Total Pancreatectomy in Management of Pancreatic Tumors

An Essay
Submitted for Partial Fulfillment of Master Degree
in General Surgery

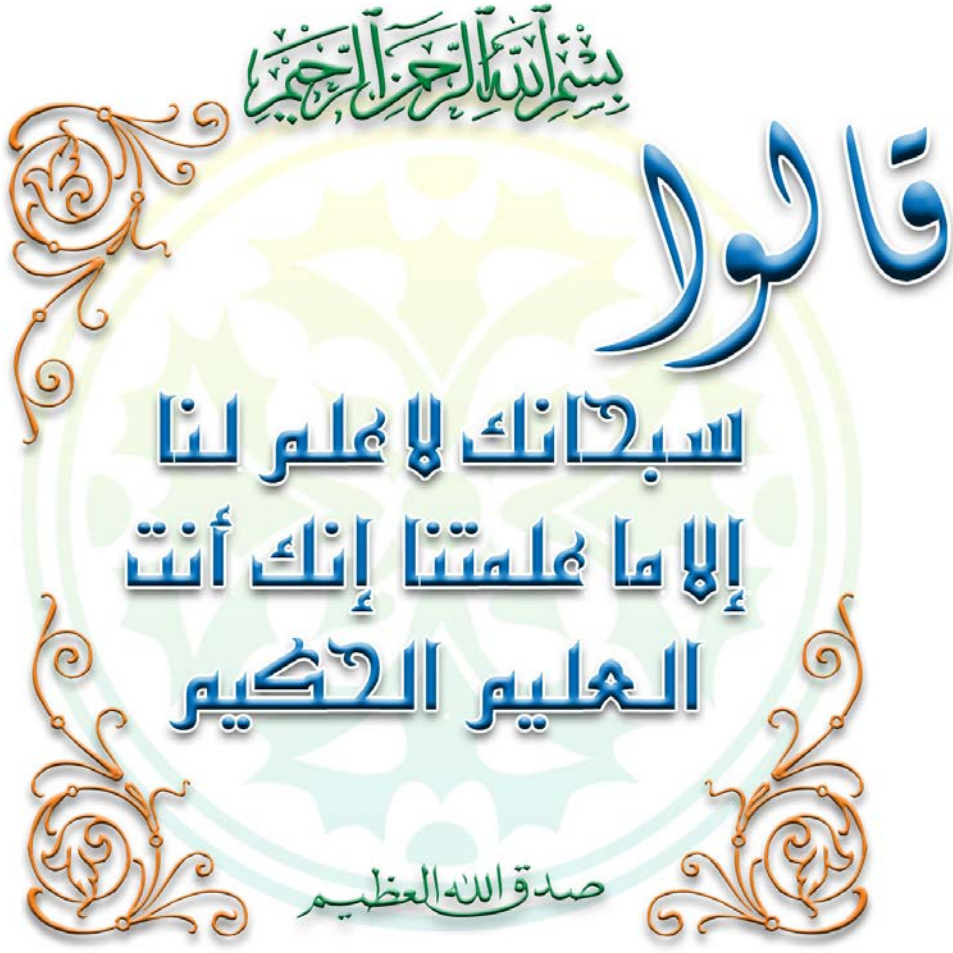
Presented By
Mahmoud Moustafa Nafie
M.B.B.Ch.
Ain Shams University

Supervised By
Prof. Dr. Abd El Rahman M. El Maraghy
Professor of General Surgery
Faculty of Medicine – Ain Shams University

Dr. Mahmoud Saad Farahat
Assistant Professor of General Surgery
Faculty of Medicine – Ain Shams University

Dr. Hisham Mohamed Omran
Lecturer of General Surgery
Faculty of Medicine – Ain Shams University

Ain Shams University
Faculty of Medicine
2013



سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost I would be thankful to Allah who enabled us to complete this work hoping to provide a useful guide to the scope of role total pancreatectomy in management of pancreatic tumors.

