

## REVIEW

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On the dissertation work for obtaining the educational and scientific degree “Doctor” of Kamen Danov MD on topic “Rotational thrombelastometry as a method for assessment of hemostasis changes and risk of varicose bleeding in patients with liver cirrhosis” in the field of Higher Education 7; Health and sports; professional field 7.1 Medicine; scientific specialty Internal medicine. Scientific supervisors: assoc. prof. Petar Yordanov Atanasov MD, PhD and assoc. prof. Oleg Georgiev 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 review is prepared according to the Regulations for application of the law for the development of the academic staff in the Republic of Bulgaria and the regulations of UMHATEM "NI Pirogov", Sofia.

The topic of the dissertation is one of the current and important issues of modern hepatology. The incidence of chronic liver disease, in particular that of liver cirrhosis and its complications, is constantly increasing. The associated serious morbidity, social costs and mortality is an important problem in modern medicine. Changes in hemostasis in liver cirrhosis are common and clinically significant, but their diagnosis by standard methods is insufficient for the needs of clinical practice. Any scientific research in this direction that would enrich our knowledge is of great importance for practical medicine.

The presented dissertation is in accordance with the requirements for structure and volume. It is written on understandable Bulgarian language. 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 author has numbered only 7 of them (from aim and tasks to contributions). It is illustrated with 81 tables and 30 figures.

The literature review contains important and up-to-date information related to the developed dissertation. The presented literature data are analyzed in depth and critically and are summarized. These include, in general, the causes of varicose bleeding in patients with liver cirrhosis, intrahepatic circulation, structural and functional changes, characteristics of hemostatic disorders in liver cirrhosis, the nature and possibilities of diagnostic tests to assess and monitor hemostasis, and alternative methods, including thrombelastometry and rotational thrombelastometry, the relationship between conventional coagulation tests and viscoelastic tests, the possibilities of the latter for use in clinical practice. The most important unresolved issues substantiating the present dissertation are also indicated.

The aim and the 5 tasks set in connection with it are formulated clearly and precisely, and fully correspond to the topic of the dissertation.

The subjects and methods used are clearly described and fully characterized, including methods for assessing hemostasis. Grouping provides subanalysis that enriches the results. The total number of 108 examined patients is sufficient for the applied statistical processing, ensuring the receipt of representative results. The inclusion and exclusion criteria are formulated clearly and concisely. A set of modern statistical methods was used. They are selected correctly in order to reliably prove or disprove the required dependencies.

The results fully correspond to the topic of the dissertation, the goal and the set tasks. Original results of clinical significance were obtained. Changes in hemostasis were characterized in patients with cirrhosis of the liver with and without hemorrhage from esophageal varices compared to healthy individuals, using a wide range of standard methods and rotational thrombelastometry. Differences in the parameters of rotational thrombelastometry between cirrhosis and healthy liver, as well as between cirrhosis without bleeding from varicose veins and with hemorrhage have been proven. Deviations in all stages of hemostasis in cirrhosis have also been found. The thrombodynamic potential index for the internal and external coagulation systems has values that

distinguish cases with and without varicose bleeding. Threshold levels of indicators in INTEM, EXTEM, FIBTEM and HEPTTEM with high diagnostic reliability have been established.

Low specificity and almost no diagnostic reliability of standard hemostasis parameters in liver cirrhosis have been shown. Platelet counts were lower in patients with cirrhosis and a bleeding episode.

The results are well interpreted and discussed in the chapters Discussion and Conclusion.

The literature reference is up-to-date. Includes 255 literature sources, 6 in Cyrillic and 249 in Latin.

There are 5 main inferences, corresponding to the results obtained, as well as the aim and tasks of the dissertation. The contributions (6) fully correspond to the results and conclusions. I accept the inferences and contributions indicated by the dissertation.

The dissertation has a significant scientific value with the possibility of applying the results in clinical practice.

The abstract fully reflects what is stated in the dissertation.

In connection with the dissertation are listed 4 scientific papers published in Bulgarian journals.

In conclusion, the dissertation of Kamen Valentinov Danov MD meets the required criteria of the Law for the development of the academic staff in our country and the Regulations for the development of the academic staff of UMHATEM "N. I. Pirogov".

Based on the above, I recommend the members of the esteemed scientific jury to give a positive vote for the award of educational and scientific degree "Doctor" to Kamen Valentinov Danov MD.

30.10.2020

Prof. Borislav Vladimirov MD, PhD