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SURVIVORSHIP SYMPOSIUM

Heart and Vascular Health after Transplant: When a Cure is Not Enough

Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022

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UT Southwestern Simmons Comprehensive Cancer Center

Heart and Vascular Health after Transplant - When Cure is Not Enough

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UT Southwestern Medical Center | Parkland

Cardiovascular Health after Hematopoietic Stem Cell Transplant (HSCT)

- Why worry about cardiovascular risks?
- What is Cardio-Oncology?
- Who has high cardiovascular risks?
- When and what tests/procedures recommended?
- How to reduce cardiovascular risks?

The Beginning

- Bone marrow transplantation - pioneered in 1950's by E. Donnall Thomas
- The Nobel Prize in Physiology or Medicine 1990: "for discoveries concerning organ and cell transplantation in the treatment of human disease."
- 1957-2012 > 1million patients transplanted

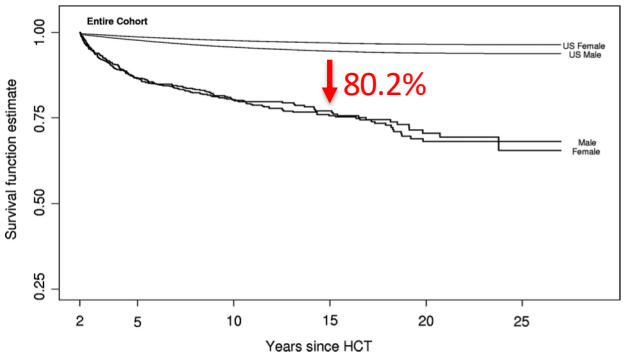
INTRAVENOUS INFUSION OF BONE MARROW IN PATIENTS RECEIVING RADIATION AND CHEMOTHERAPY*

E. Donnall Thomas, M.D.,† Harry L. Lochte, Jr., M.D.,‡ Wan Ching Lu, Ph.D.,§ and Joseph W. Ferrebee, M.D.¶
Cooperstown, New York, and Boston, Massachusetts

Thomas ED, et al. N Engl J Med. 1957 Sep 12;257(11)
https://www.nobelprize.org/prizes/medicine/1990/thomas/biographical/

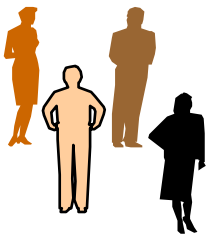
Long-term Survival after HSCT

- Bone Marrow Transplant Survivor Study
  - 1479 individuals, >2 years survival
  - Median age 25.9 years
  - Median follow-up 9.5 years
  - Survival 80.2% at 15 years
  - Standardized mortality ratio 2.2



>240,000 survivors in 2020
>500,000 survivors in 2030

Bhatia S et al. Blood. 2007 Nov 15;110(10):3784-92.



Why worry about cardiovascular risks after HSCT?

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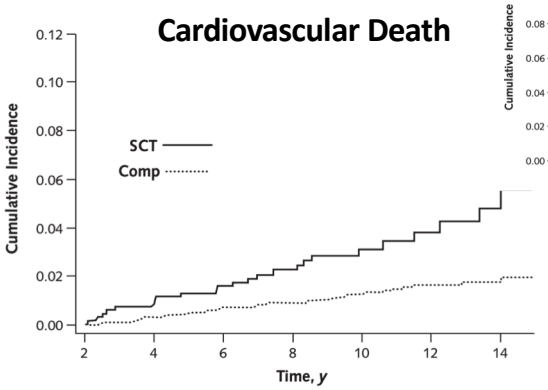
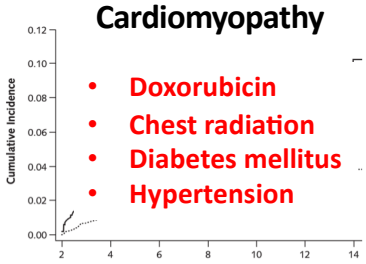
Cardiovascular Complications of HSCT

