

NCCN 10th Annual Congress:

Hematologic Malignancies™

Survivorship Issues: Late Effects of Curative Therapy in Lymphoma Survivors

Glen J. Peterson, RN, DNP, ACNP

University of Colorado Cancer Center



NCCN.org

Learning Objectives

- Discuss the variety of post therapy survivorship issues in lymphoma patients
- Describe screening, assessment and follow-up guidelines in lymphoma survivors
- Identify preventative and health maintenance strategies in lymphoma survivors

Survivorship Definition

- Any individual who is alive after a diagnosis of cancer
- Family members, friends, and caregivers are also impacted by the survivorship experience

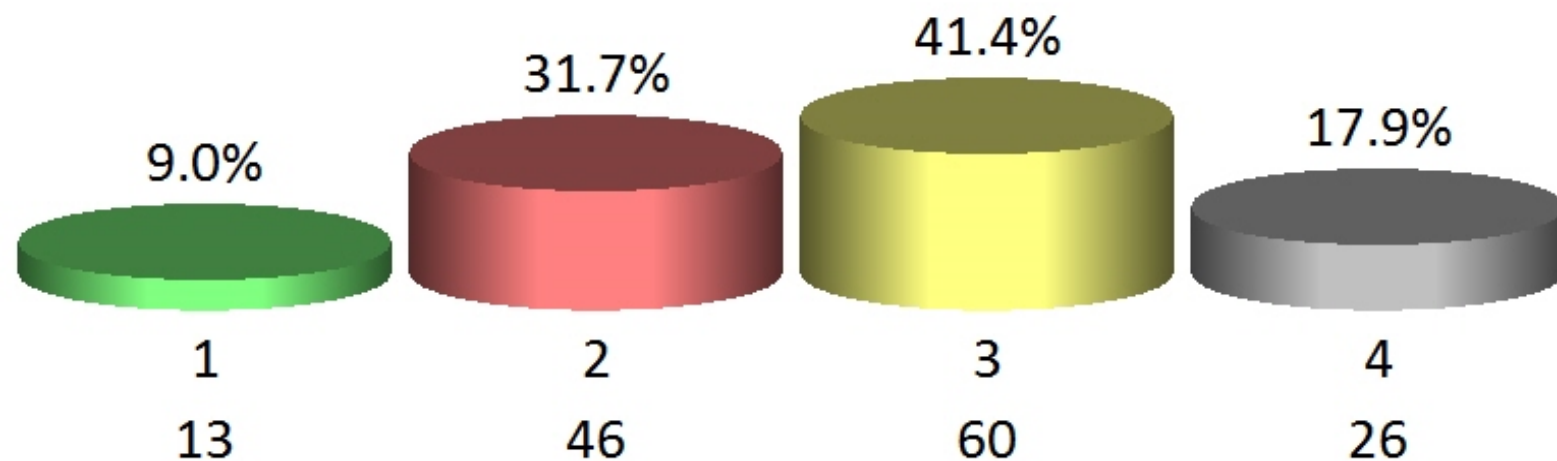
1. National Cancer Institute's Office of Cancer Survivorship

ARS Question



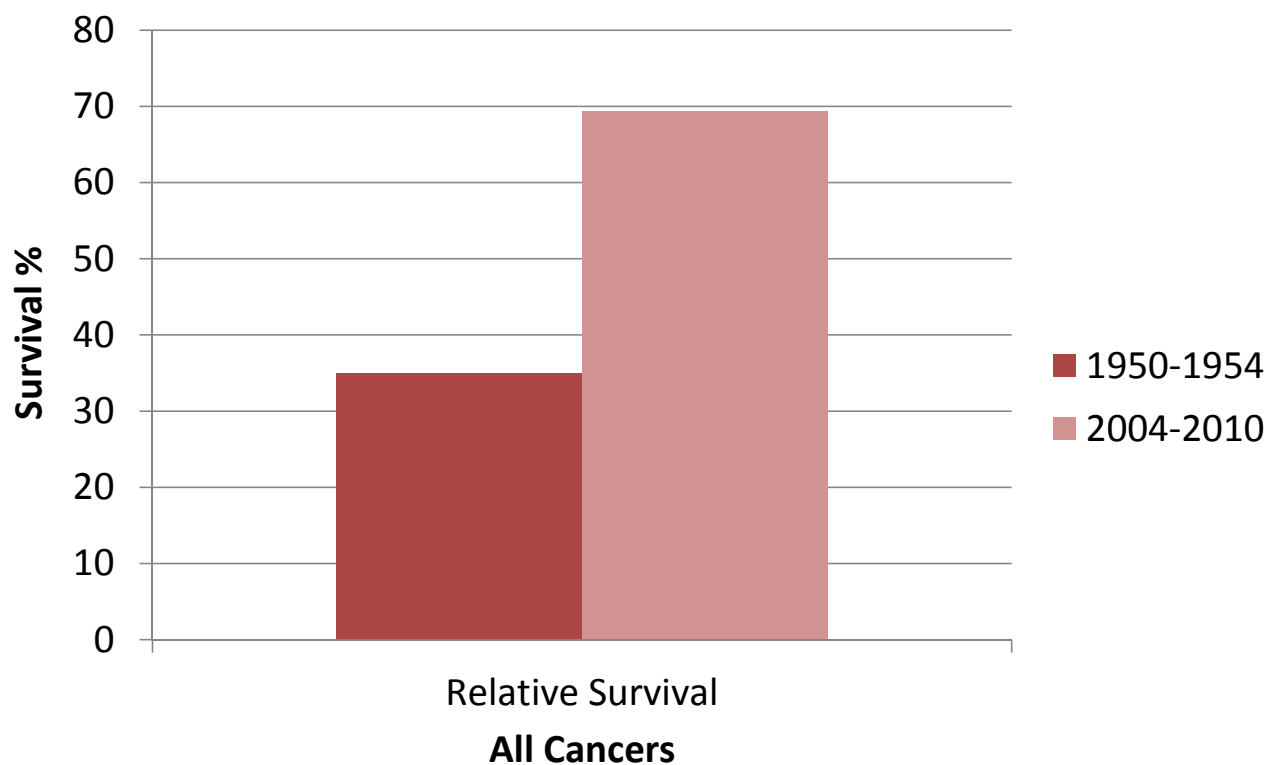
What percentage of cancer survivors experience late adverse affects of curative therapy?

