



YEAR IN REVIEW: TOP CLINICAL RESEARCH STUDIES IN CARDIO-ONCOLOGY

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Objectives

- Original published clinical research studies
 - *Pubmed search for publications during Sept 2017- Sept 2018*
- Focus
 - *Diversity in Design*
- Epidemiology, Clinical Trial/Intervention Studies
 - *Diversity of Population*
- Cancer diagnoses and Cancer treatment continuum (at diagnosis and during treatment, survivorship)
 - *Relevance to clinical practice*

Cohort Studies

Dynamic Trajectories of Left Ventricular Ejection Fraction in Heart Failure

Lupón J, Bayés-Genís A et al.
JACC 2018;72(6):591

■ Study Population/Design

- *Observational HF Clinic Registry*
- *Stage C HF, at least 2 Echos (N=1160), etiology: dilated CMP (N=160), drug induced (N=35)*

■ Primary Outcome

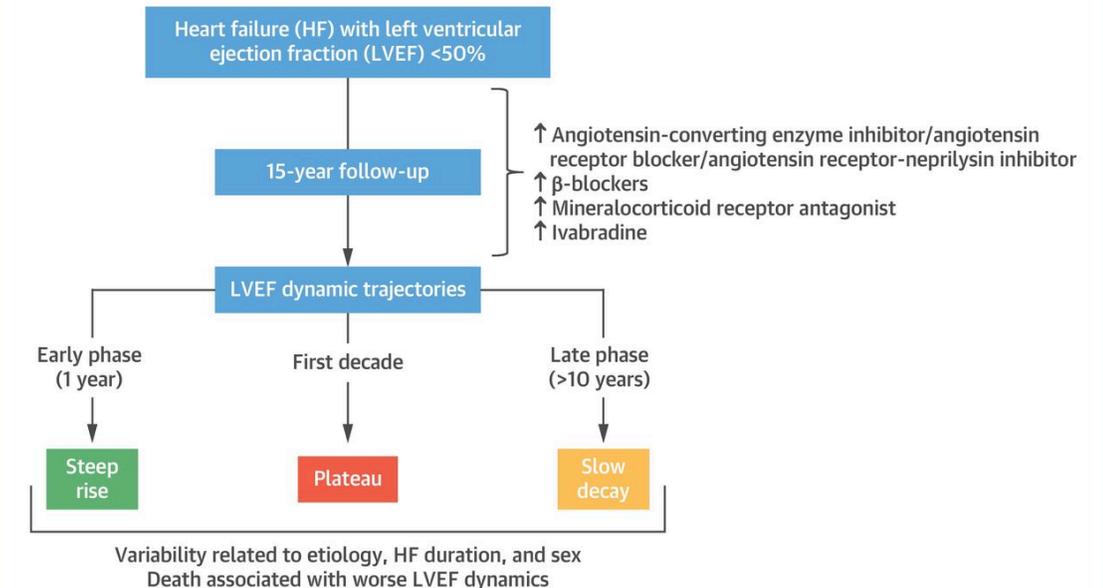
- *Change in LVEF over 15 years (Loess splines of long-term LVEF trajectories)*

■ Results

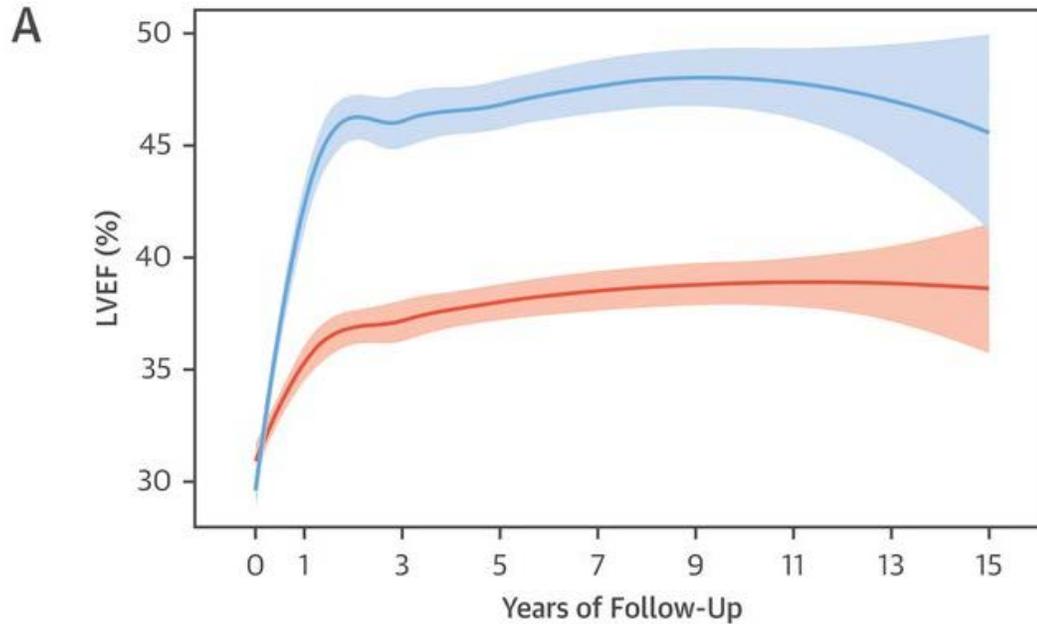
- *Rise in LVEF in the 1st year, stable LVEF period followed by decline*
- *Predictive value of LVEF*

