No Longer Neglected
Depression in Cancer Survivorship

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No Disclosures to Declare

Overview

• Survivorship and Historical Underpinnings
  • Current state of the science
  • Clinical Implications
  • Current Challenges and Controversies

Cancer Survivorship

• Success in treatment and screening
  • Increased survival
    • Most survivors living beyond 5 years
    • High prevalence/low mortality disease
  • Greater attention to long-term well-being
    • Quality of life
    • Health promotion
    • Psychological comorbidity
    • Depression

3/3/2014
Psychological Well-Being in Survivorship

- Majority of cancer survivors adjust well (Boyes et al., 2009)
  - Particularly breast cancer survivors

However
- A notable minority report long term effects
  - Primarily: Anxiety, Depression, PTSD

Risk factors based on
- Cancer site (lung, brain)
- Age (younger)
- Low resources (social support, income)
- Psychiatric History

Historical Underpinnings

- Historically, mental health concerns not routinely addressed in context of cancer diagnosis and treatment

Patient vs. Provider Barriers to Treatment
- Depression a natural part of the cancer experience
- Stigma surrounding mental health
- “Don’t ask, don’t tell policy” & “Pandora’s Box”
- “Good patient”, “yet another medication”
- Fatigue, sleep disturbance, loss of appetite (include vs. exclude?)

Many go either undetected or untreated
- Patient-provider agreement (Passik et al., 1998)
  - 33% for mild-moderate to 11% severe

Decades of Change

- Shift over past 10 to 20 years
  - Evidence base has grown
  - Depression AND Cancer

- Psychological well-being important in context of
  - Quality of life
  - Disease adjustment
  - Chronic disease management
  - Possible survival outcomes

INDEXED PAPERS MEDLINE
Depression

• One of the most frequently endorsed and studied (Massie, 2004)

• Challenges to diagnosing depression in the context of cancer
  • Common disease-related symptoms
    • Sleep and appetite disturbance, pain, fatigue, hopelessness regarding future
  • Uncommon disease-related symptoms
    • Loss of interest (“grandchild question”), guilt, self-criticism, suicidal ideation

Key Questions to Ask
• Do you have little interest or pleasure in doing things?
• Have you felt down, depressed or hopeless?

If more than half the days or all of past two weeks
• At risk for depression

Assessment of Depression

• Proliferation of self-report measures in research and clinical care – but not a diagnosis
  • 33 screening measures (Vodermaier et al., 2009)
    • Center for Epidemiology Studies Depression Scale
      • CESD: 20 items
    • Hospital Anxiety and Depression Scale
      • HADS: 14 items - patient population
    • Distress Thermometer
      • DT: One item: Visual analog scale
    • PHQ-9
      • 9 items for depression

• Future - PROMIS

Assessment of Depression

• Screening instruments not designed to offer clinical diagnosis
  • Clinical Interview (SCID): Gold Standard
    • History, differential diagnoses, clinical significance
    • Algorithm for diagnosis
    • Difficult in research setting

• In absence of a clinical interview, screening measures -
  • Provide symptom-based prevalence
  • Concept of “distress”
  • Subthreshold symptomatology
Prevalence of Depression

- Systematic Review (Hotopf et al., 2002)
  - Interview based estimate: 5% - 26%
  - Self-report based estimate: 29% (HADS)

- Review: Psycho-oncology (Krebber et al., 2013)
  - Non-palliative care setting
    - Self-report: 6% - 24% (depending on measure and cutoff used)

- Diagnostic Interview
  - Overall prevalence of major depression = 13% (49 studies)
  - Cancer site
    - Lung (5%) - Digestive tract (31%)
  - Time
    - Highest during treatment: 14% - 27%
    - < 12 months of treatment: 9% - 21%
    - > 12 months of treatment: 8% - 15%

- Meta-analysis of diagnostic interview studies (Mitchell et al., 2011)
  - 70 studies utilizing diagnostic (DSM/ICD) criteria
  - Non-palliative care settings
  - 10071 people across an international literature

- Results
  - Major Depressive Disorder: 16.3%
  - Some type of mood disorder: 30% - 40%

Prevalence of Depression

Routine Screening Study (Linden et al., 2012)

- Results
  - Clinically relevant depression: 12.9% / Subthreshold depression: 16.5%
- Notes
  - Highest rates among those diagnosed with lung and gynecological cancer
  - Rates higher among women

Are rates higher than the population?

- General population norms: MDD: 4% of population (Waraich et al., 2004)
- Mitchell meta-analytic (Mitchell et al., 2011)
  - 11.6% vs. 10.2 healthy controls - no difference -
- Long term survivors (Pirl et al., 2009)
  - Survivors did not have increased odds of MDD - no difference -
  - However survivors reported higher degrees of impairment
**Depression in Breast Cancer**

**Review Papers**

(Fann et al., 2008) (Krebber et al., 2013) (Zainal et al., 2013)

- Interview based: 5% - 15%
- Self-report: 15% - 30%

- Higher rates of depression associated with
  - Fatigue
  - Pain
  - Comorbidities
  - Low income
  - Low education
  - Single relationship status

**Depression in Survivorship**

**Clinical Studies**

- One year longitudinal study of depression (Stafford et al., 2013)
  - Majority were breast cancer survivors (CESD Self-report)

- Diagnosis: 38.8%
- 16 weeks: 29.6%
- 40 weeks: 22.4%
- 56 weeks: 19.4%

**Trajectories in Survivorship**
Implications: Adherence & QOL

Treatment Adherence (Manning & Bettencourt, 2011)
- Depression (CESD) was related to poorer medication adherence
  - Studies have shown treatment adherence and subsequent patient adherence