Cardiovascular Death



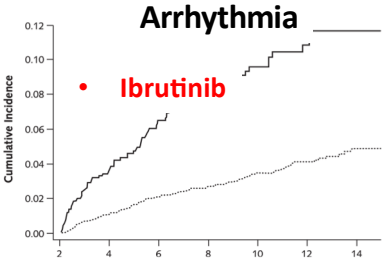
Cardiomyopathy

- Doxorubicin
- Chest radiation
- Diabetes mellitus
- Hypertension



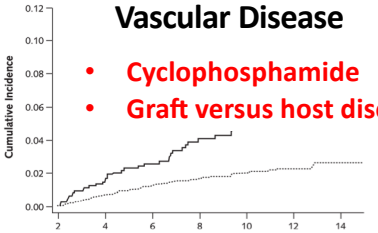
Arrhythmia

- Ibrutinib



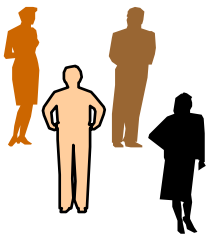
Vascular Disease

- Cyclophosphamide
- Graft versus host disease



- Fred Hutchinson Cancer Research Center
  - 1481 individuals, >2 years survival

Chow EJ et al. Ann Intern Med. 2011 Jul 5;155(1):21-32



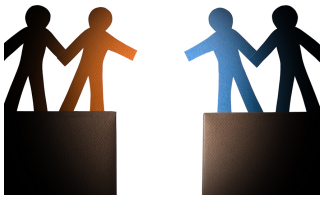
What is Cardio-Oncology?

What is Cardio-Oncology / Onco-Cardiology?

- Bridging discipline aiming to **minimize cardiovascular toxicity** while **maximizing anti-cancer effects**

How Does Cardio-Oncology Help Patients?

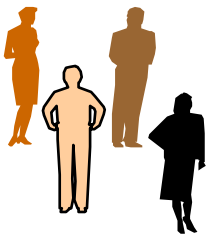
- Closing the gap between disciplines
- Preventing cardiac damage
- Recognizing early cardio-toxicity
- Improving overall outcomes after cancer treatment



Cardiovascular Risk Factors

Social Determinants of Health

Cancer	Common Risk Factors	Heart Disease
• Treatment • Cancer type	Genetic Smoking Obesity Hyperlipidemia Sedentarism Diabetes HTN	• Congenital • Underlying disease



Who has high cardiovascular risks?

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High Cardiovascular Risk

- High-dose anthracyclines (eg, doxorubicin ≥250 mg/m2)
- High-dose radiotherapy (≥30 Gy) with the heart in the treatment field
- Combined lower-dose anthracyclines (eg, doxorubicin <250 mg/m2) or molecular targeted therapies and:
  - Age ≥60 y
  - Lower-dose radiotherapy (<30 Gy)
  - ≥2 Risk factors: smoking, HTN, diabetes mellitus, dyslipidemia, CKD, obesity
- Previous heart disease
- Elevated cardiac blood biomarkers before anticancer therapy

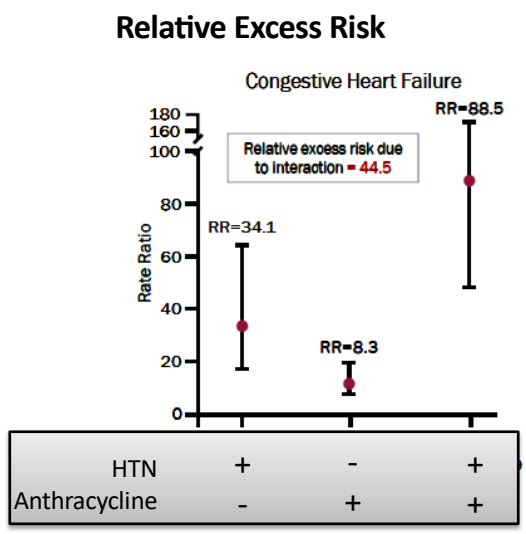
Alexandre J et al. J Am Heart Assoc. 2020 Sep 15;9(18):e018403