1. 30%
2. 50%
3. 80%
4. 100%



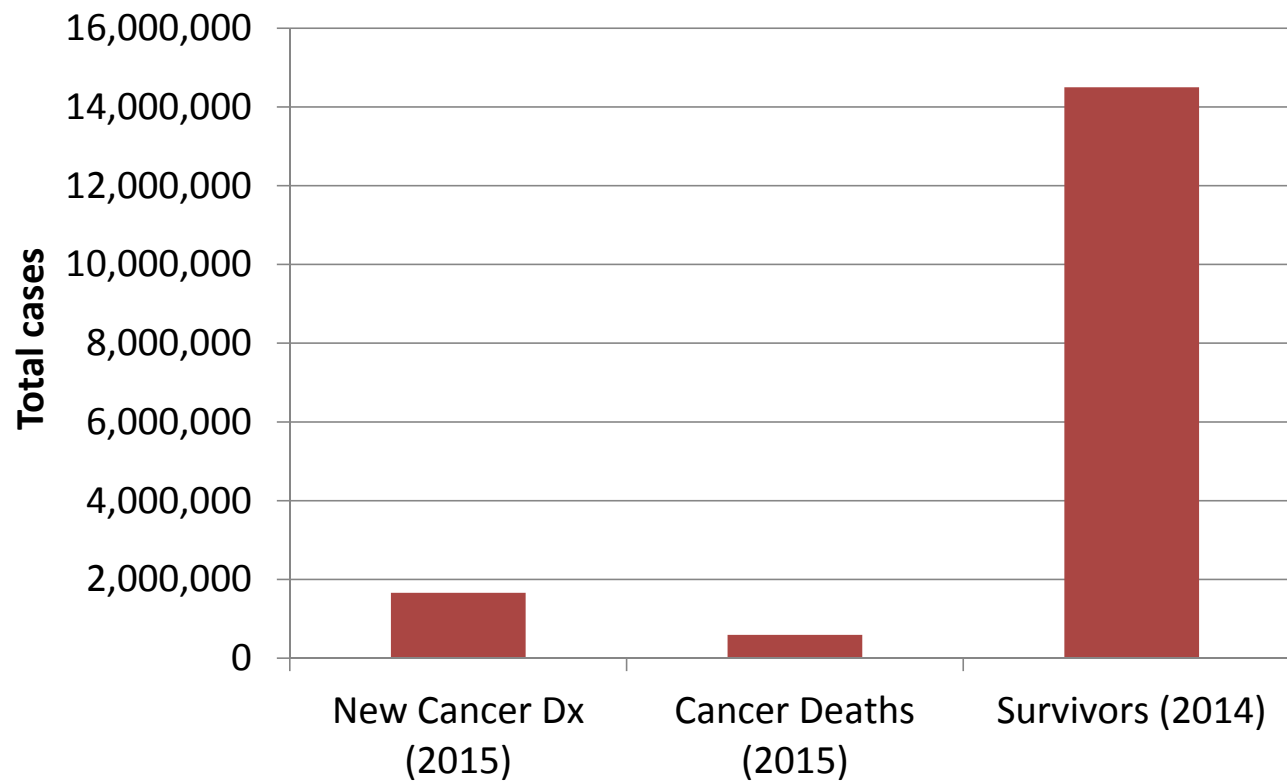
Total: 145

5 year Relative Survival-All Cancers



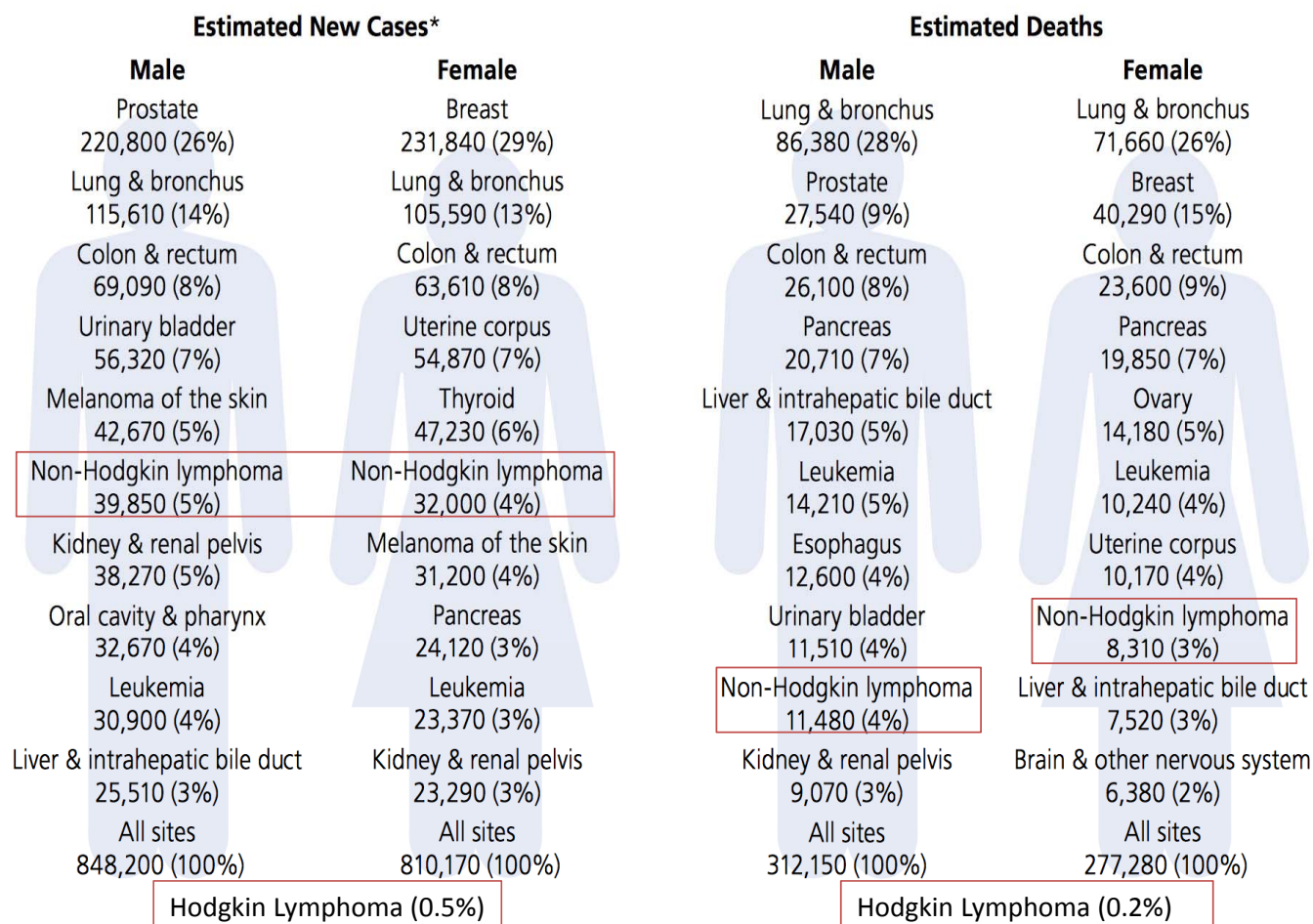
1. SEER Cancer Statistics Review, 1975-2011. National Cancer Institute; 2014.

Cancer Survivors



1. Cancer Facts and Figures. American Cancer Society 2015.

Leading Sites of New Cancer Cases and Deaths – 2015 Estimates

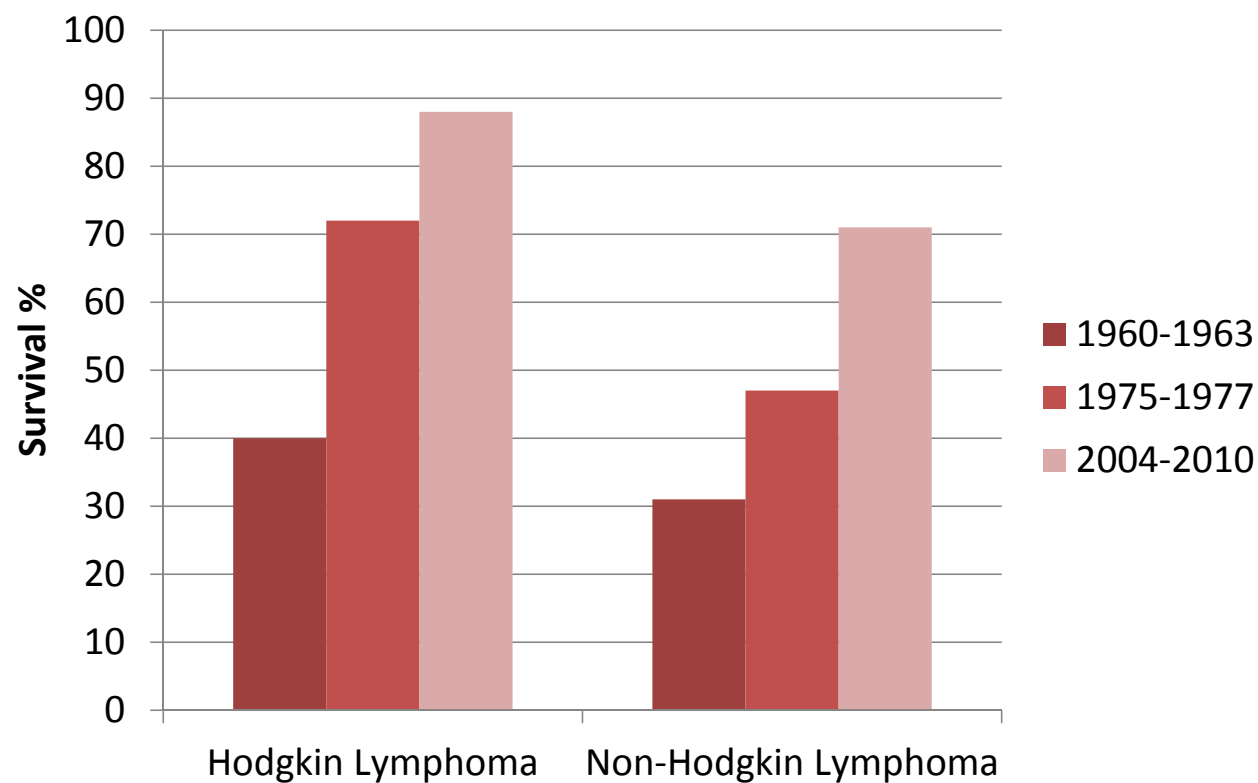


*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

SEER, 2005-2011

©2015, American Cancer Society, Inc., Surveillance Research

5-year Relative Survival-Lymphoma



1. SEER Cancer Statistics Review, 1975-2011. National Cancer Institute; 2014.

Lymphoma Treatment

Cyclophosphamide	Vinorelbine
Doxorubicin	Melphalan
Vincristine	Carmustine
Vinblastine	Thiotepa
Rituximab/other moABs	Busulfan
Prednisone/Dexamethasone	Dacarb/procarbazine
Etoposide	Mechlorethamine
Methotrexate	Brentuximab
Carbo/cis/oxaliplatin	Pralatrexate
Ifosfamide	Romidepsin
Bendamustine	Vorinostat
Fludarabine	Idelalisib
Pentostatin	Ibrutinib
Cytarabine	Radiation
Gemcitabine	Surgery

Lymphoma Long Term and Late Effects

Physical Concerns

- Consequence of Chemotherapy, Steroids and Radiation
- May affect any body system
 - General (weakness, fatigue, malaise)
 - Cardiovascular (CHF, myo/pericarditis, valv ds)
 - Pulmonary (pneumonitis/fibrosis)
 - Hepatorenal (long term liver/kidney dysfunction)
 - Musculoskeletal (pain, myopathy, osteopenia/porosis)
 - Endocrine (adrenal/thyroid/vit D, diabetes, hypogon/fert)
 - Gastrointestinal (malabsorption, motility, stricture)
 - Hematologic (2°MDS/leuk, immunosuppression)
 - Neurological (cognitive/memory def., ototox, neuropathy)
 - Ophthalmologic (cataract, dry eye)
 - Dental (periodontal disease)

1. Hewitt, Greenfield, Stovall (2006). From Cancer Patient to Cancer Survivor: Lost in Transition.

Lymphoma Long Term and Late Effects

Psychological, Social and Spiritual Concerns

- Anxiety and depression
- Fear and uncertainty
- Body image/self esteem
- Sexuality, intimacy
- Parenting, marriage
- Employment and financial
- Social support
- Spiritual/religious
- *Positive effects*

1. Hewitt, Greenfield, Stovall (2006). From Cancer Patient to Cancer Survivor: Lost in Transition.

Long Term and Late Effects

- Extreme variability
- Therapy related
 - Type and length of treatment
 - Age
 - Gender
 - Comorbidities
- Education
- Follow-up plan (screen, assess, treatment)

1. Leukemia and Lymphoma Society. Long-Term and Late Effects of Treatment in Adults Facts. No. 22. www.LLS.org.

Quality of Life and Survivorship



1. Grant M, Economou D. (2008) The Evolving Paradigm of Adult Cancer Survivor Care. *Oncology (Nurse Edition)*, 22(4):13-28.

