

**„VICTOR BABEȘ” UNIVERSITY OF MEDICINE
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HABILITATION THESIS

SURGERY – INTEGRATIVE CLINICAL RESEARCH: IMPACT AND INTERVENTIONS

A B S T R A C T

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ABSTRACT

The Habilitation Thesis contains the most important professional achievements, obtained after receiving the title of Ph D in 2005 with the thesis entitled “Liver Tumors. The conversion of tumors, initially not eligible for resection to tumors that can be resected”, awarded after its public defense.

This Habilitation Thesis is divided in three major sections: in the first section, the main academic, professional and scientific achievements are presented; the second section briefly describes the future academic, professional, and scientific perspectives; the last section of the thesis contains the references used for the research and documentation work presented in the first two sections.

My post-doctoral research and my professional path are in a close relation to the two positions appointed: senior specialist physician in General Surgery, respectively Associate Professor at the Discipline of Surgical Semiology I and Thoracic Surgery. I had the opportunity to be part of some multidisciplinary teams, being able to expand the research beyond the narrow field of surgery to a much larger one. Therefore, together with the teams I worked with, I was able to extend knowledge about liver disease, pancreatic disease, polytrauma, metabolic surgery, etc. The teams consisted of clinicians (general surgeons, intensive care doctors, gastroenterologists, internal medicine doctors), as well as fundamental science specialists (biochemistry specialists, pharmacologists). The research teams focused its research on several disease needing a multidisciplinary approach. The importance of this research is emphasized in the context of the global public health issue generated by more and more complex diseases.

At the moment of writing this thesis, I have disseminated my research work in 26 papers indexed in Clarivate’s Web of Science (23 in extenso papers and 3 meeting abstracts), which received a total of 88 citations from 87 different citing articles indexed in the Web of Science. In March 2024 I had a Hirsch index of 6 in Web of Science and of 7 in Google Scholar.

The research was published in scientific journals with high impact on the research community.

To summarize, my research was disseminated in:

- 14 *in extenso* articles indexed in Clarivate's Web of Science as principal author
- 9 *in extenso* articles indexed in Clarivate's Web of Science as co-author
- 5 *in extenso* articles indexed in international scientific databases as principal author
- 6 *in extenso* articles indexed in international scientific databases as co-author
- 3 abstracts or proceedings after conferences in supplements of journals indexed in Clarivate's Web of Science, as principal author, or co-author
- 15 abstracts in supplements of recognized scientific journals

A part of the research done was funded by one international scientific grant which were won in a competitive process. In this grant I was local project director. I was involved in global projects of state-of-the-art medical research, being an active participant in some major clinical trials from the area of surgery and oncology, as co-investigator.

Also, I participated in the publishing of 8 books in which I was author, co-author, or chapters co-author.

In this Thesis, my main scientific achievements are underlined by presenting the results of 17 of the most important studies in which I have participated.

The first important subject I have focused my research on was the surgical management of hepato-bilio-pancreatic disorders.

- 1. Postoperative morbidity and mortality after liver resection.** Liver resection as a surgical procedure is getting more and more frequent since its technique evolved and since the number of patients needing such a surgical procedure is increasing. The purpose of this study was

to analyze the postoperative morbidity and mortality of patients who underwent a liver resection in our clinic. We performed both major and minor hepatectomies and the outcome of the patients was in most cases favorable, the most frequent postoperative complication was reversible liver failure.

