.784409>

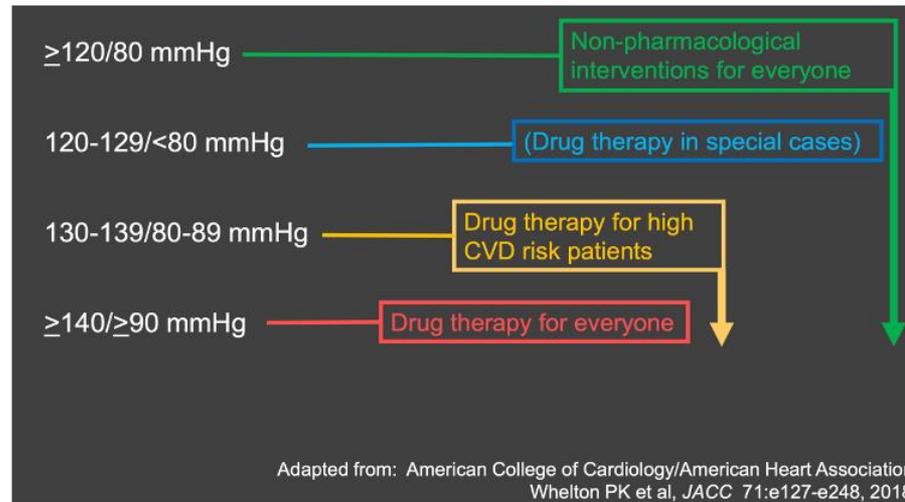
# Chemotherapy and Hypertension—Is there a link?

# 2017 Update on Guidelines for BP Management

## Blood Pressure Categories

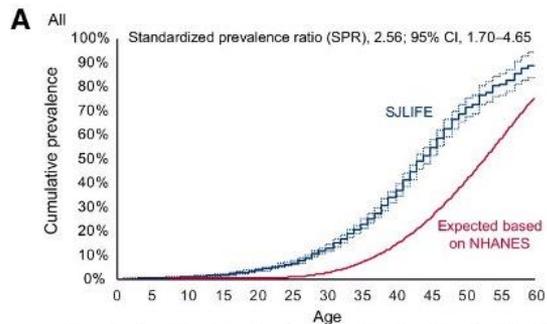


BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
<b>NORMAL</b>	<b>LESS THAN 120</b>	<b>and</b>	<b>LESS THAN 80</b>
<b>ELEVATED</b>	<b>120 – 129</b>	<b>and</b>	<b>LESS THAN 80</b>
<b>HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1</b>	<b>130 – 139</b>	<b>or</b>	<b>80 – 89</b>
<b>HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2</b>	<b>140 OR HIGHER</b>	<b>or</b>	<b>90 OR HIGHER</b>
<b>HYPERTENSIVE CRISIS (consult your doctor immediately)</b>	<b>HIGHER THAN 180</b>	<b>and/or</b>	<b>HIGHER THAN 120</b>

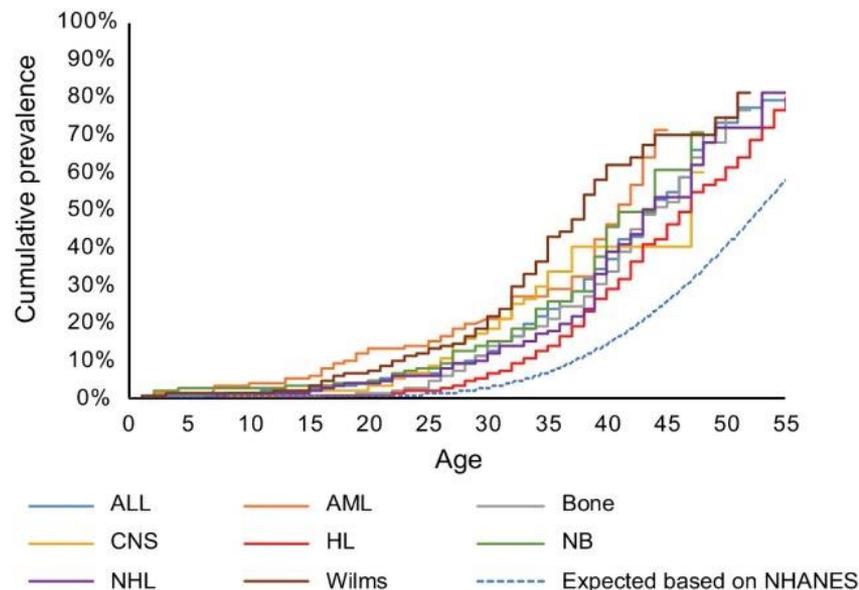
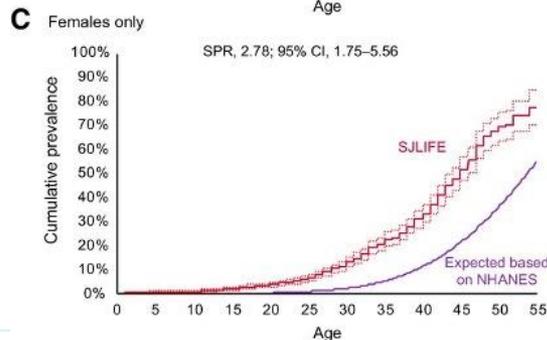
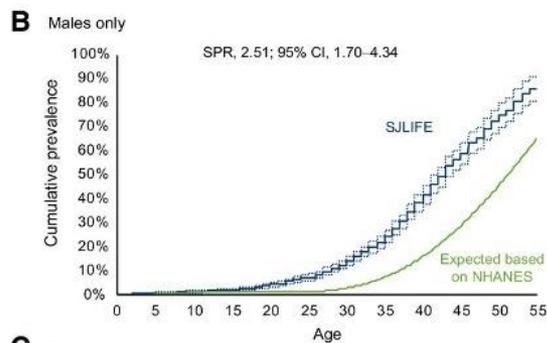


Whelton PK et al, JACC 71:e127-e248, 2018

# Blood Pressure Status in Adult Survivors of Childhood Cancer: A Report from the St. Jude Lifetime Cohort Study



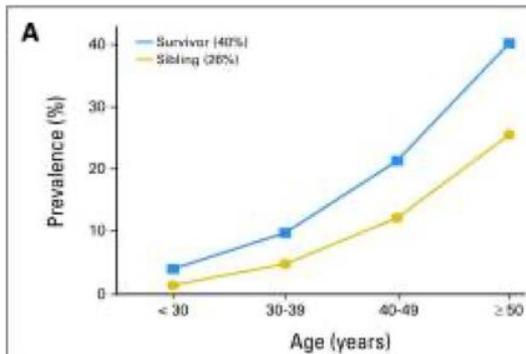
Age	5	10	15	20	25	30	35	40	45	50	55	60
N	3004	2991	2962	2839	2261	1667	1029	557	252	87	24	7



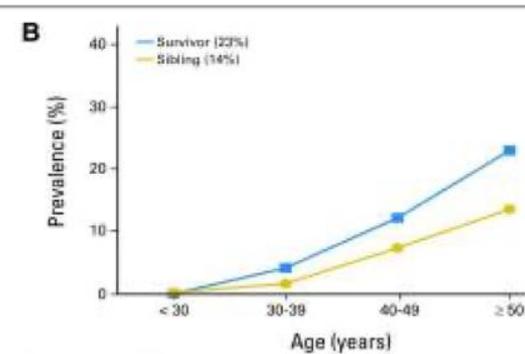
Cancer Epidemiol Biomarkers Prev. 2017;26(12):1705-1713. doi:10.1158/1055-9965.EPI-17-0510

# Prevalence of Cardiovascular Risk Factors Increase with Age

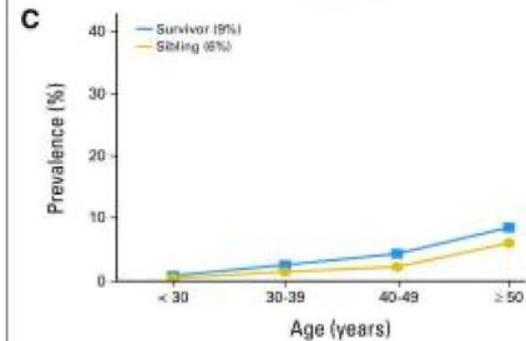
**(A) hypertension**



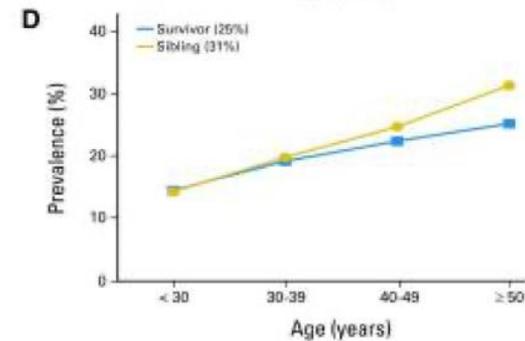
**(B) dyslipidemia**



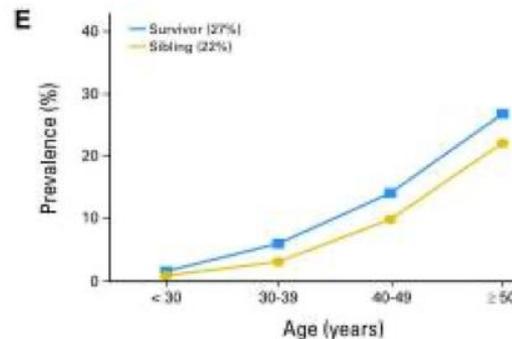
**(C) diabetes**



**(D) obesity**



**(E) Multiple cardiac risk factors**



Armstrong GT, et al. Modifiable risk factors and major cardiac events among adult survivors of childhood cancer. *J Clin Oncol.* 2013;31(29):3673-3680

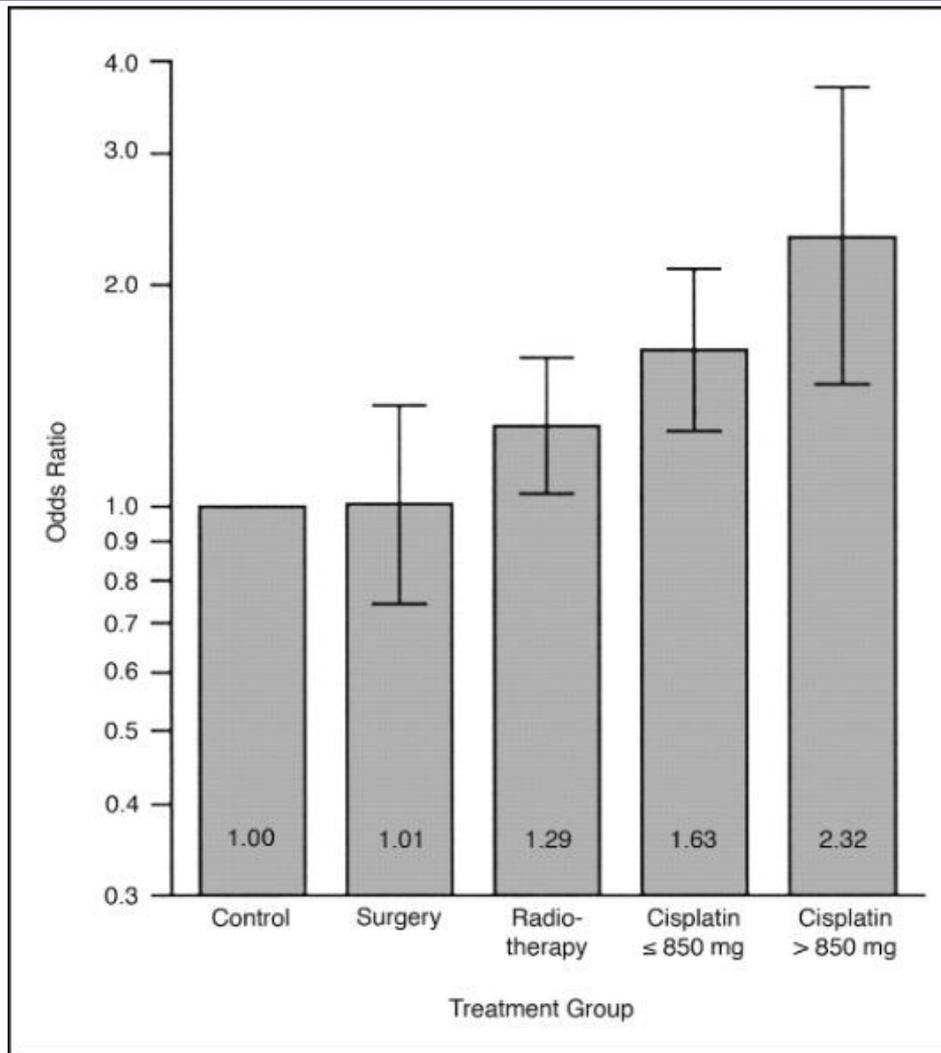
# Cancer Therapy Associated with Hypertension

- Anti-metabolites
  - Decitabine—affects DNA methylation, nucleic acid synthesis inhibitor
- Alkylating Agents
  - Cisplatin
- Monoclonal Antibodies
  - Rituximab—anti-CD 20
- Tyrosine Kinase Inhibitors
  - Monoclonal antibodies vs small molecules
- mTOR Inhibitors
  - Everolimus
- Proteasome Inhibitors
  - Bortezomib

# Cancer Therapy Associated with Hypertension

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  - Bortezomib

# Age Adjusted Odds Ratio (OR) of having Hypertension in Long Term Survivors of Testicular Cancer compared with healthy individuals.



