

"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY

BUCHAREST

DOCTORAL SCHOOL

DISCIPLINE PSYCHIATRY

ABSTRACT
OF
DOCTORAL THESIS

Scientific supervisor:

UNIV. PROF. DR. PRELIPCEANU DAN

Doctoral candidate:

CĂTĂLINA FLORESCU

2024

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ABSTRACT

DEPRESSION IN LUNG CANCER

***CLINICAL, THERAPEUTIC AND EVOLUTIONARY INTERFERENCES
IN LUNG NEOPLASM - COMPARATIVE PRE AND POSTOPERATIVE
AND ONCOLOGIC EVOLUTIONARY STUDY***

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ABSTRACT

The structure of the thesis consists of a general part, a special part, a part containing conclusions, personal contributions and originality of the thesis, an appendix containing tables related to statistics, another appendix containing ethical issues and bibliography.

The thesis aims to prove that psychiatric medication, in the oncologic context, has a salutary effect in reducing the somatic or affective symptoms of the oncologic patient, regardless of their etiology.

Cancer is one of a person's most devastating experiences. Psychological reactions to these losses initially range from demoralization to anger. In many people, a cancer diagnosis seems like a death sentence. Cancer is responsible for about 14% of all deaths. [1]

47% of cancer patients have psychiatric manifestations. 90% of these manifestations are a reaction to the diagnosis, which may become a chronic affective disorder, an affective disorder occurring in the context of oncologic disease, or a manifestation in the context of medication. [2] Of particular importance are the type of cancer, the various types of treatment, personal history of depression, previous treatments for depression.

Cancer types most commonly associated with depression are – brain (41-93%), [3, 4], pancreatic (up to 50%), [5], ENT cancers (up to 42%), [6], breast (4.5-37%), [7, 8], gynecologic (23%), [9], lung (11%) [10].

GENERAL PART

1. The first chapter of the general part addresses the epidemiology and risk factors in lung cancer. In terms of risk factors, the overwhelming role of smoking in determining lung cancer is emphasized. [11] In addition to the risk from smoking, occupational exposures, diet (diet rich in fruit and vegetables has a protective effect), socio-economic factors, personality type and chronic stress.

2. The second chapter of the general part deals with the classification of lung cancers, according to different criteria: anatomopathologic, topographic, morphologic or metastatic. [11] Of particular importance in the thesis is the classification according to metastasis, which divides cancers into primary and metastatic.
3. The third chapter of the general part deals with clinical symptoms in lung cancer. The symptomatology present in lung cancer can be systematized as follows [11, 12]:
 - *bronchopulmonary symptoms and signs*
 - *extrapulmonary intrathoracic symptoms and signs*
 - *nonmetastatic extrathoracic manifestations (paraneoplastic sdr)*
 - *metastatic extrathoracic manifestations*
 - *non-specific symptoms.*
4. The fourth chapter of the general part deals with oncologic psychiatric manifestations, with reference to acute stress disorder, cancer-substance abuse comorbidity, psychotic disorders, personality disorders.
5. The fifth chapter of the general part refers to the role of psychiatry in oncologic palliation.

Including a patient in palliative care is a borderline diagnosis. [13] and requires both the patient and the physician to adapt to the diagnosis. Sometimes this involves the physician's understanding of the possibility of extreme emotional manifestations.

Palliative care is difficult to define. It overlaps with 'terminal care', 'end-of-life care', 'comfort care', 'supportive care'. [13, A1]

The admission of a patient to palliative care assumes ***the existence of a life-threatening illness without the possibility of remission, stabilization or modification of the course of the disease.***

Sometimes patients do not accept palliative care, nor the involvement of caregivers in palliative care [14]. Palliative care must be provided by a multidisciplinary team.

