Cardio-Oncology 2022 – Heart Failure Update

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May 13, 2022

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UNIVERSITY OF TORONTO

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TED ROGERS CENTRE FOR HEART RESEARCH

Disclosures

- None

Objectives

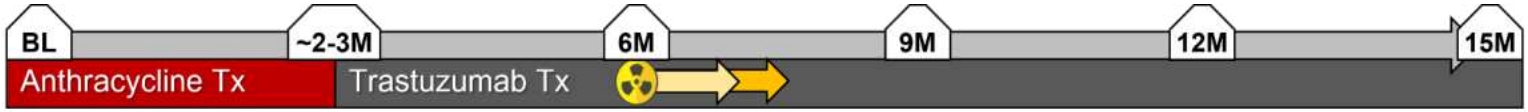
- Describe the emerging links between cancer and current or future HF
- Discuss the approach to surveillance strategies for early identification of LV dysfunction in patients receiving chemotherapy
- Discuss strategies to prevent and/or treat HF in setting of active cancer

Clinical Case

Patient in Cardio-oncology Clinic

- 51F, high risk HER2+, left sided breast cancer, stage III

- Surgery, Anthracyclines (Doxorubicin equivalent 200mg/m^2), Trastuzumab, Radiation therapy, hormonal therapy



- No cardiovascular disease history, no CV risk factors, non-smoker, no medications, excellent functional capacity

- Physical exam / ECG – normal

Question 1

What is her risk of HF during cancer treatment?

1. Low - her total cumulative dose of doxorubicin is < 250mg/m^2, she is < 60 years of age, and has no CVD risk factors

2. High – because she has HER2+ breast cancer

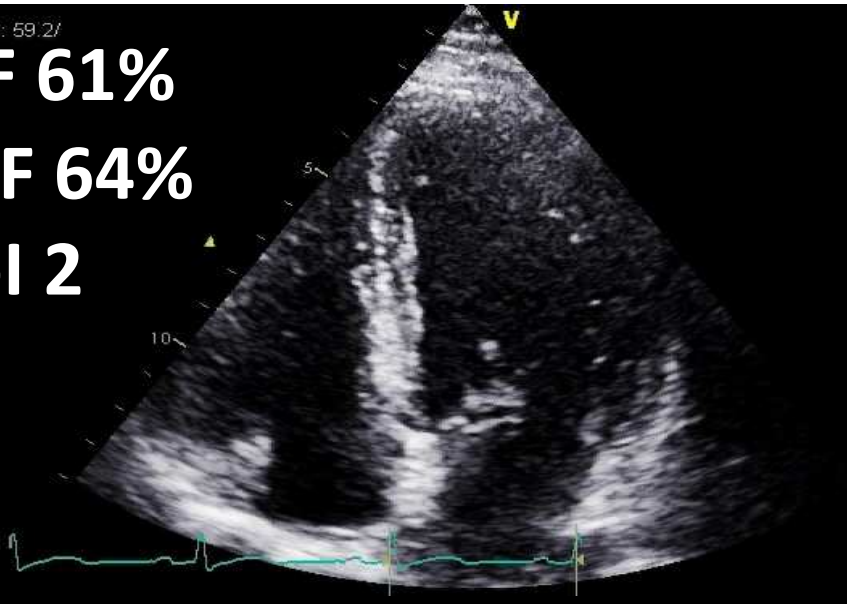
3. High – because she is receiving 3 potentially cardiotoxic therapies

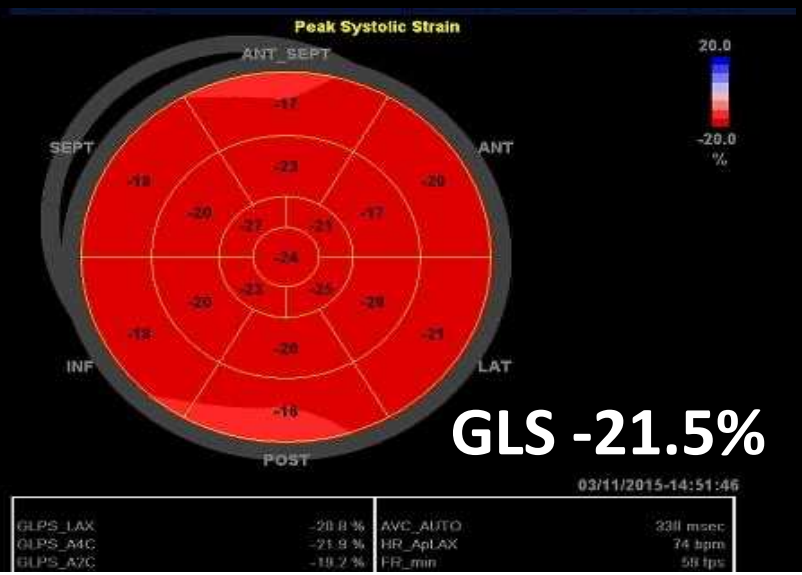
4. Not sure – but an echocardiogram will help determine risk

3DEF 61%

2D EF 64%

hsTpI 2





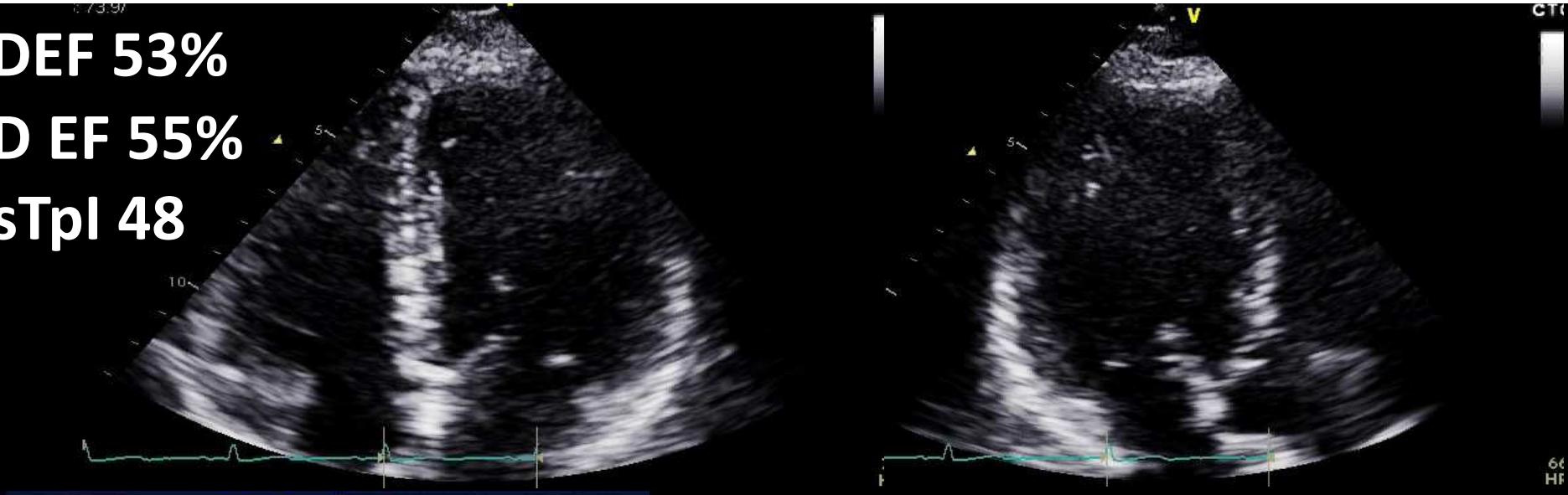
GLS -21.5%

Q: Risk of HF? Risk mitigation strategies?

3DEF 53%

2D EF 55%

hsTpI 48



(21.5 – 17.9) / (21.5) =

16.7% relative change

GLS -17.9%

Q: Do these changes alter her risk of HF?
Risk mitigation strategies?

3DEF 48%

2D EF 47%

NYHA II-III

Q: Treatment Options?

Stop / hold cancer therapy?

3DEF 56%

2DEF 54%

NYHA I

6 wks Post Cessation of Trastuzumab + BB/ACE

VO_2peak = 16 $mL \cdot kg^{-1} \cdot min^{-1}$ (67% predicted)

Q: Long Term Follow-up?

Consequences to having developed cardiotoxicity / TZM interruption?

Question 2

Which of the following regarding this patient is correct?

1. There is strong evidence from several RCTs that if HF therapy (BB/ACE/ARB) was started when GLS change occurred, HF could have been prevented.

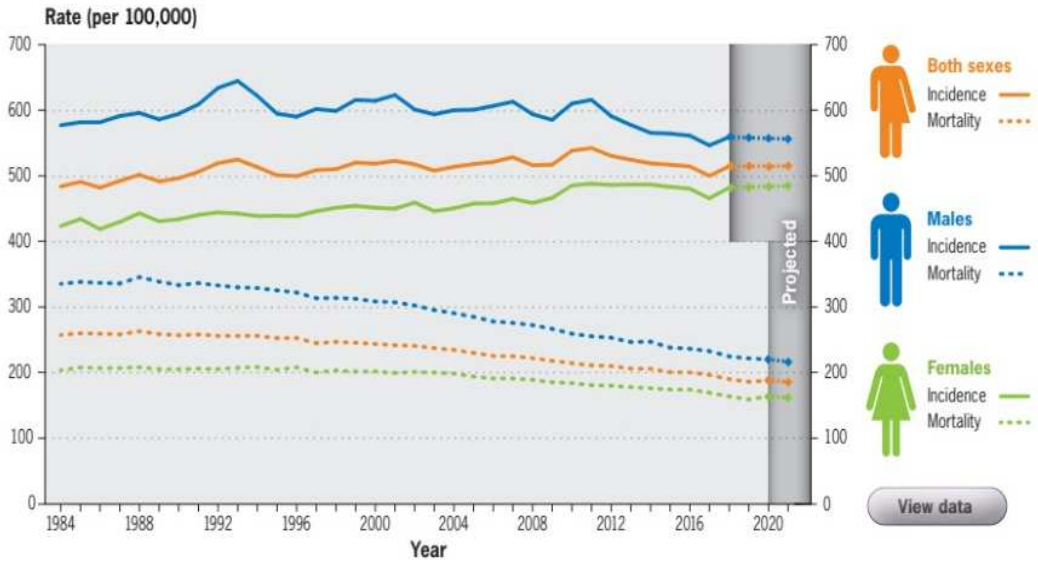
2. Stopping trastuzumab therapy transiently will affect her cancer outcomes.

3. Although her VO2peak was low post therapy in long term follow-up it will not be different from those who did not develop cardiotoxicity.

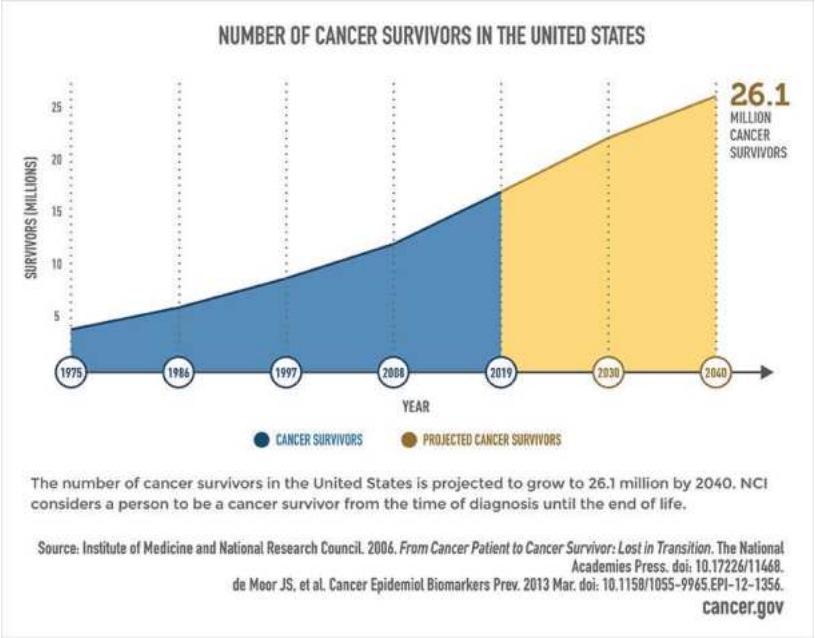
4. Troponin measurements do not have prognostic value in women with HER2+ breast cancer receiving anthracyclines.

