

To the Doctoral School  
According to Order No. R-109-274 / 20.06.2025  
of the Rector of MU – Varna

**REVIEW**  
of the dissertation  
**"Features of exocrine pancreatic function after  
duodenopancreatic resection for adenocarcinoma"**

by Dr Nikolay Veselinov Nikolov,  
PhD student at the Department of Surgical Diseases, Medical University of  
Varna  
for the award of the academic degree of **"Doctor"**  
in the scientific field of **Surgery – 03.01.37.**

Reviewer: Professor Dr. Rossen Evgeniev Madjov, MD, PhD, DSc  
Department of Surgical Diseases  
Medical University - Varna.

The dissertation work of Dr. Nikolay Nikolov addresses a serious and important clinical problem - features of exocrine pancreatic function after duodenopancreatic resection for adenocarcinoma.

Pancreatic adenocarcinoma ranks fourth as a cause of mortality among all oncological diseases, with survival rates ranking last compared to other types of neoplasms and remaining unchanged over the past 40 years. Pancreatoduodenectomy is the only treatment method that offers a potential cure for this group of patients. Despite aggressive modern intervention techniques, only 10% of newly diagnosed patients with this pathology can undergo radical surgery at the time of diagnosis.

Postoperative complications are one of the leading causes of reduced survival rates after duodenopancreatic resection for adenocarcinoma. The choice of reconstruction technique must be strictly individualized, with the degree of pancreatic fibrosis being determined prior to surgery using imaging methods (CT and MRI of the abdomen) and intraoperatively by the surgeon. The technical feasibility of performing a pylorus-preserving pancreatoduodenectomy

in combination with the choice of anastomotic technique is largely related to the postoperative exocrine function of the pancreatic remnant.

The exocrine pancreatic function after pancreatoduodenal resection is extremely important in many aspects. Studies on exocrine pancreatic function according to the type of reconstruction have controversial results and are poorly represented in the literature. Various studies by leading authors in pancreatic surgery on the relationship between the anastomotic technique used and early postoperative complications are also inconsistent.

The dissertation is written on **118** standard pages. The bibliography includes **258** titles (mostly from the last 10-15 years), of which **5** are in Cyrillic and **253** in Latin script. The visualization is done with **43** tables and **39** figures.

The literature review covers: historical data, epidemiology, etiology, clinical manifestation, modern diagnostic methods, assessment of preoperative exocrine function, treatment, the relationship between exocrine pancreatic function and surgical outcomes and overall survival.

The author is well-versed in the problem - many leading authors and schools dealing with the problems of duodenopancreatic resection and the possible complications.

The author's GOAL is to:

*"To study exocrine function after pancreatoduodenal resection for neoplasms, postoperative survival, quality of life, the relationship between maldigestion, tumor growth, and metastasis, as well as the correlation between types of reconstructive techniques (pancreatogastro- and pancreatojejunostomy) and enzyme activity."*

The overall objective is well formulated in relation to the entire dissertation. To achieve the main objective, the author sets the following 5 tasks:

1. To study the demographic and clinical characteristics of the study population.
2. To establish the most appropriate methods for assessing exocrine function after pancreatoduodenal resection and the degree of reliability when using imaging diagnostics and intraoperative gland constellation as an indicator of exocrine function.
3. To study the frequency of exocrine dysfunction after pancreatogastroanastomosis and pancreatojejunostomy and the frequency of coverage of the main pancreatic duct by gastric mucosa when using pancreatogastroanastomosis as a method of reconstruction.



4. To study the frequency of postoperative complications after pancreatogastro- and pancreatojejunostomy, as well as their effect on pancreatic gland reserve.

5. To study the relationship between enzyme insufficiency and tumor progression, and the effect of exocrine insufficiency after pancreatoduodenal resection on survival and quality of life.

The tasks are well formulated and the development of the dissertation follows their execution.

The object of the study are **92** patients with adenocarcinoma of the head of the pancreas, out of a total of 121 duodenopancreatic resections performed for neoplasms hospitalized at the Surgery Clinic of the Military Medical Academy Hospital in Varna between 2017 and 2022.

Patients were selected based on age, gender, tumor size, histological type and resection line. The criteria for selecting patients for the study were divided into inclusion criteria (TNM stage 1-2B, patient cooperation, availability of preliminary data from radiological and laboratory tests, R0 resection) and exclusion criteria (unresectable tumors, metastatic tumors).

