Cardiovascular Risk in Patients Undergoing Bone Marrow Transplant: How to Assess?

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General indications for BMT/HCT

- Dose intensity for malignant tumor
- Graft vs. Tumor
- Marrow failure
- Graft vs. Autoimmune process (GVHI)
- Gene replacement or therapy

Practical BMT/HCT

Allogeneic

- Stem cell source: other
- High dose therapy with immunotherapy
  - Anti-tumor and building better immunity
- Related
- Unrelated: matched, haploidentical
- Cord blood

Autologous: no immunologic conflict

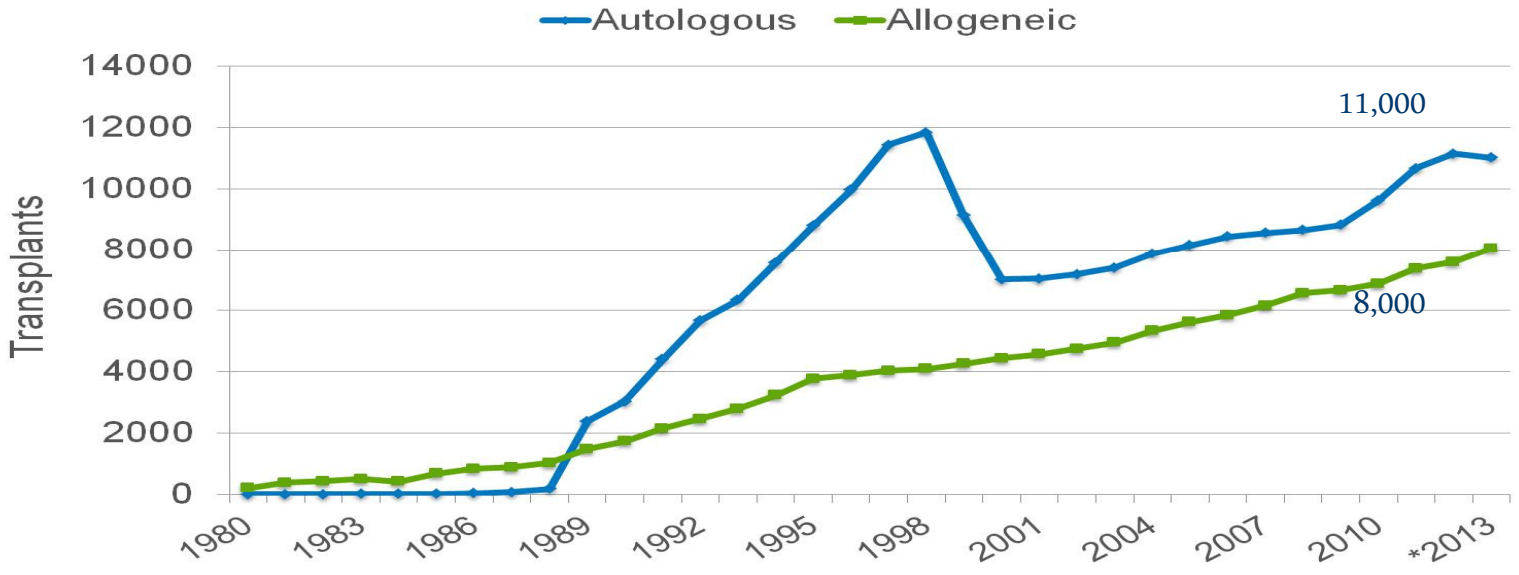
- Stem cell source: self; as “rescue” from high dose chemo
  - “marrow lethal dose”

Elements of BMT/HCT

- **Selection of donor**
  - Based on tissue typing of 6-10 HLA antigens in allogeneic transplantation
  - Tissue typing unnecessary in autologous transplantation
- **Harvest of stem cells from donor**
  - Bone marrow harvest or pheresis of peripheral blood
- **Preparative regimen**
  - Chemo-radiation for ablation and immune suppression
- **Stem cell infusion**
- **Post-transplant supportive care**
  - Autologous 100 days
  - Allogeneic 180 days or longer for tolerance to develop

Increasing number of transplants

Annual Number of Transplant Recipients in the US by Transplant type



CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

* 2013 Data incomplete

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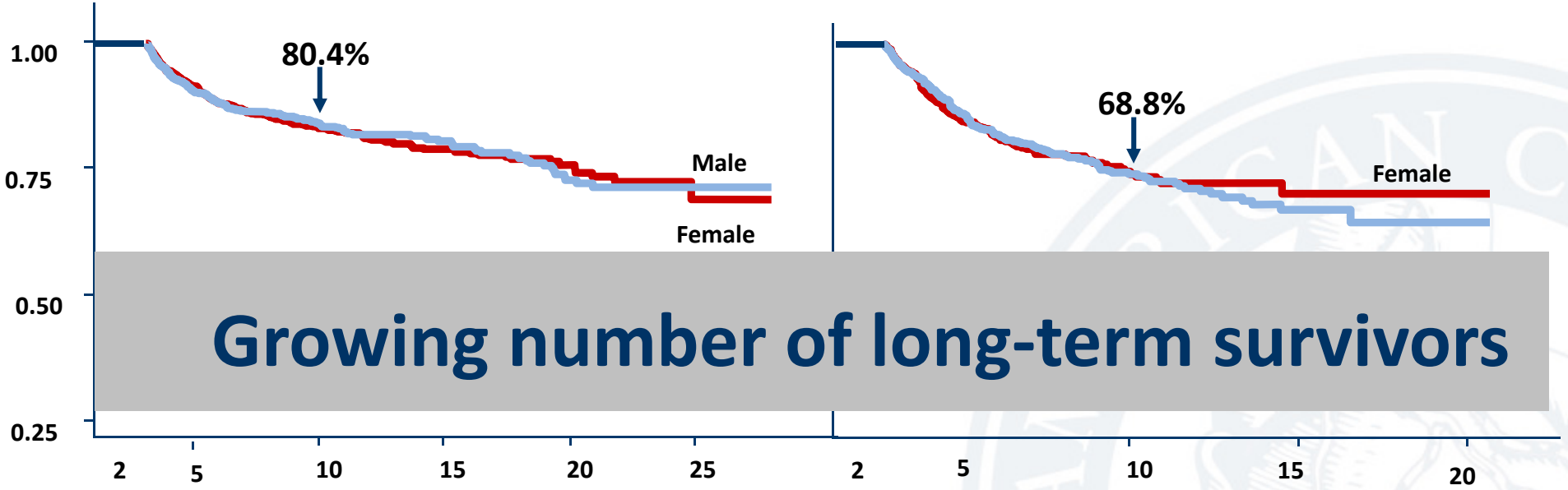
Long-term Survival after HCT



Growing number of long-term survivors

Blood, 2007, 110:3784-92

Blood, 2005, 105:4215-22

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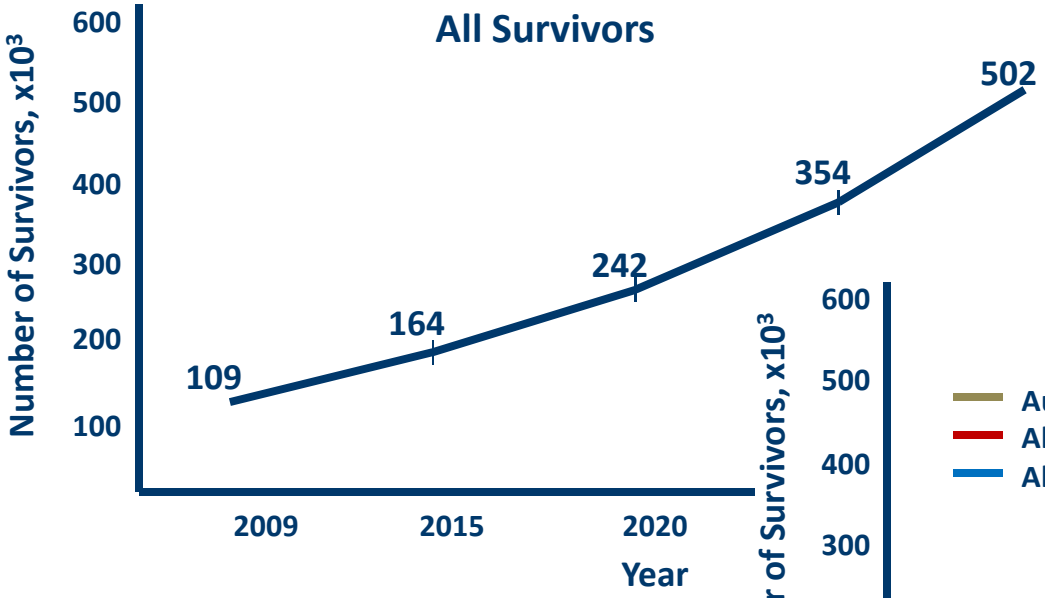
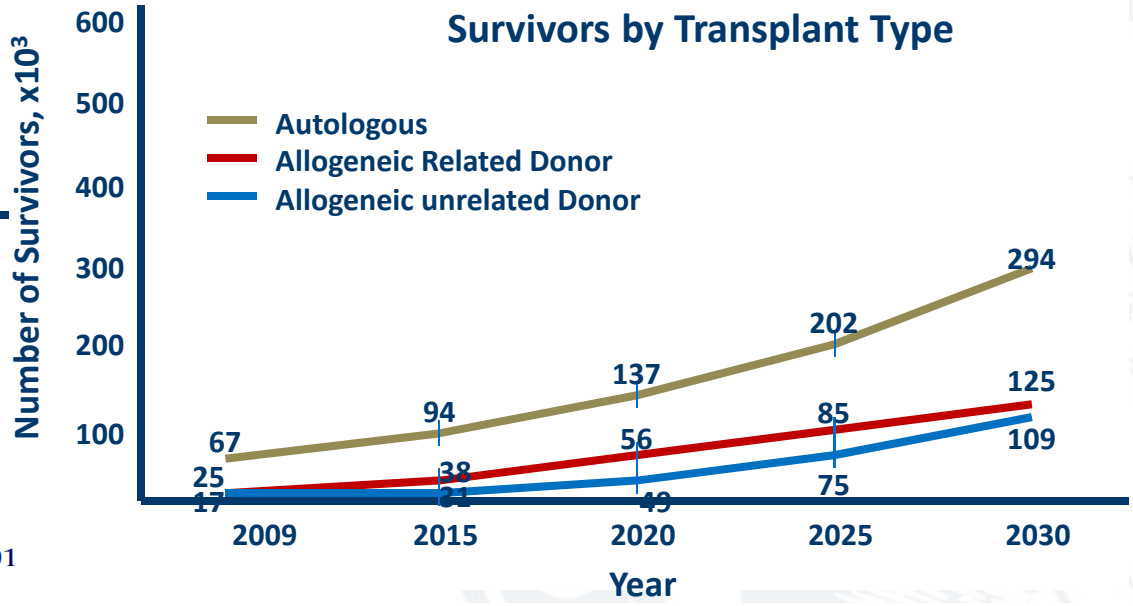
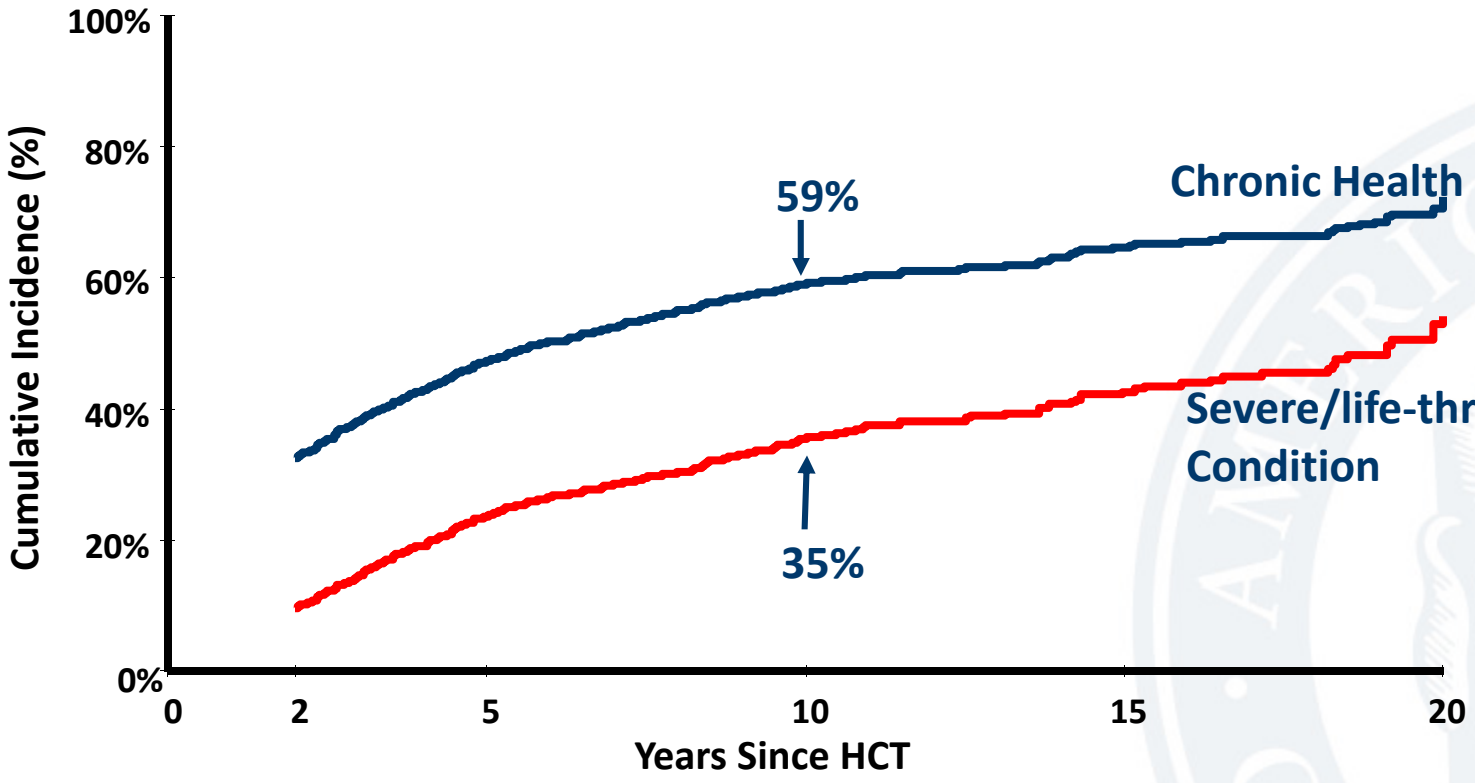
HCT Survivors: Projections