Conditioning Drugs and Cardiovascular Risks

- **Myocardial ischemia:** melphalan, etoposide, carmustine
- **Arrhythmias:** cyclophosphamide, carmustine, fludarabine
- **Myocarditis/pericarditis:** cyclophosphamide, cytarabine, busulfan
- **Endocardial fibrosis: busulfan**
- **Heart Failure:** cyclophosphamide, busulfan, melphalan, cytarabine, fludarabine, thiotepa

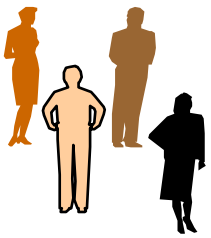
López-Fernández T et al. Cardiovascular Issues in Hematopoietic Stem Cell Transplantation. Curr. Treat. Options in Oncol. 2021

Hypertension Worsens the Risk for Heart Disease



More than additive effect with anthracycline therapy and hypertension

Armstrong G et al. JCO. 2013



When and what tests and procedures recommended?

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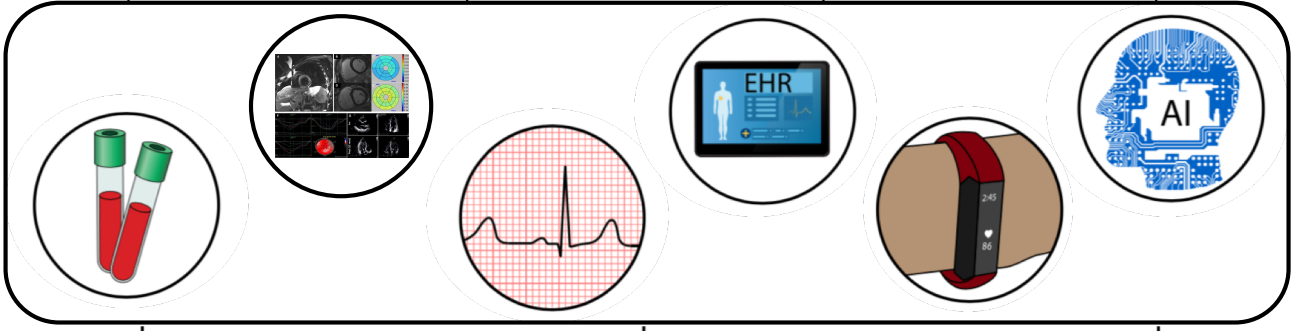
Chemotherapy | Radiation Therapy | Targeted Therapy | Immunotherapy

CARDIOVASCULAR TOXICITY

Di Carli MF et al, The Future of Cardiovascular Imaging. Circulation. 2016
Zaha VG et al, Future Perspectives of Cardiovascular Biomarker Utilization in Cancer Survivors. Circulation. 2021

Chemotherapy | Radiation Therapy | Targeted Therapy | Immunotherapy



Pre-treatment | During treatment | After treatment

Di Carli MF et al, The Future of Cardiovascular Imaging. Circulation. 2016
Zaha VG et al, Future Perspectives of Cardiovascular Biomarker Utilization in Cancer Survivors, Circulation. 2021

Pragmatic Approach to Prevent Cardiotoxicity

Systematic Cardio-Oncological Evaluation

- Clinical consultation (consider Ambulatory or Self-Measured Home BP monitoring)
- Blood glucose, lipid profile, cardiovascular tests, kidney function
- ECG
- Cardiovascular imaging studies
- Actively manage modifiable cardiovascular risk factors and diseases
- Encourage exercise on a regular basis and healthy dietary habits

Alexandre J et al. J Am Heart Assoc. 2020 Sep 15;9(18):e018403

Cardio-Oncology Approach to HSCT

CV risk factors
- Smoking
- Obesity
- Hypertension
- Diabetes
- Dislipemia

CV diseases
Heart failure/LVEF<50%
Coronary artery disease
Valvular heart diseases