2. **The evolution after liver resections.** Liver resection is the standard treatment in patients with liver tumours, both in normal as well as in cirrhotic liver. The purpose of this paper is to indicate the intraoperative and postoperative evolution of patients who underwent liver resection in our clinic.
3. **H-type portocaval and mesocaval shunts performed in patients with upper gastrointestinal bleeding induced by esophageal varices.** The purpose of this paper is the surgical treatment of portal hypertension in cirrhotic patients. This issue has been a continuous challenge for liver surgeons since few methods are safe and effective and therefore widely accepted. In our clinic, in patients with liver cirrhosis Child B and esophageal varices (grade II and III) with a recurrent bleeding after medical and endoscopic treatment, we have performed H-type portocaval and mesocaval shunts. Our results were best if using Gore-Tex prostheses of 10 mm diameter.
4. **Management of the hydatid cyst in Banat.** The hydatid cyst is disease transmitted through certain animals caused by *Echinococcus granulosus*. As adequate treatment, surgery is needed in many cases. The aim of the study was to describe the experience in the hospitals in our region in diagnosing the hydatid cyst by liver ultrasound examination and treating it through surgical procedures.
5. **Cystic echinococcosis in adult patients in Western Romania.** Cystic echinococcosis is a parasitic disease caused by *Echinococcus granulosus*. The aim of our study was to assess the frequency of this disease and its management in Western Romania. It was a retrospective study that analyzed patients hospitalized with cystic echinococcosis regarding age, gender, area of residence, localization of the cyst,

number of the cysts, management strategy, complications, duration of hospitalization.

- 6. Surgical technique in modified Whipple-Child pancreaticoduodenectomy.** Cephalic pancreaticoduodenectomy is the only management option for long-term survival in patients with periampullar tumors. Our study analyzed patients with periampullar tumors treated by modified Whipple-Child cephalic pancreaticoduodenectomy with anastomosis on the jejunal loop in continuity. We observed a postoperative rate of complications of 22.22% and of mortality of 6.66%. The survival rate at one year was 80%. These figures support the idea that our surgical technique offered a good outcome.

The second important subject for me was to identify interesting surgical cases, to find an adequate treatment strategy and to share this knowledge.

- 1. Hemobilia through aneurysm of the right hepatic artery.** Hemobilia is a rare cause of upper gastrointestinal hemorrhage that may occur after liver trauma or after surgical procedures of the area of the liver, bile and pancreas area. The procedures that lead most frequently to hemobilia are transcutaneous bile punctures, laparoscopic cholecystectomies, cateterisms of the biliary tract. Usually, hemobilia occurs after a short period after the surgical procedure. We present a case of massive hemobilia occurred 22 months after a laparoscopic cholecystectomy.
- 2. Right hepatectomy and segmental colectomy performed in the same operative time.** Colorectal cancer is one of the most frequent types of cancers worldwide. The case is about a man, 58 years old, diagnosed with cancer of the transverse colon and synchronous liver metastases. The patient underwent a surgical procedure consisting of a major hepatectomy and a segmental colon resection, performed in the same operative time, with favorable outcome.
- 3. The complications of surgical treatment of hepatic trauma.** The involvement of the liver in case of abdominal trauma represents a factor of severity and requires adequate management. We presented

a case of a young polytrauma patient presenting hepatic trauma and developing biloma and biliary fistula after the surgical intervention of liver packing.

4. **Surgical treatment of the hepatic hydatid cyst.** Biliary leakage is an important issue in case of surgical treatment of liver hydatid cysts. We presented a case having a hydatid cyst in the 2nd segment of the liver involving the left biliary duct. The cyst was treated surgically by partial pericystectomy Lagrot and primary suture of the biliary fistula, having a favorable postoperative outcome.
5. **Upper gastrointestinal bleeding caused by a portal cavernoma due to a gastric ulcer.** Long lasting gastric ulcers can lead to inflammation in the upper abdomen, to penetration in the gastric wall, toward the pancreas and the hepatic hilum, to thrombosis of the splenic vein, and the occurrence of a portal cavernoma. The portal cavernoma may lead to esophageal varices. We presented the case of a patients with multiple episodes of upper gastrointestinal bleeding, determined by esophageal varices and gastric ulcer. During surgery we found that the bleeding was caused probabely by the gastric ulcer since the portal vein was thrombosed. The surgical procedure was represented by a distal spleno-pancreatectomy, a cuneiform resection of the gastric ulcer and the resection of the hepatic tumor, with favorable postoperative outcome.
6. **Spontaneous rupture of an aneurysm of the gastroduodenal artery.** The aneurysm of the gastroduodenal artery is rare. Our case is about a man who presented about 16 hours after surgery for right inguinal hernia a state of hemodynamic shock caused by a large hematoma localized in the transvers colon mesentery and in the retroperitoneum. After removing a clot in this area, the cause of the hematoma was found to be the rupture of an aneurysm of the gastroduodenal artery. The opening was closed and the postoperative evolution was favorable.
7. **Groove pancreatitis** represents a rare type of chronic pancreatitis that involves the area between the pancreatic head and the duodenal

