PhD Candidate
RÂMBOIU DUMITRU SANDU

THE PLACE OF BILIARY DERIVATIONS IN THE TREATMENT OF BILIOPANCREATIC DISEASES

DISSERTATION THESIS

Scientific Supervisor
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Craiova
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INTRODUCTION

The obstructive jaundice is a complex syndrome with both benign aetiology (choledocholithiasis, hydatid cyst, chronic pancreatitis) and malignant (cancer of the pancreas, cholangiocarcinoma and gallbladder cancer) and it has a special place in biliopancreatic pathology, with up most importance due to changes in local and general status of the organism, difficult etiologic diagnostic problems for the clinician and whose solution requires teamwork, which involves both the surgeon, gastroenterologist, anesthesiologist etc.

The last decades have been marked on one hand by the obvious increase in the incidence of causative injuries for obstructive jaundice, especially in terms of gallstones and pancreatic cancer, but also by technological developments which have led to changes in conceptual terms regarding therapeutic options in obstructive jaundice. Thus, the introduction in the current practice of high performance imaging techniques (CT, MRI, cholangioMRI, ERCP, endoscopy, EUS) has led on the one hand to improvement of diagnosis and on the other hand has offered the possibility of an early, aggressive and radical therapy for an increasing number of patients.

This was materialized for malignant diseases, particularly cancer of the head of the pancreas, by a significant increase in resectability rate and the introduction of laparoscopic approach and upper gastrointestinal endoscopy for gallstone disease giving the opportunity to solve choledocholithiasis only by laparoscopic approach or by combining laparoscopic cholecystectomy with extraction of the common bile duct stones using endoscopic retrograde cholangiopancreatography, which greatly restricted the classical surgical indications. Moreover, the possibility of endoscopic stenting of biliary tract in patients with pancreatic head cancer or cholangiocarcinoma represents a therapeutic alternative worthy of attention, ensuring maximum patient comfort with almost no vital risk.

In these circumstances, we consider appropriate to review the place and indications of biliodigestive anastomoses in obstructive jaundice therapeutic arsenal. The above mentioned made me chose this thesis, I submitted to using the experience of two prestigious clinics from Craiova, 1st Surgery Department and Gastroenterology Department, to clarify at least in part the issues related to the treatment of extra hepatic cholestasis.

I wish to thank the entire staff of the 1st Surgery Department, who helped and encouraged me throughout the course of my study. My gratitude goes especially to Mr. Prof. Dr. Ion Georgescu, Ph.D., my Scientific Supervisor, without whose competent guidance, rigor, goodwill and understanding, the paper could not be carried out.

I extend my sincere thanks to Mr. Professor Nemes Raducu for the completion of my professional training, suggestions and contributions to accomplish this work, as well as human and professional model worth following.

MATERIAL AND METHOD

Obstructive jaundice, a plurietiologic, clinical and biological syndrome, including benign or malignant disease, acute or chronic, confronts the surgeon with difficult issues for diagnosis and treatment of whose resolution requires a multidisciplinary approach involving the surgeon, anesthesiologist, gastroenterologist and pathologist.

The aim of the thesis was at least to partly elucidate the following issues raised by the treatment of extra hepatic cholestasis:

- Establishing a diagnostic algorithm for obstructive jaundice,
- Assessment of biological and imaging investigation methods with specific guidelines based on etiopathogenesis of jaundice,
Evaluation of the place and indications of biliodigestive derivations in the therapeutic arsenal of obstructive jaundice,

Evaluation of endoscopic treatment methods as an alternative This paper is a retrospective study on a total of 340 patients with obstructive jaundice hospitalized and operated in 1st Surgery Department in the last 8 years (January 1, 2001 to December 31, 2008), divided into two groups according to the two fundamental forms of obstructive jaundice.

- Group A: obstructive jaundice of benign etiology - 149 patients
- Group B: obstructive jaundice of malignant etiology - 191 patients.

In the absence of the possibility of carrying out a randomized trial, we opted for a retrospective study applied on a consecutive series of patients diagnosed preoperatively with obstructive jaundice or which intraoperatively were found extrahepatic biliary tract changes which have imposed exploration and, possibly, making a biliodigestive derivation.

It is a single-center, multioperator study having a strong informative character by including all cases in the studied period and this prevents the tendency to distortion that may occur through the process of randomization.

Although the trend in recent years is to highlight the advantages of randomized trials, until the total disregard for other types of clinical trials, especially because of the difficulties of randomization, in surgery there is a tendency to reconsider non-randomized studies, and this not only in the latter domain.

