Carol Davila University of Medicine and Pharmacy Faculty of Medicine



ABILITY THESIS

ABSTRACT

ANESTHESIA AND INTENSIVE CARE FOR LIVER TRANSPLANTATION

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Abstract

The ability thesis entitled "ANESTHESIA AND INTENSIVA CARE IN LIVER TRANSPLANTATION", written in conformity with the decision nr. 3121/27.01.2015 of the Ministry of Education and Scientific Research and regulations of the Council of the Institute for Doctoral Studies Regulamentul of Carol Davila University of Medicine and Pharmacy Bucharest regarding the abilitation certification, presents the steps of my academic career and points out the aspects of my professional, teaching and scientific achievments.

The most relevant personal scientific contributions are resumed, after obtaining the PhD degree, in order to show achievments according to actual research and scientific international context. Attention is paid to specific activities that prove the personal organizing, coordonation, teaching and research skills, and future development in the field and perspectives regarding my career as teacher, researcher and clinician are presented.

My Hirsch index is 6 with 615 citations on Isi Thomson Web of Science

The theme of the abilitation thesis is anesthesia and intensive care for liver transplantation, and contains three sections:

Section I presents the main achievements obtained in over 25 years as clinician, teacher and researcher, focusing on the time frame since the obtainance of the PhD degree and present.

There is a short introduction showing the steps of my formation regarding the academic career at Carol Davila University and Pharmacy, Department of Anesthesiology and Intensive Care Fundeni Clinical Institute – junior assistant professor since 1991, assistant professor since 1995, lecturer since 2008 and associate professor since 2015, with one year formation with a degree in anesthesiology and emergency medicine in Paris, France at Pitie-Salpetriere Hospital (1993-1994), and numeros formation programs and degrees during 25 years of activity.

The second part of this first section points out the research activity and publications, including national and international recognition: awards and distinctions. International recognition in the field of liver transplantation is showed by the participation as executive board member of LICAGE Liver Intensive Care Group of Europe (LICAGE), the presidency

of the 35th Licage Meeting held in september 2016 in Bucharest, the honour of being founder member of the Society for the Advancement of Transplant Anesthesia (SATA), the title of Associate Professor of the State University of Medicine and Pharmacy "Nicolae Testemitanu" from Chisnev and the "Order of Honour" awarded to me by the President of Moldavia on 27th of april 2016.

The third part of this section shows the main issues regarding the theme of my ability thesis: anesthesia and intensive care for liver transplantation. A short history of LT in Romania is presented.

Liver transplantation started in Romania in 2000 at Fundeni Clinical Institute. The team that performed the first liver transplant (LT) was led by Prof Irinel Popescu-surgeon, and Prof Dan Tulbure-anesthesiologist. I had the chance to be part of the first team and to grow up with a successful LT program, from it's very beginning (starting in 1997 with the first successfull multi-organ procurement, continuing with the first LT from a cadavetic donor and with the first living related liver transplant performed in 2000 as well).

During those 20 years I actively participated in the growts, development and improvement of the LT program since 2011 since when I lead the liver transplant anesthesia team together with my colleague Dr Gabriela Droc.

Since 2011 the LT program increased substantially, becoming a high-volume program wit over 100 procedures performed yearly as shown in figure 1.

795 Liver transplants in Romania (Fundeni Clinical Institute) between 2000-2016

DDLT - Deceased Donor Liver Transplant, LDLT - Living Donor Liver Transplant

Figure 1. Increasing number of liver transplants performed at Fundeni Clinical Institute (2000-2016)

Year

This huge developement allowed the accumulation of a considerable experience in the field, permitting the introduction of national and international premieres, inovation and increased international visibility.

New surgical techniques were implemented like split liver, domino, dual graft. A highly performant anesthesia team contributed substantially to the succes of those new techniques, and a performant management of the transplant pacient, along with new intensive care measures as bridging techniques and focused care in a specialized liver unit made possible to start an emergency liver transplant program.

I pioneerd the acute liver failure management, so our team began to utilize bridging techniques and a structured admission protocol for acute liver failure, emergency liver transplantation, ABO incompatible liver transplantation, and as an international premiere we used sucsesfully hemoadsorbtion columns for acute liver failure.

In the field of LT, I combined clinical skills with teaching and research, with numeros courses, conferences and original research presented at national and international congresses.

I participated in several educational programs, and there were two regarding LT: Transplant-S.P.E.R- Specializing, preformance and efficacy and response in transplantation, and D.C.T-developing competence in transplant, where I conducted the modules dedicated to anesthesiologista and intensivists, regarding brain death, the management of the organ donor and acute liver failure.

