DEPRESSION IN CANCER PATIENTS

Maria Die Trill, PhD
Coordinator, Psycho-Oncology Unit
Hospital Universitario Gregorio Marañón
Madrid, Spain
The prevalence of anxiety and depression in patients with cancer has been reported to be on average 25%.

They significantly affect patients’ quality of life.

They generally remain underdiagnosed and undertreated in the cancer population as well as in other medical illnesses\(^1\) despite the great degree of suffering they impose on cancer patients.

\(^1\) Gregory et al., General Hospital Psychiatry, 1992; 14:36-42
A characteristic emotional response to cancer includes:

- Initial shock and disbelief

Confusion with symptoms of anxiety and depression:
- irritability,
- altered appetite and sleep patterns,
- difficulty to concentrate,
- Difficulty in carrying out usual daily activities,
- fears about the future

Symptoms begin to resolve after several weeks with family and social support as well as with the outline, by the oncologist, of a treatment plan that offers hope and reduces part of the uncertainty.
NORMAL REACTIONS TO CANCER

However, multiple losses, beginning with the loss of one´s health upon cancer diagnosis (followed by loss of: body image, professional role, family roles, social roles, loss of abilities and capacities, etc), result in grief reactions and sadness that often accompany the cancer patient throughout the disease process.
Anxiety and depression may persist in time, non-adaptively, requiring specialized attention and/or treatment.

Both may be present although only one may predominate.

Because they are different clinical entities, they will be dealt with separately in this presentation.
According to WHO:

- Depression is considered one of the most common psychiatric disorders in the world, affecting over 120 million people worldwide.
- Depression is among the leading causes of disability worldwide.
- Fewer than 25% of those affected have access to effective treatments despite the fact that it can be reliably diagnosed in Primary Care Settings.
- At its worst, depression can lead to suicide, a tragic fatality associated with the loss of about 850,000 lives every year.

http://www.who.int/mental_health/management/depression/definition/en/
DEPRESSION IN CANCER PATIENTS

PREVALENCE

- Reported prevalence rates of depression among cancer patients can be as high as 38% for major depression and 58% for depression spectrum syndromes\(^1\)

- Differences in reported prevalence rates are due to differences in assessment methods, as well as differences in stage and tumor site, among others

\(^1\)Massie MJ, J Natl Cancer Inst Monogr 2004 (32):57-71
# DEPRESSION IN CANCER PATIENTS

## PREVALENCE

<table>
<thead>
<tr>
<th>Authors</th>
<th>Cancer Site Sample Size</th>
<th>Diagnostic Method</th>
<th>Affective Disorders</th>
<th>Adjustment Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derogatis et al., 1983, JAMA</td>
<td>Mixed 215</td>
<td>DSM-III (Diagnostic Manual of Mental Disorders – III Edition)</td>
<td>6%</td>
<td>32%</td>
</tr>
<tr>
<td>Grassi et al., 1989, Gen Hosp Psych</td>
<td>Mixed 196</td>
<td>Hamilton Rating Scale for Depression+Illness Behaviour Questionnaire+Interview HADS (Hospital Anx &amp; Depression Scale)</td>
<td>26%</td>
<td>46%</td>
</tr>
<tr>
<td>Razavi et al., 1990, Brit J Psych</td>
<td>Mixed 128</td>
<td>DSM-III HADS</td>
<td>26%</td>
<td>46%</td>
</tr>
<tr>
<td>Prieto et al., 2002, JCO</td>
<td>Hematology 220</td>
<td>DSM-IV</td>
<td>13.2%</td>
<td>22.7%</td>
</tr>
<tr>
<td>Kissane et al., 2004 Aust NZJ Psych</td>
<td>Early &amp; advanced breast cancer 503</td>
<td>DSM-IV</td>
<td>8% (advanced) 11.9% (early)</td>
<td>23% (advanced) 24.8% (early)</td>
</tr>
</tbody>
</table>

Based on Grassi L and Uchitomi Y [www.ipos-society.org/education](http://www.ipos-society.org/education) and [www.e-eso.net](http://www.e-eso.net)
### Prevalence by Cancer Site

