

## REVIEW

from

Assoc. Prof. Dr. Dimitar Ivanov Bulanov, MD, PhD

**Concerning:** Defense of a dissertation for the acquisition of educational and scientific degree "PhD"

professional field 7.1. Medicine in the field of higher education 7. Health and sports

**Author:** doctor Elmira Momchilova Daskalova

**Form of doctoral studies:** full-time

**Institution:** Clinic of Hepatobiliary, Pancreatic and General Surgery of Acibadem City Clinic Tokuda Hospital EAD, convened by order 443 / 29.06.2020 of the executive director of the hospital to defense by an extended scientific board of the clinic.

**Topic:** "Pancreato-jejunostomy after duodeno-hemipancreatectomy - types, results, individual approach to selection" with scientific adviser Prof. Dr. Kiril Vassilev Draganov, Ph.D., Hepatobiliary, Pancreatic and General Surgery of Acibadem City Clinic Tokuda Hospital EAD

### 1/ **General presentation of the student and of the topic**

By order 570 / 18.09.2020 of the Executive Director of Acibadem City Clinic Tokuda Hospital Dr. Venelina Atanasova I have been appointed a member of the scientific jury for the defense of the dissertation of Dr. Elmira Daskalova on topic "Pancreato-jejunostomy after duodeno-hemipancreatectomy - types, results, individual approach to selection".

The presented set of materials on paper and electronic device is in accordance with the requirements of the Law for development of the academic staff in the Republic of Bulgaria, the Regulations for its application in " Acibadem City Clinic Tokuda Hospital " and the Regulations for acquiring scientific degrees and holding academic positions in the hospital.

The following documents are included:

- application to the executive director of Tokuda Hospital for opening the procedure for defense of the dissertation
- CV in European format with the signature of the doctoral dissertation
- a copy of the diploma of higher education - orders for enrollment in doctoral studies and for expulsion with the right to defense
- order to conduct an examination of the individual plan and the respective flow for completed doctoral minimum in the specialty
- minutes of a meeting of the extended scientific college for preliminary discussion of the dissertation and the decisions taken for opening the procedure, as well as for the composition of the scientific jury

- dissertation
- summary of the dissertation
- list of scientific publications related to the topic of the dissertation
- copies of the mentioned scientific publications
- declaration of originality and authenticity of the attached documents

The student has also attached a full-text article in which she is the sole author. The article is thematically related to the topic of the presented dissertation.

## **2/ Notes and comment on the documents**

The procedure for the defense of the dissertation, as well as the related documents, fully comply with the current legal framework in the country, mentioned above.

## **3/ Short biography**

Dr. Elmira Momchilova Daskalova graduated from the Faculty of Medicine at the Medical University, Sofia in 2014. She currently works as a doctor and specializes in surgery at the Clinic of Liver-Gall, Pancreatic and General Surgery in "Acibadem City Clinic Tokuda Hospita ". From the beginning of the academic year 2019 - 2020 she is a part-time assistant and leads the practical exercises of 3rd year students in General and Operative Surgery as well as those of 4th and 5th year - Special Surgery.

After the successful internal defense on 29.07.2020 Dr. Elmira Daskalova was expelled with the right to official defense - Order 482 / 31.07.2020 of the Executive Director Dr. Venelina Atanasova.

## **4/ Significance of the topic**

The topic of the dissertation is extremely relevant both in a fully scientific and in a scientifically applied aspect. The main reasons for this are many and well known as repeatedly researched and analyzed. Due to all this, I will not dwell on details, but only on some facts related to the research of Dr. Daskalova. Pancreatic cancer is a problem with multidisciplinary nature. The leading surgical approach has a leading role in the healing process. It is a well-known aphorism that the pancreato-jejunal anastomosis after Whipple's operation is the 'Achilles' heel' of the procedure. Obvious evidence is the high incidence of insufficiency (60% in some studies) and the formation of postoperative pancreatic fistula. In turn, this insufficiency worsens the quality of life of the patient, prolongs the hospital stay, requires additional treatment, making it more expensive. Sometimes it is an indication for reoperation. Last but not least, pancreatic fistula delays the start of adjuvant chemotherapy for a significant period of time which can lead to deteriorating long-term results.

The occurrence of this specific complication depends on a number of factors, one of which is the method of constructing a Pancreato-jejunostomy anastomosis. The existence of many methods and modifications to perform the anastomosis proves the lack of a universal, safest, relatively

fast and easy way. These, as well as a number of other factors, unequivocally prove the importance of the topic of Dr. Daskalova's dissertation.

#### **5/ General characteristics of the dissertation**

The dissertation consists of 145 pages, illustrated with 25 figures and 33 tables. The studied material used in the dissertation is part of the surgical archive of the Clinic of Liver-Gale, Pancreatic and General Surgery. The Introduction and the literature review include 49 pages, the Purpose and tasks and the Material and methods - 8 pages, the Survey results - 17 pages, the Analysis and the Discussion of results - 19 pages, the Conclusion - 3 pages. The Bibliography includes 380 sources, of which 22 in Cyrillic and 358 in Latin.