Long Term and Late Effects

Management Strategy

- Follow-up Assessment
 - Psychological, physical, social, spiritual
- Prevention and Surveillance
 - Recurrence
 - New cancer
 - Late/long term effects
- Intervention
- Coordination of care

1. Hewitt, Greenfield, Stovall (2006). From Cancer Patient to Cancer Survivor: Lost in Transition.

Lymphoma

Long Term and Late Effects

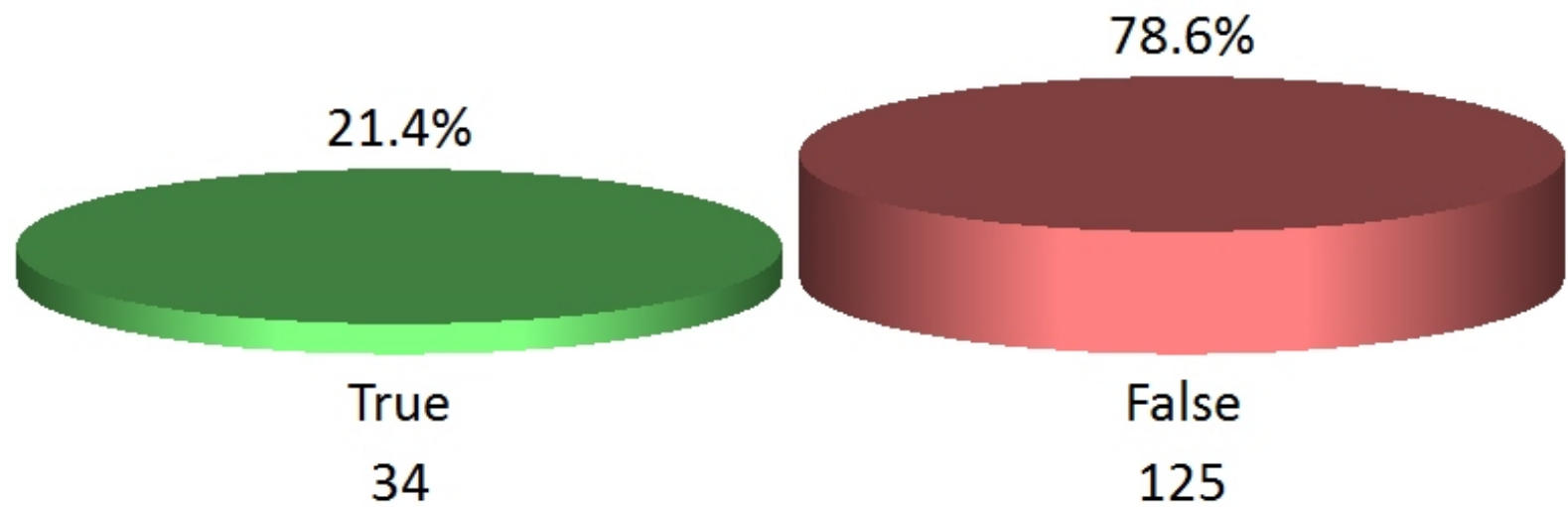
- Cardiotoxicity
- Pulmonary toxicity
- Endocrine dysfunction
- Anxiety/depression
- Cognitive dysfunction
- Fatigue
- Pain
- Sleep disorders
- Infection
- Sexual function/fertility
- Relapse/Secondary cancers
- Preventative health and maintenance

ARS Question



True or False? All patients who receive an anthracycline containing chemotherapy regimen are considered to have heart failure.

1. True
2. False



Total: 159

Cardiotoxicity

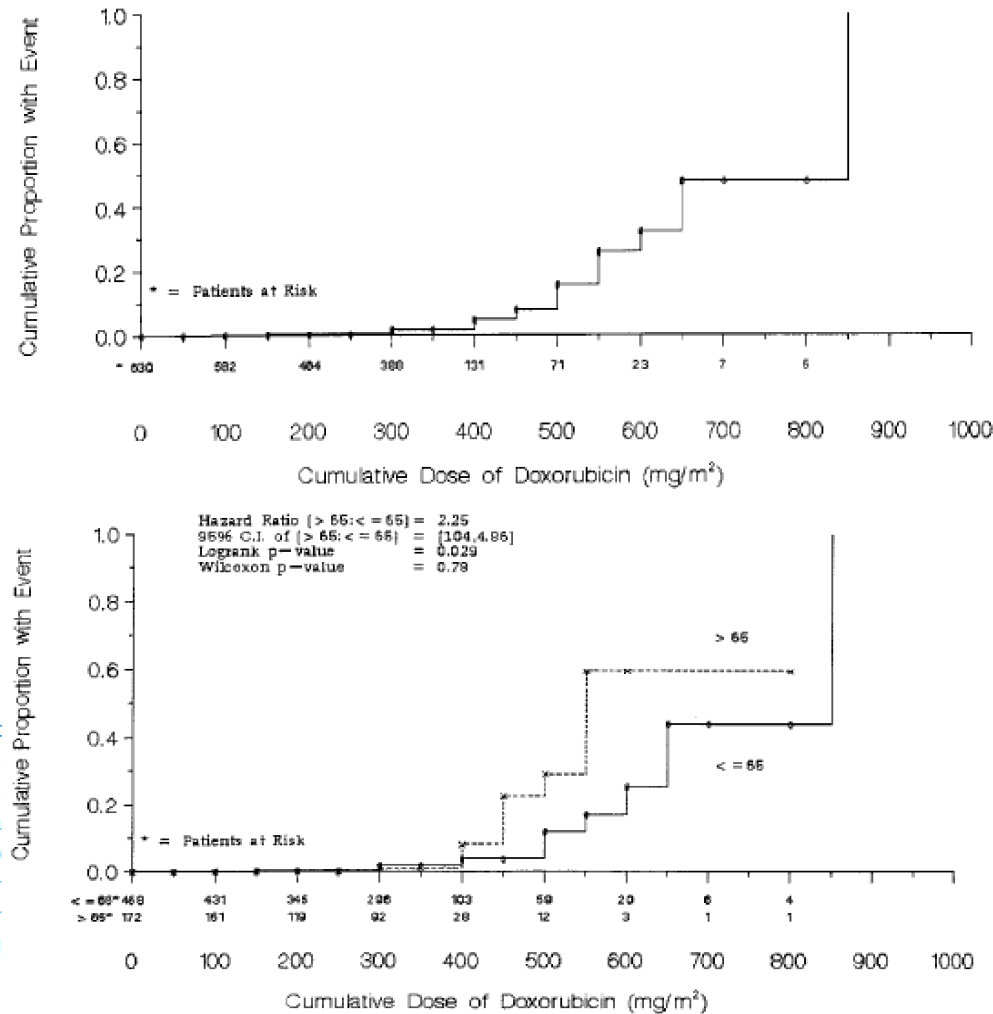
- ***Anthracyclines*** (doxo, dauno, ida)
- Antimetabolites (Flud, Pento, MTX, Cytara)
- Vincas (vinc, vinbl, vinorel)
- Alkylators (CY, Ifos, Cisplat, Bu)
- Antibiotics (Bleomycin)
- MoAbs (Ritux, Ofa, alemtuz)
- Nitrogen mustard (carmustine)
- HDACi (vorinostat, romidepsin)
- Ibrutinib
- Radiation (IFRT, TBI)
- Glucocorticoids (dex, pred)

Anthracycline-induced Cardiotoxicity

- May occur early or late
- Dose limiting toxicity
- Myocardial necrosis and dilated cardiomyopathy
- Subclinical decline in heart function (sys/dias)
- May progress to symptomatic heart failure and death
- Association with *cumulative dose*, chest radiation, pre-existing heart disease, young/old

1. Zhang, et al. (2012). Identification of the molecular basis of doxorubicin-induced cardiotoxicity. *Nature Medicine*. 18, 1639–1642
2. Hershman, et al. (2008). Doxorubicin, cardiac risk factors, and cardiotoxicity in elderly patients with DLBCL. *Journal of Clinical Oncology*. Vol 26(19); 3159-3165.
3. Carver, et al. (2007). ASCO clinical evidence review on the ongoing care of adult cancer survivors: cardiac and pulmonary late effects. *Journal of Clinical Oncology*. Vol 25(25); 3991-4008.

Cumulative Dose



1. Swain, Whaley & Ewer (2003). CHF in patients treated with doxorubicin. Cancer. American Cancer Society. 97(11):2869-79.

Anthracycline-induced Cardiotoxicity Evaluation

- H&P
 - Signs of heart failure
- Evaluate risk factors
 - Cardiac risk factors
 - Social history
 - Family history
 - Medications
 - Oncology history

Anthracycline-induced Cardiotoxicity

Prevention

- DO NOT exceed lifetime dose
 - Doxo(550mg/m²), ida(150mg/m²), dauno(550mg/m²)
- Caution in elderly, XRT, cardiac risk factors
- Infusional vs bolus
- Structural modification/Liposomal formulations
- Dexrazoxane
- Beta blockers/ACEi/ARB
- Pretreatment ECHO and surveillance

1. Zhang, et al. (2012). Identification of the molecular basis of doxorubicin-induced cardiotoxicity. *Nature Medicine*. 18, 1639–1642
2. Hershman, et al. (2008). Doxorubicin, cardiac risk factors, and cardiotoxicity in elderly patients with DLBCL. *Journal of Clinical Oncology*. Vol 26(19); 3159-3165.
3. Carver, et al. (2007). ASCO clinical evidence review on the ongoing care of adult cancer survivors: cardiac and pulmonary late effects. *Journal of Clinical Oncology*. Vol 25(25); 3991-4008.

Anthracycline-induced Cardiotoxicity

Management

- Early detection is key
- Based on risk factors and symptoms
- Echocardiogram
 - w/i one year if ≥ 1 risk factor
 - immediately if symptomatic
- ECG, troponin, BNP
- Treat based on heart failure stage
- All patients previously treated with anthracyclines are considered Stage A

1. Yancy, et al. (2013). ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 62(16).

Anthracycline-induced Heart Failure Management

- Address modifiable risk factors (PCP)
- Consider Cardiology referral

Stage A

- asymptomatic
- no structural ds.
- at risk for HF

- Address modifiable risk factors (PCP)
- Cardiology referral

Stage B

- asymptomatic
- structural ds.
- previous MI

Stage C

- heart failure S&S
- structural ds.

- Cardiology referral immediately
- BB, ACEi/ARB, diuretic

Stage D

- heart failure S&S at rest despite medical therapy

- Cardiology referral immediately
- BB, ACEi/ARB, diuretic

1. Yancy, etal. (2013). ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 62(16).

Radiation-induced Cardiotoxicity

- Hodgkin Lymphoma and mediastinal XRT
- Endothelial damage, vascular narrowing, inflam. injury, myocardial ischemia, infarct
- Effects all heart structures
- Pericardial disease, myocardial fibrosis, valvular ds, heart failure, dysrhythmia

1. Hooning, et al. (2007). Long term risk of cardiovascular disease in 10 year survivors of breast cancer. JNCI J Natl Cancer Inst. 99(5): 365-375.

