Psychosocial Care of Cancer Survivors in Post-Treatment and Extended Cancer Survivorship

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Disclosures

I have no financial disclosure or conflicts of interest related to the material presented in this presentation.

Cancer Survivorship

- National Coalition for Cancer Survivorship (1986): “one who remains alive and continues to function during and after overcoming a serious hardship or life-threatening disease.”

- A person diagnosed with cancer is considered to be a *survivor* from diagnosis until end of life.

Shifting Focus…

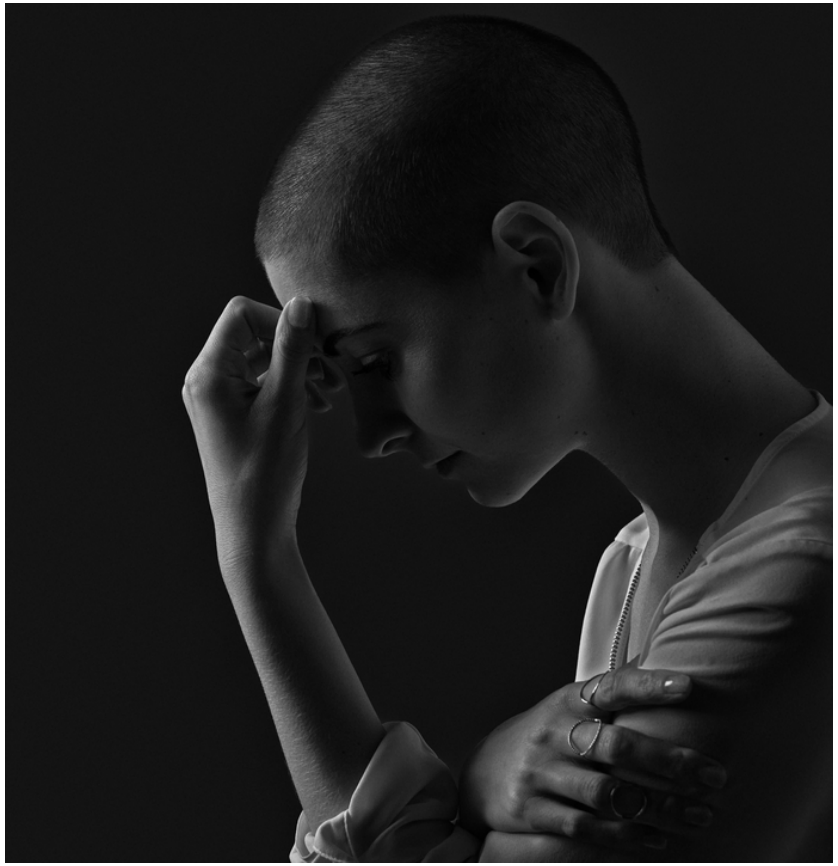
- Majority of clinical efforts and research has focused on psychological challenges faced by cancer patients in the earliest phase of diagnosis and treatment
- Lingering physical, psychological, and interpersonal challenges extend into longer-term survivorship
- Need for greater attention to psychosocial challenges in periods after treatment completion and into long-term survivorship

Phases of Survivorship

Acute	Diagnosis and Active Treatment
Re-Entry	Several months after completing treatment
Extended	Period after re-entry until end of life

Challenges of Re-Entry Phase

- Loss of safety net of active medical treatment and accompanying supportive milieu
- Fear of Recurrence (FOR)
- Physical and psychological effects of diagnosis and treatment → Fatigue/sleep disturbance, sexual dysfunction, urinary/bowel problems, and cognitive problems
- Delayed psychological impact until treatment is complete -- *"it didn't hit me until I finished treatment"*



Challenges of Re-Entry Phase

Resuming or coping with alteration of former roles within and outside the home

Decline in interpersonal support

Expectation of "quick return to normal" → survivors may feel that they are not recovering properly when experiencing distress