- **Take Home: LVEF in cancer treatment-related CMP has similar long term trajectory as in CMP of other etiologies**

CENTRAL ILLUSTRATION: Left Ventricular Ejection Fraction Trajectories and Dynamics: 15 Years

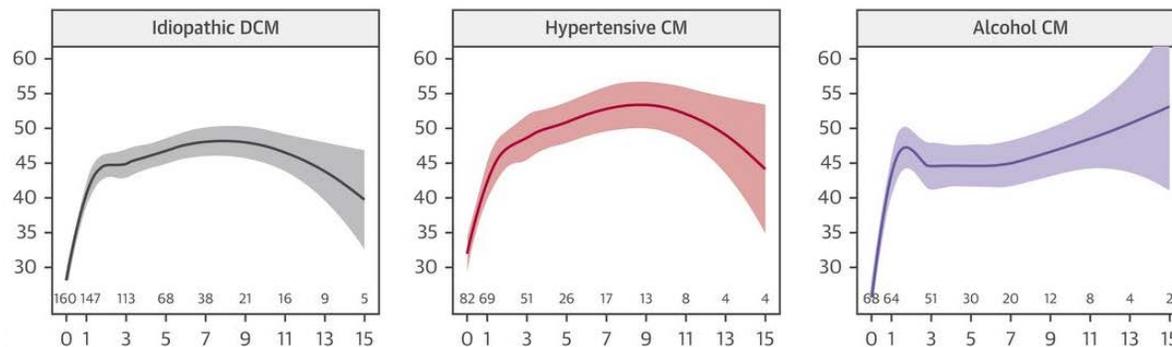
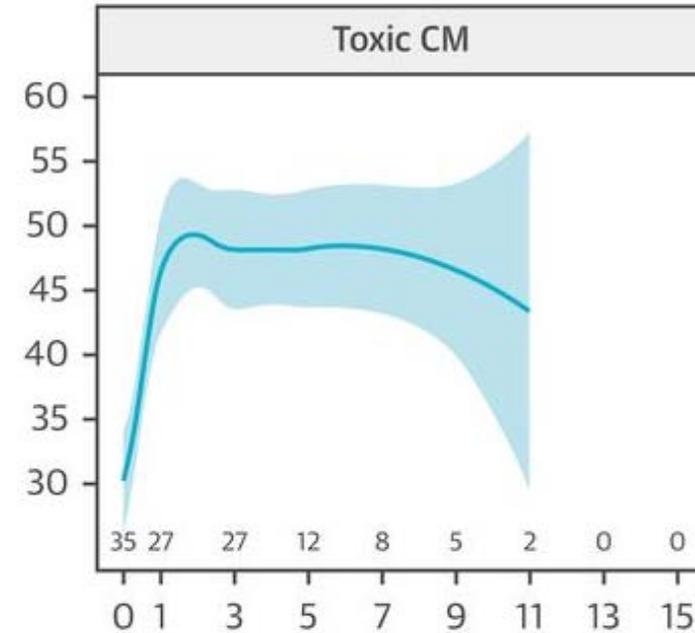


Lupón, J. et al. J Am Coll Cardiol. 2018;72(6):591-601.



