VANDERBILT UNIVERSITY
MEDICAL CENTER

Cardio-Oncology: How can collaboration improve care?

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Presenter Disclosure Information
17th Annual Benjamin Schuster Colloquium, 2.22.17
Kettering Health Network, Kettering, Ohio

- I **will not** discuss off label use or investigational use in my presentation.
- I **have** financial relationships to disclose:
  - Research support from: Takeda, Inc.
  - Consultant (modest): Roche, Amgen, Prothena, BMS

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Cardio-oncology Program - Brigham and Women's Hospital
www.brighamandwomens.org/.../**cardiooncology**/defa... ▾ Brigham and Women's Hospital ▾
May 26, 2016 - Learn about specialized cardio-oncology care during and after cancer treatment with cardiologists and oncologists at Brigham and Women's ...

Cardio-Oncology Center - Cleveland Clinic
my.clevelandclinic.org/.../**cardio-oncology**-and.../**cardio-oncology** ▾ Cleveland Clinic ▾
Cleveland Clinic's Cardio-Oncology Center includes experts from the Sydell and Arnold Miller Family Heart & Vascular Institute and the Taussig Cancer Institute ...

Burgeoning Cardio-Oncology Programs: Challenges and ...
content.onlinejacc.org/article.aspx?... ▾ Journal of the American College of Cardiology
by TM Okwuosa - 2015 - Cited by 3 - Related articles
Sep 8, 2015 - In **cardio-oncology**—as with any other **program**—institutional support is paramount to achieving success, but is not always easy to achieve.

Cardio-Oncology Program - Massachusetts General Hospital, Boston ...
www.massgeneral.org/.../treatment**programs**.aspx?id... ▾ Massachusetts General Hos
The Massachusetts General Hospital **Cardio-Oncology Program** provides care at the intersection of heart and vascular disease, and cancer. The program ...

Cardio-Oncology Program - Department of Medicine - Vanderbilt ...
medicine.mc.vanderbilt.edu › Department of Medicine ▾
The Vanderbilt **Cardio-Oncology Program** brings together Cardiologists, Oncologists and Researchers who work together in promoting the cardiovascular health ...

Cardio-Oncology Program - Cedars-Sinai
https://www.cedars-sinai.edu/.../**Programs**.../**Cardio-Onco**... ▾ Cedars-Sinai Medical C
The **Cardio-Oncology Program** is a highly specialized clinic in the Barbra Streisand Women's Heart Center dedicated to the heart health of breast cancer ...

What is Cardio-Oncology? - MedStar Heart Institute
www.medstarheartinstitute.org/conditions/**cardio-oncology**.../what-is-**cardio-oncology**
Certain cancer drugs can weaken the heart or cause abnormal rhythms. We designed our **Cardio-Oncology Program** to provide cancer patients with excellent , ...

Cardio-oncology clinics integrate specialty clinical care - For Medical ...
www.mayoclinic.org/.../**cardio**vascular/**cardio-oncology**-clinics-integrate-... ▾ Mayo Clinic ▾
Cardio-oncology clinics integrate specialty clinical care. The survival rate of cancer patients has increased in the last 25 years. In the United States, the five- year ...

Cardio-Oncology | Home page
cardiooncologyjournal.biomedcentral.com/ ▾
The editorial mission of **Cardio-Oncology** is to advance the science and practice of ... Studies Institute is accepting Letters of Intent for its THRIVE grant **program**.

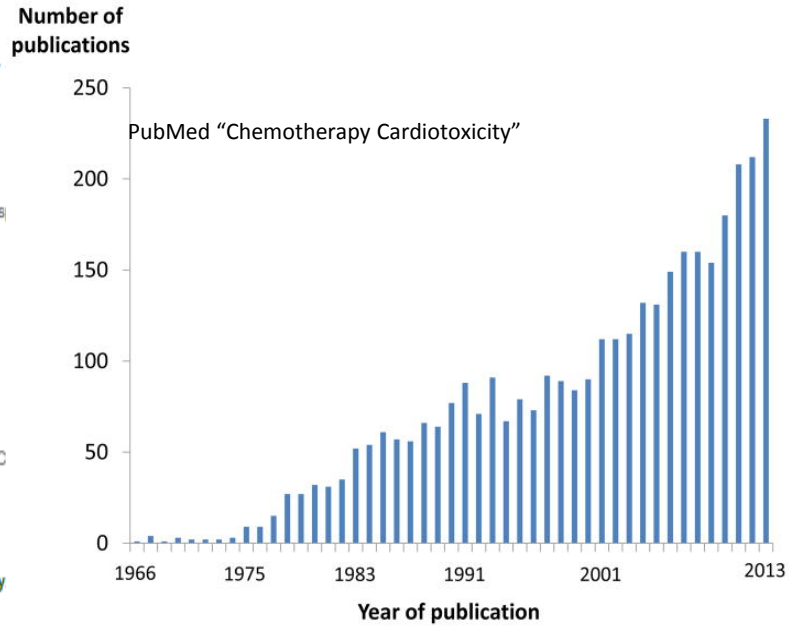
Moffitt Cancer Center: Cardio-Oncology
https://moffitt.org/.../**cardio-oncolog**... ▾ H. Lee Moffitt Cancer Center & Research Institute ▾
The **Cardio-Oncology Program** brings together oncologists at Moffitt Cancer Center and cardiologists at USF Health who collaboratively treat cancer patients ...

Wh ?

U-M Cardio-Oncology Clinic | Frankel Cardiovascular Center ...
www.umcvc.org/conditions-treatments/**cardio-oncology** ▾
To make an appointment for heart or vascular care, or to learn more about our cardio-oncology **program**, call the University of Michigan Cardiovascular Center ...

Cardio-Oncology Program - Department of Cardiology - Rochester, NY ...
www.urmc.rochester.edu › ... › Programs ▾ University of Rochester Medical Center ▾

cardio-or



customized for each participant based on their background and career ...

Greenville Health System Cardio-Oncology Program - Greenville ...
https://www.ghs.org/healthcareservices/heart/**programs**-clinics/**cardio-oncology**/ ▾
The formalized program began developing after representatives from the Vanderbilt University **Cardio-Oncology program** spoke at GHS on their success ...

Cardio-Oncology Program - Oncology > Cardiovascular Medicine ...
cardio.med.yale.edu/clinical/**cardio**onc.aspx ▾ Yale University ▾
The **Cardio-Oncology Program** at Yale School of Medicine was one of the first programs in the nation developed to address the unique cardiovascular problems ...

International Cardioncology Society, North America
icosna.org/ ▾
The Vanderbilt **Cardio-Oncology Program** brings together cardiologists, oncologists, and researchers who work to promote the cardiovascular health of cancer ...

Cardio-Oncology - MedStar Washington Hospital Center
www.medstarwashington.org › Treatments ▾
Cardio-oncology is the intersection of heart conditions in patients who have been ... MedStar Heart & Vascular Institute offers the first **cardio-oncology program** in ...

Emory Cardio-Oncology Program - Winship Cancer Institute
https://winship**cancer**.emory.edu/.../**cardio-oncology-program**-anno... ▾ Emory University ▾
Oct 20, 2014 - The proactive approach of the multidisciplinary Winship at Emory **Cardio- Oncology Program** is to provide care to patients in varying stages of ...

Cardio-Oncology | Winship Cancer Institute
ttps://winship**cancer**.emory.edu/.../**cancer**.../**cardio-oncology**.html ▾ Emory University ▾
he Winship at Emory **Cardio-Oncology Program** is one of the few programs in the nited States dedicated to the heart health of cancer patients by addressing ...

Cardio-Oncology Program - Rush University Medical Center
ttps://www.rush.edu/.../**cardio-oncology-program** ▾ Rush University Medical Center ▾
he **cardio-oncology program** at Rush helps prevent or minimize heart damage aused by cancer treatments, and helps to treat heart problems resulting from ...

Developing a Cardiology-Oncology Partnership | Physician's Weekly ...
ww.physiciansweekly.com/**cardio**logy-**oncology**-partnership/ ▾
ct 17, 2013 - The goal of the cardio-oncology program is to eliminate ardiovascular complications as a barrier to effective cancer treatment. To do so, we ...

Cardio-Oncology Program | The University of Kansas Hospital ...
ww.kumed.com/heart-care/clinical-services/**cardio-oncology** ▾
his is why cardiologists and oncologists at The University of Kansas Hospital and ancer Center developed the **cardio-oncology program**. Through this ...

Cardio-Oncology Program - Aurora Health Care
ttps://www.aurorahealthcare.org/.../**cardio-oncology-program** ▾ Aurora Health Care ▾
urora's cardio-oncology program – nationally recognized cardiology and oncology pecialists – who together, care for people at risk for cardiovascular disease.

Cardio-Oncology Services - Advocatehealth.com
www.advocatehealth.com/**cardio-oncology**-services ▾
The Cardio-Oncology service at Christ Medical Center, one of only a few in the ... to make an appointment or to learn more about the **Cardio-Oncology program**.

Cardio-Oncology - Smilow Cancer Hospital at Yale New Haven
https://www.ynhh.org/smilow/services/**cardio-oncology**.aspx ▾ Yale–New Haven Hospital ▾
Cardio-Oncology. The **Cardio-Oncology program** at Smilow Cancer Hospital at Yale New Haven is a combined inpatient and outpatient consultative service that ...

Cardio-Oncology Program — School of Medicine University of Louisville
https://louisville.edu/.../**cardio**logy/.../**cardio-oncology-progra**... ▾ University of Louisville ▾
The **Cardio-Oncology Program** at the University of Louisville is collaboration between University of Louisville Cardiovascular Medicine, James Graham Brown ...

Cardio-oncology: How can we be helpful?

- 47 y/o F, with recently diagnosed breast cancer undergoing chemotherapy, presents to assess her cardiac status while she receives treatment.
- She reports shortness of breath with walking even up to just 100 feet. She denies PND or orthopnea. She does have some lower extremity edema. She denies palpitations, syncope, or near syncope, or chest pain.

- Her cardiac related history includes:
- Aortic valve stenosis (Moderate to Severe)
  Pulmonary hypertension
  Mitral valve/Tricuspid regurgitation
  Diabetes mellitus
  Asthma
  Hodgkin's disease (previously treated)
  Chronic obstructive lung disease
  Hypertension

Past cancer history

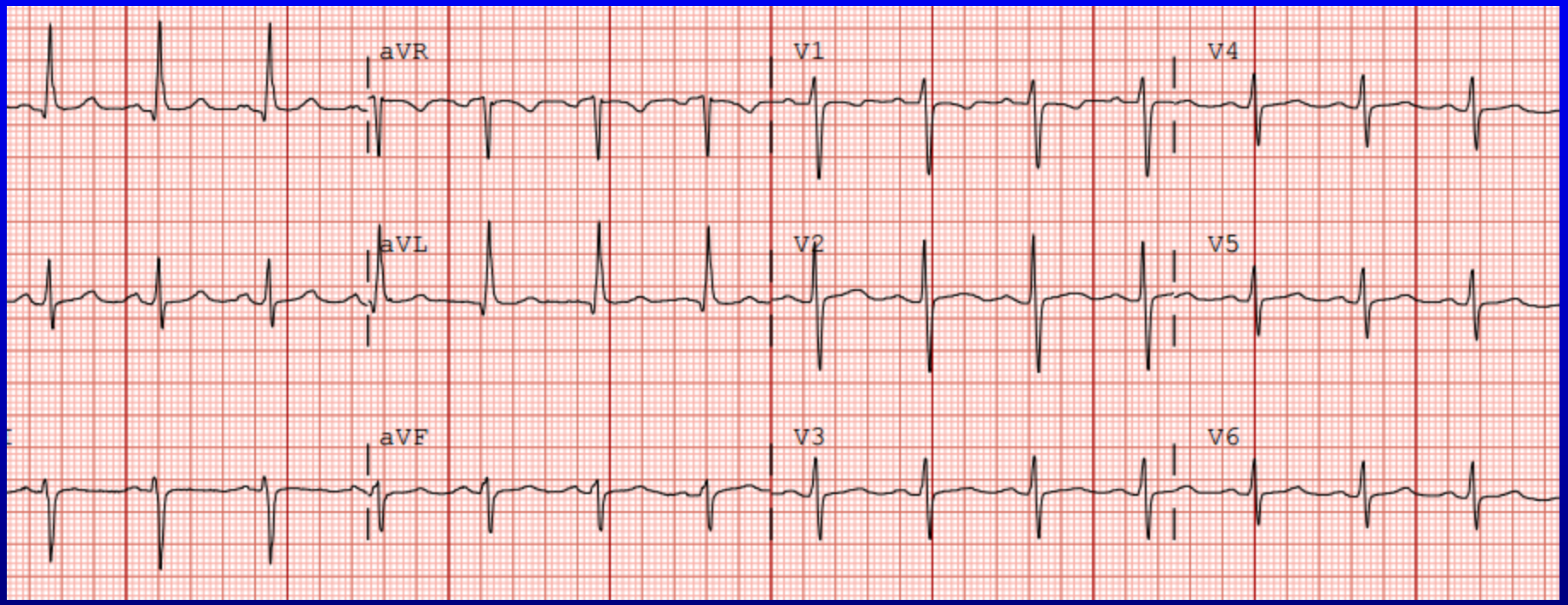
- Stage IIA Hodgkin's lymphoma in 1989 treated with mantle radiation, relapsed disease in 1992 treated with MOPP-ABVD (do you know what is in this?)
- Stage IIA (T2N0M0) R sided breast cancer (3cm), ER 3+ (99%), PR 3+ (99%), HER2-amplified by FISH (3+) s/p R total mastectomy with 0/6 SLNs in 3/2016
- Planned therapy: Adjuvant chemotherapy + HER2-directed therapy as follows: Taxol, trastuzumab (Herceptin) for 1 year, pertuzumab (Perjeta) for 8 cycles, and Lupron.
- Current MEDS: Advair Diskus 250 mg twice daily, aspirin 81 mg, levothyroxine 0.2 mg daily, omeprazole 20 mg qhs

Physical Exam and Labs

- Vital Signs: Height: 5ft 2 in; Weight: 219 lb; BMI: 40; Pulse: 92 bpm; BP: 110/58 mm Hg; O2Sat: 99 %
- JVD 4 cm above normal, bilateral carotid bruits but no decreased upstroke, lungs with few crackles. Cardiac exam: normal rate and regular rhythm; apical impulse normal in size and intensity without displacement; 3/6 systolic ejection murmur at the right upper sternal border and apex. She does have a loud S4. She has a decreased S2, pedal pulses 2+ and symmetric; 1+ extremity edema at her ankles.

- **Na**: 142 **K**: 4.1 **Cl**: **108*** **CO2**: 26 **BUN**: 13 **Creat**: 0.87 **eGFR**: > 60 **eGFRAA**: > 60 **Gluc**: **101*** **Ca**: 8.8
- **Chol**: 195 **Trigs**: 62 **HDL-C**: 52 **UricA**: **6.4*** **LDL-C**: **131***
- **TRPI**: <0.01 **BNP**: 84 **TSH**: 0.738 **TT4**: 9.0 **WBC**: 9.9 **Hgb**: **8.7***

