ACC Latin America Conference 2017

MEXICO CITY

JUNE 22 – 24, 2017

GLOBAL EXPERTS, LOCAL LEARNING

ACC Latin America Conference 2017

Drugs/Agents that Exacerbate HF

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Overall General Recommendations

- Review each drug at each and every encounter
- Specifically ask about OTC and alternatives bought at health store
- Ask about diminution of therapeutic response
- Educate and advise
- Keep medication list as “simple” as possible to only necessary meds
- Keep dosing schedule as easy as possible
- Ask pts to bring ALL their medications at each visit, including what they have at home

Today:

- Drugs that are commonly used without recognition of worsening of HF
- Medications already high in sodium
- Chemotherapeutic agents that although necessary, worsen cardiac disease, especially, HF

Drugs That May Cause or Exacerbate Heart Failure

A Scientific Statement From the American Heart Association

Circulation. 2016;134:e32–e69.

Drug or Therapeutic Class	Association With HF		Magnitude of HF Induction or Precipitation	Level of Evidence for HF Induction or Precipitation	Possible Mechanism(s)	Onset	Comments
	Causes Direct Myocardial Toxicity	Exacerbates Underlying Myocardial Dysfunction					
Analgesics							
COX, nonselective inhibitors (NSAIDs)		x	Major	B	Prostaglandin inhibition leading to sodium and water retention, increased systemic vascular resistance, and blunted response to diuretics	Immediate	
COX, selective inhibitors (COX-2 inhibitors)		x	Major	B			
Anesthesia medications							
Inhalation or volatile anesthetics							
Desflurane		x	Major	B	Myocardial depression, peripheral vasodilation, attenuated sympathetic activity	Immediate	Sole induction alone is not generally used because of hemodynamic instability and airway irritation in patients with HF
Enflurane		x	Major	B			
Halothane		x	Major	B			
Isoflurane		x	Major	B			
Sevoflurane		x	Major	B			
Intravenous anesthetics							
Dexmedetomidine		x	Moderate	B	α_2-Adrenergic agonist	Immediate	
Etomidate		x	Moderate	B	Suppression of adrenal function		Not generally used for maintenance of anesthesia
Ketamine		x	Major	B	Negative inotrope		
Propofol		x	Moderate	B	Negative inotrope, vasodilation		

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Biguanide							
Metformin		x	Major	C	Increased anaerobic metabolism and elevated lactic acidosis	Immediate to delayed (depending on renal function fluctuations)	
Thiazolidinediones		x	Major	A	Possible calcium channel blockade	Intermediate	May be reversible on discontinuation; not recommended in patients with symptomatic HF
Dipeptidyl peptidase-4 inhibitors							
Saxagliptin		x	Major	B	Unknown	Intermediate to delayed	May be a class effect
Sitagliptin		x	Major	B		Intermediate to delayed	
Antiarrhythmic medications							
Class I antiarrhythmics							
Flecainide		x	Major	B	Negative inotrope, proarrhythmic effects	Immediate to intermediate	
Disopyramide		x	Major	B		Immediate to	
Antiarrhythmic medications, continued							
Class III antiarrhythmics							
Sotalol		x	Major	B	Proarrhythmic properties, β-blockade	Immediate to Intermediate	
Other antiarrhythmics							
Dronedarone		x	Major	A	Negative inotrope	Immediate to intermediate	

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Antihypertensive medications							
α_1-Blockers							
Doxazosin		x	Moderate	B	β_1-Receptor stimulation with increases in renin and aldosterone	Intermediate to delayed	
Calcium channel blockers							
Diltiazem		x	Major	B	Negative inotrope	Immediate to intermediate	
Verapamil		x	Major	B			
Nifedipine		x	Moderate	C			
Centrally acting α-adrenergic medications							
Moxonidine		x	Major	B	Possible sympathetic withdrawal	Intermediate	
Peripheral vasodilators							
Minoxidil		x	Moderate	C	Unknown	Intermediate	

Drugs That May Cause or Exacerbate Heart Failure

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Table 3. Definitions of Evaluation Criteria

Magnitude of precipitation or exacerbation of HF
Major: Effects that are life-threatening or effects that lead to hospitalization or emergency room visit.
Moderate: Effects that can lead to an additional clinic visit, change in NYHA functional class, change in cardiac function, or worsening cardiovascular disease (eg, hypertension, dyslipidemia, and metabolic syndrome) or effects that lead to symptoms that warrant a permanent change in the long-term medication regimen.
Minor: Effects that lead to a transient increase in patient assessment/surveillance or effects that lead to symptoms that warrant a transient medication change.
Level of Evidence of precipitation or exacerbation of HF
Level A: Multiple populations evaluated. Data derived from multiple randomized, controlled trials or meta-analyses.
Level B: Limited populations evaluated. Data derived from a single randomized, controlled trial or nonrandomized studies.
Level C: Very limited populations evaluated. Data have been reported in case reports, case studies, expert opinion, and consensus opinion.
Onset of effect
Immediate: Effect is demonstrated within 1 wk of drug administration.
Intermediate: Effect is demonstrated within weeks to months of drug administration.
Delayed: Effect is demonstrated within ≥1 y of drug administration.

Table 6. Selected Intravenous and Oral Prescription Medications High in Sodium

Medication	Sodium Content Per Unit
Alendronate effervescent tablet[287]	650 mg sodium/tablet
Ampicillin/sulbactam, injection[288]	115 mg sodium/1.5 g vial
Azithromycin, injection[289]	114 mg/500 mg vial
Erythromycin ethylsuccinate[290,291]	47 mg/tablet 23.7 mg/mL
Metronidazole, injection[292]	790 mg/500 mg vial
Nafcillin, injection[293]	132 mg/2 g vial
Omeprazole/sodium bicarbonate[294]	304 mg/capsule 406 mg/packet
Oxacillin, injection[295]	128 mg/2g vial
Piperacillin/tazobactam, injection[296]	128 mg/2.25 g vial 192 mg/3.375 g vial 256 mg/4.5 g vial
Polyethylene glycol powder for solution (Colyte, Golytely)[297]	1.46 g/1 L
Ranitidine, pre-mixed bag[298]	225 mg/50 mg vial
Sodium phosphates solution (Fleet Enema)[299]	4.4 g/118 mL
Sodium polystyrene sulfonate suspension[300]	1500 mg/60 mL
Ticarcillin/clavulanate potassium, injection[301]	429 mg/3.1 g vial

