

**TO:
THE CHAIRMAN OF THE SCIENTIFIC JURY
APPOINTED BY ORDER NO P-109-
306/29.07.2021 OF THE RECTOR OF THE
UNIVERSITY OF VARNA**

REVIEW

**By Prof. Dr. Konstanta Velinova Timcheva, Ph.D.
Serdika Hospital, Sofia**

SUBJECT

A comparative analysis of the levels of distress, anxiety, depression, feelings of anger and need for help in patients with solid tumors and upcoming chemotherapy

for the award of the degree of Doctor of Science in Oncology

Candidate: Dr. Assen Ivanov Yanchev, MD

Scientific supervisor - Assoc. Prof. Eleonora Dimitrova-Gospodinova, MD, PhD

The dissertation submitted for review is intended for Scientific Jury, appointed by Order No. R-109-321/29.07.2021 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov"- Varna and Decision of the Faculty Council of the Faculty of Medicine at MU"Prof. Dr. Paraskev Stoyanov"- Varna (Protocol No.47/23.07.2021).

The review was prepared in accordance with the requirements of:

- The Law on the Development of Academic Staff in the Republic of Bulgaria;
- The Regulations for the Development of Academic Staff at MU - Varna; and the specific requirements for obtaining the scientific degree "Doctor"

For the preparation of the review I was provided with a set of documents on paper and electronic media (including copies of all full-text publications and abstracts).

Biographical sketch of the candidate

Dr. Assen Ivanov Yanchev graduated in Medicine from Medical University - Varna in 1990. Initially he worked as a resident physician at Dobrich District Hospital, from 1991 - 2012 he was a senior assistant at the Department of Internal Medicine at Medical University - Varna. Since 2015 Dr. Yanchev has been an assistant professor at the Department of Oncology at MU Varna, and since 16.07.2018 he has been a full-time PhD student at the same department.

Dr. Yanchev is a doctor with two specialties - specialty "Internal Diseases" (1996) and specialty "Oncology" (2000). He has 26 publications in the field of internal medicine and oncology.

Dr. Yanchev is a physician with more than 30 years of clinical experience, has attended numerous scientific congresses and conferences at home and abroad, has participated in presenting scientific papers.

Characteristics of the dissertation submitted for review

The dissertation is presented on 79 pages, including bibliography. The dissertation has a classical structure: 'Literature review' - 34 pages, 'Aim and objectives', 'Study design' 'Material and methods' - 4 pages, 'Results and discussion' - 24 pages, 'Discussion' - 5 pages, 'Conclusions', 'Contributions' - 2 pages. The dissertation contains 20 figures and 19 tables.

97 references are cited, 3 in Cyrillic and 94 in Latin.

The problem to which Dr. Yanchev devotes his scientific work is seemingly not directly related to his narrow specialty - Medical Oncology, i.e. treatment of oncological diseases with antitumor drugs. In fact, the thorough-going clinician perceives the close relationship between the two issues - cancer treatment and level of distress, anxiety, depression, feelings of anger, need for help.

Distress is a multifactorial, unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, spiritual, and/or physical nature that can interfere with the ability to effectively cope with cancer, its physical symptoms, and its treatment. Distress extends and ranges from ordinary, normal feelings of vulnerability, sadness, and fears, to problems that can lead to an inability to respond appropriately, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis.

According to the literature, about 20-40% of newly diagnosed cancer patients, as well as of those with proven recurrence, experience a clinically detectable (measurable) level of distress. For all cancers, the mean level of distress is about 35%, which varies by site from about 30% in patients with gynecologic malignancies to 43% in lung cancer.

In the literature review, the author discusses the characteristics of different types of drug treatment in oncology and the psychosocial problems associated with cancer treatment. He offers a comprehensive review of the existing literature on the impact of distress, depression and anxiety on the course of various cancers, and how these vary according to a number of factors, namely, location, stage, gender, ethnicity and age of the patient.

Screening and early effective treatment have the potential to reduce psychosocial distress not only for patients, but also for their caregivers. Because distress has a negative impact on treatment, quality of life and survival, early screening and timely management improve medical treatment.

At this stage, there is a problem with the identification of patients with distress, as well as with the provision of adequate psychosocial support due to poor training of the teams that serve cancer patients, lack of information, and fear of contact with specialists who deal with psychological or psychiatric problems.

Distress is a risk factor for non-adherence to treatment, especially with oral medications. The author cites international studies of significantly impaired

compliance with oral medications in patients with breast cancer. Furthermore, distress leads to poor quality of life and ultimately affects overall survival.

Early detection and treatment of distress leads to better adherence to treatment, better patient-doctor communication, fewer calls and visits to the oncology office; avoidance of patient anger and development of severe anxiety or depression.

The distress thermometer, developed by the NCCN, is now a basic initial screening tool that is similar to the pain rating scale: from 0 (no distress) to 10 (extreme distress).

Anxiety disorder is a mental disorder. It is characterised by prolonged anxiety and an irrational sense of threat, leading to feelings of constant fear and insecurity. Typical symptoms of anxiety are irrational fear, panic attacks, severe irritability, poor concentration, restlessness and incessant tenseness. These symptoms have different degrees of manifestation in different people.

In addition to the mental level, the symptoms of anxiety disorders also appear in the physical aspect through strong palpitations, sweating, high blood pressure, headaches, rapid breathing, dry mouth, dizziness and muscle tension. Anxiety disorder precedes depression. The author discusses in detail the types of anxiety disorder, the factors that determine them, and methods of diagnosis and treatment.