Nonischemic, N =	498	436	353	203	131	80	51	26	14
Ischemic, N =	662	588	450	267	171	107	75	47	24

— Nonischemic — Ischemic



Excellent read for correlation:

Detailed Echocardiographic Phenotyping in Breast Cancer Patients: Associations With Ejection Fraction Decline, Recovery, and Heart Failure Symptoms Over 3 Years of Follow-Up.

Narayan V, Ky B et al.

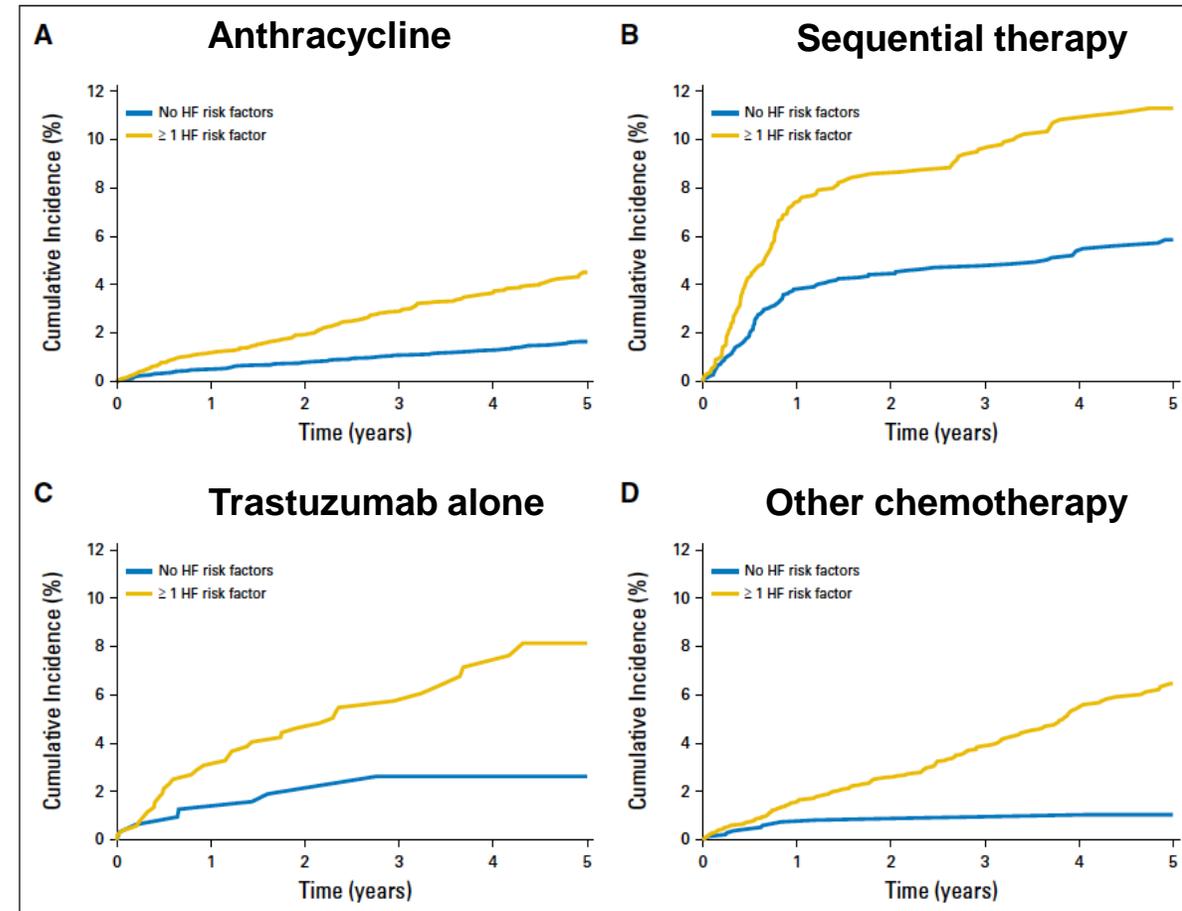
Circulation. 2017 Apr 11;135(15):1397

Lupón J et al. JACC 2018;72:591-601

Risk-Imaging Mismatch In Cardiac Imaging Practices for Women Receiving Systemic Therapy for Early-Stage Breast Cancer: A Population-Based Cohort Study