H. Sagstuen; et al; *Journal of Clinical Oncology* 2005 234980-4990. DOI: 10.1200/JCO.2005.06.882

# Cancer Therapy Associated with Hypertension

- Anti-metabolites
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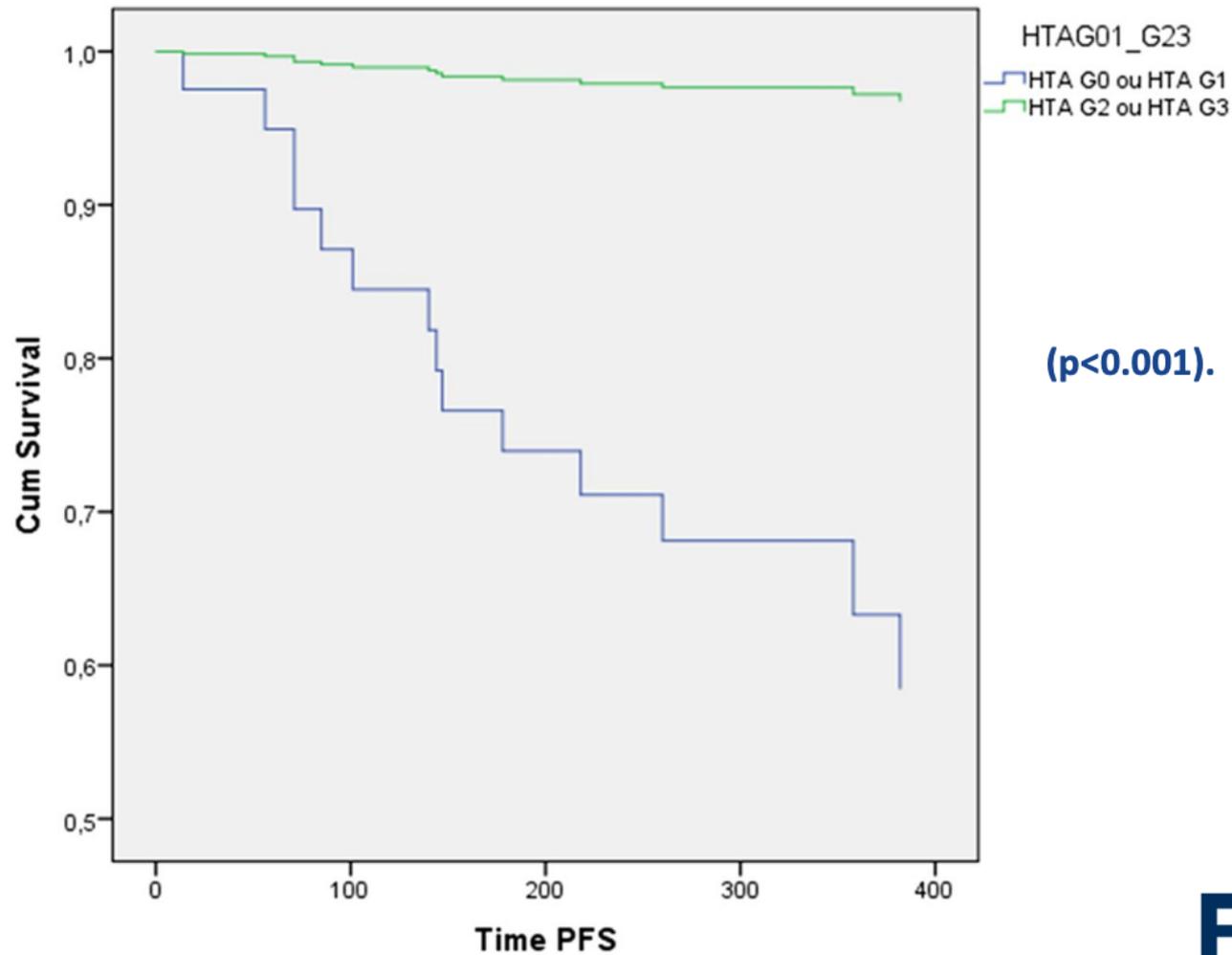
# Tyrosine Kinase Inhibitors Associated with Hypertension

- Monoclonal Antibody-based Tyrosine Kinase Inhibitors
- Small molecule tyrosine kinase inhibitors

# Tyrosine Kinase Inhibitors Associated with Hypertension

- **Monoclonal Antibody-based Tyrosine Kinase Inhibitors**
  - **Bevacizumab (Avastin)**
- HF 1-3%
- Ischemia (ATE) - 0.6- 1.5%
  - Risk factors age>65 and previous history
- HTN 4-35%

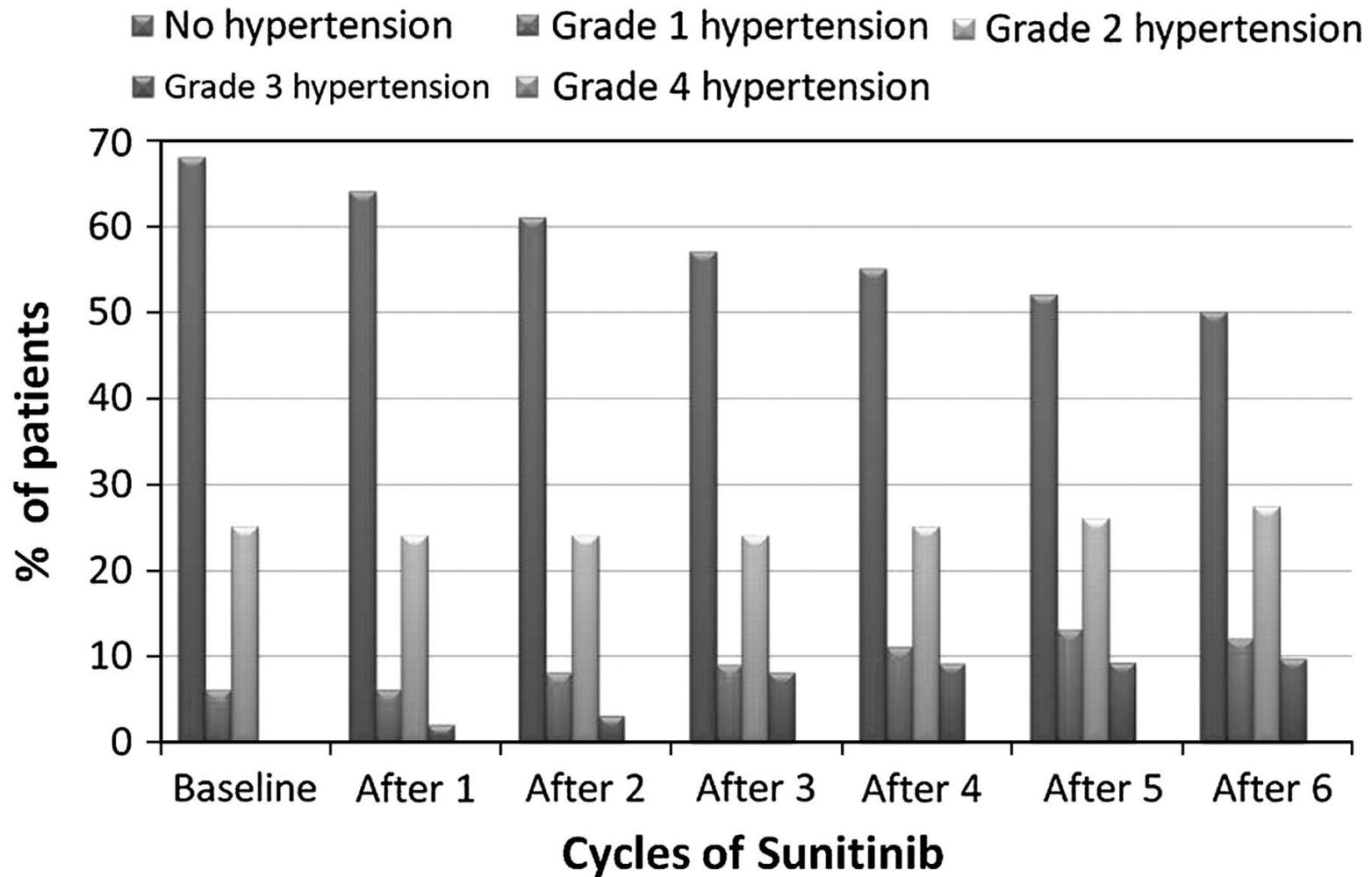
# Progression Free Survival of Patients with Colorectal Cancer with and without Grade 2-3 bevacizumab-induced HTN