Therefore, the inclusion of a patient in palliative care implies [A1]:

- *the presence of an advanced and incurable disease*
- *lack of response to specific treatment*

- *presence of severe symptoms*
- *prognosis less than 6 months*

In terminal patients, [A1] are present:

- *somatic changes: pain, dyspnea, constipation, anorexia*
- *psychiatric changes: depression, anxiety*
- *social changes: changes in social status, fear of addiction. [14]*

According to the WHO, palliative care should]:

- *provide symptom control, mainly pain control*
- *support life, but also consider death as a natural process*
- *integrate emotional symptoms, social and spiritual needs, etc. into palliative care*
- *support the patient and family until the end*
- *improve the patient's quality of life*

Palliative care should be provided by an interdisciplinary team. It should be applied as early as possible, from the earliest stages of the disease, even in conjunction with a series of cytostatic or radiotherapy treatments, with the aim of treating complications. [15]

The rights of terminally ill patients are [A1]:

- *the right to be treated as a human being*
- *the right to maintain hope, but also to express their emotions about death*
- *the right to care, even if only comfort goals exist*
- *the right not to die alone, to die with dignity*
- *the right not to be judged for their beliefs*
- *the right to have their body respected after death [16, 17]*

Palliative treatments aim to reduce the symptoms caused by the illness: nausea, pain, fatigue, etc. Palliative treatments can be medical or surgical and are represented by:

- a)** *radiotherapy - used for pain relief*

- b) chemotherapy - for palliative purposes, for tumours that may cause pain due to their large size or localization*
- c) surgery - to shrink or remove tumors that cause complications (compression, bleeding)*
- d) hormonal therapies - which slow or reduce hormone production, which can cause tumor progression*
- e) immunotherapy - which shapes the immune system response*
- f) targeted therapy - on specific cell particles that cause tumor development or progression*
- g) targeted drug therapy - alleviating specific symptoms: pain, nausea, shortness of breath*
[18, 19, A1]

Psychiatric disorders in palliative care

Patients suffering from terminal illness manifest a range of psychiatric disorders, the most common being *anxiety* and *depression*.

Anxiety

Anxiety among people with cancer or AIDS varies between 15% and 28%, the prevalence depending on the stage of the disease. Anxiety is related to the effectiveness of treatment, the results of investigations, but also to the way the results are transmitted, which is deeply influenced by the doctor-patient relationship. In the terminal stages of the disease, there is a risk of reactivation of certain pre-existing anxiety manifestations. Hypoxia, poorly controlled pain, reaction to certain oncologic treatments, may present anxiety-like symptoms. In fact, in the terminal phase of the disease, anxiety is caused by emotional and psychosocial factors as well as by medical complications, representing the organic part of anxiety. Pharmacological treatment, which is imperative in some circumstances, can be combined with supportive psychotherapy, relaxation therapy, guided imagery and hypnosis.

Pharmacological treatment consists mainly of neuroleptics, which, in this case, are the most rapidly effective treatment. Antidepressants are limited by the time needed to achieve therapeutic effect.

Psychotherapy is limited by the mental clarity of the patient. [17, 18]

Depression

Depression varies between 9% and 18% in terminally ill patients.

The patient's history of depression, or inherited history of depression may increase the risk of developing a depressive state.

Oncologic treatments such as chemotherapy, radiotherapy (more frequent in cerebral involvement), corticosteroids, hormone therapy, metabolic-endocrine complications, may increase the risk of depression.

In terminally ill patients there is a risk of minimization of depressive symptoms by clinicians as "normal reactions", leading to a deficiency in the diagnosis of depression, with decreased tolerance of stage-specific oncological symptoms.

Antidepressant medication is suitable if the terminally ill patient has a life expectancy of several months, which allows him or her to wait 2-4 weeks, i.e. the time needed for a standard antidepressant to have an effect.

A patient with a life expectancy of less than 3 weeks requires antipsychotic medication, with or without sedation.

Individual counseling, relaxation, imagery, spiritual counseling are useful in this case. [18, 20, 21]

Psychotic decompensations, at this stage, require standard pharmacologic treatment adapted to the present conditions and context.

Specific drug therapies include psychiatric drugs (antidepressants, antipsychotics, thymostabilizers) that have a beneficial effect on both secondary oncological and psychiatric symptoms, especially in the context in which most of the symptoms have a dual oncological and psychiatric determinism.

Adding psychological and spiritual counseling and relaxation techniques to this medication increases the well-being of the oncologic patient and his/her family.

