



REVIEW

by Prof. Dr. Angel Petrov Uchikov, DSc

Head of Department of Special Surgery, internal member of the scientific jury on the grounds of Letter of Appointment No. R-1540 of July 17, 2019 of the Rector of Medical University - Plovdiv

Author: Dr. Strahil Asenov Strashilov

Form of Doctoral Studies: Independent preparation.

Department: Special Surgery

Subject: "Contemporary Practical Approach in the Surgical Treatment and Monitoring of Patients with Malignant Melanoma of the Skin"

Supervisor: Prof. Dr. Rosen Stoyanov Dimov, PhD, a professor at the Department of Special Surgery of Medical University - Plovdiv

GENERAL PRESENTATION OF THE PROCEDURE AND PhD STUDENT

The presented set of materials recorded on paper and electronic device is in conformity with Article 115 (1) from Procedure for obtaining of Educational and Scientific Degree "PhD" at Medical University - Plovdiv; Regulations of Medical University - Plovdiv from November 6, 2014; and it includes the following documents:

- an application to the Rector of Medical University - Plovdiv for initiation of the procedure for defense of the dissertation work;
- an autobiography in a European format with a signature of the PhD student;
- a copy from a diploma for higher education with notarial attestation;
- orders for enrolling in doctoral studies, interruption of education (due to maternity) and continuation of education; for striking off the list with a right of defense;
- an order for implementation of an examination from the individual plan and respective protocol for a taken examination or the PhD student's minimum according to the specialty;
- a protocol from the Department's Council for preliminary consideration of the dissertation paper, and the decisions made for initiation of a procedure and for membership of a scientific jury;
- dissertation paper;
- author's summary of his dissertation;
- a list of the scientific publications on the subject of dissertation;
- copies of the scientific publications;
- a list of the participations in scientific forums;
- a list of noted citations;
- a declaration of originality and authenticity of the applied documents;
- other documents that are associated with the course of procedure.

The PhD student applied three publications, of which one is in print.

Dr. Strahil Asenov Strashilov was born on May 23, 1979 in the city of Veliko Tarnovo. He graduated from the National Professional High School of Veterinary Medicine "Prof. Dr. Dimitar Dimov", Lovech City in 1997. Dr. Strashilov graduated in medicine at the Medical University - Pleven in 2003 as a Golden Hippocrates (with excellent (6.00) grades), while in the year 2009 he gained specialty of surgery at the Clinic of Surgery - University General Hospital for Active Treatment "Tsaritsa Yoanna", Sofia City. He has been an assistant at the Department of Surgical Diseases of Medical University - Pleven City since March 1, 2008 until now. He works at the moment as a surgeon at the Clinical Department of Plastic, Reconstructive and Esthetic Surgery of University General Hospital for Active Treatment "Dr. Georgi Stranski" EAD - City of Pleven. He was put on the list as a PhD student with independent preparation in the scientific specialty General Surgery with a letter of appointment of the Rector of Medical University - Plovdiv City in the year 2018.

VOLUME AND STRUCTURE

The dissertation paper of Dr. Strahil Asenov Strashilov is written on 246 standard, typewritten pages together with the two applications, and is illustrated with 51 color figures, 22 pictures, and 38 tables. The references contain 299 literature sources, of which three are in Cyrillic alphabet and 296 are in Latin alphabet. The structure of the scientific work includes: Introduction - two pages; Literature Review - 45 pages; Aim and Taks - one page; Material and Methods - ten pages; Results and Discussion - 78 pages; Final Statements - two pages; Contributions - one page; References - 26 pages; Application I - 63 pages; Application II - three pages.

The dissertation paper was approved and directed for official defense by extended Department's Council at the Department of Special Surgery of Medical University - Plovdiv City.

The **SUBJECT** of the dissertation paper is very current, because it concerns the contemporary surgical treatment and monitoring of patients with malignant melanoma of the skin - one of the most malignant tumors in the human body.

