The Road to Improve Cardiovascular Health after Cancer

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Objective

- What are the cardiac complications in cancer survivors?
- Who is at risk for cardiac toxicity ?
- When should my primary doctor refer me to Cardiology?

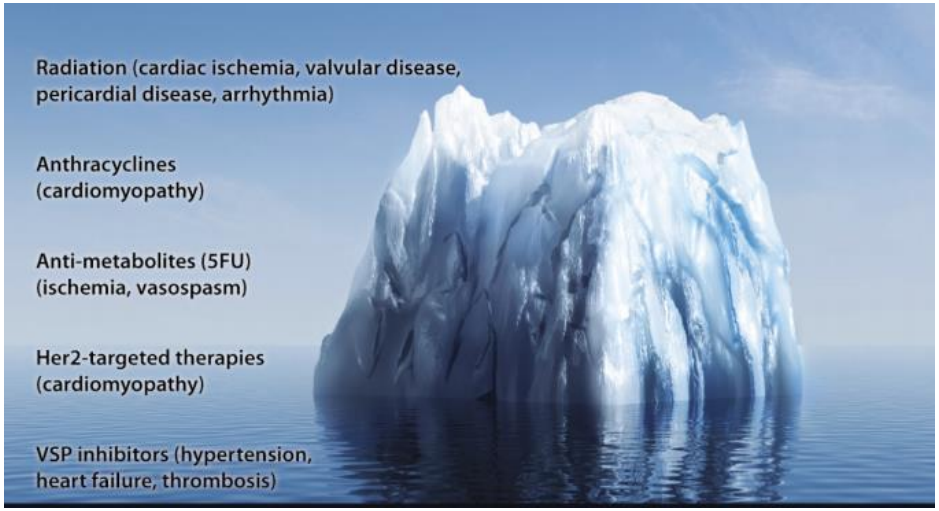
What are the Priorities in the Cardiovascular Care of Oncology Patients?

Prior to Cancer Therapy	During Cancer Therapy	After Cancer Therapy
• Identify high cardiovascular risk patients • Mitigate cardiotoxicity risk	• Monitoring to identify cardiotoxicty • Avoid dose interruptions • Prevent CV events	• Decrease risk of late Cardiovascular events • Improve long-term health

Armenian et al. J Clin Oncol 35:893-911

Improved longevity after cancer

2012: 13.7 million adult cancer survivors alive



Overall survival:

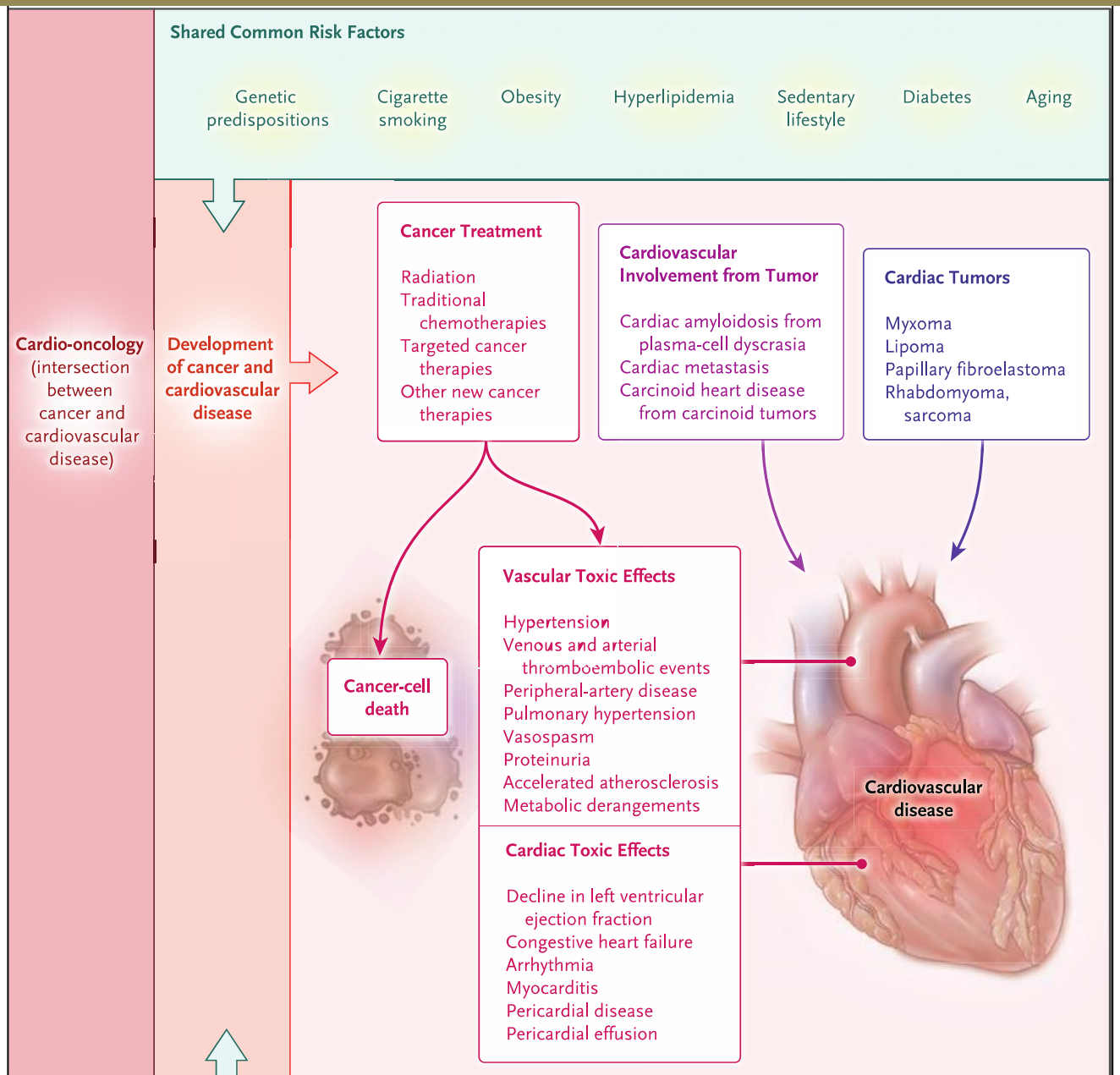
Has clearly improved in the last decade

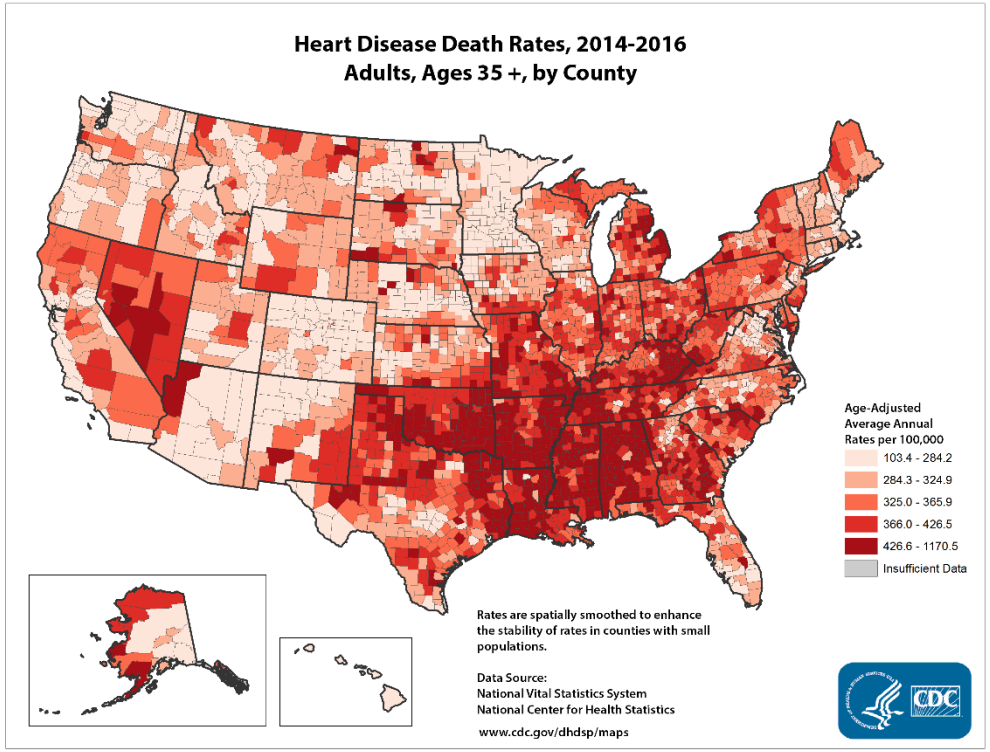
Modified from: Moslehi. Science Translational Medicine 2013.