Drugs That May Cause or Exacerbate Heart Failure

A Scientific Statement From the American Heart Association

Table 8. CAMs That Increase Bleeding Risk With Anticoagulants via Platelet and/or Clotting Factor Effects[320]

Antiplatelet Effects	Anticoagulant Effects
Danshen	Dong quai
Garlic	Motherwort
Ginkgo	Liquorice
Motherwort	
Saw palmetto	
Hawthorn	
Liquorice	

CAM indicates complementary and alterna

Table 7. CAMs With Significant Interactions With Cardiovascular Medications Used in Patients With HF[320]

CAM Product	Digoxin	ACE-I/ARBs	β-Blockers	CCB	Amiodarone	Warfarin
St. John's wort	x	x	x	x	x	x
Grapefruit juice		x	x	x	x	x
Ginseng						x
Hawthorn	x					
Danshen						x
Black cohosh		x	x		x	
Green tea						x

Heart Failure due to Chemotherapeutic Agents: Issues

- Can patients at risk be identified prior to chemotherapy
- Can very early or incipient cardiomyopathy be identified
- Once identified, will biomarkers indicate severity or prognosis.
  - Used to guide therapy?
- Can HF therapy prevent the remodeling? HFpEF vs. HFrEF
  - Onset of symptoms
  - Cardiac mortality
- How is the HF treated?
  - Standard Guideline Directed Care?
    - *Where is the evidence?*

Cardiotoxicity: Definitions

Table 1 Criteria to confirm or revise a preliminary diagnosis of cardiac dysfunction.

(1) Cardiomyopathy characterized by a decrease in LVEF that was either global or more severe in the septum
(2) Symptoms of CHF
(3) Associated signs of CHF, including S3 gallop, tachycardia, or both
(4) Decline in LVEF of at least 5% to less than 55% with signs or symptoms of CHF, or a decline in LVEF of at least 10% to below 55% without signs or symptoms

Table 2 Proposed classification of chemotherapy-related cardiomyopathy.

Type of drug	Prototype	Cumulative dose relationship	Reversibility
Type I	Doxorubicin Cyclophosphamide	Yes	No
Type II	Trastuzumab Sunitinib Sorafenib	No	Yes, in most cases

Eschenhagen T, et al. Cardiovascular side effects of cancer therapies: a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2011;13:1---10.
Seidman A, et al. Cardiac dysfunction in the trastuzumab clinical trials experience. J Clin Oncol. 2002;20:1215---21.

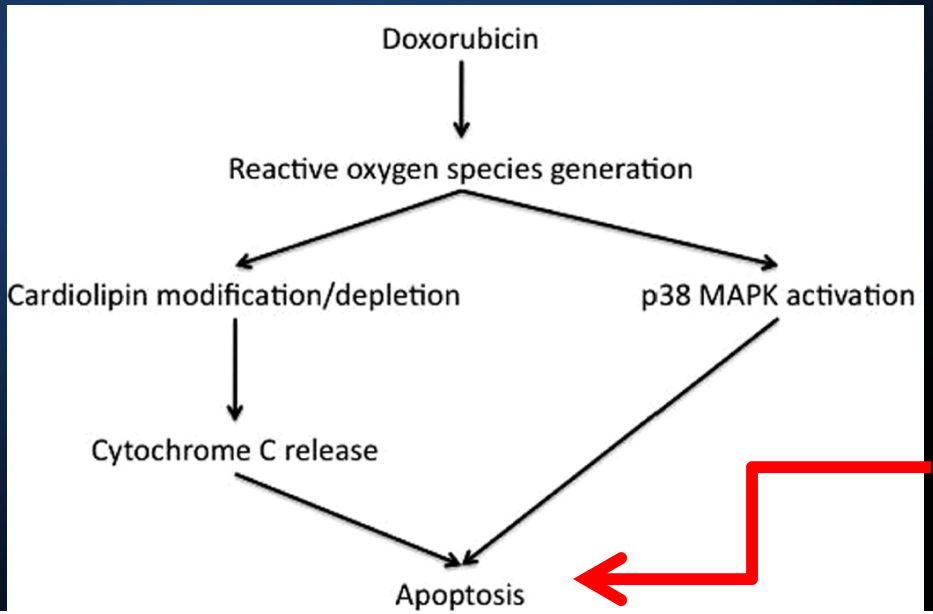
Cardiotoxicity

Table 1. Dose Related Risk of Doxorubicin-Induced Congestive Heart Failure (Based on Data from (9))

Cumulative Dose (mg/m^2)	Patients with CHF (%)
150	0.2
300	1.6
450	3.3
600	8.7

Histopathologic changes in the Myocardium can be seen with <300 mg/m2.

Billingham ME, et al.. Cancer Treat Rep 1978; 62(6): 865-72.



Troponin Release?

Volokova et al.
***Current Cardiology Reviews*, 2011, *7*, 214-220**

Mechanism of the anthracyclines

Troponin Release?

