"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY BUCHAREST

DOCTORAL SCHOOL MEDICINE

THE MANAGEMENT OF BLEEDING AND HEMOSTASIS DISTURBANCES IN PERIOPERATIVE AND ICU SETTINGS – A COMPLEX CHALLENGE IN MEDICAL PRACTICE

SUMMARY OF THE HABILITATION THESIS

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The habilitation thesis titled "Management of Perioperative Bleeding and Hemostasis Disturbances Perioperative and ICU Settings- a Complex Challenge in Medical Practice" describes the scientific, academic, and clinical activities carried out to date, focusing on the achievements that followed the completion of doctoral studies. This thesis also aims to outline the objectives and plans for professional development in scientific research and the academic field.

Perioperative bleeding is one of the most common complications in major surgery and is associated with high postoperative mortality and significant resource consumption. Hemostatic disorders, both congenital and acquired, can contribute to an increased risk of perioperative bleeding. Considering the increasing use of antithrombotic medications in the general population, understanding the physiological mechanisms involved in hemostasis, knowing the classes and effects of antithrombotic medications, and accurately assessing the hemorrhagic or thrombotic risk are essential for anesthetic practice. During surgery, the management of hemorrhagic shock includes the administration of blood products based on a fixed ratio, or the administration of red blood cell units accompanied by individualized treatment of coagulopathy based on monitoring through standard coagulation tests or "point-of-care" instruments based on viscoelastic technology. The management of post-hemorrhagic shock patients also requires a good understanding of hemostatic mechanisms, considering that after a hemorrhagic episode, there is a transition from a hemorrhagic phenotype to a prothrombotic one, similar to trauma patients. Thus, patients may develop venous or arterial thrombotic complications in the absence of adequate monitoring that reflects the patient's coagulation status and guides the administration of thromboprophylaxis or even anticoagulant treatment when necessary.

The management of perioperative bleeding, hemorrhagic shock, as well as the study and optimization of hemostatic disorders in special categories of patients, such as pediatric patients, those with chronic liver diseases, sepsis, oncological patients, or those with malignant hematological diseases, have concerned me since the early years of my residency in anesthesia and intensive care. Thus, coagulopathy in sepsis was the chosen topic for the doctoral studies

completed in 2018, but the scientific concern for hemostatic disorders in complex medical contexts, such as major surgery, liver transplantation, intensive care, and oncology, continued through research studies completed with publications in specialized journals.

The structure of the habilitation thesis includes four chapters that refer to scientific, academic, and professional achievements, as well as the proposed professional development plans for the scientific and academic career in the future.

The first chapter of the habilitation thesis contains information about the scientific achievements that followed the completion of doctoral studies. The main scientific interests and the resulting research activities have pursued several major directions: 1. evaluation and management of perioperative bleeding in major non-cardiac surgery and liver transplantation, 2. study of hemostatic disorders in intensive care patients, 3. evaluation of volemic and hemodynamic status and correlation with bleeding and transfusion requirements, 4. evaluation of cardiac dysfunction in patients with liver cirrhosis, and 5. study of hemostatic disorders in patients with solid tumors and hematological neoplastic diseases.

In the period following my doctoral studies, I obtained two research grants. The first research grant in value of 20,000 USD was obtained in 2019 with the project "Validation of the t-AUCi parameter as a measure of fibrinolysis using ROTEM and its application in the assessment of fibrinolytic resistance in septic patients" and was funded by the International Society on Hemostasis and Thrombosis (ISTH). The second research grant was obtained in 2022 with the project "Development of a New DIC Score Adapted for Chronic Liver Disease," funded by a grant from the International Society on Hemostasis and Thrombosis worth 20,000 USD. Both research projects were successfully conducted and completed. For the scientific activity carried out after completing my doctoral studies, I received three awards: two from the Romanian Society of Anesthesia and Intensive Care (in 2018 and 2024), and one from the International Society on Hemostasis and Thrombosis (ISTH).

