Living through breast cancer: The big picture and some important details

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Harvard Medical School
I have metastatic breast cancer
http://www.ecoerth.com/grieving-through-the-holidays/
Cancer sucks

- Cancer means:
  - Disability
  - Roads not travelled
  - Doors closing
  - Opportunities lost
  - Future events to be missed
  - Medicalization of life
  - Loss of control

The normal reaction to the diagnosis of cancer is to mourn what is, what cannot be, and what the future may hold.

So - feel it, own it, and embrace it.

Then - Move On
Cancer forces one to evolve

Can I do this?

- YES. You can.
- Yes. You must.
- Yes. Because you have no choice.
Overview

Among the main concerns of women with metastatic breast cancer:
- Pain
- Fatigue
- Insomnia

Management:
- Medical
- Complementary
When is a symptom a side effect?
Pain
Scope of the Problem

- Pain is common.
  - Patients requiring admission → 73% report pain
  - Chronic pain → 70 to 90% (advanced disease)
- There are a lot of types of pain
  - Nociceptive (Tissue Damage)
  - Neuropathic (Neural damage)
  - Somatic (Cancer pain)
Pain is something most are afraid of

- Very scary implications for:
  - Prognosis
  - Disability/Loss of autonomy
  - Loss of dignity
  - Barrier to enjoying life
  - Fear of overmedication
  - Fear of addiction
Medical Therapy: General principles

Up to 80% of patients benefit when applied appropriately

- Mild to moderate pain
  - Non-opioids – aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol
Think beyond Analgesics!

- Other types of medication available to alleviate pain:
  - For neuropathic pain → Antidepressants, anticonvulsants
  - For inflammatory pain → Corticosteroids
  - For bone metastases → Osteoclast inhibitors (bisphosphonates, denosumab)
Analgesics are really important

- Chronic/Constant pain require long-acting opioids
  - Fentanyl patch
  - MS Contin
- Patients require breakthrough medications as well
  - MS IR
  - Oxycodone
- All have side effects, typically GI:
  - Constipation, Dry mouth, Nausea, Emesis
- All can cause sedation, sweats
  - Uncommon: CNS side effects, Respiratory depression
Medications need not be the only solution

- Complementary therapies are entirely reasonable:
  - Accupuncture
  - Yoga
  - Massage
  - Exercise
  - Hypnotherapy

Little data it controls pain itself.

Benefit in well-being.

Significant benefits in quality of life.

May help, but data are inconclusive.
What we follow:

- The four A’s of pain control:
  - **Analgesia** → How much pain relief did you achieve?
  - **Activities of Daily Living** → How well were you able to function normally (as you yourself define that)
  - **Adverse effects** → What side effects have you experienced?
  - **Aberrancy** → Are there signs that you aren’t taking the drugs as prescribed to achieve the desired outcomes?
    - DO not let this prevent you from getting help!
When medications aren’t working...

Modified WHO Analgesic Ladder

Proposed 4th Step

The WHO Ladder

Pain persisting or increasing

Step 3
Opioid for moderate to severe pain
Nonopioid Adjunct

Pain persisting or increasing

Step 2
Opioid for mild to moderate pain
Nonopioid Adjunct

Pain persisting or increasing

Step 1
Nonopioid Adjunct

Pain

Quality of Life

Invasive treatments

Opioid Delivery

Deer, et al., 1999
Radiation therapy

- Predominantly used for bone metastases
  - Up to 40-50% have full relief (Tong, Cancer 1982)
- Often shorter course (10 days/2 weeks)
- Relief increases with time
  - May take months for full impact of treatment to be evident
- Role for Radiopharmaceuticals?
  - Strontium-89 or Samarium-153 (not typically used for MBC)
Chemotherapy plus RT can be safe and effective

  - Capecitabine plus EBRT (2 week course; capecitabine 700 mg/m2 during RT), n= 29
  - Response based on pain score (continuous scale from 0 to 10) and analgesic consumption
    - Complete (score 0, no increase in analgesics) → 48% at 12 weeks
    - Partial (-2 change, no increase in analgesics) → 38% at 12 weeks
  - Overall Response rate was 86%

- Side Effects were mild:
  - Nausea (38%), Weakness (24%), Diarrhea (24%), Mucositis (10%), Hand-Foot syndrome (7%)
Don’t discount alternative treatments

- Oh B (Acupunct Med 2013; 31: 264-71)
  - 32 patients on an aromatase inhibitor with joint pain and stiffness
  - Randomization to sham versus electroacupuncture
  - Result: Detectable positive trend in both stiffness and physical function at week 12 favoring acupuncture
  - However, no objective differences in:
    - Hand grip
    - Pain severity and intensity
    - Inflammation markers
Interventional Radiology

- Often indicated with urgent/emergent complications associated with pain
  - Cord compression due to spine metastases
  - Painful metastases in the liver