Cardiovascular complication from cancer therapy

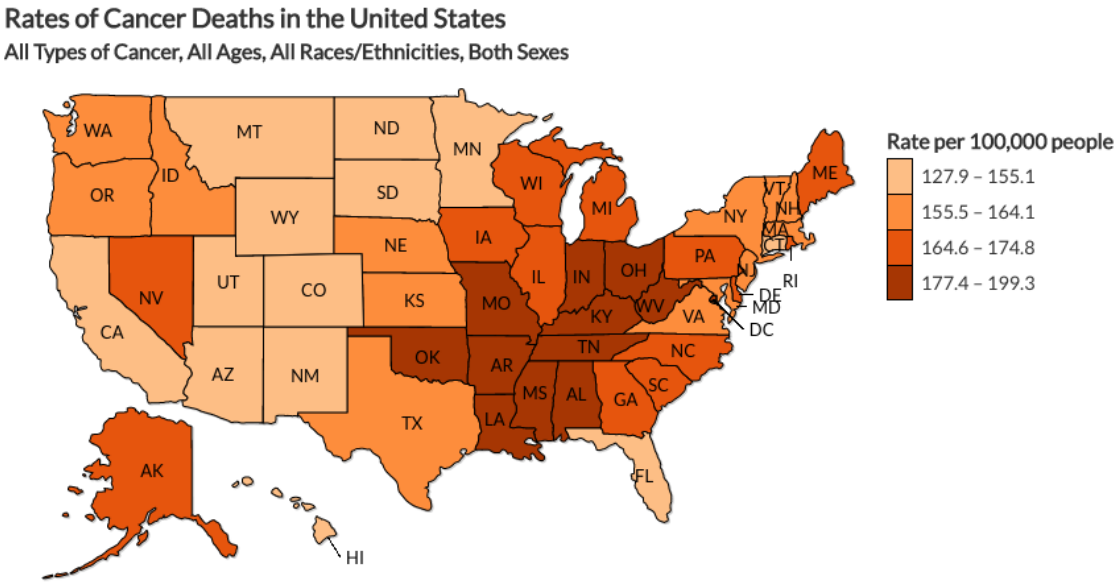
Vascular conditions	Cardiac structural problems	Cardiac dysfunction and heart failure
• Blockage of the arteries • High Blood Pressure • Deep venous thrombosis / pulmonary embolus	• Valvular heart disease • Pericardial constriction • Problem in the cardiac rhythm	• Anthracyclines – Trastuzumab • Antiangiogenic therapy • Radiation

Where Cancer and Cardiovascular Disease are met?





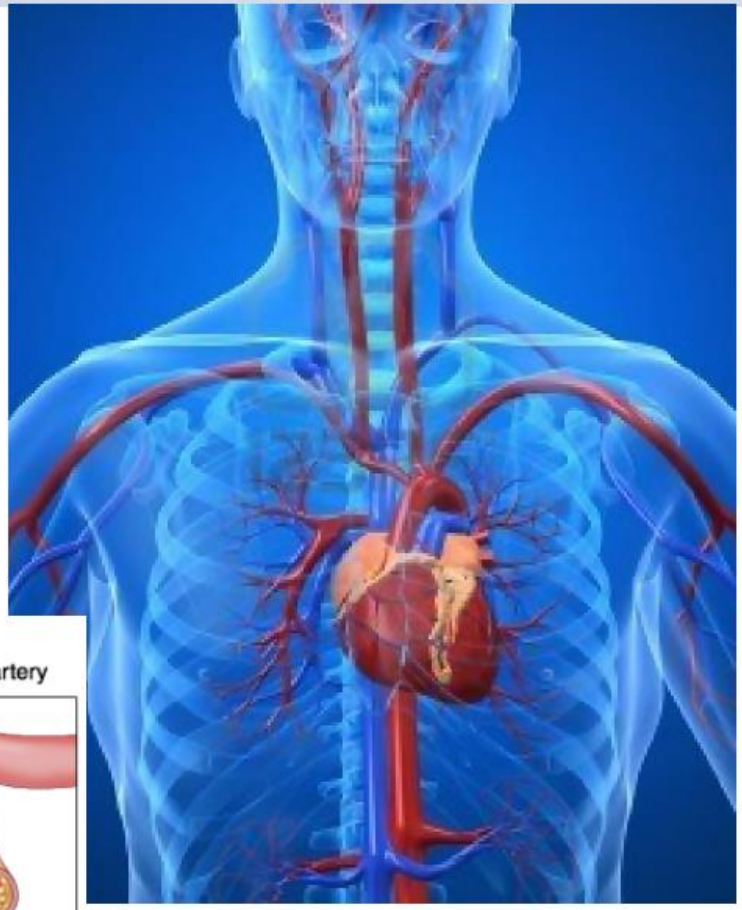
Clustering of CVD and Cancer Rates

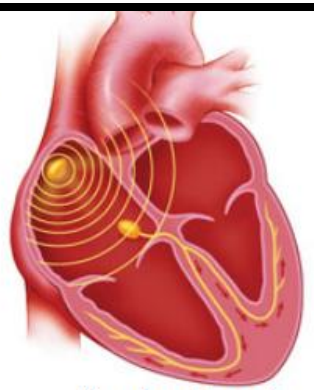


In fact, risk factors for cardiovascular disease are more prevalent in cancer survivors than in the general population