Biol Blood Marrow Transplant 19 (2013) 1498—1501

Chronic Health Conditions after HCT



Blood, 2010, 116: 3129-39

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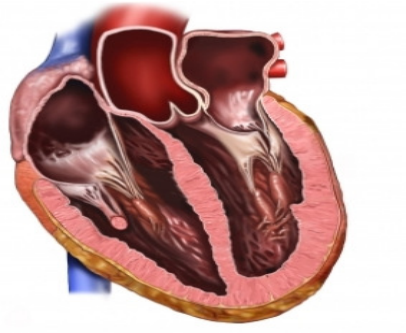
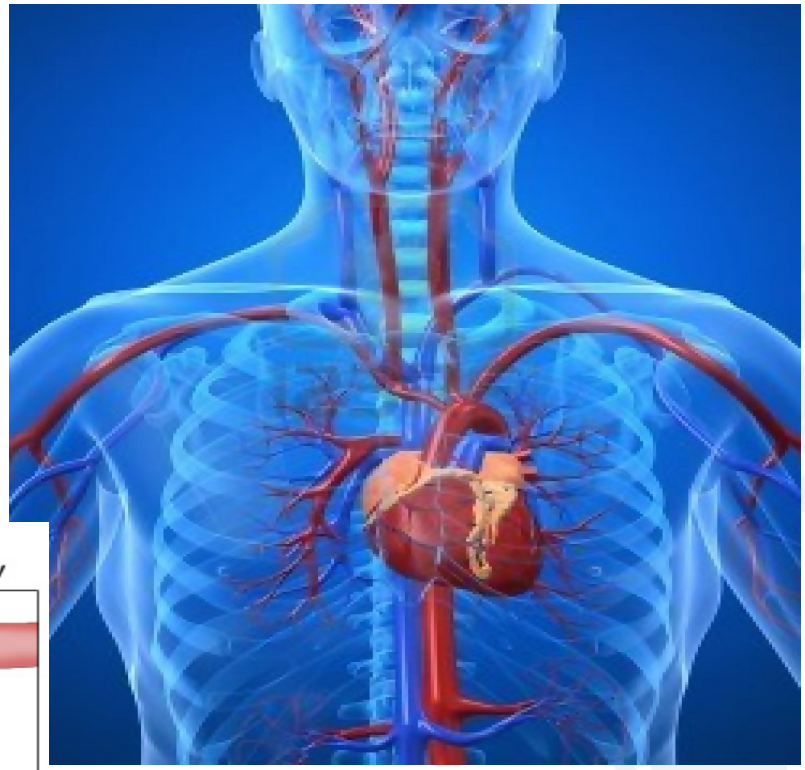
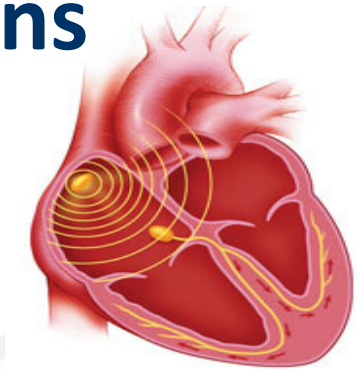
Cardiovascular complications

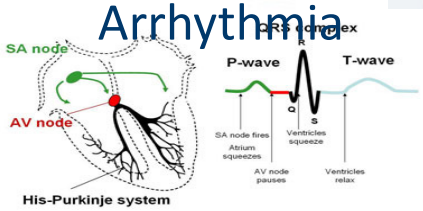


Cardiac Dysfunction/
heart failure

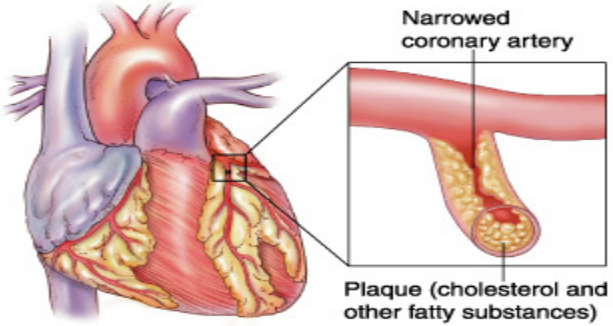




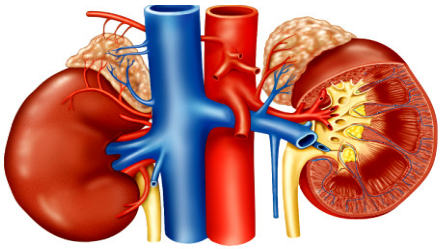
Arrhythmia



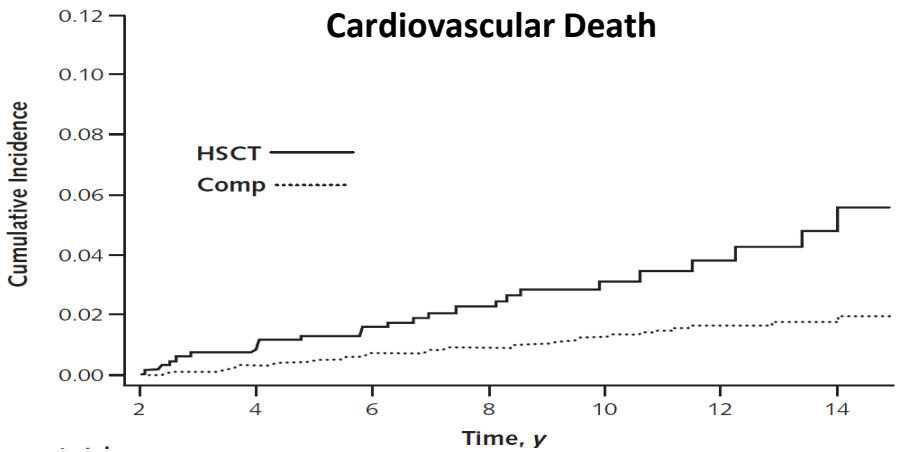
Atherosclerosis

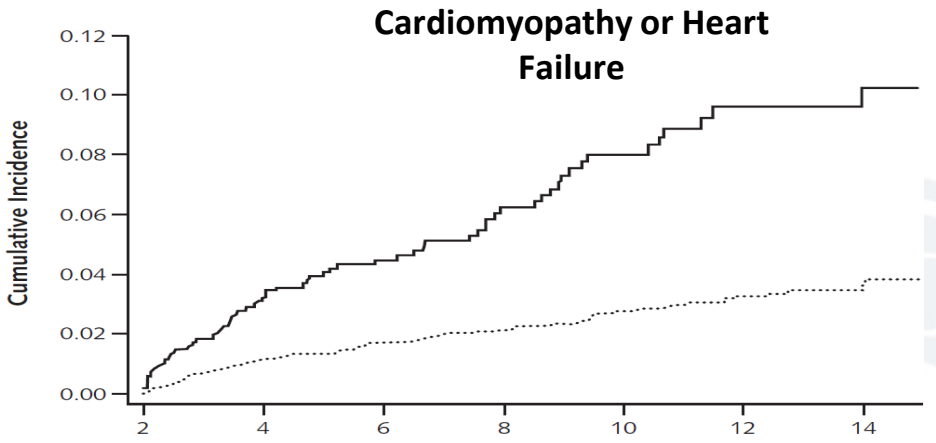


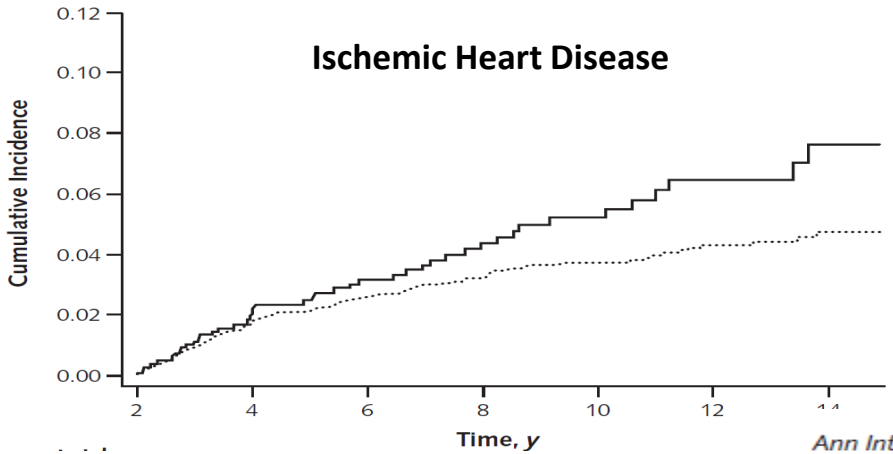
Reno-vascular

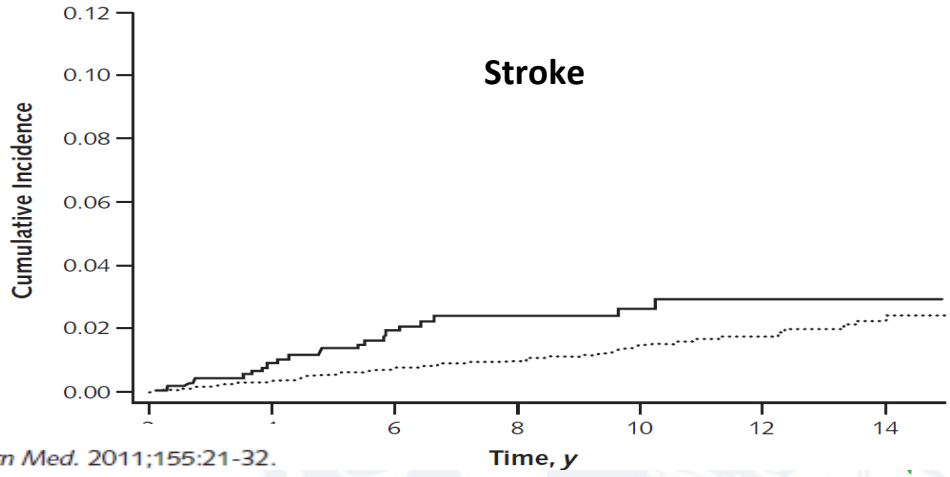


Cardiovascular disease: *HCT Survivors*



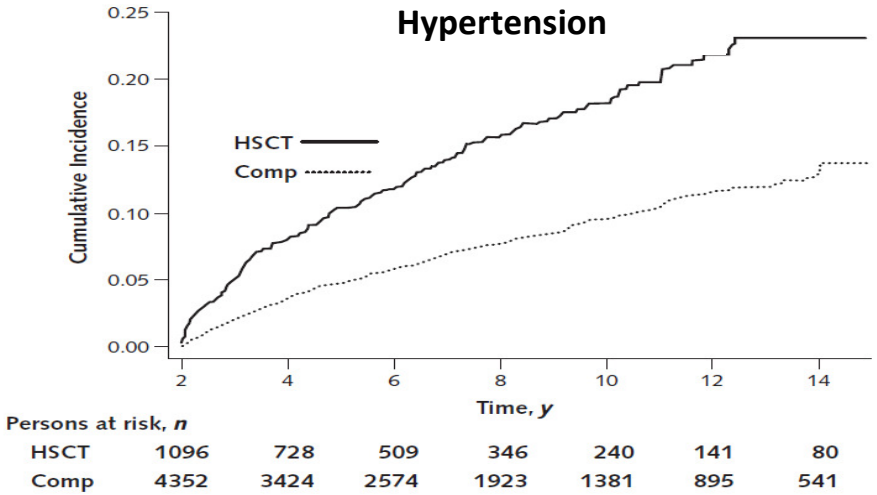


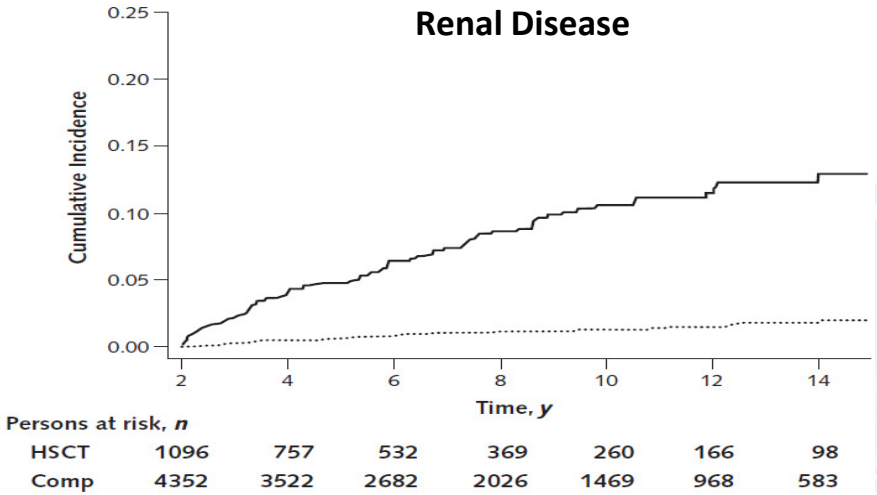


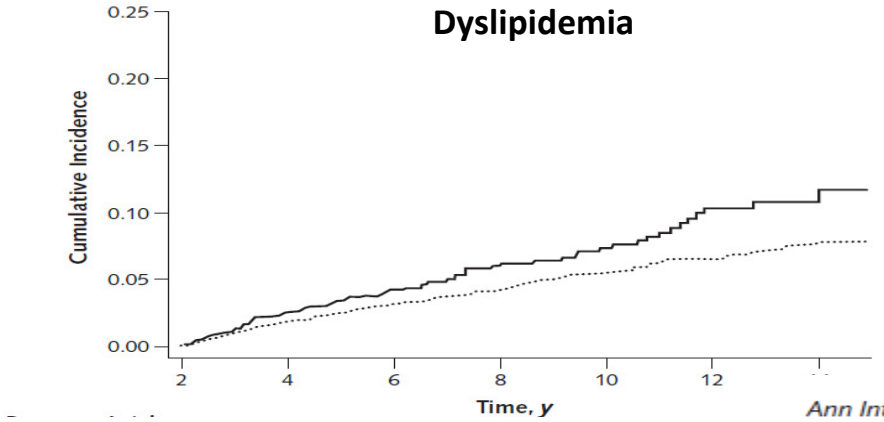


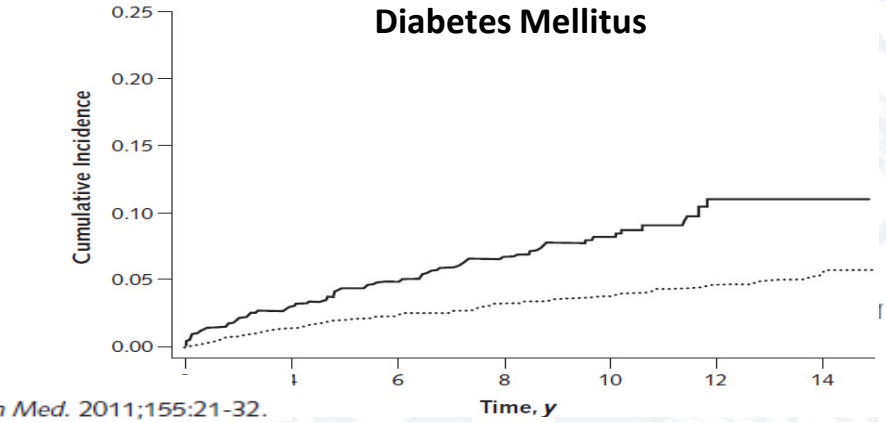
Ann Intern Med. 2011;155:21-32.