6. The sixth chapter deals with psychiatric medication used in oncology.

Patients with cancer require appropriate oncologic treatment, to which psychiatric treatment should be added as a constituent part of an integrated treatment tailored for an oncologic patient. [22]

Most studies have focused on antidepressants that have been used both for major depression but also as adjuvant treatment of cancer-related symptoms. The need for an integrated model of pharmacologic and psychiatric treatment in oncology is advocated. [23]

The prevalence of depressive symptoms, in the context of oncologic patients, is influenced by the type of cancer, stage of disease, demographic profile as well as the methods of assessment, with the diagnostic criteria being the approved ones. [24]

Oncologic patients present with certain physiologic changes, which increase the predisposition to developing psychiatric disorders, or exacerbation of pre-existing psychiatric conditions.

A study in North America shows that one in seven patients treated in outpatient or clinic settings receive antidepressant treatment. [25] All of this is due to the fact that an oncologic diagnosis triggers an emotional reaction, in addition to the symptoms caused by the disease or secondary to surgical, chemotherapy, radiotherapy or hormonal treatments. The resulting disabilities also increase the risk of depression.

Psychiatric morbidity associated with oncologic pathology varies between 18% and 40%.

Oncologic investigations and subsequent oncologic diagnosis lead to increased anxiety. In this context, the NIMHANS study on cancer patients' self-reported worries states that 90% of patients have at least one worry and 44% have one to three worries. The most important concerns are the oncologic disease, present physical symptoms, financial problems as well as worries about the future and the presence of disabilities. [26]

Anxiety symptoms may be part of a normal stress response, adjustment disorder, depressive or anxiety disorder. Somatic-type symptomatology may be in a somatoform context, manifesting as unexplained somatic symptoms such as fatigue or pain, which may sometimes be interpreted as signs of recurrence or metastasis. Thus, they can be attributed to anxiety or depression, but also to behaviors in the context of the disease.

Psychiatrists need to have a certain communication skill, which involves the ability to communicate a problematic diagnosis and the possibility of an unfavorable outcome. Communication skills could be shared with other clinicians involved in the treatment of the oncologic patient. [27]

Chemotherapy treatment may cause nausea and vomiting as a side effect. Radiotherapy can also cause secondary nausea, vomiting and increased feelings of fatigue. All these symptoms can be secondary to the treatment, but also affective secondary. [24]

The challenge in oncology, therefore, is the underdiagnosis of depression in the context of overlapping affective and physical symptoms related to cancer. In fact, behavioral changes also have dual etiology, depressive and/or influenced by the inflammatory cytokine cascade, but which can also secondarily cause depression. [28]

Barring the existence of psychiatric disorders pre-existing the oncologic diagnosis, the cancer patient should be considered a psychologically normal individual under severe stress.

The majority of studies support the efficacy of antidepressants for cancer-related anxiety and depressive disorders, but also as an adjuvant treatment for cancer-related symptoms.

Attention should also be drawn to possible interactions between psychiatric and oncologic medications.

In the context that antidepressant and antipsychotic medication can be used for dual purposes, psychiatric and oncologic symptomatic reduction, the issue of reuse of psychiatric medication, known as medication repositioning/reprofiling, arises.

It represents a new, relatively recent strategy that proposes the alternative use of well-known medications outside the original medical indications. This approach has a number of advantages, including less time for the introduction of psychiatric drugs and lower prices. Some antidepressants and certain antipsychotics are among the group of candidate medications for reuse. We refer to certain antidepressants (citalopram, fluoxetine, paroxetine, sertraline) and antipsychotics (chlorpromazine, pimozide, thioridazine, trifluorpromazine), which can be used in cancer, for their prophylactic, therapeutic action, but also for the purpose of drug reuse, which is an attractive strategy that does not imply not having to find new drugs with a well-determined purpose. [29, 30, A1]

Psychosocial oncology is a new area of interest that emphasizes the role of liaison psychiatry. In fact, psychological distress in cancer is considered the "sixth vital sign". [30]

Psychological management includes allowing expression of emotions, clarifying concerns but also involving the patient in treatment decisions, which are important in palliation.

Muscle relaxation techniques, hypnosis, are important in stress response.

Psychological management methods are individual and group psychological therapies, cognitive-behavioral therapies, desensitization, rehabilitation and mindfulness.