Data were extracted from several sources: clinical observation sheets, surgical interventions protocols, anatomo-pathological examinations, necropsy protocols.

For each patient in the study group was completed an individual form of clinical research, which included the following:

- name,
- age
- sex
- environmental provenance
- date of admission to the number of clinical observation sheet,
- main diagnosis,
- secondary diagnoses,
- personal history,
- risk factors
- subjective and objective clinical signs,
- biological exploration (CBC, urea, bilirubin, alkaline phosphatase, gammaGT, transaminases) – for jaundice syndrome and etiologic diagnosis,
- imaging (transabdominal ultrasound, computed tomography, endoscopic ultrasound, ERCP, upper gastrointestinal endoscopy)
- morphological data obtained at intraoperative exploration (gallbladder, bile duct layout, pancreas, liver)
- type of surgery,
- intraoperative incidents and accidents and how to resolve,
- local and general postoperative complications,
- postoperative course (morbidity, mortality and causes of death).
- status at discharge.

All the parameters extracted from these sheets were placed in an Excel file - spreadsheet and statistical software, which helped the statistical processing of the material.

Descriptive studies have been used to provide information on the share of each group of biliodigestive derivations for benign or malignant biliopancreatic disease.

I also made a comparative study of diagnostic imaging methods, which allowed us to assess the comparative sensitivity and specificity, positive and negative predictive values for
diagnosis of patients with extrahepatic cholestasis. The purpose of this study was to evaluate new imaging methods, such as linear endoscopic ultrasonography for preoperative determination of causes of obstructive jaundice and their predictive values in terms of resectability.

**SURGICAL TREATMENT OF OBSTRUCTIVE JAUNDICE**

Surgery is the main treatment option in obstructive jaundice and has the following objectives:
- Barrier removal and decompression of the main bile duct,
- Restoration of bile flow.

Due to the soundness of biliary obstruction for the human body it is required a preoperative patient preparation that is most often synchronous with the last stage of diagnosis (determining the etiology), surgery being considered an emergency for patients with hepatorenal failure and angiocholitis. Preoperative preparation must achieve the following goals:
- Rebalancing with crystalloids and colloidal solutions,
- Correction of anemia with blood (head of the pancreas tumors with invasion of the stomach or duodenum)
- Correction of coagulation by parenteral administration of vitamin K,
- Antibiotic therapy in forms complicated with acute cholecystitis, angiocholitis or acute pancreatitis,
- Treatment of associated diseases (cardiovascular, pulmonary, diabetes, etc.).

The objectives of surgical treatment can be carried out differently depending on the etiology. Biliodigestive derivations are also means of relief of bile duct, but also a way to restore bile flow with particular indications depending on the etiology of jaundice.

*Evaluation of biliodigestive derivations in the treatment of benign etiology obstructive jaundice*

In choosing the method of bile duct drainage we used the following criteria:
- Dilated common bile duct, vein-looking, under 15 mm diameter - external biliary drainage Kehr, possibly associated with papilosfincterotomy,
- Dilated common bile duct with a diameter over 15 mm - biliodigestive derivation (Table no.1)
### Table no. 1 Ways of providing biliary drainage in patients with bile duct stones

<table>
<thead>
<tr>
<th>Intervention type</th>
<th>No. patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choledochotomy + external biliary drainage Kehr</td>
<td>15</td>
<td>12%</td>
</tr>
<tr>
<td>Coledocholithotomy + external biliary drainage Kehr</td>
<td>31</td>
<td>24.8%</td>
</tr>
<tr>
<td>Coledocholithotomy + external biliary drainage Kehr + papilosfincterotomy</td>
<td>10</td>
<td>8%</td>
</tr>
<tr>
<td>Coledocoduodenostomy</td>
<td>52</td>
<td>41.6%</td>
</tr>
<tr>
<td>Roux-en-Y Coledocojejunostomy</td>
<td>4</td>
<td>3.2%</td>
</tr>
<tr>
<td>Coledocojejunostomy on omega loop</td>
<td>1</td>
<td>0.8%</td>
</tr>
<tr>
<td>Exploratory choledochoscopy + choledocholithotomy + trancystic biliary drainage</td>
<td>12</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

### Evaluation of biliodigestive derivations in the treatment of malignant etiology obstructive jaundice

Treatment of obstructive jaundice of malignant etiology has two major objectives:

1. oncology: tumor ablation with oncological safety limits, that will prevent relapse and / or metastases and to ensure long time survival rate;
2. functional, to solve potential complications caused by progressive tumor growth: decompression of the biliary and pancreatic ducts, solving extrinsic digestive stenosis and / or pain relief. At this therapeutic stage, therapeutic means are aimed at ensuring optimal comfort for patient survival (table no. 2).