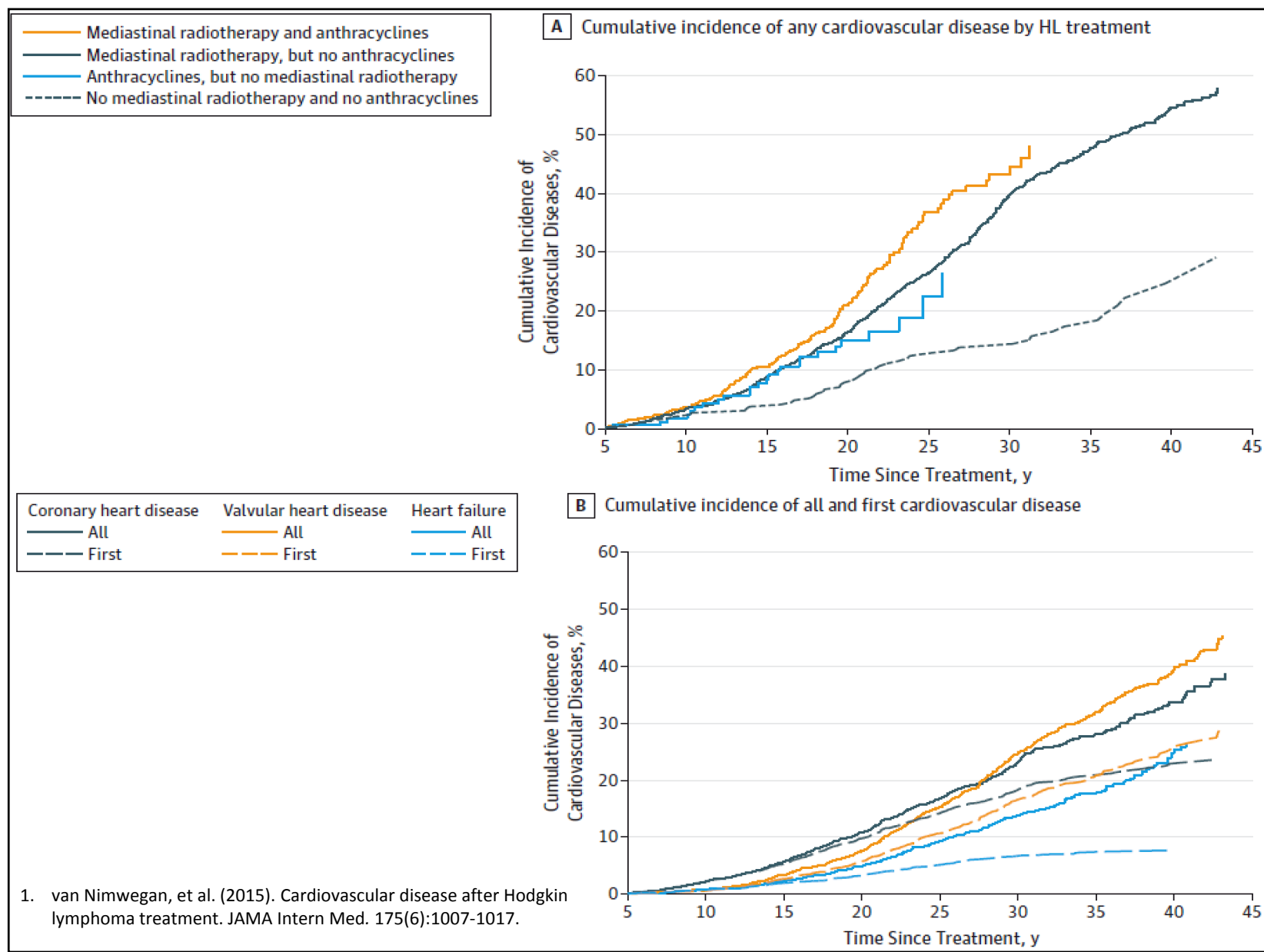
Radiation-induced Cardiotoxicity

Risk Factors

- Radiation dose
 - Exponential risk of acute coronary event with each gray XRT
 - Risk maintained for decades
- Volume of heart irradiated
- Concomitant cardiotoxins
 - *anthracyclines*
- Young
- Additional coronary risk factors

1. Moslehi (2013). The cardiovascular perils of cancer survivorship. NEJM. 368(11); 1055-1056.

2. van Nimwegan, et al. (2015). Cardiovascular disease after Hodgkin lymphoma treatment. JAMA Intern Med. 175(6):1007-1017.



Radiation-induced Cardiotoxicity Management

- Prevention is key
 - RT planning to reduce OAR exposure
 - IFRT/IMRT/ISRT/involved-node RT/resp. gating
 - Inspiration techniques
- Omit RT when appropriate (low risk, low stage)
- Eliminate cardiac risk factors when possible
- Screening techniques after therapy
 - Perfusion imaging/CT beginning at 5 years
 - ECHO/MUGA if >300mg/m² anthracycline
- Early cardiology/oncocardiology management

1. Specht, et al. (2014). Modern radiation therapy for Hodgkin Lymphoma. Int J Radiat Oncol Biol Phys. 89(4);854–862.
2. Aznar, et al. (2015). Minimizing late effects for patients with mediastinal Hodgkin lymphoma: DIBH, IMRT, or both? Int J Radiat Oncol Biol Phys. 92(1):169.

Delayed Pulmonary Toxicity

Bleomycin-induced Lung Injury

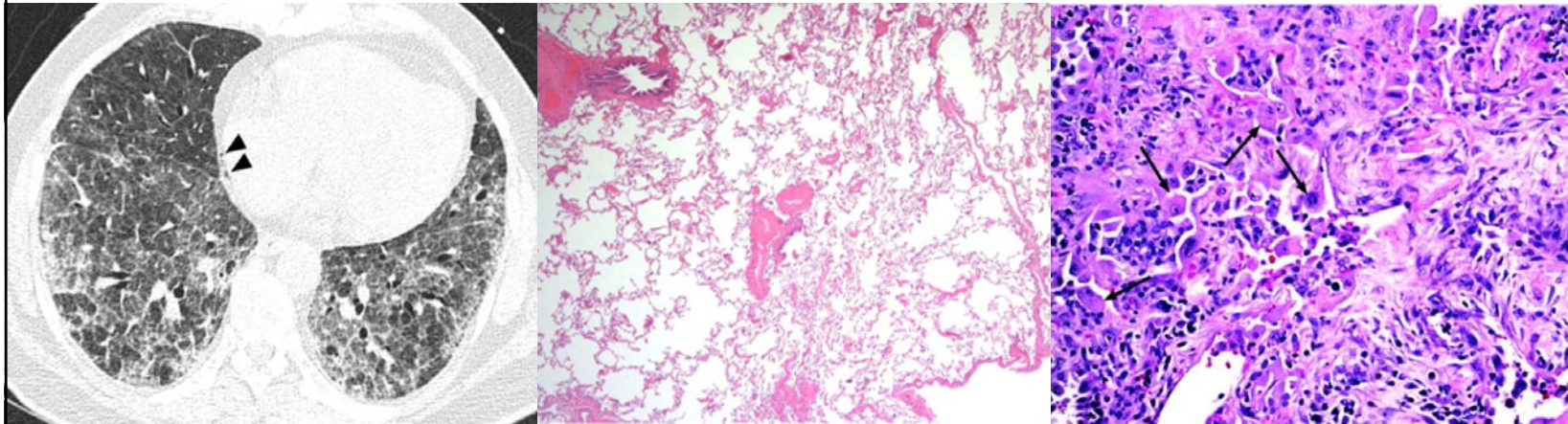
- ABVD, BEACOPP
- Pulmonary symptoms with non-infectious bilateral interstitial infiltrates
- Acute or gradual
- Interstitial pneumonitis progressing to *fibrosis*
- May occur in up to 18% of patients
- Mortality 10-27%
- Induced by oxidative damage, deficiency of bleomycin hydrolase, inflammatory cytokines
- Risk factors=age, dose, renal fxn, concomitant O₂, smoking, XRT, other chemo, G-CSF

1. O'Sullivan, et al. (2003). Predicting the risk of bleomycin lung toxicity in patients with germ-cell tumours. *Annals of Oncology*, 14(1);91–96.
2. Buchler, Bomanji, & Lee (2007). FDG-PET in bleomycin-induced pneumonitis following ABVD chemotherapy for Hodgkin's disease—a useful tool for monitoring pulmonary toxicity and disease activity. *Haematologica*, 92(11); 120–121.
3. Sleijfer, S. (2001). Bleomycin-induced pneumonitis. *CHEST*. 120(2):617-24.
4. Martin, et al. (2005). Bleomycin pulmonary toxicity has a negative impact on the outcome of patients with hodgkin's lymphoma. *Jrnl of Clin. Oncology*. 23(30);7614-7620.

Delayed Pulmonary Toxicity

Bleomycin-induced Lung Injury

Symptoms	Clinical Signs	Lab/diagnostic testing
Dyspnea	Fever	Restrictive PFT
Non-productive cough	Rales	Low DLCO
Chest discomfort	Hypoxia/cyanosis	Wide alveolar-arterial gradient
Fatigue	Tachycardia	No eosinophilia



1. Godoy, et al. (2008). Diffuse ground-glass opacities in a patient with hodgkin lymphoma and progressive respiratory failure. Chest. 2008;134(1):207-212.
2. Reinert, et al. (2013). Bleomycin-Induced Lung Injury. Jnl of Cancer Research, vol 2013, article ID 480608.