The incidence of cutaneous malignant melanoma in Bulgaria ceaselessly increases. A tendency is observed of decrease of the age of patients, which increases significantly the heaviness of problem. The mortality as a result of the disease in Bulgaria is one of the highest compared to the rest European countries.

The work of Dr. Strashilov extends the knowledge of diagnostics, treatment, and prognosis of patients with malignant melanoma of the skin. This is achieved by means of retrospective analysis of those patients, in which differences in the basic prognostic parameters, and the related to them survival rate and mortality rate are evaluated.

An exceptionally disputable subject is also touched, associated with the absence of unified approach among the doctors with respect to the early diagnostics and adequate methods of treatment and monitoring of those patients.

Raising most problems is the situation with absence of unified opinion among surgeons, associated with the realization of sufficiently wide repeated excision at the site of melanoma with the purpose of avoiding of local relapses, as well as with performing of sentinel lymph node biopsy, by means of which the metastatic involvement of the regional lymph nodes is assessed. Dr. Strashilov directs his efforts exactly in solving these problems, while he presents the most contemporary world tendencies in the surgical treatment of that disease and their application in patients in Bulgaria.

Based on the above-mentioned, a working algorithm for the diagnostics, treatment and monitoring, adapted to the conditions in Bulgaria, was created.

AIM AND TASKS OF THE DISSERTATION PAPER

The aim is formulated precisely and pragmatically; it represents a study of the differences in the basic prognostic parameters, and the associated with them survival rate and mortality rate in operated patients with cutaneous malignant melanoma with presentation of the newest practical aspects in their surgical treatment, and subsequent creation of a working algorithm for diagnostics, treatment, and monitoring, adapted to the conditions in Bulgaria. Dr. Strashilov formulates precisely and clearly four tasks for the achievement of that aim; these tasks are completely feasible, and there is an answer to each of them in the final statements of the dissertation.

LITERATURE REVIEW

The literature review takes 45 pages and it is sufficiently detailed. It presents one-third of the total volume of the dissertation and considers all aspects of the problem. It is presented regularly and is classified proportionally. The most contemporary data connected with the etiology, pathogenesis, clinical picture, anatomic pathology, diagnosis, treatment, and prognosis of malignant melanoma of the skin are correctly expressed in it. The review is balanced and informative, and it demonstrates the PhD student's good knowledge of the literature connected with the dissertation.

MATERIAL AND METHODS OF THE STUDY

The material includes 151 patients with cutaneous malignant melanoma, who were treated surgically - mainly at the Clinical Department of Plastic and Reconstructive Surgery of University General Hospital for Active Treatment "Dr. Georgi Stranski" EAD, Pleven City - for the period 2012-2016.

Patients are divided into two groups depending on whether sentinel biopsy of regional lymph nodes was performed or not; at the same time there are patients with lymph node dissection in

both groups. The group of patients with sentinel lymph node biopsy consists of 58 persons - 26 males and 32 females. The group of patients without sentinel lymph node biopsy consists of 93 persons - 52 males and 41 females. The methods of study is described in details.

All the obtained results are processed in IBM SPSS Statistics 24.0, while for level of significance - in which the null hypothesis is rejected - is accepted $p < 0.05$. The following statistical methods are used: descriptive analysis, cross-tabulation, graphical analysis, test χ^2 , Fisher's exact test, parametric T-test of Student, ANOVA - for comparison of the average values of more than two variables, correlation analysis, variational analysis, alternative analysis, Kaplan-Meier test, and Cox regression for assessment of the differences in survival rate and the factors that have influence.

RESULTS

The results follow strictly the course of the set tasks. They clarify the differences in sex, age, location, histological variant, thickness of tumor, depth of invasion, lymph node dissection, local relapse, distant metastases, stage of disease, and presence of concomitant oncological and non-oncological diseases in patients with cutaneous malignant melanoma in the groups without and with sentinel lymph node biopsy.