Isabel José Dionísio de Sousa et al. ESMO Open  
2016;1:e000045

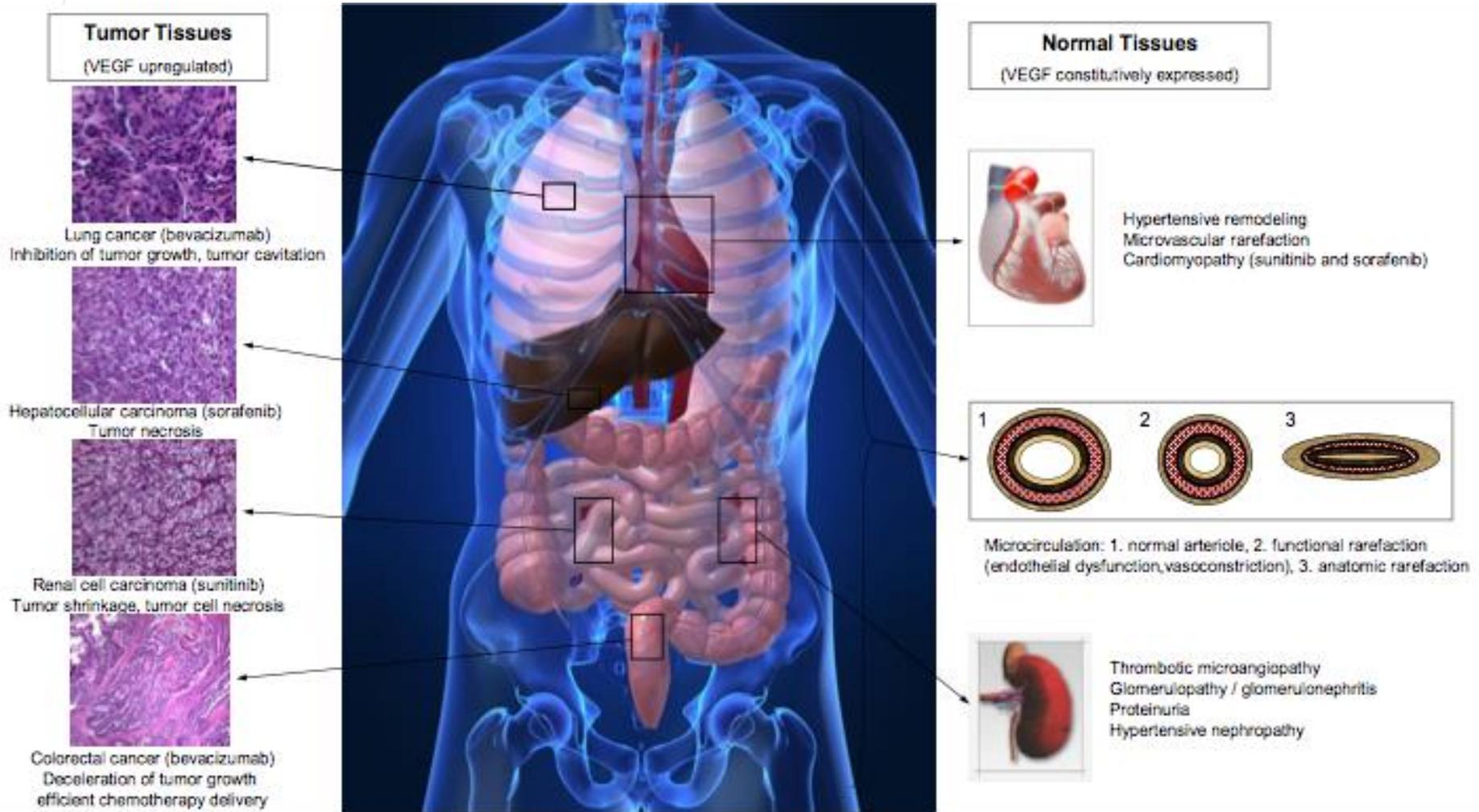
**ESMO** Open  
Cancer Horizons

# Cardiovascular Toxicity Following Sunitinib Therapy in Metastatic Renal Carcinoma: A Multicenter Analysis



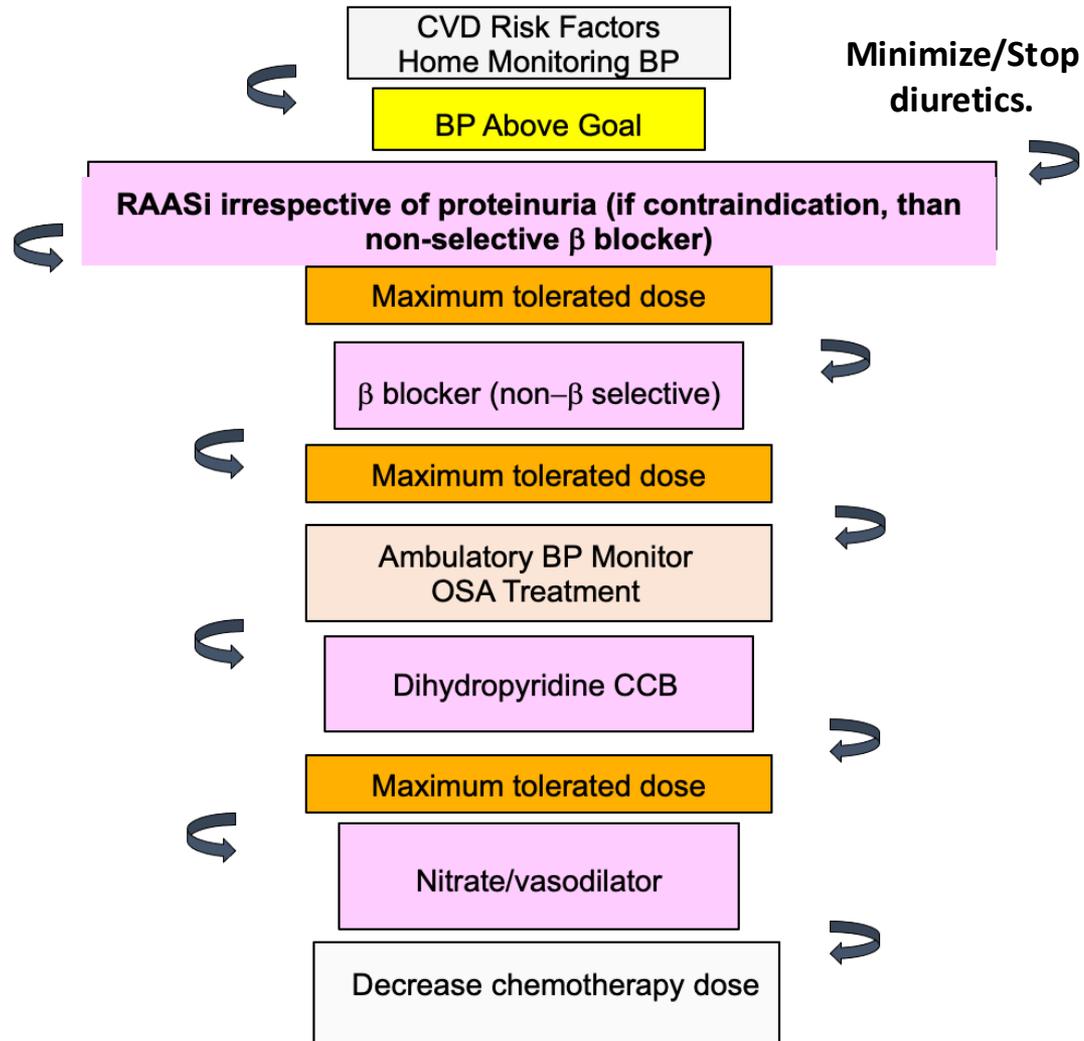
G. Di Lorenzo et al. Ann Oncol 2009;20:1535-1542

# Systemic Effects of Anti-VEGF Therapy



Vaklavos et al, Oncologist 2010, p130.

# Proposed Approach to Hypertension Management During and Post Cancer Treatment

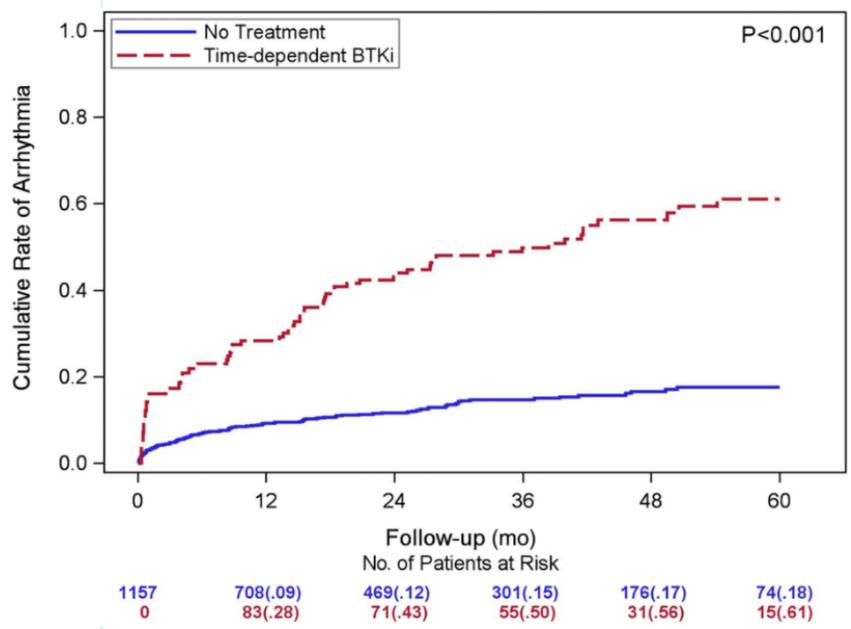


Adapted from Jordana B. Cohen et al. J Am Coll Cardiol CardioOnc 2019;1:238-251

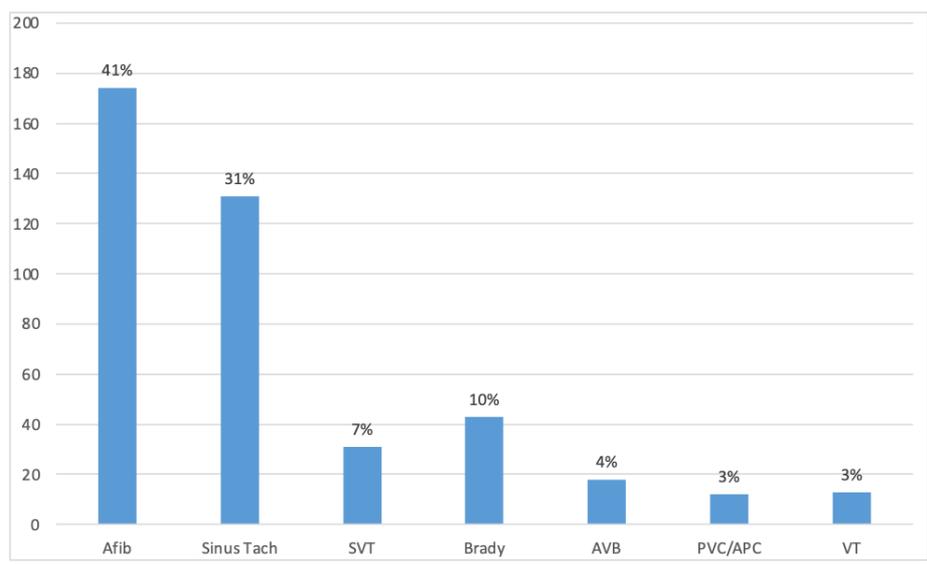
# Chemotherapy and risk of arrhythmias

# Arrhythmogenic Cardiotoxicity Associated with Contemporary Treatments of Lymphoproliferative Disorders.

Cumulative Rate of any arrhythmic event following initiation of lymphoma treatment

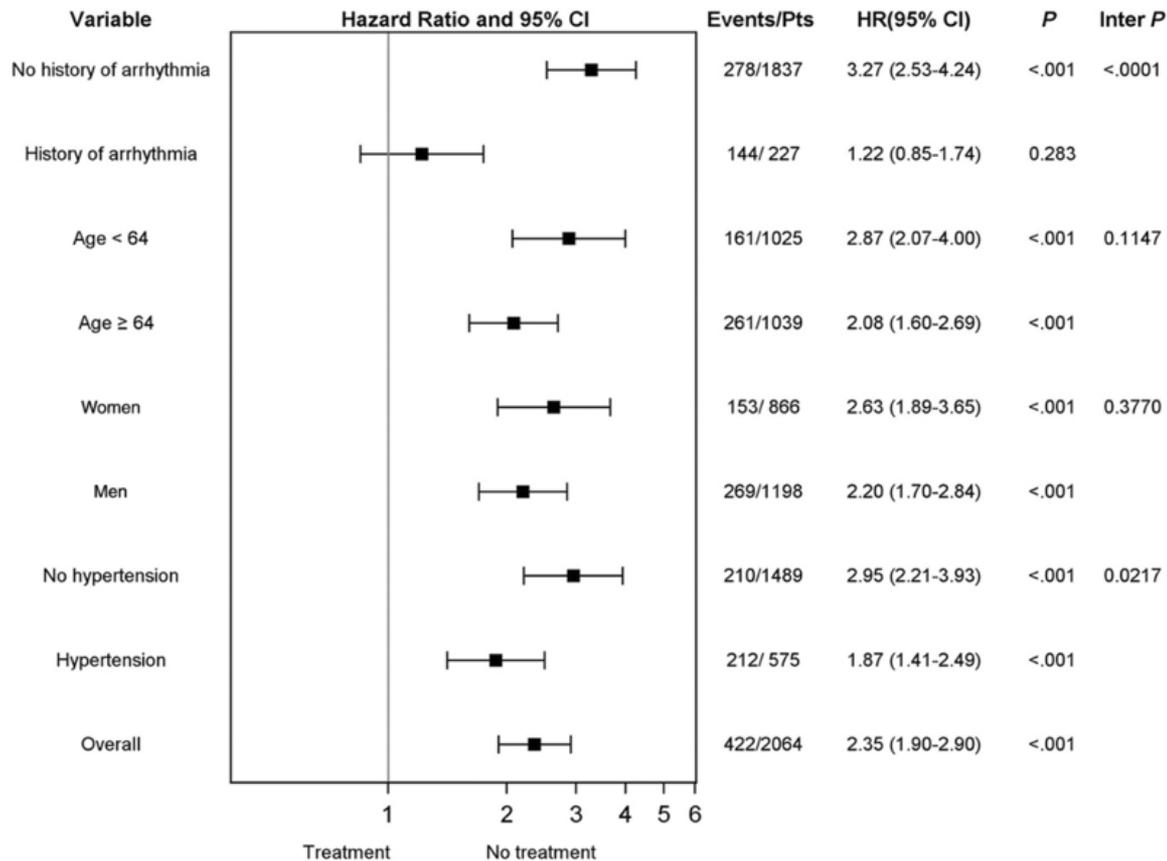


Distribution of Arrhythmia Types



Sherazi, et al. Journal of the American Heart Association. Arrhythmogenic Cardiotoxicity Associated With Contemporary Treatments of Lymphoproliferative Disorders

# Arrhythmogenic Cardiotoxicity Associated with Contemporary Treatment of Lymphoproliferative Disorders



The risk of arrhythmia during lymphoma treatment was significantly higher among patients who did not have prior history of arrhythmia.

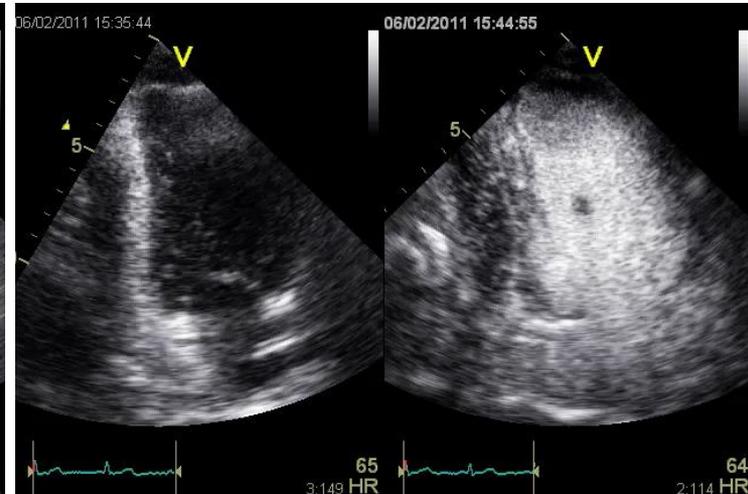
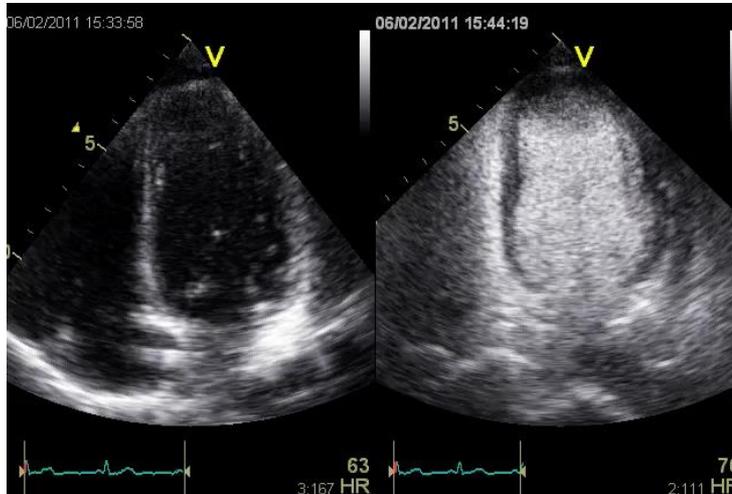
Sherazi, S., et al. Journal of the American Heart Association. Arrhythmogenic Cardiotoxicity Associated With Contemporary Treatments of Lymphoproliferative Disorders