I would like to express my deep gratitude and appreciation to **Prof. Dr. Abd El Rahman M. El Maraghy,** *Professor of General Surgery Faculty of Medicine, Ain Shams University, for his kind supervision and support, without his continous guidance and encouragement this essay would have never seen light.*

I am just as much indebted to **Dr. Mahmoud Saad Farahat,** *Assistant Professor of General Surgery Faculty of Medicine, Ain Shams University and* **Dr. Hisham Mohamed Omran** *Lecturer of General Surgery Faculty of Medicine, Ain Shams University, every step and every details in this work have been kindly assisted and supported by their effort and care.*

Last but not the least, I am also grateful to my staff, colleagues and my family who assisted me in this work.

Mahmoud Moustafa Nafie

دور عملية الاستئصال الكامل للبنكرياس فى مرضي سرطان البنكرياس

رسالة توطئة للحصول علي درجة الماجستير

فى الجراحة العامة

مقدمة من

الطبيب/ محمود مصطفي نافع

بكالوريوس الطب و الجراحة

كلية الطب – جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ عبد الرحمن محمد المراغي

أستاذ الجراحة العامة

كلية الطب – جامعة عين شمس

الدكتور/ محمـــود سعـد فرحـات

أستاذ مساعد الجراحه العامة

كلية الطب – جامعة عين شمس

الدكتور/ هشـــام محمـد عمـران

مدرس الجراحة العامة

كلية الطب – جامعة عين شمس

جامعة عين شمس

كلية الطب

2013

Contents

List of Figures

List of Tables

List of Abbreviations

Abb.	Meaning
18FDG	18 fluorodeoxy glucose
5FU	5 fluorouracil
ADCC	Antibody dependent cell mediated cytotoxicity
B-HCG	Beta subunit of human chorionic gonadotrophin
CA19.9	Carbohydrate antigen 19.9
CCK	Cholecystokinin
COX	Cyclo-oxygenase
CT	Computerized tomography
DACP	Deudenoscope assisted cholangro-pancreatoscopy
DNA	Deoxy ribonucleic acid
DT	Diphtheria toxin
EGD	Eosophago gastrodeudenoscopy
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EORTC QLQ	European organization for research and treatment of cancer quality of life
ERCP	Endoscopic retrograde cholangiopancreatography
EUS	Endoluminal ultrasound
FAMMM	Familial atypical multiple mole melanoma
FAP	Familial adenomatous polyposis
FGF	Fibroblast growth factor
FNA	Fine needle aspiration
GI	Gastrointestinal
GIP	Gastric unhibitory polypeptide
Glut-1	Glucose transporter-1
GOO	Gastric outlet obstruction
GTP	Gluteryl triphosphate
HNPCC	Hereditary non polyposis colorectal cancer

Abb.	Meaning
IDPMN	Intraductal pupillary mucinous neoplasm
IGF	Insulin like growth factor
IRG	Immunoreactive glucagons
LAR	Long acting release
MCT	Medium chain triglyceride
MEN	Multiple endocrine neoplasia
MLC	Mixed leukocyte cyloimplant
MMP	Matrix metalloprotiens
MRCP	Magnetic resonance cholangio-pancreatography
MRI	Magnetic resonance imaging
mTOR	Mammalian target of rapamycin
NF1	Neurofibromatosis type I
PET	Position emission tomography
PETs	Pancreatic endocrine tumors
PP	Pancreatic polypeptide
PPI	Proton pump inhibitors
PPPD	Pylorus preserving pancreatico-deudenectomy
PTC	Percutaneous transhepatic cholangiography
PV	Portal vein
SMA	Superior mesenteric artery
SMPV confluence	Superior mesenteric portal rein confluence
SUR	Standard uptake ratio
TGF	Transforming growth factor
TNM	Tumor-node-metastasis
TPN	Total parentral nutrition
UICC	Union of international cancer control
US	Ultrasound
VEGF	Vascular endothelial growth factor

Abb.	Meaning
VHL disease	Von hipple landau disease
VIP	Vasoactive intestinal peptide
WDHA	Watery diarrhea hypokalemia achlorhydria
WHO	World health organization

Introduction

The pancreas is an elongated organ, light tan or pinkish in color that lies in close proximity to the duodenum. It is covered with a very thin connective tissue capsule which extends inward as septa, partitioning the gland into lobules ***(Cuschieri, 2002)*.**

Pancreatic cancer is the eighth most common malignancy and the fifth leading cause of the adult cancer death in the United States. Only 1-4% of all patients diagnosed with pancreatic cancer can expect to survive 5 years. In the year 2000 about 28,300 new cases of adenocarcinoma of the pancreas were diagnosed in the United States, and about 28,200 patients died of this aggressive malignancy ***(Grau et al., 2004)***.