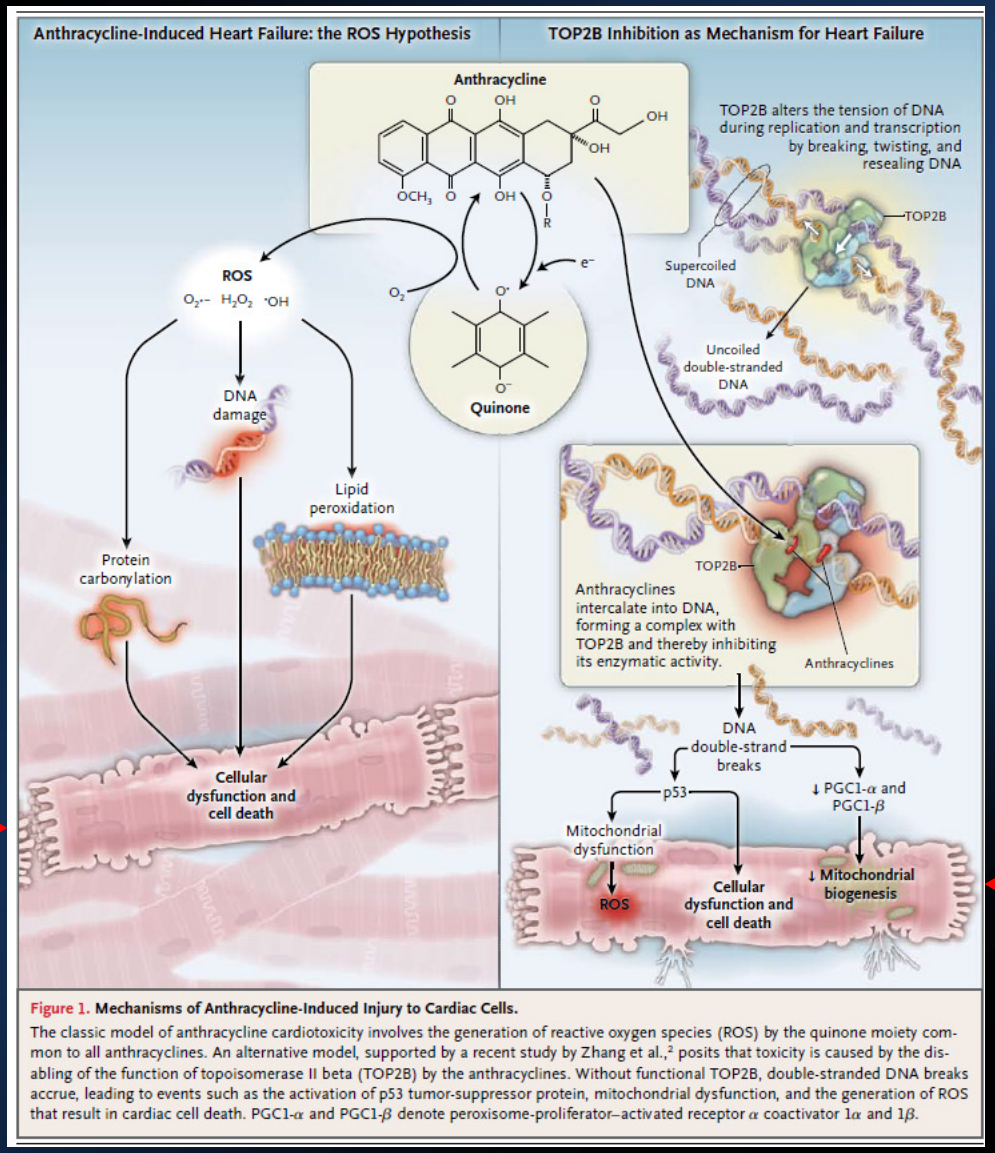


Figure 1. Mechanisms of Anthracycline-Induced Injury to Cardiac Cells.

The classic model of anthracycline cardiotoxicity involves the generation of reactive oxygen species (ROS) by the quinone moiety common to all anthracyclines. An alternative model, supported by a recent study by Zhang et al.,[2] posits that toxicity is caused by the disabling of the function of topoisomerase II beta (TOP2B) by the anthracyclines. Without functional TOP2B, double-stranded DNA breaks accrue, leading to events such as the activation of p53 tumor-suppressor protein, mitochondrial dysfunction, and the generation of ROS that result in cardiac cell death. PGC1-α and PGC1-β denote peroxisome-proliferator–activated receptor α coactivator 1α and 1β.

Troponin Release?

Sawyer DB.

N ENGL J MED 368;12 NEJM.ORG MARCH 21, 2013

Risk Factors

Can occur early (acute) or late > 1 year post chemoRx (most common)

Age >65 years or <4 years
Female gender
Hypertension
Preexisting cardiac disease
Mediastinal radiation
Treatment with cyclophosphamide, paclitaxel, or trastuzumab
Cumulative anthracycline dose
Higher individual anthracycline doses

Non-invasive Imaging

- Echocardiography has been the traditional tool +-MUGA to detect LV dysfunction
  - Manifest or early?
- Global Longitudinal Strain and strain rate (GLS) assessed using automated 2D-speckle-tracking echocardiography (STE) --recent technique for detecting and quantifying subtle disturbances in (LV) systolic function. more reproducible than ejection fraction
- Strain rate and deceleration time to detect early diastolic filling.

Table 2 Recommended cardio-oncology echocardiogram protocol

Standard transthoracic echocardiography
- In accordance with ASE/EAE guidelines and IAC-Echo

2D strain imaging acquisition
- Apical three-, four-, and two-chamber views
  - Acquire ≥3 cardiac cycles
- Images obtained simultaneously maintaining the same 2D frame rate and imaging depth
  - Frame rate between 40 and 90 frames/sec or ≥40% of HR
- Aortic VTI (aortic ejection time)

2D strain imaging analysis
- Quantify segmental and global strain (GLS)
- Display the segmental strain curves from apical views in a quad format
- Display the global strain in a bull's-eye plot

2D strain imaging pitfalls
- Ectopy
- Breathing translation

3D imaging acquisition
- Apical four-chamber full volume to assess LV volumes and LVEF calculation
- Single and multiple beats optimizing spatial and temporal resolution

Reporting
- Timing of echocardiography with respect to the IV infusion (number of days before or after)
- Vital signs (BP, HR)
- 3D LVEF/2D biplane Simpson's method
- GLS (echocardiography machine, software, and version used)
- In the absence of GLS, measurement of medial and lateral s′ and MAPSE
- RV: TAPSE, s′, FAC

Plana JC, Expert Consensus for Multimodality Imaging Evaluation of Adult Patients during and after CancerTherapy: A Report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2014;27:911-39

Echo Guidelines

- A decreased LVEF at baseline or after anthracyclines is associated with higher rates of cardiac events on follow-up.
- Although it has been suggested that alterations in LV diastolic function (as evaluated by Doppler indices of mitral inflow and e′ by pulsed DTI) precede alterations in systolic function, the evidence does not support the role of these indices for the prediction of later CTRCD.

Detecting early

- Myocardial deformation (strain) can be measured using DTI or 2D STE. The latter is favored because of a lack of angle dependency.
- GLS is the optimal parameter of deformation for the early detection of subclinical LV dysfunction.
- Ideally, the measurements during chemotherapy should be compared with the baseline value. In patients with available baseline strain measurements, a relative percentage reduction of GLS of <8% from baseline appears not to be meaningful, and those >15% from baseline are very likely to be abnormal.
- When applying STE for the longitudinal follow-up of patients with cancer, the same vendor-specific ultrasound machine should be used.

Noninvasive Cardiac Imaging

Patients with suspected or new-onset HF, or those presenting with acute decompensated HF, should undergo a chest x-ray to assess heart size and pulmonary congestion, and to detect alternative cardiac, pulmonary, and other diseases that may cause or contribute to the patients' symptoms.