Tools for measuring anxiety are various types of scales, questionnaires, which the author competently evaluates. Similar detailed information is provided by the author on the conditions of depression, anger, need for help - nature, factors that determine them, symptoms, questionnaires and scales for their assessment.

The main aim that the author of the dissertation sets is to conduct screening and identification of distress and psychoemotional categories of depression, anxiety, anger and need for help and their correlation in cancer patients with imminent initial chemotherapy by applying validated emotional thermometers.

The realization of this goal is related to the following **main tasks**:

- To screen patients who have been diagnosed with cancer and determine levels for distress, depression, anxiety, anger, and need for help using relevant emotional thermometers.
- To determine the relationship between the factors of gender, age, type of cancer, stage of cancer, performance status and levels of the above psycho-emotional states.

- To identify risk factors for high levels of distress, depression, anger and need for help
- To determine the internal consistency of the thermometers used

The methods used include: historical method - a study of literature sources; documentary method: international screening programs, current programs and guidelines for screening and action in distress in Bulgaria; methods for medical-statistical processing of data.

The study included 255 cancer patients with morphologically confirmed diagnosis, not previously treated. They must meet relevant inclusion criteria and none of the exclusion criteria. The main study instrument is a questionnaire - a validated questionnaire and a distress thermometer. Of the patients included, 53.8% had metastatic disease and 46.2% had stage II-III disease. Patients with 3 main localizations predominated: lung cancer, breast cancer and colon cancer. The remaining localizations accounted for 23.6% of the total number of patients.

Analysis of the results showed that there was no association between the level of distress and the age, sex, ethnicity, religion, and place of residence of the participants. There was a correlation between performance status, localization of carcinoma, level of education and level of distress.

The level of distress was higher in patients younger than 65 years of age and in patients with ECOG PS =1. There was a tendency for a higher level of distress in patients with higher education compared to those with primary and secondary education.

Analysis by site showed that patients diagnosed with lung and breast cancer had a significantly higher level of distress compared to those diagnosed with colorectal cancer. There was no significant difference in the level of distress between patients with lung and breast cancer.

Of the 225 patients included in the study, 127 exhibited high levels of anxiety. They were higher in female patients as well as in those with ECOG PS =1. Univariate regression analysis showed that patients with lung and breast cancer, as well as unmarried patients, were at high risk for elevated anxiety levels.

In terms of depression levels, 50 patients had high levels. These were directly related to ECOG PS and tumor location (lung cancer).

Of the patients studied, 44 (19.6%) reported feeling angry. This indicator was also correlated with the localization of the disease as well as the general condition of the patient - ECOG PS.

Strong need for help was reported by 32 patients, 14.2%. This indicator also depended on ECOG PS and tumor localization as well as disease stage. Patients in the metastatic stage had markedly higher help needs.

The author also discusses the correlation between individual thermometers.

On the basis of the scientific study, the author draws the following **conclusions**:

1. 49.3% of patients have moderate to high levels of distress, which will potentially disrupt ongoing treatment and worsen the prognosis of these patients
2. Patients in metastatic and non-metastatic stages of the disease have similar levels of distress.
3. The following factors are associated with higher risk for high levels of distress: unmarried, poor performance status, lung cancer, breast cancer, respectively
4. The following factors are associated with higher risk for high levels of distress: divorced, poor performance status, lung cancer, breast cancer
5. The following factors are associated with higher risk for high levels of depression- respectively: distance from medical center, poor performance status, lung cancer
6. The following factors are associated with higher risk for high levels of anger: poor performance status, male
7. The following factors are associated with higher risk for needing help: impaired performance status, stage of illness.

The discussed scientific work is the first of its kind research in Bulgaria. It also has a number of other **scientific contributions**, namely: for the first time in Bulgaria a correlation analysis between levels of distress and anxiety, depression, anger and the need for help in cancer patients before starting treatment. For the first time in Bulgaria, risk factors for high levels of anxiety, depression, anger and need for help were identified. For the first time in Bulgaria, the reliability of emotional

thermometers as a tool to characterize the mental status of patients before the start of systemic treatment was demonstrated.

For the first time in Bulgaria, the need for multidisciplinary teams to enter oncology practice to screen the psychological status of cancer patients before initial treatment is demonstrated.

The abstract is 60 pages long and presents in a concise form the main problems and findings presented in the thesis: formulated aim and objectives, methods used, results and discussion, conclusions and contributions of the thesis. A list of the candidate's main publications related to the dissertation topic is also presented.

The candidate's scientific output related to the topic of the dissertation includes 6 publications - 3 in Bulgarian and 3 in a prestigious foreign journal.

Conclusion

The dissertation of Dr. Assen Ivanov Yanchev is devoted to an extremely topical, neglected topic. The candidate has set himself clear, well-defined goals and tasks, which have been implemented conscientiously, precisely and thoroughly. The theoretical conclusions drawn are correct and justified. The doctoral candidate demonstrates the ability to analyze the known literature and the results of the study in a thorough and well-reasoned manner. The abstract corresponds to the dissertation content. Dr. Yanchev has serious and sufficient number of scientific publications on the topic of the dissertation, published in domestic and foreign scientific journals.

The candidate is a physician with 2 clinical specialties and extensive practical experience. He possesses both the qualities of a good professional and of a promising scientist who, along with his practical activity, sets and successfully solves serious scientific problems.

All this gives me reason to propose to the distinguished members of the scientific jury to award to Dr. Assen Ivanov Yanchev the scientific degree "Doctor" in the scientific specialty "Oncology" at the Department of Internal Diseases at MU-Varna.

14.09.2021

Reviewer: 