In 2013 I lead the anesthesia team that performed the first liver transplant in the Republic of Moldavia, and after that I participated as an international expert in the Twinning Programm, dedicated to develop the LT in Moldavia and to implement protocols for LT, for which activities I was awarded with the title of Associate Professor of the State University of Medicine and Pharmacy "Nicolae Testemitanu" from Chisnev and the President of Moldavia decorated me with the "Order of Honour" on 27th of april 2016.

Clinical, research and teaching activities combined have as result publications (books, chapters, articles in peer reviewed national and international journals), conferences as invited speaker to prestigious congresses in the field, numerous abstracts at those meetings, prizes and awards. I wrote 3 textbooks/monographs regarding liver transplantation and acute liver failure, 25 original papers published in peer-reviewed journals indexed in Isi Thomson Web of Science database as author/co-author, 8 in the field of LT and 33 original articles in journals indexed in the major databases (Pubmed, Scopus, etc), 16 in the field of LT

I had 42 oral presentations and conferences at international meetings, with abstracts published in journals indexed in ISI Thomson Reuters Web of science, and of those 33 were

in the last 5 years. From 103 accepted presentations to national and international meetings, 42 were in the field of liver transplantation.

Combining knowlege with a trained anesthesia and intensive care team made possible to develop the acute liver failure field, with educational programs, conferences, lectures, publications in this particular area. I am the national coordinator of the acute liver failure national frame program, and I was coordinating this program for 5 years in Fundeni Clinical Institute.

The thesis states out the key role of the ansthesiologist in the multidisciplinary team involved in the management of the liver transplant patient. He participates in the preoperative evaluation of the patient, during the surgical procedure and in the postoperative care of the transplanted patient.

Regarding preoperative evaluation, the anesthesiologist evaluates the patient and has a final decision to accept the patient for LT. A lot of complications of the liver disease are to be taken into account, like hepato-pulmonary sindrome, porto-pulmonary sindrome, pulmonary hypertension, cirrhotic cardiomiopathy, cirrhotic coagulopathy etc. Along with clinical skills, I developed a database for LT patiens and a sum of publications were released.

Preoperative optimisation of the patient adressed for LT is also a matter of anesthetic management, and it becomes crucial in emergency situations as acute liver failure when maintaing alive the patient until a suitable graft becomes available (the so called bridging to liver transplantation). Specific measures in order to achieve this consist of liver dialysis, critical care management, continuous veno-venous hemofiltration and the use of cytokine adsorbant colums (international premiere).

Intraoperative management during liver transplantation is complex, and consists of a standardised invasive monitoring (focused on hemodynamics), a protocolised fluid resuscitation, the goal directed management of cirrhotic coagulopaty, restrictive to bloodless transfusion approach. In the list of publications I have papers published regarding the main issues concerning liver transplant management.

The particularities of LT are widely described in this section, adressed to the phases of LT- pre-anhepatic, anhepatic and neo-hepatic phases, with a focus on reperfusion syndrome where some papers were published.

I also describe our innovative approach in LT, the early-extubation and fast track protocol and the hemostatic management of the patient during LT according to the viscoelastic tests (ROTEM point-of-care protocol). The early extubation seem to be among the first european LT programs that adopted it.

A restrictive transfusion algorithm was developed by our team.

The particularities of anesthesia for emergency LT for acute liver failure are presented, and ABO incompatible LT is also described.

Another part of this chapter shows the postoperative management of the transplanted patient, with the description of early complications and the implementation of the "fast track" concept that allows early discharge of the patient from the postanesthesia care unit.

Complications of the LT patient are widely decribed, starting with those due to the graft, and enumerating all tipes of complications related to LT, along with the management according to international guidelines and based on personal experience.

The chapter ends with the presentation of main results and inovations obtained through personal research in the field of LT and whose results were communicated and published in prestigious national and international journals, some of them awarded at our national congress.

Section II contains the main directions of personal academic and research development. I state that continuing the high standards in teaching and research imposed by my former Professors George Litarczek and Dan Tulbure is the main goal of my future academic career, though the Fundeni Clinical Institute Department of Anesthesiology and Intensive Care was and remains the main training centre for anesthesiologists in Romania. I also will continue teaching students and young anesthesiologists as professionals and researchers according to european standards.

An ambitious plan is also on it's way, to build a dedicated liver unit with funds from the World Bank, permitting to treat patients with critical liver diseases and to offer the staff (doctors and nurses) a high standard unit with peopele prone to provide dedicated professional care and superior academic training.

At the end of section II I present future directions of developement and research, many of them already in an implementation phase, others as future projects. So, I consider that the field of liver transplantation, acute liver failure, new and modern anesthesia and intensive care techniques are —each other- specific and interesting research themes for young PhD students.

Section III lists over 150 references that were used to write this thesis, and most recent articles in the field of liver transplantation are cited, along with the most relevant author's publications in the field.

Bucharest 08 mai 2017

Conf. Dr. Dana Tomescu