<table>
<thead>
<tr>
<th></th>
<th>Pancreatic head cancer</th>
<th>Gallbladder cancer</th>
<th>Cholangiocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RADICAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenopancreatectomy</td>
<td>10 (9.3%)</td>
<td>3 (23%)</td>
<td>2 (10.5%)</td>
</tr>
<tr>
<td>Partial resection of main biliary duct</td>
<td>10 (9.3%)</td>
<td>0</td>
<td>1 (5.25%)</td>
</tr>
<tr>
<td>Cholecystectomy with hepatectomy</td>
<td>0</td>
<td>0</td>
<td>1 (5.25%)</td>
</tr>
<tr>
<td><strong>PALLIATIVE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choldochoduodenostomy</td>
<td>67 (62.6%)</td>
<td>0</td>
<td>4 (21%)</td>
</tr>
<tr>
<td>Roux-en-Y choledochojejunostomy</td>
<td>13 (12%)</td>
<td>0</td>
<td>1 (5.25%)</td>
</tr>
<tr>
<td>Choledochojejunostomy on omega loop</td>
<td>6 (5.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cholecystogastrostomy</td>
<td>9 (8.4%)</td>
<td>0</td>
<td>1 (5.25%)</td>
</tr>
<tr>
<td>Transtumoral drilling with Kehr tube</td>
<td>0</td>
<td>0</td>
<td>6 (31.5%)</td>
</tr>
<tr>
<td>Hepaticogastrostomy</td>
<td>1 (0.9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Exploratory laparotomy</td>
<td>1 (0.9%)</td>
<td>10 (77%)</td>
<td>5 (26.5%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>107</td>
<td>13</td>
<td>19</td>
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</tbody>
</table>

Table no. 2 Radical and palliative surgical procedures for malignant obstructive jaundice
CONCLUSIONS

1. Obstructive jaundice remains a matter of great importance in the pathology of hepato-bilio-pancreatic pathology.

2. Pancreatic head cancer (159 patients = 46.7%) and choledocholithiasis (125 patients = 36.7%) are the most common causes of obstructive jaundice, followed in order by cholangiocarcinoma, chronic pancreatitis, hydatid cyst and gallbladder cancer.

3. The incidence of obstructive jaundice significantly increased after the age of 60 years (61.4 years for jaundice caused by lithiasis and 64.8 years for cancer of the head of the pancreas) and distribution by gender is defined according to the etiology of jaundice: the predominance of females (64, 8%) for lithiasis and male (57.8%) in malignant jaundice.

4. Hormonal dysfunction and use of oral contraceptives in women with stones and smoking, alcohol consumption and history of chronic pancreatitis at patients with pancreatic head cancer were the main risk factors.

5. Positive diagnosis of biliary obstruction was due to the presence of jaundice and biological cholestasis syndrome.

6. Biological diagnosis of obstructive jaundice can be difficult; he is established by the main clinical signs (onset, pain, fever, jaundice, itching, palpable gallbladder, etc.) and high performance imaging investigations: ultrasound, EUS, CT, ERCP, colangioMRI, etc.

7. Transabdominal ultrasound (304 patients = 89.4%) is the method of choice to detect gallstones and can highlight a series of direct and indirect signs useful in diagnosis and therapeutic indication.

8. CT (89 patients = 26.2%) considered "the golden-standard" of medical imaging for pancreatic head cancer, may provide useful data for determining resectability, but in case of endoscopic ultrasonography the predicting resectability rate in our statistics was 62 % (compared to 37% for CT), while a negative prediction is almost 100%.

9. Treatment of obstructive jaundice is now complex, multidisciplinary, but surgery is still the main treatment option and should achieve the following objectives: relief of obstruction, decompression of bile duct and assuring an efficient bile flow, effective ways of achieving these objectives are different depending on the etiology of biliary obstruction.

10. Laparoscopic cholecystectomy and restoration of bile flow using ERCP is now the main therapeutic option.

11. For main bile duct stones resolved by open surgery, treatment after relief of obstruction of bile duct is today facing external biliary drainage Kehr (44.6%), biliodigestive derivations being reserved for cases with dilated common bile duct, especially in the elderly.

12. Biliodigestive derivations are, however, the therapeutic solution for most cancers of the head of the pancreas (90.7% in our statistics), whose rate of resectability in literature does not exceed 10-20% (9.3% in our study).