#### **6/ General analysis**

The literature review is detailed, analytical and of high scientific value, rich in facts and current research and meta-analysis related to the topic. Much of the current information on the main indications for DPHE with a focus on pancreatic cancer - epidemiology, statistics, carcinogenesis, clinical manifestations, laboratory and instrumental diagnosis - is presented in detail.

An important place in the review of the literature is occupied by the description and illustration of the variety of methods for pancreatic anastomosis - the techniques of Cattle-Warren, Buchler, Blumgart, Heidelbrg, Kakita and other authors are mentioned.

The importance and the role of duct-to-mucose anastomoses in reducing the risk of occurrence and frequency of the disease are also considered.

Dr. Elmira Daskalova also draws the reader's attention to the long-standing discussions on the benefits of protective pancreatic and contact drainage. The prevailing view is that there is still no reasonable alternative to their use in pancreatic surgery.

The complications after DPHE, as well as the risk factors for their occurrence, are presented in a volume of 9 pages (39 - 48 inclusive).

As one of the most valuable moments in the dissertation in general and in the literature review in particular, I consider the conclusions from the review of the specialized literature presented on pages 48 - 49. This is a good enough motivation and justification of the surgery to the pancreas and proves the distinctive theoretical training of Dr. Daskalova

#### **7/ Research methodology**

The goal and tasks of the dissertation (10 in number) are logically and precisely formulated with a clear practical focus.

I give a high assessment of the defined working hypothesis - a logical connection between the goal and the tasks and the basis on which the whole study is based.

The material and methods are presented in sufficient detail, both with a textual description and with figures from interoperable stages.

For a 12-year period, 829 pancreatic resections were performed in different volumes and complexity in the student's clinic. Of these, 236 patients with duodeno-hemipancreaticotomy and subsequent exacerbation were selected.

Statistical methods of analysis are appropriate for this type of study and ensure that reasonable conclusions are reached.

#### **8/ Assessment of the achieved results and of the contribution of the topic**

The own results, their analysis and discussion are presented descriptively, in tabular and graphical form in Chapters 3, 4 and 5 (pp. 59 -99 inclusive).

The student has made a very well-founded interpretation of the preoperative data in the series - demography, bad habits, comorbidity, pathohistological characteristics, laboratory and instrumental studies. The surgical characteristics are also described in detail - diameter of the main pancreatic duct, consistency of the parenchyma, use of protective pancreatic and biliary drainage, supporting suture of the pancreatic remnant type 'carcass', duct-to-mucosa anastomosis, DHPE as part of larger contact multivisceral resections.

The achieved early postoperative results are comparable to those in the specialized literature. The ten conclusions are the logical conclusion of the study and have a definite scientifically applicable value. The established dependences between the frequency of anastomotic insufficiency and pre-, intra- and postoperative factors (anemia, hypoalbuminemia, their dynamics on the first day after intervention, preoperative hyperbilirubinemia, but only in males) are of original character and extremely interesting in my opinion. , etc.) Important for practice are the proven benefits of using both protective drainage and bilio-digestive anastomosis (if indicated), the 'caracas' suture, the duct-to-mucosa anastomosis, which significantly reduces the risk of pancreatic cancer, or at least the risk of a high-flow Grade C fistula. I strongly recommend to the student institution that this information be presented at national and international scientific forums in order to discuss and promote it.

#### **9/ Assessment of the student's publications and personal contribution**

The publishing activity of Dr. Elmira Daskalova on the topic of the dissertation meets the requirements of the legal normative framework in force in the Republic of Bulgaria.

#### **10/ Summary**

The summary of the dissertation meets the requirements such as volume and content, giving a clear enough idea of the essence of the work, reflecting in sufficient detail the results achieved and formulated conclusions.

#### **11/ Remarks**

I have no critical remarks on the dissertation. I had several, some of which were of a commendatory nature. I presented them during the internal defense before the extended

scientific college in which I participated. Apparently, the student and his supervisor considered them justified and fully complied with them, for which I thank them.

## 12/ **Conclusion**

After a detailed acquaintance with the dissertation, I give a positive assessment of the work of Dr. Elmira Daskalova, the problems of constructing a pancreato-jejunal anastomosis after duodeno-pancreatic resections.

The dissertation is a completed scientific research with high scientific merits and great practical orientation. The content of the dissertation corresponds to the set topic, goal and tasks. The clinical material is well and professionally analyzed in clinical and statistical aspect, ending with sound conclusions useful for clinical practice.

There are no violations of the procedure and all the requirements of the current regulatory framework for the development of the academic staff, as well as the Rules of the clinic are met. The dissertation contains scientifically applicable achievements with confirmatory and original character. It is written in a good style, the transition between the individual sections is smooth and logical, which is easy to read and enjoyable.

The presented materials and results show that the student has in-depth theoretical knowledge and professional skills in the scientific specialty "General Surgery", demonstrating qualities and skills for conducting independent research.

Due to the above, I give my unequivocal positive assessment of the research, presented by the peer-reviewed dissertation, reviewed results and contributions. I propose to the esteemed scientific jury to fully award the educational and scientific degree "PhD" to Dr. Elmira Momchilova Daskalova in a doctoral program in "General Surgery". I strongly vote YES.

19.10.2020

Sofia

Assoc. Prof. Dr. D. Bulanov, PhD