- CXR: no infiltrates, cardiac size normal, reduced volumes (poor inspiration)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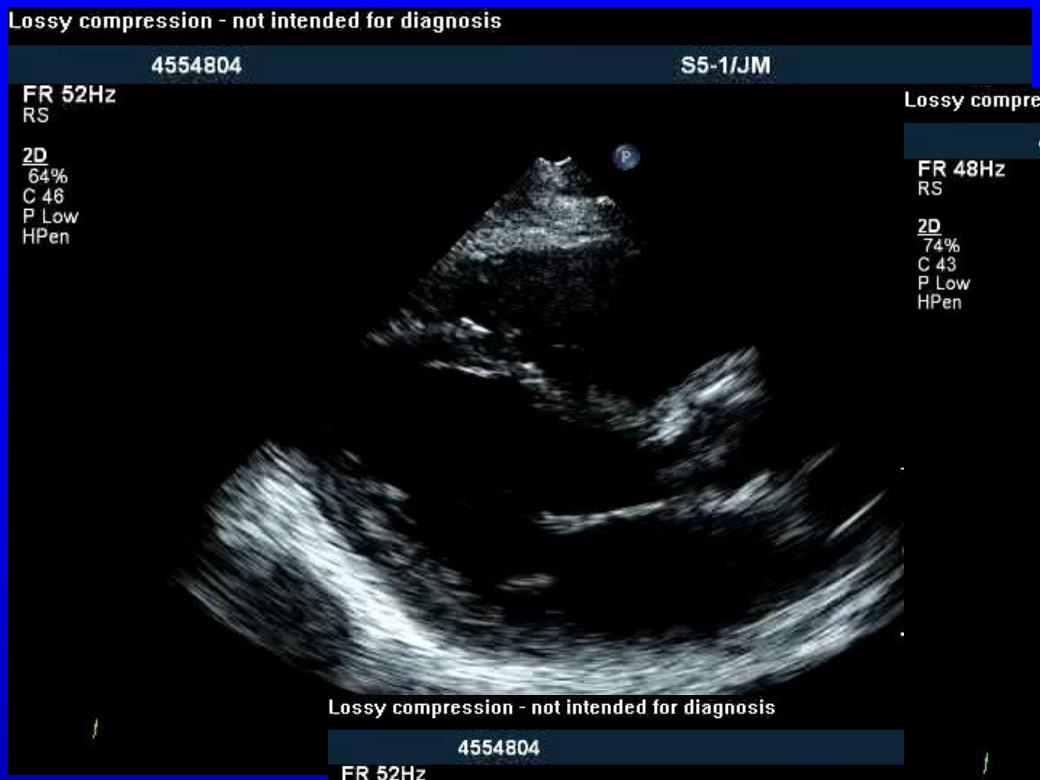
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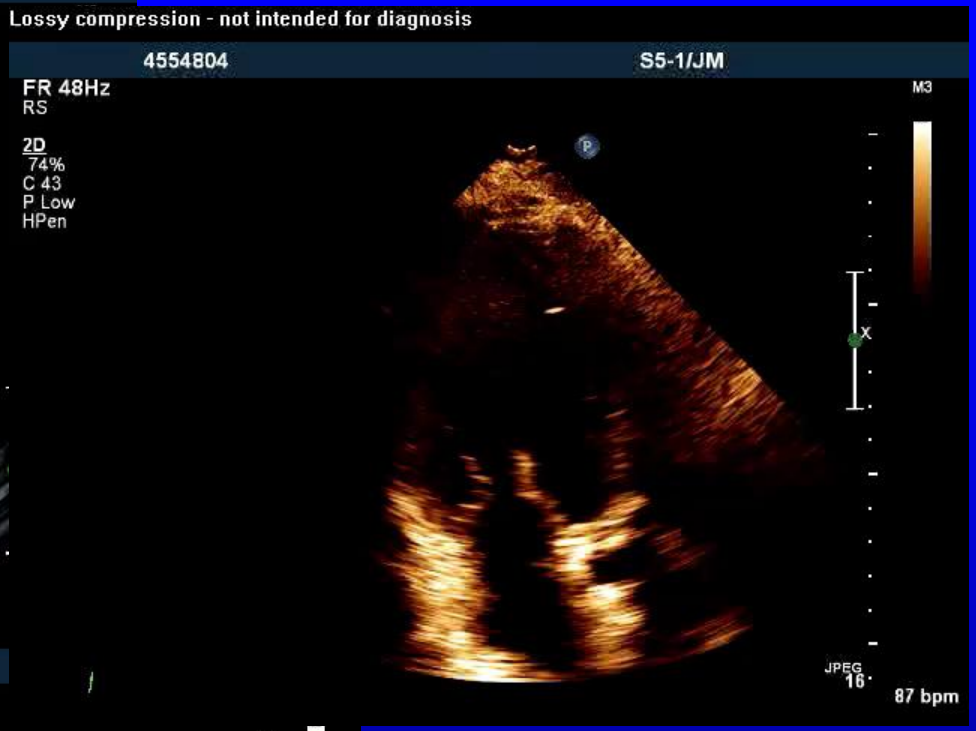
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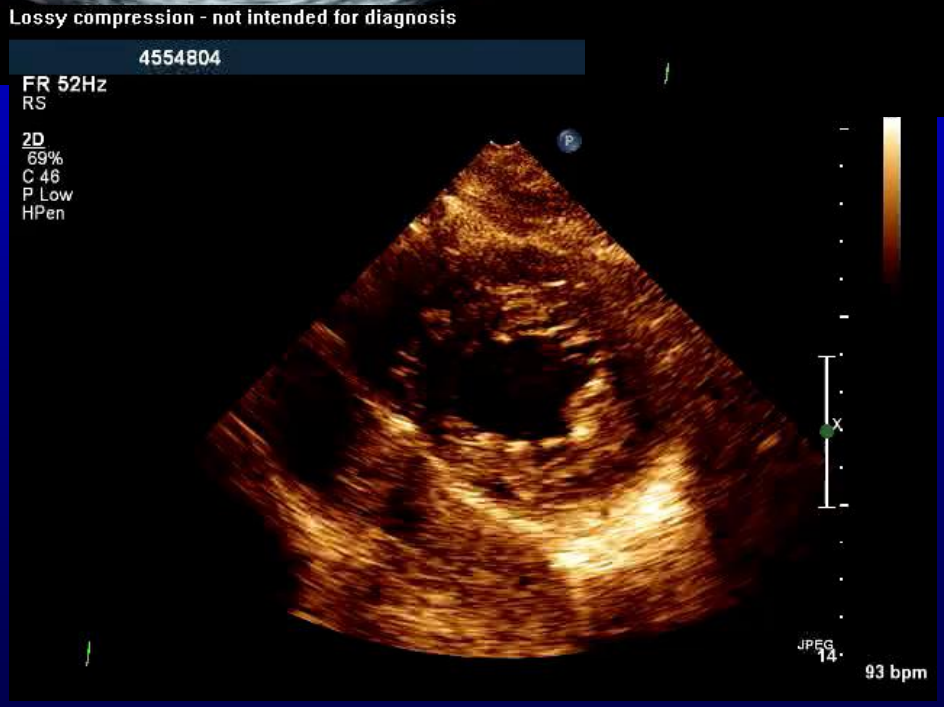
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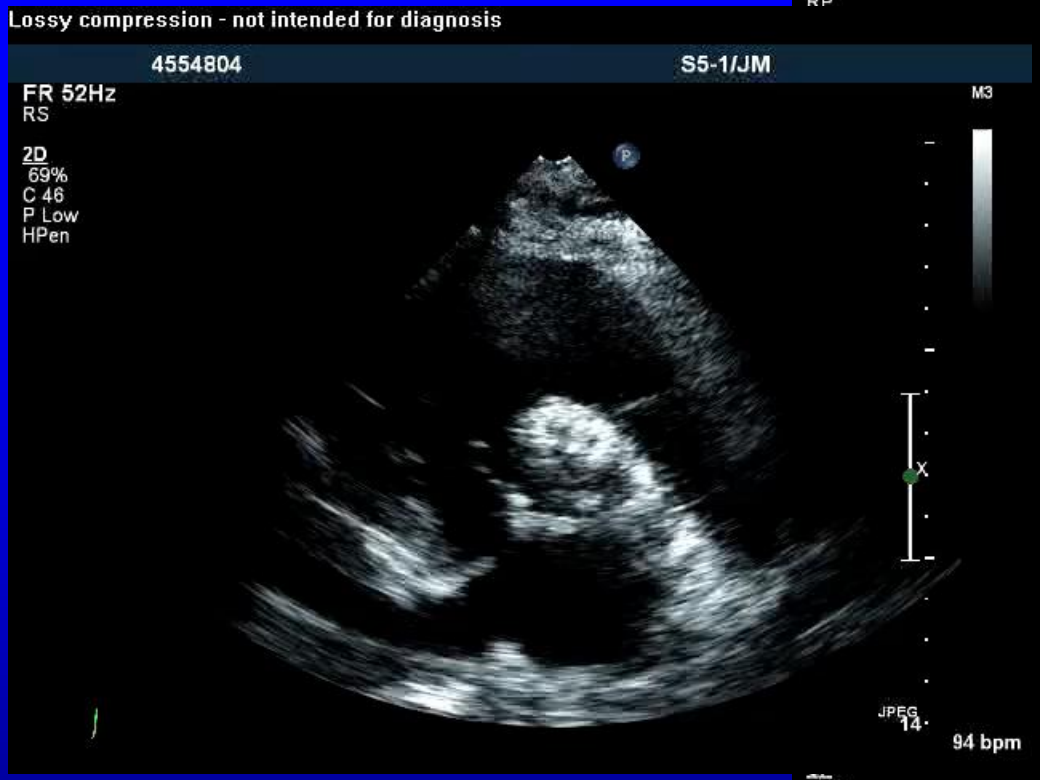
Echo Now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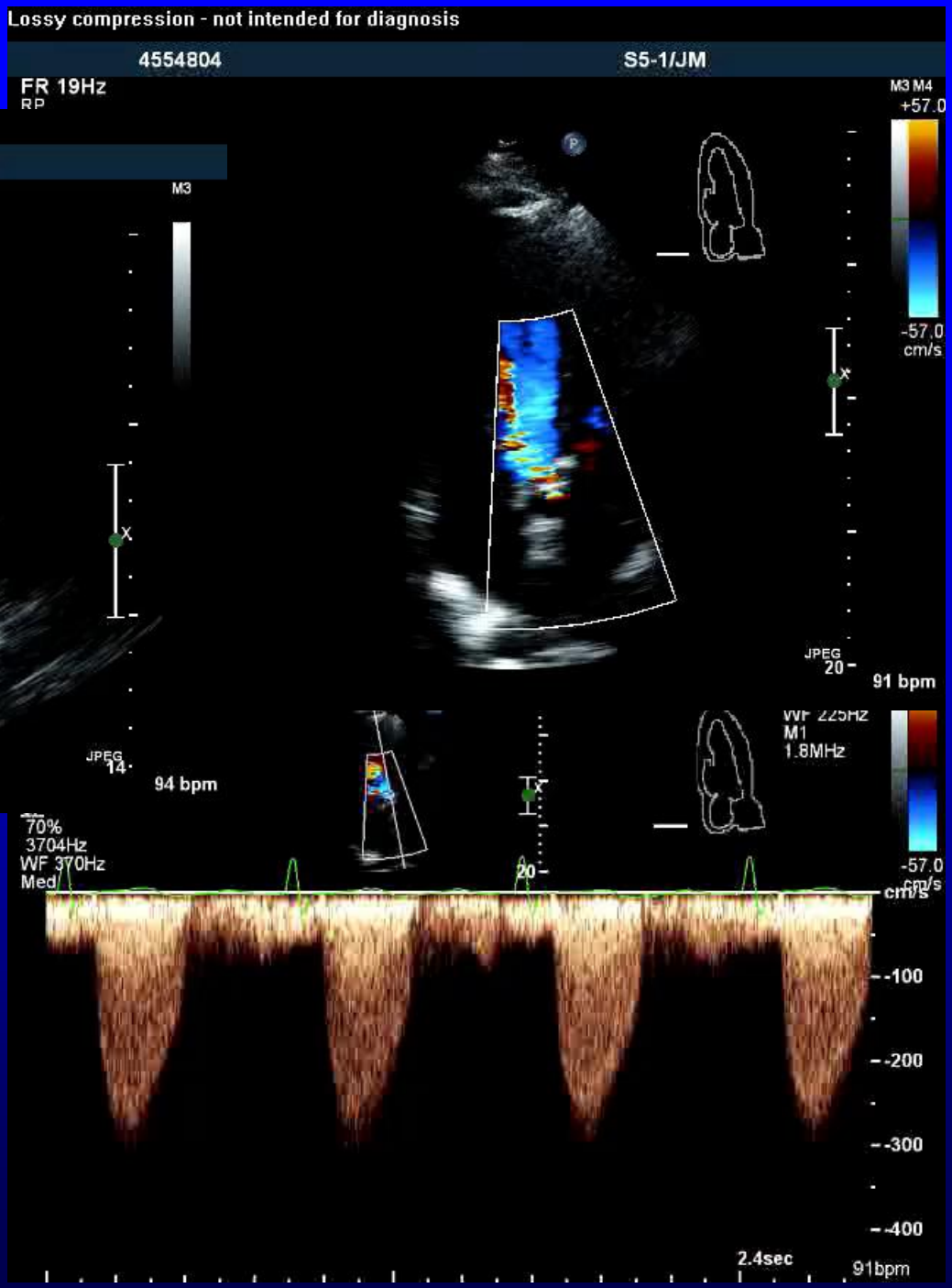
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3704Hz
WF 370Hz
Med
20
cm/s
-100
-200
-300
-400
2.4sec
91bpm

So what would you recommend?

- Any further testing?
- Add lasix?
- What kind of advice do you have for the oncologist?

Why a New Discipline in Cardio-Oncology?

- Demographics of Cardiac and Oncology Patients are similar
- There is a major biologic overlap with targeted therapy
- Sophistication of cardiac testing has increased
- Complex decision making is required for based patient outcomes

In any patient, heart disease and cancer are likely to overlap

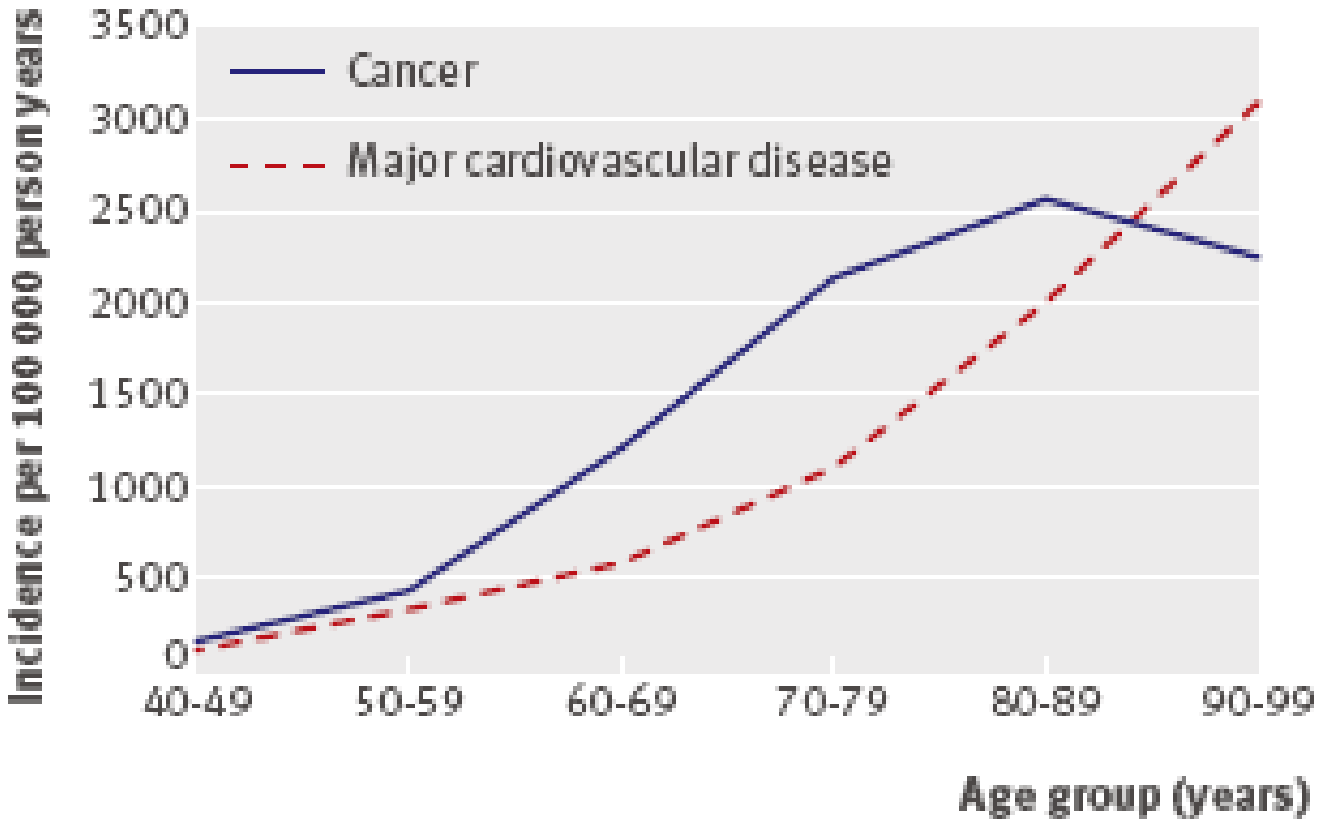


Fig 1 | Crude incidence of overall cancer and major cardiovascular disease by age

Driver BMJ 2008:337:p. 2467

Trends in Five-year Relative Cancer Survival Rates (%), 1975-2009

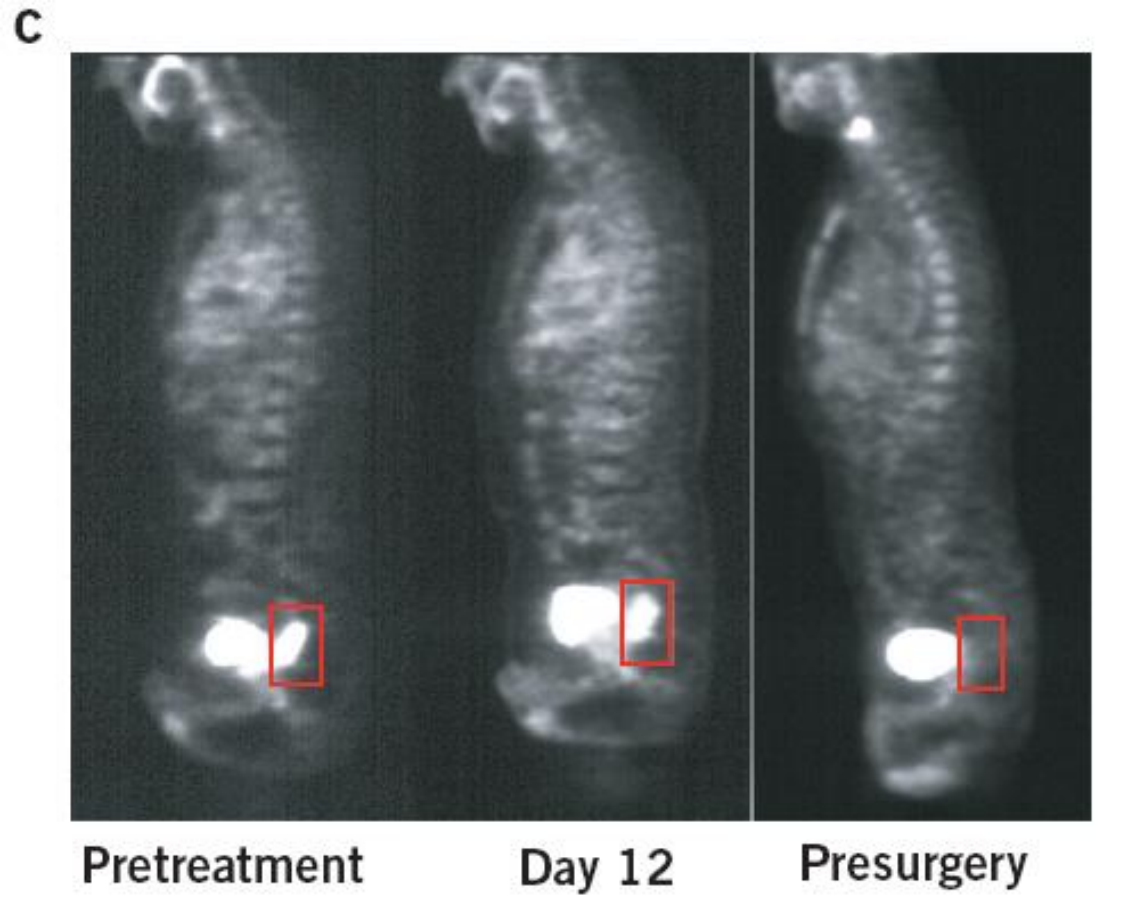
Site	1975-1977	1987-1989	2003-2009
All sites	49	55	68
Breast (female)	75	84	90
Colon	51	60	65
Leukemia	34	43	59
Lung & bronchus	12	13	18
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	71
Ovary	36	38	44
Pancreas	2	4	6
Prostate	68	83	100*
Rectum	48	58	68
Urinary bladder	72	79	80

5-year relative survival rates based on patients diagnosed in the SEER 9 areas from 1975-1977, 1987-1989, and 2003-2009, all followed through 2010.
*99.5%
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2013.

Why a New Discipline in Cardio-Oncology?

