Exercise Before, During, and After Therapy: How Much Should the Cancer Patient Do?

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Outline

• Benefits of exercise and fitness
• Cardiovascular risk in cancer survivors
• Safety and efficacy of exercise in cancer survivors
• Recommendations
Physical Activity and Cardiovascular Risk

Exercise Also Improves…

• Muscle strength (Behringer et al, *Pediatrics* 2010)
• Bone density (Meyer et al, *Bone* 2011)
• Cognitive function (Angevaren et al, *Cochrane Database Syst Rev* 2008)
• Cardiopulmonary fitness (Ross et al, *Circulation* 2016)
Benefits of Fitness

• 20% decrease in 5-year all cause mortality for each 5 kilogram increase in hand grip strength (Sasaki et al, *Am J Med* 2007)

• 13% decrease in all cause mortality and 15% decrease in cardiovascular disease for each one metabolic equivalent of increased exercise capacity (Kodama et al, *JAMA* 2009)

• 17% increase in total mortality and 13% increase in cardiovascular disease for each one standard deviation decrease in BMD (Qu et al, *Int J Cardiol* 2011)

• Fit adolescents are more than twice as likely to score in the highest tertile of academic achievement than those who are unfit (Sardinha et al, *BMC Pediatr* 2014)
Cardiovascular Risk in Cancer Survivors

- **Congestive heart failure**: HR 5.9 (3.4–9.6)
- **Myocardial infarction**: HR 5.0 (2.3–10.4)
- **Pericardial disease**: HR 6.3 (3.3–11.9)
- **Valvular disease**: HR 4.8 (3.0–7.6)


Cardiovascular Risk in Cancer Survivors

- Reduced physical function at all levels of physical activity (Hoffman et al, *J Clin Oncol* 2013)
- Exercise capacity (VO$_2$ max) reduced in many childhood cancer survivors (Berkman, *J Adolesc Young Adult Oncol* 2016)
- Metabolic syndrome more prevalent in cancer survivors than in the general population (de Haas et al, *Lancet Oncol* 2010)
Physical Function in Cancer Survivors

- Childhood Cancer Survivor Study (CCSS)
- 183 young adults (53% male)
  - Mean age at cancer diagnosis 4.2 +/- 3.0 years
  - Mean age at evaluation = 13.5 +/- 2.5 years
  - Evaluated between 2007 and 2010

- Physical function assessment
  - Lower extremity strength: isokinetic dynamometer
  - Grip strength: handheld dynamometer
  - Cardiopulmonary fitness: 6-minute walk test
  - Mobility: timed up-and-go test

Hoffman et al, J Clin Oncol 2013
Physical Function in Cancer Survivors

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Hoffman et al, J Clin Oncol 2013
Physical Function in Cancer Survivors

Traditional CV Risk Factors Potentiate Treatment-Related CV Risk

- Evaluate relative contribution of CV risk factors towards CHF
  - Longitudinal evaluation
  - 10,724 survivors, CCSS
  - Is risk simply additive?
  - Hypertension potentiates anthracycline-associated risk for CHF
  - Multiple traditional CV risk factors increase risk

![Graph showing relative excess risk due to interaction](Armstrong et al, J Clin Oncol 2013)
Modifying Risk in Survivors

Ness et al, Cancer 2014
Modifying Outcome Specific Risks in Survivors

Figure 1. Conceptual schematic of cardiomyopathy risk and modifiers in childhood cancer survivors. Factors designated by an * are under active investigation (knowledge gaps). HTN = hypertension. DM = diabetes mellitus. Ehrhardt, Fulbright, Armenian, *Curr Oncol Rep* 2014
Physical Activity and CV Risk

- Childhood Cancer Survivor Study (CCSS)
- 1,187 survivors of pediatric Hodgkin lymphoma (53% male)
  - Mean age (range) – at diagnosis = 14 years (2-21); at evaluation = 41 years (21-57)
  - Evaluated between 2007 and 2010
  - Modifiable CV risk factors: diabetes (4.4%), hypertension (24.8%), dyslipidemia (18.9%), obesity (20.1%), any of the preceding (43.6%)
  - Treatment related CV risk factors: anthracyclines <250 mg/m² (11%), ≥250 mg/m² (7.8%), chest RT >30 Gy (83.5%)
- Primary endpoint were CTCAE grades 3-5 CV events
- Exposure to vigorous intensity exercise via validated questionnaire

Jones et al, J Clin Oncol 2014
Safety

• Tailored intervention is feasible and safe in survivors exposed to anthracyclines with reduced ejection fractions (40-55%) (Smith et al, Pediatr Blood Cancer 2014)

• Exercise appears to be safe during breast cancer therapy (Markes et al, Cochrane Database Syst Rev 2006)
Efficacy

• Exercise improves quality of life, cardiorespiratory fitness, physical function, and fatigue (McNeely et al, *CMAJ* 2006)

• Exercise is feasible and may provide physiological and psychological benefits (Spence et al, *Cancer Treat Rev* 2014; Sharkey et al, *Am J Cardiol* 1993)

• Exercise during breast cancer treatment improves fitness (Markes et al, *Cochrane Database Syst Rev* 2006)

• Exercise during leukemia treatment is feasible and may improve physical function (Esbenshade et al, *Pediatr Phys Ther* 2014)
Weighing the Evidence

Evidence supporting
↓ CV risk factors
↓ CV events
Other health benefits

Questions regarding
Adverse events
Exercise Recommendations

- Regular exercise, as recommended by the AHA and ESC, offers potential benefits to survivors treated with anthracyclines or chest radiation.
- Regular exercise is recommended for survivors treated with anthracyclines or chest radiation with normal left ventricular systolic function.
- Cardiology consultation is recommended for survivors with asymptomatic cardiomyopathy to define limits and precautions for exercise.
- Cardiology consultation may be reasonable for high-risk survivors who plan to participate in high-intensity exercise to define limits and precautions for physical activity.

Armenian et al, Lancet Oncol 2015
Specifically

• ≥150 min/week of moderate-intensity or ≥75 min/week of vigorous-intensity physical activity (ACC, AHA, ACSM, and ECS)
• 2-3 sessions/week of strength training (NCCN)
• Exercise should be tailored to cancer survivor’s individual abilities and preferences (NCCN)
Summary

• Survivors incur both cancer treatment-related and traditional cardiovascular risk factors
• Exercise can be safely and efficaciously prescribed
• Cardiology consultation is recommended for survivors at high risk for cardiovascular events in order to define optimal exercise regimens