Thavendiranathan P, Lee DS et al.
JCO May 2018

- Population based retrospective cohort of 18,444 women with early stage breast cancer in Ontario, 2007-2012
- *Outcomes: 1) baseline cardiac imaging, 2) 5-year incidence of MACE (composite: hospitalization for HF/pulmonary edema/cardiomyopathy OR outpt dg of HF OR CV death)*
- Results: 5-y MACE was 2-6 higher in patients with HF risk factors across all regimens
- Take Home Message: **Baseline cardiac imaging is driven by chemotherapy regimen rather than HF risk.**

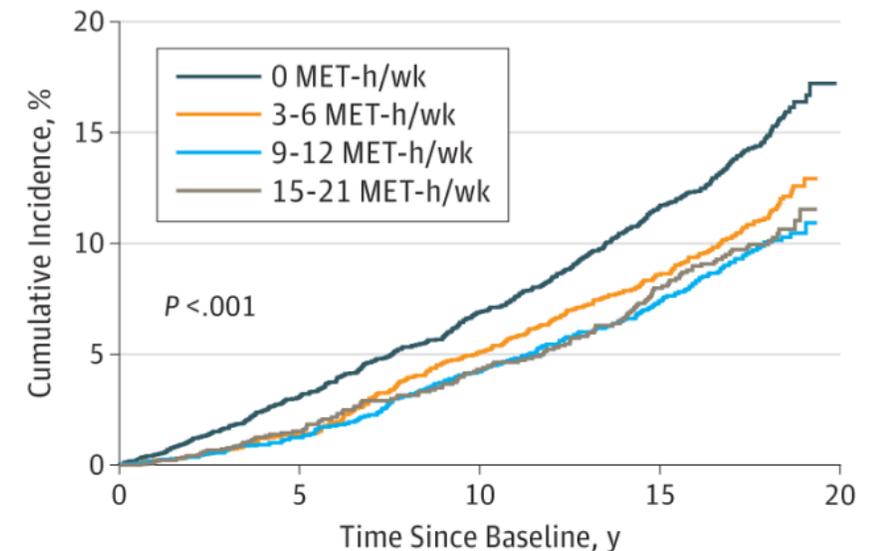


Association of Exercise With Mortality in Adult Survivors of Childhood Cancer

Scott JM, Jones LW et al.
JAMA Oncology 2018, June 3

- **Multicenter cohort analysis:** 15 450 participants of Childhood Cancer Survivor Study (enrolled 1970 -1999, follow-up through 2013)
- **Vigorous exercise** assessed based on a single questionnaire item: “on how many of the past 7 days did you exercise or do sports for at least 20 minutes that made you sweat or breathe hard”
- Primary outcome: **All-cause mortality**
- **Results**
- Increased exercise exposure was associated with a significant reduction in the cumulative incidence of all-cause, relapse, and health-related mortality at 15 years
- **Take Home:** *Adds to knowledge about benefits of exercise in a vulnerable population of survivors of childhood cancer*

A All-cause mortality



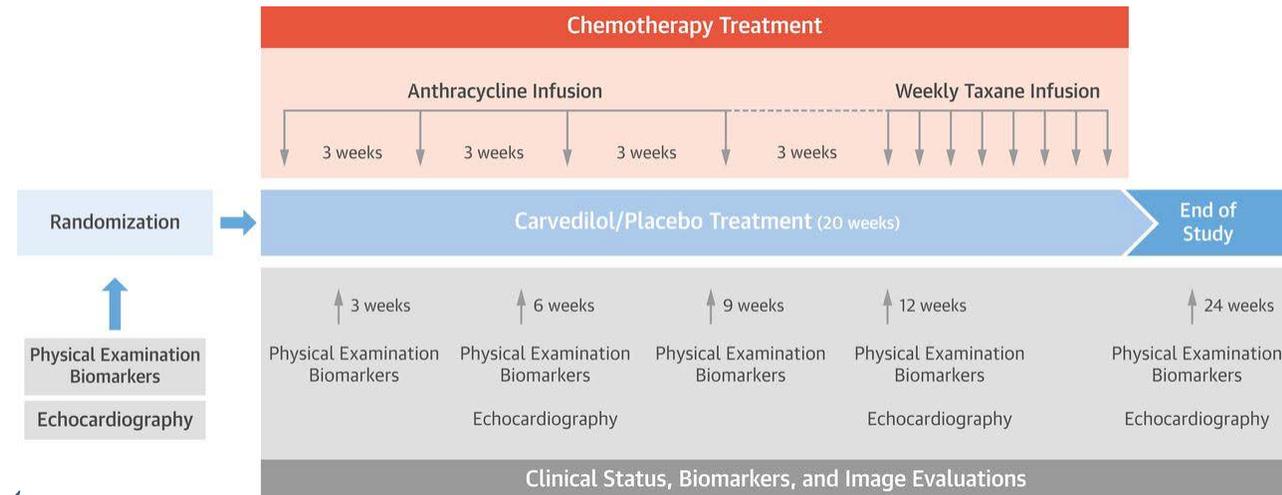
No. at risk	0	5	10	15	20
0 MET-h/wk	5059	3020	2769	2493	1425
3-6 MET-h/wk	4156	2261	2041	1897	1147
9-12 MET-h/wk	3690	1898	1724	1617	945
15-21 MET-h/wk	2545	1263	1154	1065	614