Cancer and CVD

Cancer Incidence and Survivorship



Canadian Cancer Statistics 2021

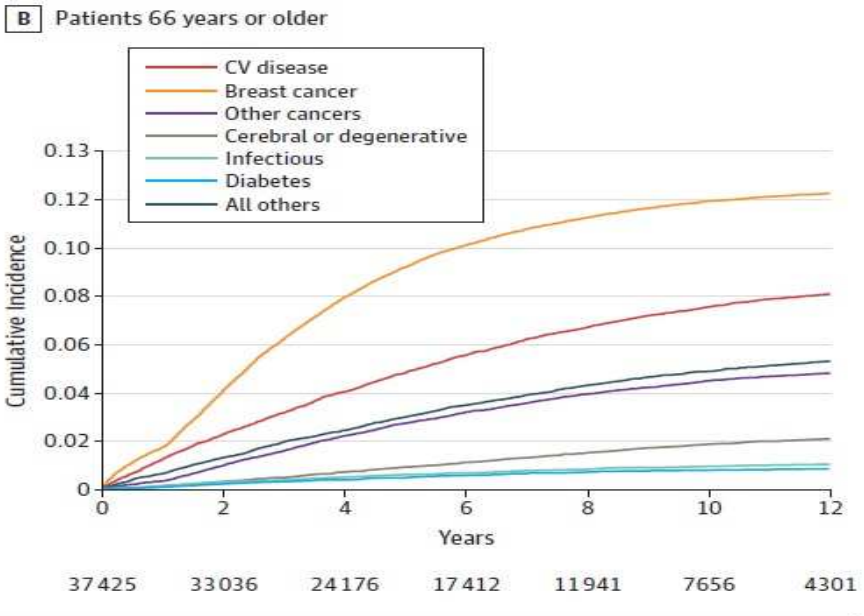


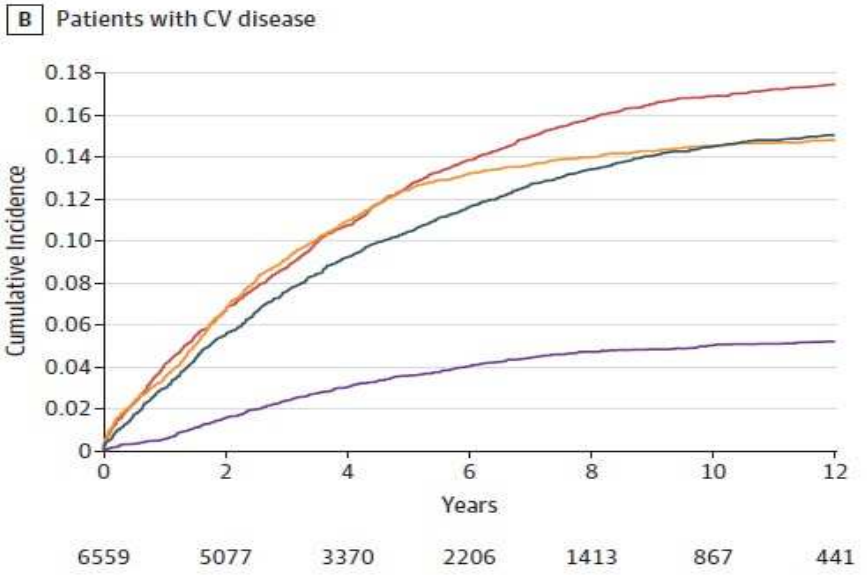
Spectrum of CVD in Patients with Cancer

	LVSD	HTN	Angina	ACS	Takotsubo	Stroke	PAD	PHTN	DVT/ PE
Anthracyclines	X								
5-FU	X		X	X	X				
Gemcitabine			X	X					
Paclitaxel		X	X	X					X
Cisplatin		X	X	X		X	X		
Bleomycin			X	X		X		X	
Vincristine		X	X	X					
Cyclophos-phamide	X		X					X	
mTOR inhibitors		X	X						X
Carfilzomib	X	X		X				X	
Bevacizumab	X	X	X	X	X	X			X
Sunitinib	X	X	X	X	X	X			X
Nilotinib			X	X		X	X		X
Dasatanib	X							X	
Thalidomide									X
Rituximab		X	X	X	X				

Chung R et al, Open Heart 2018

Older Adults – Breast Cancer

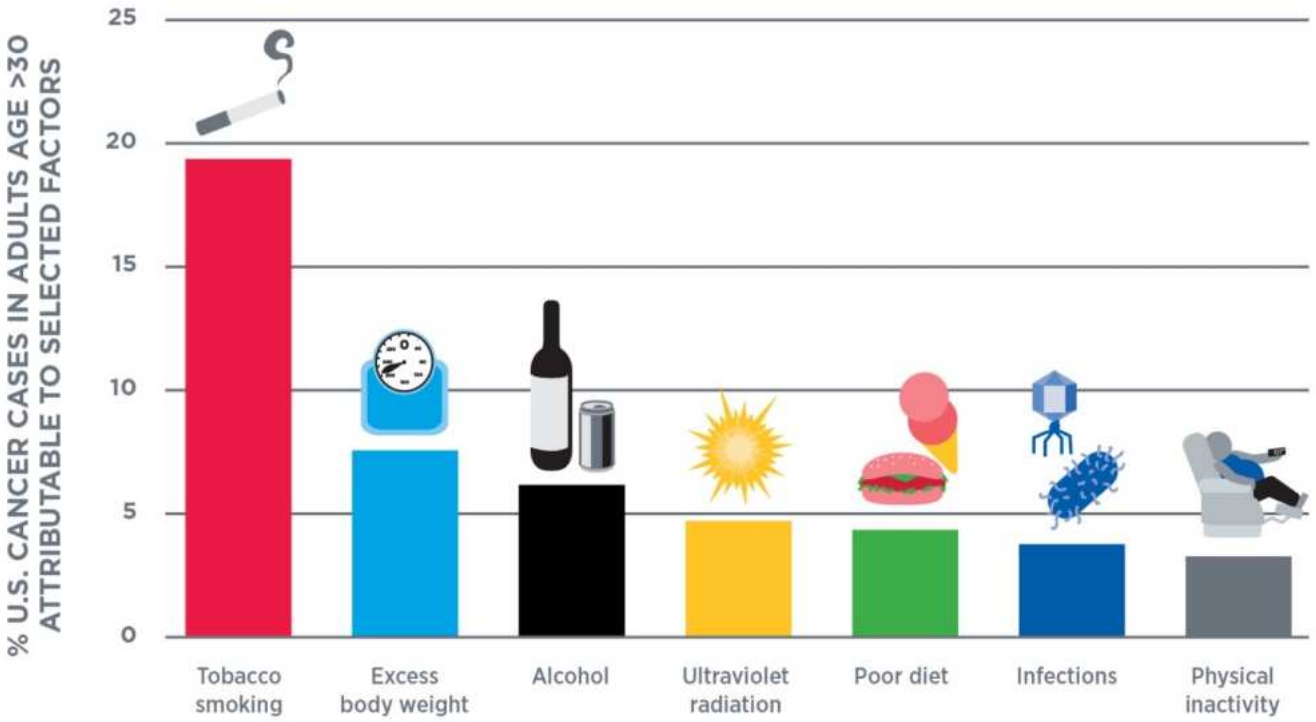




Abdel-Qadir H et al JAMA Cardiology 2016
Similar pattern in other cancers

Links Between Cancer and HF

Shared Risk Factors for Cancer and HF



Source: AACR Cancer Progress Report 2019

Novel Shared Risk Factor

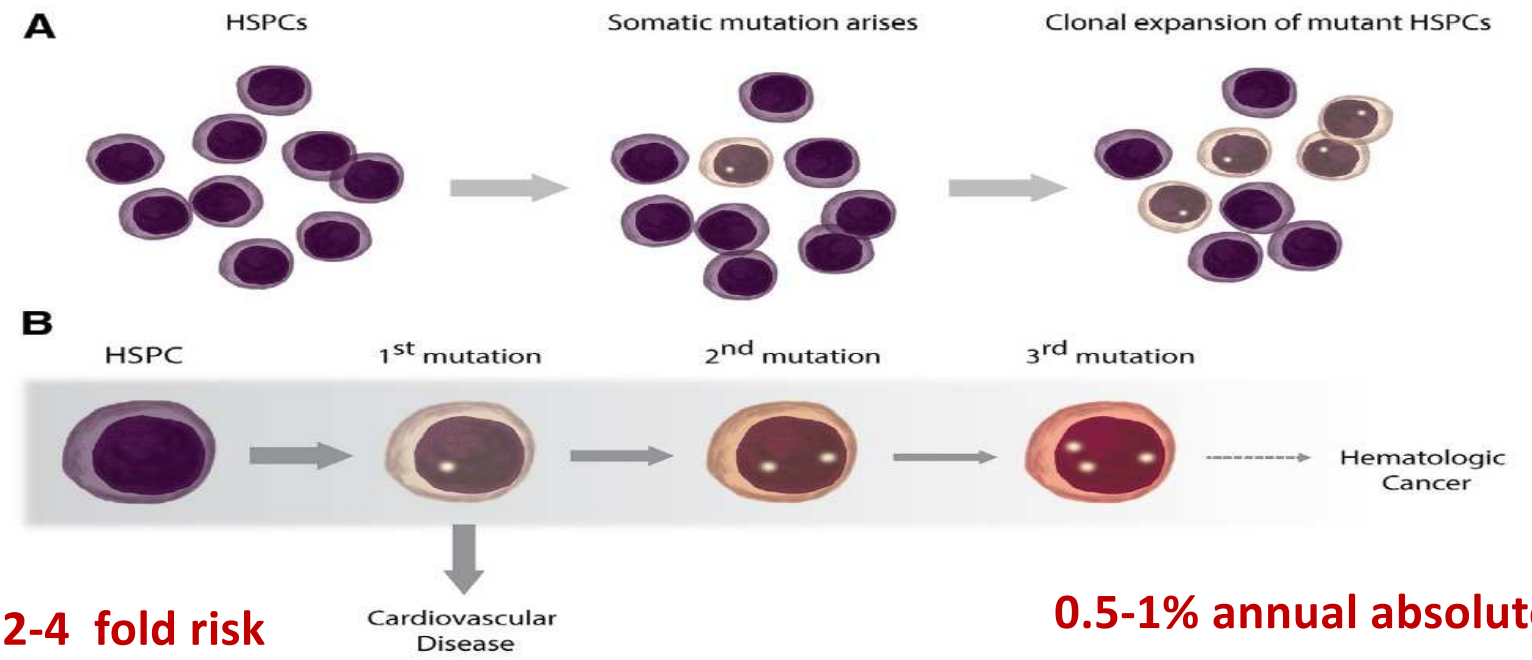
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 13, 2017 VOL. 377 NO. 2

Clonal Hematopoiesis and Risk of Atherosclerotic Cardiovascular Disease

S. Jaiswal, P. Natarajan, A.J. Silver, C.J. Gibson, A.G. Bick, E. Shvartz, M. McConkey, N. Gupta, S. Gabriel, D. Ardissino, U. Baber, R. Mehran, V. Fuster, J. Danesh, P. Frossard, D. Saleheen, O. Melander, G.K. Sukhova, D. Neuberg, P. Libby, S. Kathiresan, and B.L. Ebert

Clonal Hematopoiesis (CH)

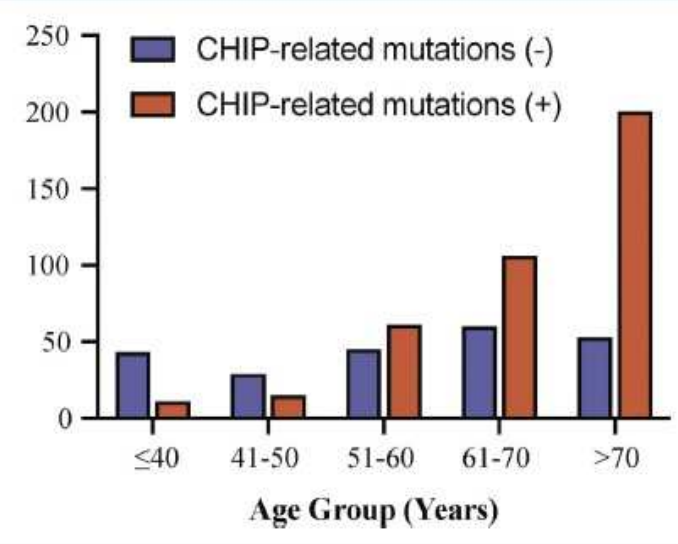


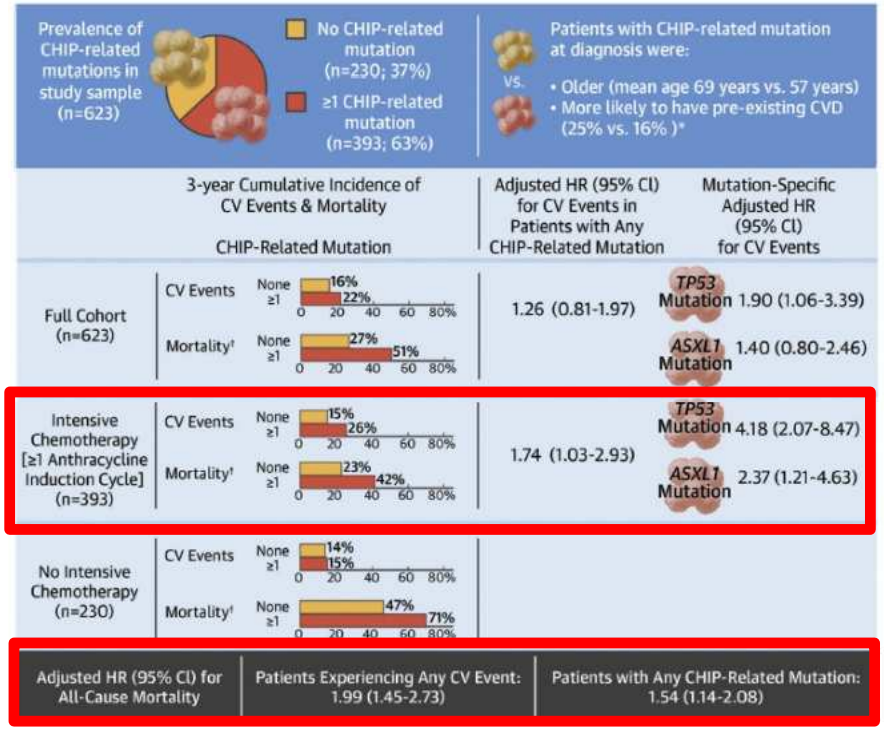
2-4 fold risk

0.5-1% annual absolute risk

Fuster JJ, Walsh K. *Circ Res.* 2018;122(3):523-532

CH-associated mutations and CVD in AML





Calvillo-Arguelles O, et al. JACC Cardioncology, March 2022

Impact of Cancer / Treatment

Moslehi J, NEJM 2016

Table 1. Cancer Therapies, Cellular Targets, and Associated Cardiovascular Toxic Effects.*