Peace of mind, spirituality, social satisfaction are considered important by 2/3 of the subjects. [31]

Self-help groups for cancer patients and their families are also helpful.

Cognitive-behavioral therapy focuses on restructuring cognitive distortions and negative automatic thoughts, changing intermediate and core beliefs. Core behavioral strategies such as gradual exposure and systematic desensitization aim to reduce avoidance and fear. [32]

These interventions are not applicable to people in advanced stages of the disease, who have disabilities involving reduced functional capacity, representing a major burden for the family. [33]

Acceptance and Commitment Therapy (ACT) is a combination of cognitive and behavioral strategies also involving different processes: acceptance, commitment, mindfulness, and behavior change. [34]

Mindfulness-based cognitive therapy helps to achieve a state of self-acceptance, decrease the focus on thoughts and change the perception of thoughts from being considered an accurate reflection of reality. [35, 36, 37]

In the following we will refer to the most common psychiatric changes occurring in patients with lung or metastatic lung cancer compared to the rest of the oncologic pathology, except pulmonary involvement.

SPECIAL PART

1. Working hypotheses and general objectives

1.1. Motivation for the study

The purpose of the study is to change the definition of palliative care from "terminal care", "end-of-life care" or "comfort care" to "**long survivorship oncologic care**" (*term proposed by Dr. Florescu Cătălina*)

An attempt is being made to change the mentality of physicians and healthcare workers with regard to the outcome of patients diagnosed with cancer, regardless of localization, regardless of the existence of metastatic or metabolic complications, etc., and with regard to the chances of survival with a good quality of life. This justifies targeting resources to improve the quality of life of cancer patients.

As for psychiatric care, it is important to introduce it as quickly as possible, for purely psychiatric, but also palliative, purposes. [A2]

1.2. General assumptions

- Does it make sense to introduce psychiatric medication, as quickly as possible, in the context in which the patient presents with physical symptoms, even if we do not know exactly whether they are secondary to the specific oncologic treatment, secondary to the disease, or with a mixed component, organic, iatrogenic or psychogenic?
- In the long term, does the early introduction of psychiatric medication have a positive effect on the reduction of both physical and affective symptoms, improving the patient's well-being, peace of mind and the well-being of his support network?

1.3. Research objectives

a. Short term

- To alleviate (until the elimination) of the discomforting physical symptoms of oncologic patients, with the contribution also of psychiatric treatment;

- To improve the affective state of oncologic patients, their feelings of peace, progressively during the treatment;

- To improve the psychological state of the people who form the support network of an oncologic patient. [A2]

b. Long term

- Early introduction of psychiatric treatment with the onset of somatic symptoms, irrespective of their amplitude and irrespective of etiology, somatic or psychological;

- Improving the quality of medical services provided to oncologic patients by changing the protocols for the introduction of certain psychiatric drugs, which currently have a more restrictive indication;

- Changing the mentality of physicians and health professionals in general towards the concept of oncological diagnosis and terminal oncological diagnosis, by adopting an optimistic, hopeful outlook in the context of new oncological drug therapies which have greatly increased the patient's life expectancy;

- Changing the notion of "palliative care" to "long-survivorship oncologic care" and concomitantly the modality of therapeutic approach. [A2]

2. General research methodology

2.1. Working assumptions and specific objectives of the study

Working assumptions: *questions we sought to answer*

- Do the physical symptoms of an oncologic patient undergoing psychiatric treatment introduced as quickly as possible change?
- Is there a correlation between improvement in the patient's physical state and improvement in the patient's affective state, concomitant with improvement in the well-being of caregivers? [A2]

Specific objectives

- Improvement in physical symptoms of oncologic patients under early psychiatric treatment;
- Improvement of affective symptoms of oncologic patients, in the context of the positive effect of psychiatric treatment on affective symptoms, but also on physical symptoms occurring in the oncologic context;

- Adherence to psychiatric treatment as a prerequisite for positive psychiatric and oncologic outcome. [A2]

2.2. Material and method

The study includes 3 groups of oncologic patients: one group with a diagnosis of primary lung cancer (group 1), one group with metastatic lung cancer (group 2), and one group including other types of cancer, excluding primary or secondary lung cancer (group 3).