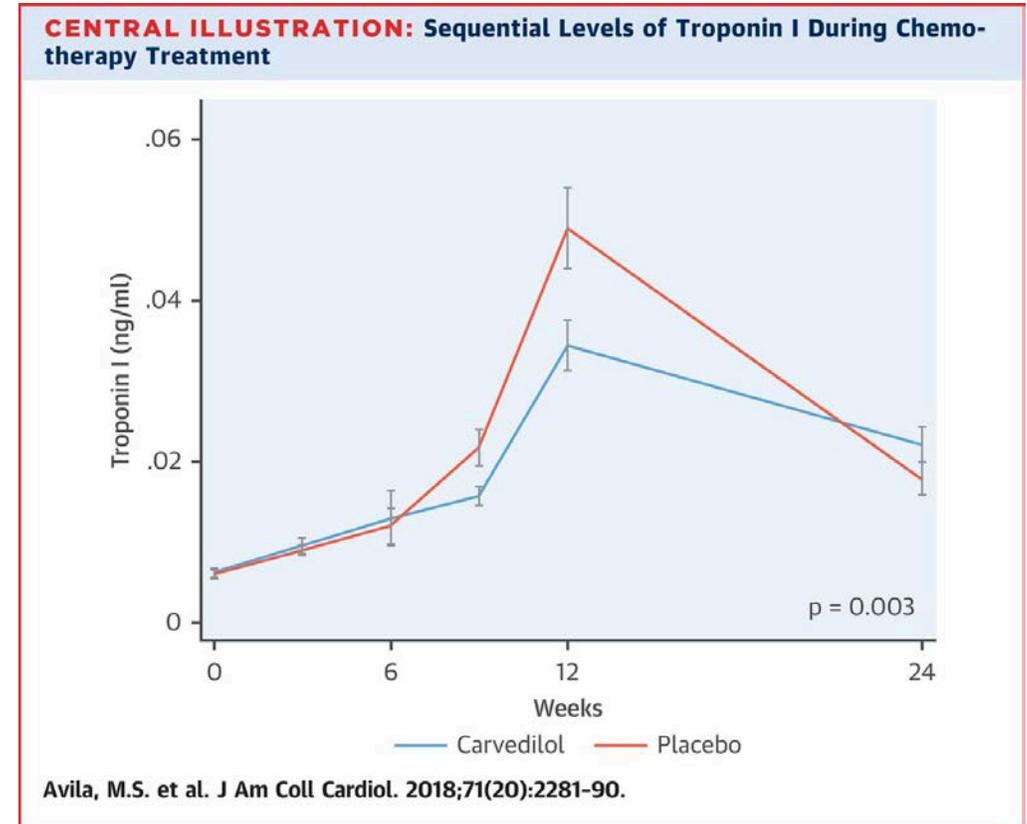
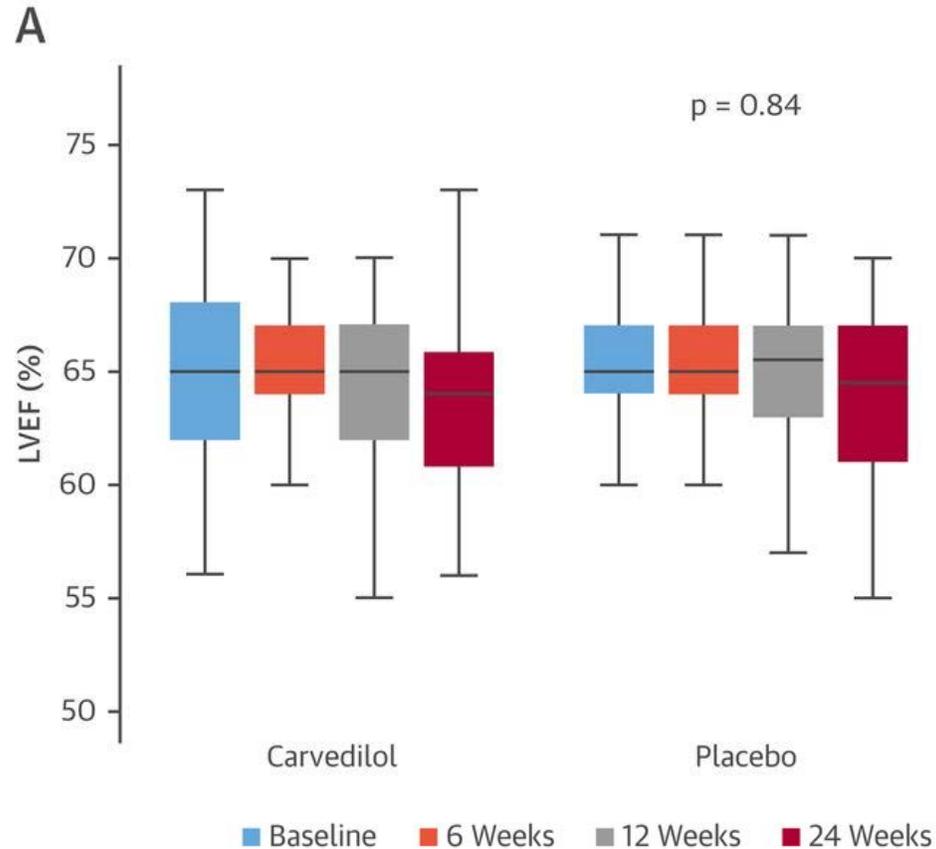
Prevention Studies