- Demographics of Cardiac and Oncology Patients are similar
- There is a major biologic overlap with targeted therapy
- Sophistication of cardiac testing has increased
- Complex decision making is required for based patient outcomes

Anti-VEGF Therapy can decrease blood flow resulting in cancer control

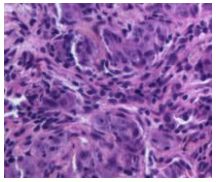


Willitt, JCO 2006

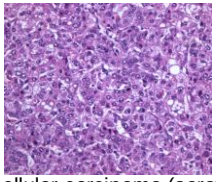
Systemic Effects of Anti-VEGF Therapy

Tumor Tissues

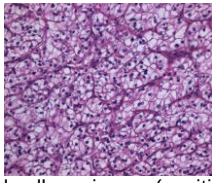
(VEGF upregulated)



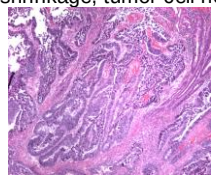
Lung cancer (bevacizumab)
Inhibition of tumor growth, tumor cavitation



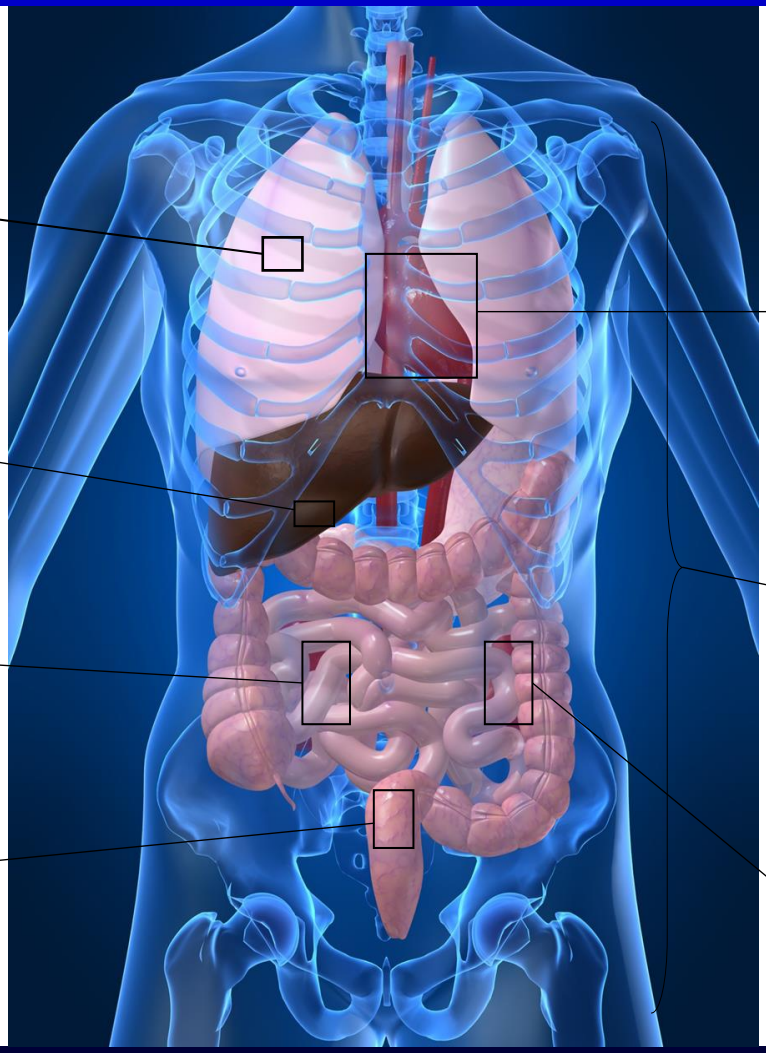
Hepatocellular carcinoma (sorafenib)
Tumor necrosis



Renal cell carcinoma (sunitinib)
Tumor shrinkage, tumor cell necrosis

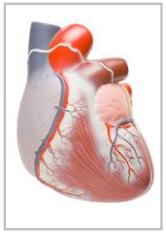


Colorectal cancer (bevacizumab)
Deceleration of tumor growth
efficient chemotherapy delivery

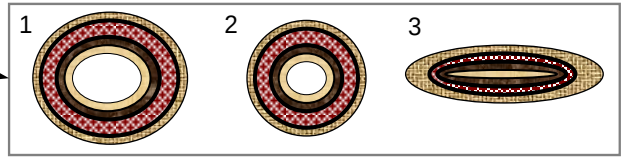


Normal Tissues

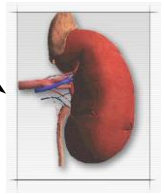
(VEGF constitutively expressed)



Hypertensive remodeling
Microvascular rarefaction
Cardiomyopathy (sunitinib and sorafenib)



Microcirculation: 1. normal arteriole, 2. functional rarefaction (endothelial dysfunction,vasoconstriction), 3. anatomic rarefaction



Thrombotic microangiopathy
Glomerulopathy / glomerulonephritis
Proteinuria
Hypertensive nephropathy

Vaklavos, et al Oncologist 2010, p 130.

Sunitinib, a novel oral chemotherapeutic agent with anti-VEGF properties, is associated with hypertension and heart failure

Table 2. Nature of Cardiotoxicity, Severity of Heart Failure, and Short Term Outcomes

Pt #	BP at baseline	Dose	Duration of drug (days)	Worst NYHA Class	BNP (pg/ml; normal ≤ 100)	LVEF post-drug	HF Therapy	LVEF post Treatment with HF Therapy	Max BP on Drug	Outcome
1	150/72	50	44	4	558	25-30%	ACE-I, B-blocker	25-30%	155/85	Expired in 6 months
2	150/80	50	4	3	3338	30-35%	Nitrates, B-blocker	45-50%	184/110	Expired in 4 months
3	140/94	25	4	4	2110	25-30%	Increased ACE-I	30%	210/110	Expired in 1 month
4*	142/67	25	29	2	409	40-45%	Increased ACE-I	60-65%	174/85	LVEF improved then worsened to 35-40% on sunitinib
5	162/92	50	20	4	409	<20%	Added ACE-I, B-blocker	-	195/97	Expired in 1 month
6	146/75	50	29	3	356	50-55%	B-blocker	-	160/80	HF symptoms improved after sunitinib was discontinued and sinus rhythm was restored

Khakoo, et al, 2008; 112:2500-8

Table 1. Angiogenesis Inhibitors

Angiogenesis inhibitors	Completed trials, phase	Therapeutic target
Monoclonal antibodies		
Bevacizumab *	On phase IV trials	VEGF
Soluble receptor		
VEGF – trap	II	VEGF, PlGF, VEGF-B
Small molecule tyrosine kinase inhibitors		
Sunitinib **	On phase IV trials	VEGFR 1-3, PDGFR-α and -β, c-Kit, FLT3
Sorafenib ***	III	VEGFR 2, VEGFR 3, PDGFR-β, Raf-1, FLT3
Vatalanib	III	VEGFR 1-3, PDGFR-β, c-Kit
Vandetanib	III	VEGFR 2, EGFR, RET
Axitinib	II	VEGFR 1-3, PDGFR, c-Kit
Motesanib diphosphate	II	VEGFR 1-3, PDGFR, c-Kit
Cediranib	II	VEGFR 1-3, PDGFR-β, c-Kit
Semaxinib (SU5416)	II	VEGFR 2, wild-type Kit, wild-type FLT3
CP-547,632[162]	II	VEGFR2, FGFR2
AEE788	II	EGFR, VEGFR1 and 2, c-Abl, c-Src,
Antisense oligonucleotides		
VEGF - AS	I	VEGF mRNA

Newer Chemotherapy with Anti-VEGF properties

Definition of a “Kinase Inhibitor”:

- A drug that interferes with *cell communication and growth* and is sometimes used to treat cancer

Chemotherapeutic Agents in Use Known to Antagonize Vascular Endothelial Growth Factor (anti-VEGF) or have Anti-Angiogenic Properties

- Bevacizumab
- Sunitinib
- Sorafenib
- Vandetanib
- Pazopanib
- Axitinib
- Cabozantinib
- Ramucirumab
- Regorafenib

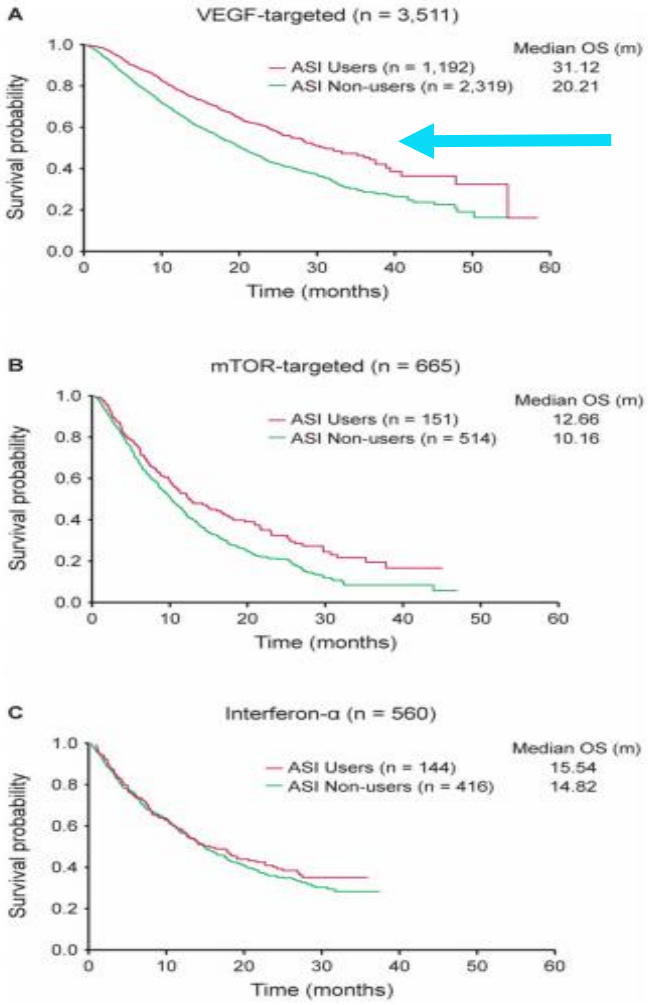


Figure 2.
Kaplan–Meier estimates of A) OS for patients receiving VEGF-targeted therapy, B) OS for patients receiving mTOR-targeted therapy, and C) OS for patients receiving IFN-a therapy stratified by ASI users versus non-users.

In Renal Cell Cancer, renin-angiotensin inhibitors are critical therapies

R McKay et al, Clin Cancer Res. 2015 Jun 1; 21(11): 2471–2479.

The problems are not always LV dysfunction

TABLE 4 Incidences and Risks of Arterial and Venous Thromboembolism Associated With VSP Inhibitors

Agent	Study (Ref. #)	Overall Incidence of VTE (%)	High-Grade VTE (Grade 3-5) (%)	RR of VTE		Study	Overall Incidence of ATE (%)	High-Grade ATE (Grade 3-5) (%)	RR of ATE	
				All-Grade	High-Grade				All-Grade	High-Grade
Bevacizumab (VEGF mAb)	Meta-analysis, 7,956 patients, 15 trials (120)	11.9	6.3	1.33	1.38	Meta-analysis, 12,617 patients, 20 trials (121)	3.3	2.0	1.44	2.14 (high-grade cardiac ischemia)
Pazopanib (TKI)	Meta-analysis, 7,441 patients, 17 trials (sunitinib: 3 trials; sorafenib: 4 trials; pazopanib: 3 trials; vandetanib: 5 trials; axitinib: 2 trials) (122)	2.76	1.92	1.10	0.85	Meta-analysis, 844 patients, 2 trials (123)	1.2	NA	4.61	NA
Sunitinib (TKI)						Meta-analysis, 4,628 patients, 4 trials (124)	1.3	NA	3.1	NA
Sorafenib (TKI)						Meta-analysis, 4,759 patients, 6 trials (124)	1.7	NA	2.39	NA
Axitinib (TKI)						Meta-analysis, 572 patients, 3 trials (123)	1.2	NA	1.17	NA
Vandetanib (TKIs)						Phase III RCT, 623 patients (123)	0	NA	0.13	NA
Regorafenib (TKI)	Phase III RCT in mCRC, 760 patients (125)	2	NA	NA	NA	NA	NA	NA	NA	NA
	Phase III RCT in advanced GIST, 199 patients (126)	No VTE or ATE events reported, but 1 patient in regorafenib arm died from cardiac arrest during treatment								
Cabozantinib (TKI)	Phase III RCT in MTC, 330 patients (112)	5.6	3.7	NA	NA	Phase III RCT in MTC (112)	2.3	0.9	NA	NA
Aflibercept (VEGF trap)	Phase III RCT in mCRC, 1,226 patients (127)	9.3	7.8	NA	NA	Phase III RCT in mCRC, 1,226 patients (127)	2.6	1.8	NA	NA
Ramucirumab (VEGFR2 mAb)	Phase III RCT in advanced gastric or GEJ adenocarcinoma, 665 patients (128)	3.98	2.45	NA	NA	Phase III RCT in advanced gastric or GEJ adenocarcinoma, 655 patients (128)	1.83	0.92	NA	NA
Lenvatinib (TKI)	Phase III trial, 261 patients (116)	5.4	3.8	NA	NA	Phase III trial, 261 patients (116)	5.4	2.7	NA	NA

ATE = arterial thromboembolic event; GEJ = gastroesophageal junction; mAb = monoclonal antibody; mCRC = metastatic colorectal cancer; MTC = medullary thyroid cancer; RCT = randomized controlled trial; TKI = tyrosine kinase inhibitor; VTE = venous thromboembolic event; other abbreviations as in Table 3.

Li, W et al, JACC 2015, p1160-78

Statins are helpful in renal cell cancer especially with anti-VEGF directed therapy

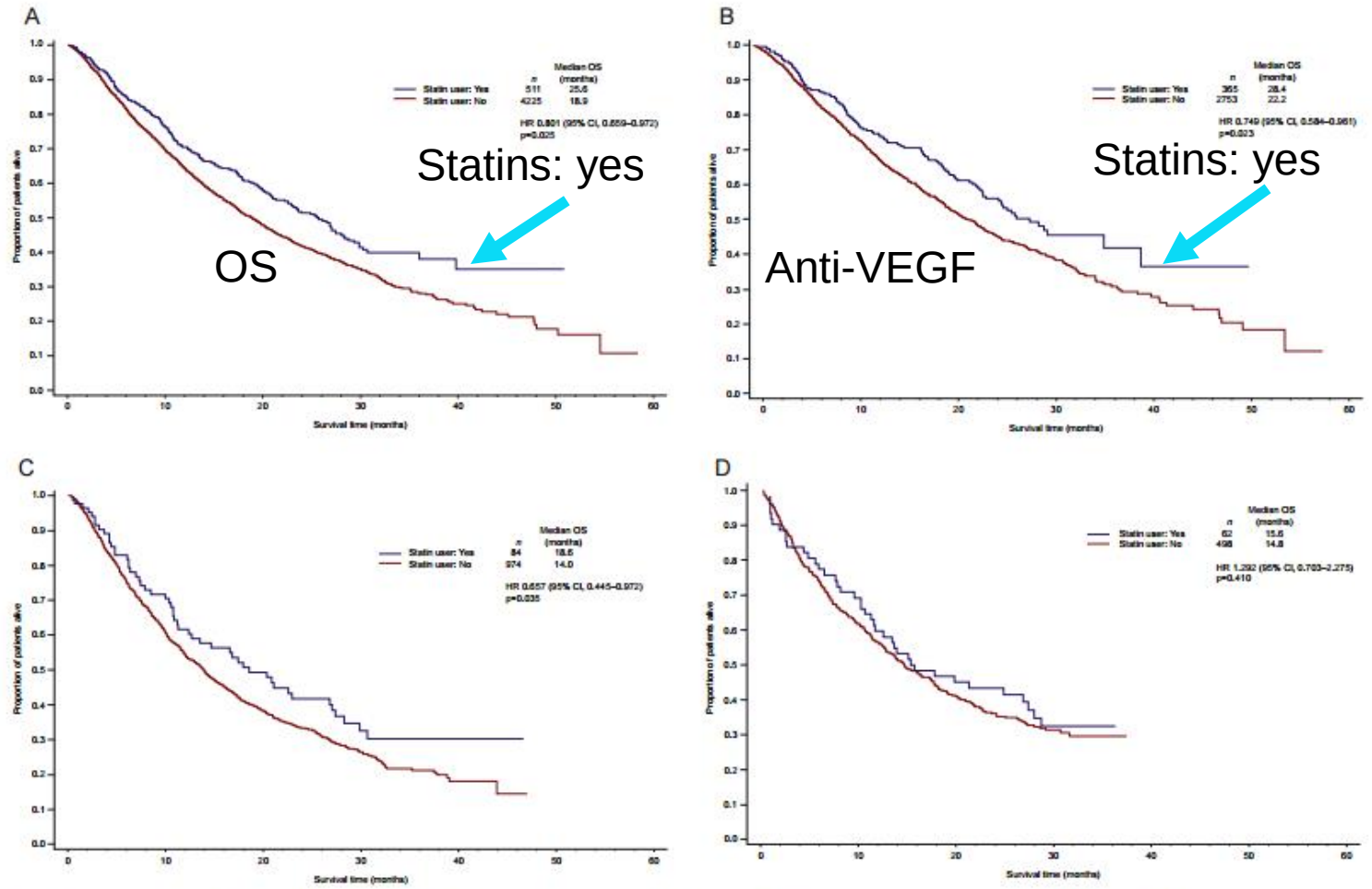


Fig. 1. Kaplan–Meier estimates of OS for (A) the overall cohort, (B) patients receiving VEGF-targeted therapy, (C) patients receiving mTOR-targeted therapy and (D) patients receiving IFN-a therapy stratified by statin users versus non-users.

R McKay et al European Journal of Cancer 52 (2016) 155-162

Why a New Discipline in Cardio-Oncology?

- Demographics of Cardiac and Oncology Patients are similar
- The is a major biologic overlap with targeted therapy
- Sophistication of cardiac testing has increased
- Complex decision making is required for based patient outcomes

How often is cardiac toxicity detected by Echo and MUGA After Four Cycles of AC Chemotherapy?

(NCI-CTC Version 2)

Method	Grade 1		Grade 2	
	No.	%	No.	%
MUGA/MUGA, n = 1,153	203	17.6	84	7.3
ECHO/ECHO, n = 305	40	13.1	12	3.9
MUGA/ECHO, n = 27	5	18.5	2	7.4
ECHO/MUGA, n = 53	10	18.9	3	5.7

Abbreviations: LVEF, left ventricular ejection fraction; NCI-CTC, National Cancer Institute Common Toxicity Criteria; AC, doxorubicin and cyclophosphamide; MUGA, multiple-gated aquisition; ECHO, echocardiogram.

