

PEER REVIEW

FROM PROF. KRASIMIR IVANOV, MD, PhD, DSc

CHAIRMAN OF SCIENTIFIC JURY

APPOINTED WITH ORDER № P-109-422/22.10.2020

OF THE RECTOR OF MEDICAL UNIVERSITY “PROF. DR. PARASKEV
STOYANOV”

IN REFERENCE TO: the dissertation thesis of Dragomir Svetozarov Stoyanov, MD, for the acquisition of scientific and educational degree “Doctor (PhD)” in Medical University „Prof. Dr. Paraskev Stoyanov“ – Varna, specialty - Oncology, entitled „The relationship between distress and time perception in cancer patients“ with scientific supervisor Assoc. Prof. Nikolay Vladimirov Conev, MD, PhD.

Biographical information of the candidate

Dr. Dragomir Svetozarov Stoyanov obtained a degree in Medicine at the Medical University - Varna in 2017. He graduated with honors and was awarded the Golden Hippocrates Award. In 2017 he started working as a resident in the Clinic of Medical Oncology at the University Hospital St. Marina - Varna and as a part-time assistant in the Department of Propaedeutics of Internal Medicine at MU - Varna. In 2018 he was appointed as a full-time assistant and a doctoral student at the same department. In 2020 he was reassigned to the newly formed Department of Oncology. He participates annually in international training courses, including those organized by ESMO and ASCO. Dr. Stoyanov actively participates in conducting clinical trials at the Clinic of Medical Oncology. He is fluent in English.

He is a member of the European Society of Medical Oncology (ESMO).

Distress, according to the National Comprehensive Cancer Network (NCCN), is 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." According to various studies, the incidence of clinically significant distress in cancer patients worldwide reaches 52%. Despite advances in the diagnosis and treatment of malignant solid tumors, there is a lack of a well-established system to address the psychosocial problems of patients and their families.

Distress has been shown to lead to worse compliance to prescribed treatment, lower satisfaction with medical care, worse quality of life, and lower survival. Adverse effects of distress could be avoided if the condition is recognized earlier in the course of the disease and if adequate therapeutic interventions are applied.

In order to optimize the management of distress in cancer patients, new methods for screening and recognizing distress are being sought. Distress screening faces a number of difficulties such as: lack of sufficient time and staff resources for screening, the need for shorter and more reliable screening questionnaires, the need to circumvent the patient's fear of stigmatization during the screening test.

These identified difficulties determine the need for development of new methods for distress screening in cancer patients in order to improve patient satisfaction and treatment outcomes.

Characteristics of the dissertation thesis submitted for review

The dissertation is presented in a volume of 135 pages and is illustrated with 6 tables and 24 figures. The scientific work has a classic structure: "Introduction" - 2 pages, "Literature Review" - 52 pages, "Aim and objectives" - 1 page, "Hypotheses" - 1 page, "Materials and methods" - 6 pages, "Results"- 24 pages, "Discussion" - 11 pages, "Summary"- 1 page, "Conclusions" - 2 pages, "Contributions" - 1 page, "Publications and participations in scientific forums related to the dissertation" - 2 pages (There are 4 scientific publications, 2 of which have been published in international journals with impact factor, and 2 participations with abstract presentation at international conferences), "Appendices" - 2 pages. The bibliographic references include 309 sources, of which 2 in Cyrillic and 307 in Latin.

In the **literature review**, the author initially reviews separately the two topics of study in the scientific work - distress and perception of time. The definition of the term distress according to the current guidelines and epidemiological data and risk factors for the development of distress are presented consistently and systematically. The author highlights the multidirectional adverse effects of distress on the patient with cancer, as well as on his relatives, treatment teams and the health system. The author reviews the globally introduced standards for distress management, the available screening methods for recognizing patients with distress, together with their advantages and disadvantages, and the algorithms for in-depth examination of patients with a positive screening test result. Dr Stoyanov gives special attention to the current problems related to the recognition of distress, which highlight the need for research in the dissertation study. The various methods for treatment of distress - through pharmacological and non-pharmacological interventions - are reviewed in detail. The other main phenomenon that is a subject of scientific research is the perception of time. The author gives definitions of the terminology used, provides detailed information about the available cognitive models that explain the perception of time, emphasizing the differences in cognitive processes used for prospective and retrospective assessment of time intervals and characterizes the strengths and weaknesses of each model. An overview of the information available in the literature on the numerous factors which affect perception of time is made. In the concluding part of the literature review, the author presents the currently scarce literature data on the relationship between the perception of time and distress in cancer patients. The need to conduct research with a more precise methodology which is in line with current global recommendations for distress management is emphasized and the author makes a smooth transition to the next chapters of the dissertation.