The significance of survival rate by sex, histological variant of melanoma, Breslow's thickness of tumor, presence of local relapse, and stage of disease, is clearly presented.

The most contemporary indications, methods, and results, deriving from them, for performing of repeated excision, sentinel lymph node biopsy, and lymph node dissection in patients with cutaneous malignant melanoma are clarified.

An algorithm - adapted to the conditions in Bulgaria - is created and is included in the printed form named "Medical Form of Patient with Malignant Melanoma of the Skin" based on the most contemporary data for diagnostics, treatment, and monitoring of patients with malignant melanoma of the skin.

The results are well illustrated in charts and tables.

The analysis of the results comprises the following: parametric (Kolmogorov-Smirnov), non-parametric (Pearson), and correlational (Kendall and Spearman) analyses.

The statistical processing is contemporary and reliable. The factors, that may influence the morality rate of disease, are analyzed.

DISCUSSION

Dr. Strashilov compares - in the discussion - the achieved results of the dissertation paper with those of leading Bulgarian and foreign authors, and at the same time he presents thorough reasoning and conclusions.

An accurate comparison is implemented with the results of different authors and logical explanations are looked for regarding the significant differences of the personal data with those cited in the literature. The achieved results are comparable with those from other similar studies.

FINAL STATEMENTS

A total of eight final statements are reached, which completely exhaust the set tasks and correspond with the achieved results and implemented discussion. They are very well presented, and they follow in complete degree the scientific analyses in the dissertation, and demonstrate a very good scientific value and significance of the explorative activity of the author.

The final statements demonstrate precisely the tendencies in the medical care of patients with malignant melanoma of the skin in Bulgaria, and have valuable scientific character. They are completely applicable in the surgical practice.

Explicit results and results of certain value are achieved in the dissertation.

CONTRIBUTIONS

I agree with the reference for contributions of the author, while the individual printed form created for the first time in Bulgaria - named "Medical Form for Patient with Malignant Melanoma of the Skin" and based on an algorithm for diagnostics, treatment, and monitoring - is of greatest worth.

ASSESSMENT OF THE PUBLICATIONS AND PERSONAL CONTRIBUTION OF THE PhD STUDENT

The study that is presented in the dissertation paper is completely work of the author, as well as the obtained results and presented contributions.

Two of the publications, that are connected with the dissertation, are published in journals refereed in Scopus with total SJR of 0.25.

One of them is in a refereed foreign journal, while in all of them the PhD student is the lead author. There are still no citations of those articles by other authors.

I do not have any critical comments to the implemented study and presented materials.

AUTHOR'S SUMMARY OF HIS DISSERTATION

The author's summary of his dissertation is of very good quality and completely corresponds to the content of the dissertation. The summary is implemented according to the requirements and reflects the basic results, achieved in the study.

CONCLUSION

The dissertation paper consists of scientific results, results of applied science and practical results, which represent original contribution in the science and correspond to all requirements of the Law for Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for Application of LDASRB, and the Regulations of Medical University - Plovdiv. The presented materials and dissertation results completely correspond to the specific requirements, accepted in connection with the Regulations of Medical University - Plovdiv for application of LDASRB.

The dissertation paper shows that the PhD student - Dr. Strahil Asenov Strashilov - has thorough theoretical knowledge and professional skills in the scientific specialty of General Surgery, and he demonstrates qualities and skills for independent realization of a scientific study.

Due to all the above-mentioned, I am convinced in giving my positive assessment of the implemented study, presented by the above-reviewed dissertation paper, author's summary for his dissertation, achieved results and contributions, and I suggest to the honorable scientific jury to confer the educational and scientific degree "PhD" to Dr. Strahil Asenov Strashilov in the doctoral program on General Surgery.

26.08..... 2019
Plovdiv City

Reviewer:
Prof. Dr. Angel Uchikov, DSc