CV complications
- Cardiac Arrhythmias
- Early CVRF
- Heart Failure
- Coronary artery disease
- Vascular events
- Pericardial diseases

Age and female sex

Pre-HSCT Tx
- Mediastinal Rt
- Alkylating agents
- Anthracyclines

Conditioning schemes

Allogenic HSCT

López-Fernández T et al. Cardiovascular Issues in Hematopoietic Stem Cell Transplantation. Curr. Treat. Options in Oncol. 2021

Cardio-Oncology Approach to HSCT

Baseline evaluation **Early F/U** **Long-term F/U**

- Blood pressure (BP)
- Glucose/HbA1c/Lipid
- Biomarkers (NPs-cTn)
- ECG
- Echo (LVEF-GLS)
- Cardiac CT (Ca^{2+} score)*

+100d

- BP
- Lipids/HbA1c
- NPs
- ECG
- Echo**

12m: Re-stratification CV Tox risk^

BP/Lipids/HbA1c/ECG/NPs/*Echo*

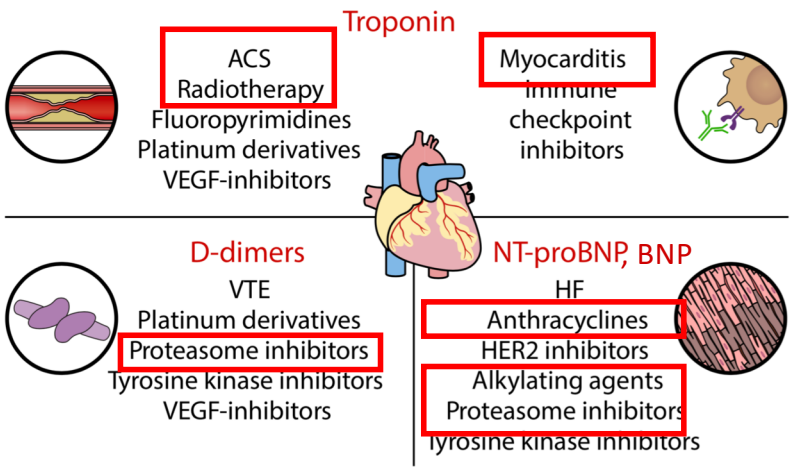
>12m: yearly follow-up

BP/Lipids/HbA1c/ECG

(*Echo* every 1-5 years according to risk)

López-Fernández T et al. Cardiovascular Issues in Hematopoietic Stem Cell Transplantation. Curr. Treat. Options in Oncol. 2021

Commonly Used Blood Tests in Cardio-Oncology

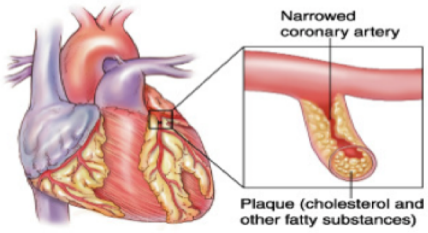


Future Perspectives of Cardiovascular Biomarker Utilization in Cancer Survivors, Circulation. 2021

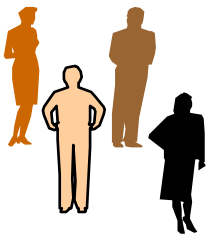
Cardiovascular Imaging in Cardio-Oncology

Novel technology in pretransplant evaluation

- Cardiac structure and function
  - 3D Echocardiography
  - Speckle-tracking echocardiography
  - Cardiac MRI
- Screening for cardiac ischemia
  - Coronary CT
  - Coronary artery calcium scoring



Hemu, M.; Zimmerman, A.; Kalra, D.; Okwuosa, T. J. Clin. Med. 2019, 8, 690



How to reduce cardiovascular risks?