Phases of Survivorship

Acute	Diagnosis and Active Treatment
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Extended Survivorship

Many patients do well…

- Psychological status is favorable over the long-term for a substantial proportion of cancer survivors
- Benefit and increased meaning from the experience
    - Greater sense of compassion
    - Heightened awareness of being valued by loved ones
    - Greater intimacy
    - Greater appreciation of life
    - Deepening of spirituality

Some struggle…

- Some patients experienced a decline in several domains of quality of life compared to those who did not receive a cancer diagnosis
- Large population-based health registry cohort study from Sweden -- MH diagnoses are elevated compared to gen population until 10 years after diagnosis
- Even when quality of life is generally positive – specific physical and psychosocial problems can persist and cause distress

Risk Factors for Compromised Psychological Health Post-Treatment

- Medical Factors
  - Systemic treatments for cancer (chemotherapy, endocrine therapies)
  - Significant medical comorbidities
  - Persisting side effects from diagnosis/treatment (ie prolonged fatigue, local pain, lymphedema, insomnia, cognitive concerns, limited mobility, alterations in bowel function, body image changes
- Demographic Factors
  - Younger age – sexuality and fertility concerns; depressive symptoms; premature menopause, challenges with intimate relationships, career disruption, sense of isolation
  - Female gender
  - Lower socioeconomic status
- Prior psychiatric history
- Distress earlier in survivorship trajectory

Risk Factors for Compromised Psychological Health Post-Treatment

- Personal attributes and resources
  - Pessimism (general expectancy for negative outcomes)
  - Avoidant coping strategies
  - Social isolation
  - Lack of emotional support
- Sociocultural factors – cultures diverge on:
  - Causes and prognosis of cancer
  - Extent of stigma associated with cancer in general and with specific cancers
  - Expected roles of health care provider, patient and family in information giving and decision making
  - Norms for psychological response to cancer and acceptability of seeking psychosocial care
  - Ex: High perceived stigma and self-blame associated with cancer are related to poorer psychological adjustment and higher distress
- Poor access to care and information

Psychosocial Issues in Cancer Survivors Post-Treatment

DISTRESS

Distress

"A multifactorial, unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope with cancer, its physical symptoms, and treatment."

Vulnerability
Sadness
Fear

Depression

DISTRESS

- Highly prevalent in cancer survivors

  Lung, pancreatic, brain, head-and-neck cancer particularly vulnerable

- Can occur at any point in survivorship and may fluctuate over time

- Comprises multiple components:
  - Fear of Recurrence (FOR)
  - Hypervigilance about new or persistent symptoms
  - Concerns about family and finances
  - Stress from managing health needs
  - Changes in self-perceptions and body image
  - Increasing awareness of vulnerability

DISTRESS

- Associated with poor outcomes
  - Poor health behaviors (ie smoking in survivors)
  - Higher utilization of medical services
  - Reduced treatment adherence
  - Poor self-care
  - Increased post-operative pain
  - Reduced quality of life
  - Higher mortality rates

FEAR OF RECURRENCE

FEAR OF RECURRENCE

- Common in cancer survivors
- ~80% reported some level of FOR
- Seen even in extended survivorship
- Risk Factors: female, <60 yo, socially isolated, 5-7 years post-diagnosis <10 years of education, recurrence, higher state anxiety, more self-reported difficulty coping
- FOR tends to increase around time of scans or other testing for recurrence

ANXIETY

Anxiety

- 18-25% of long-term cancer survivors report anxiety
- Elevated levels of anxiety at 6 months post-treatment → higher scores at 12 months
- Risk Factors: younger age, female, social isolation, advanced disease, presence of physical symptoms, higher number of comorbid conditions, diagnoses of lung cancer or melanoma, previous history of mental health treatment, avoidant coping strategies