From the perspective of scientific achievements, the activity carried out meets the minimum criteria necessary for the defense of this habilitation thesis, through the research projects materialized in the publications described in Chapter 1 of the habilitation thesis. In the scientific activity following the doctoral studies, up to the present moment, a total of 15 articles published as the first author in ISI journals with impact factor and 17 articles published as a co-author in ISI journals with impact factor can be included, meeting, along with other

requirements, the minimum conditions for supporting the habilitation thesis. From the perspective of the quality of scientific activity, I mention that to date there are 353 citations in the Web of Science - Core Collection, with a Hirsch Index - Web of Science - Core Collection of 11, a Hirsch I-10 Index - Google Scholar of 15, and a total of 869 citations in Google Scholar.

The second chapter of the thesis refers to academic activity. In 2021, I obtained the position of Lecturer within the Clinical Education Department 14, Discipline ATI 1, Fundeni Clinical Institute. I would like to mention, however, that my concern and participation in educational projects began much earlier. After obtaining the title of specialist doctor, I was constantly involved in educational events organized at the departmental level for the training of resident doctors, participated as a lecturer in workshops and webinars, and in the years 2014-2015, I was a practice tutor for students enrolled in the POSDRU 161/2.1/G/134856 project entitled Counseling Program for Medical Students and Intensive Care Practice. The position of Lecturer at the University of Medicine and Pharmacy "Carol Davila" in Bucharest involves a series of essential teaching responsibilities, which are related to ensuring high-quality professional and academic training for students. These responsibilities focus on teaching, coordination, evaluation, and mentoring activities, as essential components of a modern and efficient educational system. As part of my role as a Lecturer, I participated as a supervisor in the exams for obtaining the title of specialist physician in Anesthesia and Intensive Care Medicine (theoretical part), as a member of the examination board for the practical tests in the exams for obtaining the titles of specialist physician and primary physician in Anesthesia and Intensive Care Medicine. I have also participated as a member of examination committees or appeal committees for competitions held for obtaining positions as specialist doctors in various hospital units in Bucharest or promotion competitions within the University of Medicine and Pharmacy "Carol Davila" Bucharest. Continuous training through participation in advanced courses, conferences, and other events that contribute to the enhancement of professional competencies represents another important and necessary aspect for professional development and the quality of academic activity. Thus, during my professional development, I have become an active member of various professional societies, such as the Romanian Society of Anesthesia and Intensive Care (SRATI), the European Society of Anesthesiology and Intensive Care (ESAIC), the International Society on Thrombosis and Hemostasis (ISTH), the Liver Intensive Care Group of Europe (LICAGE), and the International Liver Transplant Society (ILTS). Within

the International Society on Hemostasis and Thrombosis (ISTH), since 2022, I have held the position of Chair of the committee that studies disseminated intravascular coagulation (DIC Subcommittee), and I am a member of the Ethics Committee and the Diversity, Equity, and Inclusion Committee. Within the European Society of Anesthesiology and Intensive Care, I am a member of the Scientific Committee and hold the position of President of the 4-Therapies Forum. I am also a member of the Board of the Liver Intensive Care Group of Europe (LICAGE) since 2024 and a member of the Scientific Advisory Board at Giganode, lecturer, and responsible for organizing educational events in collaboration with the Verein zur Förderung der Perioperativen Medizin (VFPM). The positions held within these international professional societies reflect the recognition of the quality of scientific work at an international level. Additionally, these positions involve sustained academic and educational activities through the organization of seminars, scientific meetings, the proposal and establishment of scientific programs for periodic congresses organized by professional societies, as well as constant participation in online activities such as educational webinars.