Perez EA et al. J Clin Onco. 2004:22, 3700-3704

JACC Journals

From: Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy: A Systematic Review

J Am Coll Cardiol. 2014;63(25_PA):2751-2768. doi:10.1016/j.jacc.2014.01.073

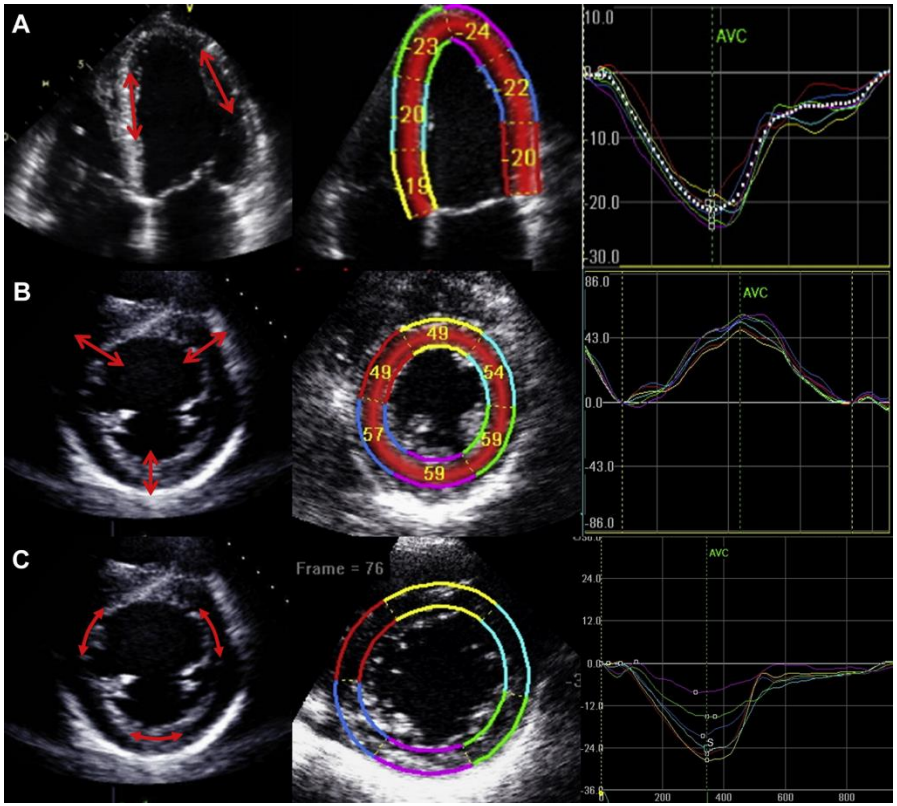


Figure Legend:

Speckle Tracking Echocardiography-Based Peak Systolic Strain Measurements in a Patient With Breast Cancer Prior to Initiation of Cytotoxic Chemotherapy

(A) Global longitudinal strain (GLS), (B) global radial strain (GRS), and (C) global circumferential strain (GCS). The left panels show the direction (arrows demonstrate the direction) in which various strain parameters are being measured. The middle panels demonstrate the segmental strain values (except for circumferential strain). The right panels illustrate the regional strain curves. Circumferential strain curves in the bottom right panel highlight the segmental variability in measurements, illustrating the challenges with this specific strain measurement. Reported normal value for GLS is −19.7% (95% confidence interval [CI] −20.4% to −18.9%), for GRS 47.3% (95% CI: 43.6% to 51.0%), and GCS −23.3% (95% CI: −24.6% to −22.1%) (68). AVC = aortic valve closure.

JACC Journals

From: Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy: A Systematic Review

J Am Coll Cardiol. 2014;63(25_PA):2751-2768. doi:10.1016/j.jacc.2014.01.073

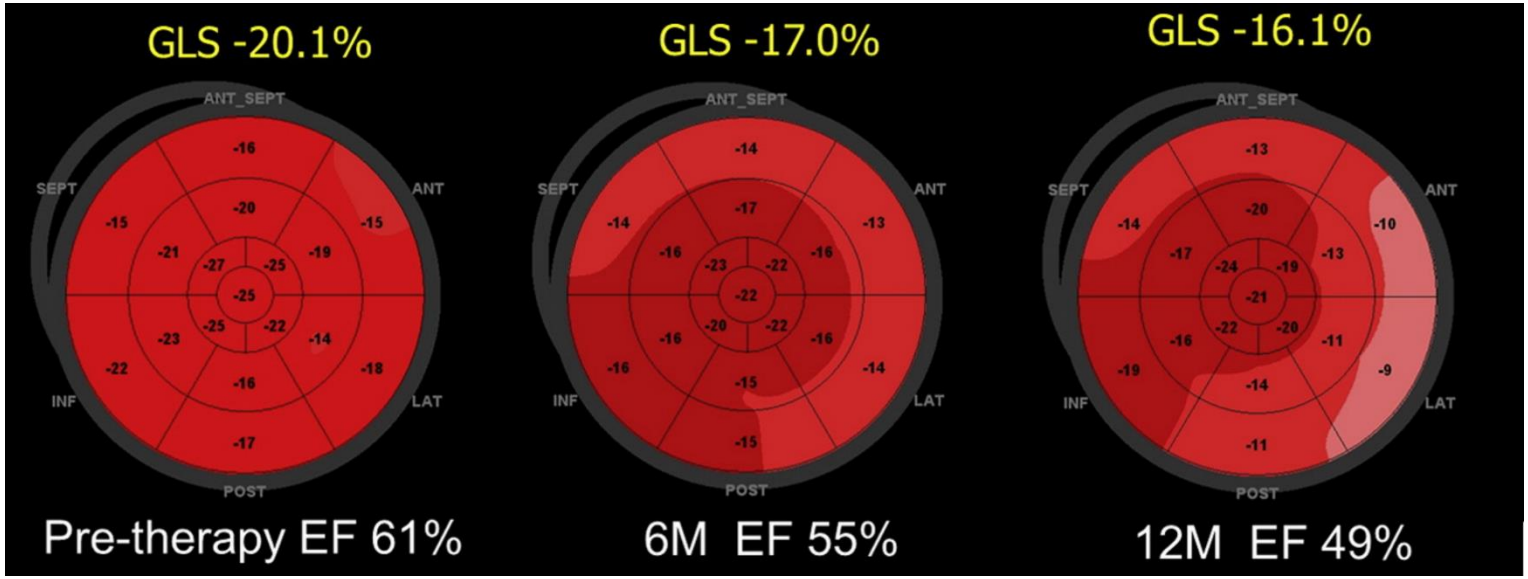


Figure Legend:

The Utility of Early Strain Changes to Predict Subsequent Cardiotoxicity

The images demonstrate a "bull's eye" plot of strain values for each of the 17 myocardial segments. A patient receiving cytotoxic chemotherapy had normal baseline strain and left ventricular (LV) ejection fraction (EF) (left). Six months into therapy, the LVEF dropped by 6% but did not meet criteria for cardiotoxicity. However, the peak systolic global longitudinal strain (GLS) fell by 15.4% (a significant change based on the literature). Then, by 12 months there was a clinically significant fall in LVEF meeting the criteria for cardiotoxicity. See Online Videos 1, 2, and 3 for 4-chamber movie images demonstrating the changes in function. LVEF was calculated using the Biplane Simpson's method. 6M = 6 months; 12M = 12 months.

In the case of HER2+ breast cancer, treatment clearly benefitted the disease but came at a cost

Table 2. Therapeutic Index for Critical Clinical Events.*

Clinical Event	AC-T	AC-T plus Trastuzumab	TCH
		number of events	
Total events	201	146	149
Distant breast-cancer recurrence	188	124	144
Grade 3 or 4 congestive heart failure	7	21	4
Acute leukemia	6	1	1†

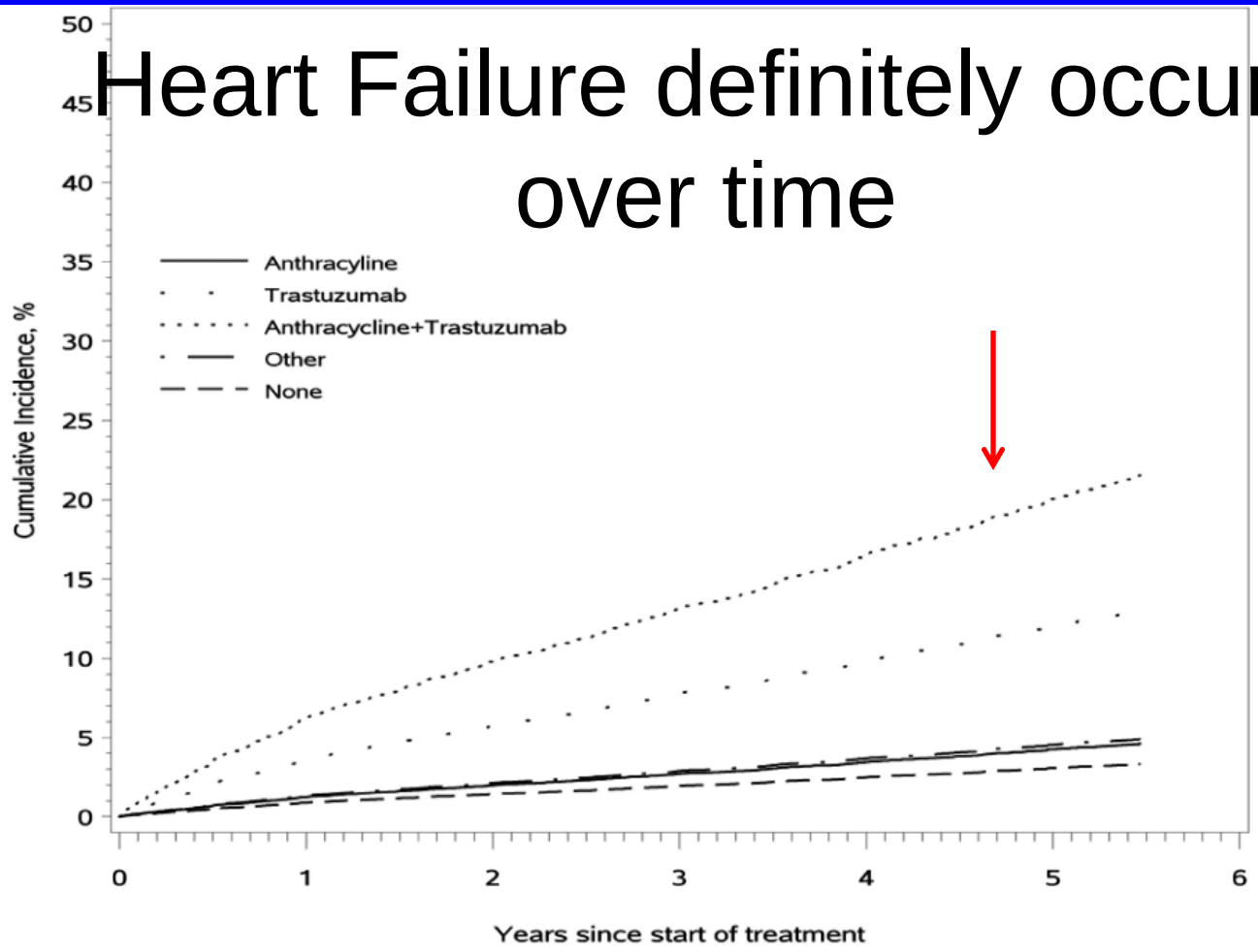
Table 4. Cardiac Risk Factors and Events.*

Variable	AC-T (N=1073)	AC-T plus Trastuzumab (N=1074)	TCH (N=1075)
		number of patients (percent)	
Risk factors			
Diabetes	38 (3.5)	36 (3.4)	28 (2.6)
Hypertension	178 (16.6)	178 (16.6)	190 (17.7)
Obesity†	214 (19.9)	242 (22.5)	234 (21.8)
Hypercholesterolemia	54 (5.0)	47 (4.4)	43 (4.0)
Left-side radiotherapy	378 (35.2)	349 (32.5)	364 (33.9)
Events			
Cardiac-related death	0	0	0
Congestive heart failure‡	7 (0.7)	21 (2.0)	4 (0.4)§
>10% relative reduction in left ventricular ejection fraction¶	114 (11.2)‖	194 (18.6)	97 (9.4)**

Is it enough to just detect cardiotoxicity?

Slamon D et al; NEJM 2011:365:1273-83

Heart Failure definitely occurs over time



No. of patients at risk	Year 1	Year 2	Year 3	Year 4	Year 5
Anthracycline only	3443	3125	2699	2146	1659
Trastuzumab only	90	78	49	24	13
Anthracycline+ Trastuzumab	347	339	263	179	94
Other chemotherapy	2159	1905	1548	1192	958
None	5235	4798	4076	3288	2590
Cumulative incidence (95% CI), %					
Anthracycline only	1.2 (1.0 to 1.5)	2.0 (1.6 to 2.4)	2.7 (2.2 to 3.2)	3.5 (2.8 to 4.1)	4.3 (3.5 to 5.0)
Trastuzumab only	3.6 (1.5 to 5.6)	5.8 (2.5 to 8.9)	7.8 (3.4 to 12.0)	9.9 (4.3 to 15.1)	12.1 (5.3 to 18.3)
Anthracycline+ Trastuzumab	6.2 (4.1 to 8.2)	9.8 (6.7 to 12.8)	13.2 (9.1 to 17.1)	16.5 (11.5 to 21.3)	20.1 (14.0 to 25.6)
Other chemotherapy	1.3 (1.0 to 1.6)	2.1 (1.7 to 2.5)	2.9 (2.4 to 3.4)	3.7 (3.0 to 4.3)	4.5 (3.7 to 5.3)
None	0.9 (0.7 to 1.0)	1.4 (1.2 to 1.7)	1.9 (1.6 to 2.3)	2.5 (2.1 to 2.9)	3.1 (2.6 to 3.5)

Bowles, Erin et al JNCI 2012 p1293

Table 5 Deaths and Cardiovascular Treatments of Patients Who Underwent MUGA Imaging Compared With Echocardiographic Imaging Before Cancer Therapy

	MUGA (n = 88)	Echo (n = 88)	p Value*
Deaths, n (%)	20 (23)	18 (20)	0.71
LVEF <55%, n (%)	16 (18)	35 (40)	0.002
Deaths within group LVEF <55%, n (%)	2 (13)	10 (29)	0.21
Cardiovascular treatments, n (%)			
Patients with LVEF <55% who received ACEI/ARB	4 (25)	14 (40)	0.30
Patients with LVEF <55% who received beta-blocker	1 (6)	18 (51)	0.002
Patients with LVEF <55% who received cardiology consultation	3 (19)	19 (54)	0.02

*p value calculated using chi-square analysis.
Abbreviations as in Tables 1 and 4.

Yoon et al JACC 2010

Table 2. Clinical Characteristics and Cardiac Events During Follow-Up of Patients With Full, Partial, and No Recovery From Cardiac Dysfunction

	Full Recovery (n=25)	Partial Recovery (n=160)	No Recovery (n=41)	*P* Value
Age, y	52±11	50±13	53±14	0.22
Women, n (%)	23 (92)	124 (77)	27 (65)	<0.001
Hypertension, n (%)	6 (24)	44 (27)	10 (24)	0.99
Diabetes mellitus, n (%)	3 (12)	7 (4)	4 (10)	0.13*
Coronary artery disease, n (%)	2 (8)	4 (3)	2 (5)	0.18*
Hypercholesterolemia, n (%)	3 (12)	14 (9)	4 (10)	0.81*
NYHA class III–IV, n (%)	2 (8)	27 (17)	14 (34)	0.02*
Creatinine clearance,† mL/min	97±34	104±29	116±51	0.56
Cumulative AC dose,‡ mg/m²	283±94	314±129	346±150	0.12
Mediastinum RT, § n (%)	1 (4)	12 (7)	3 (7)	1.00*
Body mass index, kg/m²	25±5	24±4	25±5	0.73
LVEF before ACT, %	59±3	61±4	61±4	0.002
LVEF at the end of ACT, %	57±6	56±5	55±4	0.06
LVEF before HF therapy, %	42±8	41±7	33±9	<0.001
LVEF at the end of the study, %	61±4	54±3	38±9	by definition
Mean enalapril dose, mg	10±6	10±6	8±5	0.24
Mean carvedilol dose, mg	16±7	17±10	14±6	0.42
Mean bisoprolol dose, mg	2.1±0.8	2.3±1.4	2.4±1.4	0.81
Enalapril only, n (%)	0 (0)	12 (7)	6 (15)	0.12*
β-Blocker only, n (%)	0 (0)	3 (2)	0 (0)	1.00*
Enalapril + β-blocker, n (%)	25 (100)	145 (91)	31(75)	0.004
Cumulative events, n (%)	2 (8)	27 (17)	19 (46)	0.001*
Cardiac death	0 (0)	2 (1)	4 (10)	
Acute pulmonary edema	0 (0)	2 (1)	3 (7)	
HF requiring hospitalization	0 (0)	1 (0.5)	3 (7)	
Acute coronary syndrome	0 (0)	4 (2.5)	2 (5)	
Life-threatening arrhythmias	2 (3)	14 (8)	5 (12)	
ICD implantation	0 (0)	0 (0)	(0)	
Conduction disturbances requiring pacemaker implantation	0 (0)	3 (2)	2 (5)	

Data are expressed as numbers (%) or mean±SD except for time to HF treatment expressed as median (Q1–Q3). HF indicates heart failure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and SD, standard deviation.

*By Fisher exact text.

Early detection and **treatment** is important for recovery

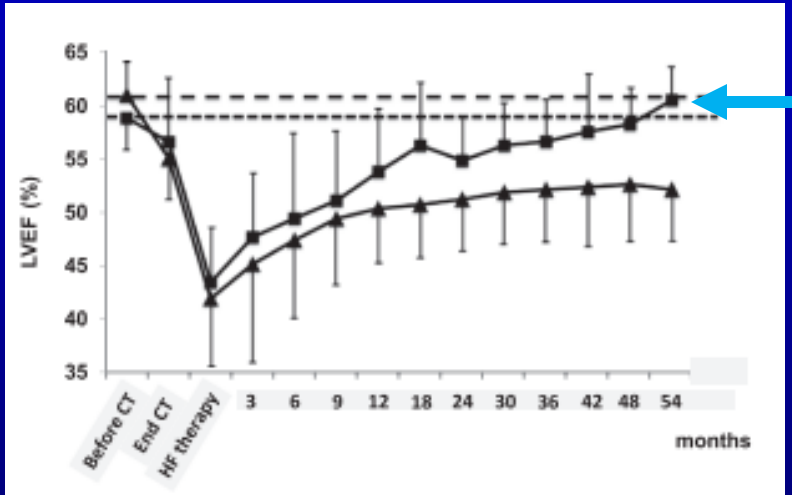
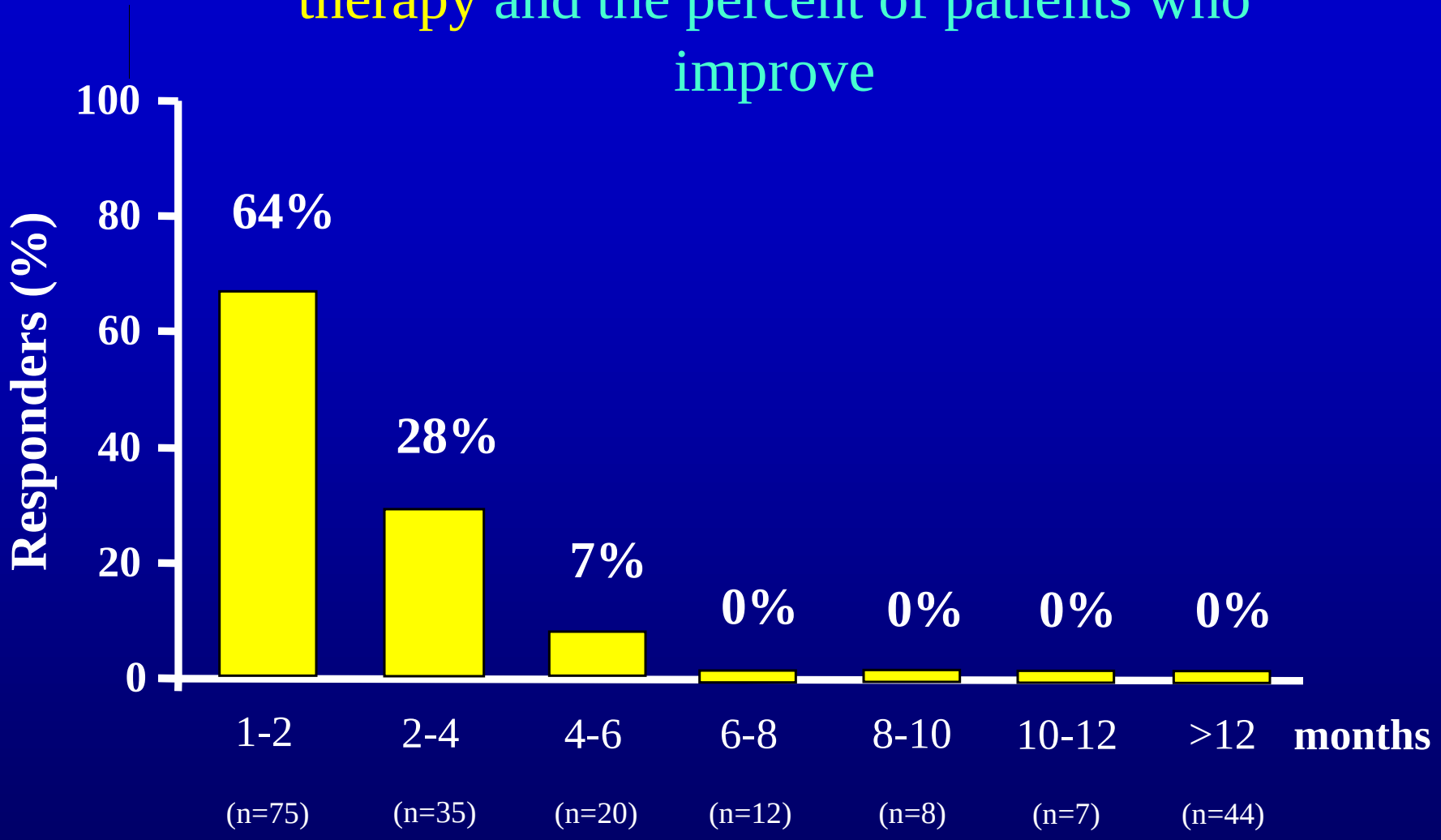


Figure 3. Left ventricular ejection fraction (LVEF) in patients with cardiotoxicity and with partial (triangle) or full (square) recovery with heart failure therapy. Data are mean±SD. CT indicates chemotherapy; HF, heart failure; and SD, standard deviation.