- Techniques:
  - Spine stabilization procedures
  - Ablative techniques (RFA, cryoablation)
  - Bone procedures (Vertebroplasty, Kyphoplasty)
  - Neural plexus blocks
Role of surgery

- Address urgent/emergent issues
  - Cord Compression
  - Bleeding metastatic lesion
  - Pending or imminent pathologic fracture
- Must consider risks and benefits of surgery
  - Anesthesia not a benign process
Talking to your providers

- Be descriptive:
  - Character
  - Onset
  - Location
  - Duration
  - Exacerbation
  - Remitting Factors
  - Associated Symptoms
  - Severity
The Bottom Line

- No person with cancer should suffer.
- Multiple modalities are available:
  - Medications can be used thoughtfully
  - Education is necessary to choose the right drugs/combinations
- Quality of life should not suffer due to cancer, or due to the drugs
- But above all else:

Fatigue
Scope of the problem

- Fatigue is very common: over 60% report some degree
  - Can be quite debilitating
  - Can create stress for the family/caregiver
- Why does it happen:
  - Tumor progression
  - Treatment (both chemotherapy and targeted treatment)
  - Anemia
  - Pain
  - Psychological distress
  - Insomnia
  - Poor nutrition
Fatigue: What works?

- **Reverse what is reversible:**
  - Anemia
  - Insomnia

- **Medications?**
  - Psychostimulants (Methylphenidate, Modafinil)
    - Data is mixed on their impact for fatigue
  - Steroids (Dexamethasone, Methylprednisolone)
    - Short courses associated with significant improvement in fatigue
    - Side effects may be problematic
  - Megestrol acetate
    - Positive impact on fatigue and on anorexia

Yennurajalingam S and Bruera E. Cancer J 2014; 20: 319-324
Fatigue: What works?

- Reverse what is reversible:
  - Anemia:
    - Blood Transfusions (Hgb<9)
    - Erythropoietin Stimuating Agents (ESAs)
      - Benefits:
      - Risks:
        - Chavez-MacGregor, et al. (Cancer 2011): ESAs associated with higher rates of thromboembolic events, including DVT (OR 1.36, 95%CI 1.05-1.75) and any clot (OR 1.26, 95%CI 1.02-1.57)
        - Hedley, et al (Clin Ca Res 2011): Mouse models show that ESA + Chemo increased metastases
  - REMS (Risk Evaluation Management System)
    - Requires consent and monitoring for outcomes by patients and their providers

Yennurajalingam S and Bruera E. Cancer J 2014; 20: 319-324
Fatigue: What works?

- Psychostimulants (eg, Methylphenidate)


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<th>Study or Subgroup</th>
<th>Methylphenidate Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
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<td>Bruera et al, 2006</td>
<td>-9.6</td>
<td>9.8</td>
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<td>-7.5</td>
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<td>53</td>
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<td>Butler et al, 2007</td>
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<td>Lower et al, 2009</td>
<td>-10.5</td>
<td>8.82</td>
<td>54</td>
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<td>9.97</td>
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<td>-3.13 [-5.55, -0.71]</td>
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Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.39, df = 2 (P = 0.82); I^2 = 0%
Test for overall effect: Z = 2.54 (P = 0.01)

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<td>Moraska et al, 2010</td>
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Heterogeneity: Tau^2 = 0.35; Chi^2 = 1.70, df = 1 (P = 0.19); I^2 = 41%
Test for overall effect: Z = 1.21 (P = 0.23)
Fatigue: What works?

- Steroids (Dexamethasone, Methylprednisolone)
  - Yennurajalingam (J Clin Onc 2013): RCT in 84 pts, Dex (4mg BID x14d versus placebo)
  - Dexamethasone:
    - Significantly improved scores in fatigue (9 versus 3 point difference, p=.008)
    - Significantly improved quality of life at day 15
    - Significant improvement in physical distress
    - No change in overall symptom distress or psychological distress
    - No difference in adverse events
  - Enrolled patients with advanced cancer

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Fatigue: What works?

- **Megestrol acetate**
  - 84 patients with advanced solid tumors (not hormone responsive):
    Megestrol 160 TID for 10 days versus placebo → Washout → Alternate treatment
  - Megestrol acetate given to 53 evaluable patients. Results:
    - Significant improvement in appetite
    - Significant improvement in activity
    - Significant improvement in well-being
    - No change in nausea, nutritional parameters, energy intake, or quality of life

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Fatigue? What else...

- Alternative therapies: Ginseng and Guarana reported to have a positive impact.

Distress plays a major role. Seek palliative care.