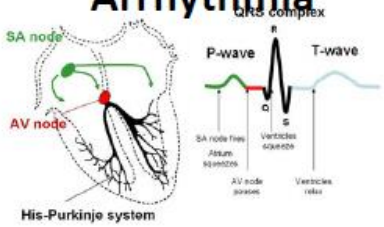
Cardiovascular Complications

Cardiac Dysfunction

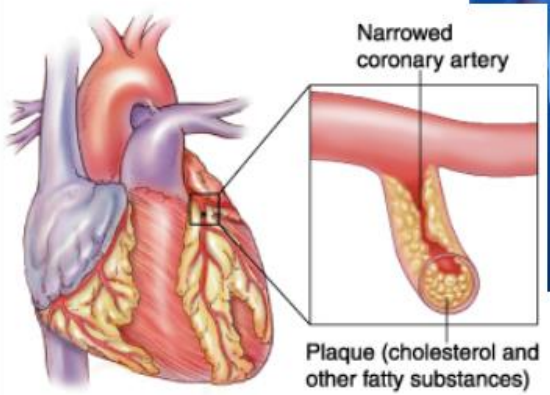




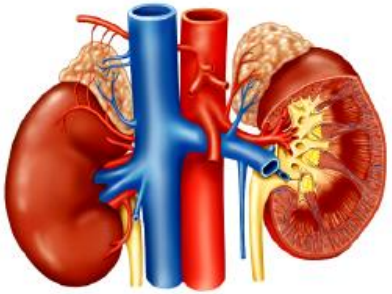
Arrhythmia



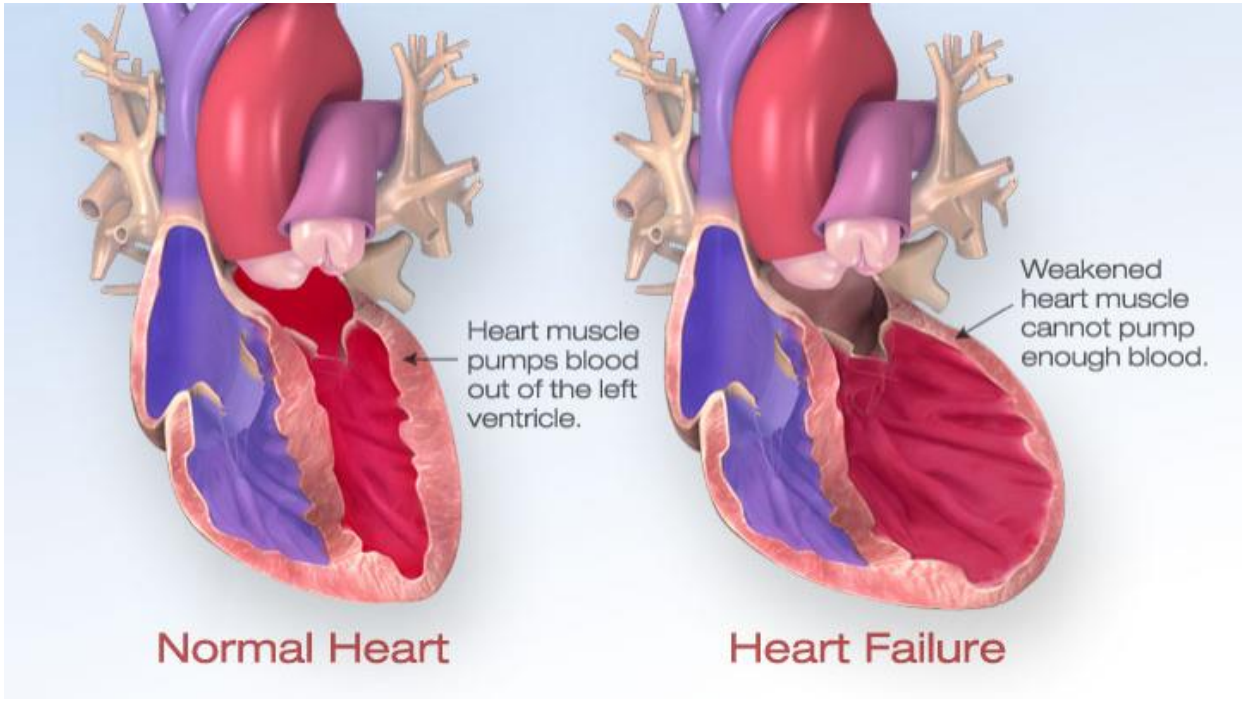
Atherosclerosis



Reno-vascular



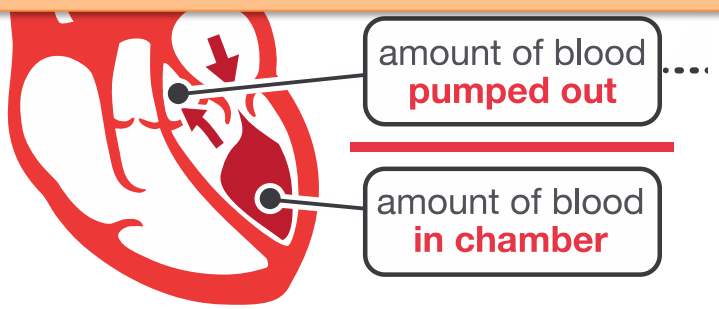
CHEMOTHERAPY INDUCED CARDIOTOXICITY



Defining cardiotoxicity

- **Decrease of the left ventricular ejection fraction below the baseline after chemotherapy**
- **Normal LVEF ~50-70 %**

The risk of symptomatic HF is 1-2 % at 10 years and 10-15 % at 25 years and beyond



amount of blood pumped out.
The fraction or percentage helps describe how well the heart is pumping blood to the body.

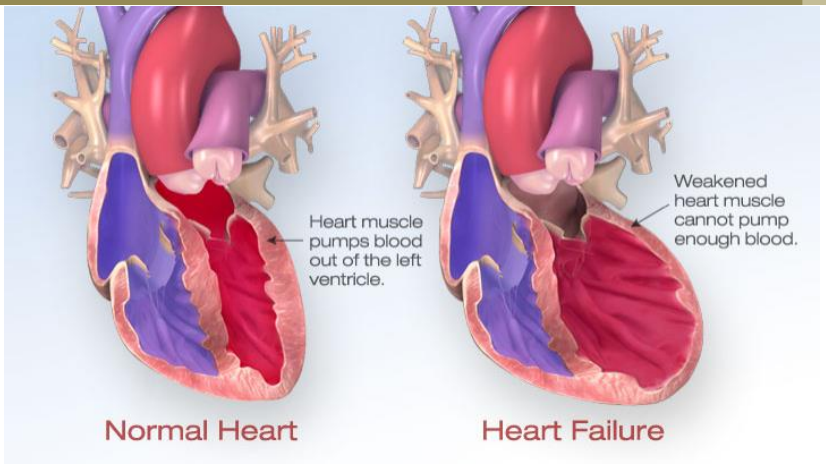
Bird BR, Swain SM. Clin Cancer Res. 2008; 14: 14-24
Plana et al. European Heart Journal (2014) 15, 1063

Cardiac Problems after chemotherapy

- Heart failure is a chronic, progressive condition in which the heart muscle is unable to pump enough blood through to meet the body's needs for blood and oxygen

- Basically, the heart can't keep up with its workload.
  - **this can be asymptomatic !**

Symptoms of Congestive Heart Failure



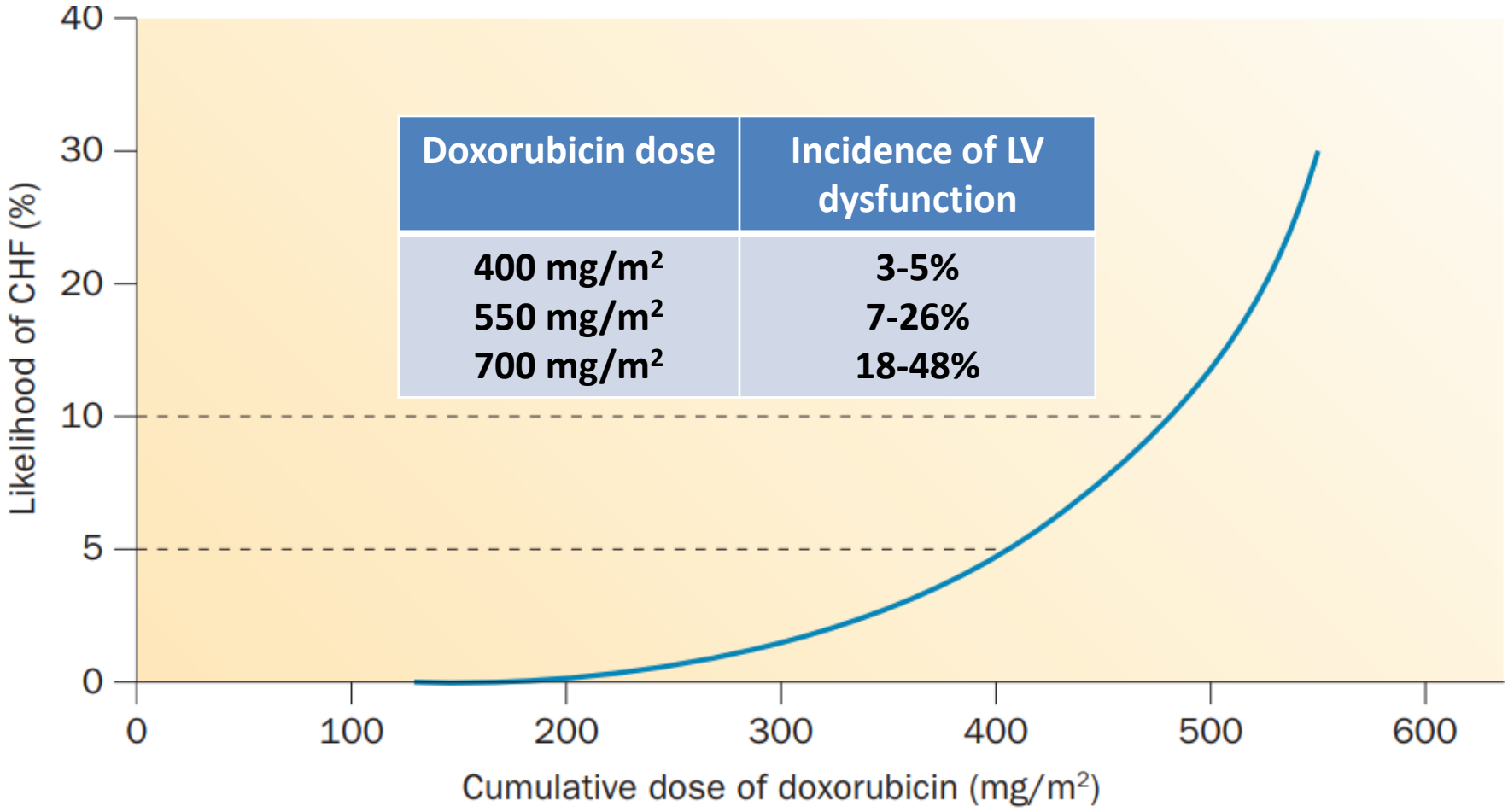
- Shortness of breath
- Severe fatigue preventing exercise or normal play
- Very swollen feet or ankles (so swollen that if a finger is pressed firmly on the area for few seconds it leaves an indentation)
- Cough and wheezing that doesn’t go away
- Lack of appetite, nausea
- Increase heart rate