Class	Drug	Cellular Target	Common Cardiovascular Toxic Effects
Traditional cancer therapies			
Radiation	NA	NA	Myocardial ischemia, pericarditis, myocarditis, valvular heart disease, arrhythmia
Anthracyclines	Doxorubicin, daunorubicin, idarubicin, epirubicin, mitoxantrone	Type II topoisomerase, DNA and RNA synthesis	Cardiomyopathy, arrhythmia, acute myocarditis or pericarditis
Platinum	Cisplatin, carboplatin, oxaliplatin	Cross-link DNA	Hypertension, myocardial ischemia
Antimetabolites	Fluorouracil	Thymidylate synthase	Myocardial ischemia
	Capecitabine	Thymidylate synthase	Myocardial ischemia, arrhythmias
Alkylating agents	Cyclophosphamide	Cross-link DNA	Congestive heart failure, myocarditis, pericarditis
Antimicrotubule agents	Paclitaxel	Microtubule	Arrhythmias (including bradycardia, heart block, premature ventricular contractions, and ventricular tachycardia), thrombosis
	Vinca alkaloids	Microtubule	Myocardial ischemia, coronary spasm
Targeted cancer therapies			
HER2 inhibitors			
HER2 monoclonal antibody	Trastuzumab	HER2	Decline in LVEF, congestive heart failure
Newer HER2 inhibitors	Pertuzumab, trastuzumab emtansine, lapatinib	HER2	Decline in LVEF, congestive heart failure
VEGF signaling pathway inhibitors		VEGF signaling pathway	Hypertension, venous or arterial thromboembolic events, proteinuria, cardiomyopathy
VEGFA monoclonal antibody	Bevacizumab		
VEGF trap	Aflibercept		
VEGFR2 monoclonal antibody	Ramucirumab		
Tyrosine kinase inhibitor with anti-VEGF activity	Sunitinib, sorafenib, pazopanib, axitinib, vandetanib, regorafenib, cabozantinib, lenvatinib	VEGF receptors (mainly VEGFR2) and other kinases; PDGFR	
Multitargeted tyrosine kinase inhibitors	Dasatinib	ABL, ABL mutants (except T315I), and other kinases; SRC, KIT, PDGFR, EGFR, BRAF, DDR1, DDR2, ephrin receptors	Pulmonary hypertension, vascular events, prolongation of QT interval corrected for heart rate
Other multitargeted tyrosine kinase inhibitors			
Anaplastic lymphoma kinase inhibitors	Crizotinib, ceritinib	Anaplastic lymphoma kinase	Bradycardia, prolongation of QT interval corrected for heart rate
PI3K–AKT–mTOR inhibitors†	Everolimus, temsirolimus	PI3K–AKT–mTOR signaling pathway	Cardiometabolic toxic effects, including hypercholesterolemia, hypertriglyceridemia, hyperglycemia
Bruton's tyrosine kinase inhibitors	Ibrutinib	Bruton's tyrosine kinase	Atrial fibrillation, other arrhythmias
MEK inhibitors	Trametinib	MEK1, MEK2	Cardiomyopathy
Immunomodulatory drugs	Thalidomide, lenalidomide, pomalidomide	Lymphoid transcription factors IKZF1 and IZKF3	Venous or arterial thromboembolic events
Proteasome inhibitors	Bortezomib, carfilzomib	Ubiquitin–proteasome system	Cardiomyopathy, hypertension, venous or arterial thromboembolic events, arrhythmia
Immune checkpoint inhibitors	Pembrolizumab, nivolumab	Programmed cell death 1	Myocarditis
	Ipilimumab	CTLA4	Myocarditis

Pre-treatment Risk Stratification

Pre-Treatment Risk Assessment - Clinical

- Patients at elevated risk – ASCO guidelines
  - Anthracycline dose (doxo ≥250mg/m^2) / radiation dose ≥30Gy/ trastuzumab / cardiovascular risk factors
  - Lower dose combinations
- Others (no clear guidelines)
  - Proteasome inhibitors, ICIs, multi-targeted TKIs, VEGFi, MEK inhibitors, EGFR

Pre-Treatment Risk Assessment - Clinical

ESC European Society of Cardiology

European Journal of Heart Failure (2020) 22, 1945–1960
doi:10.1002/ejhf.1920

POSITION PAPER

Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: a position statement and new risk assessment tools from the Cardio-Oncology Study Group of the Heart Failure Association of the European Society of Cardiology in collaboration with the International Cardio-Oncology Society

Alexander R. Lyon[1*], Susan Dent[2], Susannah Stanway[3], Helena Earl[4], Christine Brezden-Masley[5], Alain Cohen-Solal[6], Carlo G. Tocchetti[7], Javid J. Moslehi[8], John D. Groarke[9], Jutta Bergler-Klein[10], Vincent Khoo[11,12], Li Ling Tan[13], Markus S. Anker[14], Stephan von Haehling[15,16], Christoph Maack[17], Radek Pudil[18], Ana Barac[19], Paaladinesh Thavendiranathan[20], Bonnie Ky[21], Tomas G. Neilan[22], Yury Belenkov[23], Stuart D. Rosen[1], Zaza Iakobishvili[24], Aaron L. Sverdlov[25], Ludhmila A. Hajjar[26], Ariane V.S. Macedo[27], Charlotte Manisty[28], Fortunato Ciardiello[29], Dimitrios Farmakis[30,31], Rudolf A. de Boer[32], Hadi Skouri[33], Thomas M. Suter[34], Daniela Cardinale[35], Ronald M. Witteles[36], Michael G. Fradley[21], Joerg Herrmann[37], Robert F. Cornell[38], Ashutosh Wechelaker[39], Michael J. Mauro[40], Dragana Milojkovic[41], Hugues de Lavallade[42], Frank Ruschitzka[43], Andrew J.S. Coats[44,45], Petar M. Seferovic[46], Ovidiu Chioncel[47,48], Thomas Thum[49], Johann Bauersachs[50], M. Sol Andres[1], David J. Wright[51], Teresa López-Fernández[52], Chris Plummer[53], and Daniel Lenihan[54]

Table 3 Baseline cardiovascular risk stratification proforma for HER2-targeted cancer therapies (trastuzumab, pertuzumab, T-DM1, lapatinib, neratinib)

Risk factor	Score	Level of evidence	References
Previous cardiovascular disease			
Heart failure or cardiomyopathy	Very high	C	31
Myocardial infarction or CABG	High	B	31,32
Stable angina	High	B	31–34
Severe valvular heart disease	High	C	31
Baseline LVEF <50%	High	C	
Borderline LVEF 50–54%	Medium[2]	B	35–37
Arrhythmia[a]	Medium[2]	C	31,32
Cardiac biomarkers (where available)			
Elevated baseline troponin[b]	Medium[2]	B	38,39
Elevated baseline BNP or NT-proBNP[b]	Medium[2]	C	17
Demographic and cardiovascular risk factors			
Age ≥80 years	High	B	32,33
Age 65–79 years	Medium[2]	B	35,36,40,41
Hypertension[c]	Medium[1]	B	32–36,42,43
Diabetes mellitus[d]	Medium[1]	C	31,32,42
Chronic kidney disease[e]	Medium[1]	C	32
Current cancer treatment regimen			
Includes anthracycline before HER2-targeted therapy	Medium[1f]	B	32,40,41,43–45
Previous cardiotoxic cancer treatment			
Prior trastuzumab cardiotoxicity	Very high	C	
Prior (remote) anthracycline exposure[g]	Medium[2]	B	42
Prior radiotherapy to left chest or mediastinum	Medium[2]	C	41,46,47
Lifestyle risk factors			
Current smoker or significant smoking history	Medium[1]	C	34
Obesity (BMI >30 kg/m^2)	Medium[1]	C	29,34,43,45
Risk level			

Pre-Treatment Risk Assessment - Clinical

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3913–3920
doi:10.1093/eurheartj/ehz460

CLINICAL RESEARCH
Disease management

Development and validation of a multivariable prediction model for major adverse cardiovascular events after early stage breast cancer: a population-based cohort study

Husam Abdel-Qadir[1,2,3,4]*, Paaladinesh Thavendiranathan[2,5], Peter C. Austin[3,4], Douglas S. Lee[2,3,4,5], Eitan Amir[4,6], Jack V. Tu[3,4,7], Kinwah Fung[3], and Geoffrey M. Anderson[3,4]

[1]Department of Medicine, Women's College Hospital Toronto, 76 Grenville St, Room 3444, Toronto, ON M5S 1B2, Canada; [2]Department of Medicine, Division of Cardiology, Peter Munk Cardiac Centre, University Health Network, Toronto, ON, Canada; [3]Cardiovascular Research Program, ICES, Toronto, ON, Canada; [4]University of Toronto, Institute of Health Policy, Management, and Evaluation, Toronto, ON, Canada; [5]Joint Department of Medical Imaging, University Health Network, Toronto, ON, Canada; [6]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada; and [7]Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Received 17 January 2019; revised 18 May 2019; editorial decision 12 June 2019; accepted 12 June 2019; online publish-ahead-of-print 18 July 2019

See page 3921 for the editorial comment on this article (doi: 10.1093/eurheartj/ehz598)

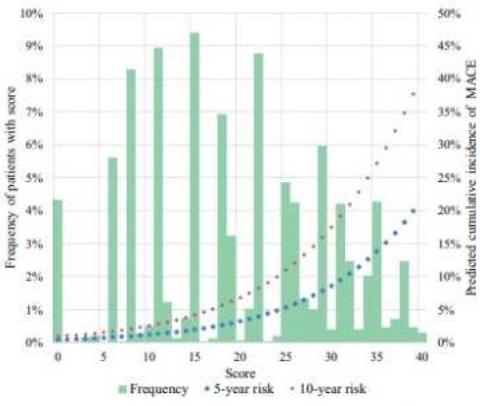
Aims Develop a score to predict the risk of major adverse cardiovascular events (MACE) after early stage breast cancer (EBC) to facilitate personalized decision-making about potentially cardiotoxic treatments and interventions to reduce cardiovascular risk.

