Oncology nurses aren’t always tuned in to the early cardiac signs and symptoms that put a patient with cancer at risk for complications. Yet with the American population aging, more individuals are likely to be diagnosed not only with cancer, but heart disease as well. During this session, you’ll boost your assessment and evaluation skills, helping you to become a watchdog for potential and actual cardiac complications.

**Content Area:** Clinical Practice  
**Content Level:** Intermediate

**Coordinator/Speaker:**  
Catherine Sargent, MS, RN, BC, AOCNS  
Oncology Clinical Nurse Specialist/Educator  
Bryn Mawr Hospital  
Bryn Mawr, PA  
sargentc@mlhs.org

**Full Disclosure:**  
Nothing to Disclose

**Speaker:**  
Brenda Shelton, RN, MS, CCRN, AOCN®  
Clinical Nurse Specialist  
Johns Hopkins Hospital  
Baltimore, MD  
sheltbr@jhmi.edu

**Full Disclosure:**  
Intends to discuss unapproved/investigational use of a commercial product/device during this educational activity

**Objectives:**  
At the end of this session, participants will be able to:  
1. Describe focused cardiac assessment of patients with cardiac complications.  
2. Evaluatecardiac complications in relation to patient treatment and prognosis.

**Content Outline:**  
I. Cardiac overview  
   A. Review of cardiac anatomy and physiology  
   B. Review of the cardiac cycle  
II. Alterations in cardiac function as it relates to cancer and its treatment  
   A. Changes in conduction pathways  
   B. Vasculature changes

1. Hypo/hypertension  
2. Capillary leak  
3. Coronary arteries (MI)  
4. Cardiomyopathy/cardiac failure

III. Cancer-related cardiac complications  
   A. Chemotherapy agents  
   B. Monoclonal antibodies  
   C. Targeted therapies  
   D. Radiation

IV. Diagnosis  
   A. Signs and symptoms  
   B. Laboratory studies  
   C. Diagnostic studies

V. Treatment  
   A. Medical management  
   B. Best supportive care

VI. Nursing considerations

**Bibliography:**


van Dalen, E.C., Caron, H.N., Dickinson, H.O., & Kremer, L.C.M.


And the Beat Goes On: Addressing Cardiotoxicity in the Patient with Cancer

Speakers:
Catherine Sargent MS, RN, BC, AOCNS
Brenda Shelton MS, RN, CCN, AOCN

Introduction

• Potential short or long term complication
• Can range from asymptomatic subclinical abnormalities to life-threatening events
• Identification of cardiovascular complications can be difficult
• Anthracyclines, monoclonal antibodies, tyrosine kinase inhibitors, as well as radiation therapy to the mediastinum

Introduction

• Is a concern for both oncology and cardiology
• Three main cardiovascular changes due to cancer treatment
  – Vascular
  – Structural
  – Conduction

Framework for Considering Cardiac Complications in Patients with Cancer

Cardiovascular Disease Affects Cancer Treatment Plan

<table>
<thead>
<tr>
<th>Affects on disease trajectory</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affects treatment options</td>
<td>Patients with pre-existing CAD may not be a good candidate for anesthesia and surgery.</td>
</tr>
<tr>
<td>Alter drug selection</td>
<td>Women with CAD and breast cancer may be higher risk for cardiotoxicities and adjuvant regimen may be altered to omit anthracyclines.</td>
</tr>
<tr>
<td>Influences medication doses</td>
<td>An individual with HIV-related KS may not be able to receive doxorubicin as would normally be given.</td>
</tr>
<tr>
<td>Contributes to toxicity profile</td>
<td>Pre-existing hypertension may be exacerbated and affect delivery of planned bevacizumab</td>
</tr>
<tr>
<td>Alters assessment or supportive care</td>
<td>Patients with low ejection fraction may require CVP monitoring, careful intake and output measurement, or more frequent echocardiograms</td>
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</tbody>
</table>
**Cardiovascular Disease in Patients with Cancer**

- Estimated incidence
  - Increasing with better supportive care
  - Increasing with greater targeted/oral cancer treatments
- High risk populations
  - Elderly
  - Diabetes
  - Hormones/corticosteroids
  - Cancer survivors
- Additive cancer or treatment-related risk factors
  - HIV disease
  - Chest masses
  - GI malignancies
  - Cardiotoxicities
  - Radiation therapy field
- Implications for nursing practice
  - Patient and family history
  - Baseline patient assessments

**Who is at risk for Cardiotoxicity?**

- Type of drug
- Rate of administration
- Delivery schedule
- Combination therapy
- Radiation to chest/abdomen
- Female sex
- African American
- Obesity
- Trisomy 21
- Pre-existing heart disease and/or hypertension
- Electrolyte abnormalities
- Infection
- Sepsis
- Smoking
- Renal dysfunction
- Pregnancy
- Drug hypersensitivity