Drugs that can induced cardiotoxicity

- Trastuzumab
- Doxorubicin
- Daunorubicin (Cerubidine)
- Epirubicin (Ellence)
- Cyclophosphamide (Genoxal, Mitoxan)
- Osemertinib (Tagrisso)

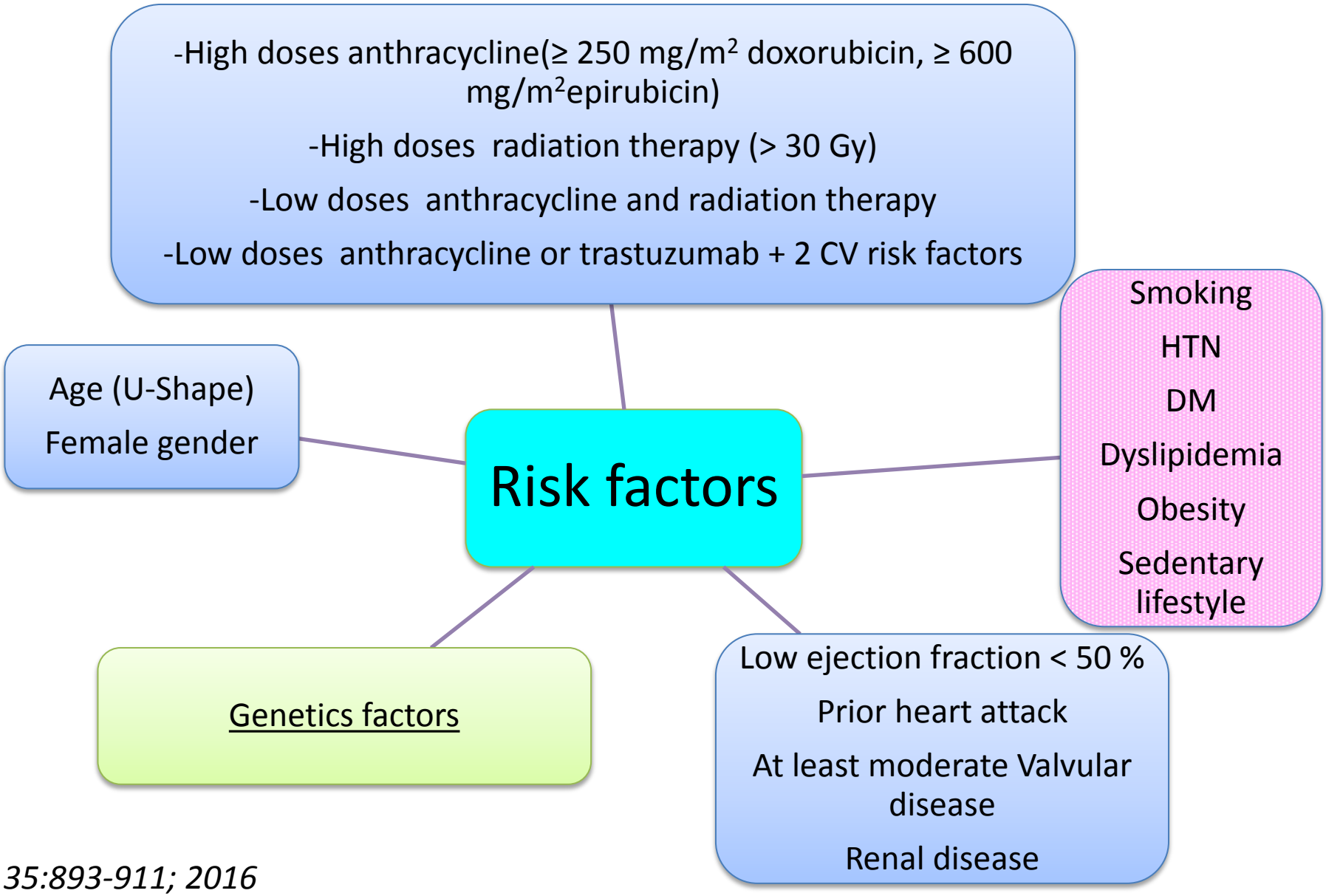
Anthracycline cardiotoxicity

Doxorubicin dose	Incidence of LV dysfunction
400 mg/m^2	3-5%
550 mg/m^2	7-26%
700 mg/m^2	18-48%



Ewer MS. Nat Rev Cardiol. 12; 547-558 2015

Which patients with cancer are at increased risk for developing cardiovascular disease?



JCO 35:893-911; 2016

AHA-proposed algorithm: Post-treatment

Following Therapy

Surveillance

Cardiac Risk Factors:

- ❑ History of MI/CAD
- ❑ Known LVD
- ❑ History of CHF
- ❑ Diabetes*
- ❑ HTN*
- ❑ Smoking
- ❑ HLD
- ❑ Family Hx CAD*
- ❑ Female gender
- ❑ Age <15 or >75[3]*