Cardiovascular risk factors: *HCT Survivors*



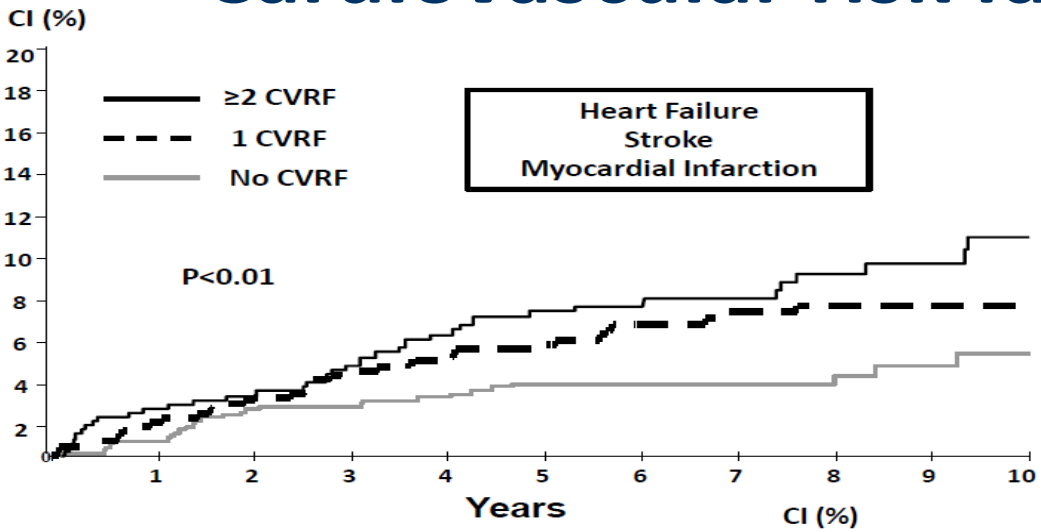


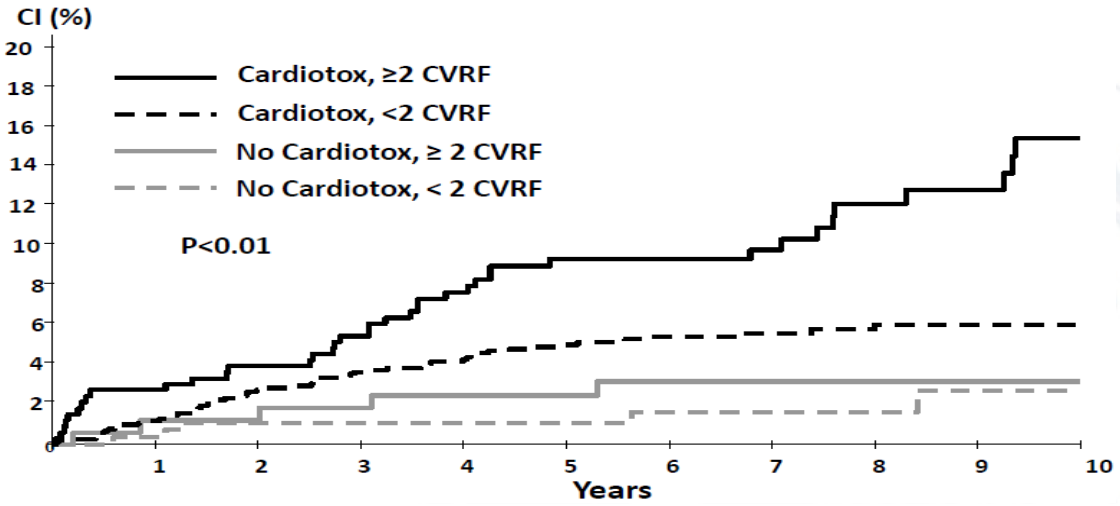




Ann Intern Med. 2011;155:21-32.

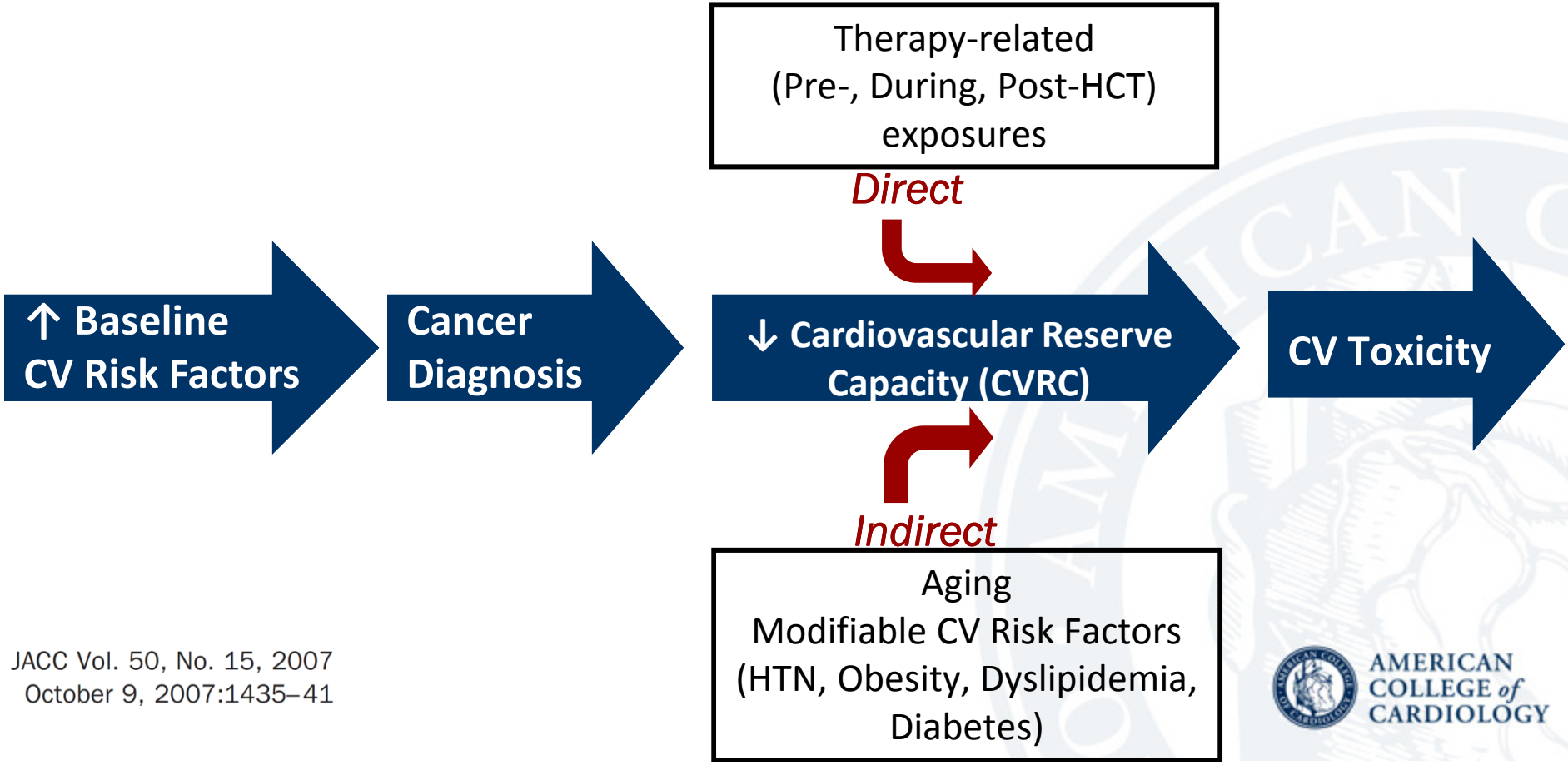
Cardiovascular risk factors and CVD





Blood, 2012, 120: 4505-12

Nature of the problem



JACC Vol. 50, No. 15, 2007
October 9, 2007:1435–41

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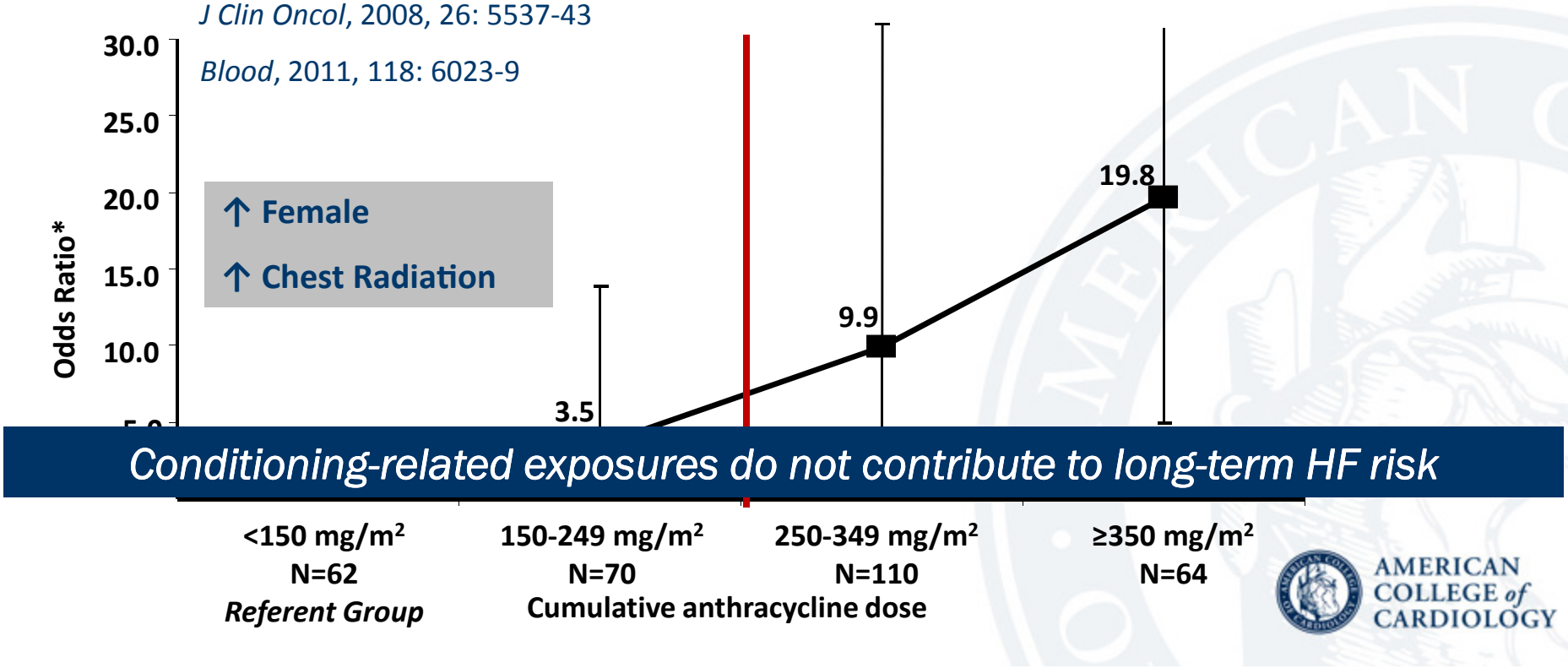
Heart failure HCT survivors:
Cumulative anthracycline dose

J Clin Oncol, 2008, 26: 5537-43

Blood, 2011, 118: 6023-9



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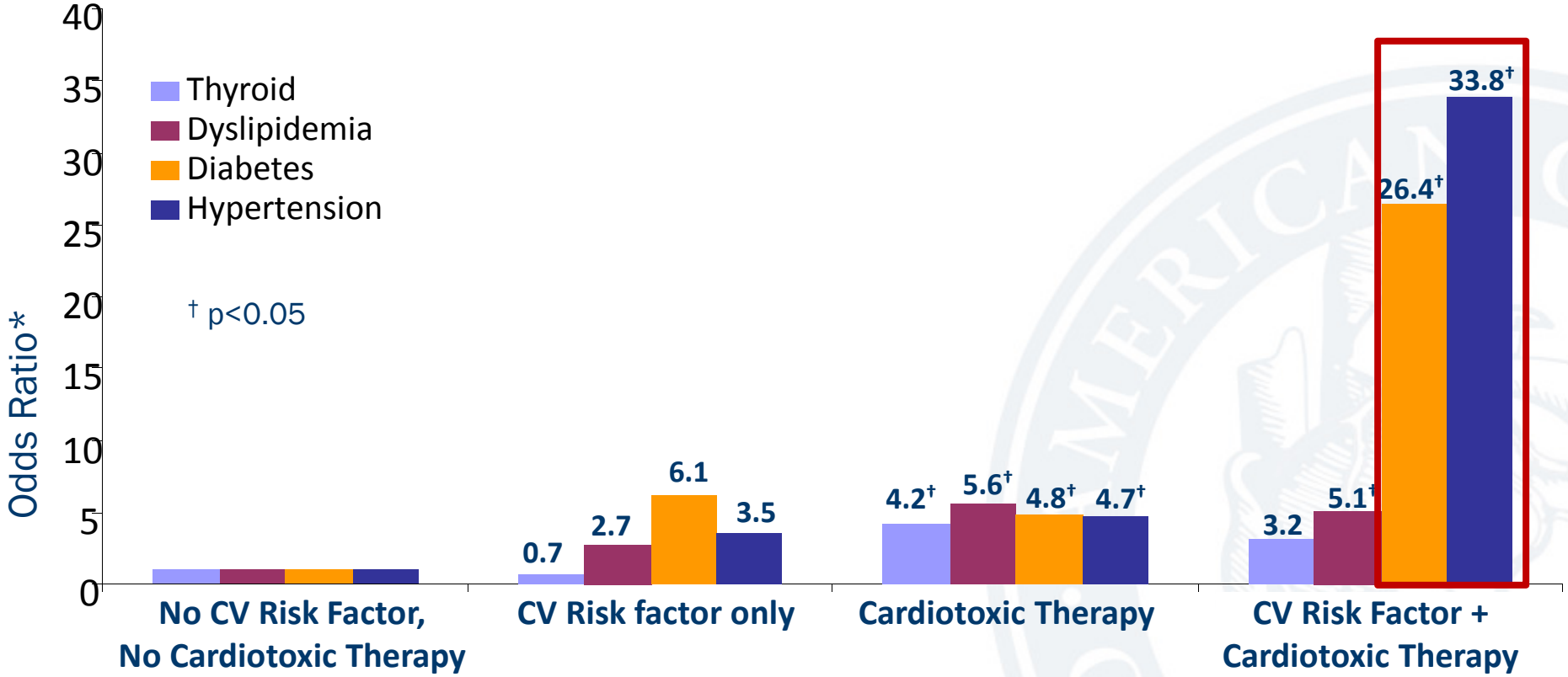
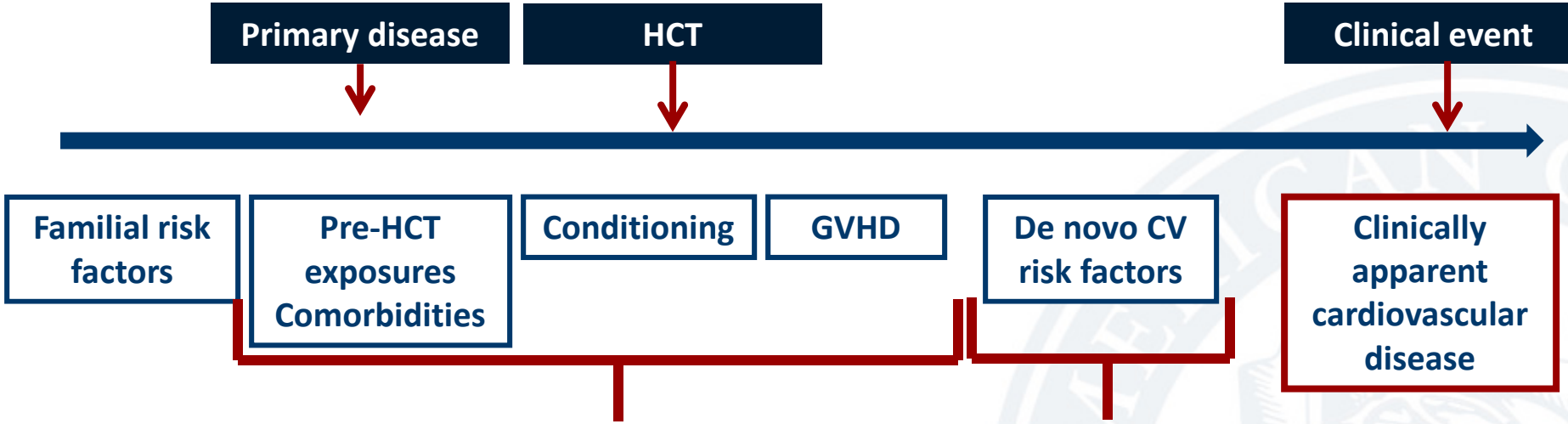
CV Risk Factors and Heart Failure:

HCT Survivors

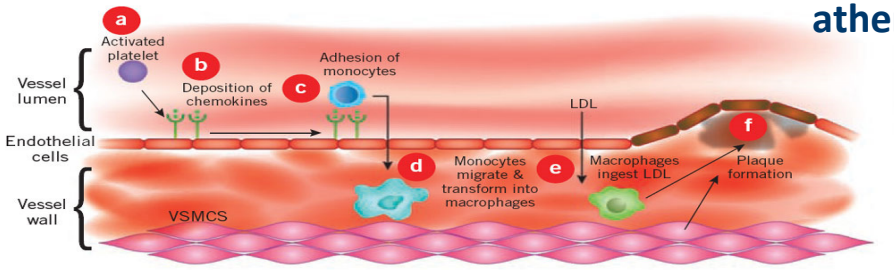
Blood, 2011, 118: 6023-9



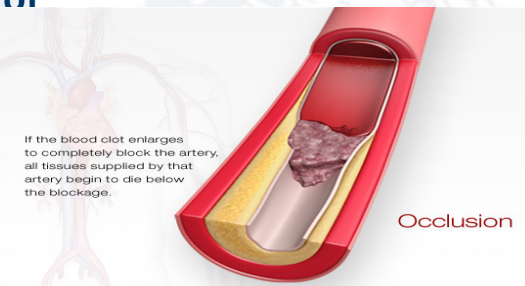
Premature atherosclerosis



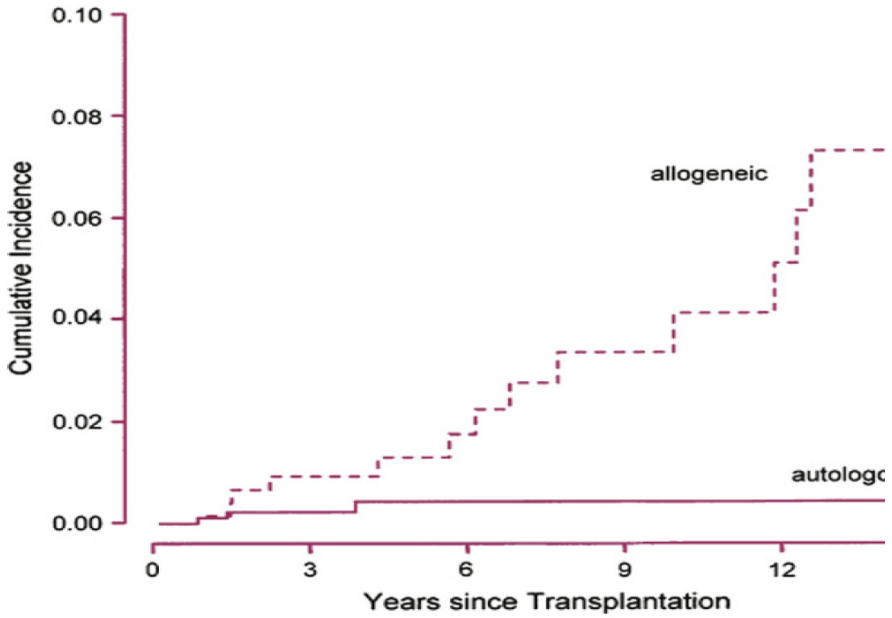
Vascular endothelial lesions

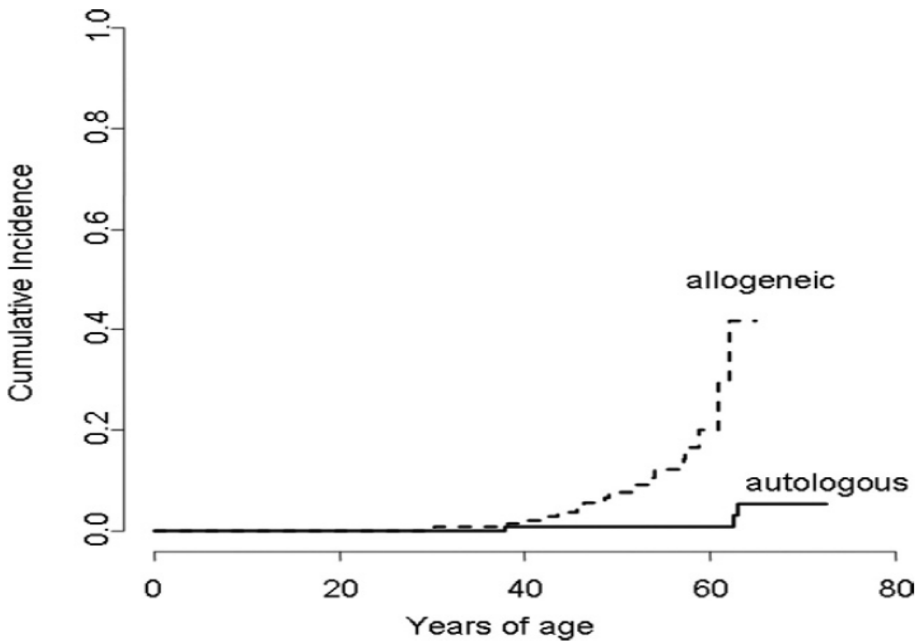


Enhancement of atheros



Arterial disease by HCT type





Blood. Tichelli A, Bucher C, Rovo A, et al. Premature cardiovascular disease after allogeneic hematopoietic stem-cell transplantation. 2007;110:3463–71. © the American Society of Hematology.[3]

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Case #1

58 yo female,

referred for Cardiology Consultation for cardiomyopathy

- No cardiopulmonary symptoms of any kind currently
- 2 months ago palpitations, dyspnea, chest tightness at the time of apheresis
- 1 month ago severe upper respiratory infection, pneumonia with respiratory failure, requiring hospitalization

Case #1 - Past Medical History

- Stage I (T1c, N0, M0) right breast infiltrating ductal carcinoma 6 years ago, s/p doxorubicin + cyclophosphamide x 4 cycles, followed by 12 weekly cycles of paclitaxel, XRT, lapatinib and Herceptin
- GIST 4 years ago, resected and treated with imatinib x 5 months

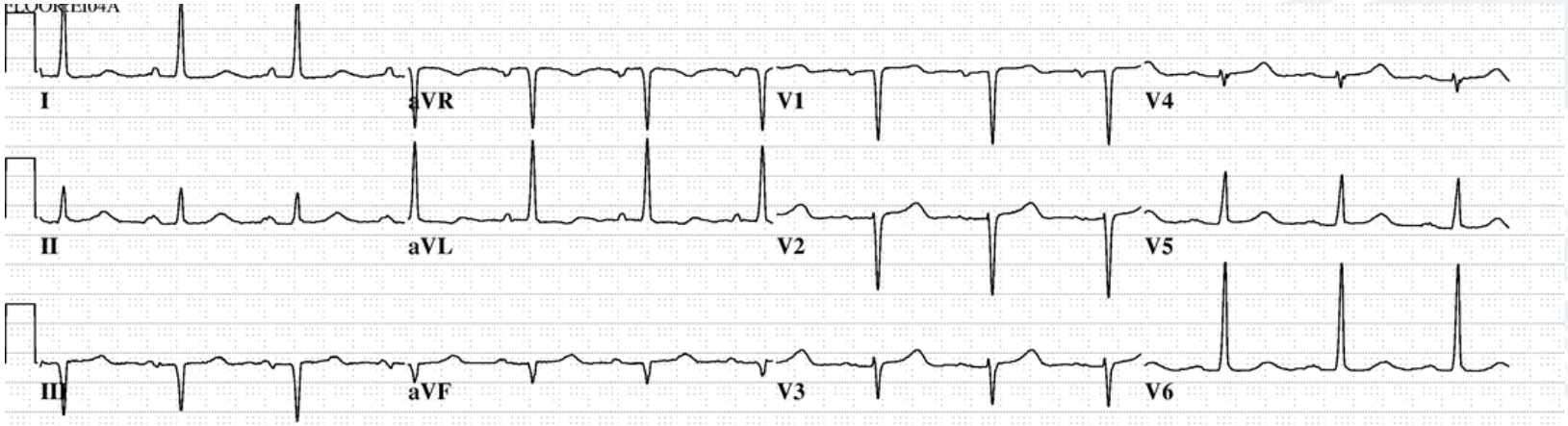
Case #1 - Past Medical History

- AML, 4 years ago, s/p induction with Idarubicin plus Cytarabine (3+7) and one cycle of high dose Cytarabine consolidation therapy, allo PBSCT with Flu/Bu conditioning
- Chronic GVHD involving skin, eyes, esophagus and liver
- Cardiomyopathy (EF 48% 3 years ago)
- Hypothyroidism
- Hyperlipidemia

Case #1 - Medications

- Carvedilol 3.125 mg BID
- Flovent HFA 220 mcg/actuation Aerosol 2 puffs BID
- Levothyroxine 100 mcg tablet 1 tablet by moth one time daily
- Lisinopril 7.5 mg one time daily
- Montelukast 10 mg every evening
- Omeprazole 40 mg one time daily
- Pravastatin 20 mg one time daily
- Sirolimus 1 mg one time daily

Case #1 - ECG



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Case #1 - Echocardiogram

Final Impressions

1. Technically difficult images.
2. Focused study per left ventricular chemotherapy protocol.
3. Left ventricular enlargement.
4. Estimated left ventricular ejection fraction range; 30 % – 35 %.
5. Generalized left ventricular hypokinesis.
6. Mild mitral valve regurgitation.
7. Indeterminate left ventricular diastolic function grade.

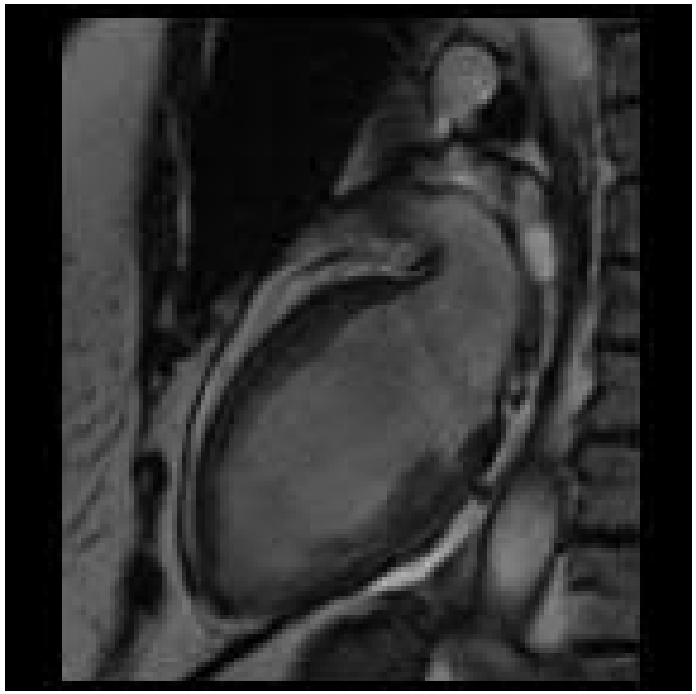
Findings

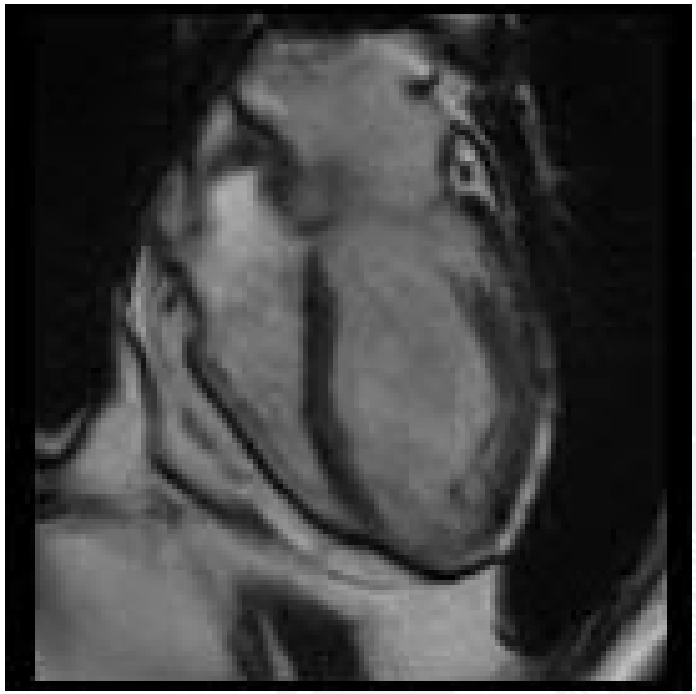
LEFT VENTRICLE: Normal left ventricular wall thickness. Calculated left ventricular ejection fraction; 34 %. RIGHT VENTRICLE: Normal right ventricular size. Normal right ventricular function. Unable to detect peak tricuspid regurgitation velocity for pulmonary artery systolic pressure calculation. ATRIA: Normal left atrial size. Normal right atrial size. CARDIAC VALVES: Tricuspid aortic valve. Normal aortic valve. No aortic valve regurgitation. Thickened mitral valve. Pulmonary valve not well visualized. Trivial pulmonary valve regurgitation. Normal tricuspid valve. Trivial tricuspid valve regurgitation. OTHER ECHO FINDINGS: No intracardiac mass or thrombus, but the left atrial appendage cannot be visualized adequately with transthoracic echo to exclude thrombus in this location. Tiny posterior pericardial effusion.

Case #1 - Serial Echocardiograms

General	05/05/14	04/26/14	12/16/13	09/24/13
BSA (m^2)	1.73	1.37	1.77	1.77
BMI(kg/m^2)	23.31	13.41	22.98	22.98
Heart Rate (BPM)	80	98	93	85
BP Systolic(mmHg)	104		102	114
BP Diastolic(mmHg)	78		68	74
LVIDd (MM)(mm)		50		50
IVSd (2D)(mm)	12	10	10	11
LVPWd (2D)(mm)	8	10	9	12
LVIDd (2D)(mm)	58	52	45	50
EF % (MM)(%)				48
EF % (2D)(%)	34		46	48
EF % (Biplane)(%)	31		43	40
SV Index(cc/m^2)	26		34	31

Case #1 – Cardiac MRI





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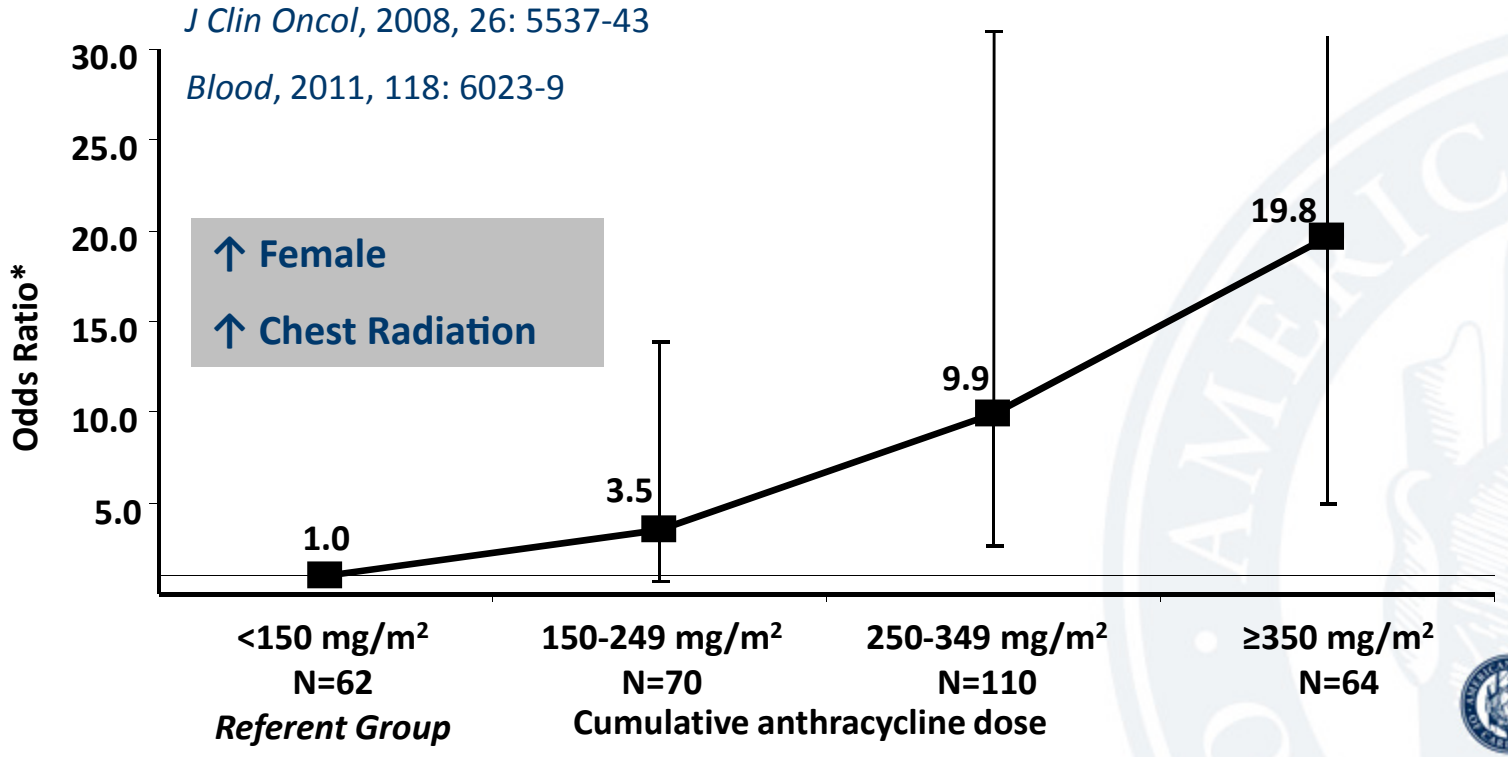
Case #1 - Cardiac MRI

- Borderline left ventricular enlargement, global hypokinesis with no regional wall motion abnormalities, LVEF 31%.
- Normal right ventricle size and systolic function. RVEF 53%.
- Mild mitral regurgitation.
- Reduced perfusion of ventricular septum at basal and mid levels, at rest and with stress. No regional wall motion abnormalities.
- No delayed myocardial enhancement.
- Small pericardial effusion. Normal pericardial thickness. Small pericardial effusion. No pericardial edema or enhancement. No MRI evidence of ventricular interdependence or constrictive physiology.