**Anthracyclines**

- Widely used class of chemotherapeutic agents
  - Includes Doxorubicin, Daunorubicin, Idarubicin, Epirubicin, Mitoxantrone
- Cardiotoxicity can develop:
  - Acute
    - Occurs within hours or days after administration
    - Disturbance in conduction or as an arrhythmia
  - Sub acute
    - Occurs within one year following treatment
    - Have EKG changes; LV dysfunction
  - Chronic manner
    - Occurs after one year after treatment
    - LV dysfunction
    - Heart failure

**Anthracyclines (cont.)**

- The best predictor of cardiotoxicity is total cumulative doses
- Lifetime cumulative for Doxorubicin $550 \text{mg}/m^2$
  - 3% incidence of HF at cumulative dose of $400 \text{mg}/m^2$
  - 7% incidence of HF at cumulative dose of $550 \text{mg}/m^2$
  - 18% incidence of HF at cumulative dose of $700 \text{mg}/m^2$

**Pathophysiology of Anthracyclines induced cardiotoxicity (cont.)**

- Generation of free radicals
- Formation of toxic metabolites
- Inhibits nucleic acid and protein synthesis
- Releases vasoactive amines
- Decreased expression of specific genes
- Impairs mitochondrial membrane binding
- Induces apoptosis
- Disturbs intracellular calcium homeostasis
- Increases certain immune functions

**Targeted Therapies**

- Initially thought to be less toxic than traditional chemotherapy
- Associated with increase risk of several cardiac effects due to targeted cells also found in cardiomyocytes
  - HER2
  - VEGFR
  - PDGFR

Sources: Jones & Barn, 2004; Leit et al., 2007; Sorensen et al., 2008; Viel & Ferrareto, 2008; Yass et al., 2008; Barry et al., 2007; Hampton, 2010; Meacham et al., 2010; Barry et al., 2007; Hallqvist-Vaile & Sanchez-Hernamonte, 2008; Wochner-Loerzel & Hassey-Dow, 2003; Cheng & Force, 2008; Force et al., 2008; Force & Kernska, 2008; Lenihan Koway, 2013.
Overview of Cardiac Diagnostic Tests

ECG (12 lead, stress) | Pictorial view of conduction pathways (stress) | Detect ischemia, injury, old infarction, electrolyte disorders, pericardial effusion
Cardiac enzymes (CPK, Troponin) | Levels of enzymes leaking from myocytes at time of injury | Detection of current acute coronary syndrome.
Echocardiogram | Ultrasound of wall thickness, internal diameter, wall motion, and fluid in pericardial space | Detects valve, global wall motion, and pericardial fluid abnormalities. Can calculate approximate EF.
MUGA scan | Accurate reflection of circulation of nuclear substance that detects coronary blood flow with/without exercise. Wall motion abnormalities w/o uptake indicates old infarction. | Detection of significant compromise of coronary blood flow. Helpful to monitor progression of CAD, or recovery from MI.
Brain natriuretic peptide (BNP) serum level | Substance produced by a ventricle in failure. Normal serum < 100 mg/dl, clinically significant if > 300 mg/dl. | Early screening for heart failure, or monitoring response to heart failure treatment.

Conduction Disturbances

- Fluid and Electrolyte disturbances
  - Platiniol, cetuximab-induced hypomagnesemia
  - Antibiotic-induced hypokalemia
  - Dehydration / fluid overload enhances atrial automaticity

- Oxygen free radicals
  - Ara-C
  - Fluoropyrimidines (e.g. 5FU)
  - Topoisomerase inhibitors
  - Tyrosine/multi kinase inhibitors
  - Cytokines

- Direct irritation/ damage to conduction pathways
  - Arsenic trioxide
  - Radiation acute and chronic effects
  - Tumor compression of atria
  - Taxanes
  - Esophagectomy, pneumonectomy

Risk Factors for QT Prolongation

- Amphetamines
- Anesthetics- e.g. furanes, propofol
- Anti-rhythmic medications- e.g. amiodarone, procarnamid 
- Antifungal agents (azolees)
- Anti-depressants
- Anti-histamines
- Arsenic trioxide
- Atenolole
- Barium
- Bradycardia
- Bulky chemotherapies- e.g. Haloparidol, Droperidol
- Caffeine
- Cimetidine
- Decongestants- ephedrine
- Dofetilide
- Dapsanamb
- Dyspyramid
- Electrolyte imbalances- K+, Mg++, calcium
- Female
- Fluoroquinolones
- Histamine receptor antagonists (e.g. ranidine) and SHT3 antagonists
- Metilopromide and related mobility stimulants
- Macrolide antibiotics
- Methadone
- Ondansetron and related serotonin antagonists
- Pentamidine
- Phenoheazines
- Protri-pump inhibitors
- Selective estrogen receptor modulators
- Sotalol
- Terfenadine
- Valproic acid