Echocardiography

Nuclear

MRI

# Contrast Echo Imaging

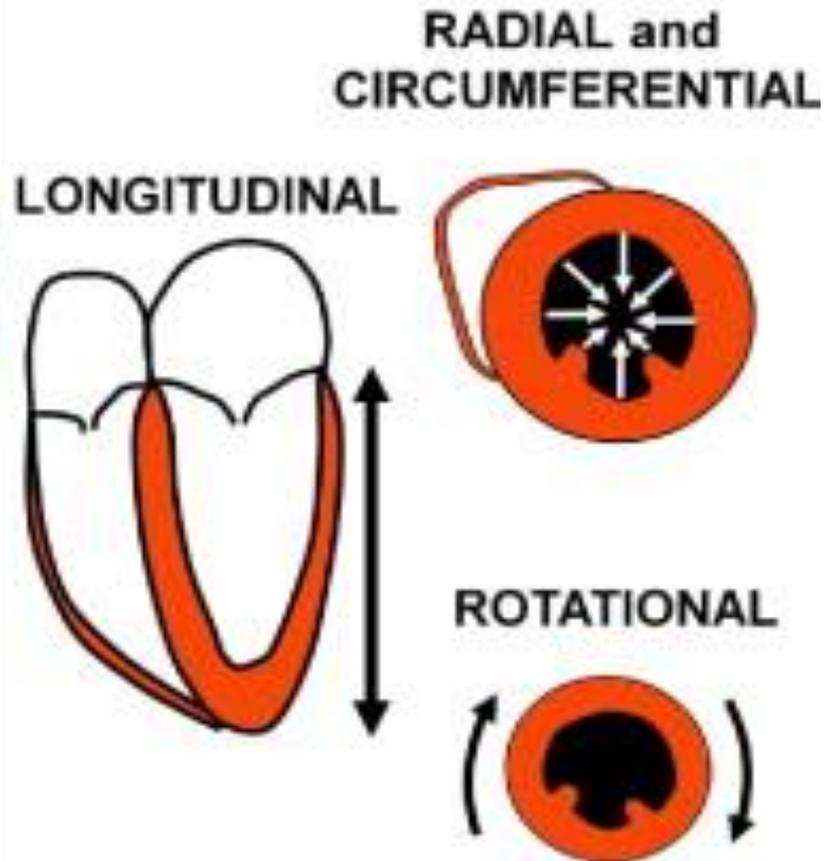


## Echo contrast indications

- Incomplete endocardial visualization
- Inadequate Doppler signal quality
- Dimension/volume quantification
- High pretest probability stress echo
- Resting WMA stress echo
- Extreme sensitivity wall motion assessment

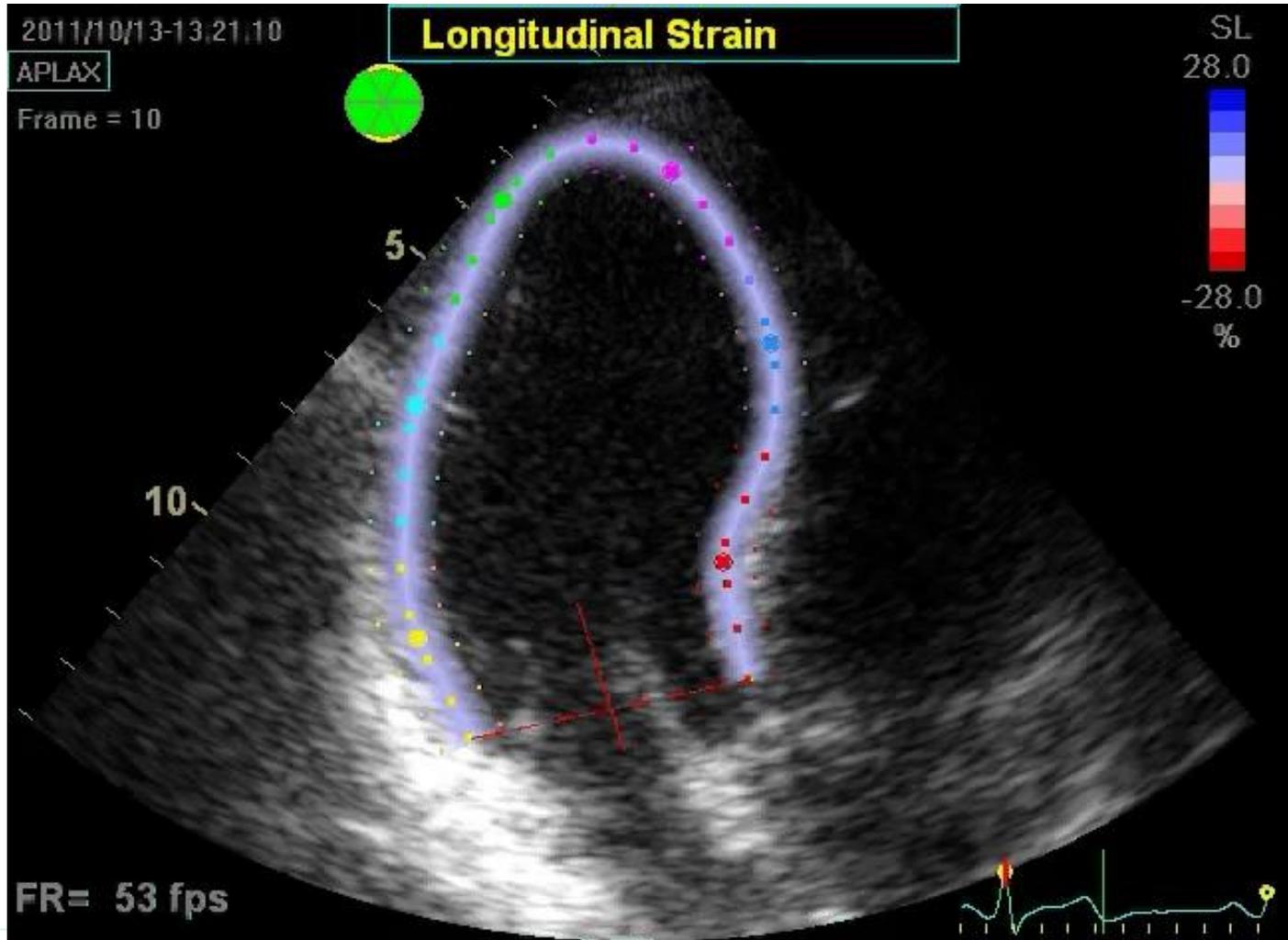


# Echocardiographic Strain Imaging

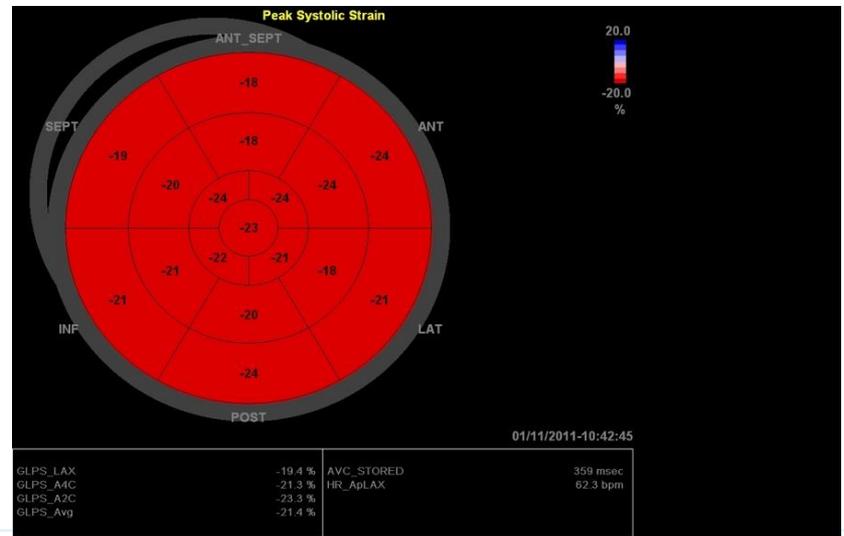
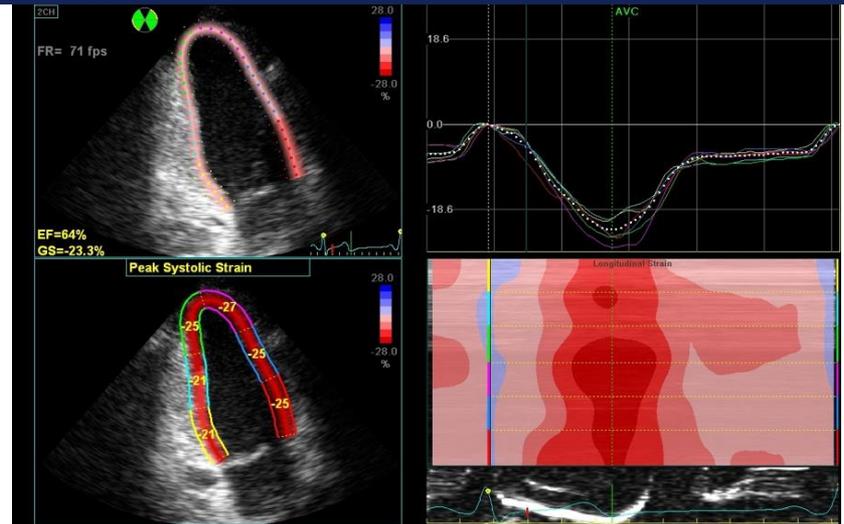