Methods and results Using administrative databases, we assembled a cohort of women diagnosed with EBC in Ontario between 2003 and 2014, with follow-up through 2015. Two-thirds of the cohort were used for risk score derivation; the remainder were reserved for its validation. The outcome was a composite of hospitalizations for acute myocardial infarction, unstable angina, transient ischaemic attack, stroke, peripheral vascular disease, heart failure (HF), or cardiovascular death. We developed the score by regressing MACE incidence against candidate predictors in the derivation sample using a Fine–Gray model. Discrimination was assessed in the validation sample using Wolber's c-index for prognostic models with competing risks, while calibration was assessed by comparing predicted and

Table 2 Risk score for prediction of major adverse cardiovascular events risk after breast cancer

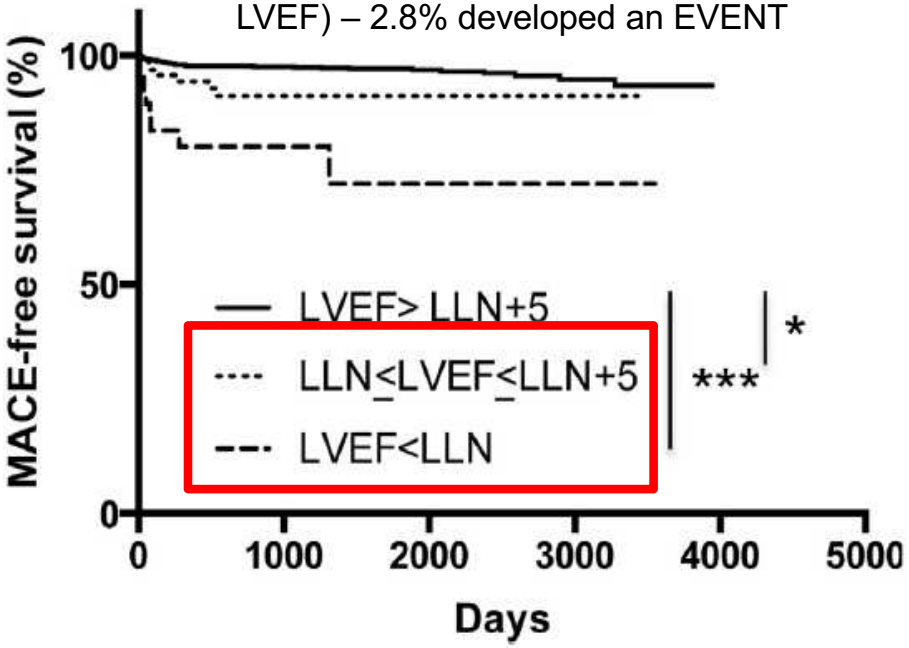
Select age category		Select past medical history	
<40 years	0	Heart failure	7
40–44 years	6	Atrial fibrillation	4
45–49 years	8	Peripheral vascular disease	4
50–54 years	11	Hypertension	4
55–59 years	15	Ischaemic heart disease	3
60–64 years	18	Diabetes	3
65–69 years	22	Chronic kidney disease	3
70–74 years	25	COPD	3
75–79 years	27	Cerebrovascular disease	2
≥80 years	31	Total score	

COPD, chronic obstructive pulmonary disease.



Pre-Treatment Risk Assessment - LVEF

Every 5% decrease in LVEF 38% relative increase in symptomatic HF + CV Death (2D LVEF) – 2.8% developed an EVENT

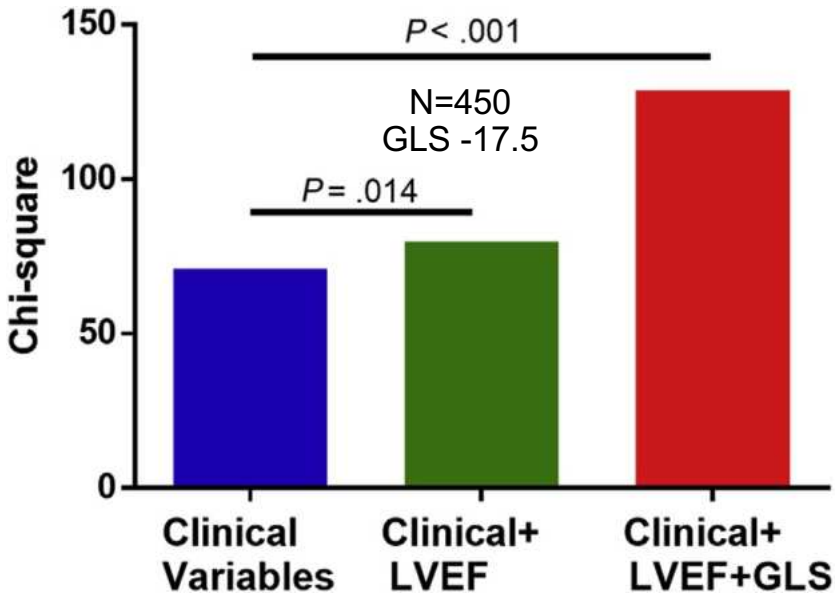


2285 Patients, BREAST, HEME, OTHER,
Anthracycline (Doxo - 223mg/m^2)
Wang L..Scherrer-Crosbie et al AJC 2015

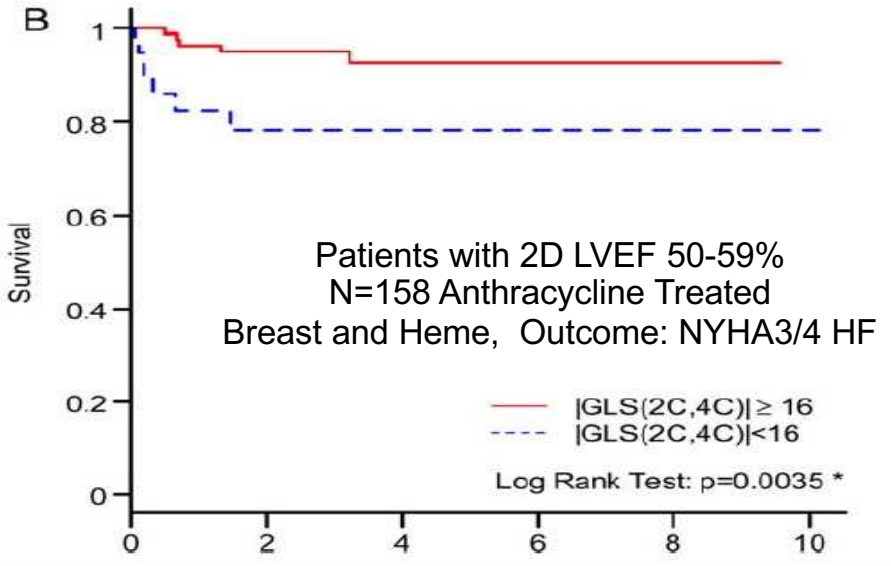
Risk Factor	# Pts	HR	p
Baseline LVEF			
≥ 65%	423	Ref	
55-64%	451	1.98	0.092
50-54%	70	6.72	<0.001
Post-AC LVEF			
≥ 65%	351	Ref	
55-64%	473	3.58	0.02
50-54%	111	11.84	<0.001

NSABP-31, 944 Patients, HER2+ BC
Cardiac Death, Clic HF (assoc with LVEF drop)
4.0% Developed an Event (by 7 years)

Pre-Treatment Risk Assessment - Strain

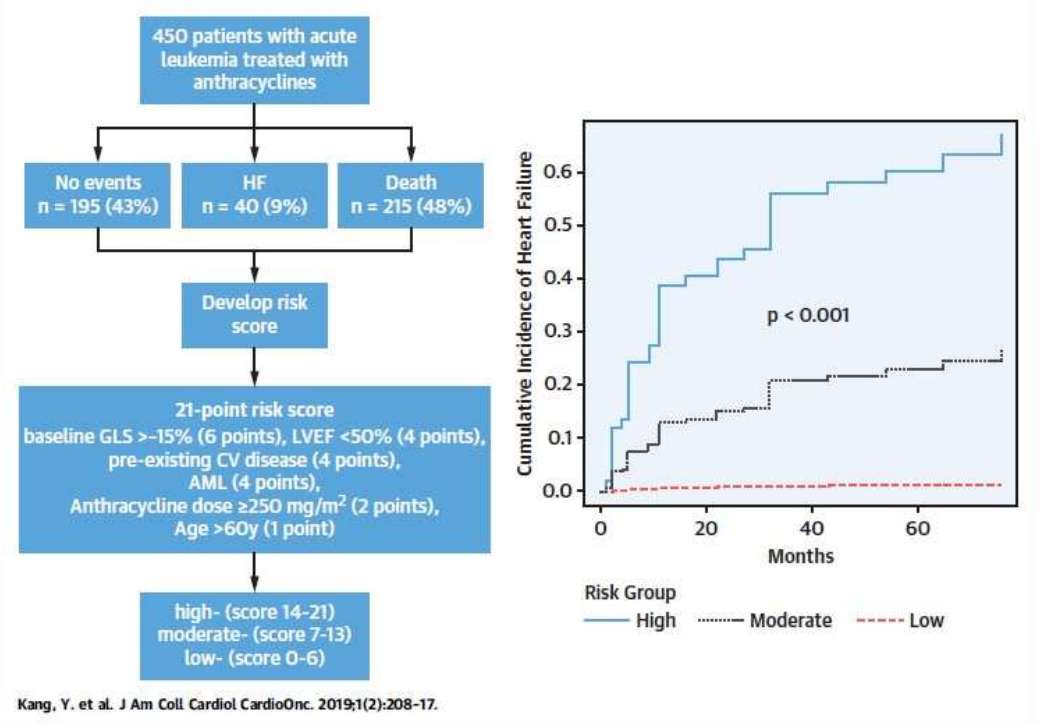


Mohammed TA, et al JASE 2016
Strain TomTec (2D CPA), n=450
Anthracycline Rx Heme Malignancies
Symptomatic HF or CV Death



Mousavi et al, EHJCVI 2015
Strain – TomTec 2D CPA, n=158
Heme, Breast, Other
Symptomatic HF or CV Death

Pre-Treatment Risk Assessment - Strain



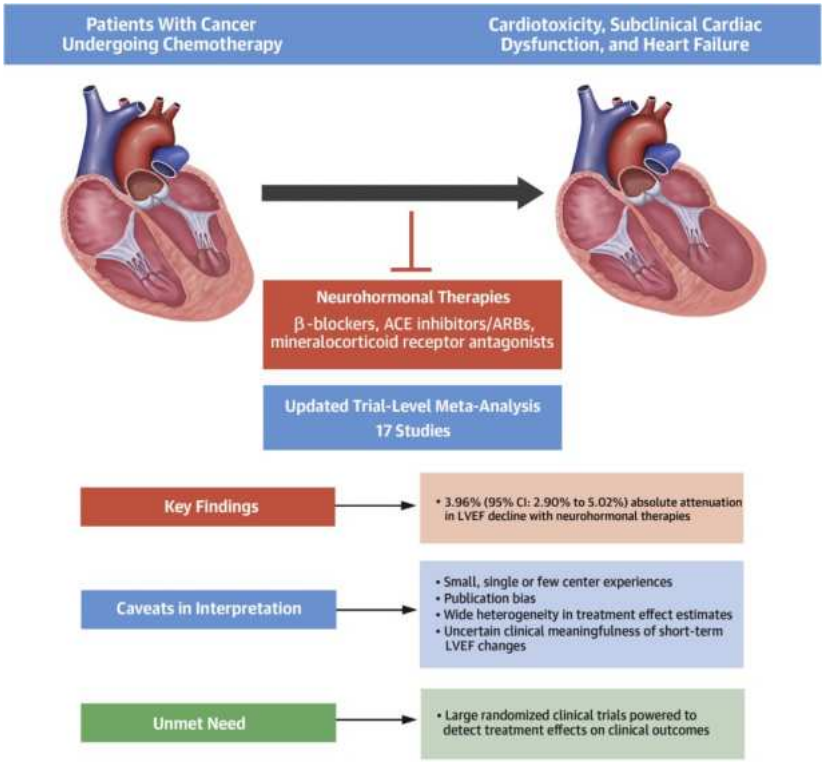
Kang, Y. et al. J Am Coll Cardiol CardioOnc. 2019;1(2):208-17.

Symptomatic HF
GLS associated with all cause death!