13. Coledocoloduodenanastomosis was the most commonly used type of bypass (62.6%) in neoplastic jaundice and its association with gastroenteroanastomosis remains a controversial issue, we have used it in a limited number of cases.

14. Endoscopic stenting (11 cases), is an alternative for biliodigestive anastomoses, which tends to gain ground in the treatment of neoplastic jaundice.
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Curriculum Vitae

PERSONAL DETAILS

LASTNAME: RAMBOIU
FIRST NAMES: DUMITRU SANDU
DATE OF BIRTH: 26.01.1981
NATIONALITY: Romanian
MARITAL STATUS: Unmarried
CONTACT TELEPHONE NUMBER: 0040740272616
CONTACT EMAIL ADDRESS: sandu_r@yahoo.com
DEPENDANTS / CHILDREN: none
FIRST LANGUAGES: Romanian
OTHER LANGUAGES: English, French
CRIMINAL OFFENCES: None
HEALTH: Very good

EDUCATION

LAST SCHOOL ATTENDED: Carol National College, Craiova, Romania
STANDARD ACHIEVED: Excellent
SUBJECTS PASSED: Romanian language, English language, mathematics, chemistry, biology
SPORTS: football, snowboarding
**HIGHER EDUCATION**

**UNIVERSITY:** University of Medicine and Pharmacy Craiova  
**DATES ATTENDED:** 01.10.1999 – 20.09.2005  
**DEGREE:** General Medicine  
**EXTRA-MURAL ACTIVITIES:** Voluntary nursing, voluntary in the emergency room, activity in the neurophysiology lab – visual evoked potentials  
Scholarship “Leonardo da Vinci” scholarship – between April 1st and June 30th 2003 at the Neurobiology Laboratory, Ernest-Moritz-Arndt University, Greifswald, Germany.  

**PhD STUDIES**  
PhD Student since 2005 at the University of Medicine and Pharmacy Craiova,  

**MASTER STUDIES**  
Master in “Management of Health Units” – 2009  

**FUTURE TRAINING**  
Advanced in Laparoscopic Surgery,  

**Employment History Summary:**

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<th>Date (start and finish)</th>
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<td>1.01.2006 – present</td>
<td>Resident at Department of General Surgery</td>
<td>Emergency County Hospital of Craiova, Romania</td>
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<tr>
<td>01.10.2006 – present</td>
<td>Lecturer in General Surgery</td>
<td>University of Medicine and Pharmacy, Craiova, Romania</td>
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EMPLOYMENT HISTORY

POST: Resident in General Surgery at the 1st Surgical Department

HOSPITAL: Emergency County Hospital of Craiova, Romania

DATES: 1.1.2006 – present

ROTATIONS/DEPARTMENTS:

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<th>Department</th>
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<td>Obstetrics and Gynaecology</td>
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<td>Anaesthetics</td>
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<tr>
<td>Cardiovascular Surgery</td>
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<tr>
<td>Plastic Surgery</td>
<td>3 months</td>
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<tr>
<td>Trauma &amp; Emergency</td>
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<td>Thoracic Surgery</td>
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<td>Laparoscopic Surgery</td>
<td>12 months</td>
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EDUCATION (Courses and postgraduate training)

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<tr>
<th>Date</th>
<th>Name and location (city of Department/Clinic of University)</th>
<th>Subject or speciality &amp; tutor’s name</th>
<th>Level of course (degree, diploma certificate, etc.)</th>
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<tr>
<td>May 2006</td>
<td>Romanian Society of Surgery</td>
<td>Biliary surgery – benign diseases</td>
<td>Certificate</td>
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<tr>
<td>September 2009</td>
<td>Elias Hospital Bucharest</td>
<td>Thyroid surgery</td>
<td>Diploma</td>
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RESEARCH

I was an active member in 2 research projects:

2. SURVIVAL AND IMUNOLOGIC IMPACT AFTER ENDOSCOPIC TRANSGASTRIC OVARIETOMY COMPARED TO LAPAROSCOPIC APPROACH, 2007-2010, Romanian National Program for Research, Development and Innovation (Program Parteneriate)
PUBLICATIONS & PRESENTATIONS

PUBLICATIONS

Books published:

TEHNICI MODERNE DE DIAGNOSTIC ȘI TRATAMENT ÎN PATOLOGIA ORGANICĂ A INTESTINULUI SUBȚIREE - sub redacția, Cristin Constantin Vere
Cap. Tumorile maligne ale intestinului subțire - pag. 105 - 117
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