

Some Issues on Cancer Epidemiology – Prevalence of Comorbid Mental Disorders

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Cancer diseases affect approximately 10 million people only in Europe. As a result of the demographic development; their prevalence is expected to double during the next 10 years. Cancer is a leading cause of death. It accounted for eight million deaths worldwide (around 15% of all deaths) in 2010 (38% more than in 1990) Meanwhile the number of survivors continues to grow, not just because of earlier detection and treatment, but also because of revolutionary new therapies. About 9 million Americans of all ages are living with a current or past diagnosis of cancer. For many individuals, this changes the landscape from a terminal illness to more of a chronic illness with periods of remission and exacerbation of symptoms. This perspective on neoplasms has broadened the scope of care from treating the disease alone to managing cancer-related symptoms at different stages of the disease trajectory including mental disorders.

Cancer-related distress was depicted as a “multifactorial unpleasant emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment” by the National Comprehensive Cancer Network of the US. Distress is related to a lower quality of life, treatment compliance and efficacy, higher mortality, and a higher risk of suicide. Therefore, clinicians should make efforts to promote patients’ quality of life and decrease medical costs by alleviating patient distress.

The NCCN clinical practice guidelines in oncology distress management have, since 1997, advocated routine screening for distress in cancer patients. Similar to the model of using pain for the 5th vital sign, the use of distress for the 6th vital sign was recommended in 2005. It was reaffirmed with International Federation of Psycho-oncology Societies. To begin, for adults diagnosed with cancer and other chronic illnesses, the “risk of psychological disability” is nearly six times higher than for adults not living with cancer. Given the prevalence of psychological disorders in cancer patients and their potential negative effects on outcomes, in the absence of adequate data, neither physicians nor patients can accurately predict the mental health impact of cancer diagnosis and treatment, thereby potentially limiting a patient’s autonomy. Comprehensive cancer care includes not only medical procedures but should also include psychosocial support if needed. Comprehensive patient-centered care in oncology has been emphasized in international guidelines and standards, implying cancer prevention and early detection as

well as high quality evidence-based medical treatment, rehabilitation and palliative care.

The issue of whether psychological care should be delivered by mental health professionals has been often debated and specifically whether hospitals should employ psycho-oncologists to deliver such care remains contested. Patients with cancer have a high rate of comorbid psychiatric disorders as well as nonspecific psychological distress. Having a clear understanding of the prevalence of common mental disorders in patients with cancer is important not only from the point of planning services geared towards holistic care but also because there is evidence to indicate that untreated psychiatric comorbidities in such patients have a significant impact on disability and quality of life and they tend to worsen if not treated adequately.

Empirical studies investigating the prevalence of mental disorders and the frequency of psychosocial burden in cancer patients have gained increasing importance during recent years. This research is of particular significance for the development and implementation of psychosocial support offers within the health care system. The prevalence of common mental disorders among people with cancer varies widely in the published literature. Recent meta-analytical evidence indicates that the overall prevalence of mental disorders among cancer patients ranges from 9.8% to 38.2% in various cancer settings. In an international review including 94 interview-based studies, the prevalence of depression by DSM or ICD criteria in oncological and hematological settings (70 studies) was 16.3%; the prevalence of dysthymia was 2.7%; the prevalence of adjustment disorder was 19.4%; and the prevalence of anxiety disorders was 10.3%. However, combination diagnoses were prevalent among up to 38.2% of patients. The prevalence of depression in palliative-care settings (24 studies) was 16.5%; the prevalence of adjustment disorder was 15.4%; the prevalence of anxiety disorders was 9.8%; and combination diagnoses were prevalent among up to 29.0% of patients. Accordingly, Singer et al. observed prevalence rates up to 32% among cancer patients in acute hospitals.

However, few trials have examined the prevalence of mental disorders in cancer patients taking into account the wide spectrum of mental disorders including substance abuse or somatoform disorders, different health care settings as well as different tumor entities and disease stages for both genders. Prevalence rate of any mental disorder varies widely among patients with different tumor

types. The highest prevalence rates in patients with breast cancer, head and neck cancer, and malignant melanoma. Dysfunction of speech and articulation and facial disfigurement are the main reasons for the distress that set head and neck cancer patients apart from other cancer patients. The lowest prevalence rates were found in patients with pancreatic cancer, stomach or esophageal cancer, and prostate cancer. We further detected different patterns of mental disorders among patients with different tumor entities. Several known risk factors might contribute to these findings, including different disease stages, treatment phases, and medical conditions, such as the presence of pain and functional impairments. The wide range of prevalence rates might also be at least partially explained by demographic characteristics such as sex, age, and educational differences, as well as socioeconomic and psychosocial factors including coping mechanisms.