Chapter three of the habilitation thesis summarizes the professional achievements. The professional journey began with graduating from the "Carol Davila" University of Medicine and Pharmacy in 2005, with a graduation average of 9.71 and a licensure exam average of 9.96. Following the national residency exam, I became an ATI resident doctor at the Fundeni Clinical Institute in Bucharest. In 2011, I passed the specialist doctor exam with an average of 10.00, and in 2016, the primary doctor exam with an average of 9.55. Since 2012, I have been employed as a specialist anesthesiologist at the Fundeni Clinical Institute. I worked continuously as a specialist doctor and later as a primary doctor in the ICU department at the Fundeni Clinical Institute, and since 2021, I have been a Lecturer at the "Carol Davila" University of Medicine and Pharmacy with clinical placement in the Anesthesia and Intensive Care Department 3 at the Fundeni Clinical Institute. The professional activity as an Anesthesiologist and ICU physician has followed a process of continuous development through constant participation in courses and educational events. I thus had the opportunity to combine scientific research with medical practice, closely following topics with applicability in clinical practice. I have participated as an invited lecturer in educational seminars and workshops held in Austria, Serbia, Macedonia, Turkey, Switzerland, Russia, Moldova, and Qatar. In 2017, I applied for and obtained a Fellowship from the International Society on Thrombosis and Hemostasis with a 3-month training period at MUMC Maastricht, Netherlands. Additionally, between 2019 and 2022, I pursued a Master's degree in the "Patient Blood Management" program at Danube University Krems, Austria, and obtained a Master of Science (MSc) in Medical Sciences in 2022, issued by Danube University Krems, Austria. Additionally, considering my scientific activity in this field, I was invited by the European Society of Anesthesia and Intensive Care to participate as a co-author in the revision of the guidelines for perioperative bleeding management, which were published in 2024. One of my significant professional achievements related to this scientific field is the development and implementation of a bleeding management algorithm at the ICU department of the Fundeni Clinical Institute.

Chapter four of the thesis presents the plan for the evolution and development of the scientific, academic, and professional career. Plans for future scientific research can be structured into several areas of interest: 1. Prediction and management of perioperative bleeding in major non-cardiac surgery and liver transplantation, 2. Study of hemostatic disorders in patients with solid cancers perioperatively and in intensive care, 3. Development of a protocol for evaluating volemic and hemodynamic status using ultrasound techniques in intensive care patients, 4. Study of disseminated intravascular coagulation in patients with complex hemostatic disorders (cirrhosis, solid cancers, or hematological diseases), 5. Study of anemia and patient blood management adapted for patients with chronic liver diseases and for cirrhotic patients candidates for liver transplantation. I aim to continue my publishing activity by disseminating research results in ISI journals with a significant impact factor (Q1), initiating new research studies involving resident doctors and PhD students in scientific projects, intensifying collaboration in multicenter, interdisciplinary studies, national and international registries to increase the impact of research, and participating with research projects in competitions for obtaining research grants at both national and international levels. Of course, the scientific objectives include continuing the activities of organizing scientific sessions with specific themes within national and international congresses, delivering presentations at conferences, seminars, and symposiums, and organizing educational events (webinars, workshops) within our discipline.

The proposed objectives for the development of academic activity are structured in three directions based on the categories involved: students of the Faculty of General Medicine, resident doctors, and doctoral candidates. The objectives include the alignment and periodic

revision of curricula according to current national and international regulations and requirements, considering the rapid emergence of new information in the field of anesthesia and intensive therapy, the use of modern learning technologies such as simulators, including the creation of clinical scenarios through simulation, and the use of artificial intelligence in learning programs. Additionally, it involves engaging students, residents, and doctoral candidates in clinical and fundamental research projects alongside experienced researchers. This objective is extremely important for the learning process of students and residents, to spark their interest in research activities.

For me, the profession of anesthesiologist and intensive care physician, along with clinical practice as an essential part of this activity, represents a passion. Therefore, I continuously invest in my professional development so that clinical practice continues to be based on solid and constantly renewed knowledge, as the field of anesthesia and intensive care is extremely dynamic. Thus, I aim to constantly improve my knowledge through continuous medical education, participation in courses and training programs in the field of anesthesia and intensive care, as well as participation in advanced courses in university pedagogy and academic management, continuing my activity and involvement in national and international professional networks, and expanding collaborations with foreign university centers for experience exchanges and joint projects.

In conclusion, I believe that these proposed objectives naturally continue my achievements so far, and I aim to reach high standards of quality in my scientific, academic, and professional activities. In my future career development plan, the priority is to support and guide researchers and doctors at the beginning of their careers and to create an academic environment based on the recognition of professional values, respect for colleagues and partners, intra- and interdisciplinary collaboration, while maintaining rigorous academic standards and adhering to ethical and deontological principles.