No consensus exists on an optimal monitoring strategy

Hamo CE et al. Circ Heart Fail. 2016; 9:e002843

Screening for Cardiomyopathy After Chemotherapy

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM OR MUGA SCAN

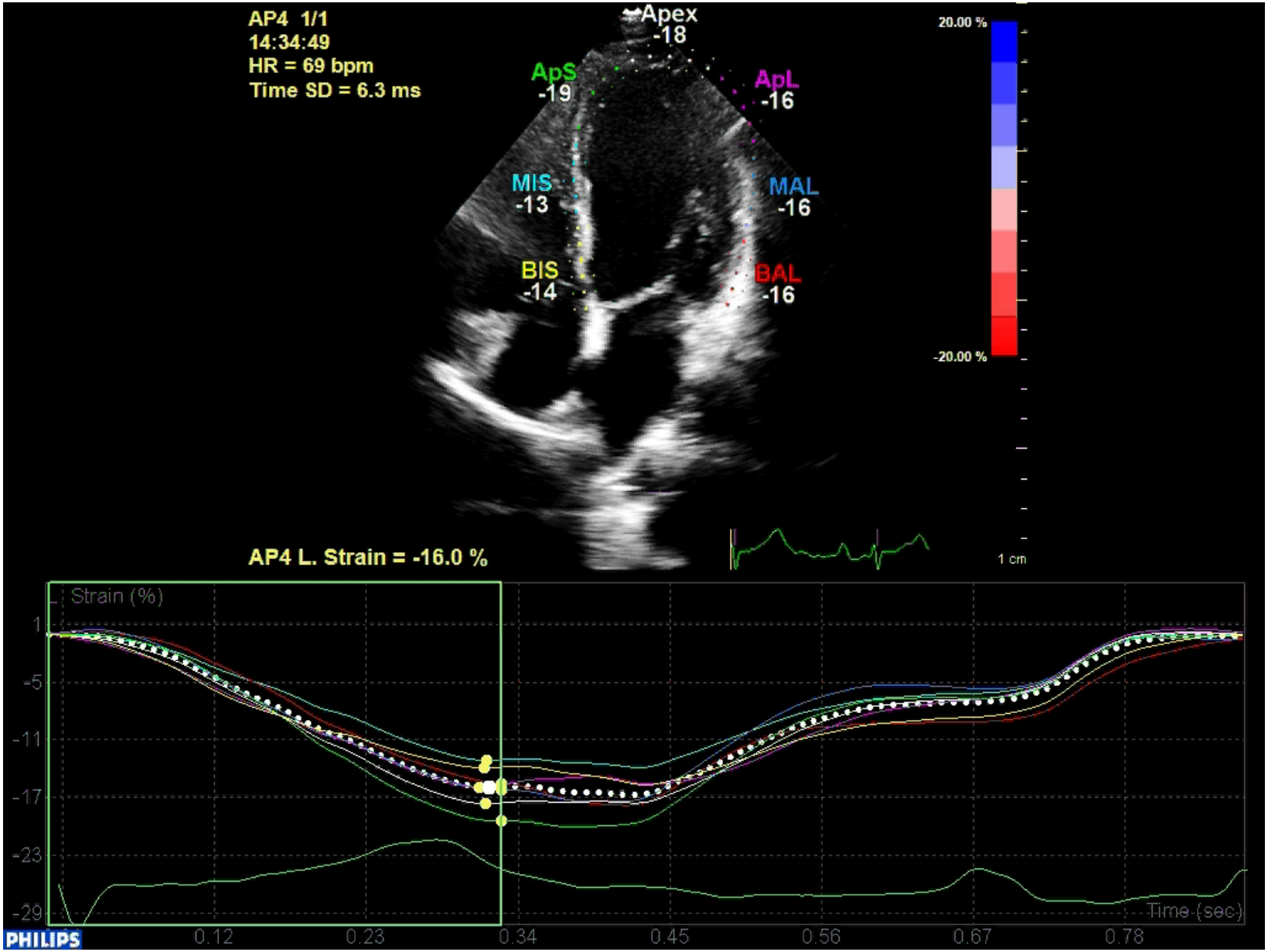
Age at Treatment*	Radiation with Potential Impact to the Heart§	Anthracycline Dose†	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	<200 mg/m^2	Every 2 years
		≥200 mg/m^2	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m^2	Every 5 years
		≥100 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
≥5 years old	Yes	<300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
	No	<200 mg/m^2	Every 5 years
		≥200 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
Any age with decrease in serial function			Every year

*Age at time of first cardiotoxic therapy (anthracycline or radiation [see fields below], whichever was given first)

§See Section 71

†Based on doxorubicin isotoxic equivalent dose [see conversion factors in Section 28 "Info Link (Dose Conversion)"]

Echocardiography is the modality of choice

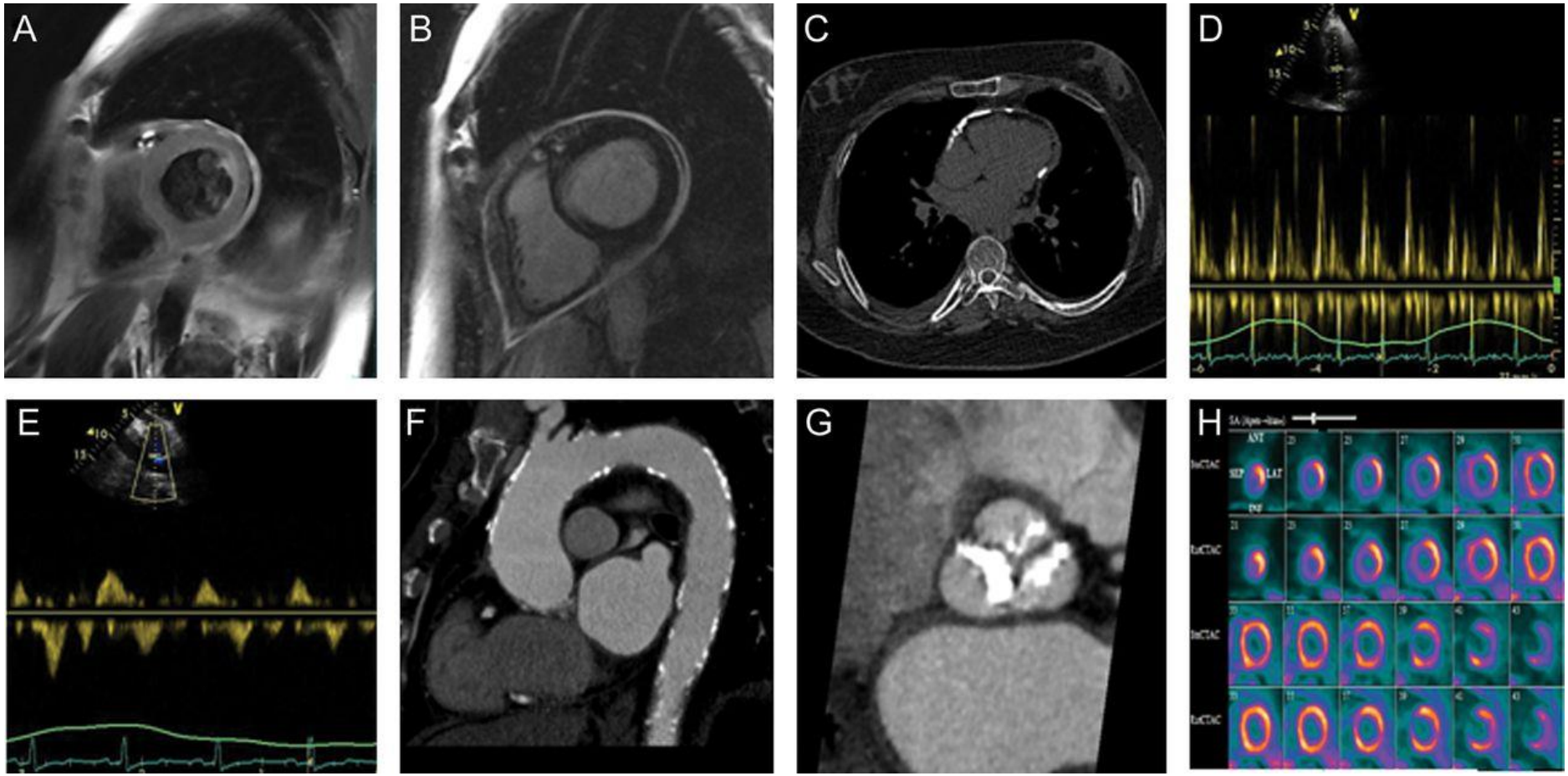


Summary: Treating cardiotoxicity

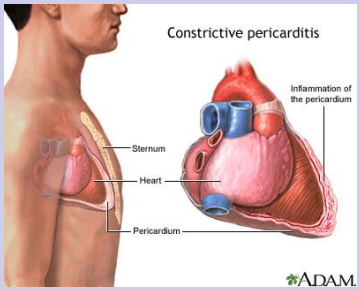
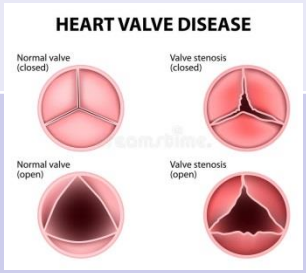
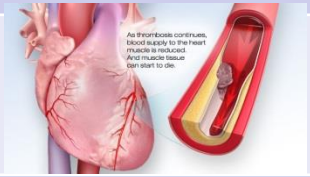
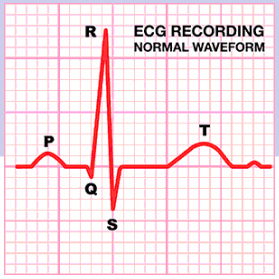
- **Medium-high risk patients need surveillance: known your treatment and your risk factors!**