The assessment method is longitudinal, over 6 calendar months, with sequential assessment at 1 month and 6 months.

The IPOS, HAM-D17, CGI-S and CGI-I questionnaires are applied, with longitudinal assessment and stage comparison, with the aim of demonstrating positive evolution under psychiatric treatment, applied from the time of enrollment. [A2]

2.2.1. Research ethics issues

Research:

- ✓ respects the person and the dignity of the human being;
- ✓ assesses the benefits and risks of research;
- ✓ involves fair selection of subjects;
- ✓ respects the autonomy, confidentiality and voluntariness of the individual.

Ethical criteria are followed in the research context:

- ✓ existence of beneficence;
- ✓ known and controllable risks that are non-lethal and do not endanger life and health;
- ✓ the individual will not be sacrificed for the good of science and society.

Research inclusion criteria:

- +18 years, male or female;
- Presence of uncomfortable symptoms attributable to oncologic and/or psychiatric pathology;
- acceptance of a psychiatric evaluation;
- the need for psychiatric treatment;
- signature of informed consent.

Research exclusion criteria:

- under 18 years of age;
- patient does not want psychiatric evaluation;
- inability to sign a valid consent (confusion, cognitive impairment);
- does not sign informed consent.

Patients included are selected among inpatients or outpatients of the Bucharest Oncology Institute who meet the criteria for inclusion in the research.

2.2.2. Conduct of the study

Patients are included in the study after the oncologic diagnosis has been established and in the context of the occurrence of physical symptoms, which may be attributable to the oncologic disease, specific oncologic treatment or reaction to the diagnosis. [A2]

The patient is initially evaluated by IPOS, HAM-D17, CGI-S and CGI-I. Psychiatric treatment is then administered. The patient is assessed at 1 month and subsequently at 6 months after inclusion in the study, at which time the mentioned scales are reapplied. We expect the outcome to be positive.

2.2.3. Socio-demographic, psychiatric and medical variables**Socio-demographic variables:**

- residence;
- gender (sex);
- age.

Medical variables:

- comorbidities;
- COVID infection;
- COVID vaccination.

Medical and psychiatric variables:

- **Physical variables** (symptoms): pain, shortness of breath, weakness or lack of energy, nausea, vomiting, lack of appetite, constipation, mouth problems, drowsiness, reduced mobility (quantified by IPOS).
- - **Psychiatric variables:** self-reported worries, emotional symptoms (scored by IPOS), communication and practical problems (scored by IPOS), medical information (scored by IPOS), specific depressive symptoms (scored by HAM-D17)

2.2.4. Procedural phases

1. Oncologic diagnosis present;
2. Initial assessment of self-reported physical symptoms;
3. Signed informed consent for inclusion in the study;
4. Assessment by psychiatric clinical examination, application of IPOS, HAM-D17, CGI-S and CGI-I scales;
5. Establishment of the psychiatric treatment regimen;
6. Dynamic assessment, 1 month after the start of treatment, by clinical examination and application of the above-mentioned scales;
7. Evaluation 6 months after the start of psychiatric treatment, by clinical examination and application of the above-mentioned scales;
8. Comparison of the values obtained by the application of the scales between the initial, 1-month and 6-month assessments.

2.3. Used psychometric instruments

a) **IPOS questionnaire** - which is an integrative palliative care scale, used for cancer but also for a range of other diagnoses with a serious course.

The questionnaire starts by rating patients' main concerns and goes on to rate the 3 categories of factors assessed: *physical symptoms, emotional symptoms and communication/practice problems*, which are quantified according to intensit. [A2]

b) **HAM-D17 questionnaire** – used for the assessment of depressive symptoms in the context of a diagnosis of depression and also used to quantify depressive symptoms in other psychiatric disorders (bipolar disorder, schizoaffective disorder). Specific depressive symptoms are rated and the final score determines the intensity of depressio. [36, 37]

c) **CGI-S scale** – which rates the severity of depression, applied in the 3 stages of assessment. [38]

d) **CGI-I scale** – which rates the intensity of change in affect, in good or bad, after treatment initiation. For this reason the scale cannot be applied at treatment initiation, but only 1 month after inclusion in the study, when treatment has already been initiated.

