**To the Chairman of the Scientific Jury,**
**determined by Order No. R-1344/20.11.2024.**
**of the Rector of Medical University – Plovdiv**
**V. Aprilov No15A**
**4002 Plovdiv**

# REVIEW

**In association with the procedure for acquiring the degree of PhD as an independent PhD student in the Second Department of Internal Medicine, Section of Gastroenterology, Faculty of Medicine, Medical University – Plovdiv**

**By Assoc. Prof. Dr. Daniel Ilianov Doykov, MD, PhD**
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**Subject: Thesis by Dr. Deyan Georgiev Radev**
On the topic **"Spleen stiffness measured by pSW elastography as a predictor of high-risk varices of the esophagus in patients with liver cirrhosis"** with scientific supervisors Prof. Dr. Vladimir Andonov, MD and Assoc. Prof. Dr. Katya Doykova, MD for acquisition of educational and scientific degree
"PhD" in the scientific specialty "Gastroenterology", professional field 7.1 Medicine, field of higher education 7.Healthcare and Sports

## 1. Relevance of the topic and appropriateness of the set goals and objectives

Hemorrhage from dilated esophageal varices is a problem of paramount importance and the leading cause of death in patients with hepatic cirrhosis and portal hypertension. Videogastroscopy in these patients is the method of choice for diagnostic specification and staging of esophageal varices. It is essential to assess the risk of bleeding in these patients in advance, thus significantly improving their survival. Mainly in the last decade, numerous attempts have been made to discover modern non-invasive methods to assess esophageal varices and rule out patients at risk in the clinical practice. This is possible without dangerous invasive procedures and

discomfort for the patient, and last but not least, it is associated with reduced economic costs.

I believe that the topic of this thesis is extremely relevant because non-invasive techniques have the potential to be routinely applied in clinical practice.

**2. Presentation of the procedure and the PhD student**

The presented set of materials, including a thesis, an abstract and an administrative set of documents, is in accordance with the Procedure for acquiring the degree of PhD at the Medical University of Plovdiv and includes all documents listed in the requirements of the Regulations.

The thesis consists of 154 standard typewritten pages and is illustrated with 22 tables and 44 figures. The style is clear and in literary language. There are 7 chapters, which include: introduction - 3 pages, literature review - 50 pages; aim and objectives - 1 page; research methods - 11 pages; Results – 62 pages; summary of the results with discussion - 10 pages; conclusions – 2 pages; Contributions – 2 pages.

The bibliography contains 135 sources, of which 4 are in Bulgarian. The majority of them have been published in the last 10 years, which confirms the relevance of the problem.

**Brief biographical data of the PhD student:**

Dr. Deyan Georgiev Radev graduated from the Medical University of Plovdiv with excellent grades. After graduating in 2017 he started his professional career at the Clinic of Gastroenterology at the University Hospital "Kaspela" in Plovdiv, where he has been working to this day. In 2022, he acquired his specialty in gastroenterology. He shows interests in endoscopic interventional procedures, as well as in liver diseases. He has third-level certificates for endoscopic and ultrasound procedures, routinely conducting elastography examinations of the liver and spleen. Dr. Radev has been an assistant professor at the Second Department of Internal Medicine, Section of Gastroenterology in Medical University of Plovdiv since 2018. He was also enrolled in the department as a PhD student. He regularly participates in national and international conferences and courses for professional development.

**3. Coverage of the literature on the problem**

The literature review covers 50 pages of the dissertation. It is detailed and well structured. It accurately analyzes the topic of the dissertation and modern scientific achievements in this field of gastroenterology. Literature data on the etiology and pathogenesis of liver cirrhosis are consecutively displayed. The currently available imaging, interventional and laboratory methods for diagnosing liver pathology and esophageal varices are presented in detail. The advantages and disadvantages of each

individual method are sufficiently analyzed. Dr. Radev emphasized the need for new methods for non-invasive assessment of the complications of portal hypertension and in particular esophageal varicose bleeding. Ultrasound elastography - its physical principles, methodology and methods of execution, are presented in detail in the review. Data from current consensus and recommendations for ultrasonic elastography were used. The chosen non-invasive diagnostic method - point shear wave - elastography is analyzed in depth, its benefits and disadvantages are presented, as well as its applicability to the spleen.

The volume of the literature review is sufficient and reflects exhaustively the available literature data on the problem.

**4. Materials and methods of the study**

184 patients were examined, divided into the following groups:

- 46 patients without liver pathology
- 46 patients with alcoholic cirrhosis
- 46 patients with liver cirrhosis with hepatitis B etiology
- 46 patients with hepatitis C liver cirrhosis

The inclusion and exclusion criteria in the survey are clear and well-structured. Clinical, paraclinical and imaging methods are used. The methodology for conducting an elastographic examination is described in detail. It has a high accuracy IQR/M <30, which outputs an average wave velocity (SWV; shear wave velocity) in m/s after ten measurements. In patients with liver pathology, a videogastroscopy is performed. Based on the presence of esophageal varices, patients are divided into 4 groups:

- patients without varices
- a group with small esophageal varices
- a group with medium-sized varices
- group with large esophageal varices

Patients from the last two groups are considered high-risk.

The statistical analysis is carried out with up-to-date versions of the programs IBM SPSS Statistics for Windows, Version 27.0(2023), Minitab 21.4.2 (2023)., MedCalc 22.016(2023).

**5. Characteristics and evaluation of the obtained results**

The aim of the dissertation is correctly stated. It is to analyze "Spleen stiffness measured by pSW elastography as a predictor of high-risk esophageal varices in patients with liver cirrhosis".

The results are extensively displayed and analyzed in 63 pages.

The study started by deriving reference limits for transverse wave velocity (SWV) in patients without data of liver disease.

The method of SW elastography of the spleen in patients with hepatic cirrhosis of alcoholic etiology is analyzed in task 2. Mean and reference values for SWV are derived and compared with the degree of esophageal varices in these patients.

Similarly, Task 3 and Task 4 also derive reference values for SWV in patients with hepatic cirrhosis with hepatitis B and C viral etiology.

In each task, ultrasound measurements of the spleen are analyzed and their relationship with the degree of varices is deduced.

The essence of the dissertation is presented in task 5, where cut-off values are set that define patients with hepatic cirrhosis as high-risk for esophageal varicose bleeding. These data have not only scientific, but clinical and practical importance. For cut-off values of SWV in patients with hepatic cirrhosis, 3.17 m/s for alcoholic cirrhosis, 2.94 m/s for hepatitis B, 2.64 m/s for hepatitis C are deduced. They are compared with current studies in this area and confirm the role of ultrasound elastography of the spleen as a non-invasive method for assessing esophageal varices in patients with hepatic cirrhosis.

In task 6, laboratory and ultrasound parameters and their relationship with the stage of esophageal varices are analyzed.

The analysis of the obtained results on the topic and their comparison with those of other authors is presented in the "Summary" section. The results are reliable and the conclusions correspond to the tasks set.

I agree with the presented contributions of original, scientifically applied and confirmatory nature.

In association with the dissertation, 3 articles were published and a poster on the topic was presented at an international forum.

**6. Conclusion**

In conclusion I believe that the thesis of Dr. Deyan Georgiev Radev on the topic "Spleen stiffness measured by pSW elastography as a predictor of high-risk esophageal varices in patients with liver cirrhosis" fully meets the requirements for acquisition of the educational and scientific degree "PhD" and I confidently give my positive assessment.



Date:10.12.2024 Assoc. Prof. Daniel Ilianov Doykov, MD, PhD