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

- **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


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

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
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.

Thavendiranathan P, Lee DS et al. JCO May 2018
Association of Exercise With Mortality in Adult Survivors of Childhood Cancer

- **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

Scott JM, Jones LW et al. JAMA Oncology 2018, June 3
Prevention Studies
Carvedilol for PrEvention of Chemotherapy-Induced CardiotoxicitY - Results of the Prospective, Randomized, Double Blind, Placebo-Controlled (CECCY Trial)

- 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
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| **Study Population**  
(N=130)  
- All epirubicin, 22% trastuzumab | **Study Population**  
(N=94)  
- All trastuzumab, 12-33% anthracycline | **Study Population**  
(N=200)  
- All doxorubicin |
| **Study design**  
- 2x2, metoprolol and candesartan | **Study design**  
- 1:1:1 bisoprolol, perindopril, placebo | **Study design**  
- 1:1 carvedilol and placebo  
- Echo |
| Primary Outcome  
- Changes in LVEF by CMR at 10-64 weeks | Primary Outcome  
- Changes in LVEDVi by CMR at 1 year | Primary Outcome  
- Reduction in Echo LVEF>10% at 6months |
| Results  
- Attenuation of LVEF decline with candesartan (order of 2-3%) | Results  
- Attenuation of LVEF decline with bisoprolol (order of 4%) | 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)
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Feasibility, safety, and efficacy of aerobic training in pretreated patients with metastatic breast cancer: A randomized controlled trial.

- 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 (≥70%)
  - Secondary: safety, objective outcomes (VO$_2$peak 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.

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 (\(P_{\text{trend}} = 0.002\)),
- Functional Assessment of Cancer Therapy-Colorectal (\(P_{\text{trend}} = 0.025\)),
- Pittsburgh Sleep Quality Index (\(P_{\text{trend}} = 0.049\)),
- Fatigue Symptom Inventory (\(P_{\text{trend}} = 0.045\))

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

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