- **If you have decrease of the function of your heart or symptoms of heart failure your doctor should referral you to see a cardiologist**

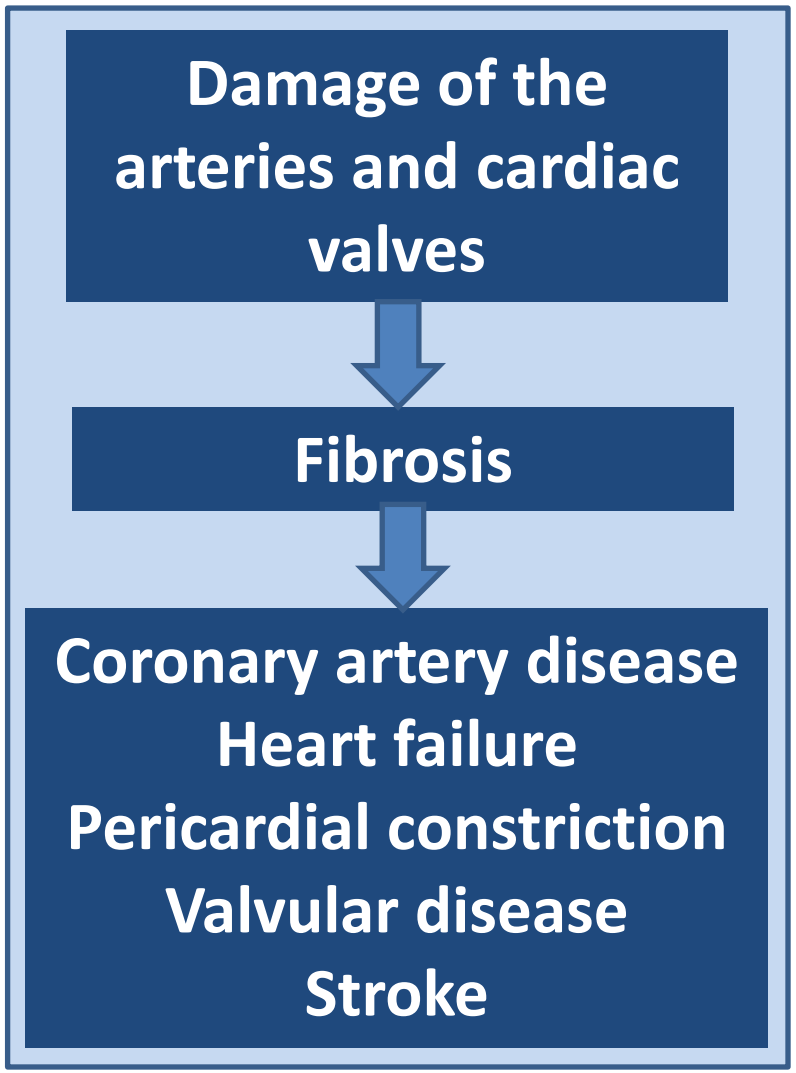
Radiation Therapy and Cardiovascular Disease



Spectrum of Radiation Damage to heart

Structure	Abnormality	Complication
Pericardium		Heart Failure Fatigue Abdominal distention
Heart Muscle		Heart Failure
Cardiac Valves damage		Murmur/ Heart Failure/Chest Pain/Lightheadedness
Blockage of the arteries		Heart Attack/ Stroke
Electrical complications		Heart Block

Radiation therapy



Risk factors:

Higher dose

Larger volume exposed

Younger age

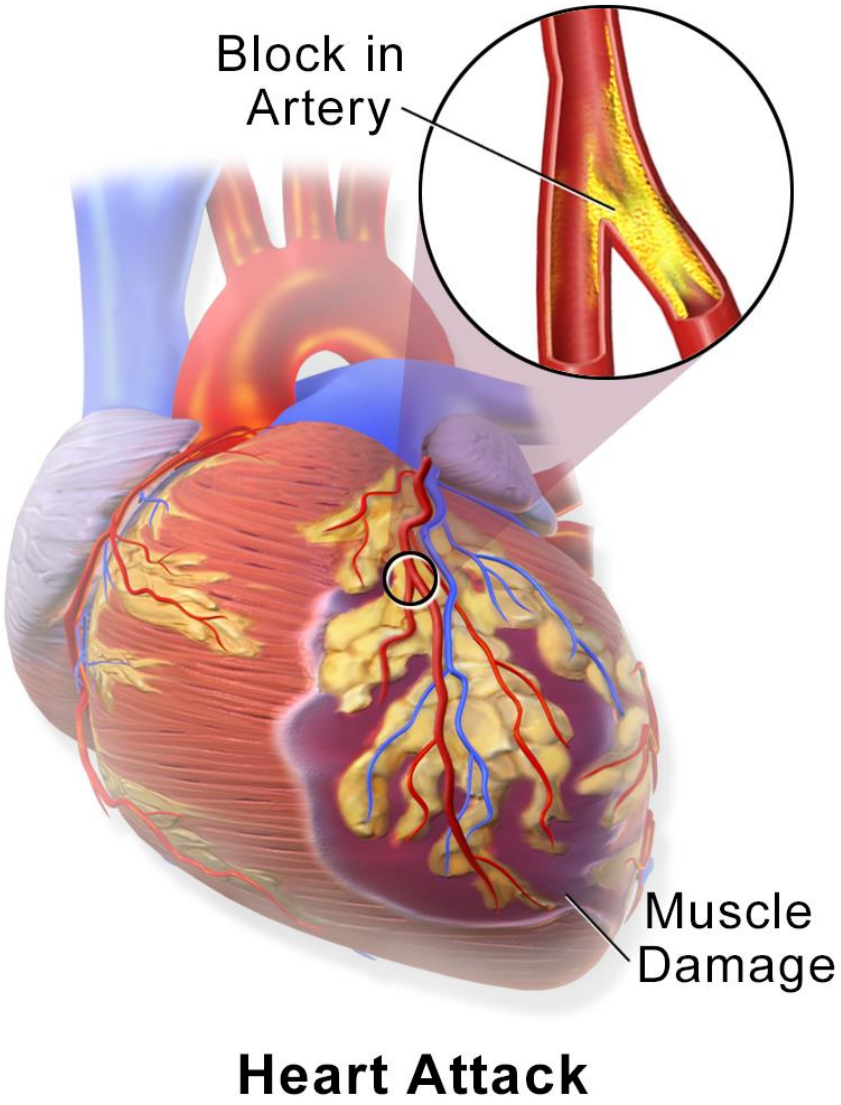
Adjuvant chemo

Type of radiation source

CV risk factors

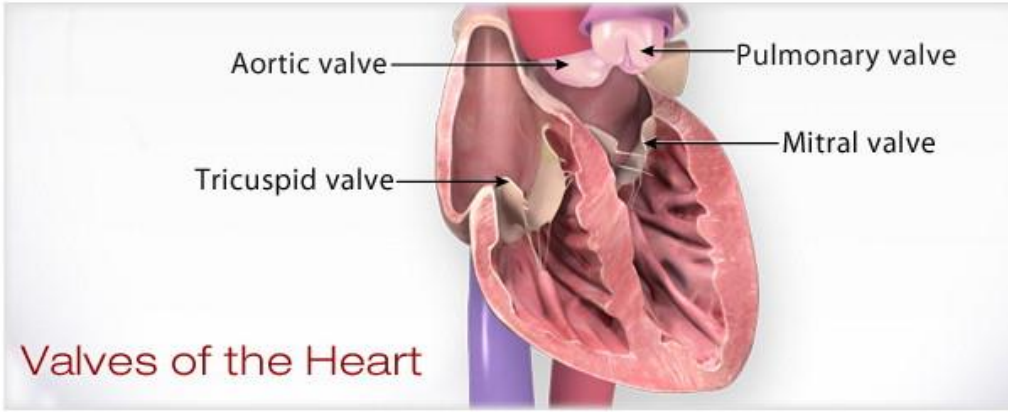
Chen-Scarabelli C et al. JNC 2016 May 25