DEPRESSION

Depression

- Associated with poor outcomes – poor quality of life, reduced satisfaction with care, and worse survival
- Predictor of increased morbidity and mortality
  - May play a causal role – poor treatment adherence; neuroimmune mechanisms
- Prevalent– some variability in literature regarding rates
- Risk factors:
  - Higher number of physical symptoms, history of multiple primary cancers, perceived low health status, two or more co-morbidities, prior history of depression, female gender, single, sedentary lifestyle, active smoking history, reduced education, lower income, unemployment, avoidant coping styles, rumination, fear of recurrence, and lack of receipt of survivorship care plan

Post-Traumatic Stress

- Cancer survivors are at increased risk of developing PTSD
  - Meta-analysis showed rates of 5-7.3% vs general population rate of 2.4%
  - Sample of long-term testicular cancer survivors 11 years after diagnosis – 10% had either subclinical or full PTSD
  - Risk factors: younger, female gender, diagnosed with later stage disease, pain
- Underdiagnosed in cancer survivors – avoidant coping
- Most times do not reach level of PTSD, but can still disrupt quality of life and functioning
- Post-Traumatic Growth: positive psychological changes that come about as a result of the cancer diagnosis and subsequent treatment journey
  - More likely to be reported by women, older adults, and those with better social support
  - 83% can identify benefits that came from their journey such as making positive changes in their lives and having a greater appreciation of life

Other Psychosocial Concerns

- Sexuality and fertility concerns

- Survivor guilt
  - Sense of having done something wrong or owing a debt that can never be fully paid as a result of having survived cancer, when others are equally worthy have died
  - Complex psychological condition that encompasses feelings of blame, grief, and loss
  - >60% reported problems with grief or identity

- Caregivers – do experience cancer-related distress, depression and anxiety.

Psychiatric Effects Associated with Cancer Treatments

Hormonal Therapies

- Aromatase Inhibitors -- adjuvant therapy for ER+ breast cancer
    - Letrozole (Femara), anastrazole (Arimidex)
    - Associated with side effects that impair quality of life: insomnia, hot flashes, depression, memory deficits

- Tamoxifen – selective estrogen receptor modulator for ER+ breast cancer
    - Can cross the blood-brain barrier and has neuropsychiatric side effects
    - Deleterious effect on cognition

- Androgen deprivation therapy
    - Reduce libido, weight gain, loss of body muscle, increase fatigue

- Corticosteroids
    - Depression, mania, psychosis, agitation, mood lability, anxiety, insomnia, delirium
    - Distractibility, intermittent cognitive concerns

Chemotherapy

- Vincristine, vinblastine: depression, fatigue, encephalopathy
- Procarbazine: depression, delirium, psychosis, somnolence, cerebellar disorder (risk of serotonin syndrome w/SSRI)
- Methotrexate: leukoencephalopathy, delirium
- Isosfamide: hallucinations, delirium, cerebellar signs, lethargy
- Gemcitabine: fatigue
- 5-flurouracil: fatigue, seizure, confusion
- Cytarabine: delirium, seizures, leukoencephalopathy
- Cisplatin: sensory neuropathy
- Taxanes: fatigue, depression, sensory neuropathy

Additional Therapies

- Biologics
  - Cytokines: encephalopathy
  - Interferon-alpha: depression, suicidality, mania, psychosis, delirium, akathisia, seizures
  - Interleukin-2: dysphoria, delirium, psychosis, seizures
- Multi-kinase inhibitors
  - Sorafenib, sunitinib, bevacizumab – posterior leukoencephalopathy syndrome
- Radiation
  - Brain irradiation: transient cognitive decline following radiotherapy; others can develop subacute or late neurotoxicity in months to years after completing radiation
  - Irradiation of gynecologic cancers – vaginal atrophy, sexual dysfunction
- BMT
  - Depression and anxiety, N/V, fatigue, adjustment d/o, dependence (dependent needs are associated with poorer survival), neurocognitive deficits due to CNS toxicity