Gorcsan and Tanaka JACC (2011) 58(14): 1401-1413

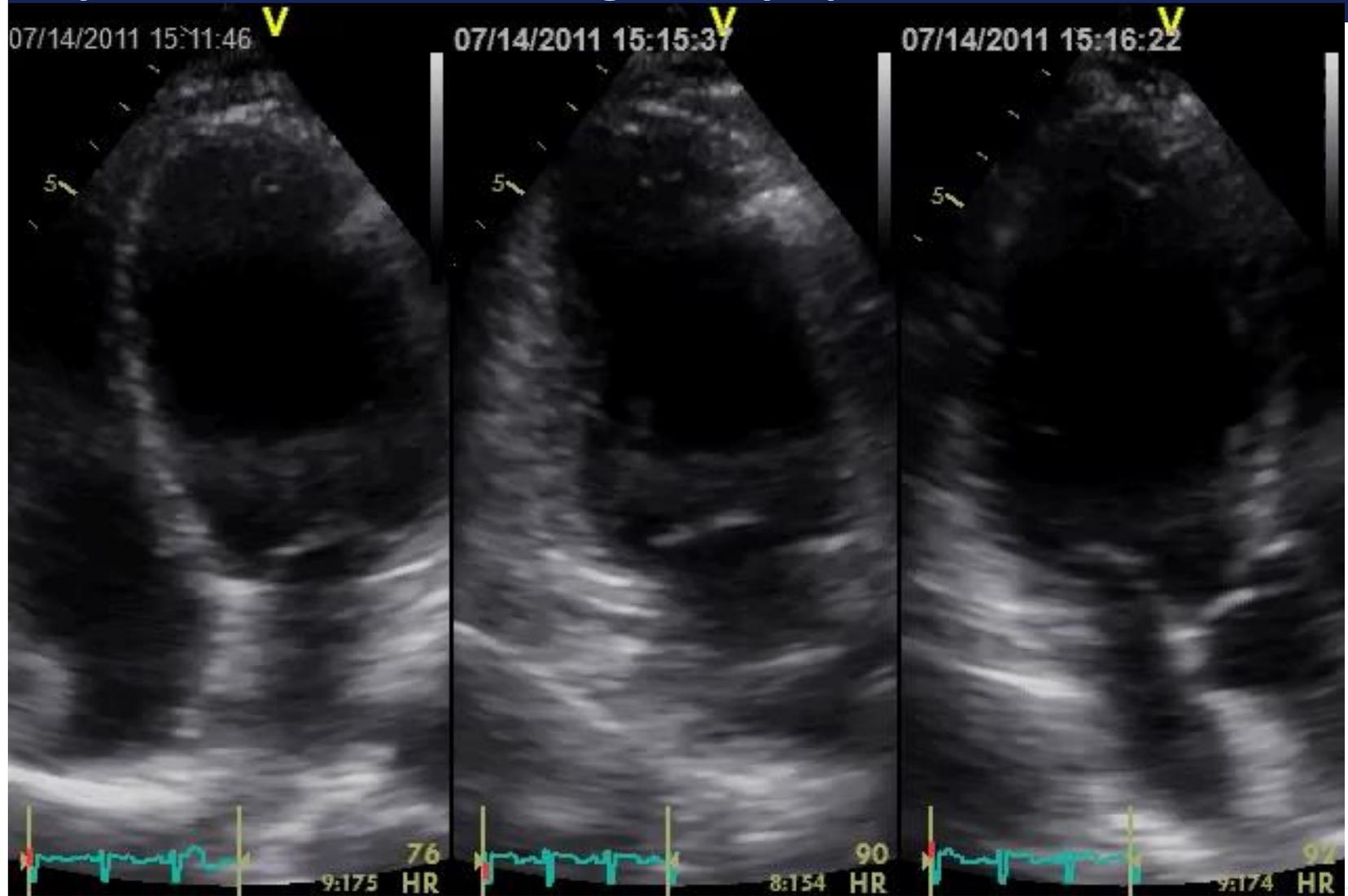
# Longitudinal Strain in Motion



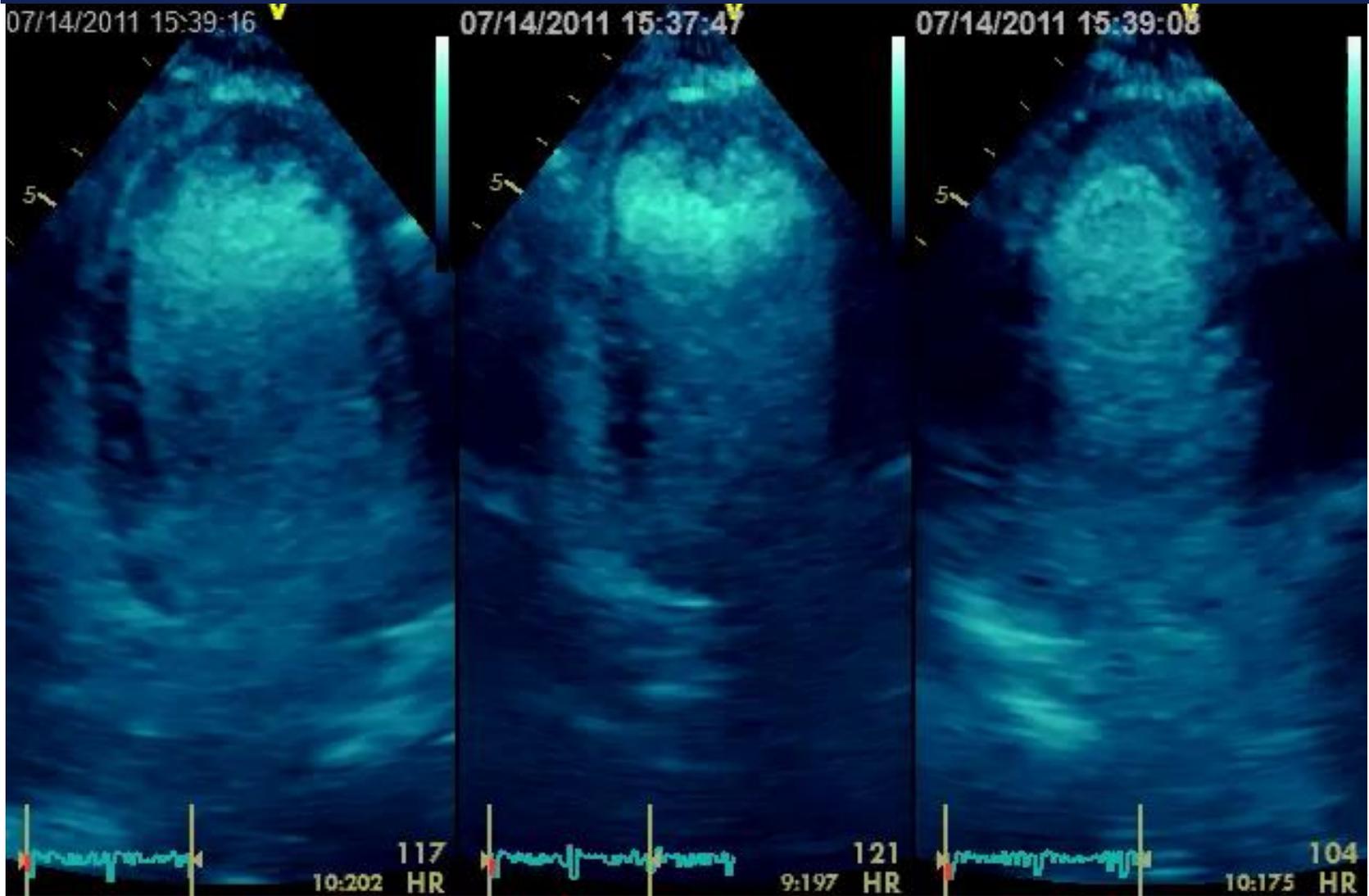
# Longitudinal Strain--Composite



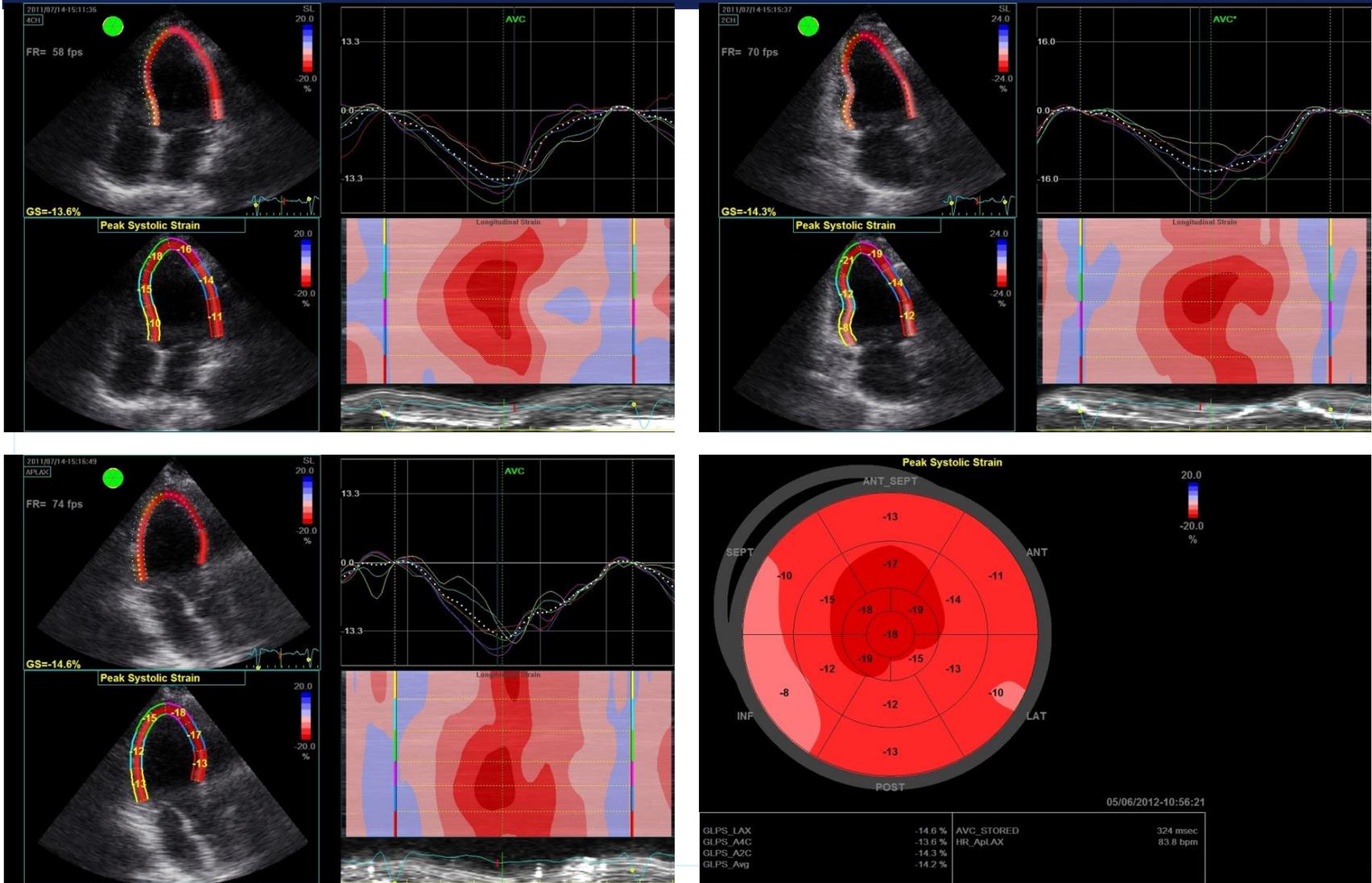
# 24 yo Female with h/o Hodgkin's Lymphoma



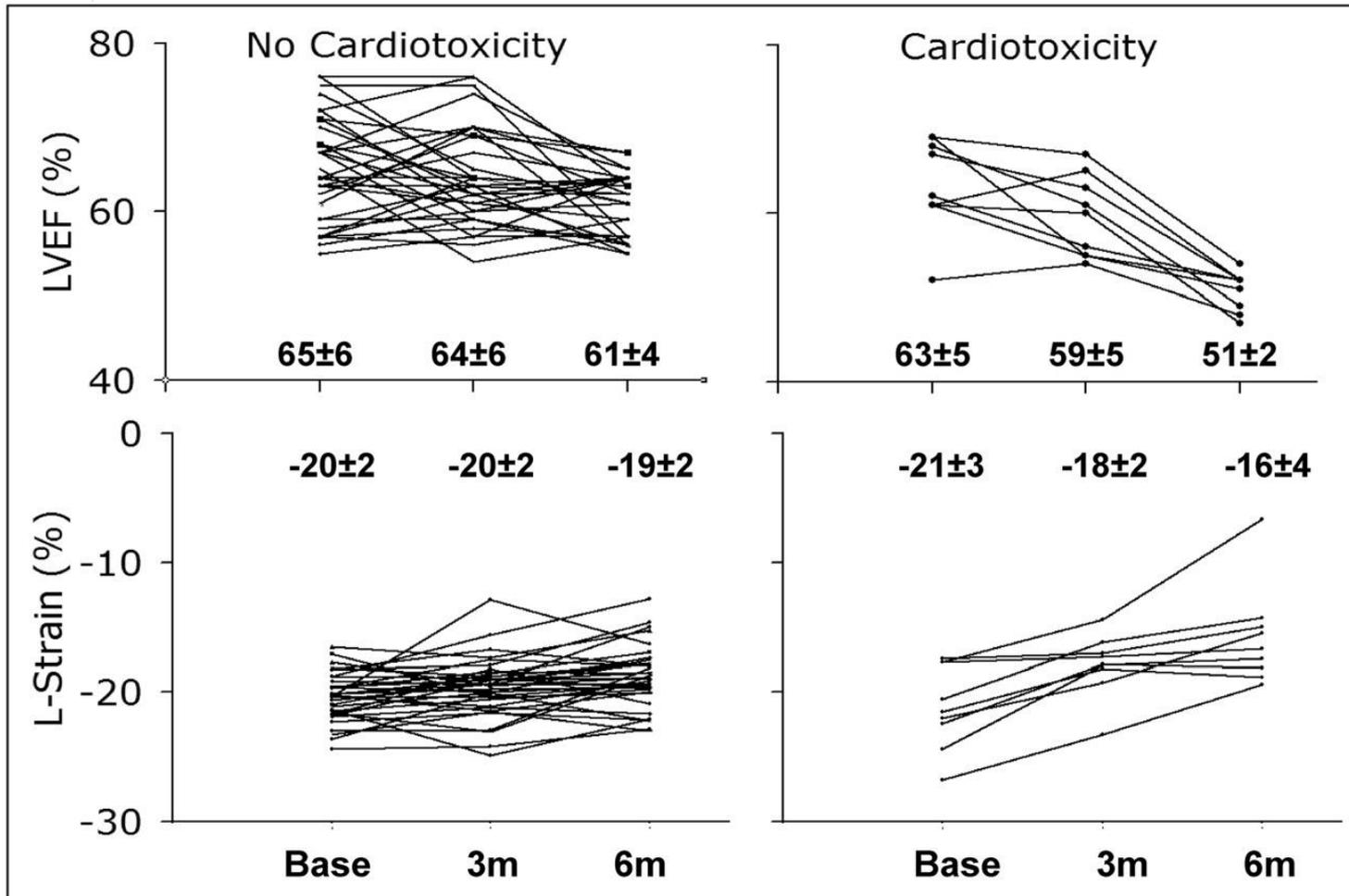
# 24 year old with h/o Hodgkin's Lymphoma



# Normal LVEF but abnormal strain



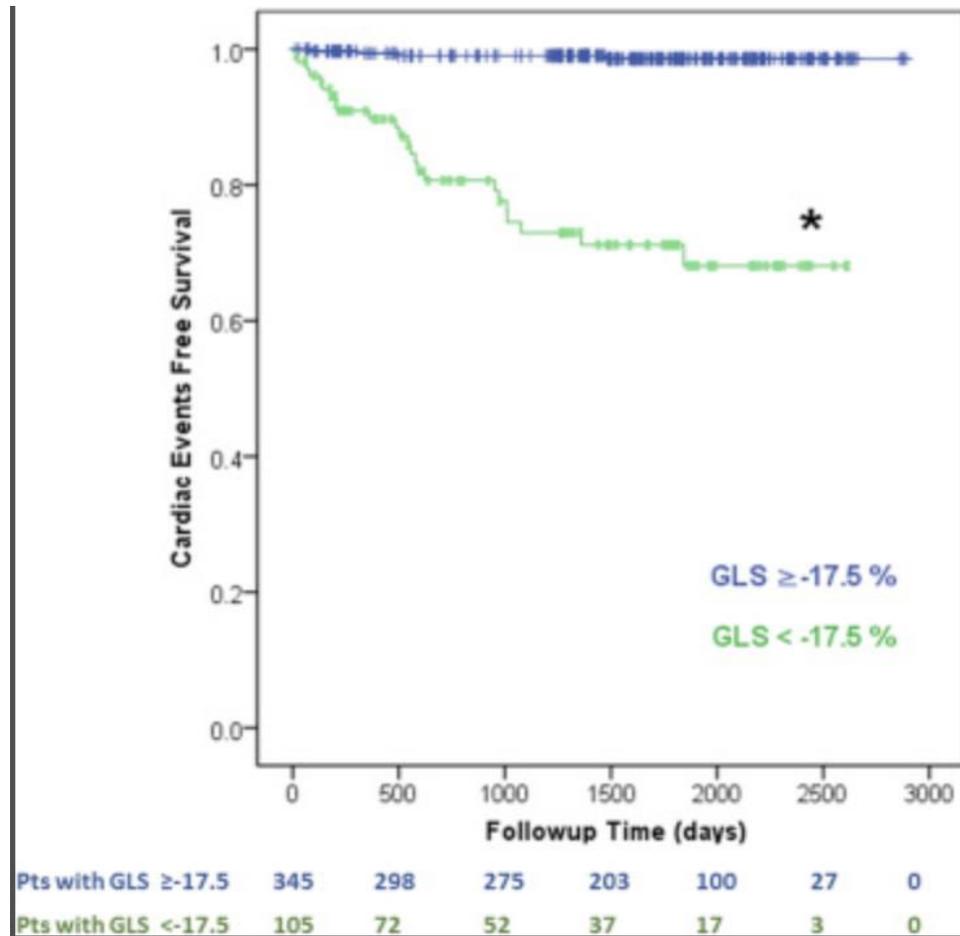
# Early Detection and Prediction of Cardiotoxicity in Chemotherapy Treated Patients



- 43 patients with breast cancer
- Treated with anthracycline and trastuzumab
- Drop in Global Longitudinal Strain at 3 months, appears to have predicted toxicity at 6 months.