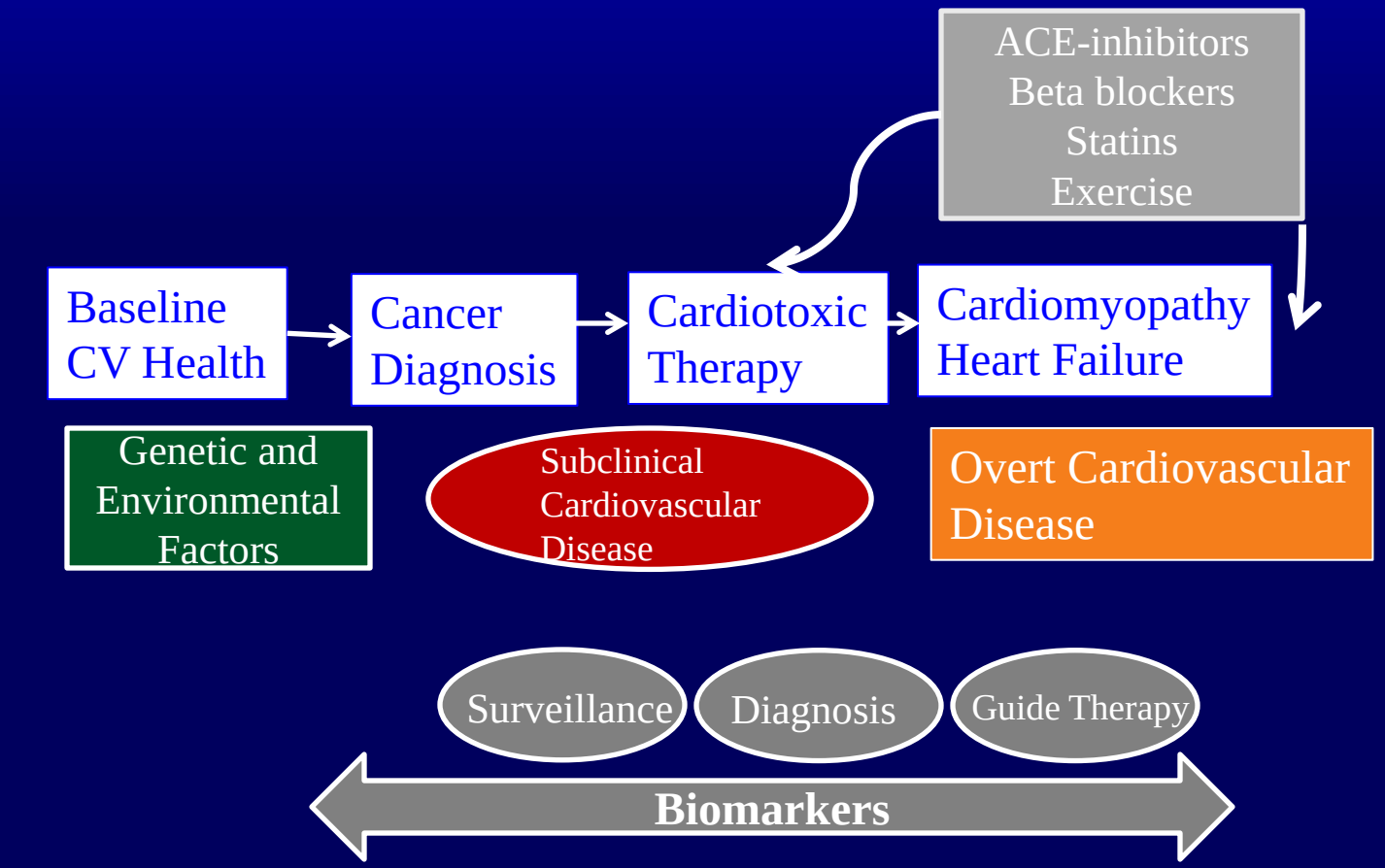
Cardinale, D Circ 6.2015; p1981-1988

The effect of time for initiation of HF therapy and the percent of patients who improve



D Cardinale, et al. JACC 2010, jan 26.

What is the Role for Biomarkers in Cardio-Oncology?



Adapted from Wang, et al. Circulation. 2011. Khouri, et al. Circulation. 2012.

Troponin I is valuable in detecting Cardiotoxicity

TABLE 3. Cardiac Events In the Study Groups

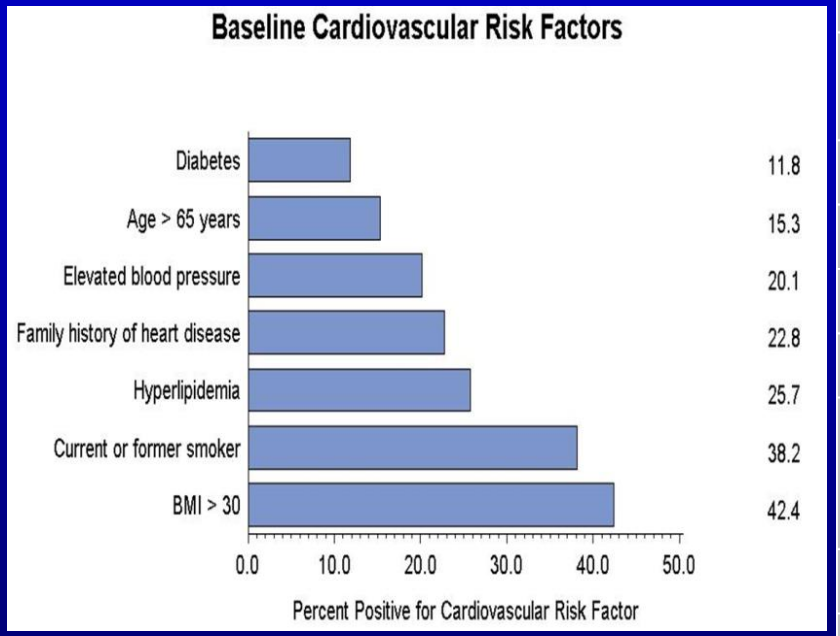
	Total (n=703)	$TnI^{-/-}$ (n=495)	$TnI^{+/-}$ (n=145)	$TnI^{+/+}$ (n=63)
Sudden death	3 (0.4)	0 (0)	0 (0)	3 (5)
Cardiac death	2 (0.3)	0 (0)	0 (0)	2 (3)
Acute pulmonary edema	3 (0.4)	0 (0)	1 (0.7)	2 (3)
Heart failure	47 (7)	1 (0.2)	18 (12)	28 (44)
Asymptomatic left ventricular dysfunction	37 (5)	2 (0.4)	24 (17)	11 (17)
Life-threatening arrhythmias	17 (2)	2 (0.4)	10 (7)	5 (8)
Conduction disturbances requiring pacemaker implantation	2 (0.3)	0 (0)	0 (0)	2 (3)
Cumulative events	111 (16)	5 (1)	53 (37)*	53(84)*†

Values are given as n (%).

*$P<0.001$ vs $TnI^{-/-}$ group; †$P<0.001$ vs $TnI^{+/-}$ group.

Cardinale et al. Circ. 2004;109:2749-2754

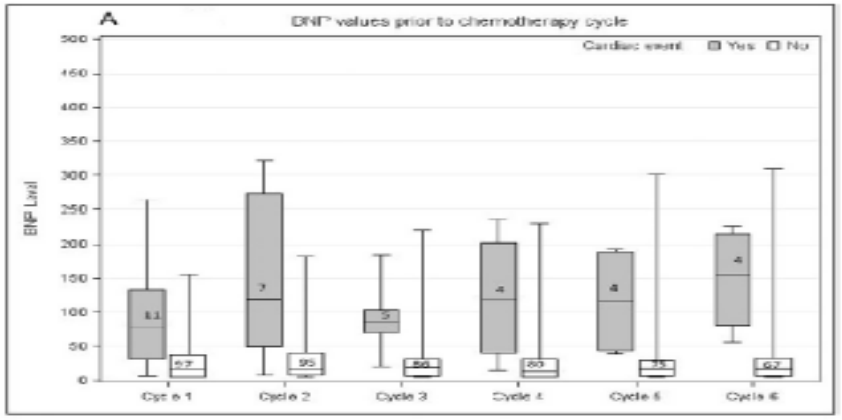
PREDICT: Demographics and risk of cardiotoxicity ASCO 2014 Abstract 9624

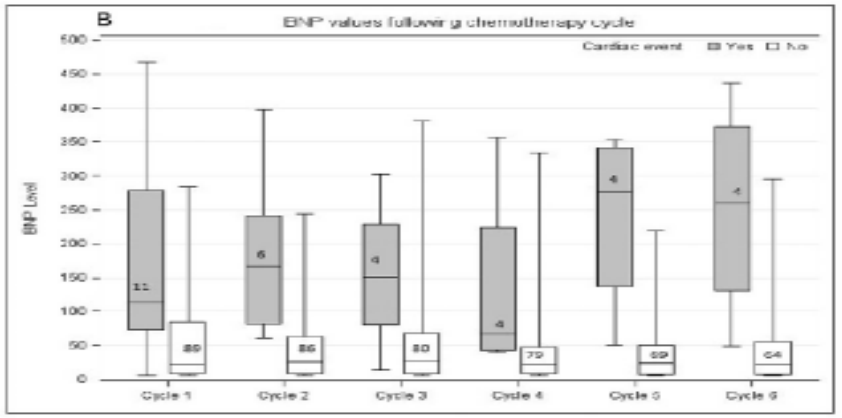


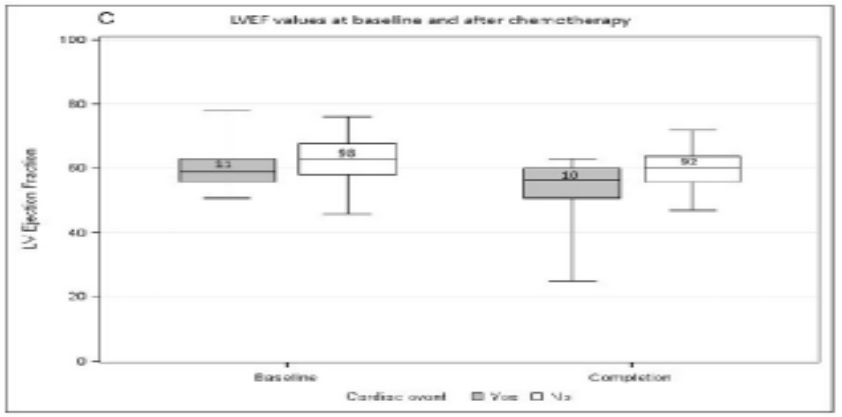
Patient Characteristic	Odds ratio (95% CI)			P
Age at registration	1.04	1.02	1.07	0.0004
Race / ethnicity, nonwhite or Hispanic (ref. Caucasian)	1.20	0.67	2.15	0.5446
Sex, Male (ref. Female)	2.68	1.45	4.96	0.0017
Number of CV risk factors including age	1.27	1.07	1.51	0.0076
Tobacco use, prior or current (ref. Never)	1.16	0.67	2.03	0.5931
Elevated blood pressure	1.45	0.77	2.74	0.2482
Hyperlipidemia	0.88	0.46	1.70	0.7037
Diabetes	1.47	0.68	3.18	0.3238
Previous cardiomyopathy	7.02	2.07	23.80	0.0018
Cancer diagnosis, Lymphoma (ref. Breast) Other (ref. Breast)	 1.98 4.97	 1.08 1.98	 3.66 12.43	 0.0285 0.0006
Prior chest irradiation	1.95	0.40	9.40	0.4070
Prior anthracycline use	12.07	1.97	73.80	0.0070
BNP > 100 pg/ml at baseline	2.08	1.09	3.97	0.0260

What factors can help us identify who to target for treatment?

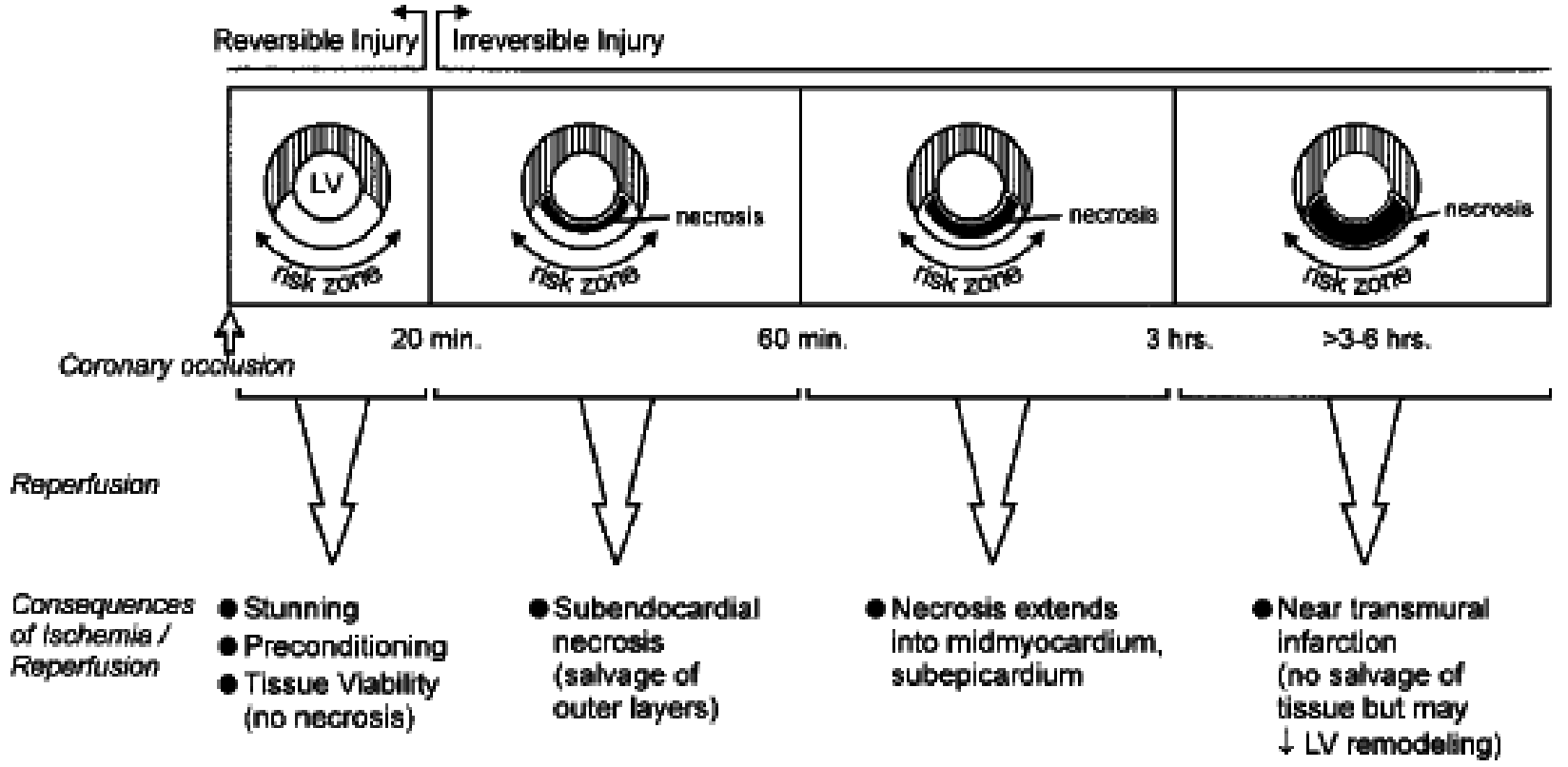
BNP was useful in detecting cardiotoxicity during each cycle whereas EF change did not appear to be sufficiently sensitive







In regards to *Ischemic* insults, we have a paradigm



Kloner et al, Circ 2001; p2981

Why a New Discipline in Cardio-Oncology?

- Demographics of Cardiac and Oncology Patients are similar
- The is a major biologic overlap with targeted therapy
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- Complex decision making is required for based patient outcomes

From: The Frequency and Severity of Cardiovascular Toxicity From Targeted Therapy in Advanced Renal Cell Carcinoma Pati

JCHF. 2013;1(1):72-78. doi:10.