Diagnosis of Conduction Disturbances

- 12 lead ECG
  - Rhythm assessment
  - QTc interval (predicts arrhythmogenic potential)
- Stress ECG
- 12, 24 hour Holter
- Electrophysiologic testing or evoked potentials

QT Prolongation Syndrome

- Prolonged time for myocardial recovery
- Corrected for heart rate= QTc
- Congenital or acquired
- Detection by 12 lead ECG
  - Bradycardia
  - Prolonged QT interval
- Highest risk- sudden death from ventricular arrhythmias
Management of Conduction Disturbances

• Acute
  – Pharmacologic
    • Correct electrolytes (K+ >4.0, Mg++ >2.0)
    • Correct fluid and acid-base imbalances
    • Correct hypoxemia
    • Adenosine
    • Calcium channel blockers
    • Beta blockers
    • Amiodarone
  – Electrical
    • Emergent cardioversion
    • Temporary transcutaneous pacing

• Chronic
  – Pharmacologic
    • Digoxin
    • Calcium channel blockers
    • Amiodarone
  – Electrical
    • Permanent pacers
    • AICD
  – Interventional
    • Biphasic cardioversion
    • Ablation therapy

Acute Coronary Syndromes (ACS)

Sudden Death

Unstable Angina

Coronary Arterial Thrombosis

Non-Q-Wave MI

Q-Wave MI

Immediate assessment (<10 minutes)
- Measure vital signs (automatic/standard BP cuff)
- Measure oxygen saturation
- Obtain IV access
- Obtain 12-lead ECG (physician reviews)
- Perform brief, targeted history and physical exam
- Focus on eligibility for thrombolytic therapy
- Obtain initial serum cardiac marker levels
- Evaluate initial electrolyte and coagulation studies
- Baggage, review portable chest x-ray (<10 minutes)

Immediate general treatment
- Oxygen at 6 L/min
- Aspirin 162 to 325 mg
- Nitroglycerin 0.4 to 0.8 mg
- Morphine IV (if pain not relieved with nitroglycerin)
- High risk patients: “MONA” greets all patients (Morphine, Oxygen, Nitroglycerin, Aspirin)

EMS personnel can perform immediate assessment and treatment “MONA”, including initial 12-lead ECG and review for thrombolytic therapy indications and contraindications.

Ischemic Chest Pain Algorithm

Cardiac Isoenzymes

• CPK (Creatine phosphokinase)
  – >175 mcg/mL abnormal
  – Marks muscle cell death
• CPK - MB (Myocardial bands)
  – Positive at 3-4%
  – Specific for cardiac muscle

• Cardiac Troponin
  – Sensitive for detecting an MI earlier than MB’s (<4 hours)
  – A protein unique to the myocardium
  – Troponin complex consists of 3 sub-units
    • Troponin I
    • Troponin T & C
    • >0.50 ng/mL abnormal

Source: Hazinski, Sampson, Schexnayder, 2010

Atrial Dysrhythmias

• Etiologies
  – Fluid imbalances
  – Lung disease
  – Electrolytes
• Pathophysiology
  – Loss of 1/3 cardiac output
  – Common rapid heart rate
  – Chronic alteration common
  – High risk pulmonary embolism or stroke
• Clinical findings
  – Initially asymptomatic
  – Dyspnea/desaturation
  – Pulse deficit
• Management
  – Electrical
  – Medical
  – Anticoagulation

Coronary Artery Disease

• Risk factors
  – Older age
  – Treatment factors
    • Chest irradiation including the heart
    • Heavily treated with alkylating agents
    • Long-term corticosteroids
    • Euthyroid regimen for testicular cancer
    • 5-FU drugs
    • Bevacizumab (Avastin™)
    • Cetuximab (Erbitux™)
  – Link between cancers and CV disease/MI – pancreatic cancer, chest lymphoma, progranulocytic leukemia

• Acute onset CAD that is not “true CAD”, but instead a temporary physiologic alteration of coronary vessels.
  – Tumor compression
  – Immunoglobulins
  – Tumor necrosis
  • Onset as early as two years after exposure
  • Peak incidence ten years after exposure

Source: Hazinski, Sampson, Schexnayder, 2010

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Management of Acute Coronary Syndromes (Acute MI, Unstable angina)