Sawaya H et al, Am J Cardiol 2011, Volume 107 (9): 1375-1380

# Myocardial Strain is Associated with Adverse Clinical Cardiac Events in Patients Treated with Anthracyclines

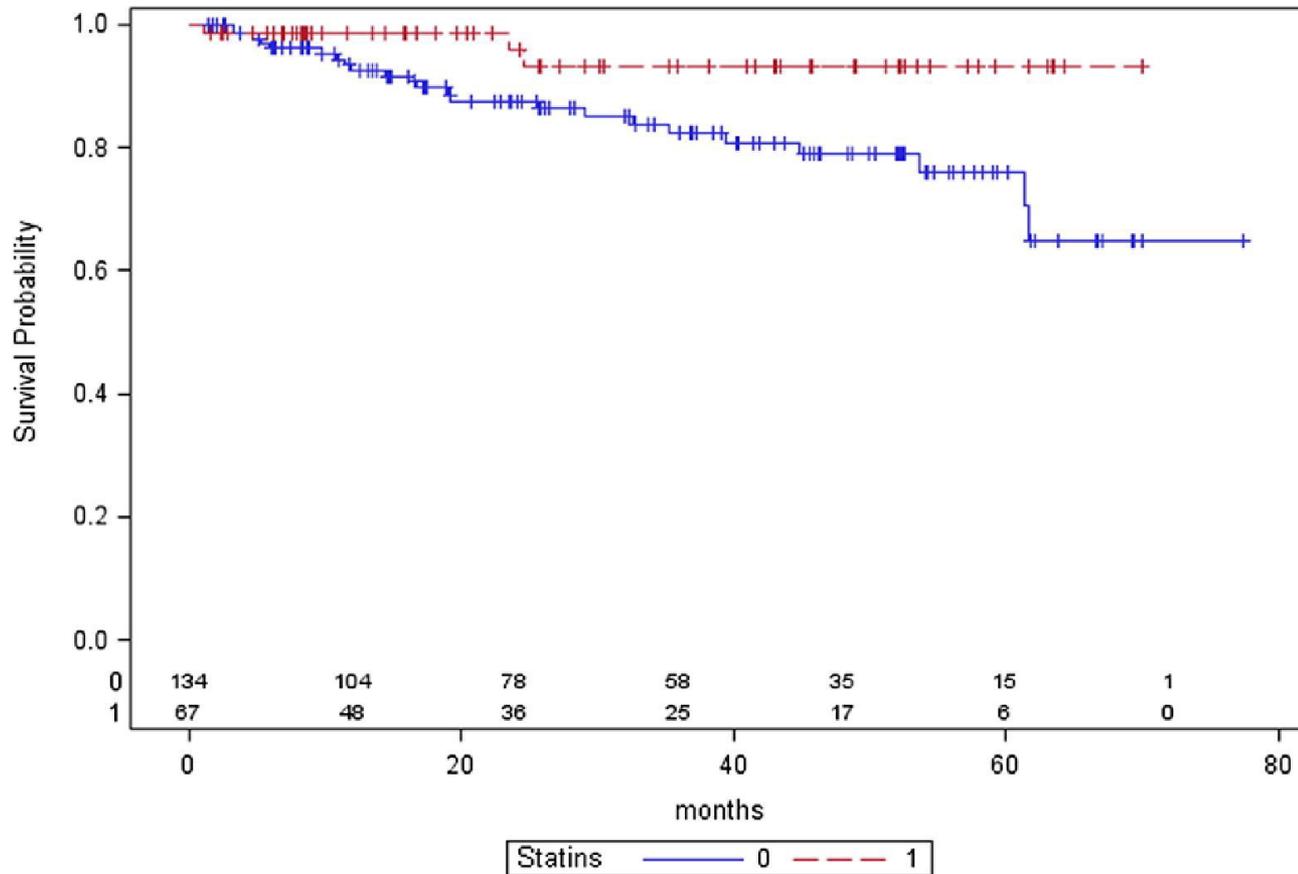


Ali MT, et al, JASE 2016(29) 522-527

# Possible Medication Interventions to Prevent Cardiovascular Complications

# Effect of Statin Therapy on the Risk for Incident Heart Failure in Patients with Breast Cancer Receiving Anthracycline Chemotherapy

## An Observational Clinical Cohort Study



Seicean et al. J Am Coll Cardiol. 2012;60(23):2384-2390.

# STOP-CA—Atorvastatin for Anthracycline Associated Cardiac Dysfunction

## JAMA

**QUESTION** Does 1 year of treatment with atorvastatin, 40 mg/d, started prior to anthracycline-based chemotherapy among patients with lymphoma, reduce the chance of a significant decrease in left ventricular ejection fraction (LVEF) compared with placebo?

**CONCLUSION** Among patients with lymphoma treated with anthracycline-based chemotherapy, atorvastatin reduced the incidence of cardiac dysfunction.

© JAMA

### POPULATION

158 Men  
142 Women



Patients with lymphoma scheduled to receive anthracycline-based chemotherapy

Mean age: 50 years

### LOCATION

9 Academic medical centers in the US and Canada



### INTERVENTION



300 Patients randomized

150

**Atorvastatin**  
Oral atorvastatin, 40 mg/d, for 12 mo starting prior to first scheduled anthracycline infusion



150

**Placebo**  
Oral placebo for 12 mo starting prior to first scheduled anthracycline infusion

### FINDINGS

Incidence of primary outcome

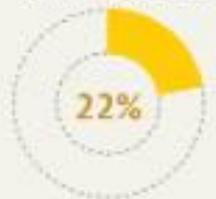
**Atorvastatin**

13 of 150 patients



**Placebo**

33 of 150 patients



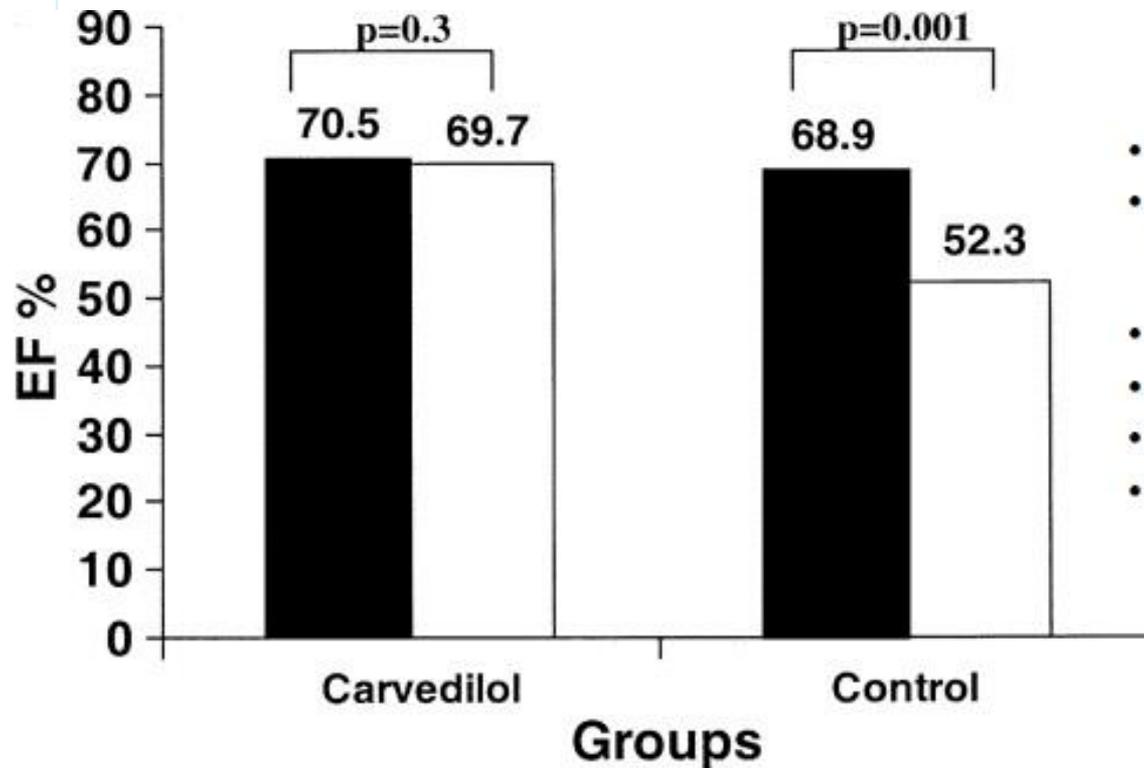
Atorvastatin significantly reduced the risk of the primary outcome:

Odds ratio of outcome with placebo vs atorvastatin, **2.9** (95% CI, 1.4 to 6.4)

Neilan TG, Quinaglia T, Onoue T, et al. Atorvastatin for anthracycline-associated cardiac dysfunction: the STOP-CA randomized clinical trial. *JAMA*. Published August 8, 2023. doi:10.1001/jama.2023.11887

Neilan, T.G., *JAMA*. 2023;330(6):528-536. doi:10.1001/jama.2023.11887

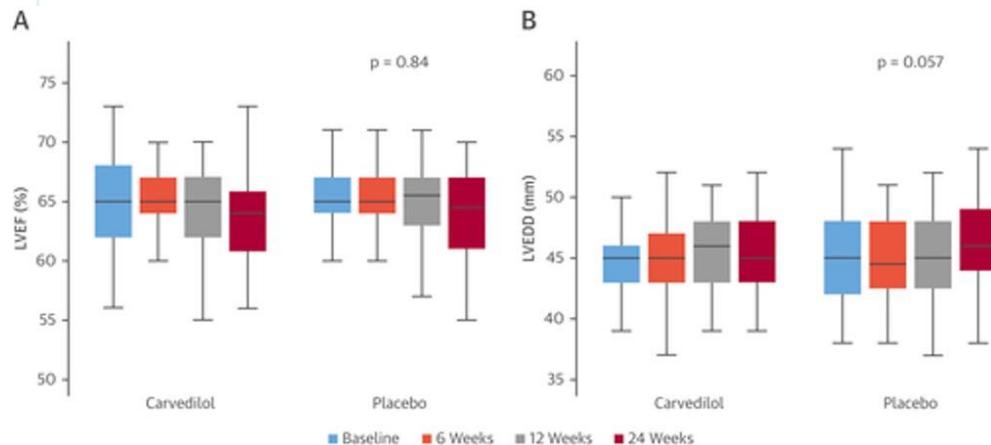
# Protective Effects of Carvedilol Against Anthracycline Induced Cardiotoxicity



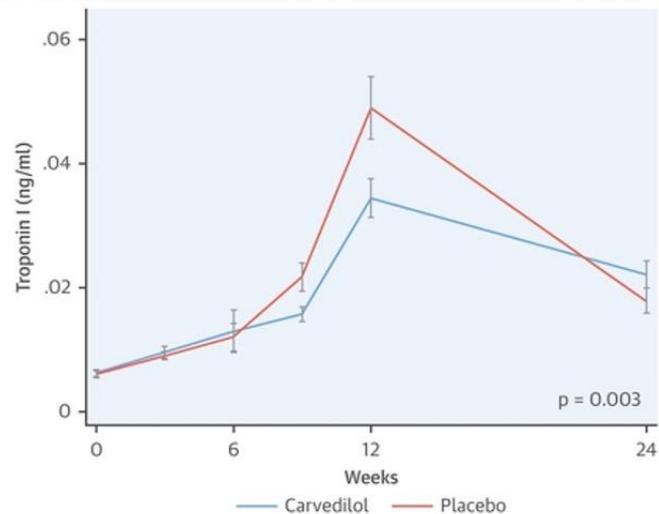
- 50 patients (breast, lymphoma, other)
- Single blind, control trial in which 25 patients were blindly assigned to 12.5 mg daily carvedilol or placebo
- Total adriamycin dose was ~ 530mg/m<sup>2</sup>
- Total epirubicin was ~790mg/m<sup>2</sup>
- Both groups had a total of 6 cycles of CHOP.
- F/u was 6 months after randomization.