2.4. Output variables

The input variables, i.e. socio-demographic, medical, medical-psychiatric and purely psychiatric, are also found as output variables.

2.5. Data analysis

We expect that, in the context of psychiatric medication administration, physical symptoms, quantifiable by IPOS, are most rapidly modified.

We expect the reduction in physical symptoms to be followed by a reduction in the patient's anxiety and depression, rated by IPOS, which leads to a reduction in family anxiety, improvement in the patient's peace of mind (rated by IPOS) and in the perception of medical information (subjective construct influenced by the doctor-patient relationship, the physical but also the emotional state of the assessor).

Regarding the HAM-D17, we expect an improvement in the scoring of items characterizing affective state, as well as in the score quantifying the severity of depression.

The CGI-S scale, which quantifies the severity of depression, is expected to show a positive trend, meaning a decrease in the severity score.

The CGI-I scale rates the intensity of change. The lower the score, the greater the change.

It should be noted that the course of oncologic disease influences affective symptomatology, perception of life and intensity of change.

The data analysis comprised two components, descriptive and analytic. Before analyzing the dataset, direct internal and cross-validations were performed to ensure the physical and logical accuracy of the dataset. Database and statistical analyses were performed in SPSS Statistics version 23.

In terms of data type, ordinal data predominate, followed by nominal dichotomous data (obtained by scoring the presence/absence of a characteristic).

Quantitative variables, measured at interval level, such as patient age, were recoded and transformed into ordinal variables to allow a comparative analysis of the subgroups created.

The analysis data are presented as absolute frequencies (n's) and percentages, with the volumes of the subgroups of analysis specified, in both tabular and graphical form.

To perform the comparative analysis, methods and techniques specific to the type of data being analyzed were used, namely McNemar test and Z-Test of proportions (for nominal variables in the within-group longitudinal analysis) and Chi-square, Fisher and Mann-Whitney U Tests (for comparison, association testing and inter-group analysis of ordinal variables).

In order to analyze the association between certain (ordinal) variables, Spearman's Rho correlation coefficient was used (showing the degree of monotonic association between the variables). A directly proportional correlation means that the values of both variables analyzed increase or decrease in the same direction (on the scales on which they are rated). An inversely proportional correlation shows that the values of one of the variables analyzed increase while the values of the other variable decrease.

The differences obtained from the comparisons were considered statistically significant at the 95% significance level ($p\text{-value} < 0.05$).

It should be mentioned that the course of oncologic disease influences affective symptomatology, perception of life and intensity of change. [A2].

Research results prove that psychiatric medication improves physical symptoms, regardless of their etiology (oncologic, affective or mixed), affective symptoms and improves the affective state of the support network.

CONCLUSIONS AND PERSONAL CONTRIBUTIONS. ORIGINALITY OF THE THESIS

CONCLUSIONS

1. In terms of *location*, the incidence of lung and metastatic cancers are significantly higher in urban than in rural areas. For primary and metastatic lung cancer, there are no significant urban/rural differences. This proves the role of pollution in lung cancer incidence.

2. *Age*. Cancer incidence is higher in the 50-79 age range for all cancers, with no statistically significant differences between groups, this range representing a risk range for the development of oncologic symptoms.

Metastatic lung cancer has the highest incidence in the age range 40-49 years, this range being determined by the heterogeneity of the oncologic disease.

3. *Sex*. The incidence of lung cancer is significantly higher in males than in females due to the role of a major etiologic factor, smoking. For other cancers, the higher incidence in females is due to other factors (including hormonal)

4. *The incidence of co-morbidities* is higher in primary or metastatic lung cancer than in other cancers, which increases the risk of complications and decreases quality of life and survival

5. Regardless of the oncologic location, in terms of concerns mentioned by oncology patients, the disease ranks first in all groups and regardless of the time of assessment, with financial and family problems having a lower weight.

6. *Physical symptoms* occurring in the oncologic context: pain, shortness of breath, weakness or lack of energy, nausea, vomiting, lack of appetite, constipation, mouth problems, drowsiness, reduced mobility, decrease during the 6 months of follow-up in all groups, with the introduction of psychiatric medication being of particular importance.