What is the Most Likely Etiology of the Reduced Cardiac Function?

A. Hypothyroidism
B. Coronary artery disease
C. Viral myocarditis
D. Anthracycline exposure
E. High dose conditioning therapy for allogenic HCT
F. HER-2 inhibitors (Trastuzumab/Lapatinib)

Heart failure HCT survivors:
Cumulative anthracycline dose



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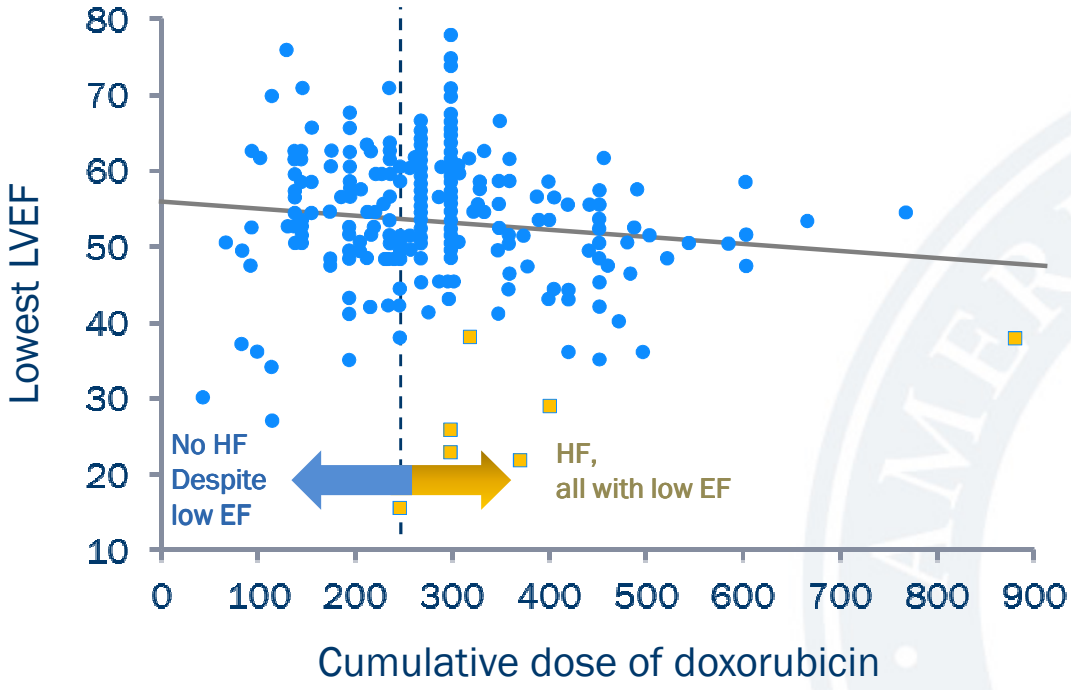
Anthracycline Dose and Correlation With LVEF Reduction and Heart Failure



Mitani I et al: J Nucl Cardiol 2003;10:132-9

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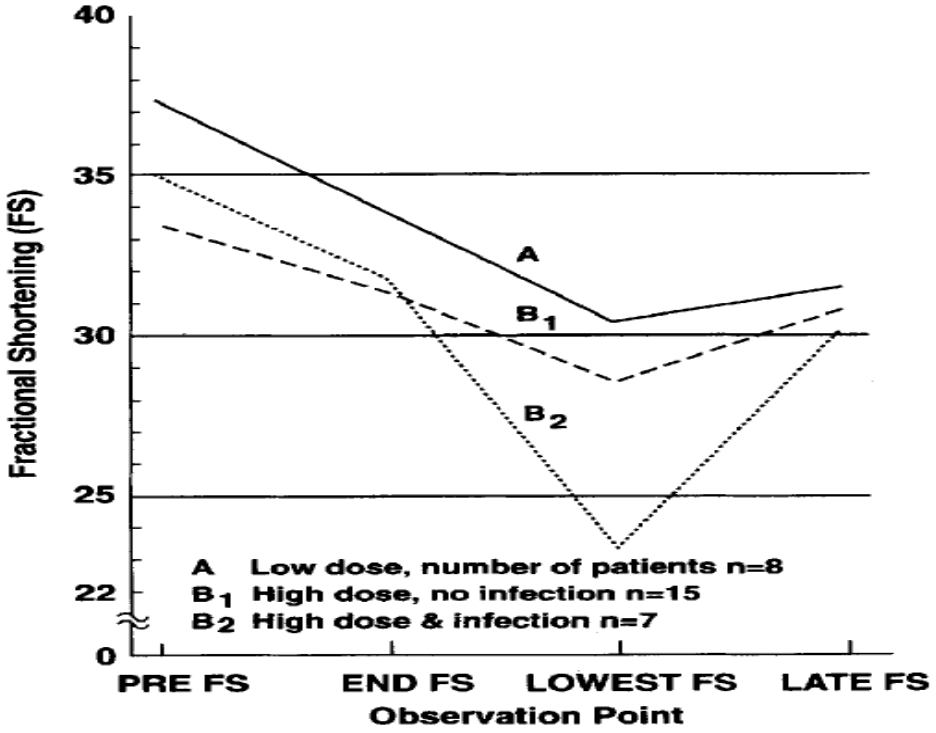
Cardiac Function Dynamics

Pediatric Cancer Patients After Doxorubicin



Ali M et al: Cancer 74:182, 1994

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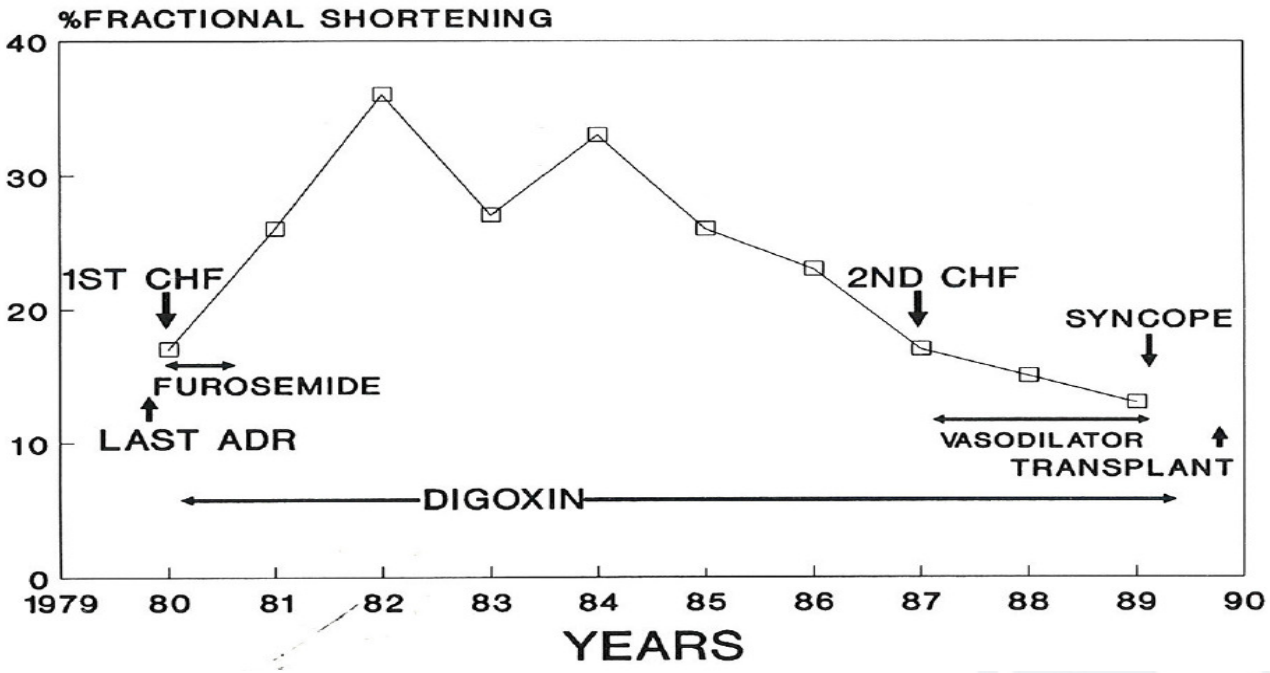
Cardiac Function Dynamics

Pediatric Cancer Patients After Doxorubicin



Steinherz et al: Med Ped Oncol 24:352, 1995

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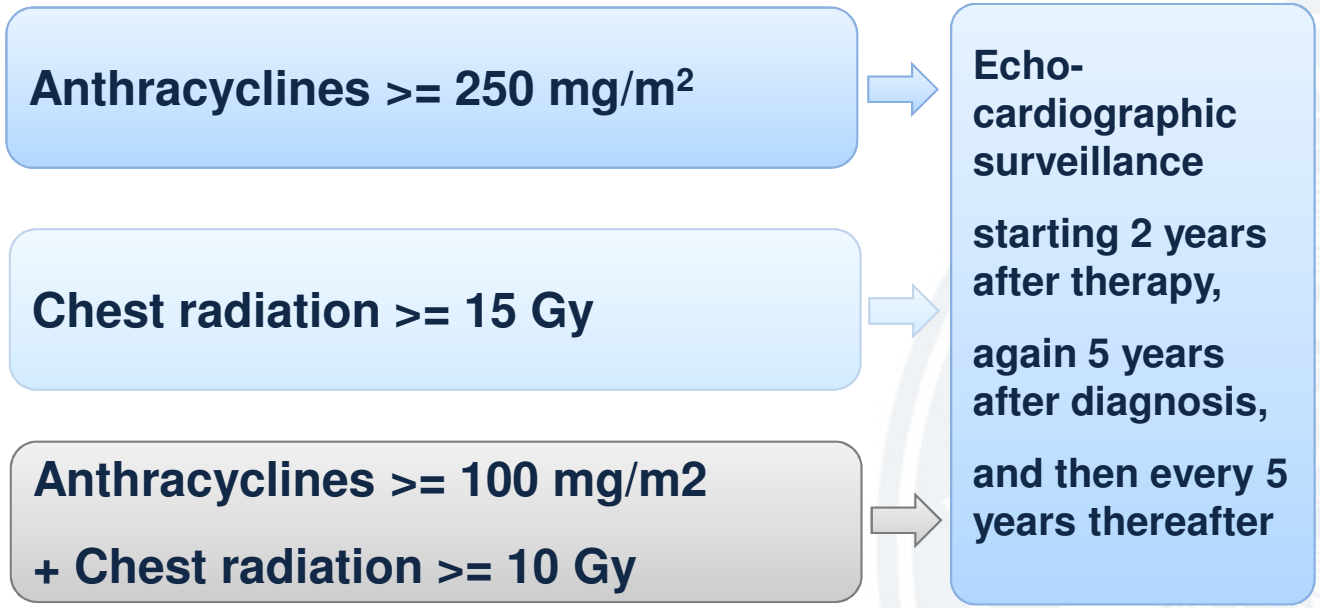
International Late Effects of Childhood Cancer Guideline Harmonization Group



Armenian SH et al: Lancet 15:e123, 2015

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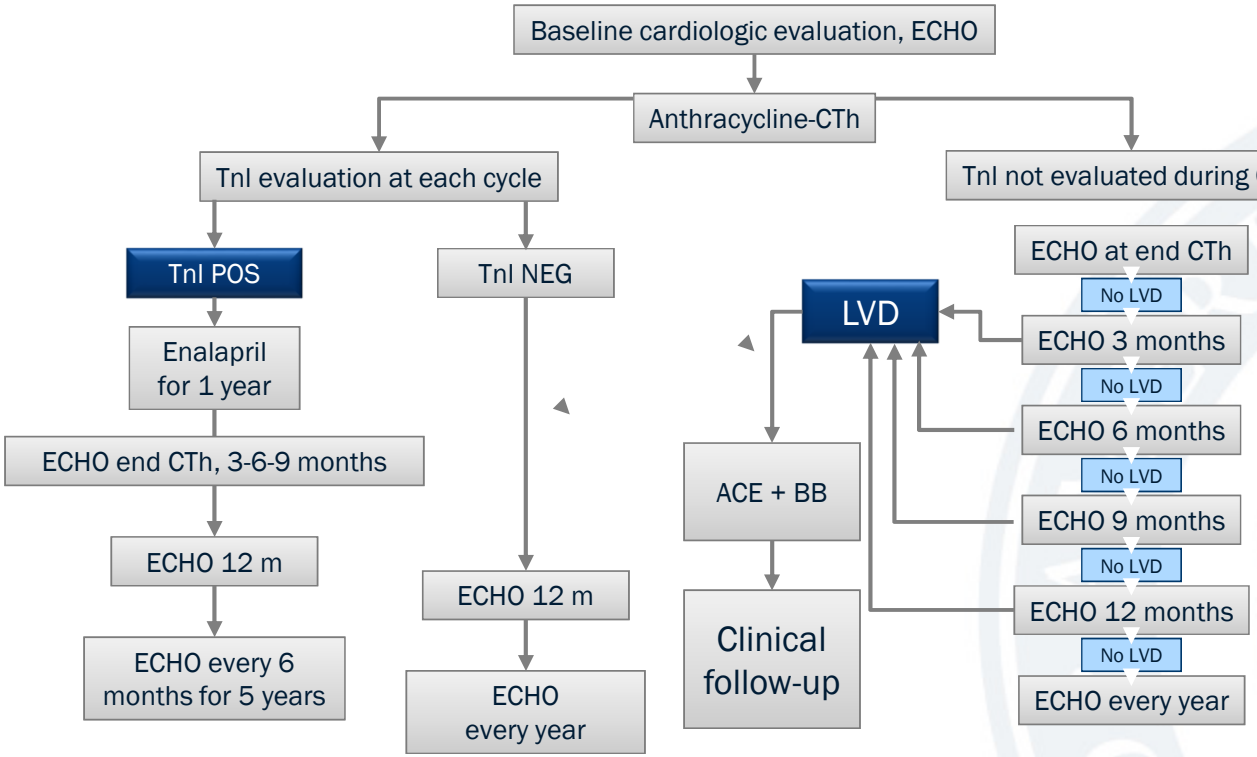
ESMO Clinical Practice
Guideline 2012



Curigliano G. et al: Ann Oncol 2012:23 (Suppl. 7): vii155-vii166

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Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline

Saro H. Armenian, Christina Lacchetti, Ana Barac, Joseph Carver, Louis S. Constine, Neelima Denduluri, Susan Dent, Pamela S. Douglas, Jean-Bernard Durand, Michael Ewer, Carol Fabian, Melissa Hudson, Mariell Jessup, Lee W. Jones, Bonnie Ky, Erica L. Mayer, Javid Moslehi, Kevin Oeffinger, Katharine Ray, Kathryn Ruddy, and Daniel Lenihan

Author affiliations appear at the end of this article.