Kalay et al. J.A.C.C. (2006) 48; 11: 2258-2262

# CECCY Trial: Carvedilol for Prevention of Chemotherapy-Related Cardiotoxicity



**CENTRAL ILLUSTRATION: Sequential Levels of Troponin I During Chemotherapy Treatment**



Avila, M.S. et al. J Am Coll Cardiol. 2018;71(20):2281-90.

Total Adriamycin dose 240 mg/m<sup>2</sup>

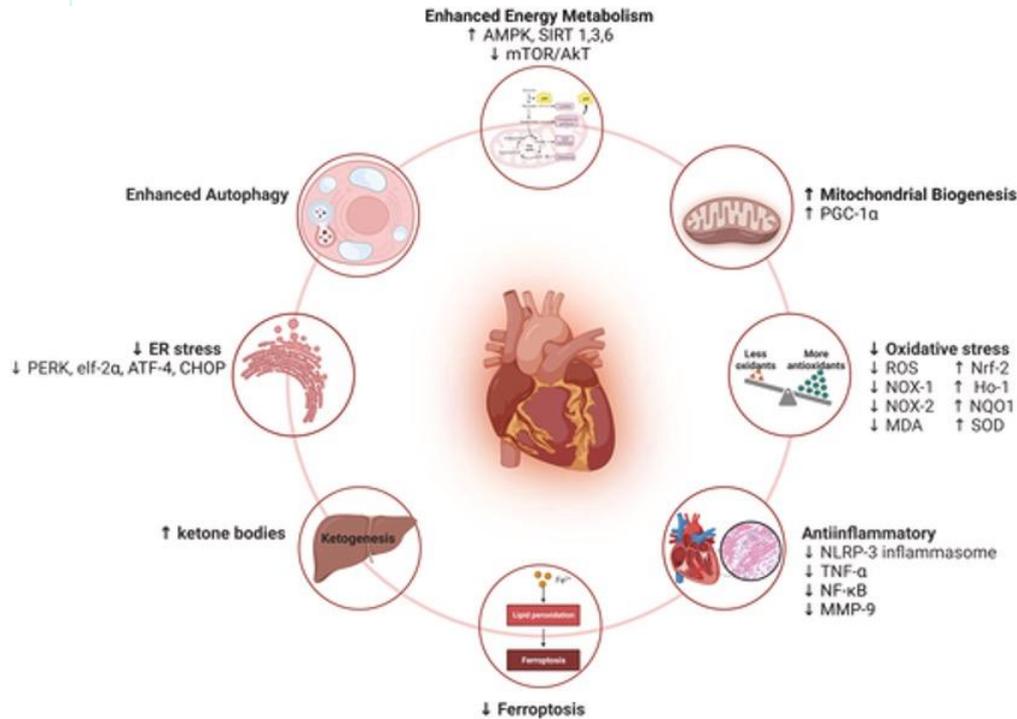
Primary endpoint: LVEF < 10% decrease at 6 months

Secondary endpoint: Effects of carvedilol on troponin I, B-type natriuretic peptide, and diastolic dysfunction.

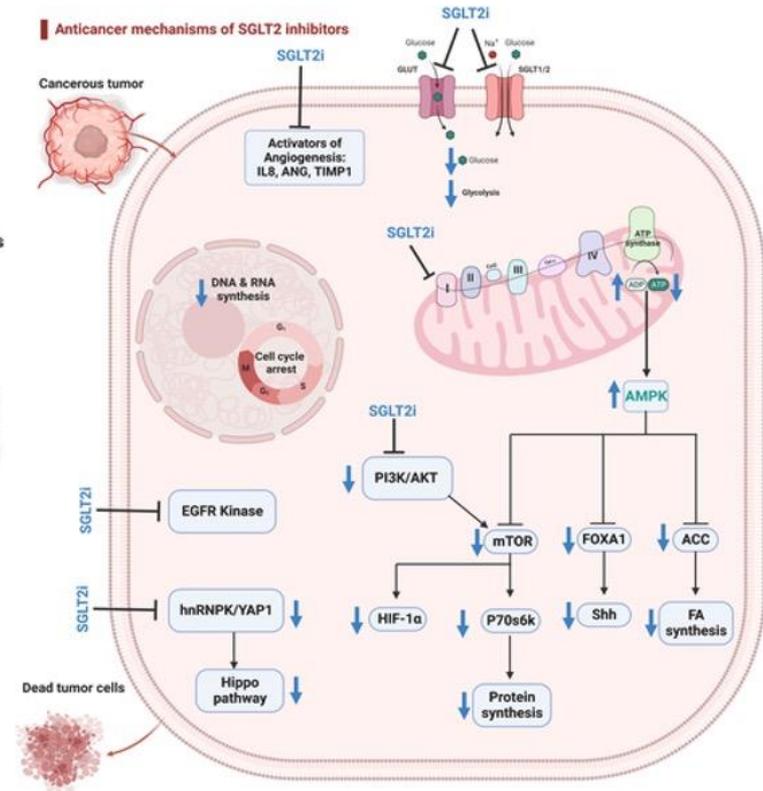
Primary endpoint occurred in 14 patients (14.5%) in the carvedilol group and 13 patients (13.5%) in the placebo group ( $p = 1.0$ ).  
 Secondary Endpoint: No differences in changes of LVEF or B-type natriuretic peptide were noted between groups.  
 A significant difference existed between groups in troponin I levels over time, with lower levels in the carvedilol group ( $p = 0.003$ ).  
 Additionally, a lower incidence of diastolic dysfunction was noted in the carvedilol group ( $p = 0.039$ )

# SGLT2 inhibitors

## Cardio-protective



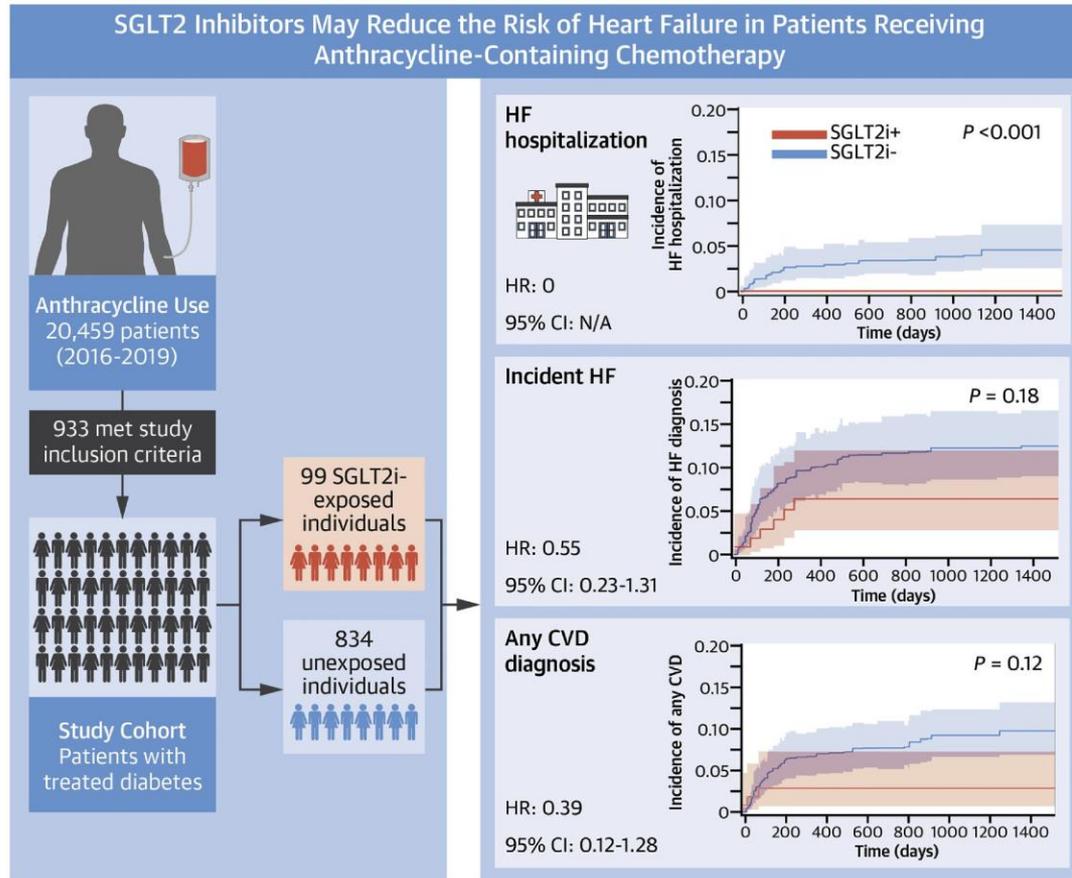
## Tumor-Destroying



Mohamed S. Dabour et al. *J Am Coll Cardiol CardioOnc* 2024; 6:159-182

# Do SGLT2-I reduce Anthracycline Cardiotoxicity?

## CENTRAL ILLUSTRATION: The Association Between Sodium-Glucose Cotransporter 2 Inhibitors and Anthracycline Cardiotoxicity



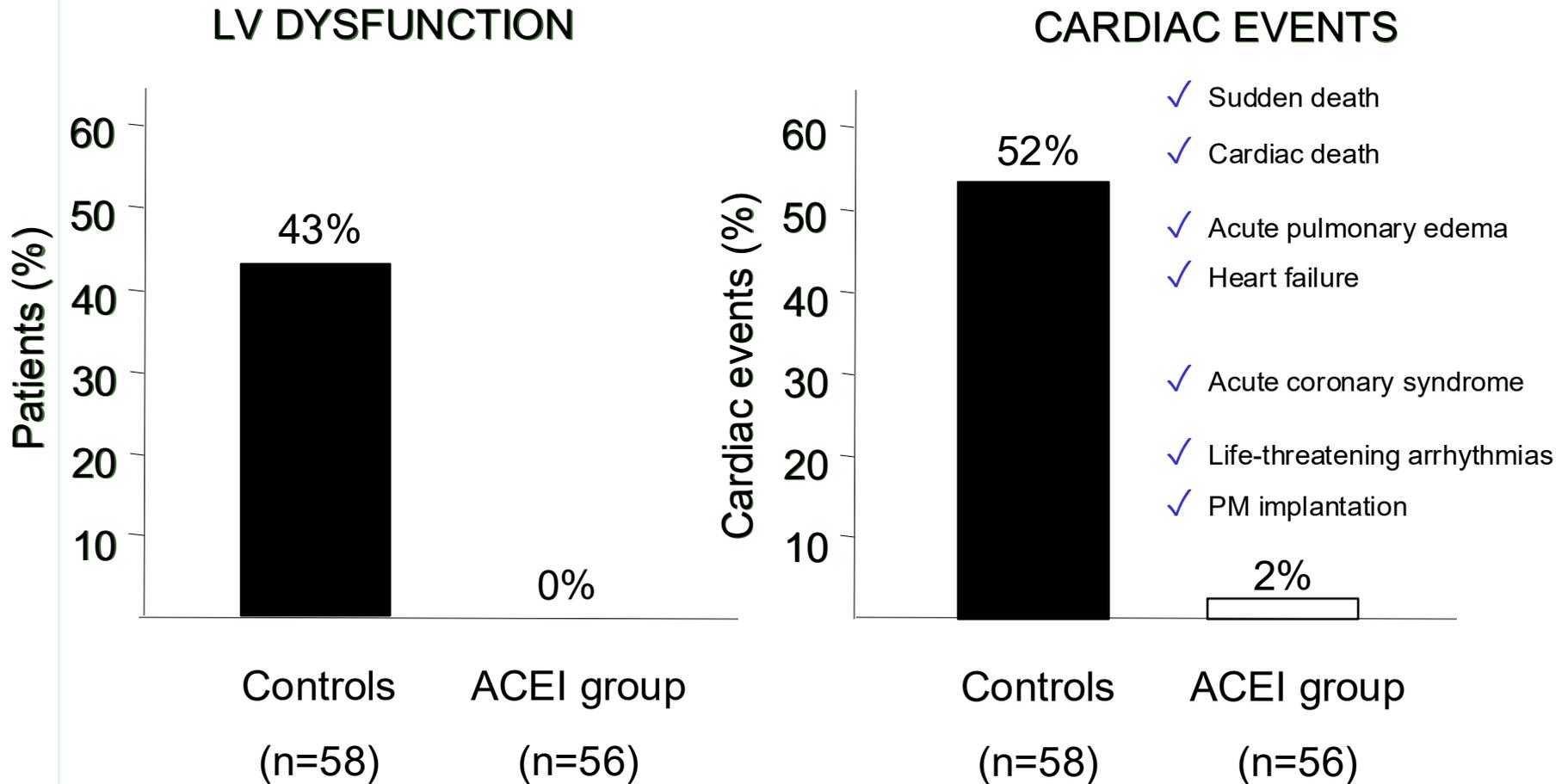
Abdel-Qadir H, et al. J Am Coll Cardiol CardioOnc. 2023;5(3):318-328.