Kang et al JACC CO 2020

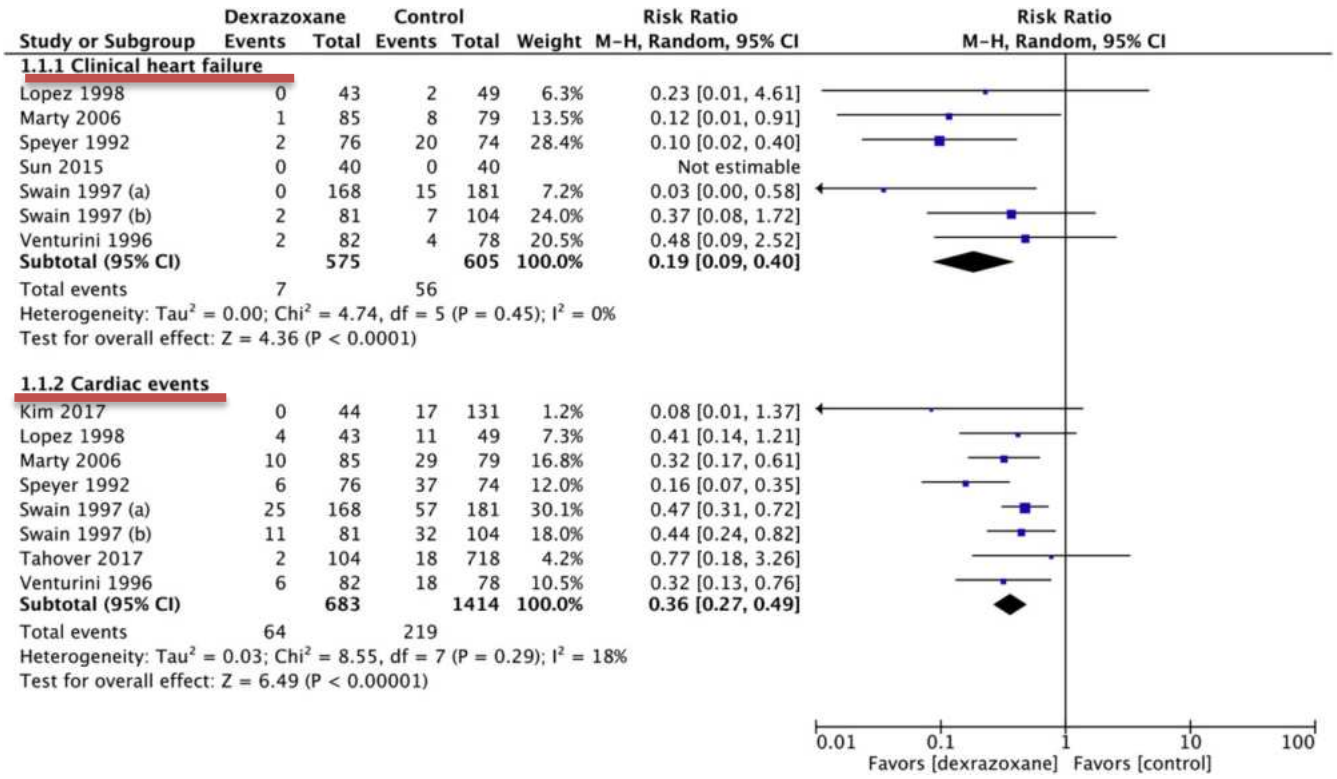
Universal Primary Prevention

Neurohormonal Blockade



Vaduganathan M et al, JACC Cardio-oncology 2019

Dexrazoxane



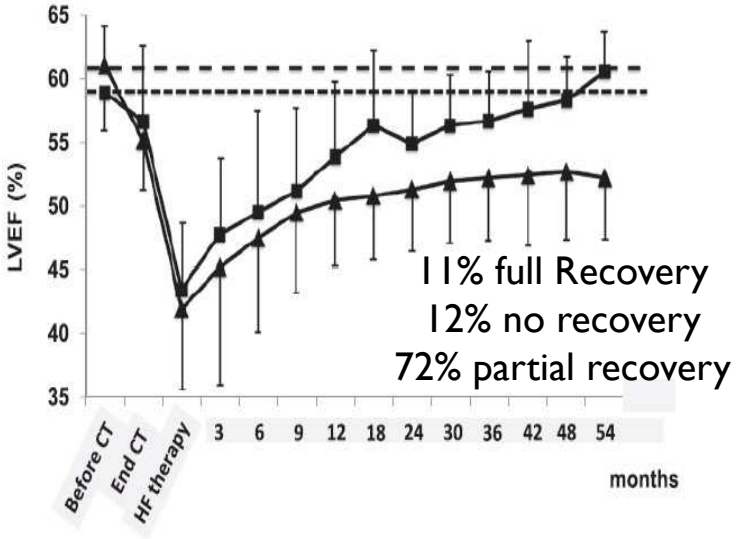
Study or Subgroup	Dexrazoxane Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Clinical heart failure						
Lopez 1998	0	43	2	49	6.3%	0.23 [0.01, 4.61]
Marty 2006	1	85	8	79	13.5%	0.12 [0.01, 0.91]
Speyer 1992	2	76	20	74	28.4%	0.10 [0.02, 0.40]
Sun 2015	0	40	0	40		Not estimable
Swain 1997 (a)	0	168	15	181	7.2%	0.03 [0.00, 0.58]
Swain 1997 (b)	2	81	7	104	24.0%	0.37 [0.08, 1.72]
Venturini 1996	2	82	4	78	20.5%	0.48 [0.09, 2.52]
Subtotal (95% CI)		**575**		**605**	**100.0%**	**0.19 [0.09, 0.40]**
Total events	7		56			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.74$, df = 5 (P = 0.45); $I^2 = 0\%$						
Test for overall effect: Z = 4.36 (P < 0.0001)						
1.1.2 Cardiac events						
Kim 2017	0	44	17	131	1.2%	0.08 [0.01, 1.37]
Lopez 1998	4	43	11	49	7.3%	0.41 [0.14, 1.21]
Marty 2006	10	85	29	79	16.8%	0.32 [0.17, 0.61]
Speyer 1992	6	76	37	74	12.0%	0.16 [0.07, 0.35]
Swain 1997 (a)	25	168	57	181	30.1%	0.47 [0.31, 0.72]
Swain 1997 (b)	11	81	32	104	18.0%	0.44 [0.24, 0.82]
Tahover 2017	2	104	18	718	4.2%	0.77 [0.18, 3.26]
Venturini 1996	6	82	18	78	10.5%	0.32 [0.13, 0.76]
Subtotal (95% CI)		**683**		**1414**	**100.0%**	**0.36 [0.27, 0.49]**
Total events	64		219			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 8.55$, df = 7 (P = 0.29); $I^2 = 18\%$						
Test for overall effect: Z = 6.49 (P < 0.00001)						

Macedo et al, JACC CO 2019

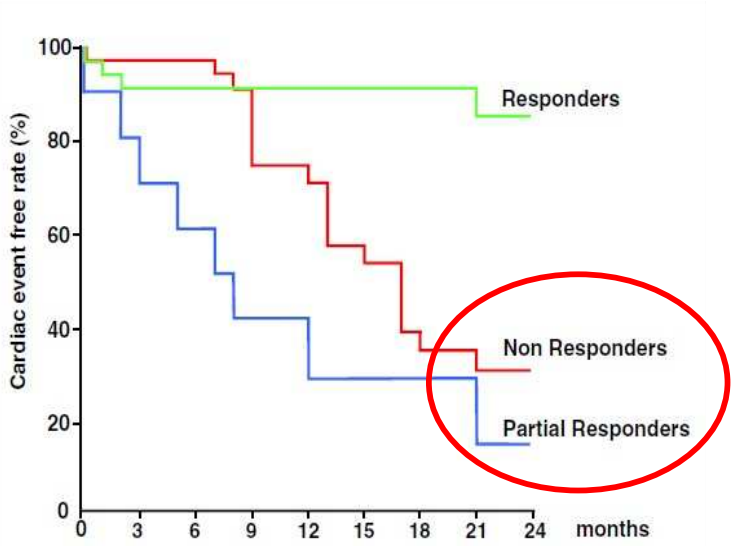
Risk Assessment During Cancer Treatment

Limitations of an LVEF Only Approach

Anthracyclines ± Trastuzumab

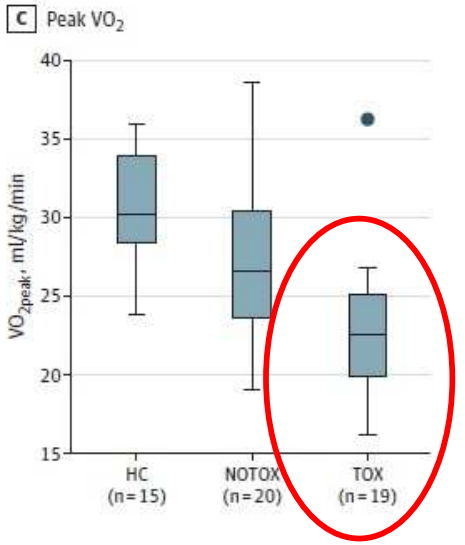


Cardinale D et al, Circulation 2015



Death, acute pulmonary edema, HF hospitalization, life threatening arrhythmia, conduction abnormalities requiring PM

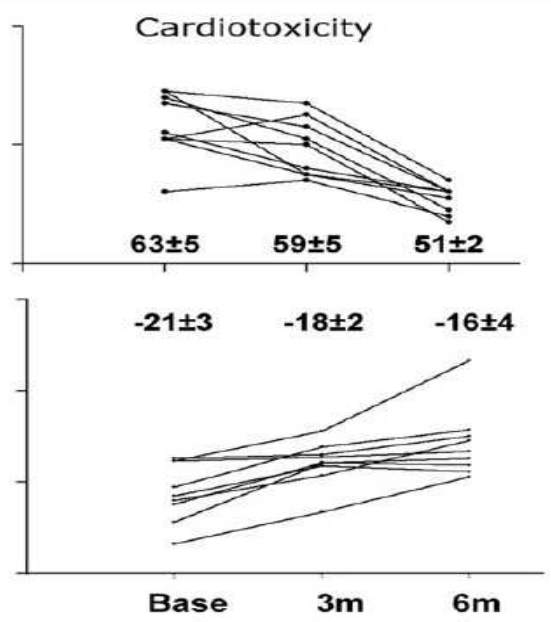
Cardinale D et al, JACC 2010



MEDIAN 7.0 Years Post Therap

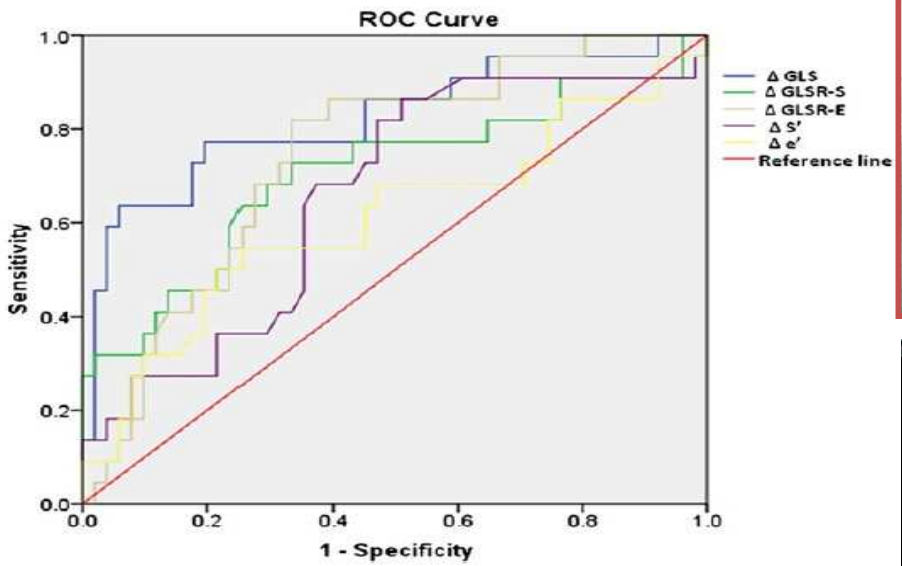
Yu A et al, JAMA Cardiology, 2019

Global Longitudinal Strain



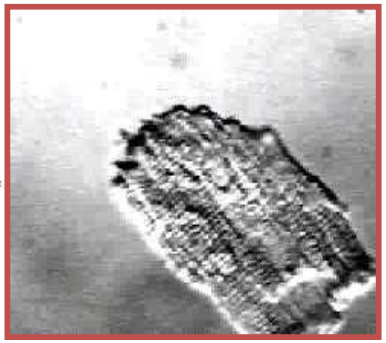
N=43, 21% CTOX, AC followed by TZM

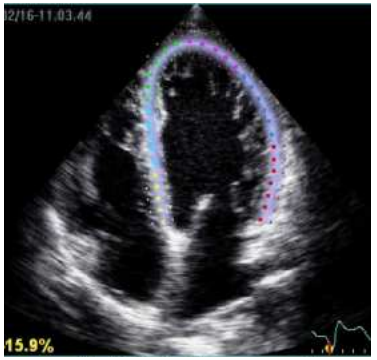
Sawaya H et al. Am J Cardiol 2011;107:1375