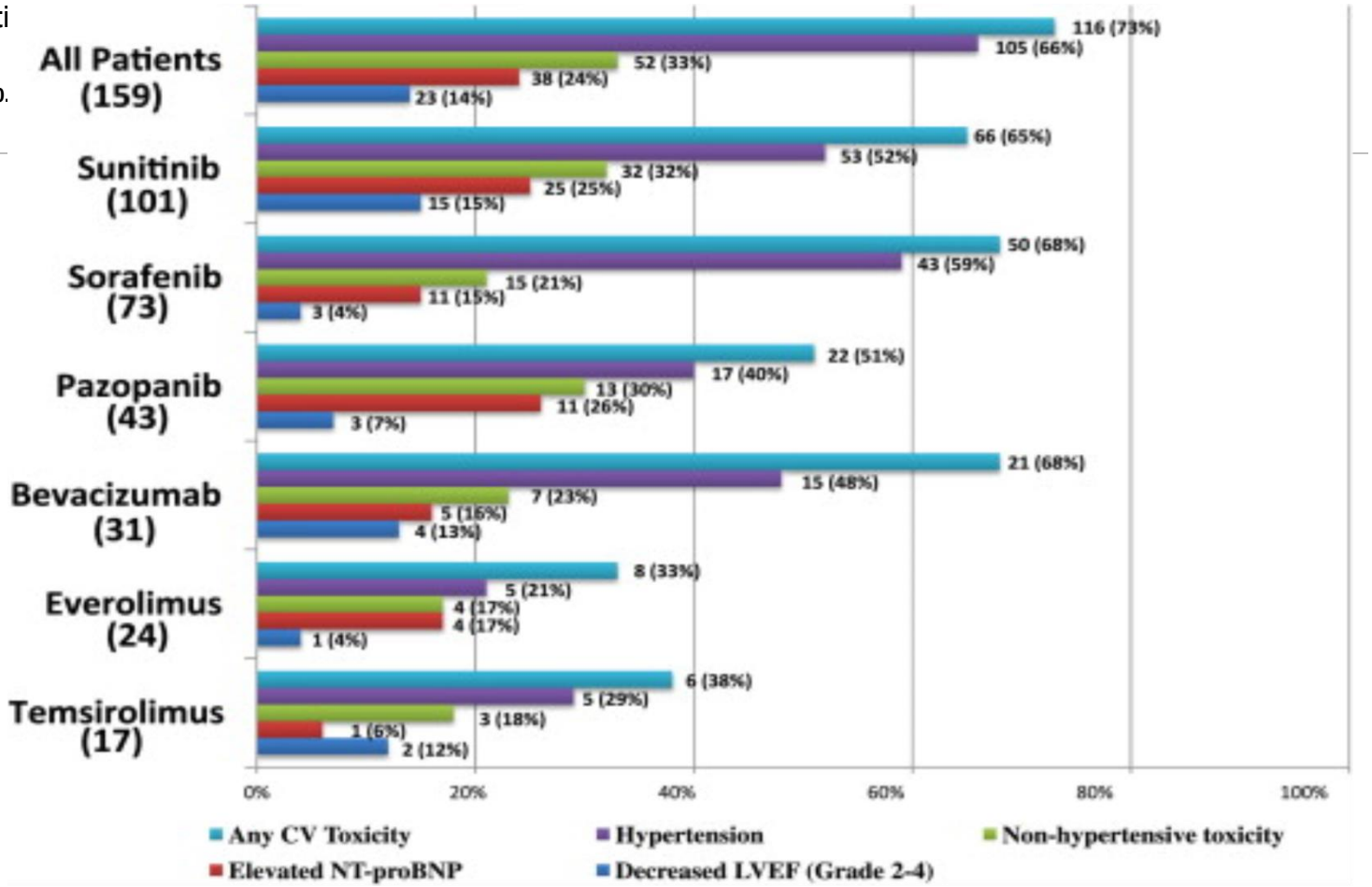

Figure Legend:

Incidence of Cardiovascular Toxicity by Type

The incidence of cardiovascular toxicity varied by type of toxicity and by chemotherapy agent received. Many patients received multiple therapies in succession and are included only once in "All Patients." CV = cardiovascular; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal B-type natriuretic peptide.

From: The Frequency and Severity of Cardiovascular Toxicity From Targeted Therapy in Advanced Renal Cell Carcinoma Patients

JCHF. 2013;1(1):72-78. doi:10.1016/j.jcl

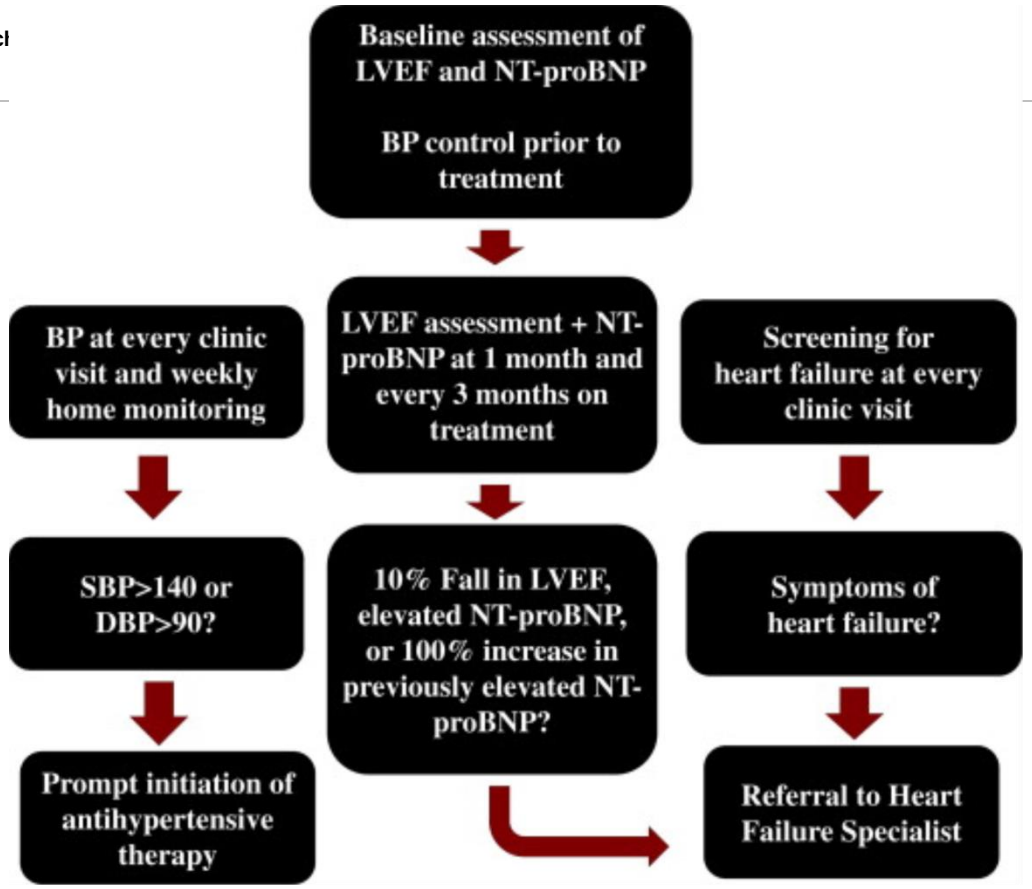

Figure Legend:

The Stanford Monitoring Algorithm for Targeted Therapies

Cardiovascular monitoring algorithm for patients with renal cell carcinoma receiving targeted chemotherapy. BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure; other abbreviations as in Figure 1.

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC)

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[1] **Representing the International CardiOncology Society (ICOS)**

Pocket Guidelines and smartphone app also available!

Table 6 Proposed diagnostic tools for the detection of cardiotoxicity

Technique	Currently available diagnostic criteria	Advantages	Major limitations
Echocardiography: **- 3D-based LVEF** **- 2D Simpson's LVEF** **- GLS**	• LVEF: >10 percentage points decrease to a value below the LLN suggests cardiotoxicity. • GLS: >15% relative percentage reduction from baseline may suggest risk of cardiotoxicity.	• Wide availability. • Lack of radiation. • Assessment of haemodynamics and other cardiac structures.	• Inter-observer variability. • Image quality. • GLS: inter-vendor variability, technical requirements.
Nuclear cardiac imaging (MUGA)	• >10 percentage points decrease in LVEF with a value <50% identifies patients with cardiotoxicity.	• Reproducibility.	• Cumulative radiation exposure. • Limited structural and functional information on other cardiac structures.
Cardiac magnetic resonance	• Typically used if other techniques are non-diagnostic or to confirm the presence of LV dysfunction if LVEF is borderlines.	• Accuracy, reproducibility. • Detection of diffuse myocardial fibrosis using T1/T2 mapping and ECVF evaluation.	• Limited availability. • Patient's adaptation (claustrophobia, breath hold, long acquisition times).
Cardiac biomarkers: **- Troponin I** **- High-sensitivity Troponin I** **- BNP** **- NT-proBNP**	• A rise identifies patients receiving anthracyclines who may benefit from ACE-Is. • Routine role of BNP and NT-proBNP in surveillance of high-risk patient needs futher investigation.	• Accuracy, reproducibility. • Wide availability. • High-sensitivity.	• Insufficient evidence to establish the significance of subtle rises. • Variations with different assays. • Role for routine surveillance not clearly established.

ACE-Is = angiotensin converting enzyme inhibitors; BNP = B-type natriuretic peptide; ECVF = extracellular volume fraction; GLS = global longitudinal strain; LV = left ventricular; LLN = lower limit of normality; LVEF = left ventricular ejection fraction; MUGA = multigated radionuclide angiography; NT-proBNP = N-terminal fragment B-type natriuretic peptide.

- Can Cardiotoxicity be Prevented?

"An ounce of prevention is worth a pound of cure"

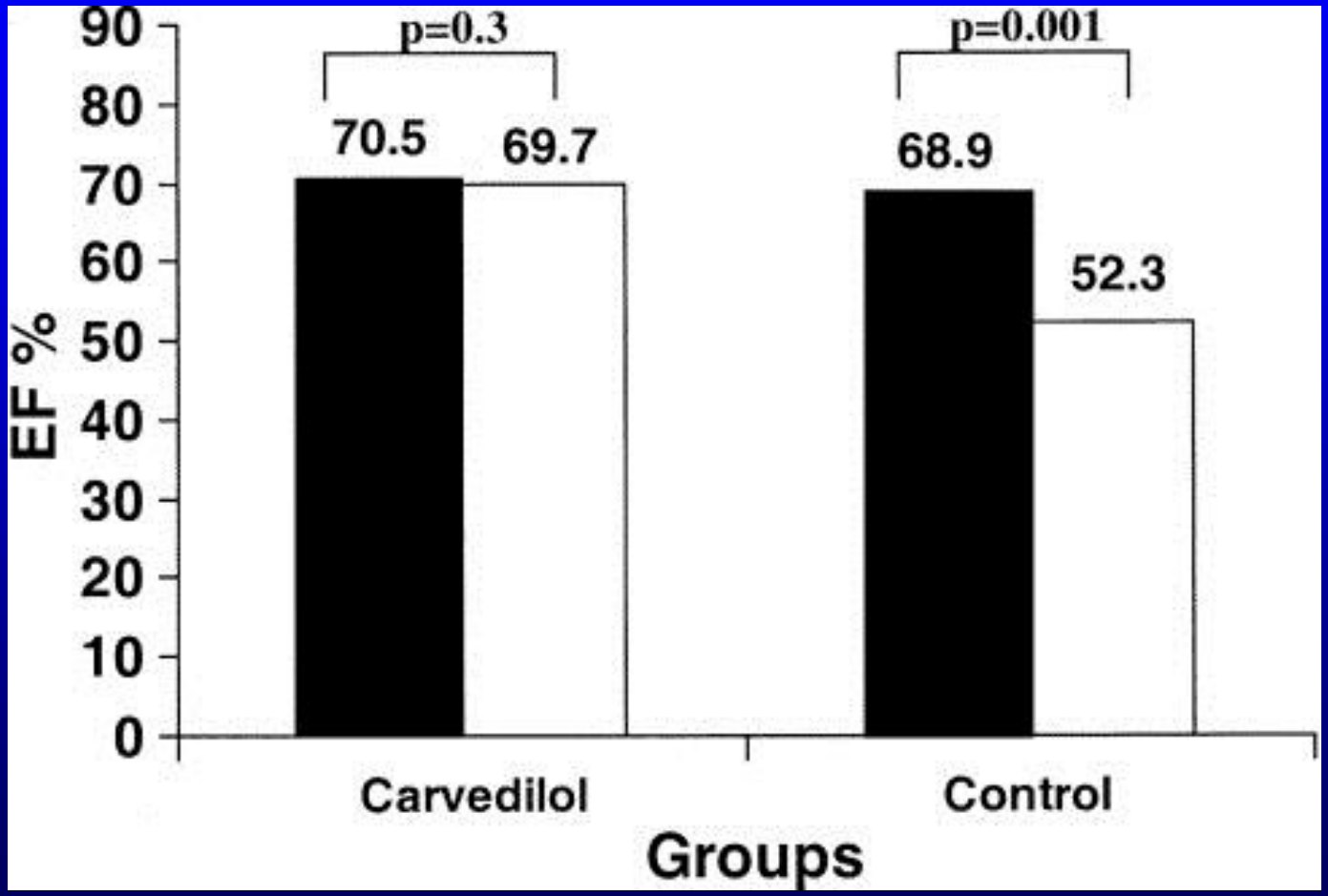
ACE Inhibition appears quite important in preventing heart failure

	Total (n=114), n (%)	ACEI Group (n=56), n (%)	Control Subjects (n=58), n (%)	*P*
Sudden death	0 (0)	0 (0)	0 (0)	1.0*
Cardiac death	2 (2)	0 (0)	2 (3)	0.49*
Acute pulmonary edema	4 (3)	0 (0)	4 (7)	0.07*
Heart failure	14 (12)	0 (0)	14 (24)	<0.001
Arrhythmias requiring treatment	11 (10)	1 (2)	10 (17)	0.01
Cumulative events	31	1	30	<0.001

*Fisher exact test.

Cardinale D et al. Circulation. 2006;114:2474-2481

Carvedilol appears protective during adriamycin based chemotherapy



Data expressed as mean values.

Kalay et al. JACC. Dec 2006. 48:2258-62

Statin therapy prior to and during chemotherapy prevented HF

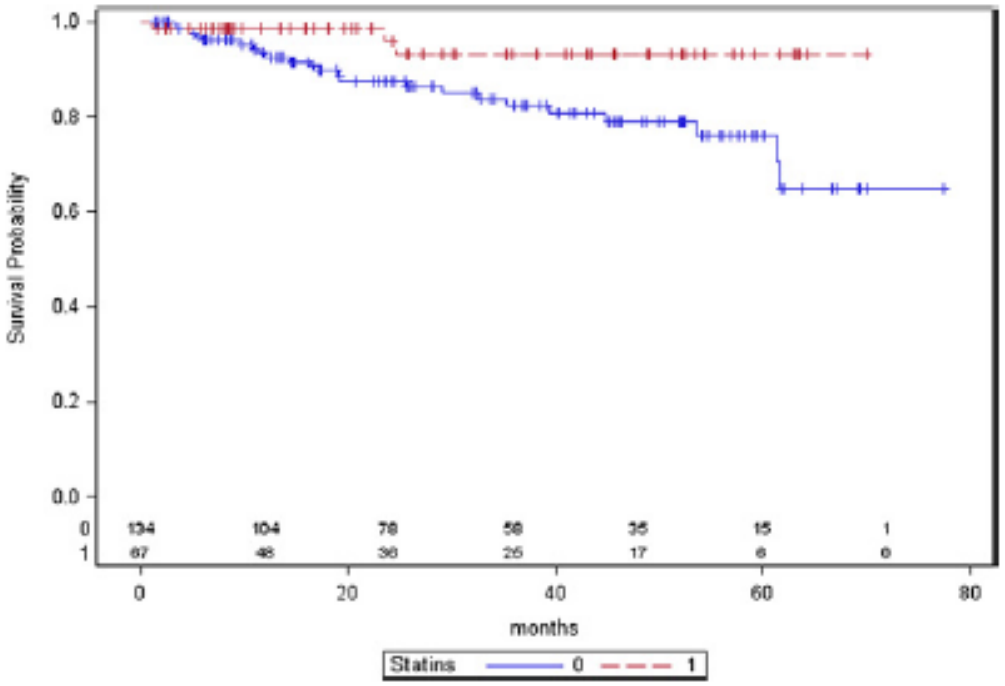


Figure 1 **Heart Failure-Free Survival**

These survival curves illustrate survival in statin **(red)** and non-statin **(blue)** treated groups. Figures above the abscissa relate to numbers of patients surviving without heart failure at each 12-month interval.