A 2-dimensional echocardiogram with Doppler should be performed during initial evaluation of patients presenting with HF to assess ventricular function, size, wall thickness, wall motion, and valve function.

Repeat measurement of EF and measurement of the severity of structural remodeling are useful to provide information in patients with HF who have had a significant change in clinical status; who have experienced or recovered from a clinical event; or who have received treatment, including GDMT, that might have had a significant effect on cardiac function; or who may be candidates for device therapy.

Stage A

Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF.

Other conditions that may lead to or contribute to HF, such as obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents, should be controlled or avoided.

(*Circulation*. 2006;114:2474-2481.)

Prevention of High-Dose Chemotherapy–Induced Cardiotoxicity in High-Risk Patients by Angiotensin-Converting Enzyme Inhibition

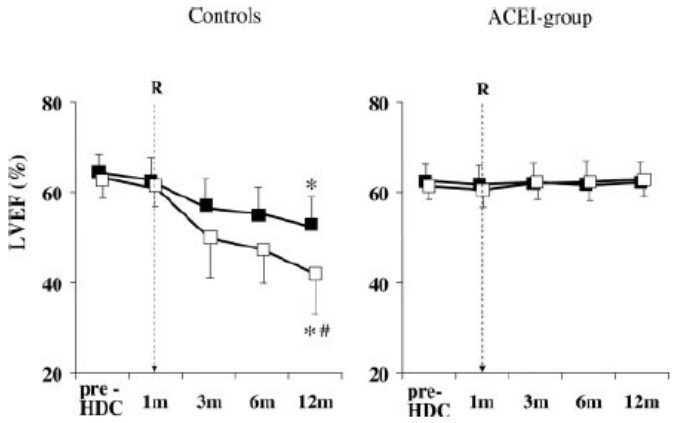
Daniela Cardinale, MD; Alessandro Colombo, MD; Maria T. Sandri, MD; Giuseppina Lamantia, MD; Nicola Colombo, MD; Maurizio Civelli, MD; Giovanni Martinelli, MD; Fabrizio Veglia, PhD; Cesare Fiorentini, MD; Carlo M. Cipolla, MD

TABLE 3. Echocardiographic Parameters During the Study Period

	Baseline	Randomization	3 mo	6 mo	12 mo	*P**
EDV, mL						
ACEI group	101.7±27.4	100.2±26.1	98.1±27.8	97.5±24.5	101.1±26.4	0.045
Control subjects	103.2±20.1	103.9±21.0	106.4±21.0	107.1±23.9	104.2±25.6	
ESV, mL						
ACEI group	38.6±10.8	38.7±10.4	37.3±10.9	37.4±10.3	38.5±11.2	<0.001
Control subjects	38.8±10.2	40.5±12.2	49.8±17.6	51.8±16.9	54.4±20.1†	
LVEF, %						
ACEI group	61.9±2.9	61.1±3.2	61.9±3.3	61.6±3.9	62.4±3.5	<0.001
Control subjects	62.8±3.4	61.8±4.3	54.2±8.1	51.9±7.9	48.3±9.3†	

TABLE 4. Cardiac Events in the Study Groups

	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



Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 48, No. 11, 2006
ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2006.07.052

Protective Effects of Carvedilol Against Anthracycline-Induced Cardiomyopathy

Nihat Kalay, MD,* Emrullah Basar, MD,* Ibrahim Ozdogru, MD,* Ozlem Er, MD,† Yakup Cetinkaya, MD,* Ali Dogan, MD,* Tugrul Inanc, MD, Abdurrahman Oguzhan, MD,* Namik Kemal Eryol, MD,* Ramazan Topsakal, MD,* Ali Ergin, MD*

Table 1. Baseline Characteristics of Patients

	Carvedilol (n = 25)	Control (n = 25)	p Value
Age (yrs)	46.8 ± 14	49.0 ± 9.8	NS
Female (%)	88	84	NS
BMI (kg/m^2)	1.75 ± 12.7	1.71 ± 21.1	NS
Baseline LVEF (%)	70.6 ± 8.0	69.7 ± 7.3	NS
LVDd (mm)	47.7 ± 5.3	45.5 ± 4.8	NS
LVSd (mm)	31.4 ± 5.0	30.2 ± 4.7	NS
Type of cancer, n (%)			
Breast	18 (72)	16 (64)	NS
Lymphoma	4 (16)	5 (20)	NS
Other	3 (12)	4 (16)	NS
CT strategy, n (%)			
CEF/CAF	17 (68)	16 (64)	NS
CHOP/ABVD	4 (16)	4 (16)	NS
Other	4 (16)	5 (20)	NS
Total adriamycin dose (mg/m^2)	525.3	513.6	NS
Total epirubicin dose (mg/m^2)	787.9	770.4	NS
Number of cycles	6	6	
Control echocardiography time (months)	5.0 ± 1.1	5.4 ± 1.3	NS