N=81, 30% CTOX, All trastuzumab, 40% A

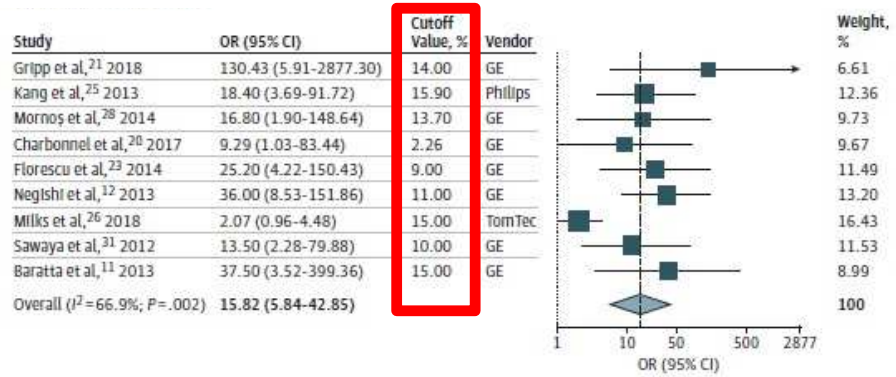
Negishi K et al, JASE 2013, 26: 493-8



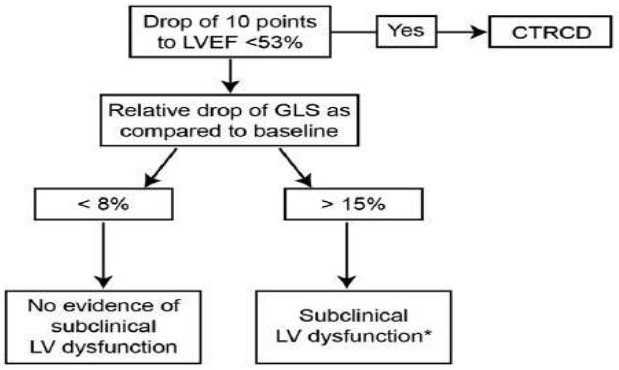


Global Longitudinal Strain – Meta-analysis

- Relative GLS (n=9)
  - Median 13.7%
- Absolute GLS (n=9)
  - Median -18.0%



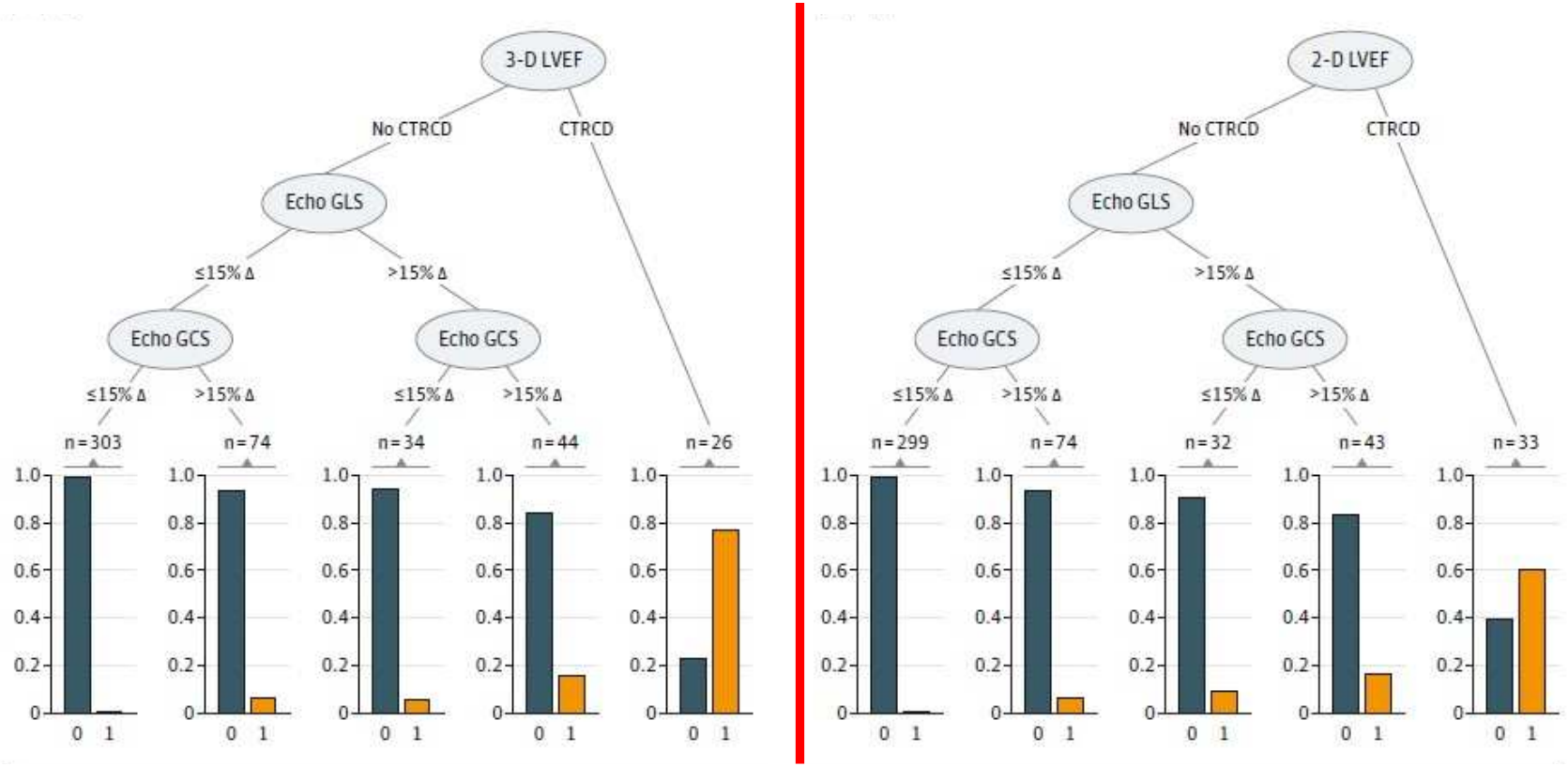
Study	OR (95% CI)	Cutoff Value, %	Vendor	Weight, %
Gripp et al,[21] 2018	130.43 (5.91-2877.30)	14.00	GE	6.61
Kang et al,[25] 2013	18.40 (3.69-91.72)	15.90	Philips	12.36
Mornoş et al,[28] 2014	16.80 (1.90-148.64)	13.70	GE	9.73
Charbonnel et al,[20] 2017	9.29 (1.03-83.44)	2.26	GE	9.67
Florescu et al,[23] 2014	25.20 (4.22-150.43)	9.00	GE	11.49
Negishi et al,[12] 2013	36.00 (8.53-151.86)	11.00	GE	13.20
Milks et al,[26] 2018	2.07 (0.96-4.48)	15.00	TomTec	16.43
Sawaya et al,[31] 2012	13.50 (2.28-79.88)	10.00	GE	11.53
Baratta et al,[11] 2013	37.50 (3.52-399.36)	15.00	GE	8.99
Overall (I^2=66.9%; P=.002)	**15.82 (5.84-42.85)**			**100**



Oikonomou EK et al P, JAMA Cardiology 2019

Plana et al, JASE 2014

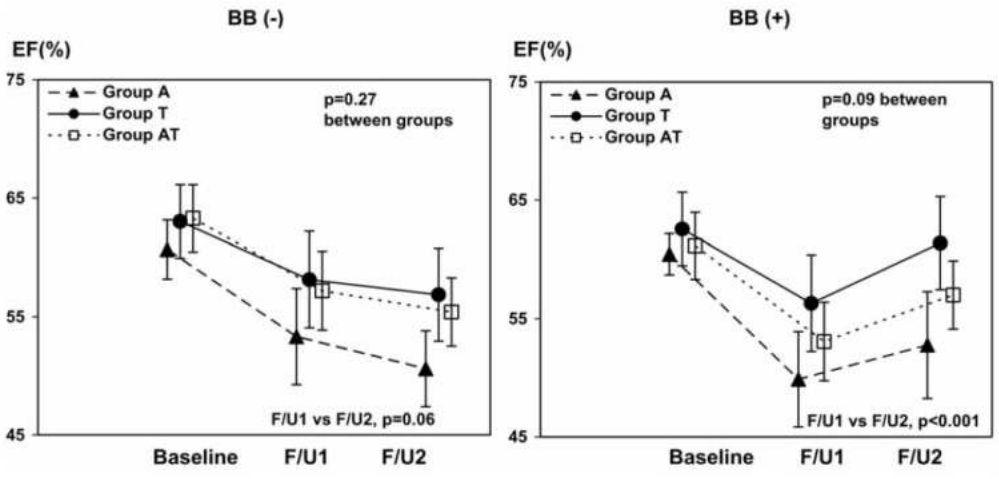
Integrated Approach to The Diagnosis

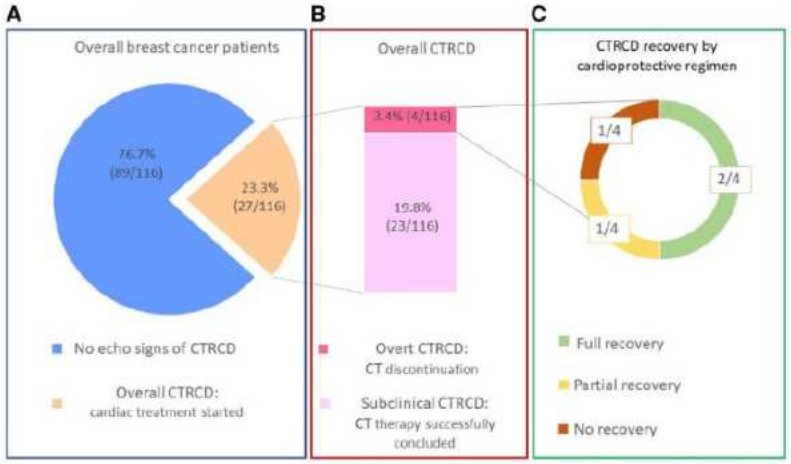


Probability of MRI defined CTRCD

Esmaeilzadeh M et al JAMA Cardiology, Feb 2022

GLS Guided Cardioprotection





Negishi K et al, EHJ CVI 2014; Santoro C et al EHJ CVI 2019

SUCCOUR TRIAL

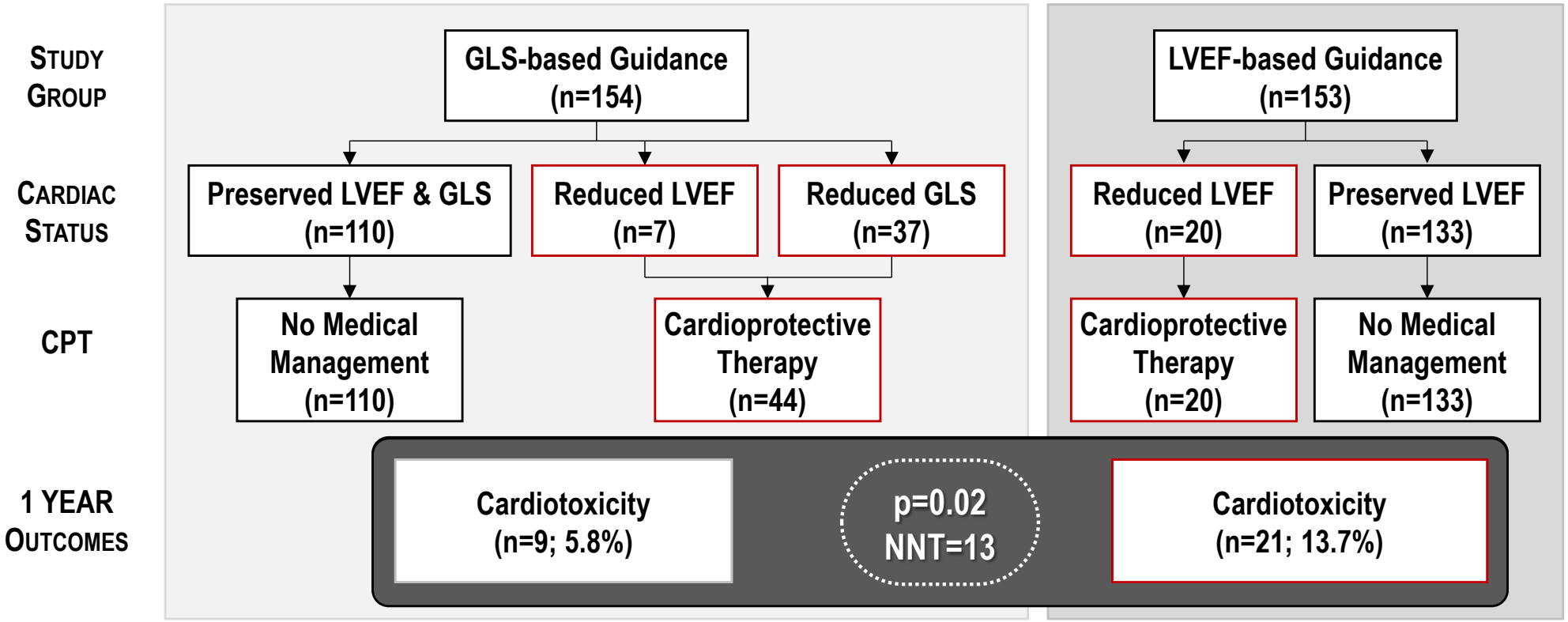
Strain- vs LVEF-based Guidance for Cardio-protection

OBJECTIVE

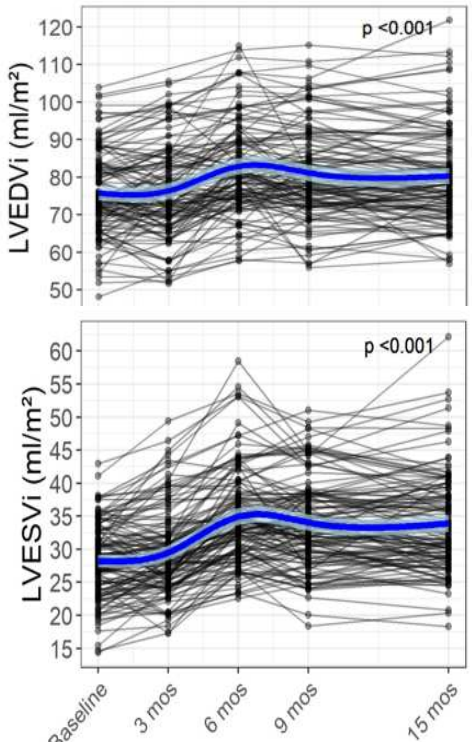
To determine whether a strain guided approach to CPT can prevent reduction in LVEF and development of cardiotoxicity compared to standard of care (LVEF based CPT) in patients receiving anthracycline based cancer therapy at elevated cardiotoxicity risk