The presence of a mental disorder or psychological symptom burden is not necessarily associated with subjective needs of patients for professional psychosocial support and the utilization of relevant offers. Although a variety of psychological interventions have been shown to be effective in the reduction of psychosocial symptom distress and the improvement of quality of life, however, improving distress screening and the access of cancer patients to adequate psychosocial care remains a critical concern. Thus, epidemiological data about mental comorbidity, psychological symptom burden and supportive care needs are essential for the evidence-based implementation of psychosocial support offers within oncological health care.

Mental health effects should be evaluated at diagnosis, throughout treatment and the post-treatment phase, and in survivorship. The psychopathological status of persons with cancer often remains undetected and untreated [1-12]. Approximately, only a third of severely distressed persons with cancer are recognized by their oncologists, and only 15%-50% of them are referred to specialized services. The possible reasons for the limited referral rate are a low level of psychological awareness among medical doctors, the stigma attached to psychiatric disease by clinicians, and the traditional idea that a clinician's main mission is saving life rather than dealing with psychological distress. We could improve the referral rates through promotion in formal hospital meetings and offering website learning to the physicians. Furthermore, many cancer inpatients have severe psychosocial problems (e.g., lack of social support). These failures may have detrimental effects on the course of illness and quality of life, they contribute to the treatment gap - the difference between the true and treated prevalence of mental health disorders among persons with cancer). The difference between true and the treated prevalence rates for psychiatric disorders and distress is generally substantial. It exceeds 50% worldwide; fewer than 50 percent of cancer patients with psychiatric disorders are identified and referred for appropriate care, in the least resourced countries it approaches 90% for common mental disorders. A WHO review of 37 studies worldwide estimated that the treatment gap for major depression and dysthymia reached 56%. The frequent failed recognition of mental problems due to objective barriers, e.g., availability and accessibility of services, and subjective factors, e.g. stigma, may lead to the treatment gap.

This treatment gap is frequent, even for people with cancer. For example, a community study conducted in the US showed that only 35% of cancer survivors who reported mental problems accessed

specialized services. Another study, conducted among persons with cancer treated in a public hospital, showed that only 12% of those diagnosed with depression received antidepressant medications, and even a smaller percentage (5%) saw a mental health counselor. Muriel et al. found that while oncologists estimated that over a third of their patients experience psychological distress needing intervention, only half of them reported making a referral to the mental health services.

Derogatis et al. reported the prevalence of psychiatric disorders in a random population of 215 hospitalized and ambulatory cancer patients at three major American cancer centers and revealed that almost half of the cancer patients were diagnosed as having a such disorder. Each patient was assessed in a common protocol via a psychiatric interview and standardized psychological tests. Results indicated that 47% of the patients received a *DSM-III* diagnosis, with 44% being diagnosed as manifesting a clinical syndrome and 3% with personality disorders. Approximately 68% of the psychiatric diagnoses consisted of adjustment disorders, with 13% representing major affective disorders (depression). The remaining diagnoses were organic mental disorders, personality disorders, and anxiety disorders. On psychiatric consultation of 546 cancer patients there was revealed that 54% of the referrals were diagnosed as having adjustment disorders, 15% delirium and 9% major depression. The results showed elevated risk of comorbid common mental health disorders among persons who at the time of the study were undergoing treatment for cancer across all countries studied compared with either cancer survivors or cancer-free respondents. Regarding cancer site, the proportion of adjustment disorders and major depression was highest among patients with pancreatic cancer, while the proportion of delirium was highest in patients with liver cancer.