The author sets a clearly stated **aim**, namely: to investigate the relationship between time perception and levels of distress in patients with malignant solid tumors. To achieve the set goal, the author outlines the following **objectives**:

Selection of patients with malignant solid tumors who are referred for initiation of systemic antineoplastic therapy. Assessment of distress levels in patients who agreed to participate in the study. Comparison of the levels of distress in the studied patient population with the accumulated global data. Assessment of time perception in the patient population. Collection of basic clinical and pathological characteristics of patients. Establish correlations between distress levels,

perception of time and various clinical and pathological factors. Determination of the specificity and sensitivity of a prospective one-minute time estimation test as an indicator of distress level. Identification of predictors for high levels of distress.

A separate chapter of the dissertation defines the **hypothesis** of the scientific research, which is formulated on the basis of a critical synthesis of the summarized literature data.

Dr Dragomir Stoyanov has prospectively examined 262 patients who have been treated at the Clinic of Medical Oncology at the University Hospital Sveta Marina EAD - Varna. The study was conducted in the period from August 2016 to December 2017. Inclusion and exclusion criteria are clearly defined in order to select suitable patients for the study. The **materials and methods**, including the type of information collected, the methods for assessment of distress levels and perception of time, and the statistical design of the research are duly presented by the author.

Results

The study analyzed data from 262 patients with malignant solid tumors. A descriptive analysis of the patient population was performed, and the main demographic and clinicopathological characteristics are well illustrated in tabular form and with the help of figures. The cohort is well balanced in terms of gender, performance status, disease stage, and primary tumor location. According to the type of cancer, patients are grouped into 4 groups, which are presented equally, namely: lung cancer, breast cancer, colorectal cancer and other types of cancer (over 14 different locations).

Correlations between the perception of time, the levels of distress and the main clinicopathological and demographic characteristics of the patients were studied. The author presents and illustrates the results well with the help of tables and figures with an accurate description of the type of statistical analysis and the degree of statistical significance. Predictors of high levels of distress were derived by univariate and multivariate regression analysis.

Several highlights from the results

The main highlight of the results is the detection of statistically significant higher levels of distress in patients with a faster assessment of a one-minute time interval. Faster median estimates of a one-minute time interval with increasing levels of distress have been demonstrated.

The ROC analysis establishes the possibility of using the test proposed in the dissertation for assessment of time perception as a screening method to distinguish patients with high and low distress with satisfactory accuracy.

The regression analysis identified risk factors for high levels of distress, namely: younger age, breast and lung cancer, worse performance status, and faster assessment of a one-minute time interval.

The **discussion** is a critical analysis of the obtained results in the context of the reviewed literature. The discussion is closely related to the set aims and objectives and the formulated hypotheses. The author is self-critical, pointing out some of the limitations of the dissertation and offers guidelines for future research in the field.

Conclusions: 12 clear conclusions are formulated, which represent a synthesis of the whole study and correspond to the set aim and objectives. The results and conclusions of the scientific work lead to logical **contributions**, which are indicated as contributions related to communications for the first time worldwide and contributions related to communications for the first time in Bulgaria.

The **dissertation summary** is presented in a volume of 72 pages and contains the main chapters of the dissertation. The aim and objectives of the research, the hypotheses, the materials and methods, the results, the discussion with the summary, the conclusions and the contributions of the dissertation are presented. The scientific publications and participations related to the dissertation are also attached.

Critical remarks and recommendations:

There is insufficient data in the research methodology chapter on how the test for assessment of time perception is applied. The literature review highlights many factors on which the momentary perception of time depends. The author did not specify the environment in which the research is conducted - whether the test is conducted in a secluded room and whether the environmental factors during the assessment are standardized.

Another disadvantage of the scientific work is that the proposed test for assessment of subjective perception of time is compared only with the NCCN distress thermometer. The distress thermometer is a validated scale, but it is a quick screening method. The assessment of time perception should be compared with other more detailed validated scales which are available. Given the self-criticism shown by the doctoral student regarding the listed problems, I believe that this scientific work will be expanded and optimized in the near future.

The **scientific production** of the candidate, related to the topic of the dissertation, includes 4 publications, 2 of which are in international journals with impact factor. The author has 2 participations with abstract presentation of the results of the dissertation at international forums.

Conclusion

The dissertation thesis of Dr Dragomir Stoyanov entitled "The relationship between distress and time perception in cancer patients" is a fully completed and properly structured scientific work. It contains results with original contribution to science and meets all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (ЗПАСРБ), the Regulations for implementation of ЗПАСРБ and the Regulations of MU-Varna.

The dissertation thesis shows that the doctoral student Dr. Dragomir Svetozarov Stoyanov has in-depth theoretical knowledge and demonstrates qualities and skills for independent research.

Due to the above, I confidently give my positive assessment of the dissertation.

I propose to the highly respected Scientific Jury to award Dr Dragomir Svetozarov Stoyanov an educational and scientific degree "DOCTOR (PhD)".

Date:

Prof. Krasimir Ivanov, MD, PhD, DSc

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