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Editor's note: This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a Data Supplement with additional evidence tables, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/cardiac-guideline.

Endorsed by the American Heart Association.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

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0732-183X/16/3499-1/$20.00

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A B S T R A C T

Purpose
Cardiac dysfunction is a serious adverse effect of certain cancer-directed therapies that can interfere with the efficacy of treatment, decrease quality of life, or impact the actual survival of the patient with cancer. The purpose of this effort was to develop recommendations for prevention and monitoring of cardiac dysfunction in survivors of adult-onset cancers.

Methods
Recommendations were developed by an expert panel with multidisciplinary representation using a systematic review (1996 to 2016) of meta-analyses, randomized clinical trials, observational studies, and clinical experience. Study quality was assessed using established methods, per study design. The guideline recommendations were crafted in part using the Guidelines Into Decision Support methodology.

Results
A total of 104 studies met eligibility criteria and compose the evidentiary basis for the recommendations. The strength of the recommendations in these guidelines is based on the quality, amount, and consistency of the evidence and the balance between benefits and harms.

Recommendations
It is important for health care providers to initiate the discussion regarding the potential for cardiac dysfunction in individuals in whom the risk is sufficiently high before beginning therapy. Certain higher risk populations of survivors of cancer may benefit from prevention and screening strategies implemented during cancer-directed therapies. Clinical suspicion for cardiac disease should be high and threshold for cardiac evaluation should be low in any survivor who has received potentially cardiotoxic therapy. For certain higher risk survivors of cancer, routine surveillance with cardiac imaging may be warranted after completion of cancer-directed therapy, so that appropriate interventions can be initiated to halt or even reverse the progression of cardiac dysfunction.

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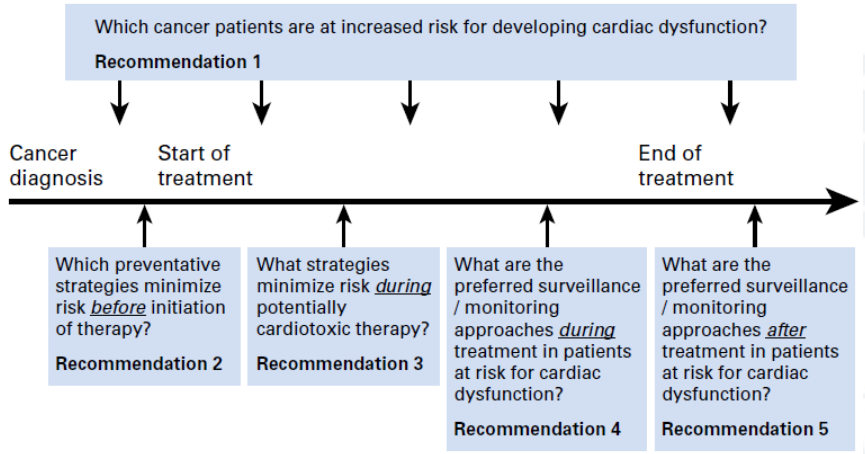
INTRODUCTION

Recent advances in cancer treatment and supportive care have resulted in a growing number of survivors of cancer.[1] With longer survival, attention to the chronic and long-term adverse treatment effects has become increasingly important. Heart failure (HF), presenting during or after completion of cancer treatment, is a well-recognized complication impacting survival and quality of life. The American College of Cardiology (ACC) and American Heart Association (AHA) describe HF as a progressive disorder.[2] This process begins with risk factors known to be associated with the development of HF, including the toxicity of chemotherapy and/or radiation (RT; stage A), and is commonly progressive after structural changes to the heart occur. The initial manifestation may be asymptomatic cardiac dysfunction (stage B), which precedes eventual development of overt signs and symptoms (stages C and D). In patients with cancer, onset of either asymptomatic or symptomatic disease may also be responsible for interruption or discontinuation of cancer-directed therapy, potentially reducing



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5. What are the preferred surveillance and monitoring approaches after treatment in patients at risk for cardiac dysfunction?

Recommendation 5.1. Clinicians should complete a careful history and physical examination in survivors of cancer previously treated with potentially cardiotoxic therapies.
(Informal consensus; benefits outweigh harms; Evidence quality: insufficient; Strength of recommendation: strong)

Recommendation 5.1.1. In individuals with clinical signs or symptoms concerning for cardiac dysfunction, the following approaches should be offered as part of recommended care:

- Echocardiogram for diagnostic workup

(Evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong)

- Cardiac MRI or MUGA if echocardiogram is not available or technically feasible (eg, poor image quality), with preference given to cardiac MRI

(Evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)

- Serum cardiac biomarkers (troponins, natriuretic peptides)

(Evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)

- Referral to a cardiologist based on findings

(Informal consensus; benefits outweigh harms; Evidence quality: insufficient; Strength of recommendation: strong)

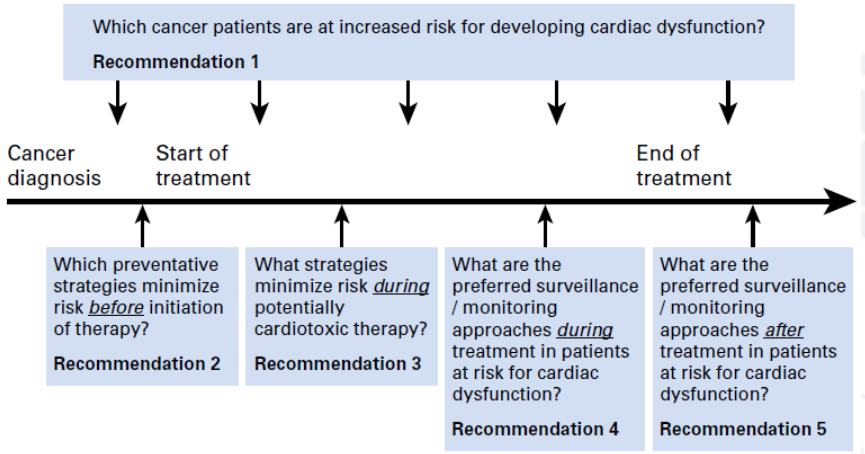
Recommendation 5.2. An echocardiogram may be performed between 6 and 12 months after completion of cancer-directed therapy in asymptomatic patients considered to be at increased risk (Recommendation 1.1) of cardiac dysfunction.
(Evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)

Recommendation 5.2.1. Cardiac MRI or MUGA may be offered for surveillance in asymptomatic individuals if an echocardiogram is not available or technically feasible (eg, poor image quality), with preference given to cardiac MRI.
(Evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)

Recommendation 5.3. Patients identified to have asymptomatic cardiac dysfunction during routine surveillance should be referred to a cardiologist or a health care provider with cardio-oncology expertise for further assessment and management.
(Informal consensus; benefits outweigh harms; Evidence quality: insufficient; Strength of recommendation: strong)

Recommendation 5.4. No recommendations can be made regarding the frequency and duration of surveillance in patients at increased risk (Recommendation 1.1) who are asymptomatic and have no evidence of cardiac dysfunction on their 6- to 12-month post-treatment echocardiogram.
(Informal consensus; relative balance of benefits and harms; Evidence quality: insufficient)

Recommendation 5.5. Clinicians should regularly evaluate and manage cardiovascular risk factors such as smoking, hypertension, diabetes, dyslipidemia, and obesity in patients previously treated with cardiotoxic cancer therapies. A heart-healthy lifestyle, including the role of diet and exercise, should be discussed as part of long-term follow-up care.
(Evidence based and consensus; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate)



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Case #1 – Take Home Points

- pre-HCT anthracycline dose and CV risk factor assessment to determine risk status (low vs. high) is the key initial step for post-HCT cardiomyopathy surveillance efforts
- echocardiogram in at risk patients recommended 6-12 after completion of anthracycline-containing chemotherapy, thereafter the surveillance schedule remains undefined (unless pediatric patients and radiation therapy)
- Important to evaluate for factors that cause cardiomyopathy by itself or reduce the anthracycline threshold

Case #2

39 yo female, referred for Cardiology Consultation

- 10 days ago chest discomfort while lying in bed, initially sharp, then heaviness into the arms
- mild dyspnea and diaphoresis
- resolution of symptoms after 30 minutes

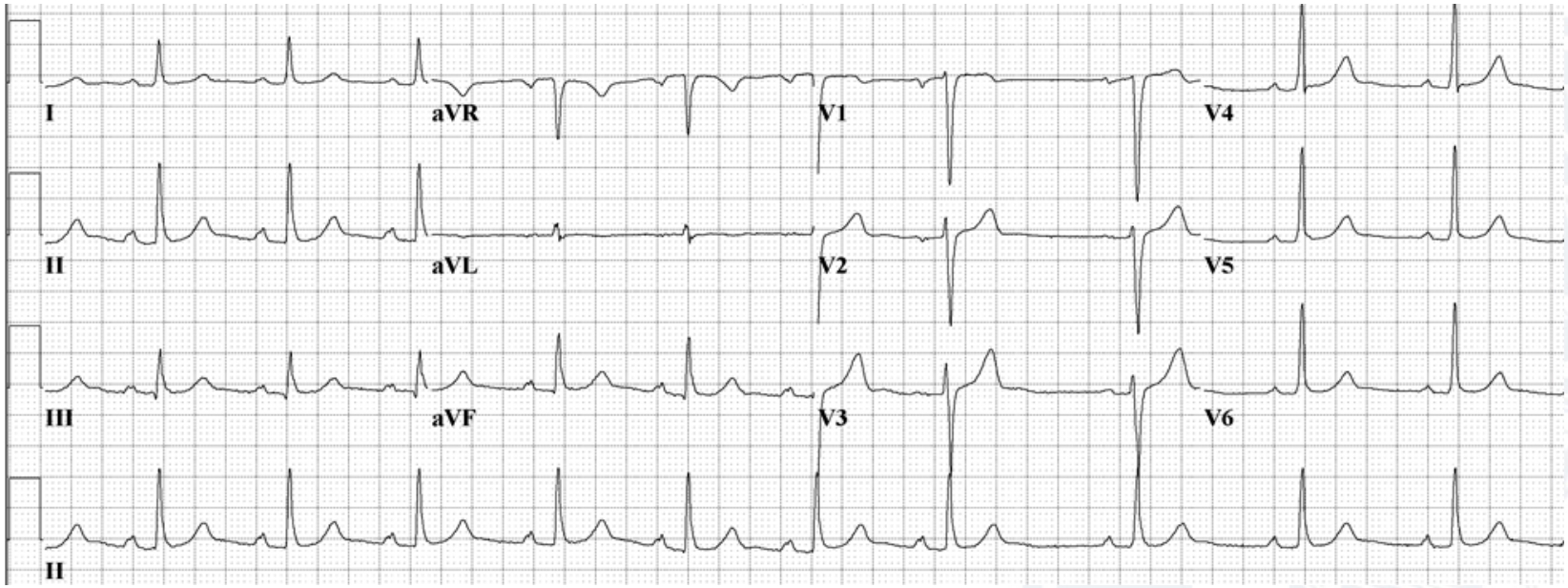
Case #2 – Past Medical History

- AML, dx 10 years ago, s/p chemotherapy (daunorubicin, cytarabine, etoposide, high-dose Ara-C) and matched unrelated donor allogeneic BMT 8 years ago, complicated by late-onset chronic graft-versus-host disease involving skin and GI tract
- Steroid-related DM
- Hyperlipidemia
- Nicotine dependence
- Depression

Case #2 - Medications

- Albuterol 90 mcg/Act 2 puffs q4h PRN
- Aspirin 81 mg per day
- Atorvastatin 80 mg per day
- Metoprolol 25 mg twice a day
- Xanax 0.5 mg twice a day PRN

Case #2 - ECG



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What is Your Recommendation?

A. No further testing
B. Chest CT PE protocol
C. Exercise treadmill stress test
D. Exercise stress echocardiogram
E. Coronary angiogram
F. Cardiac troponin T

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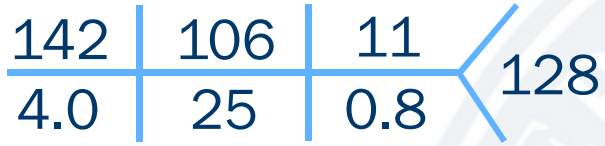
Case #2 – Laboratory Parameters

CBC

E'lytes

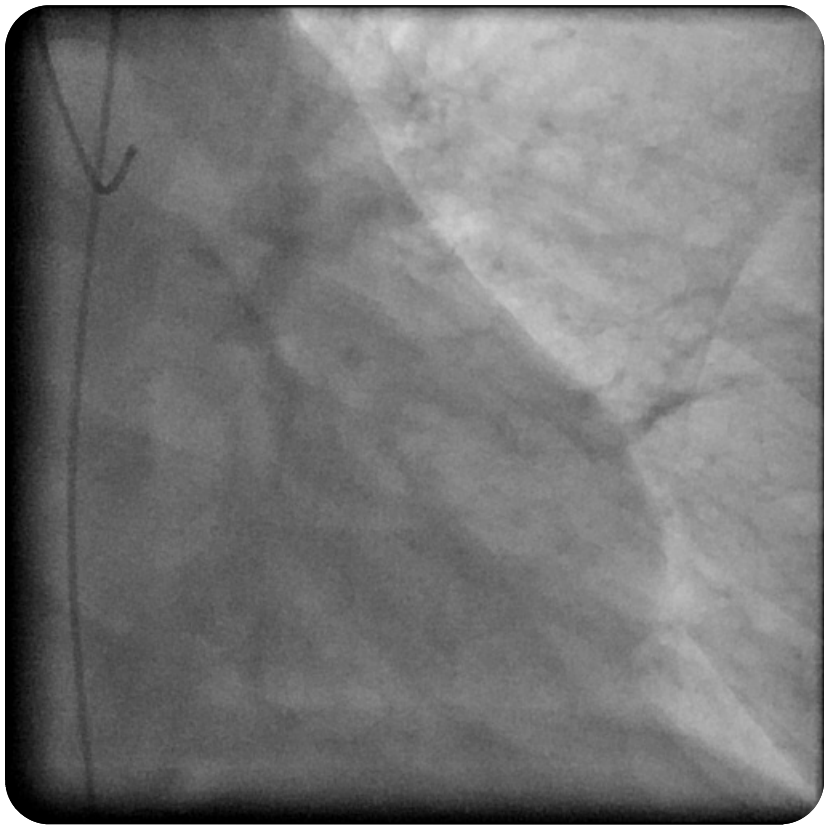


Cardiac biomarkers

cTnT 0.18, CK-MB 1.7

NT-pro-BNP 749

Case #2 – Coronary Angiogram



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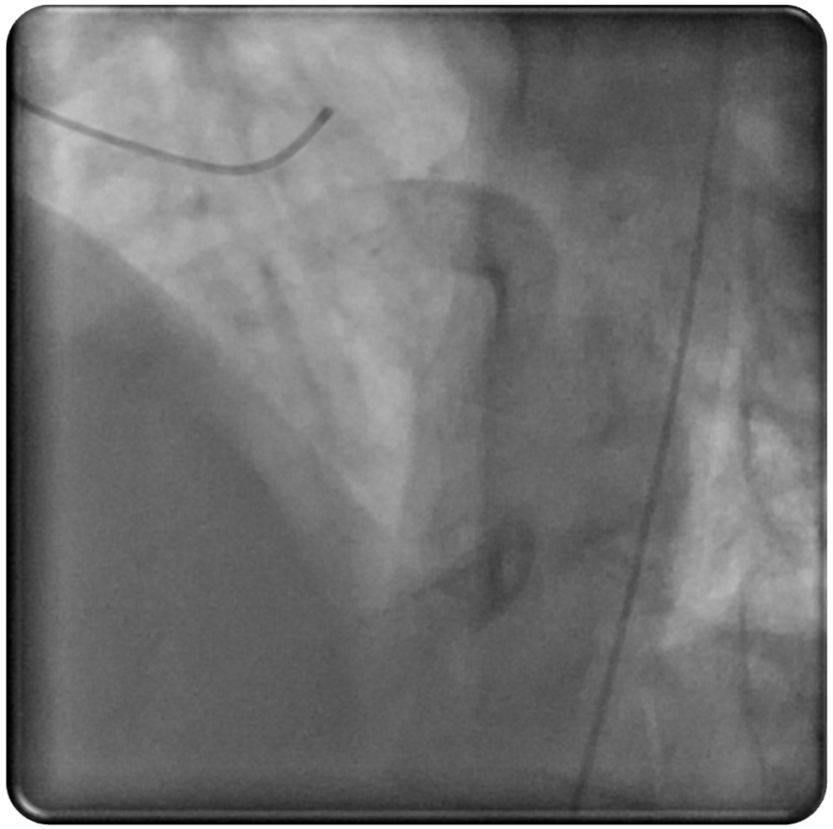