In a meta-analysis of studies published from 1980 to 1994, the authors concluded that the prevalence of all mental disorders, but depression in cancer patients, was the same as in the general population. However, this meta-analysis was on the basis of studies that used screening instruments instead of comprehensive clinical interviews, which remain the gold standard for diagnosing mental disorders. Validated and comprehensive instruments internationally regarded as being valid instruments for the assessment of mental disorders are the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders (DSM) (SCID), the Composite International Diagnostic Interview (CIDI), the Clinical Interview Schedule (CIS), and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN).

For patients, caregivers, and families, going through cancer can be a devastating experience with many stresses and emotional upheavals. Because cancer is potentially life threatening, the psychological impact of its diagnosis on patients has been an important aspect of clinical oncology. Recent standards in cancer care require that all patients with cancer be screened for psychological distress. Cancer patients often have delirium particularly ones with far-advanced disease. Delirium has been defined as a disorder of global cerebral function characterized by disordered awareness, attention, and cognition. The term *acute confusional state* has also been used to describe this syndrome, which is, in addition, associated with behavioral manifestations. Occurrence rates range from 28% to 48% in patients with advanced cancer on admission to hospital or hospice, and approximately 90% of these patients will experience delirium

in the hours to days before death, the condition sometimes referred to as terminal restlessness probably represents a terminal delirium.

Among the nosological forms of comorbid mental pathology in cancer patients, affective disorders (depression and anxiety) predominate. This predominance is most distinct in long-term cancer survivors. Cancer-related depression can exist before the diagnosis of cancer or may develop after the cancer is identified. An interaction between genetic predisposition and life history appear to determine a person's level of risk. Episodes of depression may then be triggered by stress, difficult life events, side effects of medications, or other environmental factors. Whatever its origins, depression can limit the energy needed to keep focused on treatment for other disorders, such as cancer. The reported prevalence of depressive symptoms in cancer has been variable, depending on cancer type and stage, timing and method of assessment, diagnostic criteria applied, and demographics of the population studied. The mean prevalence of depression using diagnostic interviews is around 13% and using all assessment methods it varies from approximately 4 to 49%. This wide variation is due to several factors including the treatment setting, type of cancer included and method used to screen for symptoms (e.g. interview by trained psychiatrist or self-report instrument). The estimated prevalence of depression was found to be 3% in patients with lung cancer, compared to 31% in patients with cancer of the digestive tract, when diagnostic interviews were used. A meta-analysis of 15 studies meeting a number of quality criteria, including the use of diagnostic interviews, found that the estimated prevalence of depression varied across treatment settings (5 to 16% in outpatients, 4 to 14% in inpatients, 4 to 11% in mixed outpatient and inpatient samples, and 7 to 49% in palliative care). This wide variability can be explained by the lack of consensus regarding the appropriate diagnostic criteria to utilize in the setting of advanced illness, as well as by the differences in various assessment methods. There is no universal standardized tool, which is recommended for depression screening in patients with cancer, and the method used is likely to differ depending on the treatment setting. A meta-analysis of screening and case finding tools for depression in cancer settings identified 63 studies that used 19 different screening tools for depression. Common screening methods for depression include semi-structured diagnostic interviews, the Hospital Anxiety and Depression Scale - depression subscale and Center for Epidemiologic Studies Depression Scale (CES-D), which are designed to measure the severity of depressive symptoms.

Major depressive disorder is present in 16% of individuals with cancer, while minor depression and dysthymia occur in about 22% of patients; these presentations are milder, but also are associated with significant distress. Clinical depression & depressive symptoms have been reported to increase mortality and reduce survival in different populations.

As to cancer patients, one study's authors have presented such comparison: about 25% of people with cancer have depression, only 2% of them receive antidepressant medication. The impressive comparison, isn't it? Persons with cancer, their families and friends, and even their physicians and oncologists (physicians specializing in cancer treatment) may misinterpret depression's warning signs, mistaking them for inevitable accompaniments to cancer. Depressive syndromes are highly correlated with a reduced quality of life, increased difficulty managing the course of disease, decreased adherence to treatment, and earlier admission to inpatient or hospice

care. Psychological distress is a major cause of concern among patients with advanced cancer. A meta-analysis revealed that minor or major depression increases the rate of mortality among people with different types of cancer by up to 39% during the follow-up period than people without depression; in addition, patients displaying even a few depressive symptoms may be at a 25% increased risk of mortality as measured using validated measures.