Bleomycin-induced Lung Injury

Diagnosis and Management

- Exclude other causes of pulmonary failure
- CXR, ILD CT scan, PET/CT
- Pulmonary consultation
- BAL/open lung biopsy
- D/C Bleomycin
- Consider steroids if symptomatic
- Imatinib
- Use O2 sparingly
- Supportive care for pulmonary fibrosis/transplant consideration

1. Reinert, et al. (2013). Bleomycin-Induced Lung Injury. Jnl of Cancer Research, vol 2013, article ID 480608.
2. Raghu, et al. (2011). Idiopathic pulmonary fibrosis: Evidence based guidelines for diagnosis and management. American Thoracic Society.
3. Carnevale-Schianca, et al. (2011). Complete resolution of life-threatening bleomycin-induced pneumonitis after treatment with imatinib mesylate in a patient with HL: Hope for severe chemo induced toxicity? JCO. 29(24); e691-e693

Delayed Pulmonary Toxicity

Radiation-induced Pulmonary Fibrosis

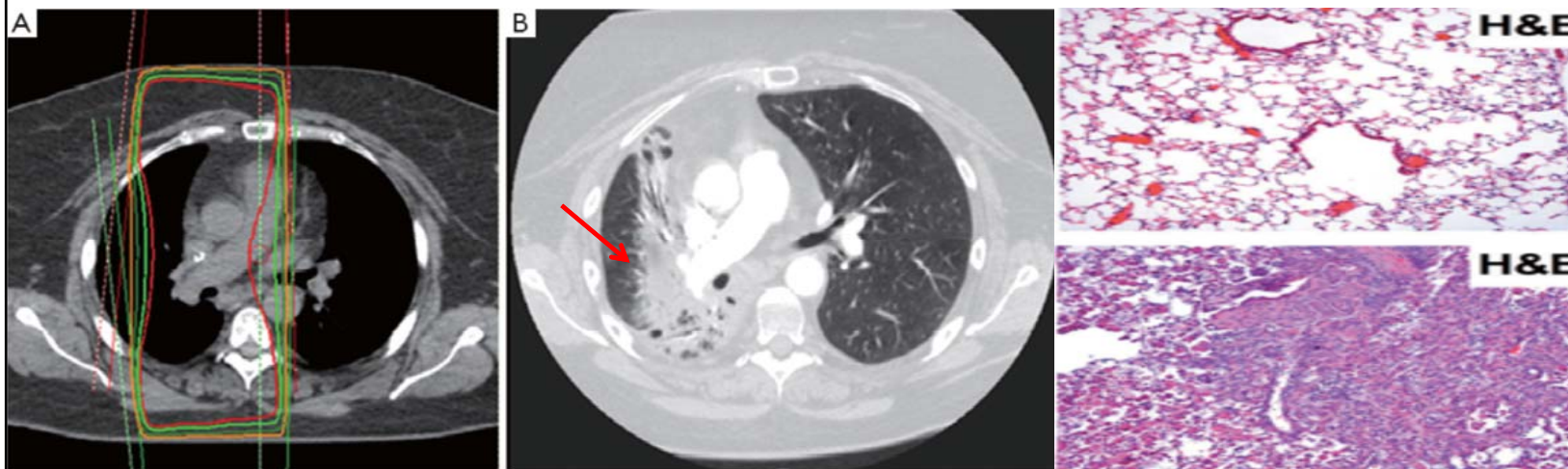
- May occur 6 months after initial exposure and progress for years
- Direct cytotoxicity of ionizing XRT
- Cytokine mediated fibrosis
 - TGF-beta, TNFa, IL-1a, IL-6, PDGF, bFGF
- Risk factors
 - Lung volume irradiated, XRT dose, concurrent chemo, prior XRT, smoking/ COPD

1. Cella, et al. (2014). Pulmonary damage in hodgkin's lymphoma patients treated with sequential chemo-radiotherapy: predictors of radiation-induced lung injury. *Acta Oncology*; 53(5)613-9.
2. Mazon, et al. (2010). Predictive factors of late radiation fibrosis: a prospective study in non-small cell lung cancer. *Int J Radiation Oncol Biol Phys*. 77(1):38.

Delayed Pulmonary Toxicity

Radiation-induced Pulmonary Fibrosis

Symptoms	Clinical Signs	Labs/diagnostic testing
Dyspnea	Fever	Restrictive PFT
Non-productive cough	Rales/pleural rub	Low DLCO
Chest discomfort	Hypoxia/cyanosis	Wide alveolar-arterial gradient
Fatigue	Tachypnea, tachycardia	Pleural eff., pulmonary HTN



1. Matonen, et al. (2014). New techniques for assessing response after hypofractionated radiotherapy for lung cancer. *Jrnl of Thoracic Disease*. 6(4); 375–386.

Radiation-induced Pulmonary Fibrosis

Diagnosis and Management

- Prevention
 - RT planning to reduce OAR exposure
 - IFRT/IMRT/ISRT/involved-node RT/respiratory gating/hold
- Exclude other cause of pulmonary failure
- CXR, ILD CT scan, PET/CT
- Pulmonary consultation
- BAL/open lung biopsy
- Prednisone ($\geq 60\text{mg/day}$) x 2 weeks with gradual taper over 3-12 weeks
- Azathioprine, CSA, pentoxifylline
- Improvement may occur within 18 months. after XRT, less likely if delayed >18 months

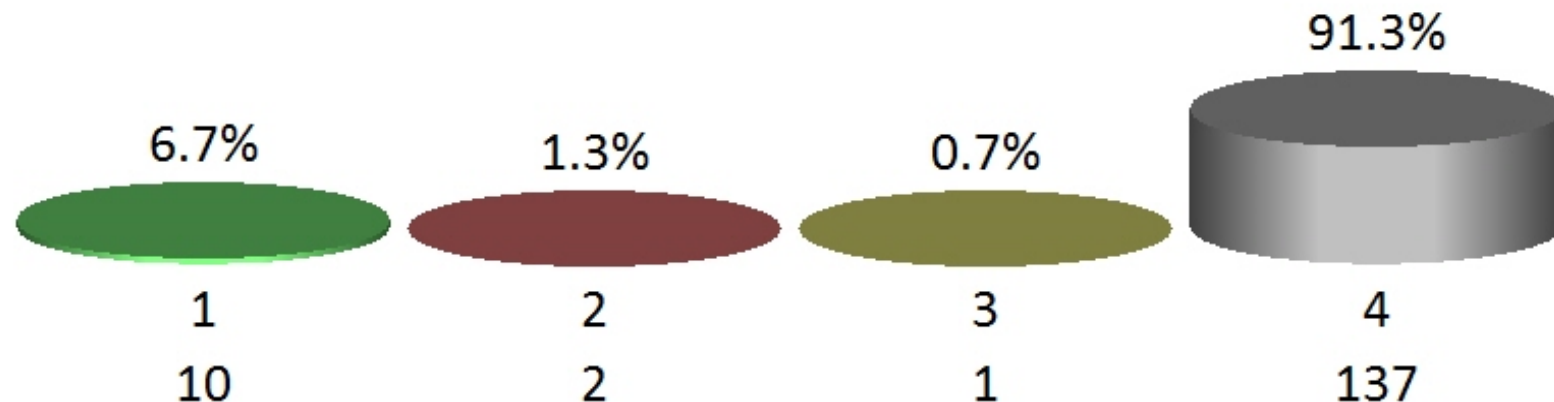
1. Choi, et al. (2004). Effects of radiation on the lung: radiologic appearance and differential diagnosis. *Radiographics*; 24(4):985.
2. Robins, et al. (2012). Imaging radiation-induced normal tissue injury. *Radiat Res.* 177(4):449-66.
3. Ozturk, Egehan, Atavci, Kitapci (2004). Pentoxifylline in prevention of radiation-induced lung toxicity in patients with breast and lung cancer: a double blind randomized trial. *Int J Radiat Oncol Biol Phys.* 58(1):213.
4. Bradley J, Movsas B. (2006). Radiation pneumonitis and esophagitis in thoracic irradiation. In: Small W, Woloschak GE, eds. *Radiation Toxicity: A Practical Guide*. New York, NY: Springer Science+Media Business, Inc.;43–52.

ARS Question



M.J. is a 45 y/o male with a history of DLBCL treated with REPOCH chemotherapy 2 years ago. He is in remission, but has been experiencing continued fatigue, trouble sleeping and anxiety over the possibility of relapse. You have ruled out medical causes of M.J.'s symptoms. What intervention would be most appropriate at this time?

1. Continue to follow M.J. with a PET/CT scan every 3 months
2. Tell M.J. to start exercising 5 days per week
3. Have M.J. reschedule a follow-up appointment in 3 months
4. Refer M.J. to your program Survivorship Clinic as soon as possible



Total: 150

Fatigue in Lymphoma

- Persistent sense of tiredness/exhaustion related to cancer or treatment
- Most common and distressing complaint in individuals undergoing cancer therapy
- B-symptom
- Underlying cause
 - anemia, poor nutrition, organ dysfunction, pain, anxiety, depression, lack of exercise or sleep
- May persist for an extended period of time for some cancer survivors

1. Bower, JE., et al. (2014). Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation. JCO, 32(17): 1840-1850.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Fatigue in Lymphoma

Screening

- H&P
 - Fatigue history
 - Fatigue scale
 - Disease status
 - Contributing factors
- Laboratory evaluation
- Imaging
- Specialty referral if appropriate

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Fatigue in Lymphoma

Treatment

- Treat underlying medical etiology
 - Cardiopulmonary dysfunction
 - Endocrine
 - Hepatorenal
 - Neurologic
 - Anemia
 - Arthritis
 - Infection
 - Relapse
- Medication management
- Pain
- Emotional distress
- Sleep disturbances
- Nutrition/exercise

1. Bower, JE., et al. (2014). Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation. JCO, 32(17): 1840-1850.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Fatigue in Lymphoma

Treatment

- Exercise program
 - Physical therapy
 - Exercise specialist
- Complementary/Alternative Medicine (CAM)
 - Acupuncture, biofield, massage, music, herbals
- Psychostimulants
 - Caffeine, methylphenidate, modafinil
- Education and counseling
 - What is normal?
 - Monitoring and follow-up plan

1. Bower, JE., et al. (2014). Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation. JCO, 32(17): 1840-1850.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue (version 2.2015).

Pain in Lymphoma

- An unpleasant sensory and emotional experience associated with actual or potential tissue damage in oncology
- One of the most common symptoms reported in cancer survivors
- Affects quality of life of cancer survivors, families, caregivers and friends
- May adversely affect survival

1. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, et al. (2007). Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol*;18:1437-1449.
2. Te Boveldt N, Vernooij-Dassen M, Burger N, et al. (2013). Pain and its interference with daily activities in medical oncology outpatients. *Pain Physician*; 16:379-389.