- Other modalities that address mind-body connection:
  - Yoga
  - Meditation
  - Sleep hygiene
Insomnia
Scope of the problem

- Very common: Over 50% of patients have disturbed sleep patterns
  - Difficulty “staying” asleep
  - Difficulty “getting to” sleep
- Insomnia can be secondary to:
  - Pain
  - Worry
  - Vasomotor symptoms
Insomnia is a rarely an isolated factor

- Physical Symptoms
  - Breathlessness, Cough, Hiccups (Glynn J, et al. BMC Support Pall Care 2014; S1: 156)

- Psychiatriac conditions
  - Anxiety and/or Depression associated with more nightmares, less restorative sleep (Mercadante S, et al. Support Care Ca 2004; 12: 355-9)

- Environmental issues
  - Loud or active stimuli, bright lights, tv, books
  - Children
  - Pets
For women with metastatic disease

- Insomnia can be tied to distress:
  - “I’m afraid of sleeping because I might not wake up.”
  - “I just don’t want to miss anything.”
- Insomnia can be a manifestation of disease progression:
  - More time somnolent
  - More time bed-bound
  - Less active
- Secondary to Medications
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal

- CBT consists of:
  - Sleep restriction
  - Stimulus control
  - Sleep hygiene
  - Cognitive restructuring
  - Relaxation training
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal

- CBT consists of:
  - Sleep restriction → Addresses mismatch between “Opportunity” and “Ability” for sleep
  - Stimulus control
  - Sleep hygiene
  - Cognitive restructuring
  - Relaxation training
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal

- CBT consists of:
  - Sleep restriction
  - Stimulus control → Addresses the non-sleep behaviors in the bedroom
  - Sleep hygiene
  - Cognitive restructuring
  - Relaxation training
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal

- CBT consists of:
  - Sleep restriction
  - Stimulus control
  - Sleep hygiene → Promotes behavior and practice that promote sleep
    - Reserve the bed for sleep and sex
  - Cognitive restructuring
  - Relaxation training
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal
- CBT consists of:
  - Sleep restriction
  - Stimulus control
  - Sleep hygiene
  - Cognitive restructuring → Identification of thoughts and beliefs that might contribute to pre-sleep arousal and performance anxiety
  - Relaxation training
Insomnia: Role of Cognitive Behavioral Therapy

- Insomnia associated with cognitive, physiologic, and cortical hyperarousal
- CBT consists of:
  - Sleep restriction
  - Stimulus control
  - Sleep hygiene
  - Cognitive restructuring
  - Relaxation training → Aims to reduce arousal and calm the mind
Does CBT work?

- Evidence of benefit exists outside of cancer populations
- No studies in patients with metastatic disease
- Trials in patients after cancer treatment suggest CBT is effective
- More data are needed for CBT in metastatic breast cancer
Managing Insomnia: Helpful Hints

- Address sleep-wake cycles:
  - Stay physical activity
  - Get out of the house: Natural light is important
  - Continue with familiar routines
What about medications?

- Anti-depressants - Use of those with sedative properties
  - Doxepin (6 mg)
  - Trazodone (12-25 mg)
- Benzodiazepines (limit to 2 weeks or shorter- rapid tolerance)
- Not recommended:
  - Diphenhydramine - Side effects can be problematic (dry mouth, delirium, decreased cognitive function)
  - Melatonin - No impact for insomnia; preparations vary
What I have learned about living

Pragmatism
Realism
Optimism
**PRAGMATISM**

**pragmatism**  [prag-muh-tiz-uh m]  

**noun**
1. character or conduct that emphasizes practicality.
2. a philosophical movement or system having various forms, but generally stressing practical consequences as constituting the essential criterion in determining meaning, truth, or value.

Compare **pragmaticism**, **instrumentalism**.

**Origin:**
1860–65; pragmat(ic) + -ism
Pragmatism

http://osopher.files.wordpress.com/2012/07/pragmatist.gif
Because no one else has to walk in your shoes
Being pragmatic means prioritizing

When facing cancer, it’s all about you...
And those you love.

http://media.salon.com/2013/11/nj-governor.jpeg-1280x960.jpg
REALISM

real·ism [ree-uh-liz-uh m]  
noun
1. interest in or concern for the actual or real, as distinguished from the abstract, speculative, etc.
2. the tendency to view or represent things as they really are.
Realism

Prepare for an uncertain present, and an even more uncertain future.
OPTIMISM

optimism
/ˈɑːptəˌmizəm/

noun

1. hopefulness and confidence about the future or the successful outcome of something.
   "the talks had been amicable, and there were grounds for optimism"
   synonyms: hopefulness, hope, confidence, buoyancy, cheer, cheerfulness, good cheer, sanguineness, positiveness, positive attitude

2. the doctrine, esp. as set forth by Leibniz, that this world is the best of all possible worlds.
Optimism=Hope

Optimism is a Clinical Trial

Don S Dizon @drdonsdizon
People who participate in clinical trials are not guinea pigs. They are trailblazers! Partners as we fight for better. #hcsm

25 Jul

8 RETWEETS 3 FAVORITES

10:33 AM - 25 Jul 13 · Details
Hope for better is what drives clinical research... on all fronts.
Diagnosed with #breastcancer? Eat cake and have sex. @drdonsdizon is my kind of oncologist. #YSC2015
Conclusions

- Side effects are common
- Toxicities can be treated
- Goals of care: Cancer control is as important as quality of life
Thank you