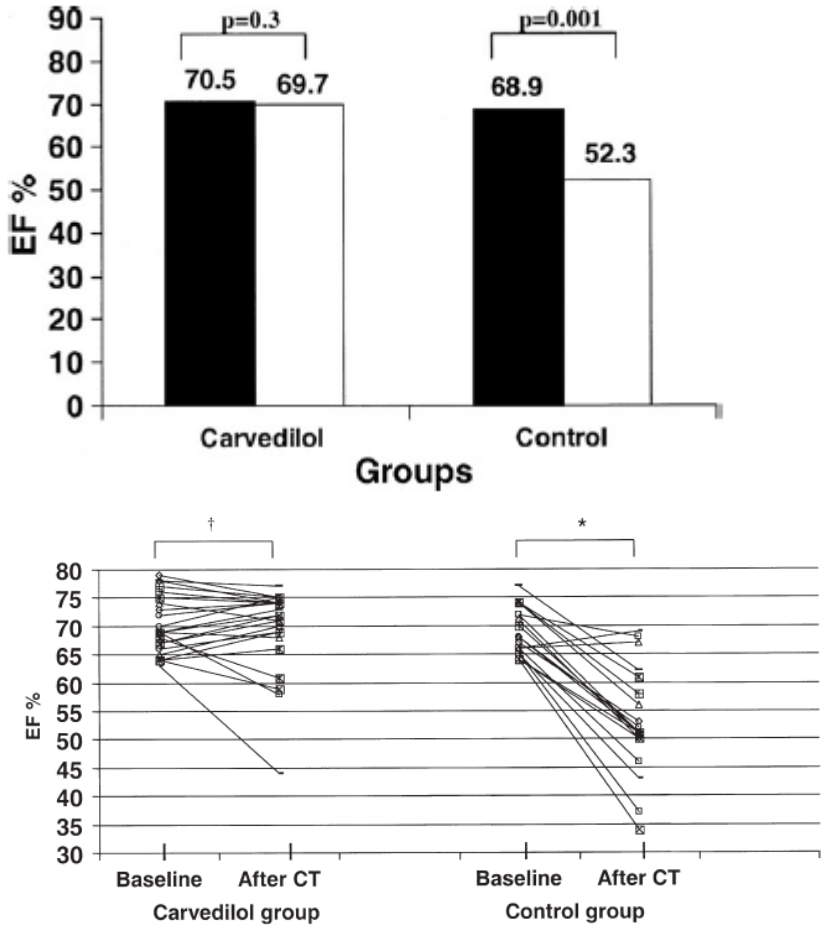

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Table 2. Results of Doppler Examination on Carvedilol Group

	Baseline	After CT	p Value
Peak E velocity (cm/s)	80.2 ± 18.4	70.5 ± 17.1	0.03*
Peak A velocity (cm/s)	75.1 ± 13.9	73.9 ± 14.3	0.79
E/A ratio	1.08 ± 0.2	0.98 ± 0.2	0.23
IVRT (ms)	64.3 ± 19.9	75.6 ± 17.8	0.1
IVCT (ms)	57.6 ± 19.6	72.3 ± 23.1	0.1

*$p < 0.05$ considered statistically significant. Data expressed as mean ± SD.
CT = chemotherapy; IVCT = isovolemic contraction time; IVRT = isovolumic relaxation time.

Table 3. Results of Doppler Examination on Control Group

	Baseline	After CT	p Value
Peak E velocity (cm/s)	69.8 ± 15.2	58.4 ± 17.9	0.019*
Peak A velocity (cm/s)	68.7 ± 13.0	68.0 ± 14.2	0.79
E/A ratio	1.03 ± 0.2	0.87 ± 0.2	0.02*
IVRT (ms)	72.7 ± 16.1	72.7 ± 2.0	0.9
IVCT (ms)	73.3 ± 18.7	78.8 ± 18.3	0.5

*$p < 0.05$ considered statistically significant. Data expressed as mean ± SD.
CT = chemotherapy; IVCT = isovolemic contraction time; IVRT = isovolemic relaxation time.

European Journal of Heart Failure (2015) **17**, 81–89
doi:10.1002/ejhf.196

Protective effects of spironolactone against anthracycline-induced cardiomyopathy

Mahmut Akpek[1]*, Ibrahim Ozdogru[1], Omer Sahin[1], Mevlude Inanc[2], Ali Dogan[1], Cevat Yazici[3], Veli Berk[2], Halit Karaca[2], Nihat Kalay[1], Abdurrahman Oguzhan[1], and Ali Ergin[1]

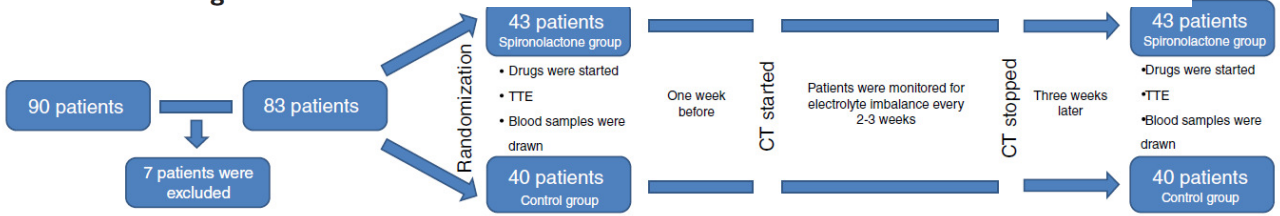
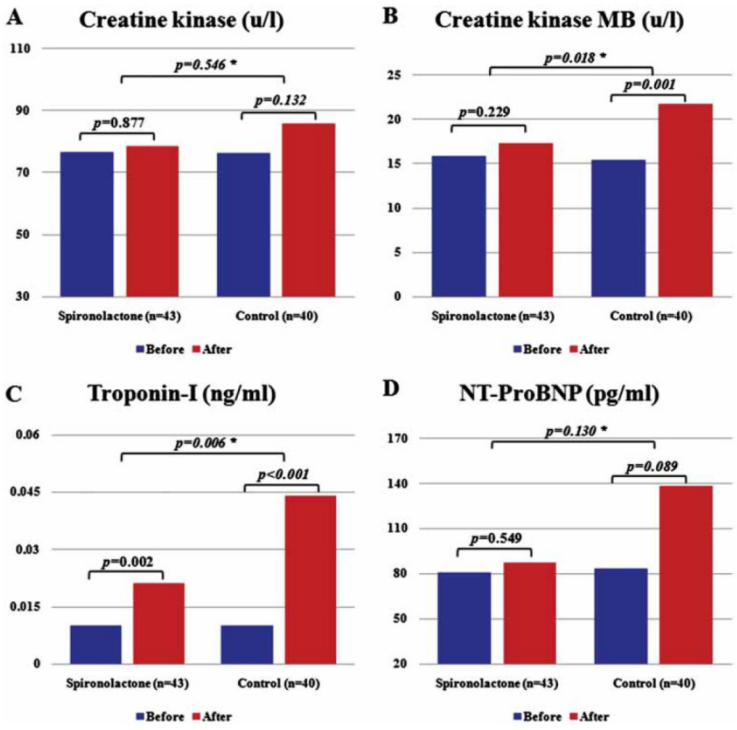


Figure 1 Study flow. CT, chemotherapy; TTE, transthoracic echocardiography.