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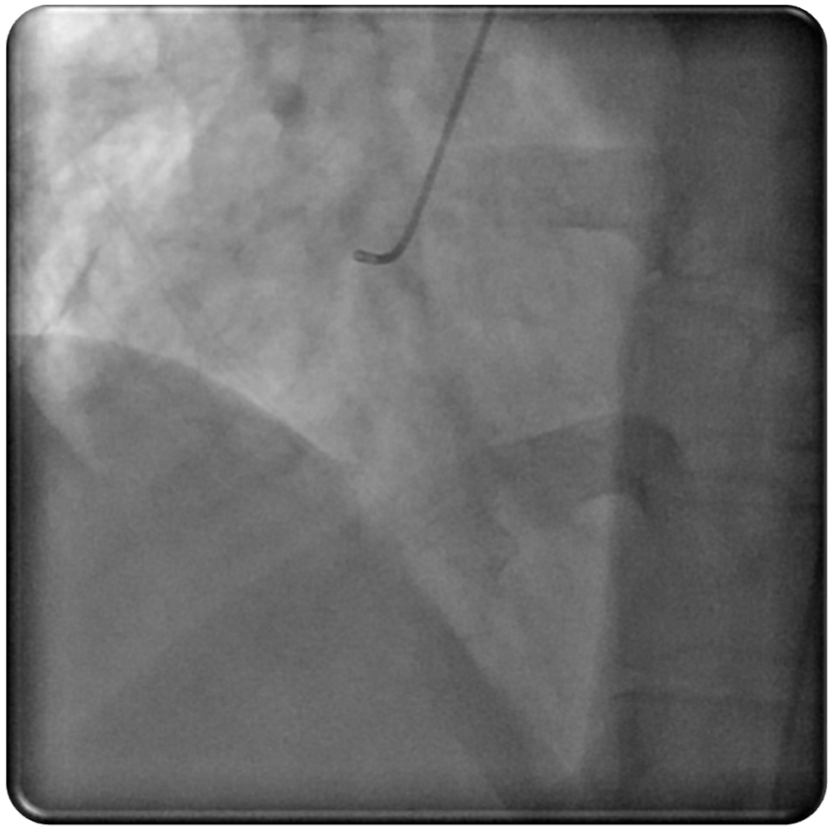
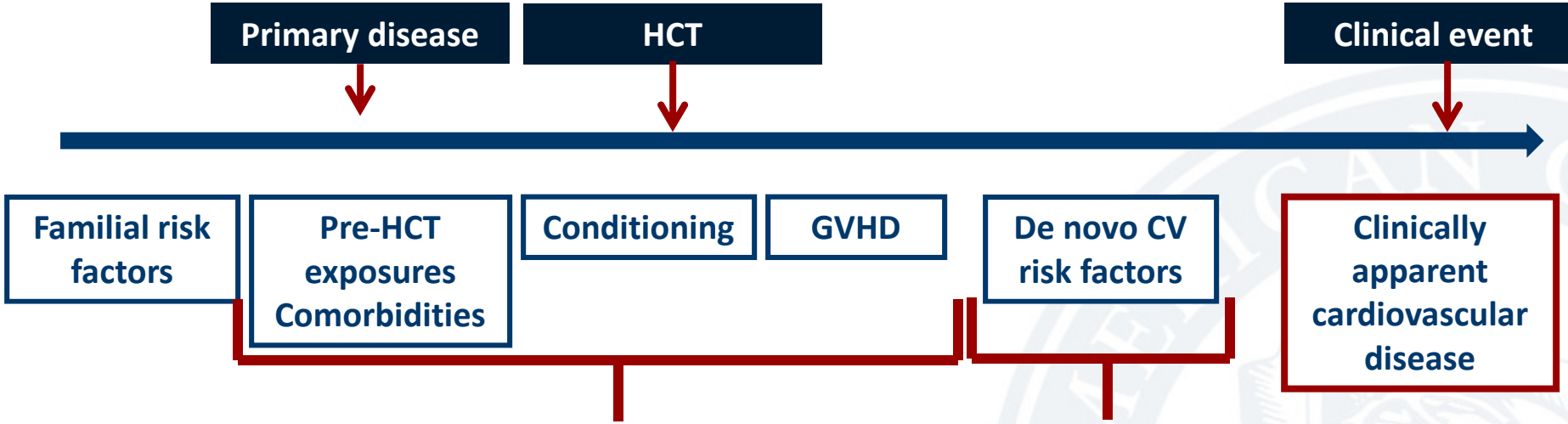


Case #2 – CV Risk Evaluation 3 months prior

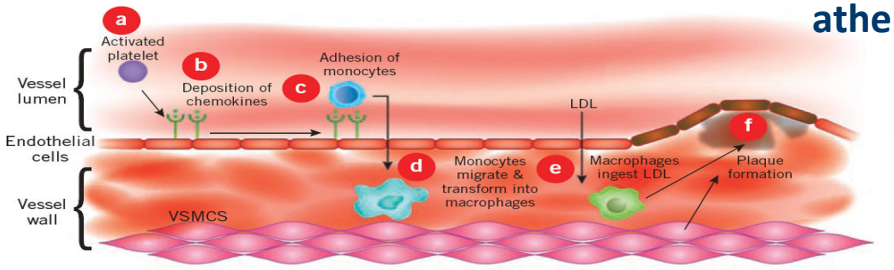
- FRS 2.6%
- TC 212, HDL 36, LDL 127, TG 243 mg/dL
- BP 116/81 mmHg
- FPG 93 mg/dL
- BMI 19 kg/m2

- Chest CT: “scattered arterial calcifications including coronary”

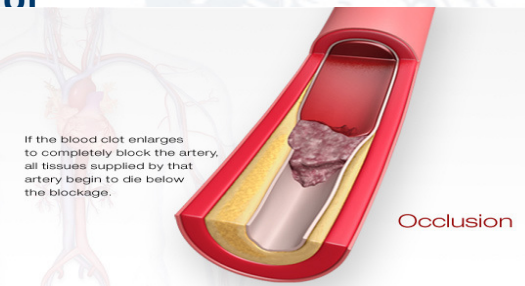
Premature atherosclerosis



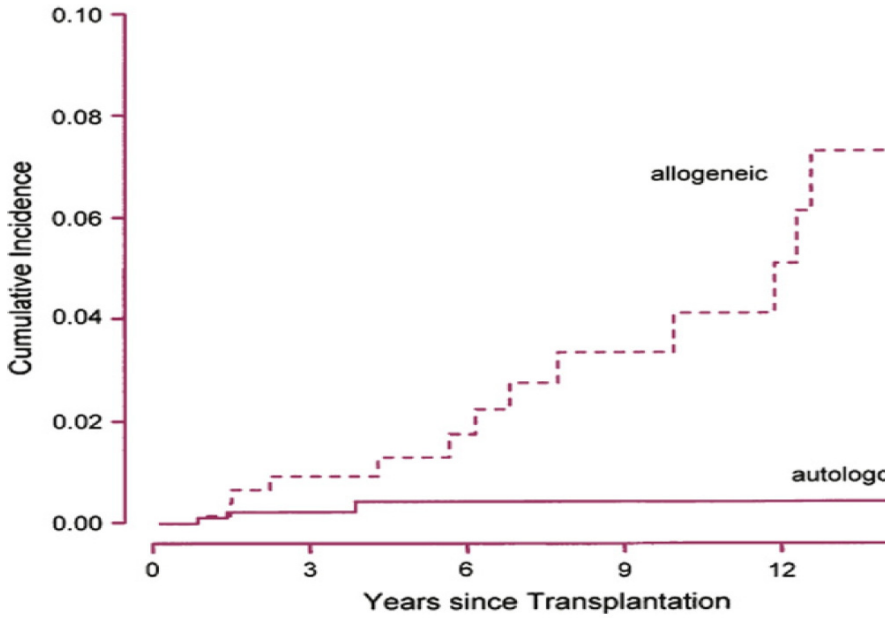
Vascular endothelial lesions

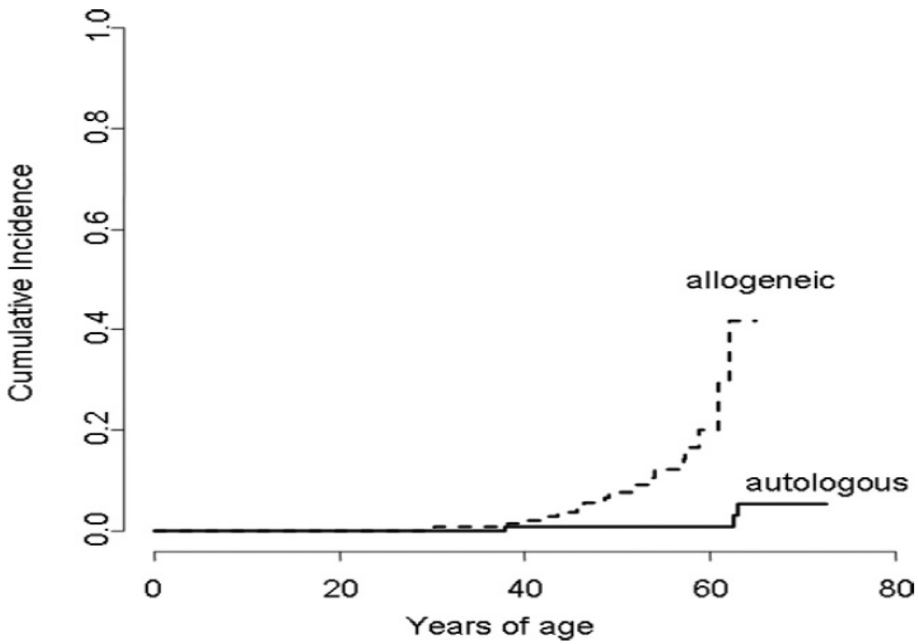


Enhancement of atheros



Arterial disease by HCT type





Blood. Tichelli A, Bucher C, Rovo A, et al. Premature cardiovascular disease after allogeneic hematopoietic stem-cell transplantation. 2007;110:3463–71. © the American Society of Hematology.[3]

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Late cardiovascular events after allogeneic hematopoietic stem cell transplantation: a retrospective multicenter study of the Late Effects Working Party of the European Group for Blood and Marrow Transplantation

Original Article
haematologica | 2008; 93(8) | 1203 |

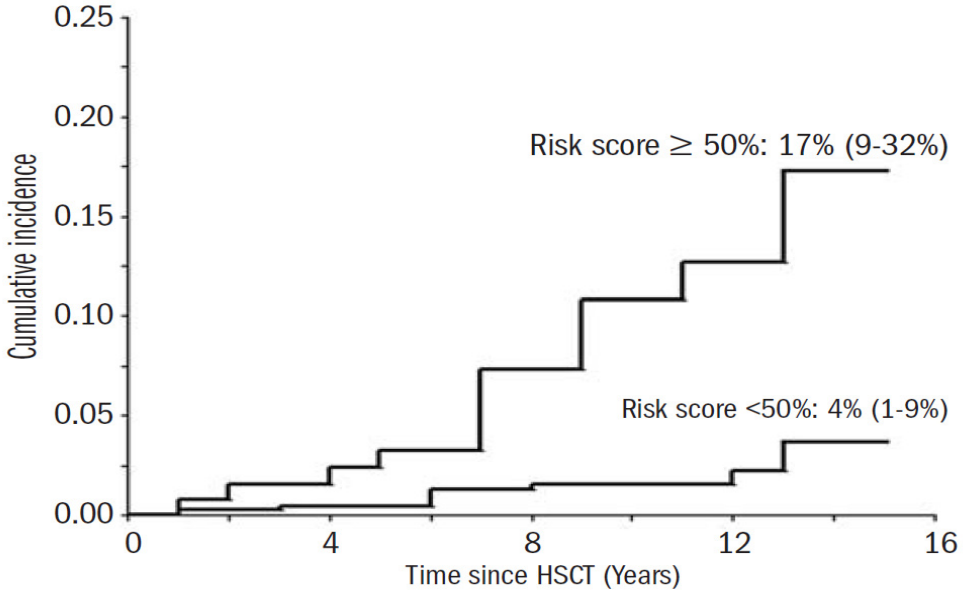

Table 4. Results of multivariate analysis of the risk factors for arterial complications.

Factor	*Relative Risk (OR)*	*95% confidence interval*	*p value*
Age at transplantation			
< 30 years	1	—	0.003
≥30 years	6.43	1.87-22.06	
Global cardiovascular risk score			
< 50%	1	—	<0.001
≥50% (i.e. 3 or more)	9.81	3.75-25.66	

Risk score:

arterial hypertension, dyslipidemia, diabetes, being overweight, smoking, physical inactivity (1 point each)

GVHD, radiation, and age not included!

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Case #2 - Take Home Points

- Patients after HCT have an increased risk of (premature) atherosclerosis and represent a vulnerable population
- Traditional risk scores (Framingham) may not be adequate for this population
- Unique risk factors include chemotherapy and radiation exposure as well as graft versus host disease
- Modifiable risk factors should be managed as optimally as possible

Case #3

67-year-old woman, referred for a cardiology consultation

- Starting a few days ago, exertional dyspnea and significant bilateral lower extremity swelling
- Subsequently orthopnea and chest tightness
- Also fever, mucositis, urinary spasms, diarrhea, nausea, and general malaise

Case #3 – Past Medical History

- Stage IV Hodgkin lymphoma, 2 years ago, initial remission after ABVD chemotherapy, recurrence 6 months ago, treatment with bendamustine and brentuximab with CR, then autologous bone marrow transplant 2 weeks ago after BEAM conditioning (BiCNU (Carmustine), Etoposide, Ara-C (Cytarabine), Melphalan)
- Depression

Case #3 - Medications

- Pantoprazole 40 mg IV BID
- Acyclovir 400 mg PO BID
- Cefepime 2 gr IV BID
- Filgrastim 300 mcg SQ per day
- Fluconazole 400 mg IV per day

Case #3 – Vital Signs

- Height: 160.0 cm
- Weight: 62.70 kg
- BMI: 24.492 KG/M2
- Blood pressure: 110/57 mmHg
- Pulse rate: 115/minute
- Respiratory rate: 20/ minute

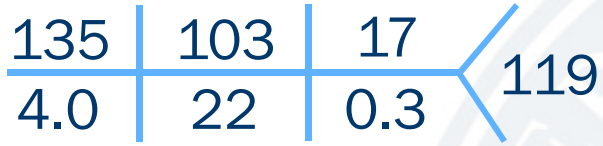
Case #3 – Physical Exam

- General: Patient appears tired.
- Skin: No stasis dermatitis or ulceration.
- Vessels: No carotid bruits. Normal pedal pulses.
- Heart: Normal palpation. Normal first and second heart sound. No murmurs, gallops, or rubs. Normal JVP and pulsation.
- Lungs: Normal respiratory effort and air movement. Clear to auscult.
- Abdomen: Normal-sized liver and spleen. No abdominal masses or tenderness.
- Extremities: No clubbing or cyanosis. Pitting 2+ to 3+ lower extremity edema to the level of the knee.