Carvedilol for PrEvention of Chemotherapy-Induced CardiotoxicitY - Results of the Prospective, Randomized, Double Blind, Placebo-Controlled (CECCY Trial)

Avila MS et al.
JACC 2018; 71: 2281

- Double-blind, randomized, placebo-controlled trial
- 200 patients with HER2 negative breast cancer treated with anthracycline-based chemotherapy
- Intervention: concomitant carvedilol OR placebo and placebo
- Cardiotoxicity definition
 - *Decline in LVEF by 10% from baseline by echocardiography*
- Endpoints:
 - *Prevention of a $\geq 10\%$ reduction in LVEF at 6 months*
 - *Changes in troponin, DD, BNP*





- Take Home:
 - *Incidence of cardiotoxicity 13.5% to 14.5%*
 - *No effect of carvedilol on primary endpoint (change in LVEF from baseline to 6 months)*
 - *Carvedilol was associated with reduction in troponin increase and diastolic dysfunction*

PRADA

- Study Population (N=130)
 - All epirubicin, 22% trastuzumab
- Study design
 - 2x2, metoprolol and candesartan
- Primary Outcome
 - *Changes in LVEF by CMR at 10-64 weeks*
- Results
 - *Attenuation of LVEF decline with candesartan (order of 2-3%)*

Gulati G et al. Eur Heart J. 2016

MANTICORE

- Study Population (N=94)
 - All trastuzumab, 12-33% anthracycline
- Study design
 - 1:1:1 bisoprolol, perindopril, placebo
- Primary Outcome
 - **Changes in LVEDVi by CMR at 1 year**
- Results
 - **Attenuation of LVEF decline with bisoprolol (order of 4%)**