Thavendiranathan P, Negishi T….Marwick TH et al, JACC 2021

Results

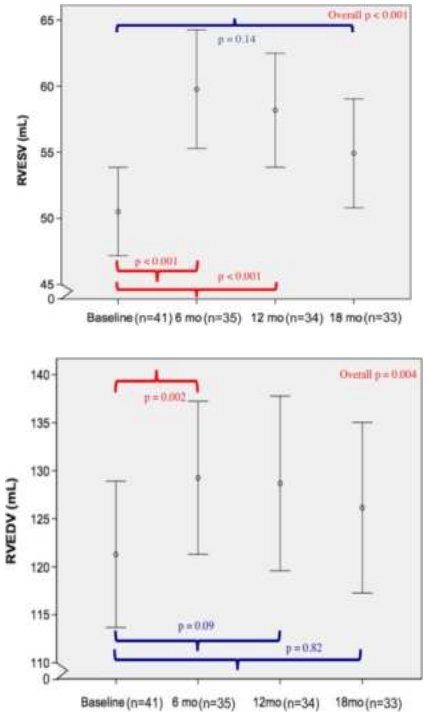

STUDY GROUP
GLS-based Guidance (n=154)
LVEF-based Guidance (n=153)
CARDIAC STATUS
Preserved LVEF & GLS (n=110)
Reduced LVEF (n=7)
Reduced GLS (n=37)
Reduced LVEF (n=20)
Preserved LVEF (n=133)
CPT
No Medical Management (n=110)
Cardioprotective Therapy (n=44)
Cardioprotective Therapy (n=20)
No Medical Management (n=133)
1 YEAR OUTCOMES
Cardiotoxicity (n=9; 5.8%)
p=0.02
NNT=13
Cardiotoxicity (n=21; 13.7%)

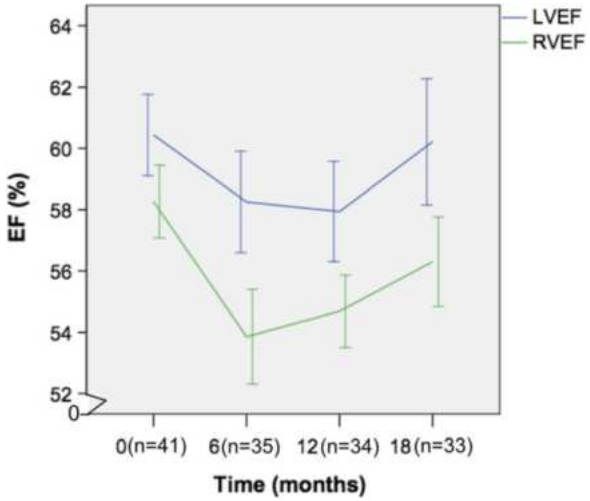
CMR - Ventricular Remodeling



HER2+ BC, FEC-DH, N=125

Hubois C, Thavendiranathan P et al, JACCi; 2021





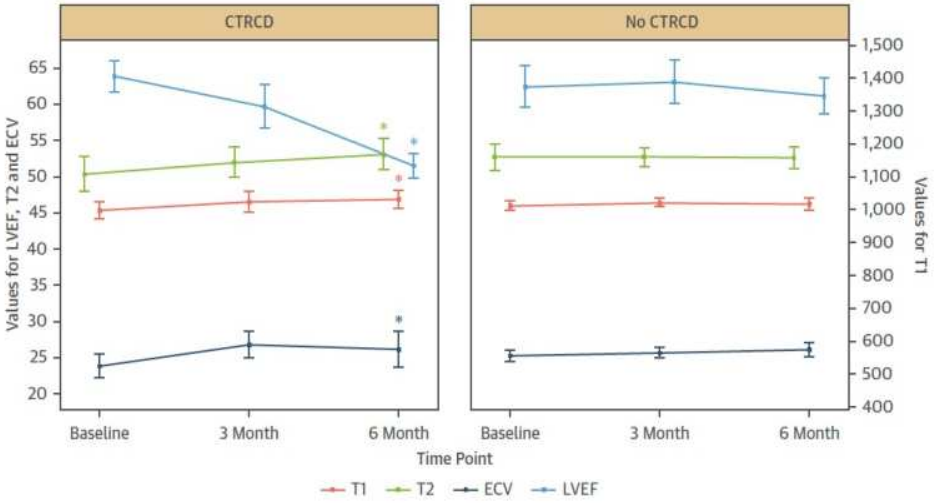
HER2+ BC, 56% Anthracyclines, N=41

Barthur A, Yan AT et al SCMR 2017, 19:44

CMR Tissue Characterization

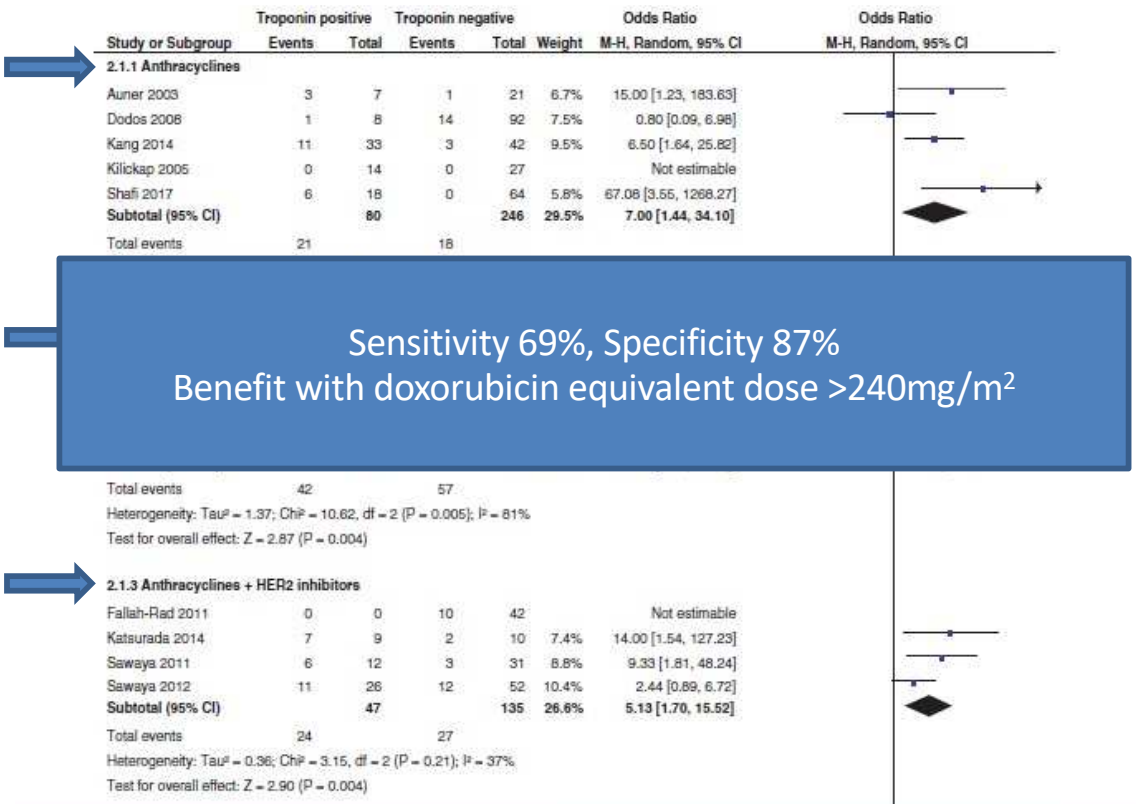
	Anthracycline (N=40)		Non-anthracycline (N=16)	
	Baseline (N=40)	3 months (N=40)	Baseline (N=16)	3 months (N=16)
Native T1, ms	1,058 ± 100	1,071 ± 85.2*	1,036 ± 41	1,041 ± 38
T2, ms	50.8 ± 2.9	51.6± 3.5	51.5 ± 2.2	52.4 ± 2.9
T2 Septum, ms	50.7 ± 2.7	51.9± 3.8*	51.6 ± 3.1	52.3±3.2
ECV, %	26.9 ± 3.1	28.6 ± 3.0*	26.7 ± 3.3	27.7 ± 3.8

CMR pre and ~3 months post initiation of Rx
Doxorubicin equivalent mean - 375mg/m2
Melendez GC et al. JACCi 2017



FEC-DH, N=20
Doxorubicin equivalent mean 200mg/m2
Altaha M et al JACCi 2020

Role of Serum Biomarkers

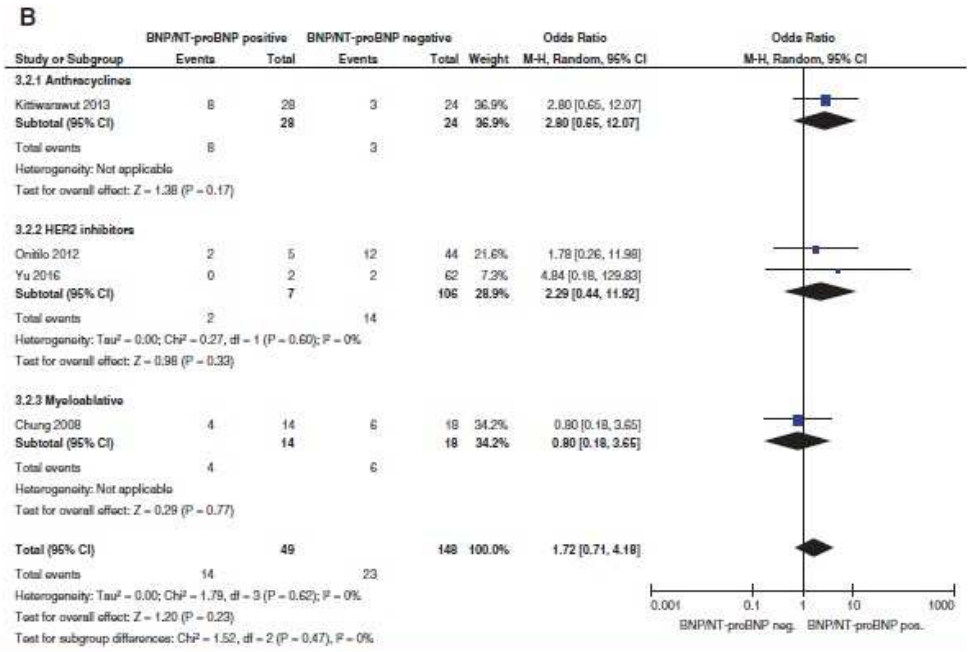


Study or Subgroup	Troponin positive Events	Total	Troponin negative Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
2.1.1 Anthracyclines						
Auner 2003	3	7	1	21	6.7%	15.00 [1.23, 183.63]
Dodos 2008	1	8	14	92	7.5%	0.80 [0.09, 6.98]
Kang 2014	11	33	3	42	9.5%	6.50 [1.64, 25.82]
Kilickap 2005	0	14	0	27		Not estimable
Shafi 2017	6	18	0	64	5.8%	67.08 [3.55, 1268.27]
Subtotal (95% CI)		**80**		**246**	**29.5%**	**7.00 [1.44, 34.10]**
Total events	21		18			
Total events	42		57			
Heterogeneity: Tau² = 1.37; Chi² = 10.62, df = 2 (P = 0.005); I² = 81%						
Test for overall effect: Z = 2.87 (P = 0.004)						
2.1.3 Anthracyclines + HER2 inhibitors						
Fallah-Rad 2011	0	0	10	42		Not estimable
Katsurada 2014	7	9	2	10	7.4%	14.00 [1.54, 127.23]
Sawaya 2011	6	12	3	31	8.8%	9.33 [1.81, 48.24]
Sawaya 2012	11	26	12	52	10.4%	2.44 [0.89, 6.72]
Subtotal (95% CI)		**47**		**135**	**26.6%**	**5.13 [1.70, 15.52]**
Total events	24		27			
Heterogeneity: Tau² = 0.36; Chi² = 3.15, df = 2 (P = 0.21); I² = 37%						
Test for overall effect: Z = 2.90 (P = 0.004)						

Odds Ratio M-H, Random, 95% CI

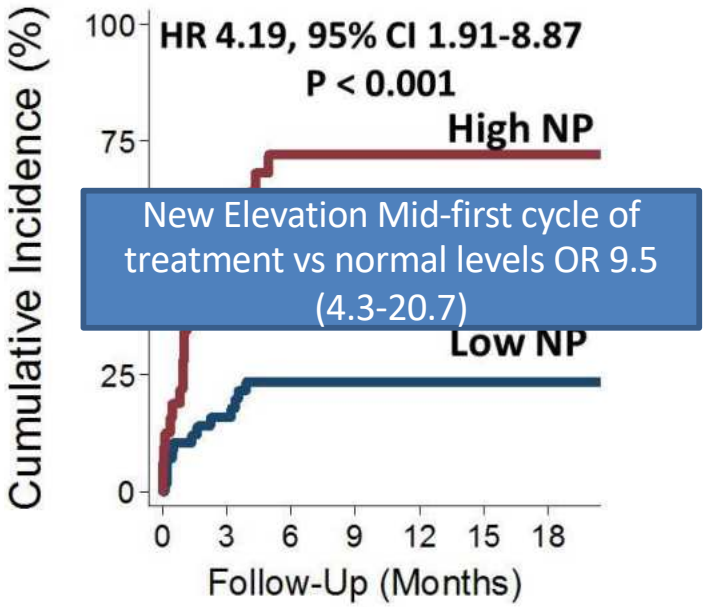
Sensitivity 69%, Specificity 87%
Benefit with doxorubicin equivalent dose >240mg/m^2

