

REVIEW

By Prof. Deyan Emilov Yordanov, M.D., Ph.D.,

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Concerning: dissertation work of **Todor Yuriev Dzhendov M.D.**,

Specialist doctor, Clinic of Surgery, University Hospital, Linköping,
Sweden

for the award of the educational and scientific degree

“Philosophy Doctor”

On topic: **“Multimodal approach in the treatment of esophageal carcinoma.
Prognostic and predictive markers.”**

The dissertation paper submitted for review is written on 146 pages and is structured as follows:

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| 1. | Table of contents | - 3 pages |
| 2. | Abbreviations | - 2 pages |
| 3. | Introduction | – 3 pages |
| 4. | Literature review | – 39 pages |
| 5. | Goals and objectives | – 1 page |
| 6. | Materials and methods | – 13 pages |

7.	Results	– 23 pages
8.	Discussion	– 19 pages
9.	Conclusion	– 2 pages
10.	Consequences	– 1 page
11.	Publications	– 1 page
12.	Appendices	– 6 pages
13.	Bibliography	– 22 pages

The dissertation work is illustrated with 13 tables, 33 figures and 6 appendices. There are 301 titles listed in the bibliography, of which only the citation from the National cancer registry is in Cyrillic. I consider the lack of knowledge of Bulgarian publications concerning esophageal cancer to be a known shortcoming.

The literature is very up-to-date – there are almost no titles before 2010. In terms of structuring the dissertation work, the relatively large volume of the literature review, which occupies almost a third of the entire work, is impressive.

In the literature review, the doctoral student examines in detail the incidence and prevalence, etiology, pathogenesis, clinical presentation, diagnostic methods and prognosis in esophageal cancer. The author examines in detail the staging of esophageal cancer, as it has a direct relation on both the therapeutic process and the prognosis.

Logically and necessarily, the emphasis of the literature review accentuates on treatment methods, divided according to the stage of development as well as on the prognostic factors, which are divided into two groups – from the patient's side and according to the applied treatment.

Consideration of genetic factors and the influence of human papilloma virus in the carcinogenesis of esophageal cancer deserves admiration. These studies are extremely current and not yet finished. I believe that the dissertation work would have gained more if the literature review ended with analytical conclusions that would highlight the unresolved issues and substantiate the goals and objectives of the dissertation work.

The **purpose** of the dissertation work is clearly and briefly stated – to evaluate the current methods for treatment of esophageal cancer and to define the prognostic markers for the optimization of the therapeutic protocol. To achieve this goal, the author sets himself six tasks. They are specific and clearly worded.

Patients. The author's study included 129 patients operated in UMHATEM "N.I.Pirogov", Sofia, from which 12 inoperable patients were excluded. The second group of patients consists of 115 patients who were operated in University Hospital, Linköping, Sweden. The two groups were compared by almost all possible criteria – gender, age, stage of disease, applied surgical treatment, postoperative results and postoperative survival. The data has been processed with modern statistical methods that prove or disprove the statistical claims with high probability.

Accordingly, the obtained results are extremely interesting not only from a surgical point of view – there is room for many conclusions from oncologists, sociologists, psychologists and specialists in demography. For example, very interesting is the fact that only a quarter of the patients in Sweden are of working age, while in Bulgaria they are 50%. 90% of the patients in Sweden received neoadjuvant therapy and 60% had negative nodal status (N0). Perhaps this is related to the postoperative survival, which in Bulgaria is – three-year survival 12.8% and five-year survival 11.1%, and in Sweden 53% and 43.5% , respectively. The dependence is hardly so simple, considering that in the Bulgarian cohort there are no T0 patients, with T1 is only one patient and 81

patients are with T3 tumors. In the Swedish cohort, only 34 patients are with T3 tumors and this clearly shows the difference in the levels of diagnosis and prevention in the two countries.

The author thoroughly analyzes the prognostic value of nodal status, and his conclusions coincide with those of most globally recognized experts. Analysis of the significance of neoadjuvant chemotherapy alone or in combination with preoperative radiotherapy on postoperative survival is of interest. The issue is still debatable and pending worldwide resolution.

The author's first in the country genetic study of patients with esophageal cancer and the sought after combination with papilloma virus deserves admiration. The potential of these analyzes is probably very high and the future will prove it.

The author offers a detailed therapeutic algorithms based on the TNM classification and according to the clinical stage, which would be a useful practical guide.

Consequences. As a result of the in-depth examination of the problem, D-r Dzhendov drew 6 consequences.

I accept seven main contributions of the dissertation work, namely:

1. An analysis of the contemporary methods of treatment of esophageal carcinoma by stages is performed.
2. New methods of treatment in the early stages of the tumor and in patients who are not candidates for surgical resection are presented.
3. An ambispective clinico –epidemiological study was conducted in two esophageal surgery centres in two European countries and data on the incidence, clinico-histological characteristics and survival of patients with esophageal carcinoma were presented.

4. The role of the perioperative oncological therapy in the complex treatment of this type of carcinoma has been confirmed.
5. Additional prognostic indicators regarding survival were derived.
6. A therapeutic algorithm was developed according to the histological type and the stage of the tumor.
7. A DNA bank for esophageal tumors has been established and is stored in the Centre for Molecular Medicine and can be used for future studies.

In conclusion, the presented dissertation paper is based on a large clinical material relevant to clinical practice from the point of view of the severity of the disease and the volume of the operative intervention. The achieved results, formed in conclusions, are important for the clinical practice not only of thoracic surgeons and intensive care physicians, but also of gastroenterologists, medical oncologists and radiation oncologists. I believe that the critical remarks I made do not reduce the scientific value of the work, and the dissertation submitted for review has all the qualities to award Todor Yuriev Dzhendov M.D. the scientific and education degree “Philosophy doctor”.

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Sofia

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