Tamoxifen: A Closer Look

- Metabolized to active metabolite (endoxifen) by CYP2D6
- Preferred use: Effexor XR (minimal to no 2D6 inhibition), Remeron is ok.
- Second line: Lexapro, Celexa – weak CYP2D6 inhibitors
- MINIMIZE moderate CYP 2D6 inhibitors: Cymbalta
- AVOID strong CYP 2D6 inhibitors: Paxil, Prozac and Wellbutrin

MANAGING PSYCHIATRIC DISORDERS/SYMPTOMS IN CANCER SURVIVORS

IMPORTANT CONSIDERATIONS IN SELECTING PSYCHOPHARMACOLOGY IN CANCER PATIENTS

- Medical comorbidities
- Potential drug interactions
- Route of administration
  - Mucositis/GI obstruction – PO may not be an option
  - Thrombocytopenia – may want to avoid IM formulations
- Onset of action in context of prognosis
- Associated somatic symptom profile in patient (ie pain, insomnia, agitation, hot flashes)
- Adverse effect profile of the intended psychotropic medication
- Low albumin levels and ascites – can affect volume of distribution of drugs

PHARMACOTHERAPY FOR DEPRESSION IN CANCER SURVIVORS

- SSRIs first line management
- SNRIs
  - Venlafaxine → vasomotor symptoms
  - Duloxetine → pain, chemotherapy-related neuropathy
- Mirtazapine – appetite, nausea, insomnia
- Bupropion
  - Activating profile is positive in patients with lethargy
  - **Seizure risk in malnourished or CNS tumors**
  - May assist with smoking cessation

PHARMACOTHERAPY FOR DEPRESSION IN CANCER SURVIVORS

- TCAs -- neuropathic pain syndromes
- Stimulants
  - Cancer-related fatigue
  - Neurocognitive effects of chemo
  - Improvement within hours to days
  - Improves appetite
  - Counteract sedating effects of opioids
  - Prognosis of days to few weeks

- Low dose atypical antipsychotics in augmentation – some may also provide benefit for nausea, appetite, sleep

PHARMACOTHERAPY FOR ANXIETY IN CANCER SURVIVORS

- SSRIs, SNRIs, buspirone, mirtazapine
- Benzodiazepines – given for acute anxiety and/or insomnia as well as to augment antiemetics during chemotherapy
    - Ativan, Xanax – favored in acute setting: rapid onset of action, increased benefit for as-needed basis.
    - Caution w/ concurrent opioids
- Low doses of antipsychotics are useful in patients who are unresponsive to or intolerant of benzodiazepines or in patients who have severe anxiety and agitation

Psychological Interventions in Cancer Survivors

- **Psychological interventions are effective**
  - Most studies assessing the efficacy of psychosocial and behavioral interventions were conducted in the diagnostic or active medical treatment plans

  - RCTs indicate that interventions offered at re-entry are effective – CBT, stress interventions (relaxation, mindfulness), and psychoeducational interventions
    - Limited studies
    - Most are focused on breast and prostate cancer
    - Interventions themselves are not uniform

  - Studies show that interventions for health behavior change (physical activity, diet, smoking) are effective → important to promote good health behaviors after treatment

Promoting Adaptive Survivorship

- Proactive psychosocial care can aim to prevent or minimize distress/challenges associated with re-entry or extended survivorship → can promote adaptive survivorship and maintain quality of life.
  - Monitoring of patients' psychological and physical concerns is warranted throughout survivorship – in particular during the re-entry/extended phases in light of survivors' shifting concerns and evidence that external sources of support erode over time
  - Routine screening for distress is essential, but alone not sufficient: must be paired with referral to appropriately trained professionals and with evidence-based treatment of symptoms and problems
  - Helping individuals know what to expect at completion of medical treatment and how to address anticipate problems.
  - Increasing awareness of risk factors for distress so that psychosocial care can be targeted to those most in needed
  - Proactively providing patients with information about resources for support or psychosocial care

Thank you

Questions?

Please feel free to email me at jmolinaro@mcw.edu

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