Higher rates of depressive symptoms in cancer have been found toward the end of life and in specific cancers, such as pancreatic, gastric, and oropharyngeal ones. Although depression has been reported to be 2 to 3 times more common in women than in men in the general population, this disparity has not been observed in cancer, perhaps because the burden of disease may be equally distributed by sex. More severe symptoms of depression are of clinical concern because of their association with marked distress, more prolonged hospital stays, physical disorders, poorer treatment compliance & adherence to therapy, disability, lower quality of life, increased desire for hastened death, and completed suicide. Depression is the most common mental illness associated with suicide, which has been documented in 75% of cancer-related suicides. Depression incurs a 25-fold increased risk of suicide compared with those without depression, irrespective of cancer.

The number of patients with cancer who are age 65 years or older are increasing dramatically worldwide. 3 of 4 cancer cases are diagnosed in those older than 60 years. Life expectancy and the likelihood of developing comorbid dementia & cancer are thereby growing. In nursing home cohort was appeared 14% to 26% of patients to be given a diagnosis of cancer. The prevalence of cancer has proved to be significantly higher among patients without dementia than among those with dementia. Population-based cohort studies report lower rates of dementia in cancer survivors. Studies on rates of cancer in individuals with dementia have found that the converse is also true, with lower rates of cancer in people with dementia. There are several explanations put forward to explain this disconnect. Most commonly there has argued advanced dementia is the leading cause for no referral of patients with suspected cancer.

A recent study found that approximately half of the population of individuals with dementia were accidentally discovered to have cancer (48%) or had unexpected unfolding of clinical signs (44%), whereas most cognitively intact patients (63%) voluntarily sought medical evaluation. Under diagnosis of cancer is one possible explanation – one study reported that individuals with prevalent Alzheimer's disease had a 69% lower risk of being admitted to hospital for cancer. Individuals with dementia tend to under-report symptoms, such as gastrointestinal discomfort, joint pain and vision problems, which leads to delays in medical attention being sought. Thus, they are diagnosed with more advanced stages of cancer, often too late to be treated. One study on individuals with colon cancer found that those with dementia were twice as likely to be diagnosed without tissue sampling and that they were half as likely to receive surgical resection or adjuvant treatment. A study on individuals with breast cancer reached similar conclusions – women with dementia were likely to have a more advanced stage of cancer and less likely to have treatment.

Cognitive impairment consistent with dementia was found in majority of patients

Dementia, of which the most common cause is Alzheimer's disease, is an incurable and progressive condition. It affects 35 million people

worldwide—a number expected to almost double in the next 2 decades. In general, dementia results in the decline of the person's cognition and physical function. Up to 90% of people with dementia experience neuropsychiatric symptoms such as agitation, depression, and delusion, during the course of their disease. Cancer symptoms are potentially more onerous for people with both conditions because they are no longer able to give a valid self-report—a prerequisite for adequate treatment. Dementia is associated with poorer cancer outcomes although the reasons for this are not yet clear. Patients with severe dementia and cancer are at a great risk of having untreated advanced cancer pain because they are no longer able to account for their suffering.

The patient's level of dementia is classified by the Clinical Dementia Rating (CDR) scale (range, 0–3). The instrument consists of 6 categories with scores for no dementia of 0, possible dementia of 0.5, and mild, moderate, and severe dementia of 1, 2, and 3, respectively. The cutoff point for the presence of dementia is CDR of 1 or greater. The CDR scoring algorithm weights memory as the primary domain and the other domains as secondary.

The last but not least chapter. In addition to the dementia syndrome, there is a syndrome of cognitive impairment without functional disorders, which is most commonly termed mild cognitive impairment. Many individuals with such impairment are experiencing age-related changes in multiple organ systems, including the brain, which complicates decisions about systemic therapy. They will go on to develop dementia. In community samples, rates of conversion from MCI to dementia average 12 to 15 % per year.