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Percentage Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>33% - 50%</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>22% - 57%</td>
</tr>
<tr>
<td>Breast</td>
<td>13% - 46%</td>
</tr>
<tr>
<td>Lung</td>
<td>11% - 44%</td>
</tr>
<tr>
<td>Colon</td>
<td>13% - 25%</td>
</tr>
<tr>
<td>Gynecological</td>
<td>12% - 23%</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>8% - 19%</td>
</tr>
<tr>
<td>Gastric</td>
<td>11%</td>
</tr>
</tbody>
</table>

DEPRESSION IN CANCER PATIENTS

RISK FACTORS

- Young age
- Personality factors (pessimism, tendency to repress feelings such as anger)
- Social isolation and lack of support
- Poverty
- Previous negative experience with cancer in the family or personal experiences of physical illness
- Advanced disease (metastatic or terminal illness)
- Physical deterioration
- Tumor location (lung, pancreatic, head and neck)
- Presence of physical symptoms from cancer, especially if not well controlled
- History of multiple losses
- Previous psychiatric disorders, especially episodes of major depression or suicide attempts
- History of substance abuse
THE DIAGNOSIS OF DEPRESSION IS A CHALLENGE IN THE CANCER SETTING

- Depressive symptoms occur along a spectrum that ranges from sadness to major affective disorder.

- Mood change may be difficult to assess in a patient who feels his life threatened by disease.

- Diagnosis of depression in physically healthy individuals depends heavily on the presence of somatic symptoms (anorexia, fatigue, insomnia & weight loss).

  Somatic symptoms are indicators of little value in cancer patients: they are common to cancer and depression.
MAJOR DEPRESSIVE EPISODE: DIAGNOSTIC CRITERIA (I)

A) At least 5 of the 9 symptoms below for the same 2 weeks or more, most of the time almost every day, and this is a change from his prior level of functioning. One of the symptoms must be either (a) depressed mood, or (b) loss of interest:

a. Depressed mood
b. Loss of interest or pleasure in most or all activities
c. Weight loss or gain
d. Insomnia or hypersomnia
e. Agitated or slowed down behavior
f. Feeling fatigued or reduced energy
g. Thoughts of worthlessness or extreme guilt (not about being ill)
h. Reduced ability to think, concentrate or make decisions
i. Frequent thoughts of death or suicide

MAJOR DEPRESSIVE EPISODE: DIAGNOSTIC CRITERIA (I)

B) Symptoms don’t indicate a mixed episode

C) Symptoms cause great distress or difficulty in functioning at home, work or other

D) Symptoms are not caused by substance use (alcohol, drugs) or a medical condition

E) Symptoms are not due to normal grief for the loss of a loved one; they persist for more than 2 weeks, or they include great difficulty in functioning, frequent thoughts of worthlessness, thoughts of suicide, psychotic symptoms, or psychomotor retardation
DEPRESSION IN CANCER PATIENTS

DIAGNOSIS

Four approaches have been described in the assessment of depression in the medically ill:

1) **INCLUSIVE APPROACH**: Counts all symptoms of depression, whether or not they may be secondary to physical illness. High sensitivity, low specificity; does not focus on etiology

2) **ETIOLOGIC APPROACH**: Counts a depressive symptom only if it is presumed not secondary to physical illness

3) **EXCLUSIVE APPROACH**: Eliminates symptoms such as anorexia and fatigue, which can be secondary to cancer, and employs other depression criteria. Increases specificity, lowers sensitivity which may result in lower prevalence and underdiagnosis.

4) **SUBSTITUTIVE APPROACH**: Replaces indeterminate symptoms such as fatigue (frequently secondary to physical illness) with cognitive symptoms such as indecisiveness, brooding and hopelessness.¹

---

¹Endicott J, Cancer 1984, 53: 2243-2248

DEPRESSION IN CANCER PATIENTS

DIAGNOSIS

- The diagnosis of depression in the oncology setting should depend on psychological not somatic symptoms, in cancer patients:
  - dysphoric mood,
  - feelings of helplessness and hopelessness,
  - loss of self-esteem,
  - feelings of worthlessness or guilt,
  - anhedonia,
  - thoughts of wishing for death or suicide

1Massie MJ et al., Handbook of Psycho-oncology: Psychological Care of the Patient with Cancer, New York, Oxford University Press, 1989; 273-282
DEPRESSION IN CANCER PATIENTS

IMPORTANT DIAGNOSTIC CONSIDERATIONS

In order to design effective treatments differential diagnosis should include:

- Normal reactions to illness and loss
- Adjustment disorders with depressed and/or anxious mood
- Determine whether organic factors underlie the depressive syndrome: the evaluation of every depressed cancer patient must consider medical, endocrin, metabolic and neurological factors

Depressive syndromes caused by the direct physiologic effects of cancer are called **MOOD DISORDERS DUE TO A GENERAL MEDICAL CONDITION**
MOOD DISORDERS DUE TO A GENERAL MEDICAL CONDITION

DIAGNOSTIC CRITERIA*

A) A person has significant disturbance in mood that includes either (or both):
   - Depressed mood or significantly reduced level of interest or pleasure in most or all activities
   - Mood that is euphoric, heightened or irritable

B) The person’s symptoms are directly related to the presence of a medical condition (which should be identified)

C) Another disorder does not better explain the mood disturbance

D) The mood condition is not present only when a person is delirious

E) Symptoms are a cause of great distress or difficulty in functioning at home, work or other important areas

## MEDICAL CONDITIONS ASSOCIATED WITH DEPRESSION IN CANCER PATIENTS

<table>
<thead>
<tr>
<th>ENDOCRINE ABNORMALITIES</th>
<th>INFECTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cushing’s Disease</td>
<td>Epstein-Barr virus</td>
</tr>
<tr>
<td>Addison’s Disease</td>
<td>Encephalitis</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>HIV</td>
</tr>
<tr>
<td>Hypopituitarismo</td>
<td>Influenza</td>
</tr>
<tr>
<td>Thyroid dysfunction (hypo or hyperthyroidism)</td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>Syphilis</td>
</tr>
<tr>
<td></td>
<td>Hepatitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MEDICATIONS</th>
<th>ONCOLOGICAL DISEASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Tumors of the SNC</td>
</tr>
<tr>
<td>Interferon</td>
<td>Lung Cancer</td>
</tr>
<tr>
<td>Interleukin 2</td>
<td>Pancreatic Cancer</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Methyldopa</td>
<td></td>
</tr>
<tr>
<td>Reserpine</td>
<td></td>
</tr>
<tr>
<td>Some antibiotics</td>
<td></td>
</tr>
<tr>
<td>Some chemotherapy</td>
<td></td>
</tr>
<tr>
<td>agents (Vincristine, L-Asparginase, Procarbazine, Vinblastine)</td>
<td></td>
</tr>
</tbody>
</table>

# MEDICAL CONDITIONS ASSOCIATED WITH DEPRESSION IN CANCER PATIENTS

## Neurological Disorders
- Cerebrovascular Diseases
- Huntington’s Disease
- Alzheimer’s Disease and other forms of Dementia
- Parkinson’s Disease
- Multiple Sclerosis
- Subaracnoid Hemorrhage

## Metabolic Disorders
- Hyponatremia
- Hypokalemia
- Hyperkalemia
- Folic Acid Deficiency
- Pellagra
- Uremia
- Wilson’s Disease

## Other Medical Conditions
- Systemis Lupus Erithematosus
- Rheumatoid Arthritis
- Alcoholism
- Uncontrolled Pain
- Anemia
- Hypertension

PSYCHOMETRIC INSTRUMENTS IN THE MEASUREMENT OF DEPRESSION

- Beck Depression Inventory\(^1\)
- The Hospital Anxiety and Depression Scale (HADS) \(^2\)
- The Brief Symptom Inventory- 18 (BSI-18)- Depression Subscale\(^3\)
- Profile of Moods State – POMS\(^4\)
- The Distress Thermometer (DT)\(^5\)

---

\(^1\) Beck A, *Depression Inventory*, Philadelphia, PA, Center for Cognitive Therapy, 1961
\(^3\) Derogatis LR & Melisaratos N, Psychological Medicine, 1983, 13:595-605
\(^4\) McNair D. *et al.*, *Education and Industrial Testing Service, San Diego, CA*. 1971
\(^5\) Holland J & Bultz B, National Comprehensive Cancer Network, . 2007, 5:3-7
A single-item question:

“Have you been depressed, most of the day, nearly every day, for the past two weeks or more?”

was able to identify all cancer patients diagnosed as depressed using the Research Diagnostic Criteria.

