

POSITION

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Regarding dissertation work for acquiring educational and scientific degree "Doctor" in the field of higher education 7. Healthcare and sports, by professional field 7.1. Medicine and scientific specialty "Internal Medicine" of Kamen Valentinov Danov MD, with topic "Rotational thrombelostometry as a method for assessing hemostatic changes and the risk of varicose bleeding in patients with liver cirrhosis", with supervisors Assoc. Prof. Petar Atanasov MD, PhD and Assoc. Prof. Oleg Cholakov, MD, PhD

The procedure for the defense of the dissertation is determined by an order of the head of the scientific organization №RD-26-1707 / 09.10.20. The dissertation was discussed and proposed for defense on 09.09.2020. Discussed, adopted and directed for defense by a decision of the Scientific Council of 23.09.2020.

The topic of the dissertation is related to one of the most current issues of modern clinical gastroenterology and in particular hepatology. The incidence of chronic liver disease remains high, and with it the associated mortality. Bleeding from esophageal varices is one of the serious complications and timely assessment of these patients can help to differentiate the approach to them, including monitoring and therapy in intensive care units.

The dissertation contains 198 pages, of which 1 page - title, 1 page - content, 2 pages - abbreviations used, 4 pages - introduction, 49 pages - literature review, 1 page - purpose and tasks, 6 pages - materials, 3 pages - methods, 94 pages - results, 5 pages - discussion, 1 page - conclusion, 2 pages - inferences, 1 page - contributions, 27 pages - bibliography, 1 page - publications.

The literature review is composed of strictly selected information, which summarizes all the points of view presented in the literature on the researched problem. Regardless of the specificity of the considered issues and the study of the possibilities for application in hepatology of a new methodology, the available scientific reports on the topic are cited in detail. Both the traditional

theories for the formation of portal hypertension and the innovative theories and hypotheses, which include newly established facts and presumed mechanisms, are moderately and exhaustively considered. Attention is drawn to theories related to the mechanisms of hemostasis that affect the risk of bleeding in patients with cirrhosis of the liver and esophageal varices.

Danov's approach to the data from the world literature is analytical and shows knowledge of the matter by asking the unresolved issues that the dissertation deals with.

The purpose of the dissertation is specifically formulated. 5 tasks have been formulated, which completely correspond to the set purposes.

The section "Materials" is presented in 7 chapters and describes the selection of patients, including and excluding criteria, the main groups of patients included in the study and their distribution by individual characteristics. Patients were divided into three groups - with cirrhosis of the liver and an episode of bleeding from esophageal varices, with cirrhosis of the liver without evidence of bleeding from esophageal varices and a control group of healthy individuals.

The section "Methods" describes the methods for testing hemostasis and the statistical methods used to process the data. Routine haemostasis tests, platelet count and conventional haematological and biochemical markers were studied. All patients underwent thrombelastometry in a volume of four panels - EXTEM, INTEM, FIBTEM and HEPTEM.

The "Results" section contains 11 chapters. The clinical characteristics of the patients, the routine clinical and laboratory parameters and the severity of liver cirrhosis are reflected. The results of all panels of rotational thrombelastometry were processed and with the help of statistical methods reference limits were derived for each parameter, adapted for patients with liver cirrhosis. It is proposed to calculate the thrombodynamic potential index to be calculated based on the parameters of hemostasis in the internal and external coagulation systems. The results of the processing of the values of the thrombodynamic potential index show a high statistical significance of this parameter. The relationship between the results of rotational thrombelastometry and the presence of an episode of bleeding from esophageal varices with conventional hemostasis tests was considered. Insufficiently significant correlation of INR with the actual state of hemostasis and lack of correlation of aPTT with the real state of hemostasis have been demonstrated. The parameters of the study of the internal and external

coagulation systems show a significant correlation with the presence of bleeding from esophageal varices, demonstrating a relative balance of hemostasis in patients with liver cirrhosis and no bleeding.

The section "Discussion" analyzes the essence of the dissertation. Summarizes the accuracy of each studied method for the study of hemostasis and draws conclusions about its clinical application. The discussion is clinically oriented, competent and critical. The established changes in blood clotting in patients with liver cirrhosis are commented, which confirm the theory of the presence of consumptive coagulopathy in patients with liver cirrhosis. Emphasis is placed on the strong correlation of the risk of bleeding with the values of the thrombodynamic potential index and being offered as an easy-to-use algorithm for assessing the state of hemostasis in patients with liver cirrhosis. The question of the importance of conventional methods for the study of blood clotting and their importance in the assessment of patients with liver cirrhosis is discussed.

The conclusion summarizes and comments concisely and clearly on the significance of the researched problem and the significance of the obtained results for the clinical practice.

The inferences in the dissertation are 5, strictly follow the results obtained, correspond to the set tasks and are accurate.

The bibliography contains 255 titles - 6 in Bulgarian and 249 in Latin, which are current.

The contributions of the dissertation work are 6 and are correctly deduced.

In connection with the dissertation, 3 scientific publications and 1 scientific report presented at a national conference were marked.

In conclusion, the dissertation work of Kamen Valentinov Danov MD meets the required criteria of the Law for the development of the academic staff for obtaining the educational and scientific degree "Doctor". The style of the dissertation is clear, orderly, with strictly processed data, detailed original results, accurate conclusions and contributions. The dissertation is emphatically clinically oriented, but also clarifies issues of basic science, which shapes it as important for everyday clinical practice.

I recommend to the members of the respected Scientific Jury to give a positive vote for awarding the educational and scientific degree "Doctor" to Kamen Valentinov Danov MD.

10/12/2020

Prof. Raina Teodosieva Robeva MD, PhD