Clinical, laboratory, imaging, instrumental, and statistical methods were used, and the surgical aspects of pancreatic drainage according to the type of reconstruction were examined in detail.

The discussion of patients by a multidisciplinary team in order to determine operability and treatment strategy for each case is of paramount importance for the favorable outcome of treatment in this group of patients.

The use of abdominal CT with a pancreatic scan protocol as the first method of choice, followed by abdominal MRI in cases of suspected generalized disease or inoperability is the gold standard for accurate diagnosis.

The most common clinical manifestations of adenocarcinoma of the head of the pancreas are mechanical jaundice in about 80% of cases, pain, chronic pancreatitis, weight loss, and impaired exocrine and endocrine function of the pancreas. In patients with severe exocrine insufficiency, the author reports a significant increase in the frequency of hematogenous metastasis and local recurrence compared to patients with moderate insufficiency or normal function of the residual pancreas.

The leading cause of post-pancreatectomy exocrine insufficiency is preoperative obstruction of the main pancreatic duct and underlying chronic pancreatitis. Surgical intervention disrupts the mechanisms responsible for secretion of the pancreas, and there is also a relative loss of pancreatic

parenchyma. Postoperative effects on these processes include pancreatic fistulas, postoperative pancreatitis, and intra-anastomotic obstruction of the pancreatic duct. In patients undergoing pancreatogastric anastomosis, the buffering properties of food have a beneficial effect on the action of pancreatic enzymes, with this effect being more pronounced in pylorus-preserving operation.

As a result of careful analysis of the literature and interpretation of their own clinical data, the author and the clinic team consider pancreatogastroanastomosis to be the preferred method of reconstruction due to lower rate of severe postoperative complications compared to pancreatojejunostomy, shorter hospital stay, better exocrine function, improved survival and quality of life. An algorithm has been developed for performing a follow-up gastroscopy after pancreatogastric anastomosis due to the tendency for the anastomotic surface to be covered by gastric mucosa.

The reported mortality rate in the first postoperative month was zero, while in the second postoperative month it was 4.30% in the PGA group and 6.50% in the PYA group. In the third postoperative month, mortality doubled, with 13% in the PGA group and 15.20% in the PYA group.

The conclusions – six in total – are well formulated and correspond to the main objective and tasks set by the author.

The contributions which the doctoral student has listed at the end of the dissertation (five in total) have a scientific-applied character and are the result of the personal activity of the author, as well as of the team at the Surgery Clinic of the Military Medical Academy Hospital in Varna.

The abstract is very well structured and fully reflects the essence of the dissertation work. The excellent stylistic and design layout, as well as the quality of printing, make a very good impression.

Dr. Nikolay Nikolov graduated Medicine at MU – Varna in 2006.

From 2006 to 2013, he has been a resident surgeon at the Surgery Clinic at “St. Anna” Hospital – Varna. In 2014, he obtained a specialty in General Surgery. From 2014 to 2015, he has been a head of the surgical team at the Surgery Clinic of “St. Anna” Hospital - Varna. From 2015 to 2022, he works as a surgeon at the Surgery Clinic of the Military Medical Academy Hospital in



Varna. Since 2022 until now, he has been a head of the surgical team at the Surgery Clinic of "St. Anna" Hospital - Varna.

Dr. Nikolov has completed postgraduate training in 2009 in "Laparoscopic Colorectal Surgery" in Paris, France and a course in 2023 on topic "Hepatocellular Carcinoma – a multidisciplinary Approach." He regularly participates in national scientific congresses, conferences and symposiums on surgery. He regularly participates in national scientific congresses, conferences, and symposiums on surgery.

He is fluent in written and spoken English and French. He is a member of the Bulgarian Surgery Society and the Bulgarian Medical Association.

Dr. Nikolay Nikolov has three publications related to his dissertation work of which he is the first author in all of them.

### CONCLUSION

The presented dissertation is thorough and thought-provoking, clearly and accurately outlining the characteristics of exocrine pancreatic function after duodenopancreatic resection. It has results of contributory character and journalistic manifestations.

Dr. Nikolay Nikolov fully meets the minimum national requirements according to the ZRASRB and its implementation regulations, as well as the regulations of the Medical University of Varna.

All of this gives me the right and the basis to recommend to the members of the Scientific Jury to give their **positive vote** and award the educational and scientific degree of "**Doctor**" to Dr. Nikolay Nikolov.

20.08.2025  
Varna

Reviewer:  
/Prof. Dr. R

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