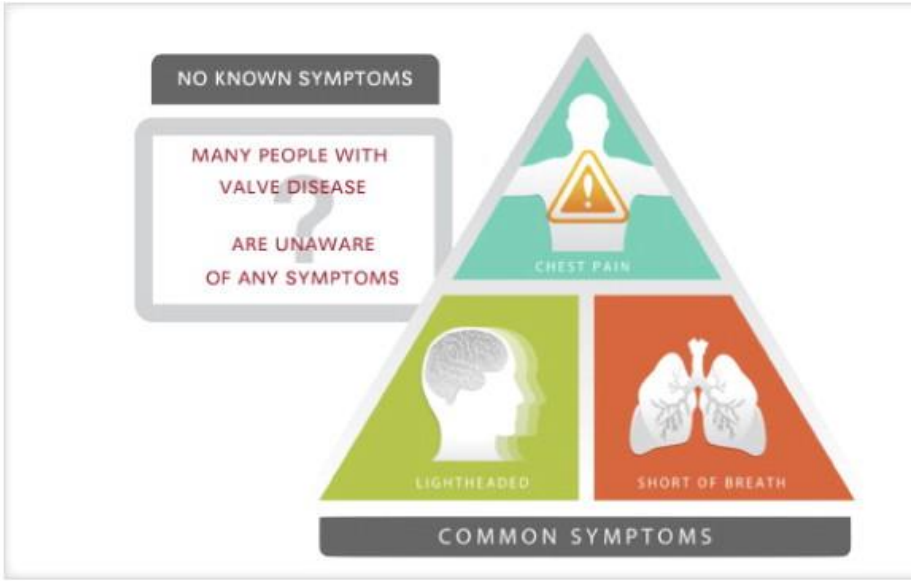
Symptoms of Heart Attacks (coronary artery disease)

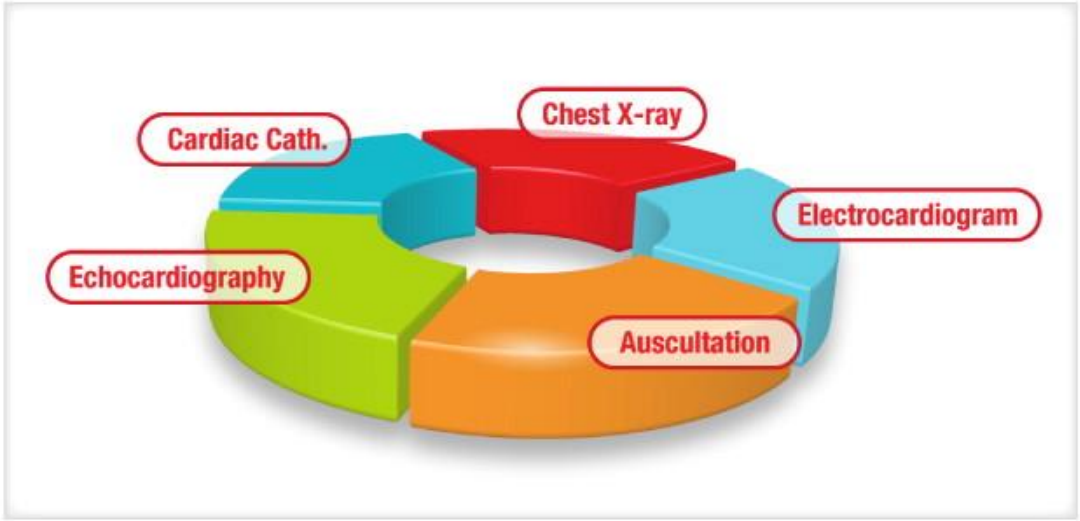


- Chest discomfort
- Discomfort in upper body
- Cold sweat
- Nausea
- Lightheadedness

Cardiac Valvular Disease and Radiation







After Radiation

Electrocardiogram, echocardiogram , Lipids and cardiac risk factors

Treat and known your Risk Factors (hypertension , lipids, diabetes, obesity, smoking, exercise)

Yearly follow up: Electrocardiogram and echocardiogram if clinically indicated

At 5 year : Electrocardiogram and echocardiogram

10 year f/u: Electrocardiogram, echocardiogram , stress test

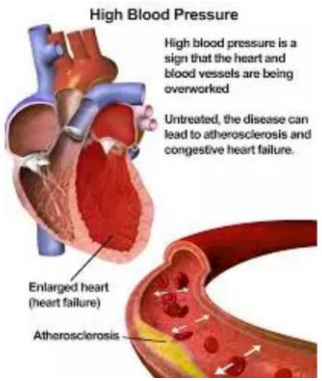
What are the Risk Factors?

What You Can Change?

- Physical Activity
- Life Stress
- High Blood Pressure
- Obesity
- Diabetes
- High Cholesterol & Triglycerides
- Smoking
- Unhealthy Diet (HIGH in saturated fat
  & calories; LOW in fresh fruit, veggies, whole grains & fish)

What You Can't Change?

- Age
- Gender
- Family History



Hypertension: Facts

- Its prevalence before chemotherapy is similar to that in the general population (29%)
- After the initiation of certain chemotherapeutic agents HTN increase significantly ~ 30%–80%

Drugs that target blood vessel formation (VEGF)

Bevacizumab (Avastin, Mvasi)
Sorafenib (Nexavar)
Sunitinib (Sutent)

Always Know Your Numbers!

Total Cholesterol	<200 mg/dl
Triglycerides	<150 mg/dl
Fasting Glucose	<100 mg/dl
Blood Pressure	<120/80 mmHg
Body Mass Index	<25
Waist Circumference	<35 inches
Exercise	Minimum 30 minutes most of the days

American Heart Association.

How often do discussions about CVD risk factors occur in cancer survivors ?

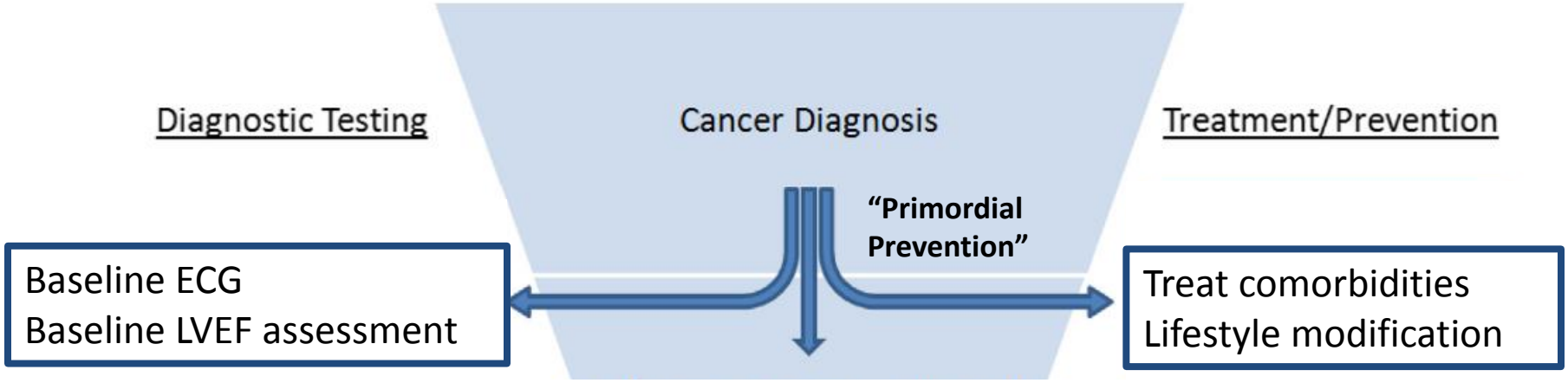
One in three survivors with one or more risk factors for CVD did not report a health promotion discussion with their health care providers

