

REVIEW

ON DISSERTATION PAPER

By D-r Alexander Valeriev Yordanov, on the topic: "Risk factors and clinical follow-up of patients with acute bleeding from upper gastrointestinal tract" for awarding the educational and scientific degree "doctor" in the field of higher education 7 "Health care and sport", professional direction 7.1 "Medicine" by scientific specialty 01.03.14. "Gastroenterology".

Scientific supervisor: Assoc. Prof. D-r Milko Bozhidarov Mirchev, MD PhD

REVIEWER

Assoc. Prof. D-r Irina Ivanova Ivanova, MD PhD

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By decision of the order of the Rector of the Medical University - Varna No. 189/19.05.2026 and protocol 1 of the meeting of the scientific jury on 1.6.2026, I am determined to present this review.

1. Brief biographical and professional data of the PhD student

Dr. Alexander Yordanov graduated with full honors and received the Golden Hippocrates Award of MU - Varna in 2020. Since the beginning of 2021, he has been working as a physician and assistant at the Gastroenterology Clinic and since autumn of 2025 in the Department of Gastroenterology for Endoscopic Diagnostics of UMBAL St. Marina and in the Second Department of Internal Medicine, currently the Department of Gastroenterology, Hepatology and Nutrition at MU-Varna. Dr. Yordanov completed his doctoral studies in full-time form at this academic structure. In 2025, he acquired the specialty "Gastroenterology". In a short period of training and specialization, Dr. Yordanov has emerged as a competent physician with broad interests in diagnostic and therapeutic endoscopy and with excellent knowledge in the field of clinical medicine and perfect training in the field of gastroenterology. In addition to the field of GIT bleeding, the colleague's scientific interests are also focused on oncology in gastroenterological practice, rare diseases, therapy of portal hypertension, precancerous lesions of the upper GIT. Dr. Yordanov works dedicatedly, also participating in the teams for emergency endoscopic examinations at St. Marina University Hospital. He is a competent and beloved lecturer of students and a young scientist with annual participation in scientific conferences in our country and abroad with the potential for a quality academic career.

2. Relevance of the dissertation topic

Despite a well-developed management algorithm, acute upper gastrointestinal (GI) bleeding remains an emergency with persistent significant morbidity and mortality. The use of

antisecretory and vasoactive medications in the first steps of treatment is well-established, but insufficient to influence severe bleeding and to completely prevent recurrent bleeding. An increasing number of patients are elderly, have comorbidities, and are taking risky medications for bleeding. Each clinical center should learn from the accumulated experience, predict the individual approach and adapt the algorithms of behavior according to the local characteristics of patients and opportunities; based on its own studies, optimize the approach to frequent, socially significant and potentially lethal conditions. Therefore, this dissertation is relevant and necessary for scientific knowledge and clinical practice.

3. Characteristics, volume, structure, and evaluation of the dissertation work

Dr. Alexander Yordanov's dissertation is a large book, in the considerable volume of 231 pages and follows the traditional structure: introduction - 1 page; literature review - 46 pages; goal and objectives - 1 page; clinical material and methods of the study - 8 pages; results together with a discussion of over 140 pages; conclusions, conclusion and contributions on 1 page each; literature review of 266 sources. The own results are excellently arranged and illustrated in 149 tables and 76 figures. The dissertation has balanced content; it is written in clear, correct Bulgarian. Despite the large volume, it is easy and enjoyable to read.

The literature review competently presents both the main and the most current publications, in consideration of the topic. The excellent knowledge of the problem and the systematic arrangement of the data are impressive. An important place in the review is occupied by the systems for stratification of patients, for predicting the severity of non-variceal and variceal bleeding from the GIT and endoscopic methods for hemostasis. The topicality and good and extremely competent presentation make the review a recommended guide for behavior in acute upper GIT bleeding.

The aim of the dissertation is to analyze the clinical, laboratory, endoscopic and therapeutic characteristics of patients with acute upper GI bleeding in order to specify the risk factors for severe bleeding and for an adverse outcome. The tasks are categorical and clearly formulated. In a retrospective study, Dr. Yordanov included a group of 209 patients of St. Marina University Hospital with consecutive hospitalizations for a period of 3 years. The data were extracted from emergency upper endoscopy protocols and the documentation of the history of the disease. The selection of patients was based on clearly defined inclusion criteria. Although the protocol design is "retrospective", Dr. Yordanov has a personal contribution as an endoscopist in a significant part of the patients. With much effort and hard work, the dissertation student extracts the laboratory and clinical indicators that will serve to calculate the prognostic models: pre-endoscopic /Glasgow-Blatchford Score, AIMS65, ABC-score, CANUKA-score, MAP(ASH)-score and Rockall score/ and post-endoscopic, i.e. including data from the upper endoscopy, such as the full Rockall score, PNED and Cedars-Sinai Medical Center Predictive Index (CSMCPPI). These systems have not been validated in clinical studies in the Bulgarian patient population. Although the main parameters involved overlap, each of the risk stratification systems has its own characteristics,

advantages, or limitations, which Dr. Yordanov, based on the analysis conducted, competently discusses.