JACC 2012, p 2384

The combination of ACE/BB can prevent cardiotoxicity

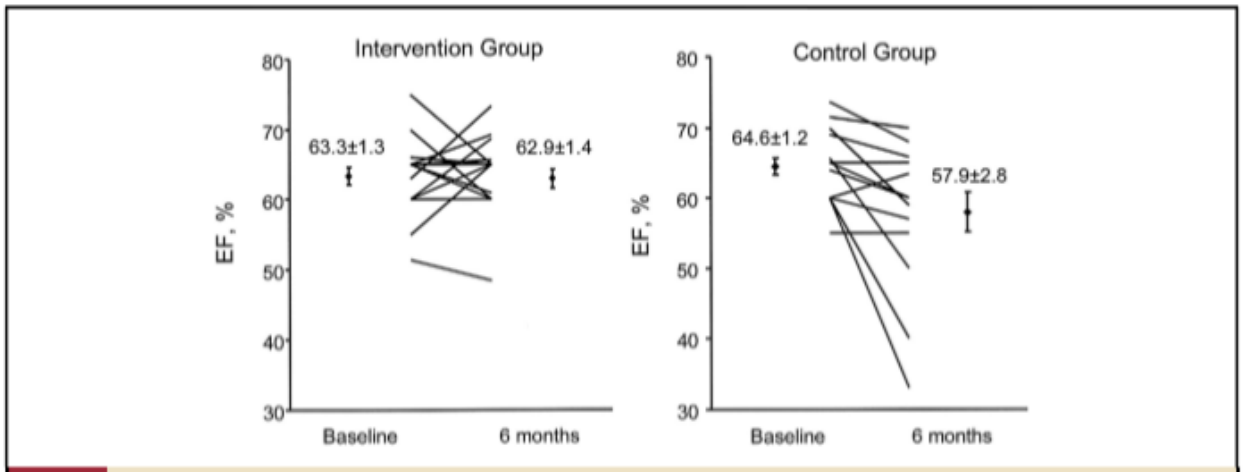


Figure 2 Change From Baseline in LVEF in Acute Leukemia Patients Undergoing Chemotherapy in the Intervention and Control Groups

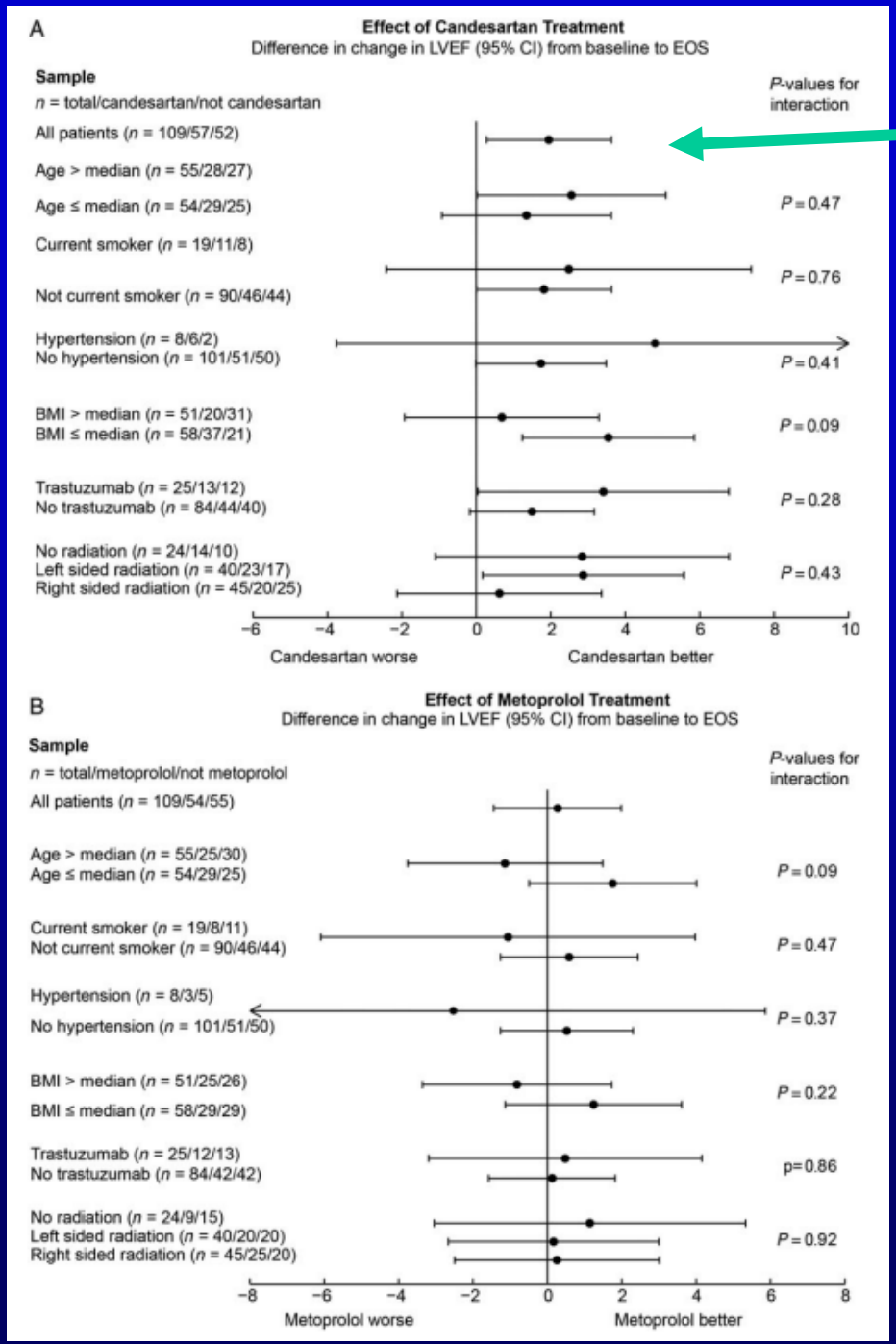
While no differences were observed in the intervention group, patients in the control group had a 6.7% absolute decrease in their mean left ventricular ejection fraction (LVEF) ($p = 0.025$), with all but 3 patients having some degree of LVEF reduction. Values are mean ± SEM.

Table 4 Clinical Endpoints

	Enalapril + Carvedilol	Control	p Value
Premature end of the study (%)	3 (6.7)	11 (24.4)	0.02
Total mortality (%)	3 (6.7)	8 (17.8)	0.11
Death or heart failure (%)	3 (6.7)	10 (22.2)	0.036
Death, heart failure or final LVEF<45% (%)	3 (6.7)	11 (24.4)	0.020
≥10% decrease in LVEF with a final LVEF<50% (%)	2 (4.8)	2 (5.4)	0.90
Heart failure or ≥10% decrease in LVEF (%)	4 (9.5)	7 (19)	0.22
Severe adverse events* (%)	9 (20)	15 (33)	0.15

Values are n (%). *Defined as a serious adverse event that resulted in death or was life-threatening.
LVEF = left ventricular ejection fraction.

Bosch, X et al, JACC 2013, p 2355



Candesartan is modestly protective, but not metoprolol

PRADA. Gulati, G et al. European Heart Journal 2016 doi:10.1093/eurheartj/ehw022

Are there **inhibitors** on the cancer therapy horizon that could be concerning for the development of Cardiovascular Events??

There is a balance between protein synthesis and degradation

The NEW ENGLAND JOURNAL of MEDICINE

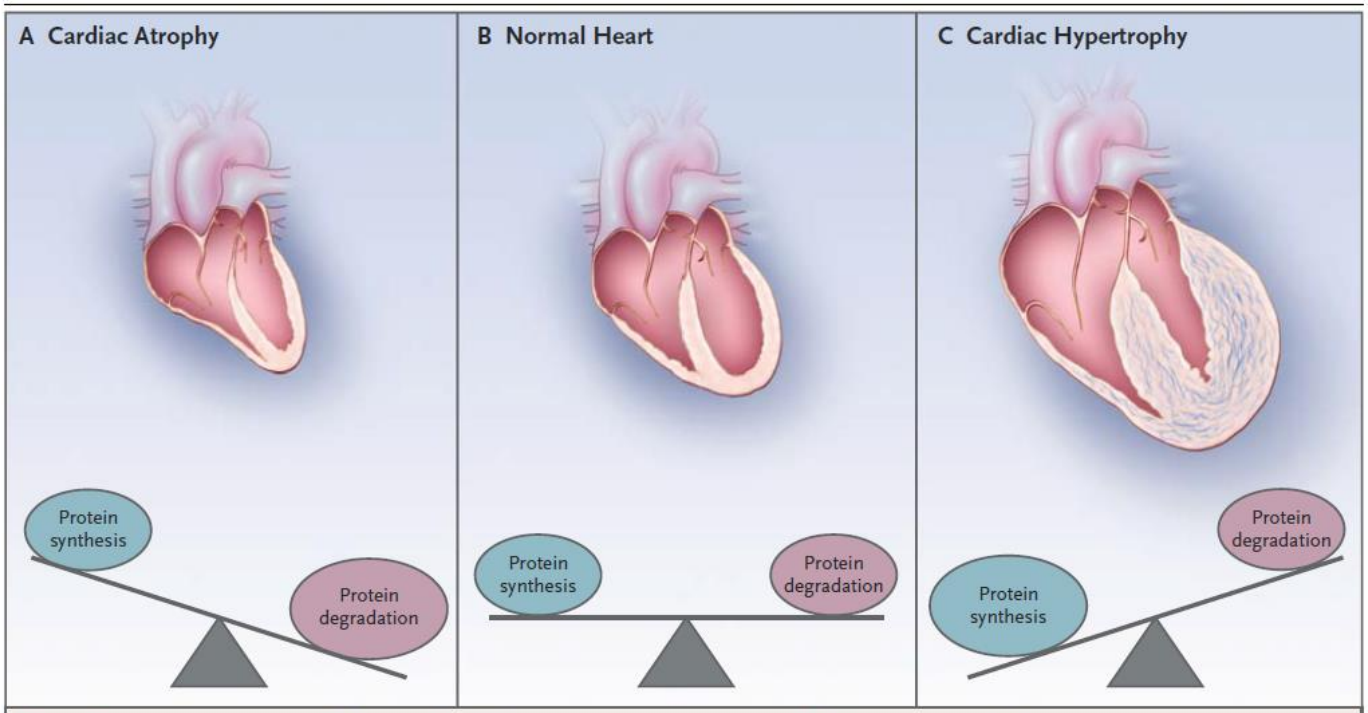


Figure 1. Association of the Development of Cardiac Atrophy and Hypertrophy with Changes in the Balance between Protein Synthesis and Protein Degradation.

The development of cardiac atrophy involves both the inhibition of protein synthesis and a simultaneous increase in the rates of protein degradation (Panel A), resulting in shorter half-lives of individual cardiac proteins, as compared with the half-lives of proteins in a steady state, when protein synthesis and degradation are balanced (Panel B). The development of cardiac hypertrophy involves both an increased fractional synthesis rate of proteins and the suppression of protein degradation (Panel C), resulting in longer half-lives of cardiac proteins.[7-10]

Monte S. Willis, M.D., Ph.D., and Cam Patterson, M.D., M.B.A.
NEJM 2013;368:455-64.

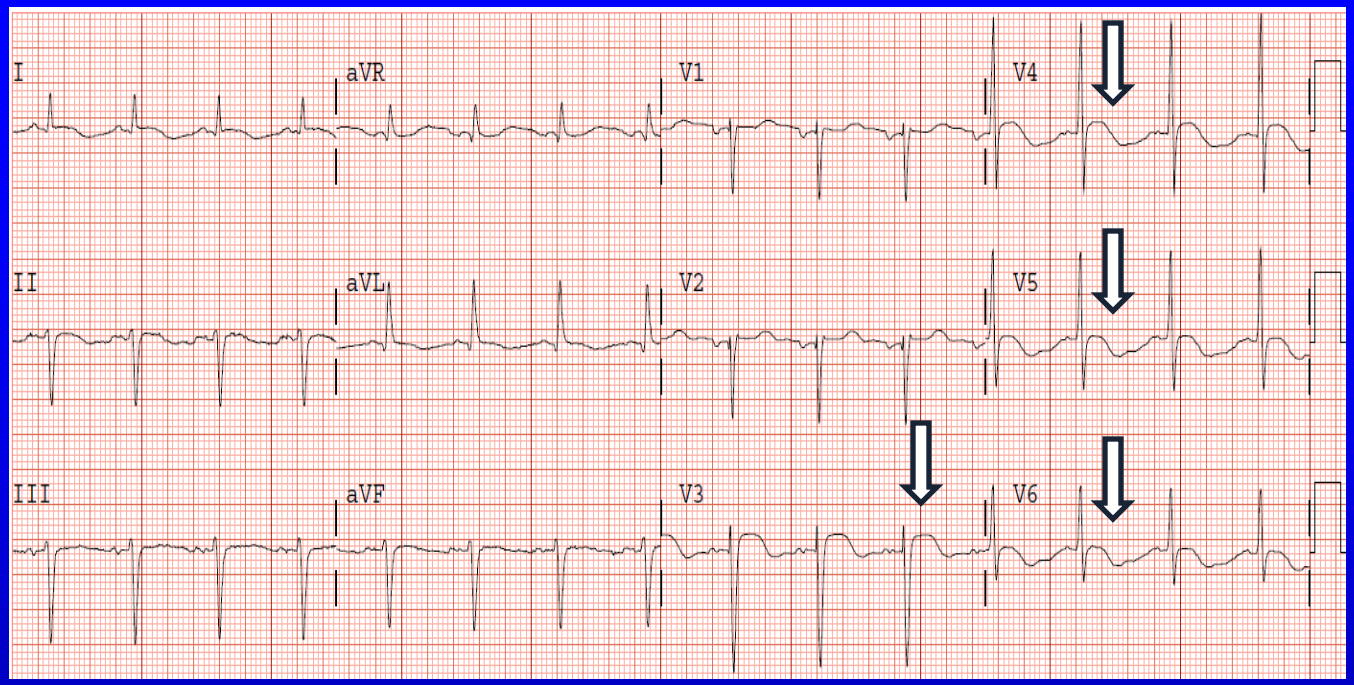
Properties of bortezomib and the second-generation proteasome inhibitors

Proteasome inhibitor	IC_{50} $\beta5/\beta2/\beta1$ (nM)	IC_{50} NF-κB (nM)	Dissociation $t_{1/2}$ (min)
Bortezomib	2.4–7.9/590–4200/24–74 [16,18,25]	36–40 [18,25,39]	110 [18]
MLN9708 [18]	3.4/3500/31	62	18
CEP-18770 [19,20]	3.8/>100/<100	NR	NR—slowly reversible
Carfilzomib [16]	6/3600/2400	NR	Irreversible
PR-047 [21]	36/NR/NR	NR	Irreversible
NPI-0052	3.5/28/430 [25]	13–20 [25,39]	Irreversible

Abbreviations: IV, intravenous; MCL, mantle cell lymphoma; MM, multiple myeloma; NR, not reported; SC, subcutan

Dick, LR and Fleming, PE
Drug Discovery Today ;15 (5/6) March 2010

A


I
aVR
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III
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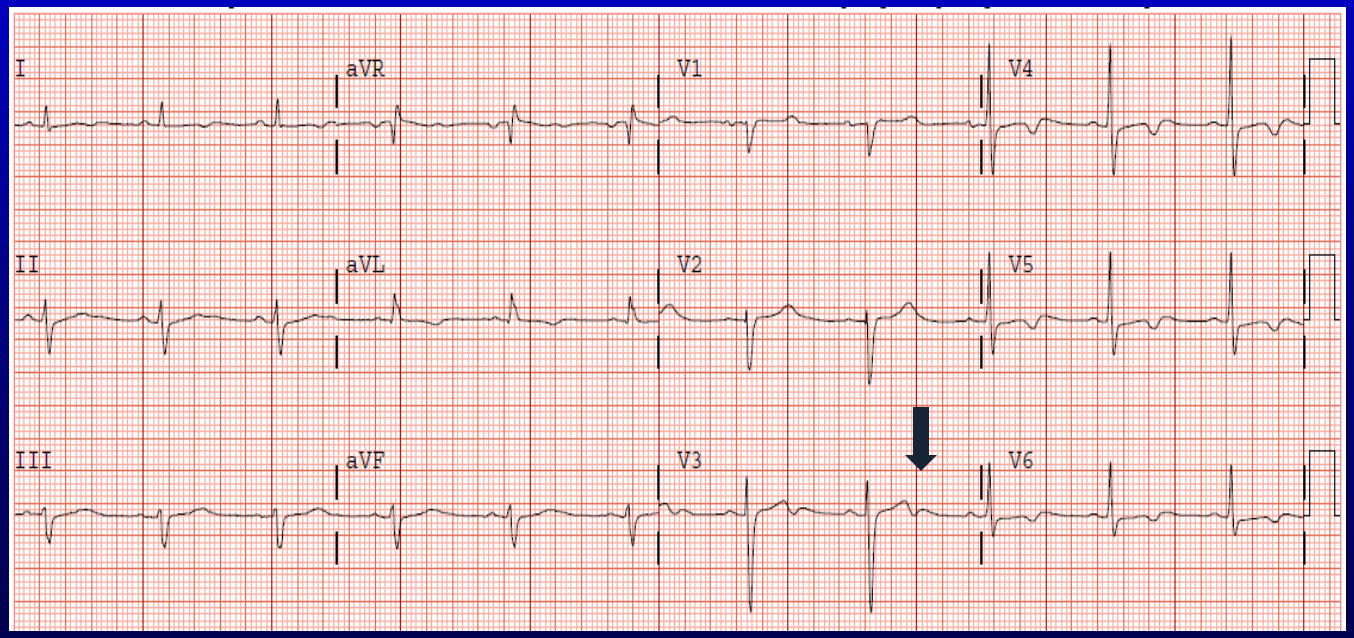
V3
V6

B


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

A report of 6 cases describing carfilzomib related cardiac dysfunction and the patterns of cardiotoxicity

Table 2. Summary of Clinical, Echocardiography, and Biomarker Response During and After Carfilzomib Therapy

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Carfilzomib exposure						
Dosing (mg/m^2)	20×1 then 27	27	20	20	27	20×1 then 27
Duration of therapy (mo)	3	5	6	1	3	3
Total cumulative dose (mg/m^2)	405	903	972	141	540	444
Baseline						
NYHA	I	I	I	I	I	I
LVEF	50–55	60–65	55	55–60	58	68
BNP (pg/mL)	N/A	79†	594*,†	N/A	N/A	N/A
Troponin (ng/mL)	N/A	N/A	<0.05	N/A	N/A	N/A
With carfilzomib						
Worst NYHA	III	II	III	III	III	III
Nadir of LVEF (%)	25–30	47	50	<20	25–30	44
Highest BNP or NT-proBNP† (pg/mL)	1,837†	170†	2,988†	2,026	640	744
Highest troponin	<0.05	<0.05	<0.05	2.5	0.01	<0.05
Summary of Cardiac Events	**HF, LV dysfunction**	**Mild LV and RV dysfunction**	**HF**	**ACS, HF, prolonged QTc, LV dysfunction**	**HF, LV dysfunction**	**HF, LV dysfunctio**

proBNP, N-terminal pro–B-type natriuretic peptide; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HF, heart failure; LV, left ventricular; RV, right ventricular; ACS, acute coronary syndrome; QTc. QTc prolongation.

*NT-proBNP 3 months before starting carfilzomib therapy.

†NT-proBNP.