Case #3 – Laboratory Parameters

CBC

E'lytes



Additional parameters

AST 33, ALP 96, total bilirubin 0.7, albumin 3.0

NT-pro-BNP 7396

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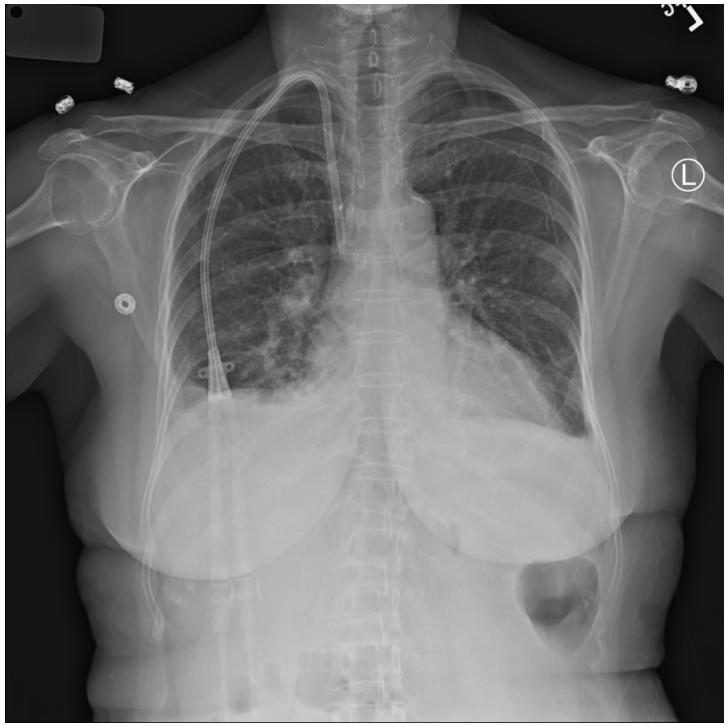
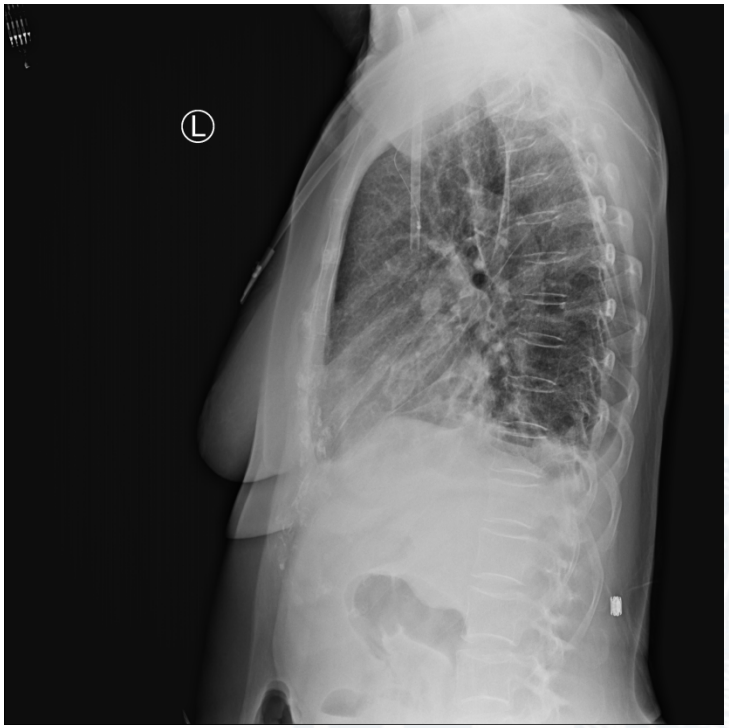
Case #3 - CXR





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Case #3 - Echocardiogram

Final Impressions

1. Normal left ventricular chamber size.
2. Estimated left ventricular ejection fraction; 35 %.
3. Generalized left ventricular hypokinesis. Systolic function of the apical segments is best preserved.
4. Borderline decrease in right ventricular systolic function.
5. Moderate mitral valve regurgitation (2 jets).
6. Bilateral pleural effusion.
7. Compared to the report of 09/04/2014 the following changes have occurred: The left ventricular ejection fraction has decreased. Mitral regurgitation is now moderate and there are bilateral pleural effusions..

Findings

Focused echo exam. LEFT VENTRICLE: Normal left ventricular chamber size. Normal left ventricular wall thickness. Estimated left ventricular ejection fraction; 35 %. Generalized left ventricular hypokinesis. Systolic function of the apical segments is best preserved. Findings consistent with increased left ventricular filling pressure. RIGHT VENTRICLE: Normal right ventricular size. Borderline decrease in right ventricular systolic function. Estimated right ventricular systolic pressure 28 mmHg (systolic blood pressure 128 mmHg). ATRIA: Left atrial enlargement. Normal right atrial size. CARDIAC VALVES: Tricuspid aortic valve. Thickened aortic valve. No aortic valve regurgitation. Thickened mitral valve. Moderate mitral valve regurgitation (2 jets). Normal pulmonary valve. Trivial pulmonary valve regurgitation. Normal tricuspid valve. Trivial tricuspid valve regurgitation. OTHER ECHO FINDINGS: Normal inferior vena cava size with normal inspiratory collapse (>50%). Normal abdominal aorta Doppler flow pattern. No intracardiac mass or thrombus, but the left atrial appendage cannot be visualized adequately with transthoracic echo to exclude thrombus in this location. No pericardial effusion. Bilateral pleural effusion. Echo pictures not adequate for strain imaging.

Case #3 – Baseline Echocardiogram

Final Impressions

1. Global averaged left ventricular longitudinal peak systolic strain is normal at −19 % (normal = more negative than −18%).
2. Normal left ventricular chamber size.
3. Calculated 2−D biplane volumetric left ventricular ejection fraction; 59 %.
4. Left atrial enlargement.
5. Mild tricuspid valve regurgitation.
6. Estimated right ventricular systolic pressure 32 mmHg (systolic blood pressure 122 mmHg).

Findings

LEFT VENTRICLE: Normal left ventricular wall thickness. Calculated left ventricular ejection fraction; 54 %. No regional wall motion abnormalities. Indeterminate left ventricular diastolic function grade. RIGHT VENTRICLE: Normal right ventricular size. Normal right ventricular function. ATRIA: Left atrial volume index 34 cc/m^2. Normal right atrial size. CARDIAC VALVES: Tricuspid aortic valve. Mildly thickened aortic valve. No aortic valve regurgitation. Normal mitral valve. Trivial mitral valve regurgitation. Normal pulmonary valve. Normal pulmonary valve systolic velocity. Trivial pulmonary valve regurgitation. Normal tricuspid valve. OTHER ECHO FINDINGS: Normal inferior vena cava size with normal inspiratory collapse (>50%). Normal ascending aorta dimension. No abdominal aortic aneurysm. Normal abdominal aorta Doppler flow pattern. No shunt at atrial level by color flow imaging. No intracardiac mass or thrombus, but the left atrial appendage cannot be visualized adequately with transthoracic echo to exclude thrombus in this location. No pericardial effusion.

Which HCT Conditioning Drug has the Highest Cardiotoxicity Risk?

A. Carmustine
B. Cytarabine
C. Cyclophosphamide
D. Fludarabine
E. Ifosfamide
F. Melphalan

Cardiotoxicity of Conditioning

Single agent/combination	*Risk factors*		*Type/incidence (%)*	*Increased mortality (%)*	*Number of patients/reference*
	Cardiac dysfunction[a]	*Doxo* $\geqslant 400\,mg/m^2$ [b]			

Two single center series from the 1977-1997 era[1,2] :

<5% cardiovascular complications

0.9-1.8% life-threatening CV event

[1] Bone Marrow Transplant 2001;28:283
[2] J Clin Oncol 1994; 12:998

Morandi P et al. Bone Marrow Transplant 2005;35:323-34

Risk Factors and Prevention

Dosage	Total dose ⩽maximum-tolerated dose as single agent
Schedule of administration	Adopt the least cardiotoxic schedule (eg multifractionated schedule for HD cyclophosphamide)
Concomit… agents	…atment
History c… chest wal…	…luation
History c…	…luation …ne (ie
Older age	…aluation including 2D echo, particularly if there is history of anthracycline exposure
Overweight	Calculate HD chemotherapy dose on ideal body weight
LVEF <50%	Thorough cardiologic monitoring ACE inhibitors

>10 studies - overall balance in favor of:

Baseline resting LVEF is not predictive of severe CV events

Morandi P et al. Bone Marrow Transplant 2005;35:323-34

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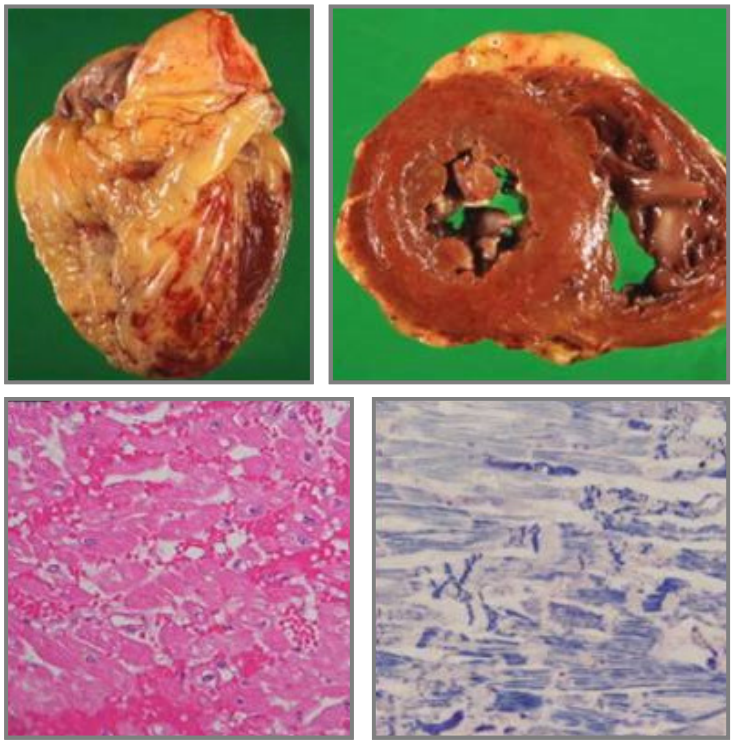
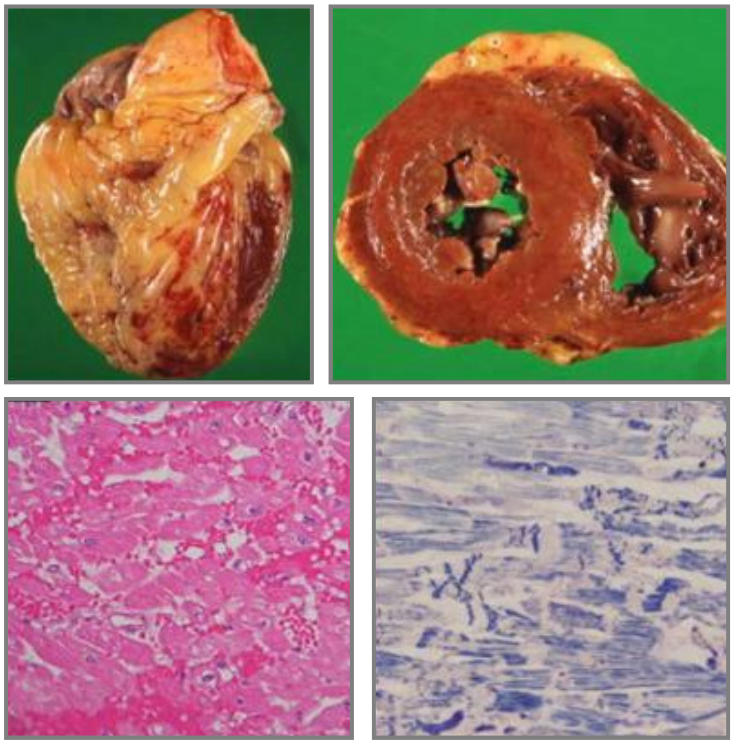
Cyclophosphamide-Induced Heart Disease



- Fulminant acute heart failure in 5-28% and pericardial tamponade in 19% with high dose therapy (180 mg/kg over four days), commonly with cytarabine
- toxic endothelial damage with extravasation of toxic metabolites ⇒ cardiomyocyte dysfunction
- interstitial hemorrhage and edema ⇒ LV wall thickening
- fibrinous pericarditis with spotty pericardial hemorrhage

Gottdiener et al: Arch Intern Med 141:758, 1981; Katayama et al: J Cardiol 54:330, 2009

Cyclophosphamide-Induced Heart Disease



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- LV function with wall thickening 5-15 days after initiation of therapy

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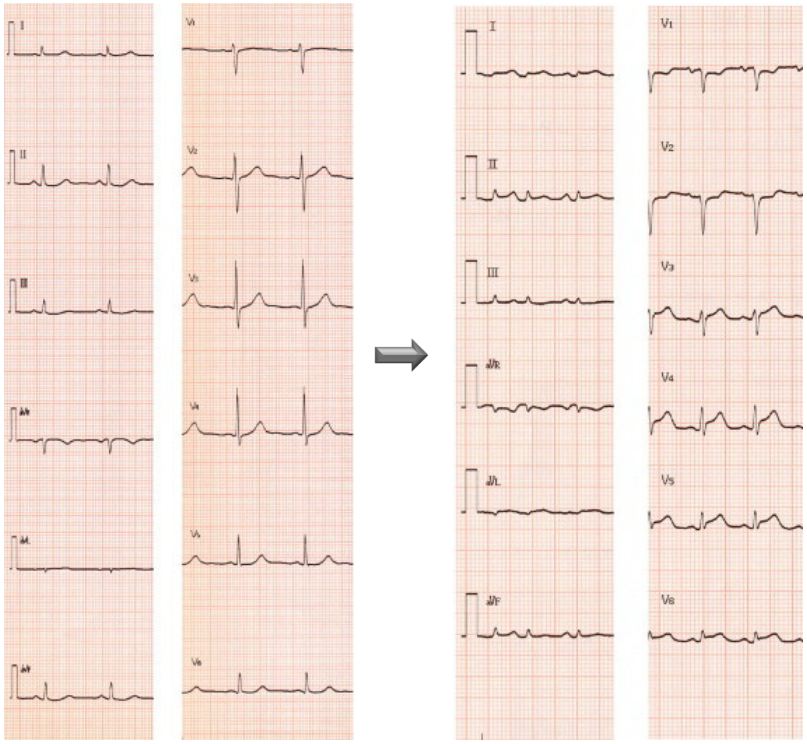
Cyclophosphamide-Induced Heart Disease



- Fulminant acute heart failure in 5-28% and pericardial tamponade in 19% with high dose therapy (180 mg/kg over four days), commonly with cytarabine
- LV function with wall thickening 5-15 days after initiation of therapy
- Ominous sign: declining ECG voltage
- Acute mortality up to 20%
- Long-term prognosis good
- Aggressive support, even use of mechanical support devices to bridge to recovery

Gottdiener et al: Arch Intern Med 141:758, 1981; Katayama et al: J Cardiol 54:330, 2009

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Case #3 - Take Home Points

- Conditioning therapies for HCT have variable acute (and largely reversible) cardiotoxicity risk
- Any variables that influence drug distribution and metabolism are important (e.g. obesity, older age)
- Risk is increased with combination therapies, prior anthracycline exposure or radiation exposure of the heart and possibly with any reduced cardiac function
- No established CV drug prevention strategies

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