Pain in Lymphoma

- In general, pain improves dramatically after treatment for lymphoma
- Chronic cancer pain
 - Neuropathic
 - Myalgia/arthralgia
 - Skeletal pain
 - Post-radiation pain
- Severe pain is a medical emergency
- Acute, unusual pain requires immediate attention

Pain in Lymphoma

Screening and Diagnosis

- Assess pain at each visit
 - WILDA (**W**ords to describe, **I**ntensity, **L**ocation, **D**uration, **A**ggravating or **A**lleviating factors)
 - Etiology
 - Current pain regimen
 - Medical and Oncologic history
 - Physical exam
 - Disease status
 - Current psychosocial support

1. Fink, R. (2000). Pain assessment: the cornerstone to optimal pain management. Proc (Bayl Univ Med Cent).13(3): 236–239.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain (version 2.2015).

Pain in Lymphoma

Treatment

- Treatment based on type of pain
- Neuropathic
 - Gabapentin, pregabalin, duloxetine, amitriptyline, opioids, local/topicals
 - Nonpharmacologic, CAM, TENS
 - Referral to neuro-oncology
- Myalgias/Arthralgias
 - NSAIDS, cyclobenzaprine/baclofen, lorazepam, diazepam, gabapentin, pregabalin, duloxetine, amitriptyline, opioids, local/topicals
 - PT, hot, cold, CAM
 - Referral to pain team, PM&R

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain (version 2.2015).

Pain in Lymphoma

Treatment

- Skeletal pain
 - NSAIDS, amitriptyline, cyclobenzaprine/baclofen, opioids
 - PT, brace, vertebroplasty/kyphoplasty
 - Referral to IR/spine, Pain Team, PM&R
- Post radiation pain
 - NSAIDS, gabapentin, pregabalin, duloxetine, amitriptyline
 - PT, surgical lysis of adhesions
 - Referral to Radiation Oncology, Pain Team

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain (version 2.2015).

Sleep Disorders in Lymphoma

- Disturbances in sleep related to insomnia, excessive sleepiness and sleep related movement or breathing disorders
- Affects 30-50% of cancer patients/survivors
- Often associated with other disorders
- Often contributes to other disorders

1. Ancoli-Israel S. (2009). Recognition and treatment of sleep disturbances in cancer. J Clin Oncol; 27:5864-5866.

Sleep Disorders in Lymphoma

Screening

- Assess sleep at each visit
- Screening questionnaire
 - Insomnia
 - Excessive sleepiness
 - Obstructive sleep apnea
 - Restless legs syndrome
 - Parasomnias
- H&P
 - Contributing factors
 - Oncologic history
 - Current coping strategies

1. Chung, et al. (2008). STOP questionnaire: a tool to screen patients for OSA. *Anesthesiology*; 108(5):812-21.
2. Buchfuhrer, MJ. (2012). Strategies for the treatment of RLS. *Neurotherapeutics*; 9(4):776-90.
3. Morgenthaler, et al. (2007). Practive parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep*; 30(12):1705-1711.
4. Lippman, Mazour, Shahab (2001). Insomnia: therapeutic approach. *South Med Jrnl*; 94(9):866-73.

Sleep Disorders in Lymphoma

Diagnosis and Treatment



Insufficient sleep time

- Increase sleep time
- Sleep hygiene education



Obstructive sleep apnea

- Sleep study
- CPAP
- Weight loss
- Surgery
- Oral appliance
- Refer to sleep specialist



Restless legs syndrome

- Ferritin
- iron if deficient
- Ropinirole, pramipexole, carbidopa-levodopa
- Gabapentin
- Pregabalin
- Opioids
- Clonazepam, lorazepam
- CAM
- Refer to sleep specialist



Other Sleep Disorders

- Prolonged wakefulness or awakenings (insomnia)
- Prolonged sleep (hypersomnia)
- Cataplexy (narcolepsy)
- Excessive day sleepiness
- Reverse underlying causes
- Medication management (stimulants or sleep aids), CBT
- Sleep hygiene
- Sleep specialist

1. Chung, et al. (2008). STOP questionnaire: a tool to screen patients for OSA. *Anesthesiology*; 108(5):812-21.
2. Buchfuhrer, MJ. (2012). Strategies for the treatment of RLS. *Neurotherapeutics*; 9(4):776-90.
3. Morgenthaler, et al. (2007). Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep*; 30(12):1705-1711.
4. Lippman, Mazour, Shahab (2001). Insomnia: therapeutic approach. *South Med Jnl*; 94(9):866-73.

Anxiety and Depression in Lymphoma

- Occurs during times of worry and distress related to a variety of challenges and stressors affecting cancer survivors
- Common with and as a result of other survivorship issues
- Risk factors include cognitive impairment, medical illness, uncontrolled symptoms, substance abuse, prior psychiatric disorder, social concerns
- Negatively impacts quality of life

1. Bellizzi, Miller, Arora, Rowland (2007). Positive and negative life changes experienced by survivors of non-Hodgkin's lymphoma. *Ann Behav Med*; 34(2):188-99.
2. Smith, et al. (2011). Post-traumatic stress symptoms in long-term non-Hodgkin's lymphoma survivors: does time heal? *J Clin Oncol*; 29(34): 4526–4533.

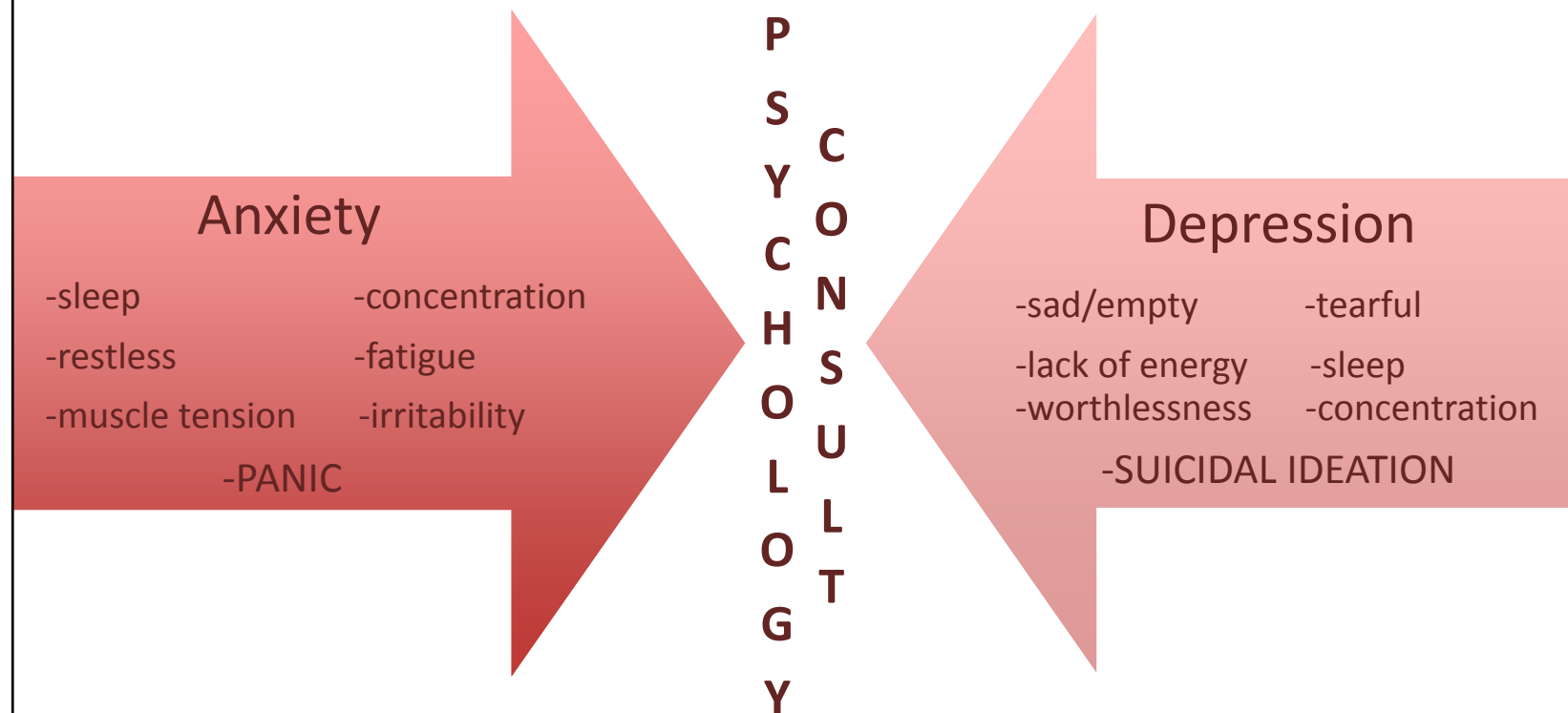
Anxiety and Depression in Lymphoma Screening

- Screening should occur during change in clinical status, treatment, life events, symptoms
- Signs of anxiety and depression
 - Nervous, worry
 - Fear
 - Inability to control fear and worry
 - Sleep difficulties
 - Trouble concentrating
 - Lack of interest/enjoyment
 - Feelings of sadness or depression
 - Difficulty with ADL's
- H&P to assess for medical etiology

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Anxiety and Depression in Lymphoma

Screening and Diagnosis



1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Anxiety and Depression in Lymphoma Treatment

- Assure safety
- Address non-psych medical etiology
- Isolate and minimize contributing factors
- Psychology/Psychiatry support
 - Reassurance/education
 - Exercise
 - Chaplain
 - Social work
 - Therapy
 - SSRI/SNRI
 - Benzodiazepines
 - Monitor closely
 - Follow-up plan

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Cognitive Dysfunction in Lymphoma

- May be directly related to cancer or cancer therapy
- Approximately 50% of cancer survivors
- Not typically progressive
- Deficits in executive function, learning, memory, attention, processing speed
- Cytokine release, white matter changes, anxiety, depression, sleep, pain, etc.
- Symptoms may persist for years or decades
- Adversely affects QOL and function