Role of Serum Biomarkers



Michel L et al, EJHF 2020

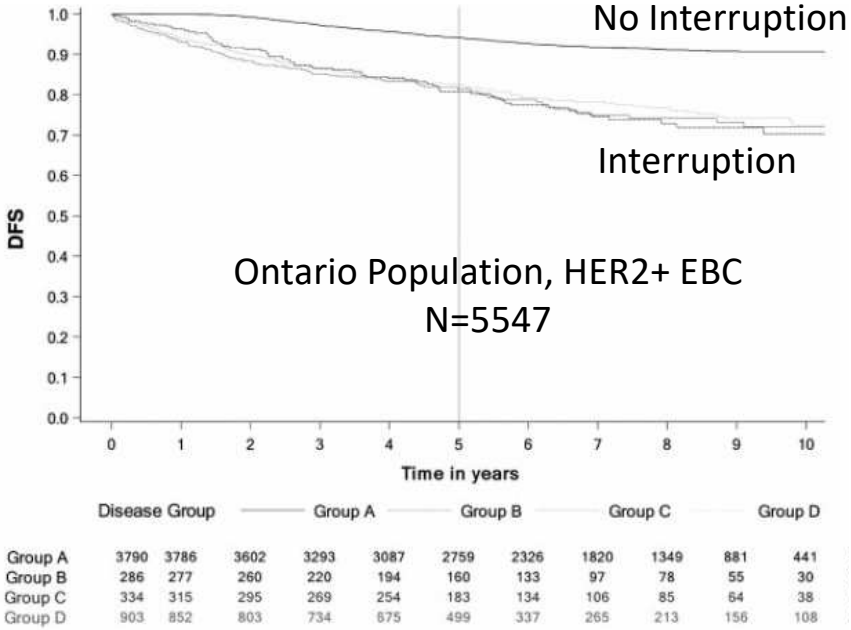
Multiple Myeloma PI



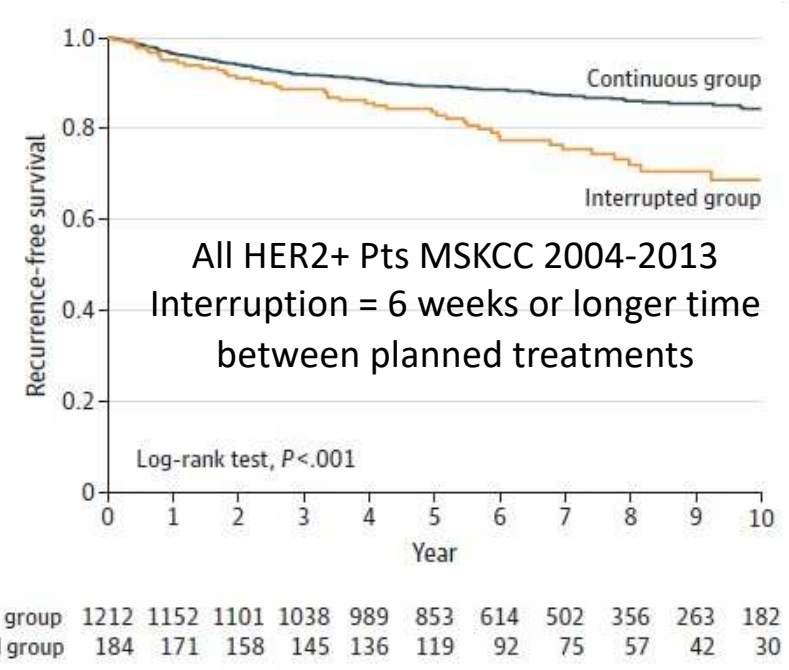
Cornell F …Lenihan D et al, JCO 2019

Interruption of Cancer Therapy?

Consequences of Trastuzumab Interruption



Rushton M et al, JNCI 2020



Copeland-Halperin R et al, JAMA Oncol2020

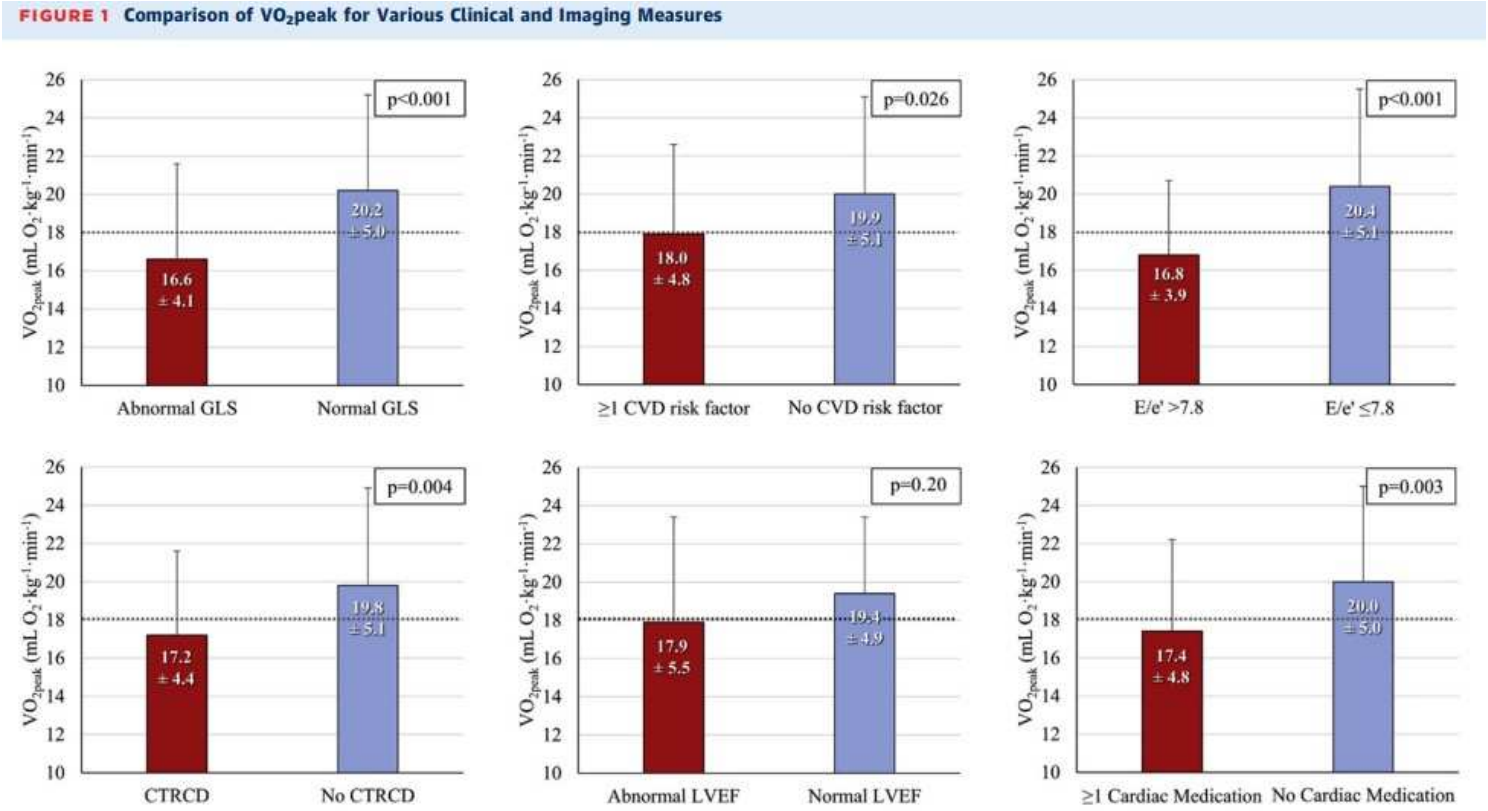
Treatment of HF

Pillars of Therapy

- Decision regarding cancer therapy (lean towards continuing)
- The 4 foundations of therapy for HFrEF apply (majority LVEF >40%)
  - Focus on BB/ACE/ARB
  - Goal is rapid recovery to enable cancer therapy
- Early imaging follow-up to assess recovery
- Advanced HFrEF – no different from other NICM/HF

Identifying Subclinical Injury / CVD Risk Assessment in Survivors

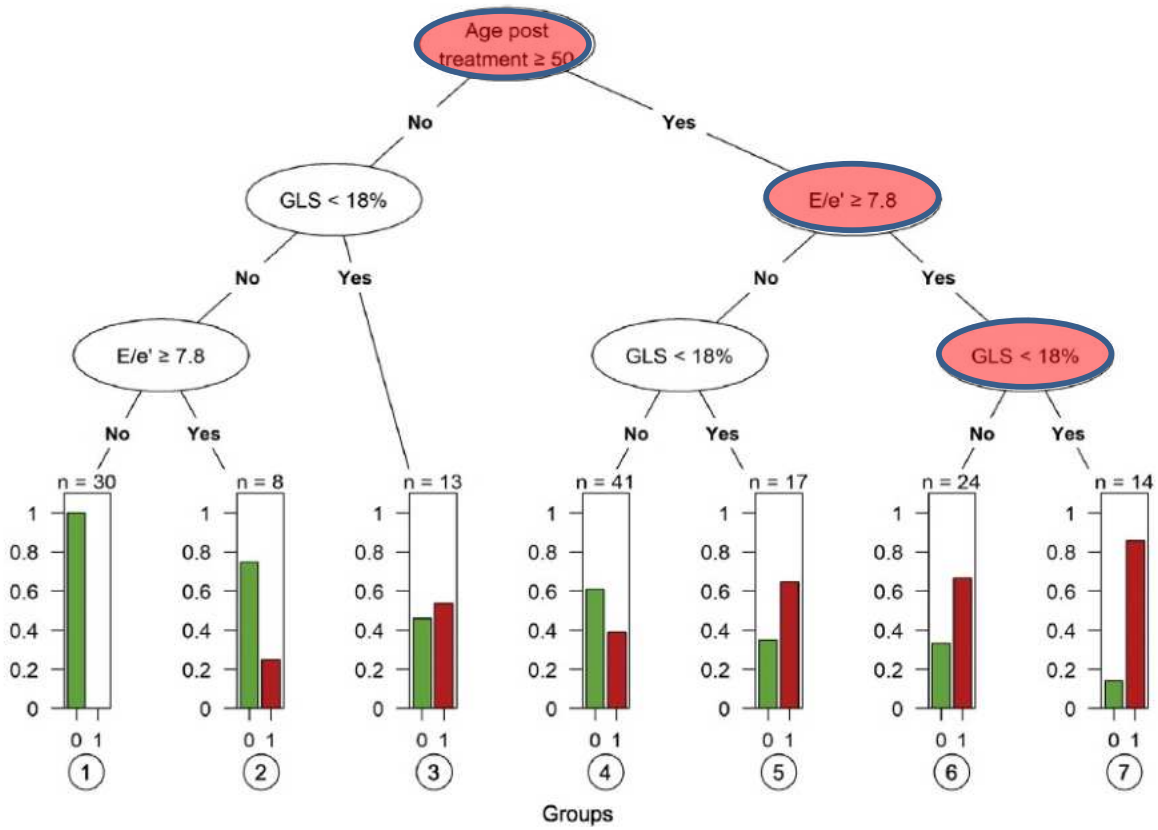
End of Treatment Variables and CRF



Bonsignore A et al JACC CardioOncology, 2021

End of Treatment Variables and CRF

Probability of loss of functional independence



Bonsignore A et al JACC CardioOncology, 2021

Summary

- CVD important competing risk for morbidity / mortality
- Pre-treatment risk stratification challenging
  - LVEF / GLS
  - No established primary prevention strategies (statins / SGLT2?)
  - High risk patients – BB, ACE/ARB, statins, dexrazoxane
- Early detection of cardiovascular injury attractive
- Global longitudinal strain
  - Identifies subclinical injury / GLS guided Rx reduces cardiotoxicity

Summary

- Troponin and BNP may have a role with select treatments
  - Measured after each cycle
- Interruption of cancer therapy should be minimized
- HF treatment – as per HFrEF
- Assessing long term risk / determining follow-up challenging
  - Cardiotoxicity history, imaging abnormalities – may be helpful

Canadian Cancer Society
Société canadienne du cancer

CIHR IRSC
Canadian Institutes of Health Research
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Thank you
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