„C” loop (the groove area), usually occurring in men with alcohol and tobacco misuse. Our report is about a 66 years old woman, heavy smoker, presenting with weight loss, nausea, and upper abdominal pain. Investigations showed the presence of pancreatitis, dilatation of the main pancreatic duct, a cyst of the pancreatic head, and enlargement of the biliary tract. Because no other therapeutical option was feasible, we performed pancreatoduodenectomy, with favorable outcome.

8. **Conventional grade 1 chondrosarcoma.** Chondrosarcoma is a malignant tumor of the soft tissue with involvement of the cartilages very rarely situated in the head and neck region. The cases we presented were represented by conventional condrosarcoma, one localized in the scapula and the other one in the trachea, both with microscopic features of conventional low-grade tumors (grade 1). We performed conservative surgical curative treatment, with a favorable postoperative outcome.

The third important subject for me was the challenge represented by the diseases with an increasing prevalence in our century and the multidisciplinary approach in order to provide an adequate management.

1. **Non-invasive assessment of liver steatosis and fibrosis in patients with type 2 diabetes mellitus.** Despite the fact that nonalcoholic fatty liver disease is common in the present time, especially in patients with insulin resistance and type 2 diabetes mellitus, it is still difficult to diagnose early. The aim of our team was to find a correlation between elastographic parameters and lab results and to imagine and diagnostic algorithm. We used transient elastography and measured liver stiffness as a marker of the degree of fibrosis and liver steatosis, by controlled attenuation parameter in patients with type 2 diabetes mellitus. We observed that almost all patients in our group had some degree of liver steatosis and there was a correlation between steatosis, fibrosis and the ratio between triglycerides and HDL cholesterol.

2. **Complications of Roux-en-Y gastric bypass.** Bariatric surgery is used more and more frequently in case of severe obesity and comorbidities. We performed Roux-en-Y gastric bypass, an intervention that is both restrictive and malabsorptive, and therefore efficient in terms of weight loss. Our research aimed to evaluate the complications that occurred in our patients. We found wound infections and incisional hernias as complications and succeeded to adapt the method of suturing the abdominal wall in order to avoid the infection of the wound.
3. **The impact of certain biomarkers on mortality in patients with liver metastasis derived from a colorectal cancer.** Colorectal cancer has an increasing prevalence, its morbidity and mortality being related also to the presence of metastases. We evaluated the relation between different clinical and biological parameters in patients with metastatic colorectal cancer and found an association between a shorter survival and several parameters: low body mass index and lymphocyte count, high values of neutrophil-hemoglobin-lymphocyte score, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and systemic immune-inflammation index. The presence of hepatic metastasis at diagnosis was related to a reduced survival.

The second part of the Habilitation Thesis focuses on my future perspectives, from academic, professional, and scientific perspectives. From an academic point of view, I would like to develop the current existing teaching and knowledge base regarding surgical semiotics and surgery. I aim to develop new lectures for medical students, broadening the spectrum of the existing topics and integrating them in the context of state-of-the art medical research areas.

From the researcher's point of view, I aim to continue the research topics already started, a work in which PhD students will have a central place being pro-actively involved in applied and theoretical state-of-the-art medical research. Part of the approached areas of research will be continuing the already started ones: surgery of the liver, interdisciplinary approach of the surgical patient.

Of course, this short list of further perspectives doesn't intend to comprise the entire area of future research since the development of science rises unforeseen new areas of research and new perspectives regarding the entire medical pathology and since the surgical techniques are getting more and more complex and safe.

Finally, having the premises of my previous training and experience and considering my future plans, I hope that by achieving the previously mentioned goals I will be a member of the academic staff who will reach the expectations of the University which formed me, my Alma Mater, the "Victor Babes" University of Medicine and Pharmacy from Timisoara.

LIST OF THE 10 REPRESENTATIVE PAPERS

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