Grandin, E J Cardiac Failure 2015; p138-144

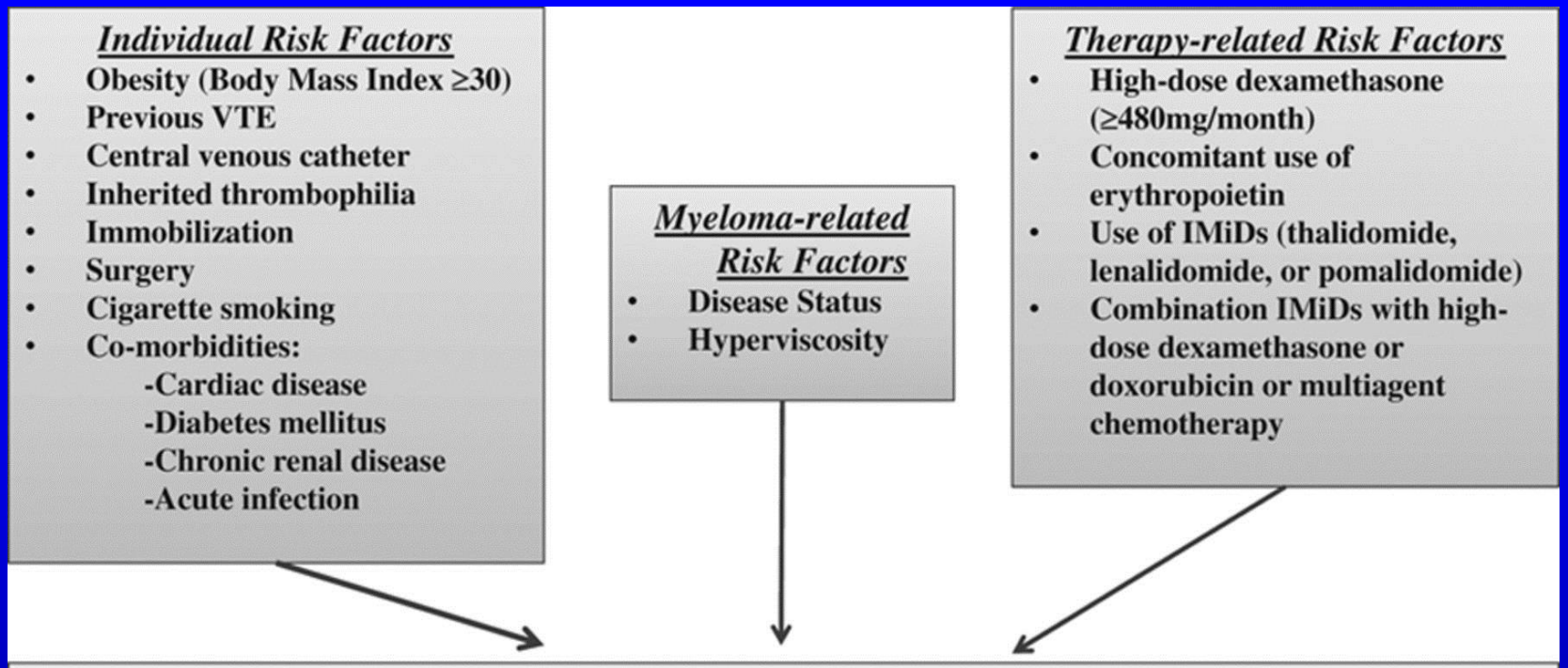
Cardiovascular SAEs in RCTs
Phase 3 Carfilzomib Trials

- ASPIRE Trial

Table 3. Adverse Events in the Safety Population.*

Event	Carfilzomib Group (N=392)		Control Group (N=389)	
	All Grades	Grade 3 or Higher	All Grades	Grade 3 or Higher
	number of patients (percent)			
Dyspnea	76 (19.4)	11 (2.8)	58 (14.9)	7 (1.8)
Hypertension	56 (14.3)	17 (4.3)	27 (6.9)	7 (1.8)
Acute renal failure†	33 (8.4)	13 (3.3)	28 (7.2)	12 (3.1)
Cardiac failure‡	25 (6.4)	15 (3.8)	16 (4.1)	7 (1.8)
Ischemic heart disease§	23 (5.9)	13 (3.3)	18 (4.6)	8 (2.1)

Total Cardiac AEs	26.6%	11.4%	15.6%	5.7%
Total Cardiac AEs + Dyspnoea	46%	14.2%	30.5%	7.5%
DVT/PE	10.2%		6.2%	



Recommendations

- Aspirin 81-325mg once daily should only be recommended for low-risk patients (≤ 1 individual or myeloma-related risk factor)
- LMWH (equivalent of enoxaparin 40mg once daily) or full-dose warfarin (target INR 2-3) should be recommended in the presence of ≥ 2 individual or myeloma-related risk factors
- LMWH or full-dose warfarin should be considered in all patients who receive high-dose dexamethasone or doxorubicin or multiagent chemotherapy, independent of the presence of additional risk factors
- The dose of LMWH should be adjusted according to renal function. LMWH is generally not recommended for patients with creatinine clearance < 30ml/minute
- Thromboprophylaxis should be provided for the first 4 to 6 months of treatment, until disease control is achieved or as long as the risk of VTE remains high

Weijuan Li et al. Circulation. 2016;133:908-912

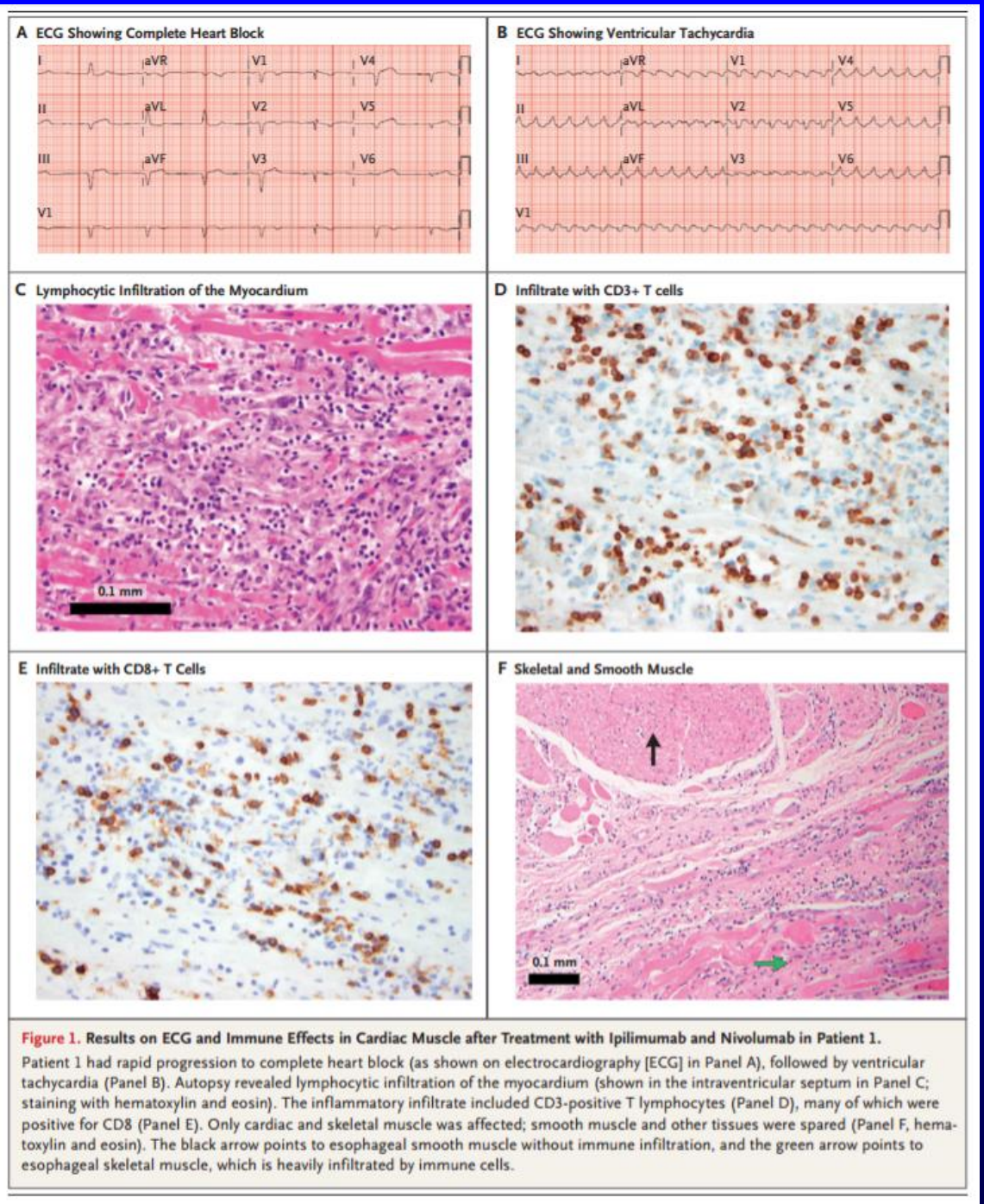


Figure 1. Results on ECG and Immune Effects in Cardiac Muscle after Treatment with Ipilimumab and Nivolumab in Patient 1.

Patient 1 had rapid progression to complete heart block (as shown on electrocardiography [ECG] in Panel A), followed by ventricular tachycardia (Panel B). Autopsy revealed lymphocytic infiltration of the myocardium (shown in the intraventricular septum in Panel C; staining with hematoxylin and eosin). The inflammatory infiltrate included CD3-positive T lymphocytes (Panel D), many of which were positive for CD8 (Panel E). Only cardiac and skeletal muscle was affected; smooth muscle and other tissues were spared (Panel F, hematoxylin and eosin). The black arrow points to esophageal smooth muscle without immune infiltration, and the green arrow points to esophageal skeletal muscle, which is heavily infiltrated by immune cells.

Combination checkpoint inhibitors may have important cardiac effects

Table 1. Incidence of Myocarditis and Myositis in Patients Receiving Nivolumab or Ipilimumab plus Nivolumab.

Characteristic	Nivolumab (N=17,620)	Nivolumab plus Ipilimumab (N=2974)
	no. (%)	
Myocarditis		
Any*	10 (0.06)	8 (0.27)
Fatal events	1 (<0.01)	5 (0.17)
Myositis		
Any	27 (0.15)	7 (0.24)
Fatal events	2 (0.01)	1 (0.03)

* The number of patients with myocarditis includes six patients with concurrent myocarditis and myositis.

N Engl J Med 2016;375:1749-55.
DOI: 10.1056/NEJMoa1609214

Case Study revisited:
So what would you recommend?

47/y/o with moderate to severe AS/MR/TR, normal LVEF, COPD, hx of RTx, Breast cancer on anti-HER2 therapy, with evidence of some pulmonary HTN by physical exam, BP 110/62, and P 92

- Any further testing?
- Add lasix?
- What kind of advice do you have for the oncologist?

Suggestions I made

- Follow BNP periodically during treatment
- Increase activity
- Check BP, weight and pulse daily
- If cardiac symptoms (especially of worsening AS) develop or worsen, will re-evaluate
- I did not start any vasoactive meds but did start Lipitor 20mg qhs

- What is Cardio-Oncology?

It is a clinically-based discipline focused on the cardiovascular health of cancer patients and cancer survivors

- Who is a cardio-oncologist?

A health care provider who is focused on the prevention, early detection, management, and recovery of cardiovascular function potentially resulting from cancer therapies.

Consensus Statement

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

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

ABSTRACT

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

Key Words: Cardio-oncology, training, cardiotoxicity, survivorship.

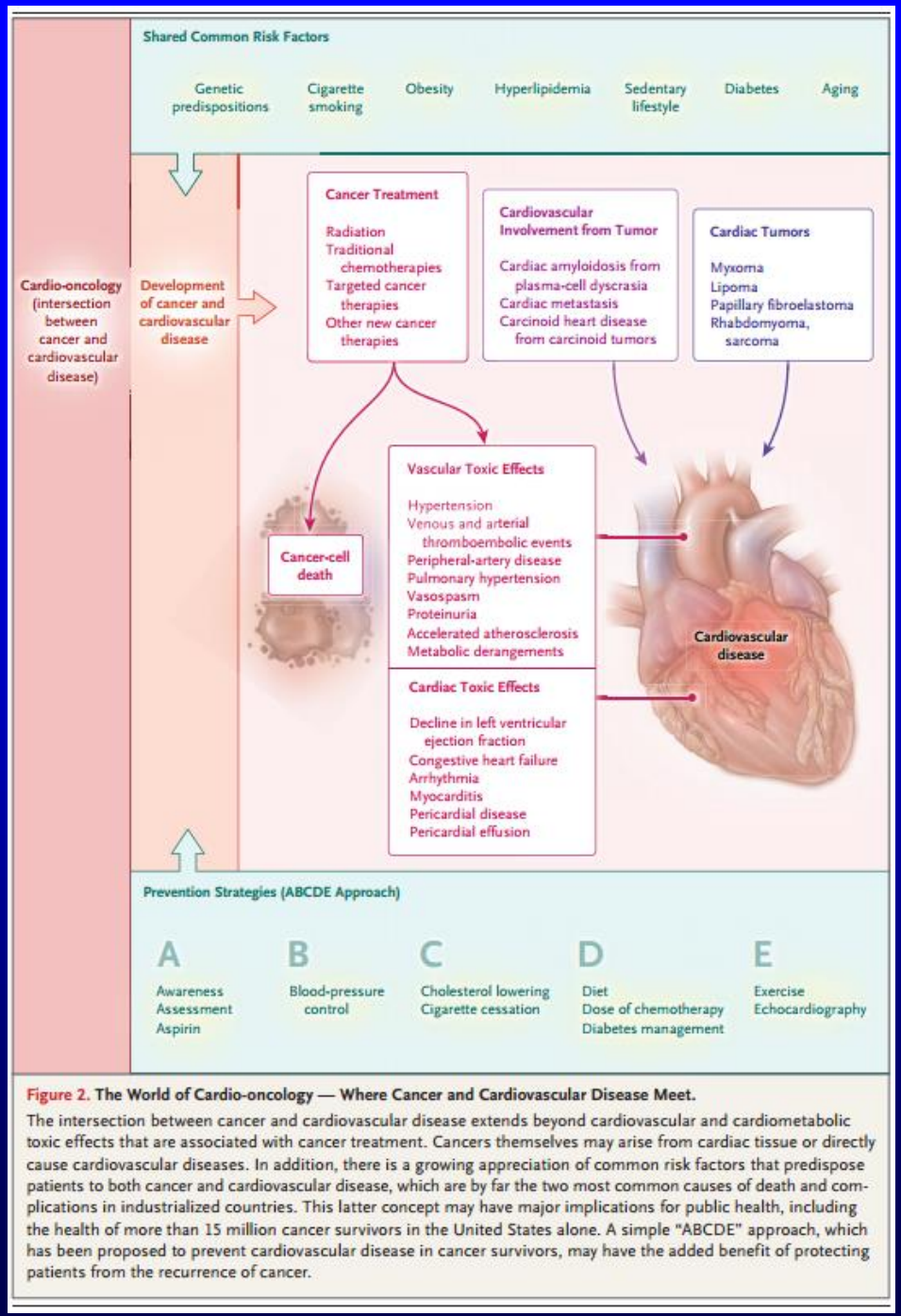


Figure 2. The World of Cardio-oncology — Where Cancer and Cardiovascular Disease Meet.

The intersection between cancer and cardiovascular disease extends beyond cardiovascular and cardiometabolic toxic effects that are associated with cancer treatment. Cancers themselves may arise from cardiac tissue or directly cause cardiovascular diseases. In addition, there is a growing appreciation of common risk factors that predispose patients to both cancer and cardiovascular disease, which are by far the two most common causes of death and complications in industrialized countries. This latter concept may have major implications for public health, including the health of more than 15 million cancer survivors in the United States alone. A simple "ABCDE" approach, which has been proposed to prevent cardiovascular disease in cancer survivors, may have the added benefit of protecting patients from the recurrence of cancer.

The World of Cardio-Oncology

Moslehi, J. N Engl J Med 2016;375:1457-67.

The State of the Art of Cardio-Oncology

- The demographic profile for cancer patients being treated with chemotherapy is identical to typical cardiac patients
- Optimal management of cardiac disease includes prevention, early detection and careful medication choices
- Close collaboration between cardiology and oncology is feasible and essential
- Ongoing research will further define the best collaborative practice

Save the Date

Global Cardio-Oncology Summit 2017

September 20-21, 2017

London, UK

Additional details to follow.

British Cardio-Oncology Society
BC-OS.org

Canadian Cardiac Oncology Network

International CardiOncology Society

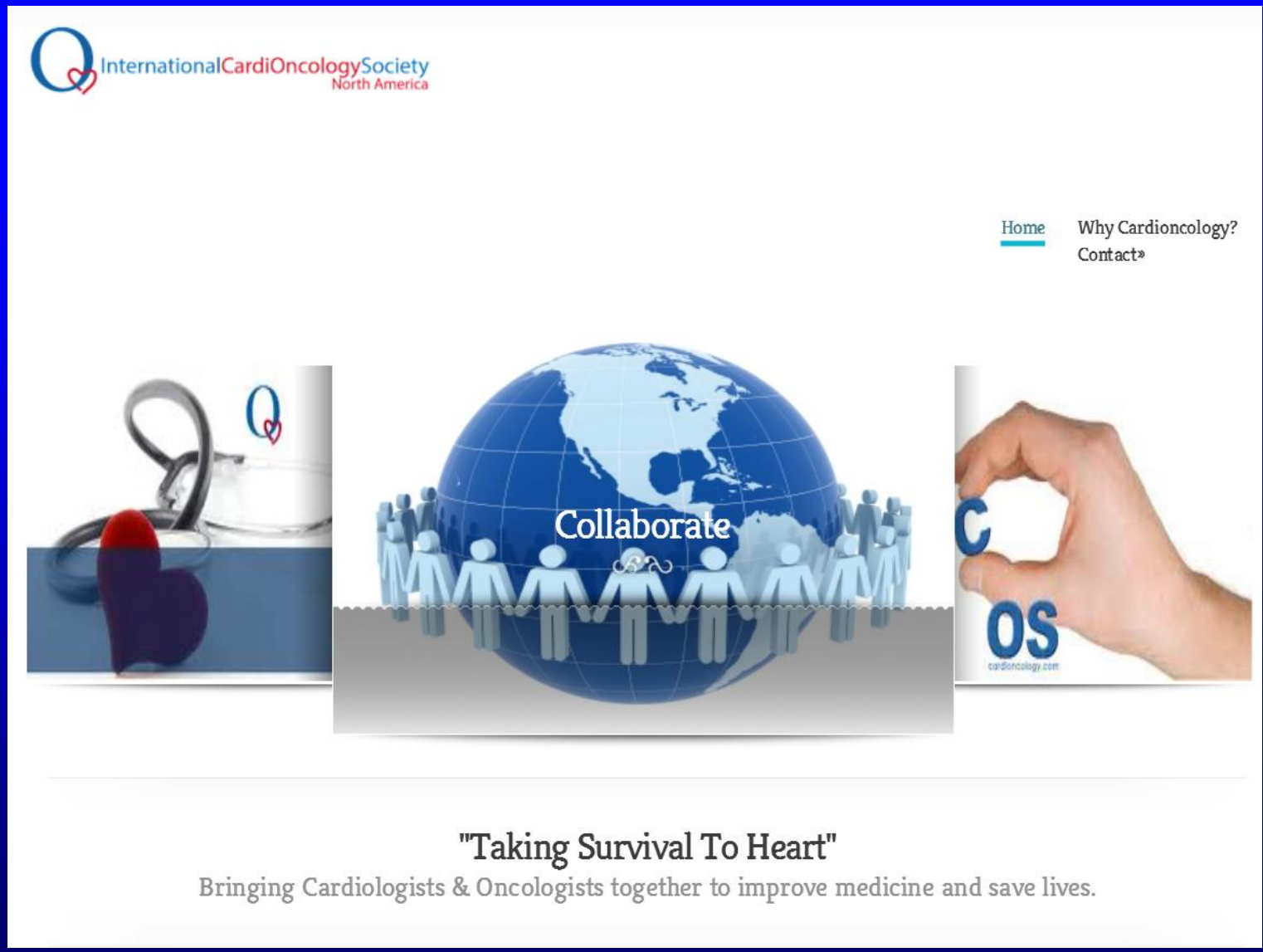
British Cardiovascular Society

WE ARE MACMILLAN. CANCER SUPPORT

Royal Brompton & Harefield NHS
NHS Foundation Trust

Topics include:

- How to deliver a Cardio-Oncology service
- Training in Cardio-Oncology
- eHealth and Cardio-Oncology
- How do I measure the quality of my service?
- Role of primary care in cancer survivors
- Immunotherapy and emerging cardiotoxicity
- Personalised medicine & genetics
- EP session –who should have ablation, ICDs, CRT?
- Anticoagulation and antithrombotic (AF, ACS)
- Radiation-induced cardiotoxicity
- Managing cardiac issues during BMSC transplants
- Cardiac tumours, carcinoid valvular disease, amyloid
- Hormone therapy and CV risk



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