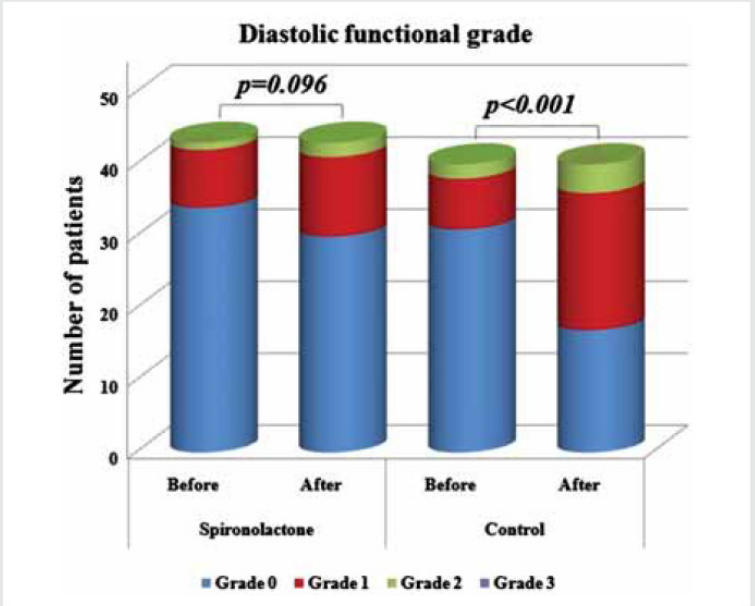


Figure 5 Changes in diastolic functional grade.

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Table 3 Cardiac and oxidative biomarkers

	Spironolactone group ($n = 43$)			Control group ($n = 40$)			
	Before	After	*P*-value	Before	After	*P*-value	*P*-value*
Creatine kinase (U/L)	74 (55–77)	69 (53–98)	0.877	70 (55–98)	87 (70–102)	0.132	0.546
Creatine kinase-MB (U/L)	15.8 ± 5.3	17.3 ± 6.0	0.229	15.4 ± 6.8	21.7 ± 9.5	0.001	0.018
Troponin-I (ng/mL)	0.010 (0.001–0.020)	0.015 (0.004–0.032)	0.002	0.010 (0.001–0.021)	0.026 (0.010–0.053)	<0.001	0.006
NT-proBNP (pg/mL)	71 (48–125)	85 (51–100)	0.549	70 (56–72)	100 (89–138)	0.089	0.130
TAC (μmol/L)	286.1 ± 44.7	275.4 ± 37.6	0.083	295.0 ± 47.5	250.4 ± 19.7	<0.001	0.001
TOC (μmol/L)	449.7 ± 222.5	487.0 ± 211.0	0.449	465.0 ± 256.4	594.8 ± 372.1	0.057	0.259
OSI	1.61 ± 0.80	1.79 ± 0.79	0.282	1.60 ± 0.90	2.37 ± 1.45	0.004	0.055

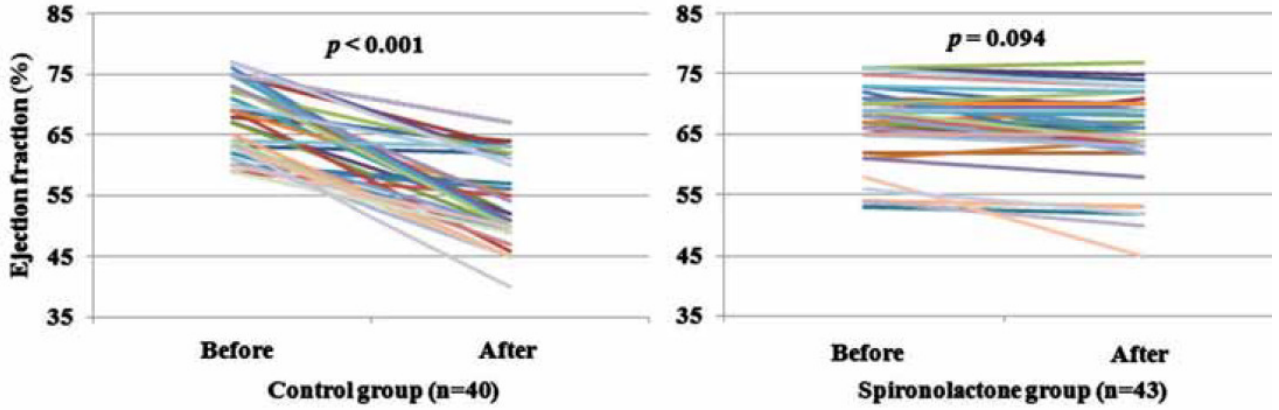
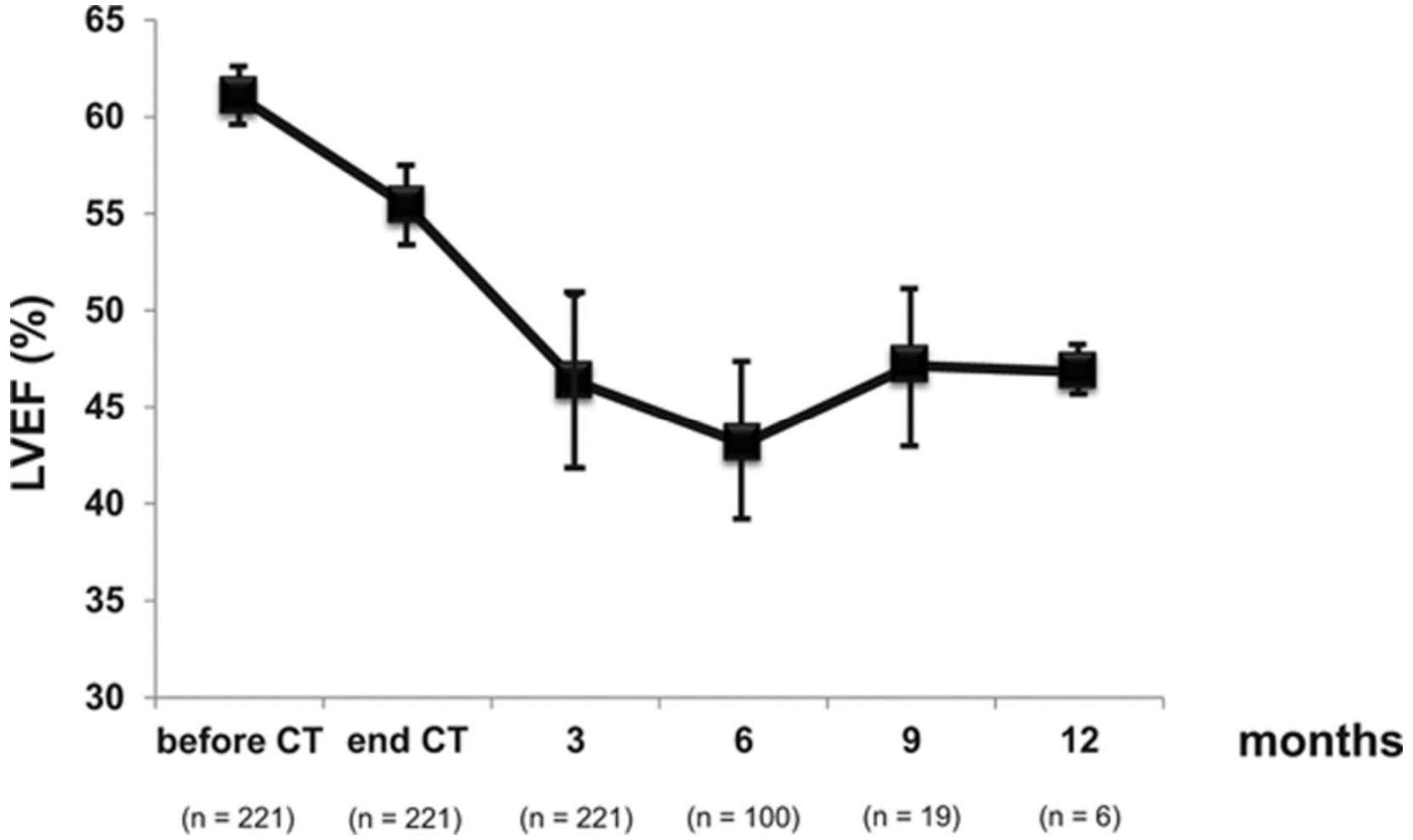