Study of 95 breast cancer patients (Paranjape et al., 2005)
- Depressed women: 51.3% vs. 92.2% accepted and received treatment

Quality of Life
- Depression associated with significant impairment in quality of life domains
  - Interpersonal relationships
  - Occupational functioning
  - Extraverted physical symptoms
  - Emotional functioning
- Depression also associated with less satisfaction with care

Implications: Health Behaviors

Cancer as a chronic disease
- Importance of health promotion (Alfano et al., 2013; Rock et al., 2012)
- Long-term management and potential role of mental health
- Depression and depressive symptoms can limit survivors’ engagement in health promoting behaviors
- Weight-loss efforts
- Physical activity
- Dietary changes
- Cancer screening

ACS Guidelines for Cancer Survivors
- Achieve and maintain a healthy weight.
- Engage in regular physical activity.
- Achieve a dietary pattern that is high in vegetables, fruits, and whole grains.

Long-term Implications

Depression as a predictor of survival
- Meta-analysis (Somashekar et al., 2009; Pinquart & Duberstein, 2010)
  - Mortality rates up to 25% higher in those with depressive symptom
  - This rose to 39% for those diagnosed with major or minor depression

Patient Populations
- Metastatic non-small cell lung cancer (Pirl et al., 2012)
  - Depression predicted worse survival (N=351, HR: 1.6)
- Renal cell carcinoma (Somashekar et al., 2009)
  - CESD depression symptoms significant predictor of survival (N= 217, HR: 1.5)

Potential Mechanisms (Jang et al., 2012)
- Biological – inflammation/stress/cortisol
- Adherence to treatment
- Engagement in health behaviors
Prison of Positive Thinking

1990's Culture of Positivity
• Psychosocial Support Group → Increased Survival
• Positive thinking → Increased survival
Therefore
• Negative Thoughts & Depression → Reduced Survival

Tyranny of Positive Thinking
• Fortunately less widespread now
• But still a cultural element

Author: Barbara Ehrenreich

Interventions Targeting Survivors

For those who are identified or seek help
• Efficacy of psychological interventions and psycho-pharmacology generally effective in treating depression in cancer

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<thead>
<tr>
<th>Psychosocial Interventions (Li et al., 2012)</th>
<th>Other Interventions</th>
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<tbody>
<tr>
<td>Supportive</td>
<td>Inter-personal</td>
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<tr>
<td>Psychoeducation</td>
<td>Problem-solving</td>
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<tr>
<td>Relaxation Training</td>
<td>Counseling</td>
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<td>Cognitive behavioral</td>
<td>Emotional and expressive</td>
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Review of systematic reviews and meta-analyses
• Results to 60% - 80% of reviews / medium to large effect sizes in meta-analyses
• However:
  - neck et al., 2007: Only 60% of interventions significant reduction of depressive symptoms
  - Williams et al., 2006: Only 3 positive RCTs of psychosocial interventions in cancer

Interventions Targeting Breast Cancer Survivors

Randomized Clinical Trial: Cognitive Therapy (Savard et al., 2006)
• 45 women → randomized to treatment or wait-list control
• Treatment: 8 weekly sessions (60-90min) + 3 booster calls

Results
• CT Group had significantly lower depression scores
  • Although not on all scales
• Reductions in depression symptoms associated with:
  • Anxiety
  • Fatigue
  • Insomnia
• Effects sustained at 3 and 6 months
Empirical Challenges

Which cancer survivors do we enroll in psychotherapy trials?

• Historical context of intervention development
• Many patients are subthreshold
• Which measure to use?

• Meta-analysis of entry threshold trials
• Interventions targeting depressive symptoms in adults with cancer
• Examined only trials with entry threshold to trial (N=14)

CONCLUSION: Both psychological and pharmacological interventions reliably reduced symptoms of depression
- Should be targeted to patient symptoms

Future Steps: How do we ask?

• Dual Question Format
  • Are you depressed, distressed, anxious?
  • Do you desire support?

• How well do routine screening measures:
  • Detect those in Need AND Desiring help

Notre Dame Long-Term Survivor Cohort

• 317 Survivors, primarily diagnosed with breast cancer
• 63 years old, married, Caucasian
• 5–7 years post primary treatment

Notre Dame Long-Term Survivor Cohort

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<tr>
<th>Stressor</th>
<th>Endorsed by 30% of Survivors</th>
<th>Endorsed by 10% of Survivors</th>
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<tbody>
<tr>
<td>Financial</td>
<td>27%</td>
<td>3%</td>
</tr>
<tr>
<td>Sexual</td>
<td>24%</td>
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<tr>
<td>Social</td>
<td>23%</td>
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Although still not straightforward

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<tr>
<th>Desire for Follow-up</th>
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<td>Yes</td>
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<td>20</td>
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<td>192</td>
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CONCLUSION: Both psychological and pharmacological interventions reliably reduced symptoms of depression
- Should be targeted to patient symptoms
Unanswered questions...

• What is the most effective way to identify those in need?

• Who should provide treatment?

• How can treatment be delivered?

• How can treatment be covered?

Summary

• Prevalence of major depression ranges depending on study
  • GOLD STANDARD: 13%
  • Higher rates of subthreshold depression

• Untreated depression can have important consequences
  • Quality of life
  • Adherence to treatment and screening
  • Engagement in healthy behaviors

*Psychosocial and pharmacological treatments are generally effective in the context of cancer*

• Survivorship presents new challenges to identifying those in need and providing evidence-based treatment

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Follow-up questions or comments
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