The use of psychiatric medication has a rapid effect on nausea and vomiting, but also on pain, a major discomfort factor for oncology patients.

Shortness of breath, weakness or lack of energy, drowsiness or reduced mobility are more difficult to overcome under psychiatric treatment, and are more influenced by the course of the disease.

7. The patient's depression lessens under psychiatric treatment. Decreasing physical oncologic symptoms plays an important role in decreasing the patient's depressive symptoms.

8. *Familial anxiety and depression* are manifested in any type of cancer, with minimal differences from lung cancer and metastatic lung cancer. The conclusion is that it is not the localization of cancer that determines anxiety, but the oncologic diagnosis.

9. *Improved communication* with friends or family positively influences the patient's emotional state.

10. The oncologic patient needs *medical information* and active participation in the therapeutic decision, which also helps to reduce depression and anxiety.

11. Psychiatric medication modifies feelings of guilt and autolytic ideation.

12. Discomforting manifestations of depression, such as insomnia, agitation, gastrointestinal and general somatic manifestations, as well as appetite and genital symptoms, rated by HAM-D17, are progressively modified under psychiatric treatment in all groups.

13. *Work capacity and ability to concentrate* change in all groups under psychiatric treatment, but more slowly.

14. The CGI-S depression severity rating follows the course of the HAM-D17 depression rating.

15. The decrease in depression values, obtained by the CGI-S, is followed by the decrease in values by the CGI-I.

PROPOSALS

Short-term:

1. Psychiatric evaluation as soon as possible after the oncologic diagnosis, even if the physical symptoms present are minimal, as are the affective symptoms.
2. Psychiatric treatment should be introduced as soon as possible, with the aim of curing the physical symptoms as well as the affective symptoms, even in their minimal context.
3. Increasing psychological involvement, through relaxation exercises, supportive therapy, in order to direct attention towards pleasant activities that prevent intrusive negative thoughts.
4. Family therapy to decrease caregiver anxiety.

5. Providing the most complete medical information possible, offered throughout the oncologic treatment. Pointing out essential medical information at each patient assessment to improve the doctor-patient relationship..

Long-term:

1. Intensification of education methods to avoid polluted areas and smoking quit smoking.
2. Amend environmental protection legislation and increase environmental methods in order to ensure a healthier living environment.
3. Preventive screening from the age of 35-45 years for any cancers that may become symptomatic between the ages of 40-79 years. It is proposed that routine medical tests, tumor markers as well as CT scans should be carried out from the age of 35.
4. Longitudinal evaluation of the oncologic patient, in order to adapt psychiatric medication and, at the same time, maintain adherence to oncologic and psychiatric treatment.

ORIGINALITY OF THE THESIS

1. The thesis aims to change the perspective of a patient included in palliative care from a patient for whom the major importance is the supportive care to a patient for whom the quality of life is important. We are trying to change the notion of palliative care to **long survivorship oncologic care** (*term proposed by Dr. Florescu Cătălina*) which is adapted to the increase in survival time in the context of new oncologic treatments. In this context, the introduction of psychiatric medication plays a major role in improving the physical and emotional state of the oncologic patient.
2. Emphasizing the spiritual intervention in maintaining the patient's wellbeing, which at the same time influences family and friends, contributes to the affective development of the oncologic patient. Medical information and the possibility of active participation in the therapeutic decision have a salutary role in the positive evolution of the oncologic patient.

RESEARCH LIMITATIONS

1. Patients were assessed only for depressive disorder and some anxiety symptoms, other psychiatric symptoms (e.g. psychosis) were not considered;
2. Patients were assessed in the study only for a period of 6 months, not being assessed longitudinally after this period, especially in the context of increased life expectancy of the oncologic patient.

ANNEX 1

-contains the study data in tabulated form

ANNEX 2

-contains the informed consent to participate in the study and the opinion of the ethics committee

The thesis concludes with the appropriate bibliography

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A2. Florescu, C; Vasiliu, O; Prelipceanu, D. – The Palliative care in patients with Oncological diseases. A New medical and Therapeutic Approach, Medicina Modernă, 175-185, June 2024