One age-related change that is often cited as a particular concern of older patients and survivors is impairment in one or more cognitive domains, which could have important effects in the daily lives. With over 13 million cancer survivors in the United States, up to 4.5 million individuals may be living with long-lasting cognitive difficulties resulting from cancer and cancer treatments. Approximately 30%–40% patients experienced cognitive impairment before any type of cancer treatments. These impairments have been well documented. They are defined as one or more impaired functions of interrelated cognitive process. Such patients describe their condition as frequent forgetfulness (e.g., names, date, or telephone numbers), slow-progressing speeds, and difficulties in concentration, multitasking, and word retrieval. Up to 75% of breast cancer patients have such impairment. 'Chemo brain' or 'chemo fog' are terms found in the literature and on numerous cancer support websites that include a heterogeneous cluster of cognitive symptoms: verbal and visuospatial memory deficits, verbal fluency & other language problems, frontal executive dysfunction, and disturbances of attention and concentration. 11%–27% cancer patients who are recovering from surgical removal for tumor were found to have moderate or severe impairment on verbal fluency and 14%–17% complained of memory impairment. Of those who experienced cognitive impairment before cancer treatments, approximately 60% reported persistent disorders after the completion of cancer treatments. A meta-analysis showed that majority of the cognitive deficits were in verbal and visuospatial ability.

One of the largest longitudinal studies of perceived such disorders showed that 45.2% of patients with breast cancer complained of cognitive decline after receipt of chemotherapy compared with 10.4% of healthy age-matched controls. This decline persisted 6

months after receipt of chemotherapy for 36.5% of patients with breast cancer and 13.6% of healthy controls. In other study, 71% of patients showed acute and late cognitive decline 7.7 months after chemotherapy, and 61% of patients performed worse on the late evaluation compared with evaluation during or right after chemotherapy. Hence, cognitive impairment could progress to long-term disorders. Koppelmans et al. evaluated 196 patients with breast cancer treated with cyclophosphamide/methotrexate/fluorouracil at more than 20 years after treatment. Compared with a control population, cancer survivors performed worse in verbal memory, processing speed, executive function, and psychomotor speed. Older cancer patients with such impairment have 10% to 15% probability of developing dementia per year compared to about 1% to 2.5% among those without cognitive impairment. Some studies have suggested that changes can be reversible. Collins et al. showed that cognitive effects from chemotherapy largely resolved after 1 year; the negative impact of chemotherapy on verbal ability resolved over time, although this was not true of decrease in processing speed. Hormonal therapy for both men with prostate cancer and women with breast cancer can have an impact on cognition. Patients who received tamoxifen for 1 year performed significantly worse on verbal ($p < .01$) and executive function ($p = .01$) tests compared with healthy controls, although this was not true for patients who received exemestane. Patients who received chemotherapy alone had deterioration in verbal working memory, whereas patients who received chemotherapy and tamoxifen had deficits in visual memory and verbal working memory.

Therefore, oncology care providers will need to be familiar with the risks for adverse cognitive effects of cancer when prescribing systemic therapy to older patients and be able to screen for symptoms of cognitive impairment when providing care for this age group. Our experience includes the results of evaluation 4789 patients (men 2367, women 2422, mean age 64.8 ± 5.6 years). They were examined at home because their condition precluded a standard examination in a medical facility. The patients have variety of malignancies, the commonest being breast, lung, colorectal & skin cancers. They were classified as having mental comorbidity based on clinical judgment, which was added with routine tests if necessary.

Mental disorders were detected in 2064 (43.1% of total cohort), in this group nosologic prevalence was as follows: depression & other mood disturbances 725 cases (35.1%), cognitive impairments - 445 (21.6 %), delirium (hyperactive, hypoactive & mixed) 865 (41.9%), other disorders - 29 (1.4%). The most difficult for differentiating were cases when delirium superimposed on dementia (58 pts). The delirium's fluctuating consciousness permitted it to set apart from dementia. During final days of life, the delirium prevalence increased.

Improving the quality of care requires recognition and addressing patients' distress, mental disorders and supportive care needs during treatment and after care. Thus, psychosocial and psycho-oncological support services considerably contribute to improving the quality of life of patients as a central outcome criterion of oncological care. It is clear that a more personalized approach to supporting the psychological health of people with cancer is needed. Some people may not want or require support or treatment, others will be able to self-manage, and some may have more complex needs that require more intensive follow-up and support. At diagnosis, the psychological health of patients should be considered alongside their

physical health and sources of support offered. Needs and symptoms may also change over time. Being mentally aware is a preference reiterated by seriously ill patients.

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