J Cancer Surviv 7(2): 253-261

Screening (no evidence-based guidelines in adults)

Screening (condition)	US Preventive Services Task Force	COG	AAP / AHA
Blood pressure	Annually for adults	Annually if treatment risk factors present	Check at every visit if >3 yo
Fasting lipids (dyslipidemia)	Males 20-34 yo / females 20-44 yo with CHD risk	2y after completing therapy and q2y	All cancer survivors
EKG / Echo (cardiomyopathy)	N/A	EKG 2y after therapy / Echo q1-5y depending exposures	NA
Fasting glucose	Only asymptomatic adults with BP> 135/80 mmHg	Q2y in cancer survivors exposed to specific treatments	Baseline for all cancer survivors

Full range of disease



Modified from: Yu et al. J Card Failure. 2014. 20(11): 841.

Conclusions

- It is clear that both the disease (cancer) and the treatment itself carry risk.
- Known your cancer treatment
- Early detection and treatment of cardiotoxicity, even when asymptomatic, helps cardiac function to recovery and decrease cardiac events
- Management of risk factors is important not only during treatment and post treatment, but also in the prevention of these two diseases

Resources

- American Society of Clinical Oncology
- National Comprehensive Cancer Network
- American Cancer Society
- Children's Oncology Group "Survivorship Guidelines"
- AHA website

Resources available at UW: : **Cardio-oncology**

- Richard K. Cheng, MD (HF/transplant cardiologist):
  rkcheng@uw.edu

- Daniel Fishbein, MD (HF/transplant director):
  dfish@uw.edu

- Jim Kirkpatrick, MD (Echo director/imaging):
  kirkpatj@uw.edu

- Carolina Masri, MD (HF/transplant cardiologist):
  cmasri@uw.edu

- Patient care coordinators:
  Laura Yale: lauranne@uw.edu
  Kristelle Calma: kcalma@uw.edu

Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions

Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

Nonpharmacologi-cal Intervention		Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mm Hg	-3 mm Hg
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5/6 mm Hg	-2/3 mm Hg
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg

Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension* (cont.)

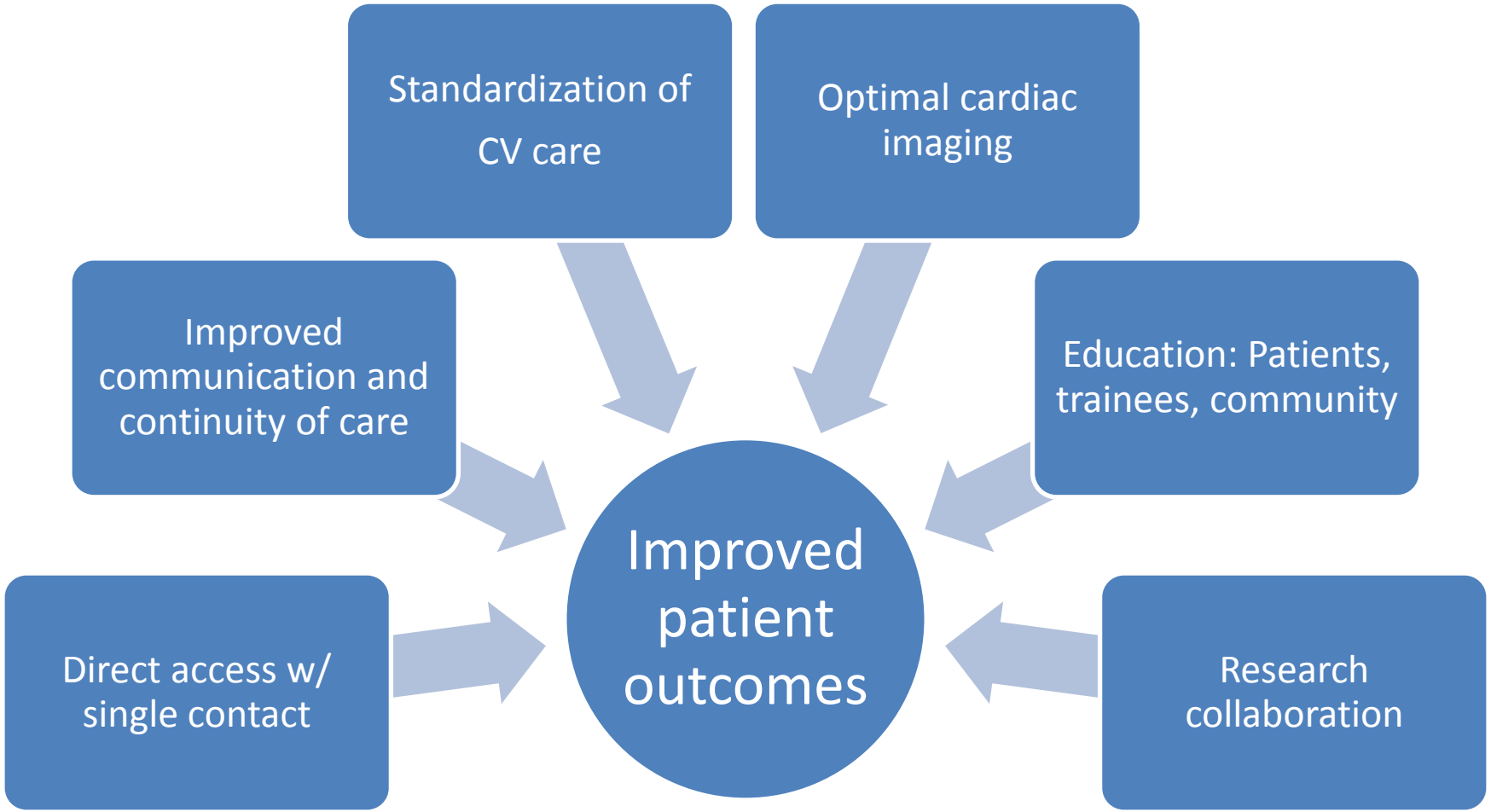
	Nonpharmacological Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Physical activity	Aerobic	● 90–150 min/wk ● 65%–75% heart rate reserve	-5/8 mm Hg	-2/4 mm Hg
	Dynamic resistance	● 90–150 min/wk ● 50%–80% 1 rep maximum ● 6 exercises, 3 sets/exercise, 10 repetitions/set	-4 mm Hg	-2 mm Hg
	Isometric resistance	● 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ● 8–10 wk	-5 mm Hg	-4 mm Hg
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: ● Men: ≤2 drinks daily ● Women: ≤1 drink daily	-4 mm Hg	-3 mm

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.
†In the United States, one “standard” drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).

Cholesterol (Lipid) Recommendations You May Be Familiar With

Total Cholesterol Goal:	<200 mg/dL
“Bad Cholesterol” LDL Goal: (Low Density Lipoprotein Cholesterol)	<100 mg/dL
“Good Cholesterol” HDL Goal: (High Density Lipoprotein Cholesterol)	>50 mg/dL
Triglycerides Goal:	<150 mg/dL

Potential benefits of Cardio-Oncology



Cardiovascular complication from cancer therapy

Vascular conditions	Cardiac structural problems	Cardiac dysfunction and heart failure
• Atherosclerosis • Hypertension • Arterial Thrombosis • Deep venous thrombosis / pulmonary embolus	• Valvular heart disease • Pericardial constriction • Conduction system disease	• Anthracyclines – Trastuzumab • Antiangiogenic therapy • Radiation