1. Wefel JS, Schagen SB. (2012). Chemotherapy-related cognitive dysfunction. *Curr Neurol Neurosci Rep*;12:267-275.
2. Jean-Pierre P, Winters PC, Ahles TA, et al. (2012). Prevalence of self-reported memory problems in adult cancer survivors: a national cross-sectional study. *J Oncol Pract*;8:30-34.
3. Deprez S, Amant F, Smeets A, et al. (2012). Longitudinal assessment of chemotherapy-induced structural changes in cerebral white matter and its correlation with impaired cognitive functioning. *J Clin Oncol*;30:274-281.
4. Schmidt JE, Beckjord E, Bovbjerg DH, et al. (2015). Prevalence of perceived cognitive dysfunction in survivors of a wide range of cancers: results from the 2010 LIVESTRONG survey. *J Cancer Surviv*. DOI 10.1007/s11764

Cognitive Dysfunction in Lymphoma

Screening

- H&P
 - Cancer history and risk factors for CNS disease and cognitive dysfunction
 - Onset, duration, trajectory
 - Characterize deficits
 - Focal neuro deficits
- Assess contributing/reversible factors
 - Medications/drugs/alcohol
 - Anxiety, depression, sleep/fatigue, pain
 - Medical comorbidities

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Cognitive Dysfunction in Lymphoma Management

- Treatment of contributing/reversible factors
- Reassurance/counseling
- Psychology consultation/CBT/OT
 - Relaxation/stress management
 - Cognitive function
 - Exercise
- Memory coping strategies
- Pharmacologic interventions
 - Methylphenidate, modafinil, caffeine

1. Goedendorp MM, Knoop H, Gielissen MF, et al. (2014). The effects of cognitive behavioral therapy for postcancer fatigue on perceived cognitive disabilities and neuropsychological test performance. *J Pain Symptom Manage*;47:35-44.
2. Kohli S, Fisher SG, Tra Y, et al. (2009). The effect of modafinil on cognitive function in breast cancer survivors. *Cancer*;115:2605-2616.

Sexual Function and Fertility

- Important issue affecting patient QOL
- Induced by chemotherapy, surgery, XRT, steroids, disease
- May be affected by other survivorship concerns (anxiety, depression, pain, fatigue)
- *Often not discussed by providers*
- Should be assessed at regular intervals
- Address impact of cancer treatment on sexual function as early as possible

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Sexual Function and Fertility Management

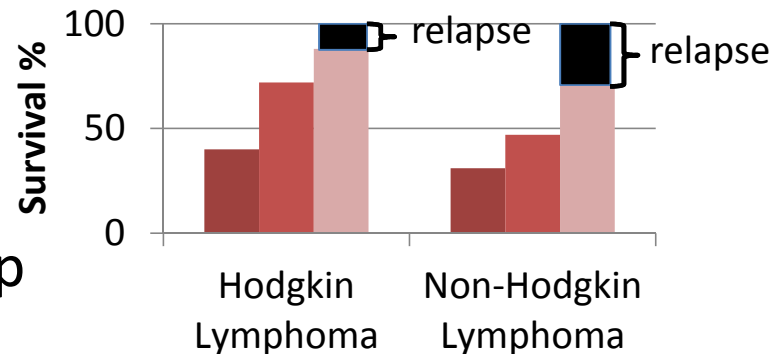
- H&P (*ask the question*; symptom checklist)
- Identify traditional risk factors for sexual dysfunction
- Guide treatment based on specific type of sexual dysfunction
- Referral to Specialist as indicated
 - Psychotherapy
 - Sexual/couples counseling
 - Gynecologic care/Urologist/Fertility specialist
- A variety of therapeutic interventions exist
- ***DON'T IGNORE THE ISSUE***

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).

Relapse and Secondary Cancers

Incidence

- Relapse
 - 10-30%
 - Assessment/follow-up
- Secondary Cancers
 - Induced by chemo and XRT
 - Most are solid tumors: lung, breast, GI
 - Blood cancers: MDS/AML, NHL
 - Incidence increases over time (8-10% at 15 years)



1. Forrest, et al. (2005). High-dose therapy and autologous SCT does not increase the risk of second neoplasms for patients with hodgkin's lymphoma: a comparison of conventional therapy alone vs conventional therapy followed by autologous SCT. J of Clin. Oncol; 23:7994-8002.
2. Tarella, et al. (2011). Risk factors for the development of secondary malignancy after high-dose chemotherapy and autograft, with or without rituximab: a 20-year retrospective follow-up study in patients with lymphoma. JCO; vol. 29(7), 814-824.

Relapse and Secondary cancers

Surveillance

- Relapse (Follow-up After Completion of Treatment up to 5 Years)
 - H&P every 3-6 months for 1-2 years, then every 6-12 months until year 3 and annually thereafter.
 - Labs: CBC, platelets, ESR (if elevated at time of initial diagnosis), chemistry profile as clinically indicated
 - Scans: CT scan once during the first 12 months, then as clinically indicated. PET/CT should only be obtained if last PET was Deauville 4-5, to confirm CR.
- Secondary Cancers (Follow-up and Monitoring After 5 Years)
 - H&P annually
 - Counseling: Reproduction, health habits, psychosocial, cardiovascular, breast self-exam, and skin cancer risk
 - Labs: CBC, platelets, chemistry profile annually; TSH at least annually if RT to neck; Biannual lipids
 - Low-dose CT if increased risk of lung cancer
 - Annual breast screening (mammography 8-10 years post therapy or age 40 (whichever comes first); if chest/axillary XRT at age 10-30 years, breast MRI in addition to mammography)
 - Colonoscopy every 10 years for patients age ≥ 50 , if high risk begins at age 40

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma (version 2.2015).

Preventative Health and Maintenance

- Cancer survivors are at increased risk due to therapy related comorbidities
- Promote healthy behavior and lifestyle
 - Exercise
 - Nutrition
 - Weight management (high and low)
 - Immunizations
 - Infection prevention
- Survivorship Team

1. Underwood, et al. (2009). Surveillance of demographic characteristics and health behaviors among adult cancer survivors—behavioral risk factor surveillance system. MMWR Surveill Summ; 61:1-23

What About Us?

- Oncology is difficult and demanding
- Caring for *others* vs. caring for *self*
- Healthcare provider burnout
- Provider satisfaction and well being affects patient care
- Obtaining and maintaining *balance*
- We must have an action plan for caring for providers

1. Skovholt & Trotter-Mathison (2011). The Resilient Practitioner. Burnout prevention and self-care strategies for counselors, therapists, teachers, and health professionals. 2nd ed.

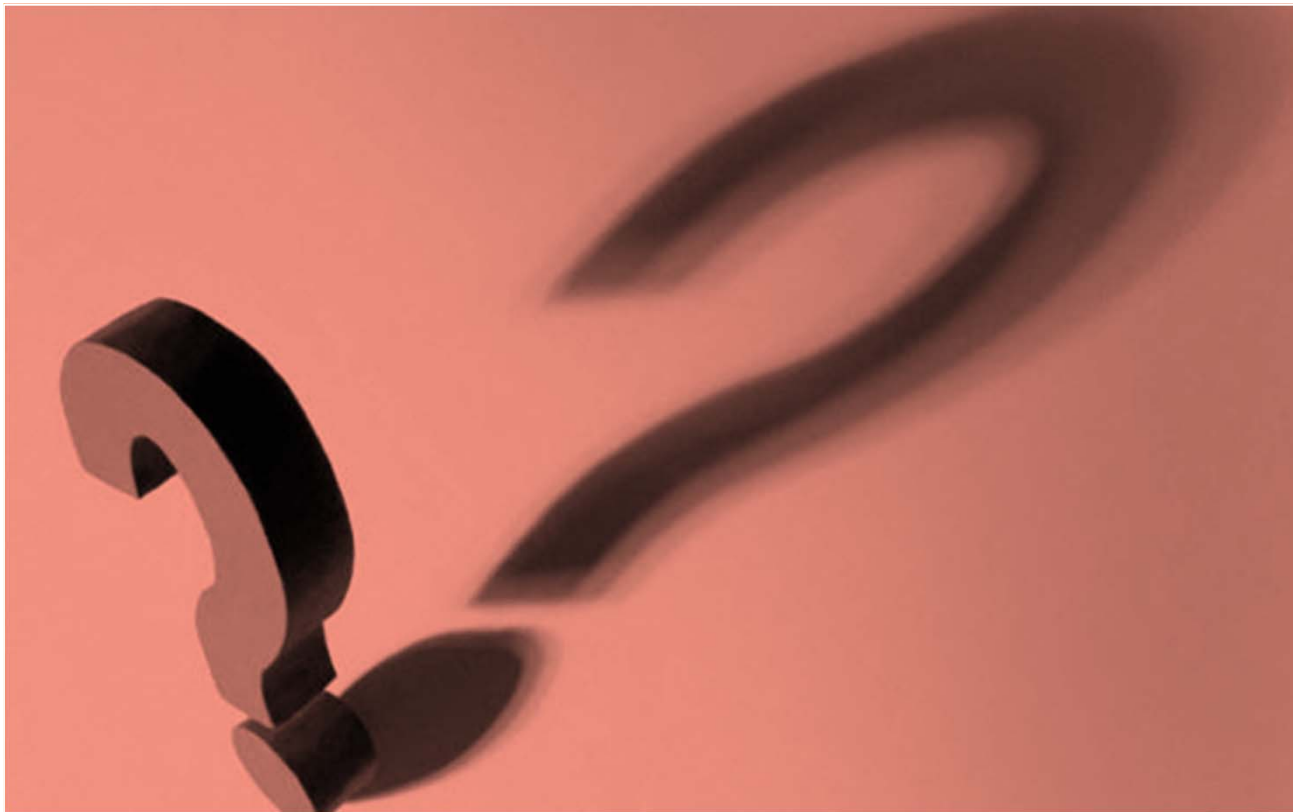
Survivorship Team

- MD/APP
- Psychologist
- Social worker
- Case manager
- Nursing
- Pharmacist
- Dietician
- PT/OT
- Specialty Services
 - Cardiology
 - Pulmonary
 - Endocrine
 - Reproductive Med
 - Pain Team
 - PCP/Internist