Chochinov HM et al., Am J Psychiatry 1997; 154:674-676
Vast literature showing the association between depression and an increase in pro-inflammatory cytokines (e.g., interleukin-1, interleukin-6, and tumor necrosis factor alpha)

Cancer itself and its treatment (medications and surgery) in general can be responsible, together with the individual stress response, for the production of pro-inflammatory cytokines which may contribute to the development of depressive symptoms

Riba M. and Grassi L., 2008 World Psychiatric Association, WPA Educational Programme on Depressive Disorders – Vol. 2 Physical Illness and Depression Disorders in Physical Illness, 2008: 73-87
CONSEQUENCES OF DEPRESSION IN CANCER PATIENTS*

- Increased length of stay in hospital\(^1\)
- Maladaptive coping and abnormal illness behavior\(^2\)
- Reduced adherence to treatment\(^3\)
- Reduced efficacy of chemotherapy in breast cancer patients\(^4\)
- Reduced quality of life\(^5\)
- Increased psychosocial morbidity within in the family
- Complicated family relations and patterns of communication within the family
- Increased risk of suicide\(^6\)

\(^1\)Prieto JM et al., J Clin Oncol 2002; 20:1907-1917
\(^2\)Grassi L. et al., Psycho-Oncology, 1993; 2 (1): 11-20
\(^3\)Diamate et al., Arch Intern Med 2000; 160:2101-2117
\(^4\)Walker LG et al., British Journal of Cancer 1999; 80: 262-268
\(^5\)Parker KP. et al., Health and Quality of Life Outcomes, 2003:1-68
\(^6\)Hem E. et al., J Clin Oncol 2004; 22: 4209-4216
Mary is a 19 year old diagnosed with treatment-resistant lymphoma.

Treatment protocols have been unable to achieve periods of prolonged remission. Her condition is terminal, although death is not imminent.

When she is not in remission she suffers intense uncontrolled pain. The amount of analgesia required to control her pain leaves her “…too drugged to do anything” according to her.

During her last hospitalization she mentioned ending her life if she had further uncontrolled pain episodes in the future.

She appears in the outpatient clinic today without previous appointment. She looks for various staff members who had cared for her to thank them. As she gives a few personal belongings to staff members to whom she felt close, one of them realizes that Mary has enough analgesic medication at home to end her life.

What actions would you take?
CANCER AND SUICIDE: A CLINICAL VIGNETTE

1) Empathize with patient

2) Validate patient’s feelings: “Many cancer patients have transient thoughts of suicide or desire death, especially if they feel hopeless”

3) Maintain a supportive therapeutic relationship

4) Adequate pain control (and other physical symptoms)

5) Assessment of current emotional state:
   - Is the patient depressed? Is there a wish to have ultimate control over intolerable symptoms? Is suicide an alternative to suffering?
Psychiatric history:

- Previous depressive episodes? Suicide attempts? Suicide in family?

Is there a defined PLAN, INTENTION and what is the VIABILITY of such plan? (24-hour companion if needed)

What has kept the patient from committing suicide?

What are the patient’s support systems?

- What type of family, social relationships does she maintain?

What are the patient’s belief systems?
CANCER AND SUICIDE: A CLINICAL VIGNETTE

- What is her sense of meaning in life?
- What meaning do death and pain have for the patient?
- What are the patient’s interests in life?: Help maximize values
- Convey that things can be done to improve the quality of life even in the context of a poor prognosis
- Involve and evaluate patient’s family
CANCER AND SUICIDE

- Suicide has been reported to be 1.5-2 times higher in cancer patients than in the general population\(^1\)

- Among terminally ill patients with cancer the request for euthanasia is about 4 times higher in patients with depression than in those without depression\(^2\)

- Desire for death in terminally ill cancer patients is frequent, and has been shown to be associated to depression and is transitory\(^3\)

---

\(^1\) Hem E. *et al.*, J Clin Oncol 2004; 22: 4209-4216
\(^3\) Chochinov HM *et al.*, Am J Psychiatry 1995; 152:1185-1191
## Risk Factors

- Family/personal history of suicide or suicide attempts
- **Psychiatric history:**
  - Delirium, depression with hopelessness, psychotic features, irrational thinking, loss of control and impulsivity
- Uncontrolled pain or other symptoms, advanced disease
- Cancer site (head & neck, lung, gastrointestinal)
- Poor social support
- Older age
- Gender: Males
## DEMORALIZATION SYNDROME IN CANCER PATIENTS