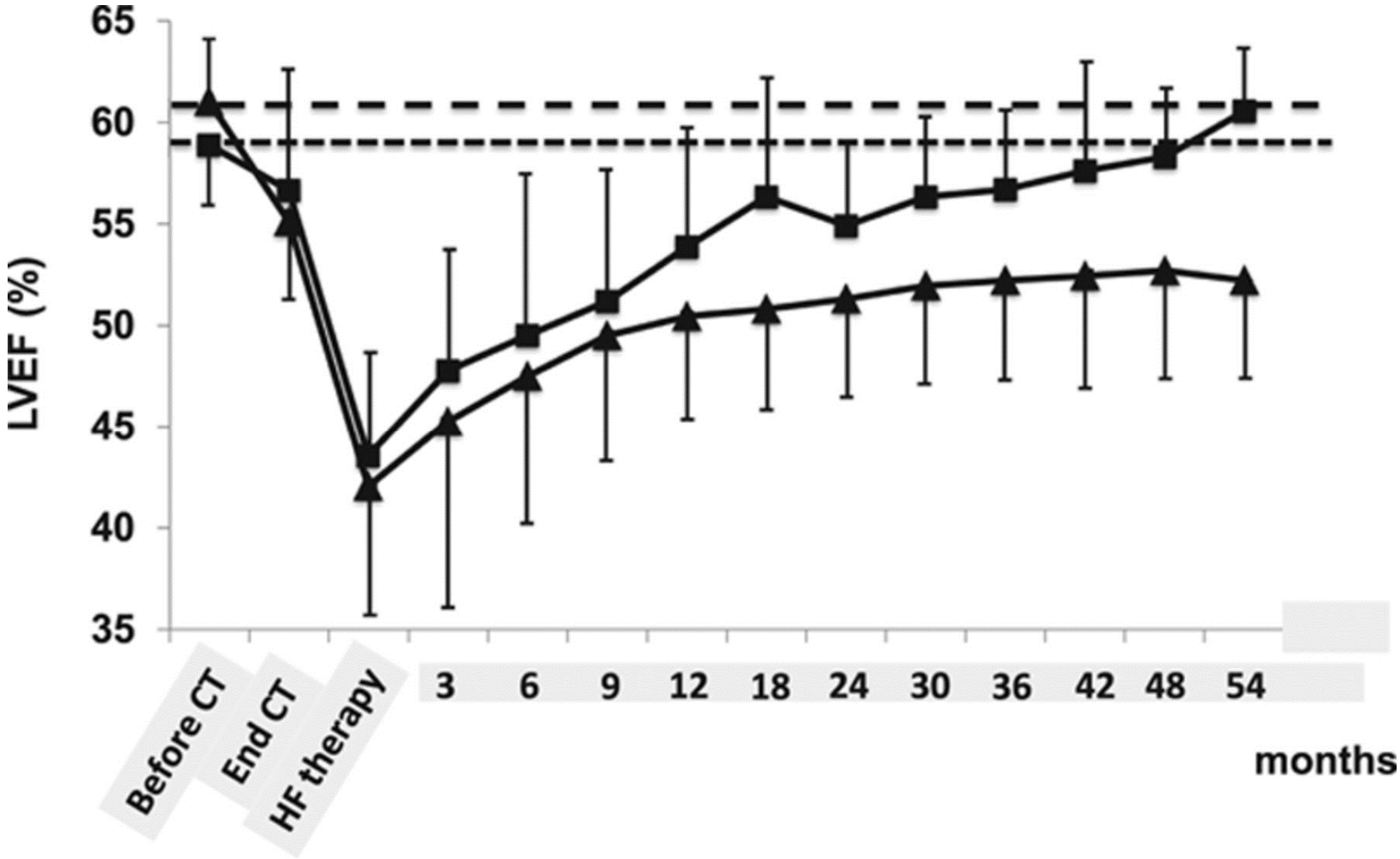
Figure 3 Individual systolic function data at baseline and after chemotherapy in the control and spironolactone groups.

Left ventricular ejection fraction (LVEF; mean±SD) behavior in patients developing cardiotoxicity in the first year, from baseline (before starting chemotherapy) to the initiation of heart failure therapy.



Daniela Cardinale et al. Circulation. 2015;131:1981-1988

Left ventricular ejection fraction (LVEF) in patients with cardiotoxicity and with partial (triangle) or full (square) recovery with heart failure therapy.