Conclusion

- 100% of cancer survivors are affected
- May result in permanent physical, emotional and social impairment
- Many suffer for months or years
- *Organize a Survivorship Team*
- *Remember to care for one another*
- *Your patients depend on you!!*

Questions



References

- van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, et al. (2007). Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol*;18:1437-1449.
- Te Boveldt N, Vernooij-Dassen M, Burger N, et al. (2013). Pain and its interference with daily activities in medical oncology outpatients. *Pain Physician*; 16:379-389.
- Fink, R. (2000). Pain assessment: the cornerstone to optimal pain management. *Proc (Bayl Univ Med Cent)*. 13(3): 236–239.
- Ancoli-Israel S. (2009). Recognition and treatment of sleep disturbances in cancer. *J Clin Oncol*; 27:5864-5866.
- Fiorentino L, Ancoli-Israel S. Sleep dysfunction in patients with cancer. *Curr Treat Options Neurol* 2007;9:337-346.
- Liu L, Ancoli-Israel S. Sleep Disturbances in Cancer. *Psychiatr Ann* 2008;38:627-634.
- Omachi TA. Measures of sleep in rheumatologic diseases: Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S287-296.
- Savard MH, Savard J, Simard S, Ivers H. Empirical validation of the Insomnia Severity Index in cancer patients. *Psychooncology*, 2005;14:429-441.
- Chung, et al. (2008). STOP questionnaire: a tool to screen patients for OSA. *Anesthesiology*; 108(5):812-21.
- Buchfuhrer, MJ. (2012). Strategies for the treatment of RLS. *Neurotherapeutics*; 9(4):776-90.
- Morgenthaler, et al. (2007). Practive parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep*; 30(12):1705-1711.
- Lippman, Mazour, Shahab (2001). Insomnia: therapeutic approach. *South Med Jrnl*; 94(9):866-73.
- Leukemia and Lymphoma Society. Long-Term and Late Effects of Treatment in Adults Facts. No. 22. www.LLS.org.
- Underwood, et al. (2009). Surveillance of demographic characteristics and health behaviors among adult cancer survivors—behavioral risk factor surveillance system. *MMWR Surveill Summ*; 61:1-23
- Grant M, Economou D. (2008) The Evolving Paradigm of Adult Cancer Survivor Care. *Oncology (Nurse Edition)*, 22(4):13-28

References

- Bellizzi, Miller, Arora, Rowland (2007). Positive and negative life changes experienced by survivors of non-Hodgkin's lymphoma. *Ann Behav Med*; 34(2):188-99.
- Smith, et al. (2011). Post-traumatic stress symptoms in long-term non-Hodgkin's lymphoma survivors: does time heal? *J Clin Oncol*; 29(34): 4526–4533.
- Ahles TA, Root JC, Ryan EL. Cancer- and cancer treatment- associated cognitive change: an update on the state of the science. *J Clin Oncol* 2012;30:3675-3686.
- Hodgson KD, Hutchinson AD, Wilson CJ, Nettelbeck T. A meta- analysis of the effects of chemotherapy on cognition in patients with cancer. *Cancer Treat Rev* 2012;39:297-304.
- Wefel JS, Schagen SB. (2012). Chemotherapy-related cognitive dysfunction. *Curr Neurol Neurosci Rep*;12:267-275.
- Jean-Pierre P, Winters PC, Ahles TA, et al. (2012). Prevalence of self- reported memory problems in adult cancer survivors: a national cross- sectional study. *J Oncol Pract*;8:30-34.
- Deprez S, Amant F, Smeets A, et al. (2012). Longitudinal assessment of chemotherapy-induced structural changes in cerebral white matter and its correlation with impaired cognitive functioning. *J Clin Oncol*;30:274-281.
- Schmidt JE, Beckjord E, Bovbjerg DH, et al. (2015). Prevalence of perceived cognitive dysfunction in survivors of a wide range of cancers: results from the 2010 LIVESTRONG survey. *J Cancer Surviv*. DOI 10.1007/s11764
- Goedendorp MM, Knoop H, Gielissen MF, et al. (2014). The effects of cognitive behavioral therapy for postcancer fatigue on perceived cognitive disabilities and neuropsychological test performance. *J Pain Symptom Manage*;47:35-44.
- Kohli S, Fisher SG, Tra Y, et al. (2009). The effect of modafinil on cognitive function in breast cancer survivors. *Cancer*;115:2605-2616.
- Cancer Facts and Figures. American Cancer Society 2015.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain (version 2.2015).

References

- Godoy, et al. (2008). Diffuse ground-glass opacities in a patient with hodgkin lymphoma and progressive respiratory failure. *Chest*. 2008;134(1):207-212.
- Reinert, et al. (2013). Bleomycin-Induced Lung Injury. *Jrnl of Cancer Research*, vol 2013, article ID 480608.
- Matonen, et al. (2014). New techniques for assessing response after hypofractionated radiotherapy for lung cancer. *Jrnl of Thoracic Disease*. 6(4); 375–386.
- Carnevale-Schianca, et al. (2011). Complete resolution of life-threatening bleomycin-induced pneumonitis after treatment with imatinib mesylate in a patient with HL: Hope for severe chemo induced toxicity? *JCO*. 29(24); e691-e693
- Ozturk, Egehan, Atavci, Kitapci (2004). Pentoxifylline in prevention of radiation=induced lung toxicity in patients with breast and lung cancer: a double blind randomized trial. *Int J Radiat Oncol Biol Phys*. Vol. 58(1):213.
- Bradley J, Movsas B. Radiation pneumonitis and esophagitis in thoracic irradiation. In: Small W, Woloschak GE, eds. *Radiation Toxicity: A Practical Guide*. New York, NY: Springer Science+Media Business, Inc.; 2006:43–52.
- National Cancer Institute’s Office of Cancer Survivorship.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue (version 2.2015).
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Survivorship (version 2.2015).
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma (version 2.2015).

References

- Mazon, et al. (2010). Predictive factors of late radiation fibrosis: a prospective study in non-small cell lung cancer. *Int J Radiation Oncol Biol Phys.* 77(1):38.
- Forrest, et al. (2005). High-dose therapy and autologous SCT does not increase the risk of second neoplasms for patients with hodgkin's lymphoma: a comparison of conventional therapy alone vs conventional therapy followed by autologous SCT. *J of Clin. Oncol*; 23:7994-8002.
- Tarella, et al. (2011). Risk factors for the development of secondary malignancy after high-dose chemotherapy and autograft, with or without rituximab: a 20-year retrospective follow-up study in patients with lymphoma. *JCO*; vol. 29(7), 814-824.
- Skovholt & Trotter-Mathison (2011). *The Resilient Practitioner. Burnout prevention and self-care strategies for counselors, therapists, teachers, and health professionals.* 2nd ed.
- Kohli S, Fisher SG, Tra Y, et al. The effect of modafinil on cognitive function in breast cancer survivors. *Cancer* 2009;115:2605-2616.
- O'Sullivan, et al. (2003). Predicting the risk of bleomycin lung toxicity in patients with germ-cell tumours. *Annals of Oncology*, 14(1);91–96.
- Buchler, Bomanji, & Lee (2007). FDG-PET in bleomycin-induced pneumonitis following ABVD chemotherapy for Hodgkin's disease—a useful tool for monitoring pulmonary toxicity and disease activity. *Haematologica*; 92(11); 120–121.
- Sleijfer, S. (2001). Bleomycin-induced pneumonitis. *CHEST.* 120(2):617-24.
- Martin, et al. (2005). Bleomycin pulmonary toxicity has a negative impact on the outcome of patients with hodgkin's lymphoma. *Jrnl of Clin. Oncology.* 23(30);7614-7620.
- Robins, et al. (2012). Imaging radiation-induced normal tissue injury. *Radiat Res.* 177(4):449-66.
- SEER Cancer Statistics Review, 1975-2011. National Cancer Institute; 2014.
- Hewitt, Greenfield, Stovall (2006). *From Cancer Patient to Cancer Survivor: Lost in Transition.*

References

- Zhang, et al. (2012). Identification of the molecular basis of doxorubicin-induced cardiotoxicity. *Nature Medicine*. 18, 1639–1642
- Hershman, et al. (2008). Doxorubicin, cardiac risk factors, and cardiotoxicity in elderly patients with DLBCL. *Journal of Clinical Oncology*. Vol 26(19); 3159-3165.
- Carver, et al. (2007). ASCO clinical evidence review on the ongoing care of adult cancer survivors: cardiac and pulmonary late effects. *Journal of Clinical Oncology*. Vol 25(25); 3991-4008.
- Swain, Whaley & Ewer (2003). CHF in patients treated with doxorubicin. *Cancer*. American Cancer Society. 97(11):2869-79.
- Yancy, et al. (2013). ACCF/AHA Guideline for the Management of Heart Failure. *J Am Coll Cardiol*. 62(16).
- Hooning, et al. (2007). Long term risk of cardiovascular disease in 10 year survivors of breast cancer. *JNCI J Natl Cancer Inst*. 99(5): 365-375.
- Moslehi (2013). The cardiovascular perils of cancer survivorship. *NEJM*. 368(11); 1055-1056.
- van Nimwegen, et al. (2015). Cardiovascular disease after Hodgkin lymphoma treatment. *JAMA Intern Med*. 175(6):1007-1017.
- Specht, et al. (2014). Modern radiation therapy for Hodgkin Lymphoma. *Int J Radiat Oncol Biol Phys*. 89(4);854–862.
- Aznar, et al. (2015). Minimizing late effects for patients with mediastinal Hodgkin lymphoma: DIBH, IMRT, or both? *Int J Radiat Oncol Biol Phys*. 92(1):169.
- Cella, et al. (2014). Pulmonary damage in hodgkin's lymphoma patients treated with sequential chemo-radiotherapy: predictors of radiation-induced lung injury. *Acta Oncology*; 53(5)613-9.
- Choi, et al. (2004). Effects of radiation on the lung: radiologic appearance and differential diagnosis. *Radiographics*; 24(4):985.
- Bower, JE., et al. (2014). Screening, Assessment, and Management of Fatigue in Adult Survivors of Cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation. *JCO*, 32(17): 1840-1850.

NCCN Member Institutions