- Rest and recline
- Remember Nurse MONA greets them
- Cardiac monitor and 12 lead ECG, 18 leads if changes in II, III, or AVF, ST segment monitoring
- IV access and blood draw for electrolytes, CK enzymes, troponin I, Beta natriuretic peptide (BNP)
  - Limit fluids if left heart involved
  - Avoid volume depletion if right heart involved
- Consider beta blockade with ischemia on ECG
- Consider interventional cardiology interventions

Emergent Medications: MONA + B

- **Morphine**
  - Reduced sympathetic stimulation
  - Reduced preload (volume returning to heart)
  - Reduces pain
- **Oxygen**
- **Nitrates**
  - Improved coronary perfusion
  - Reduces preload
- **Aspirin**
  - Immediate anti-platelet action
  - Easily reversed with transfusion
  - One adult aspirin (325 mg) chewed

- **Beta Blockers**
  - Reduces sympathetic stimulation
  - Decreases oxygen consumption
  - Minimizes infarct size
  - Metoprolol 5 mg IV.PK three 5-15 minutes apart
  - Evaluate heart rate, blood pressure, breath sounds

Source: Hazinski, Sampson, Schexnayder, 2010

Management of CAD Risk Factors

- **Preventive measures**
  - Cardiac shielding, IMRT
  - Screening chemotherapy candidates for risk factors
  - Monitoring for hyperlipidemia
  - Address hypercoagulable conditions

- **Treatment**
  - Anticoagulation
  - Nitrates
  - Beta blockers
  - ACE inhibitors
  - Interventional cardiology

Source: Yahalom & Portlock, 2008

Hypotension/Hypertension

- Defines as a systolic blood pressure of ≥ 140 mm Hg or a diastolic blood pressure of ≥ 90 mg Hg

- Hypertension is a common class effect from angiogenesis inhibitors and VEGF inhibitors

Source: Curgliano et al, 2010; Nazer, Humphreys, & Mosleh, 2011; ONS Chemotherapy & Biotherapy Guidelines, 2014

Hypotension/Hypertension (cont.)

- Rate if HTN depends upon which agent was used

Risk Factors for Hypotension/Hypertension

- Pre-existing HTN or cardiovascular disease
- Treatment with:
  - Bevacizumab
  - Sorafenib
  - Sunitinib
  - Pazopanib
  - Vandetanib
- Renal insufficiency
- Hypothyroidism
- Cushing syndrome
- Increased intracranial pressure
- Hypomagnesaeimia
Case Study

- J. P. is a 62 year old male patient recently diagnosed with stage 3 renal cell carcinoma; S/P nephrectomy 5 weeks ago
- PMH: arthritis and hypertension
- On an ACE Inhibitor and a beta blocker
- Vital signs: HR=96, RR= 20, BP= 174/104

Case Study (cont.)

- Concerned over patient’s hypertension
- What would be the best treatment option(s) for this patient?
  - Chemotherapy
  - Biotherapy
  - Monoclonal Antibodies
  - Targeted Therapy

Cardiomyopathy

- Defined as:
  - Inadequate contractile force to eject the required amount of blood for perfusion of the body
- Classified as primary or secondary based on the primary etiology and has 3 types:
  - Acute
  - Chronic early
  - Chronic late

Case Study

- D. B. is a 75 year old female with diagnosed with CML in 2012
- Initially placed on Imatinib, but relapsed in spring 2013
- Placed on Nilotinib but continued to progress
- Received Busulfan and Cyclophosphamide (BU-CY) for transplant

Case Study (cont.)

- It is now Day 8 post transplant
  - Vital signs: T= 101.8, HR = 138, RR=26, BP=102/58
  - Pt states she feels like her heart is racing
  - EKG performed showing tachycardia and low QRS voltage
  - Assessment
    - Cardiac: murmur and split heart sounds presents, lower extremity edema
    - Respiratory: dyspnea, crackles
    - Electrolytes: Potassium = 2.9

Radiation-Induced Cardiotoxicity

- Radiation to any vascular location, places the patient at increased risk for early atherosclerosis
- Mediastinal irradiation is a major risk
- Causes scar tissue to build up in the heart
- Pericardial disease usually appears within 6 months to one year

Curgiano, et al. 2010; Heart Failure Society of America, 2010; ONS Chemotherapy & Biotherapy Guidelines, 2014
Radiation-Induced Cardiotoxicity (cont.)

- Related cardiac injuries
  - Acute pericarditis
  - Delayed pericarditis
  - Pancarditis
  - Myopathy (in absence of pericardial disease)
  - Coronary Artery Disease
  - Function valve injury
  - Conduct defects

Radiation-Induced Cardiotoxicity (cont.)

- Total body radiation linked to a 5.5 fold increase
- Irradiation to the chest and abdomen have a 2.2 fold increase

Perez & Brady, 2010