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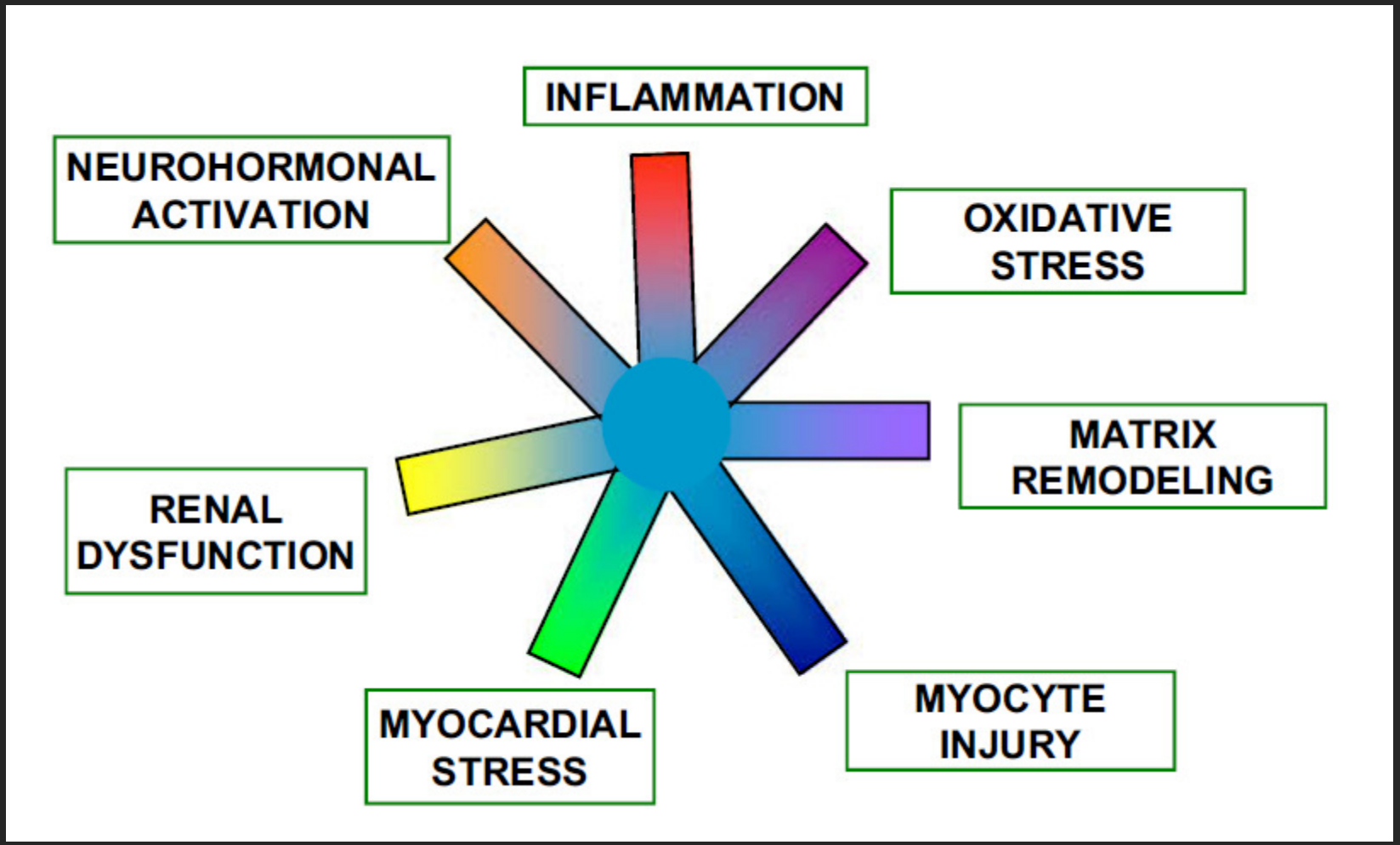
Multimarker Risk Prediction



Braunwald, E. NEJM. 2008.
Braunwald, E. JACC HF. 2013.

What is the Role of Multimarker Risk Prediction in Breast Cancer Therapy?

- Objective: To determine the utility of biomarkers in the early identification of breast cancer patients at risk of cardiac dysfunction

- Biomarkers hypothesized to be mechanistically relevant:
  - TnI (cardiomyocyte injury)
  - NT-proBNP (neurohormonal activation)
  - hsCRP (inflammation)
  - PlGF (angiogenesis)
  - sFlt-1 (angiogenesis/vascular remodeling)
  - GDF-15 (inflammation and oxidative stress)
  - MPO (oxidative stress)
  - Gal-3 (fibrosis)

Biomarkers to detect cardiotoxicity in breast cancer before LVEF drops?

- 19% of pts stop trastuzumab due to drop in EF
- 36 pts with normal EF at least 3 weeks after trastuzumab
- BNP and troponin at baseline at 24 hours
- No elevation in troponin
- 39% had elevation of proBNP, 8 at both baseline and 24 hrs, 11 had previous anthracycline, 3 hx of HTN

	Pre-trastuzumab infusion (t_0)	Post-trastuzumab infusion (t_{24})
N	36	31
Mean	163.5	168.1
SEM	56.6	49.3
Median	86.4	74.6
Wilcoxon signed ranks *P* value		0.97

ULN: 110 pg/mL (<75 years); 589 pg/mL (>75 years).

Goel et al. Asia–Pac J Clin Oncol 2011; 7: 276–280

Troponin to detect early myocardial damage

- Troponins commonly used for Dx of ACS. Rise & fall.
- Any insult including ADHF – with cell death will elevate troponin
- Older assays --circulating cardiac troponins.
- High sensitivity troponins—even normals spill troponins but at low levels.
- Labs vary, how measured varies, 99th percentile vs. ULN.
- How measured? How often? Relation to dosing of ChemoRx. May be missed if not measured longitudinally

Witteles R., Biomarkers as Predictors of Cardiac Toxicity From Targeted Cancer Therapies, JCF (2016), http://dx.doi.org/doi: 10.1016/j.cardfail.2016.03.016.

Troponin to detect early myocardial damage

- Troponin elevations with trastuzumab therapy -- almost exclusively in patients who have been pretreated with anthracyclines. Early (2-3 mos)
- Normalize in 3 months --even if trastuzumab is continued and whether cardiac medications (e.g. carvedilol/enalapril) are initiated
- Predictive of future LVEF reductions in some but not all studies.
- Cardinale et al. 2006 -- a significant association between troponin elevations and major adverse cardiac events.

Witteles R., Biomarkers as Predictors of Cardiac Toxicity From Targeted Cancer Therapies, JCF (2016), http://dx.doi.org/doi: 10.1016/j.cardfail.2016.03.016.

Summary

- Heart failure associated with chemotherapy can be severe and include both elements of HFrEF and HFpEF
- Risk factor identification is critical
- HF associated with chemotherapy can respond to GDMT
- GDMT may also be protective if administered with chemotherapy although the data are not consistent
- GDMT may reverse LV dysfunction previously thought non-reversible
- A panel of biomarkers may be predictive of cardiotoxicity and could serve as markers of improvement .
- Further research is needed in mREF patients whose LV function improves