### DIAGNOSTIC CRITERIA

- Affective symptoms of existential distress including hopelessness or loss of meaning and purpose in life
- Pessimism, helplessness, a sense of being trapped, personal failure or lacking a worthwhile future
- Absence of motivation to cope differently
- Associated features of social alienation or isolation and lack of support
- These phenomena persist for more than two weeks, with fluctuation in emotional intensity
- A major depressive episode or other psychiatric disorder is not present as the primary condition

Kissane DW *et al.*, Journal of Palliative Care, 2001; 17:12-21
DEMORALIZATION SYNDROME IN CANCER PATIENTS

Occurs in at least 20% of patients who do not meet DSM-IV criteria for the diagnosis of a mental disorder

TREATMENT OF DEPRESSION IN CANCER PATIENTS

Combination of:

- Control or elimination of potential organic causes of depression when possible
- Psychotherapy
- Pharmacotherapy
- Working with the patient’s family and staff members
Adjust psychotherapeutic modality to patient’s needs and disease stage

Crisis-intervention models involving an active therapeutic role

Educational interventions: Clarifying information, explaining emotional reactions to patient and family

Cognitive techniques to help correct misconceptions and exacerbated fears
Interventions directed to enhance the spiritual aspects in advanced disease and dying

Interventions designed to maintain patients’ dignity

Cognitive-Behavioral Interventions

GROUP THERAPIES: Supportive-Expressive Group Psychotherapy; Cognitive-Existential Group Therapy; Multidimensional structured group psychotherapy

1 Breitbart W., Support Care Cancer, 2002; 10(4):272-280
2 Chochinov HM et al., J Clin Oncol, 2005; 23 (24): 5520-5525
3 Greer S. et al., British Medical Journal, 1992; 304 (6828):675-680
5 Kissane DW, et al., J Clin Oncol, 2004; 22(21): 4255-4260
PHARMACOTHERAPY FOR DEPRESSION IN THE CANCER SETTING: General Rules

CHOOSE THE DRUG DEPENDING ON:

- Which is the safest drug or which has the fewest side-effects for the cancer patients
- What the characteristics of the depressive episode are
- Which is the best way of administration for a particular patient (pills vs. liquid vs. parenteral)
- The most recent scientific advances in the treatment of depression

Riba M. and Grassi L., 2008 World Psychiatric Association, WPA Educational Programme on Depressive Disorders – Vol. 2 Physical Illness and Depression Disorders in Physical Illness, 2008: 73-87
PHARMACOTHERAPY FOR DEPRESSION IN THE CANCER SETTING: General Rules

- Start dose according to patients’ condition (usually half dose for a few days, then titrate)
- It would be important to wait for the effects of the drugs (latency: usually 4 weeks)
- Provide continued treatment for 6-9 months (more if depression or depressive episode are recurrent)
- Discontinue gradually by tapering the dose and followup
- Monitor on a continued basis to watch for potential drug interactions that may occur between antidepressants and certain chemotherapeutic agents

Riba M. and Grassi L., 2008 World Psychiatric Association, WPA Educational Programme on Depressive Disorders – Vol. 2 Physical Illness and Depression Disorders in Physical Illness, 2008: 73-87
STAFF INTERVENTIONS TO REDUCE DEPRESSIVE SYMPTOMS IN CANCER PATIENTS

- Training in communication skills
- Use of simple screening instruments to detect depressive symptoms
- Explain to patient and family that depressive symptoms can be treated
- Provide continuity in patient care
- Monitor patient’s sense of wellbeing and needs in a continued manner along the disease continuum
- Work with the family: Provide basic caretaking guidelines and support for family members
- Explore one’s own attitudes towards illness, suffering, death and dying
STAFF INTERVENTIONS TO REDUCE DEPRESSIVE SYMPTOMS IN CANCER PATIENTS

- Increase patient’s perception of control:

  - Provide options
  - Inform adequately
  - Anticipate patient’s needs
  - Facilitate adaptive coping mechanisms
  - Respect defense mechanisms as long as they don’t interfere with treatment administration
  - Normalize patient’s feelings
  - Help maintain realistic hope
  - Remain available to listen to patient’s worries and fears
Combination of psychological interventions and pharmacotherapy tailored to specific patient needs is the most effective approach.

Guidelines for screening, diagnosis and psychological and pharmacological treatment are available.*

Holland JC & Bultz BD, J Natl Compr Canc Netw, 2007; 5:3-7; NCCN, 2008
THANK YOU!