Pituskin E et al. J Clin Oncol. 2016

CECCY

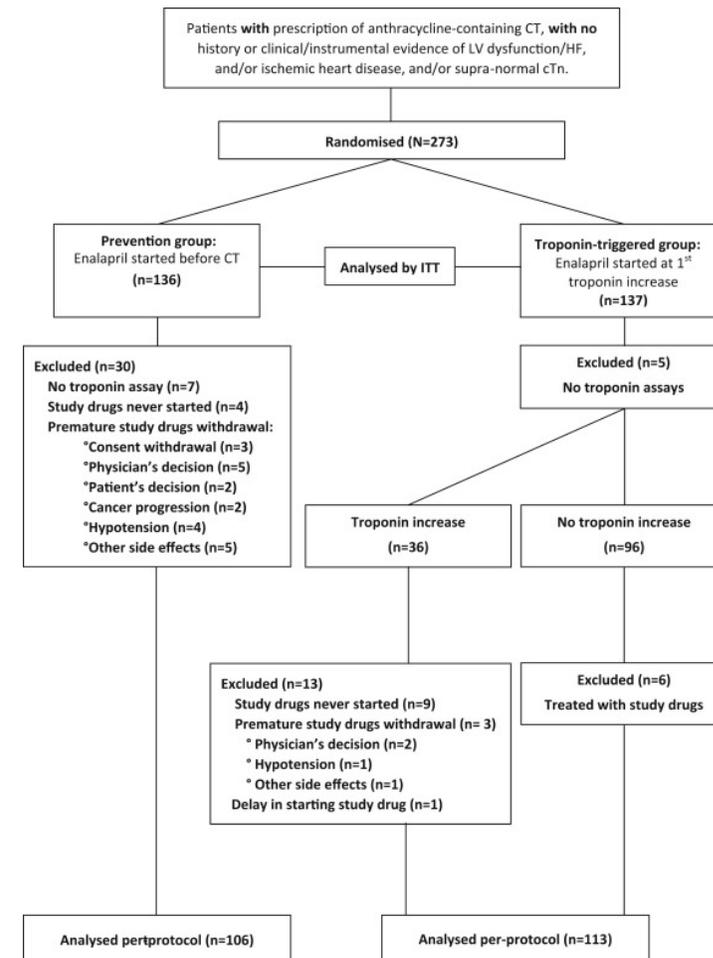
- Study Population (N=200)
 - All doxorubicin
- Study design
 - 1:1 carvedilol and placebo
 - Echo
- Primary Outcome
 - **Reduction in Echo LVEF>10% at 6months**
- Results
 - **No significant difference in LVEF decline (13.5% vs 14.5% for placebo and carvedilol)**

Avila MS. J Am Coll Cardiol. 2018

Anthracycline-induced cardiotoxicity: A multicenter randomised trial comparing two strategies for guiding prevention with enalapril: The International CardioOncology Society-one trial.

- Randomized, open-label trial in 21 Italian hospitals
- 273 patients (76% breast cancer)
- **Prevention arm** (Enalapril before chemo to all) vs **Troponin-triggered arm**
- **Primary outcome**
- *incidence of troponin elevation above the threshold*
- **Results**
- 23% in the prevention and 26% in the troponin-triggered group (p = 0.50)

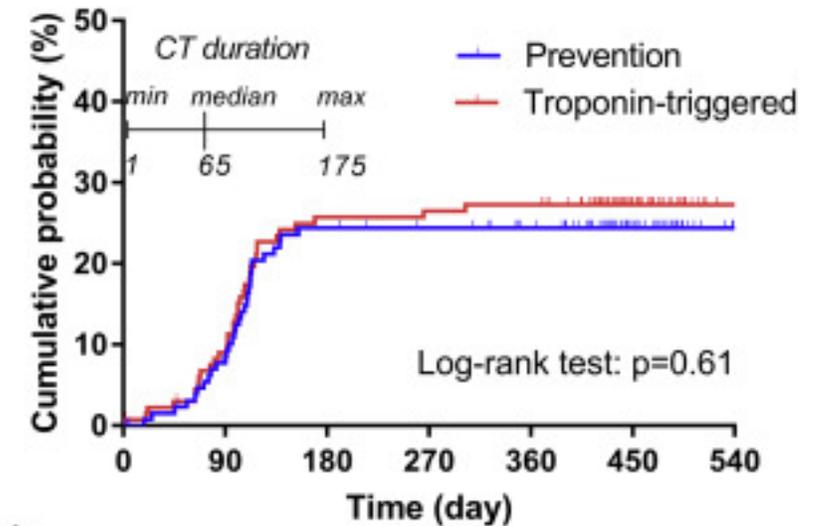
Cardinale D .. ICOS Investigators
 Eur J Cancer. 2018 May;94:126-137



