

**REVIEW**

**By Assoc. Prof. Mariana Penkova Radicheva, MD, PhD**

**Department of Propaedeutics of Internal Medicine and Clinical Laboratory,  
Trakia University – Stara Zagora**

of the presented thesis

**"Spleen stiffness measured by pSW elastography as a predictor of high-risk  
esophageal varices in patients with hepatic cirrhosis"**

**by Dr. Deyan Georgiev Radev**

for the acquisition of the educational and scientific degree "PhD"

in the scientific specialty "Gastroenterology",

Professional field 7.1 "Medicine"

field of higher education 7. "Health and Sports"

Supervisorand:

Prof. Vladimir Andonov, MD, PhD

Assoc. Prof. Katya Doykova, MD, PhD

**1. Relevance of the topics and appropriateness of the goals and set objectives**

Esophageal varices are one of the most significant complications of portal hypertension in patients with hepatic cirrhosis. Bleeding from dilated varices of the esophagus is still a problem of paramount importance and a leading cause of death in these patients. Timely diagnosis and staging of this pathology, as well as a preliminary assessment of the risk of bleeding, are vital for avoiding complications and improving survival. Videogastroscopy is still the gold standard for the diagnosis and therapy of esophageal varices, but in recent years more and more attempts have been made to introduce new non-invasive methods into clinical practice. Spleen is considered a direct reflection of portal hypertension and is increasingly recognized in international consensuses.

I believe that the topic of the dissertation is relevant and has great clinical application, and the results of such studies can be the basis for a lasting adoption of non-invasive techniques in everyday practice.

**2. Structure of the dissertation**

The presented set of materials, including a dissertation, an abstract and an administrative set of documents, is in accordance with the Procedure for acquiring a PhD

degree at Medical University - Plovdiv and includes all documents listed in the requirements of the Regulations.

The dissertation is in a form and volume corresponding to the requirements and consists of 154 standard pages. It is illustrated with 22 tables and 44 figures. The style is accessible, in literary language.

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

The literature review is comprehensive and detailed. Literature data on the pathomorphological characteristics of hepatic cirrhosis, portal hypertension and their complications are presented. The need for new techniques for early non-invasive assessment of patients at risk for varicose hemorrhage is convincingly motivated. In the next section, the method of ultrasonic elastography is discussed in detail. Its physical foundations are presented, as well as the existing types of elastography techniques - quantitative and qualitative. Particular attention is paid to the method of point shear wave - elastography. The technical aspects are presented and its applicability on the spleen is proved. Finally, the studies carried out so far on the topic, the results obtained and the questions that should be answered are presented.

The structure and volume of the literature review reflects exhaustively existing literature data and shows excellent knowledge of the problem.

The literary reference includes 135 sources, of which 4 are by Bulgarian authors and 131 are in Latin. The majority of them have been published in the last 10 years, which confirms the relevance of the problem.

### **4. Materials and methodology of the survey**

The study included 184 patients - 46 healthy subjects, 46 patients with alcohol cirrhosis, 46 patients with hepatic cirrhosis with hepatitis B viral genesis, as well as 46 patients with hepatitis C etiology. The criteria for inclusion in the study were defined. All patients had anamnestic, physical and laboratory data, as well as B-mode ultrasound. The method for performing point shear wave was explained in details. Examination with high accuracy  $IQR/M < 30$  was performed and the average wave velocity (SWV; shear wave velocity) was displayed in m/s after ten measurements. The methods also include videogastroscopy, through which patients are divided into 4 groups - a group without varices and groups with small, medium and large varices. The data analysis was carried out with up-to-date versions of the statistical 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 goal to analyze "Spleen stiffness measured by pSW elastography as a predictor of high-risk esophageal varices in patients with hepatic cirrhosis" is specific.

The results obtained are presented in 63 pages. The complete overlap between the set tasks and the corresponding results is impressive. After each task, a short discussion of the data obtained and their comparison with other available studies is added.

The results of task 1 are the starting point of the study by deriving reference limits for shear wave velocity (SWV) in patients without liver pathology.

Task 2 aims to investigate the method of SW elastography of the spleen in patients with hepatic cirrhosis of alcoholic etiology. It derives mean and reference values for SWV and compares them with the degree of esophageal varices in these patients. It was concluded that the majority of patients in this group had high-risk esophageal varices and a high positive association was found between the presence of varices and SWV values ( $r_s = 0.734$ ).

In the next two tasks, reference values for SWV in patients with hepatitis B and C viral etiology were also derived. In all patient groups, SWV values showed a high association with varices degrees, with the highest in patients with hepatic cirrhosis of alcoholic etiology.

Ultrasound measurements (transverse and longitudinal size of the spleen) and their relationship with SWV and the degree of varices were also analyzed.

Task 5 presents cut-off values defining patients with liver cirrhosis of various etiologies as high-risk for esophageal varicose bleeding. The data obtained are clearly presented and illustrated and are of high practical importance. Cut-off values for SWV in patients with alcoholic, HBV and HCV etiology were derived respectively 3.17 m/s, 2.94 m/s, 2.64 m/s and they have a high specificity of about 90% and a sensitivity between 71% and 87.5%. These results are close in value to the data obtained in similar studies and have the potential to be successfully applied in clinical practice as a non-invasive method for assessing esophageal varices.

The last 6th task analyzes laboratory parameters and other ultrasound measurements and their relationship with the presence and severity of esophageal varices.

In the "Summary" section, the results are analyzed and compared with those of other authors. Similarity was found in most of them, which proves their credibility. The conclusions correspond to the tasks and results set. There are contributions of original, scientifically applied and confirmatory nature.

In connection with the dissertation, 3 articles were published as the leading author, one of them in an Scopus indexed journal. A poster on the topic was also presented at an European Conference.

## **6. Critical remarks and recommendations**

1. Factors such as smoking, high BMI and the presence of ascites and their relationship to elastography measurements could be examined.
2. Groups of patients with other etiologies of liver cirrhosis, for example, autoimmune pathology, can also be included.

## 7. Conclusion

As a member of the scientific jury, 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" is extremely relevant and of high scientific and practical value. It meets all the requirements for awarding the degree of "PhD", which is why I give my positive assessment.

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Stara Zagora

Assoc. Mariana Penkova Radicheva, MD, PhD