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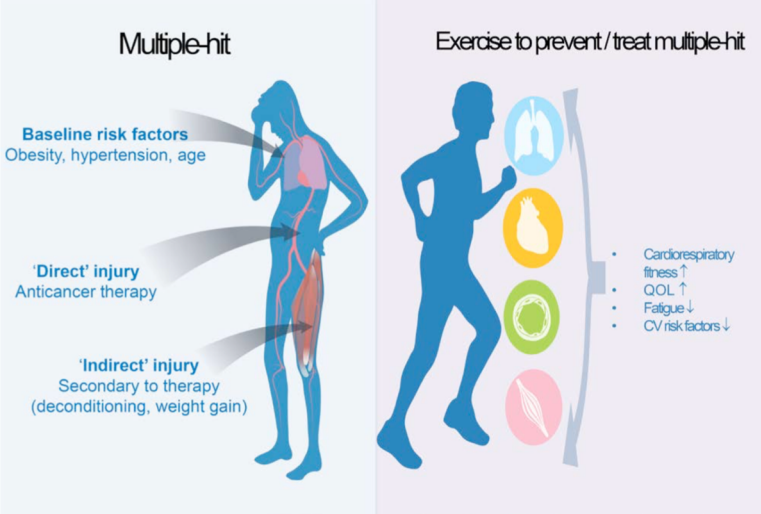
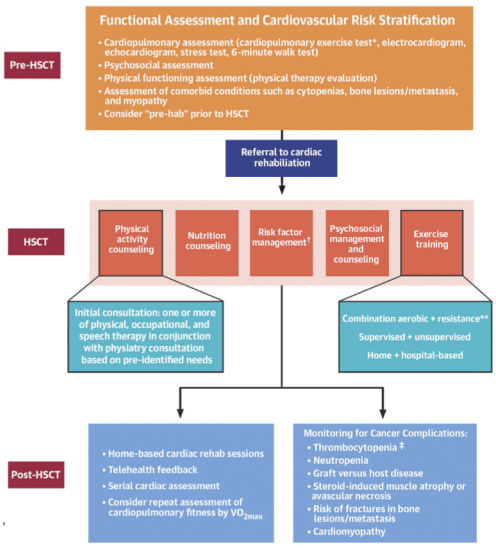
Potential Benefits of Exercise



Gilchrist S, et al. Cardio-Oncology Rehabilitation to Manage Cardiovascular Outcomes in Cancer Patients and Survivors. Circulation. 2019

Cardiac Rehabilitation Timeline in HSCT



Mohananey D, et al. JACC Cardiooncology. 2021

Cardiac Rehabilitation Timeline in HSCT

Pre-HSCT

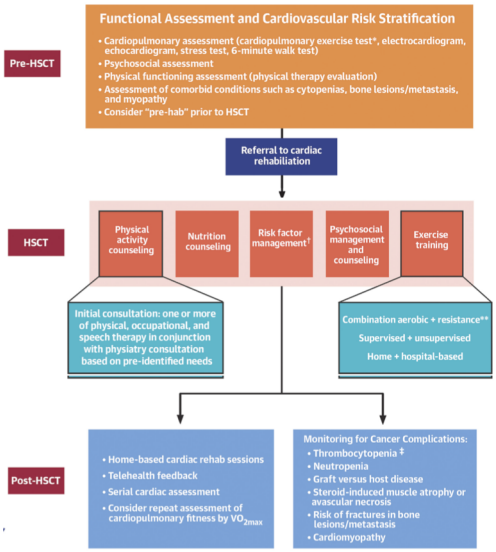
Functional Assessment and Cardiovascular Risk Stratification

- Cardiopulmonary assessment (cardiopulmonary exercise test*, electrocardiogram, echocardiogram, stress test, 6-minute walk test)
- Psychosocial assessment
- Physical functioning assessment (physical therapy evaluation)
- Assessment of comorbid conditions such as cytopenias, bone lesions/metastasis, and myopathy
- Consider "pre-hab" prior to HSCT