# Management Chemotherapy Induced Cardiovascular Toxicity

# Enalapril prevents cardiac dysfunction and cardiac events in TNI+ patients

403 patients with HD Chemo

114 with TNI +



Cardinale et al. Circulation 2006

# Effects of Sacubitril/Valsartan on Prevention of Cardiotoxicity in High Risk Patients Undergoing Anthracycline Chemotherapy: The SARAH Trial



## PRIMARY ENDPOINT

SARAH Trial met the Primary Endpoint

Primary Endpoint	ARNi (n=56)	Placebo (n=56)	OR (95% CI)	P value
GLS decrease >15%, n (%)	4 (7.1%)	14 (25%)	0.23 (0.07 to 0.75)	0.015

Relative Risk Reduction = 77%

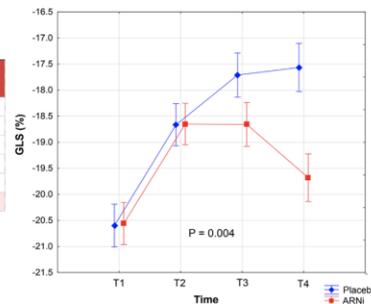
NNT = 5.59

The differences between groups occurred independently of risk factors such as: mean indexed cumulative dose of ANT, HER2 positivity, presence of hypertension and age

## SECONDARY ENDPOINT

GLS variation after 24 Weeks

Secondary Endpoints	ARNi (n=56)	Placebo (n=56)	P value
GLS (%)			
End of treatment	-19.5 ± 3.1	-17.6 ± 3.6	0.004
Absolute change	-0.5 (-12.7 to 10.3)	1.5 (-12.2 to 12.7)	<0.001
Percentual change	Improvement 2.5 %	Decline 7.6 %	<0.001

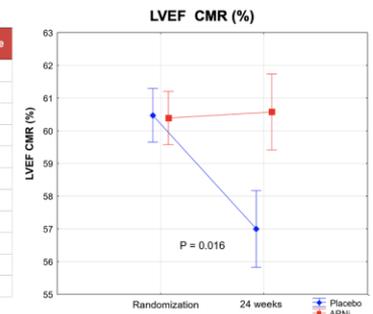


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## SECONDARY ENDPOINTS

Echo and CMR parameters after 24 Weeks

Secondary Endpoints	ARNi (n=56)	Placebo (n=56)	P value
LVEF decrease >10% with final value <53%			
• ECHO, n (%)	4 (7.1%)	4 (7.1%)	1
• CMR, n (%)	2 (3.7%)	6 (11.3%)	0.161
LVEF			
• ECHO (%)	64 (42 to 79)	62 (28.5 to 72)	0.052
• CMR (%)	61 (27 to 73)	58 (23 to 70)	0.027
LVEDV (ECHO) (mL)	83.1 (42 to 160)	92.4 (47.4 to 182)	0.026
LVESV (CMR) (mL)	43 (19 to 166)	48 (24 to 190)	0.036



Other secondary endpoints, such as variations in Echo or CMR parameters, were similar between groups.

# Interventional Cancer Trials in Progress

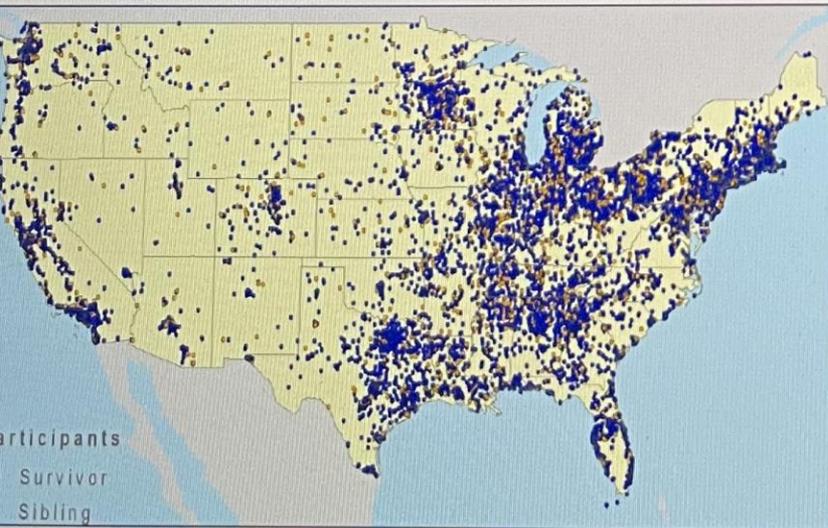
Intervention (study name, estimated study completion)	Study population	Estimated enrollment	Trastuzumab patients included?	Endpoints	Follow-up (months)
Bisoprolol/Ramipril (SAFE Trial, 2023)	Breast cancer	480	Yes	Primary: Change in LVEF Secondary: Not reported	24
Carvedilol (TACTIC Trial, 2024)	Breast cancer	450	Yes	Primary: Rate of asymptomatic and symptomatic cardiac dysfunction, rate of reversible cardiac function decline Secondary: Change in LVEF, genetic variation and risk of cardiotoxicity and response to therapy	24
Lisinopril (PLAID Trial, 2020)	Any cancer type	200	N/A	Primary: Change in GLS/GLS rate Secondary: LVD with HF symptoms	12
Sacubitril/valsartan (PRADA II Trial, 2022)	Breast cancer	300	Yes	Primary: Change in LVEF Secondary: Change in GLS and LVESV	18
Ivabradine (N/A, 2020)	Any cancer type	128	N/A	Primary: Change in GLS Secondary: Incidence of myocardial injury, incidence of LVD, incidence of symptomatic HF	6
Ivabradine (IPAC Trial, 2021)	Any cancer type	160	N/A	Primary: Reduction in GLS Secondary: Composite of mortality and major cardiac outcomes (AMI, HF, IST, arrhythmia), incidence of myocardial injury, incidence of LVD	12
Atorvastatin (SPARE-HF Trial, 2022)	Breast cancer, aggressive lymphoma, leukemia or sarcoma	112	N/A	Primary: Change in LVEF Secondary: Change in LVEDV and LVESV	4
Atorvastatin (STOP-CA Trial, 2022)	Non-Hodgkin's lymphoma	300	N/A	Primary: Change in LVEF Secondary: Incidence of new onset HF	24
Atorvastatin (PREVENT Trial, 2020)	Breast cancer	279	N/A	Primary: Change in LVEF Secondary: Cognitive function, self-reported quality of life	24

Vedeer, JA, et al. *Pharmacotherapy*, (2021) 41 (12) 1066-180

# Cardiovascular Risk Prediction Calculator

## CCSS

Childhood Cancer Survivor Study Cohort  
U24 CA55727 (PI: Armstrong)  
38,036 Survivors (25,665 participants)



## SJLIFE

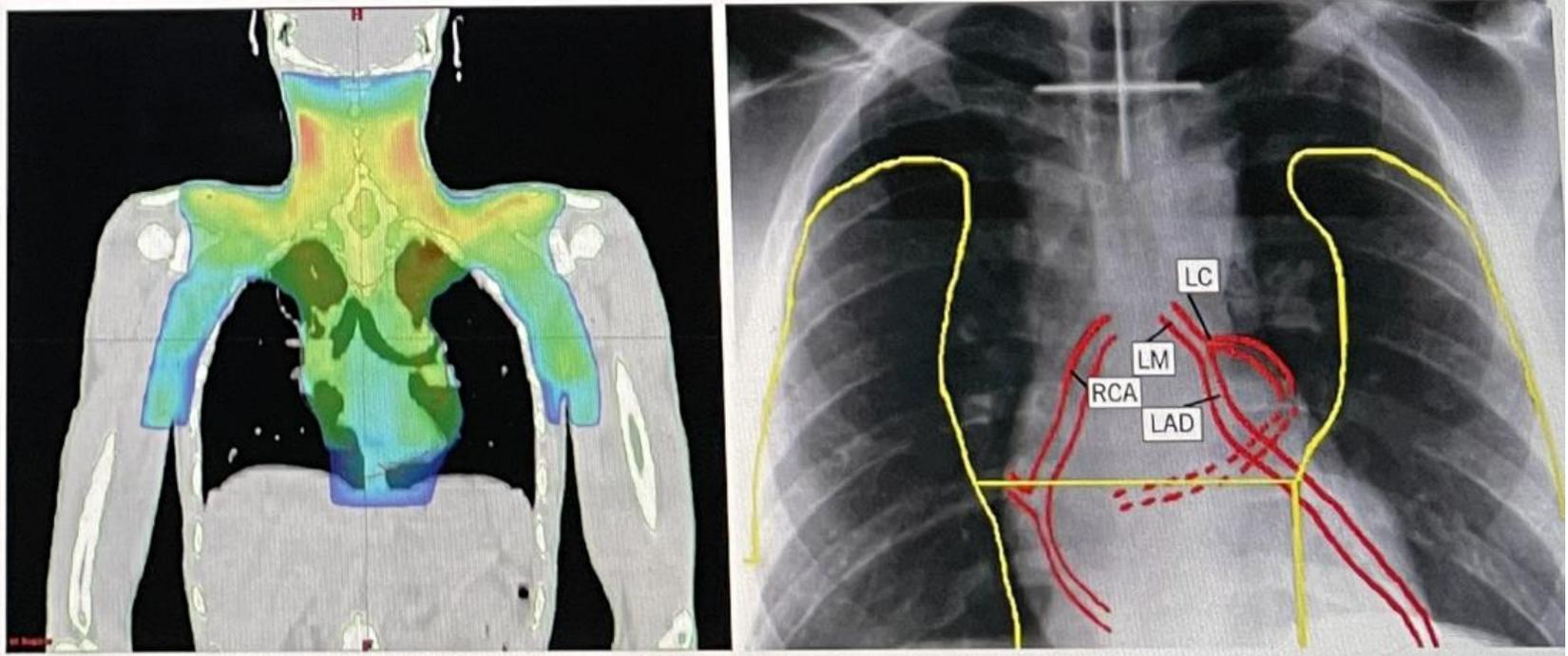
St. Jude Lifetime Cohort  
U01 CA195547 (MPI: Hudson/Ness)  
10,020 Survivors (6000+ clinically assessed)



from Dr. Stephanie Dixon, St. Jude's Hospital

# Case Study

- 45 yo female Hodgkin's doxorubicin (300 mg/m<sup>2</sup>) followed by 21 Gy mediastinal radiation at age 16
- Total Chol 210, HDL 40, LDL 115, TG 165, HgA1c is 5.5% BMI >30
- no tobacco, drugs, no meds



What do you estimate her 10 year CVD risk to be?

Adapted from Dr. Stephanie Dixon, St. Jude's Hospital

# ASCVD Estimator



ASCVD  
Risk Estimator

Estimator

Recommendation

10-Year ASCVD Risk  
**1.6%** calculated risk

**0.5%** risk with optimal risk factors

Lifetime ASCVD Risk  
**39%** calculated risk

**8%** risk with optimal risk factors

## ASCVD Risk Estimator

Reset All

Intended for patients with LDL-C < 190 mg/dL (4.92 mmol/L), without ASCVD, not on LDL-C lowering therapy

### Demographics

Sex

Male

Female

Age

45

Age must be between 20-79

Race

White

African American

Other

# CCSS Estimator

Using the **Standard Model** for survivors who are 5-years from cancer diagnosis::

- **Risk Group is High**
- The overall risk score is **7**
- The estimated probability of developing Heart Failure by 50 years of age is **12.4%** (95% confidence interval = **9.3-15.6%**)
- The relative risk of developing Heart Failure compared to a non-cancer sibling comparison is **41.5** (95% confidence interval = **22.7-75.9**)
- Data Used For Calculation
  - Gender? **Female**
  - Patient's age at diagnosis? **≥ 15**
  - Were any anthracyclines used? **Yes, cumulative dose known**
  - What was the anthracycline dose? **≥ 250 mg/m<sup>2</sup>**
  - Was there radiation to the chest? **Yes, chest radiation dose known**
  - What was the chest radiation dose? **15 - 34 Gy**

---

## Ischemic Heart Disease

Using the **Standard Model** for survivors who are 5-years from cancer diagnosis:

- **Risk Group is Moderate**
- The overall risk score is **2**
- The estimated probability of developing Ischemic Heart Disease by 50 years of age is **11.9%** (10-year probability = **8.6-15.3%**)
- The relative risk of developing Ischemic Heart Disease compared to a non-cancer sibling comparison group is **7.2** (95% confidence interval = **4.7-11.2**)
- Data Used For Calculation
  - Gender? **Female**
  - Was there radiation to the chest? **Yes, chest radiation dose known**
  - What was the chest radiation dose? **15 - 34 Gy**

<https://ccss.stjude.org/resources/calculators/cardiovascular-risk-calculator.html>

# Prevention of Cancer Treatment Related Cardiovascular Complications

- **Cardiovascular Risk Factor Modification**
  - Healthy Lifestyle—Nutrition—Mediterranean Diet or such—fruits, vegetables, lean meats or fish, protein intake, reduce salt intake.
  - Moderate Intensity Exercise for 30 mins at a time for 4-5 times per week.
  - Know your numbers—blood pressure, lipids (cholesterol), blood glucose (sugar)
  - Optimizing baseline inflammation--Inflammation increases the likelihood of plaque build-up in the arteries
    - -The level of CRP predicts cardiovascular risk independently of other risk factors
    - -High levels of CRP (greater than 3 mg/L) predict cardiovascular risk in women better than high levels of LDL cholesterol
    - -Studies are underway to see if lowering CRP reduces cardiac risk
- Tobacco Cessation
- Moderate alcohol intake
- Optimize medical treatment of hypertension and high cholesterol when lifestyle changes are not sufficient.

# Questions?



# Jefferson Health

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