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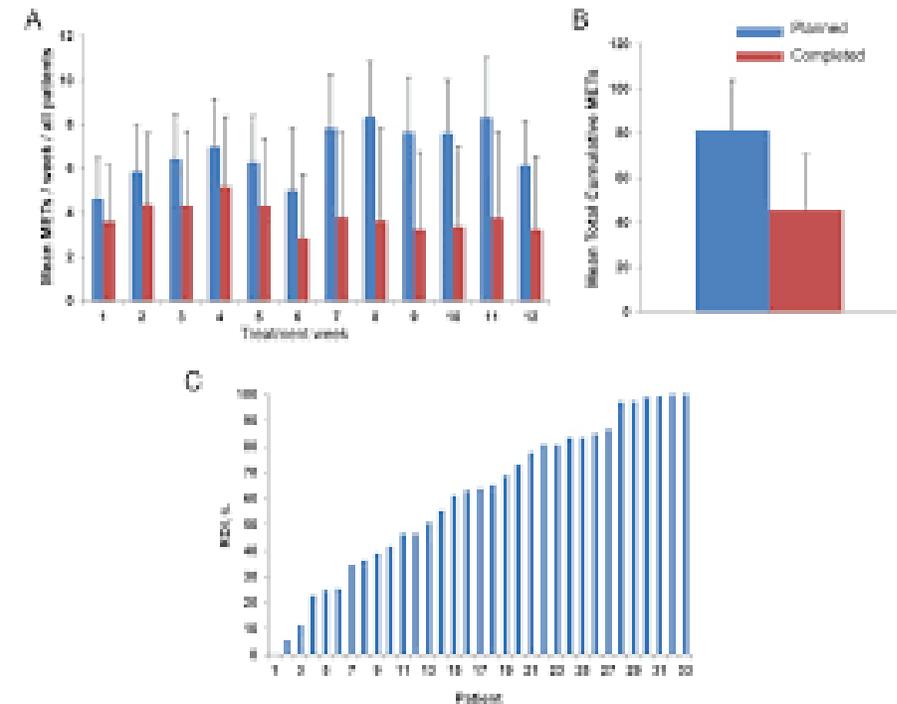
Patients at risk		0	90	180	270	360	450	540
Prevention	136	117	94	91	85	40	6	
Troponin-triggered	137	120	97	97	95	45	10	

Feasibility, safety, and efficacy of aerobic training in pretreated patients with metastatic breast cancer: A randomized controlled trial.

Scott JM, Jones LW et al.

Cancer. 2018 Jun 15;124(12):2552-2560

- Study Population: 65 women with metastatic breast cancer randomized to **aerobic training group** (n = 33) or **stretching group** (n = 32)
- Endpoints
 - *Aerobic training feasibility* = lost to follow-up (LTF) rate (<20%) and attendance ($\geq 70\%$)
 - *Secondary: safety, objective outcomes* (VO_{2peak} and functional capacity), and *patient-reported outcomes*
- Take Home
 - Aerobic training at the dose and schedule tested is safe but **not feasible** for a significant proportion of patients with metastatic breast cancer



A randomized dose-response trial of aerobic exercise and health-related quality of life in colon cancer survivors.

Brown JC, Schmitz KH. et al.
Psychooncology. 2018. 27:1221

■ Study Population and Design

- 39 stage I-III colon cancer survivors
- Randomized 1) usual-care control, 2) 150 min·wk⁻¹ of aerobic exercise (low-dose) and 3) 300 min·wk⁻¹ of aerobic exercise (high-dose) for 6 months
- Primary Outcome: **HRQoL** (questionnaires)

■ Results: Exercise dose-related improvement in

- Physical component summary score of the SF-36 ($P_{trend} = 0.002$),
- Functional Assessment of Cancer Therapy-Colorectal ($P_{trend} = 0.025$),
- Pittsburgh Sleep Quality Index ($P_{trend} = 0.049$),
- Fatigue Symptom Inventory ($P_{trend} = 0.045$)

■ Take Home: Adds to evidence based data on the benefit of exercise. No hard CV outcomes.

Thank YOU