A group of consecutive patients with a median age of 68 years, with at least one cardiovascular disease and a cancer incidence of 20%, was analyzed. At baseline, the patients had significant circulatory disorders: systolic blood pressure (SBP) ≤ 90 mmHg in 41.6%; heart rate ≥ 100 beats/min in 63.2%; shock index ≥ 1.0 in 37.8%; mean hematocrit value was 0.25. The frequency of taking medications associated with the risk of GI bleeding was in descending order: 34% anticoagulants; 26% antiplatelet agents; 13% NSAIDs; 5% steroids; 1.4% SSRIs. On the other hand, anamnestic data on gastroprotection preceding acute bleeding in the studied population was available in only 16%. The largest proportion of patients underwent endoscopic examination within the first hours after admission, with 50.2% being examined by the 2nd hour and 67.5% by the 3rd hour. The high frequency of immediate endoscopy within 6 hours of hospital admission /of 82.8%/ Dr. Yordanov critically analyzes related to the severity of acute bleeding on the one hand and the peculiarities of local emergency care on the other. 90% of the analyzed cases are with non-variceal bleeding, with the main source being gastroduodenal erosions, peptic ulcer disease and to a lesser extent erosive esophagitis, as well as other rarer causes. Active bleeding during emergency upper endoscopy was present in 20.8% of the studied patients, endoscopic hemostasis was performed in 37.8%, and recurrence of hemorrhage requiring repeated hemostasis in 22%. The analysis of clinical outcomes during the hospital stay is important, with a high mortality rate recorded – in 59 out of 209 (28.2%). The described cohort with non-variceal bleeding is graded and divided into groups of severe and non-severe bleeding, based on the presence of severe endoscopic findings and A-B-C criteria (hemodynamic instability, hemoglobin below 80 g/l, adverse clinical outcome), and thus 115 patients are categorized with severe bleeding. Using 3 models of multivariate regression analysis, Dr. Yordanov investigated the factors associated with the clinical course of severe non-variceal bleeding. He identified the key importance of active peptic ulcer disease localized in the stomach, the need for oxygen therapy due to respiratory failure, hypoalbuminemia and impaired renal function as predictors of severe bleeding. Although in a small number of 41 patients, multivariate analysis identified a trend for severe bleeding in hepatic synthetic disorders /MELD score/ and a higher degree of portal hypertension /thrombocytopenia/. Another very strong aspect of the dissertation is the study of the significance of nine scoring systems in predicting key clinical outcomes, such as in-hospital mortality, recurrent bleeding, need for blood transfusion, endoscopic or possibly surgical intervention for hemostasis. The analysis was conducted as an individual assessment and as a comparison of the 9 validated scoring systems in total. Thus, the dissertation proves the leading role of PNED and ABC in predicting death within hospitalization. The main predictor of the risk of rebleeding is PNED (at AUC=0.894), with a threshold ≥ 6.5 for high sensitivity (97.7%), balanced by moderate specificity (64.1%). In cases of non-variceal bleeding, the strongest predictor of the need for blood transfusion in the studied cohort is the GBS score. Dr. Yordanov analytically arranges the success of all the studied scoring systems in a summary table, respectively for variceal and non-variceal bleeding. Additionally, in search of factors predicting clinical outcome,

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the dissertation demonstrates that significant initial hemodynamic instability/shock is a powerful predictor of in-hospital mortality and recurrence of acute upper GI bleeding. Through a logistic regression model including multiple hemodynamic, hematological, renal, and coagulation parameters, it is demonstrated that serum albumin is the only independent quantitative predictor of in-hospital mortality. A logical consequence of the above results and discussion are nine clearly formulated and informative conclusions. I confirm that the conclusions are supported by the conducted study. The dissertation work of Dr. Alexander Yordanov has undeniable contributions of a scientific and applied nature. The systematic and precise analysis of clinical, endoscopic and laboratory predictors for severe non-variceal bleeding allows for more precise early recognition of high-risk patients in hospital practice. The comparison of nine prognostic scoring systems in real practice for predicting an unfavorable outcome in acute upper GI bleeding is initial for Bulgaria and deserves to be popularized in the gastroenterological national and international community.

In connection with the dissertation work, Dr. Alexander Yordanov offers 5 materials published as full-text articles and 2 independent reports at national conferences.

Evaluation of the contributions of the dissertation work

I fully accept the stated conclusions and contributions of the dissertation work. The significance of the work is supported by the competent and precise statistical analysis and the intelligent comprehensive discussion, which demonstrates the professionalism and knowledge of the dissertation author in the field of GIT diseases.

4. Critical remarks

There are no grounds for any critical remarks.

5. Conclusion

The thesis of Dr. Alexander Valeriev Yordanov on the topic: "Risk factors and clinical follow-up in patients with upper gastrointestinal bleeding" presents results and conclusions with an original contribution to science and meets the requirements of the Law for the Development of the academic staff of the Republic of Bulgaria and its Regulations for the implementation.

The dissertation work shows that Dr. Yordanov has the qualities and skills to independently conduct scientific research based on in-depth theoretical knowledge and professional skills in the scientific specialty "Gastroenterology." In addition, my personal impressions from more than 4 years of joint work show that Dr. Yordanov has deserved and should continue his successful start in academic and clinical work in order to contribute with his personal qualities to the development of gastroenterology practice at St. Marina University Hospital.

In connection with this, I convincingly give my positive assessment of the work of Dr. Alexander Yordanov and propose to the Scientific Jury to award Dr. Alexander Valeriev Yordanov an educational and scientific degree "Doctor".

Date: June 10, 2026

Varna

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/ Assoc. Prof. Dr Irina Ivanova, PhD /