Referral to cardiac rehabiliation

Mohananey D, et al. JACC Cardiooncology. 2021

Cardiac Rehabilitation Timeline in HSCT



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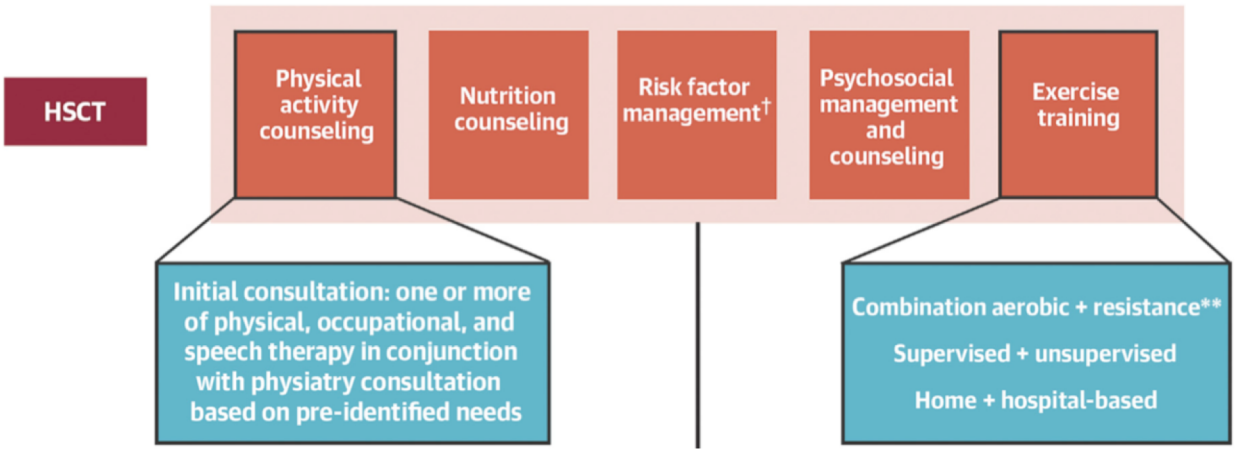
Cardiac Rehabilitation Timeline in HSCT



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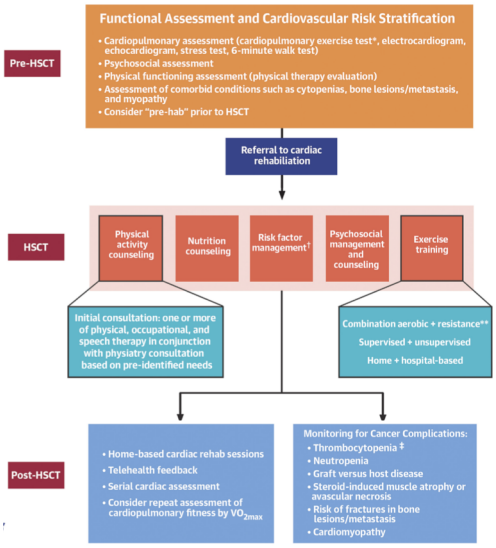
Cardiac Rehabilitation Timeline in HSCT



Mohananey D, et al. JACC Cardiooncology. 2021

Cardiac Rehabilitation Timeline in HSCT

Post-HSCT

- Home-based cardiac rehab sessions
- Telehealth feedback
- Serial cardiac assessment
- Consider repeat assessment of cardiopulmonary fitness by VO_{2max}

Monitoring for Cancer Complications:

- Thrombocytopenia ‡
- Neutropenia
- Graft versus host disease
- Steroid-induced muscle atrophy or avascular necrosis
- Risk of fractures in bone lesions/metastasis
- Cardiomyopathy

Mohananey D, et al. JACC Cardiooncology. 2021

Take Home Messages

- Cardiovascular disease = significant risk after HCT
- Risk prediction is challenging but important
- Survivors are particularly sensitive to hypertension
- Physical exercise is beneficial
- New diagnostic and treatment options are being developed

Thank you!

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Questions?


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