Depending on the extent of the tumor at the time of diagnosis, the prognosis is generally regarded as poor, with few victims still alive five years after diagnosis, and complete remission still extremely rare ***(Cuschieri, 2002)*.**

Risk factors for pancreatic cancer include age, male gender, African ethnicity and smoking. Cigarette smoking causes a 75% risk increase, and the risk persists for at least a decade after quitting. Diets high in red meat, obesity, diabetes mellitus and chronic pancreatitis have been linked, but are not

known to be causal. Helicobacter pylori infection, occupational exposure to certain pesticides, dyes, and chemicals related to gasoline are among the risk factors. 5-10% of pancreatic cancer patients have a family history of pancreatic cancer ***(Iodice et al., 2008)***.

Epithelial neoplasms of the pancreas include tumors that arise from ductal, acinar, or endocrine cells. The most common are adenocarcinomas of the ductal phenotype. Ductal adenocarcinoma is therefore the prototype of pancreatic cancer, and that is what is meant whenever epidemiological and clinical data on pancreatic cancer are discussed. All other epithelial tumors are uncommon, but they include a number of neoplasms with special biological features. Non-epithelial tumors of the pancreas are exceedingly rare ***(Kloppel, 1997).***

The recently published World Health Organization (WHO) classification of pancreatic exocrine tumors divides the tumors on the basis of their biological behavior into benign tumors, borderline tumors (uncertain malignant potential), and malignant tumors ***(Kloppel et al., 2011)***.

Early diagnosis of pancreatic cancer is difficult because the symptoms are so non-specific and varied, pancreatic cancer is sometimes called a "silent disease". Common symptoms include pain in the upper abdomen, loss of appetite, nausea,

vomiting significant weight loss and painless jaundice related to bile duct obstruction (carcinoma of the head of pancreas), diabetes mellitus ***(Bakkevold et al., 2002).***

Pancreatic cancer is usually discovered during the course of the evaluation of one of the forementioned symptoms. Liver function tests may show a combination of results indicative of bile duct obstruction (raised conjugated bilirubin, y-glutamyl transpeptidase and alkaline phosphatase levels). CA19-9 (carbohydrate antigen 19.9) is a tumor marker that is frequently elevated in pancreatic cancer, Imaging studies such as ultrasound or abdominal CT scan may be used to identify tumors. Endoscopic ultrasound (EUS) is another procedure that can help to visualize the tumor and obtain tissue biopsy to establish the diagnosis, ERCP (endoscopic retrograde cholangiopancreatography), PTC (percutaneous transhepatic cholangiography) and MRI (magnetic resonance imaging) are used for diagnosis and staging of pancreatic cancer ***(Ghaneh et al., 2007).***

People with pancreatic cancer may have several treatment options. Depending on the type and stage, pancreatic cancer may be treated with surgery, radiation therapy or chemotherapy. Some patients have a combination of therapies. The surgeon may remove all or part of the pancreas. The extent of surgery depends on the location and size of the tumor, the

stage of the disease and the patient's general health, the mortality rates for the pancreatic resection have fallen substantially over the last two decades. This is related to the better quality of peri-operative care, improvement in the skill and experience of the surgeons and the concentration of these patients in specialist centers ***(Evans et al., 2001).***

Total pancreatectomy (TP) for pancreatic cancer was first reported by Rockey in1943. Subsequently, it was considered that partial pancreatectomy (PP) would help to avoid pancreatic fistula. Because of high tumour recurrence rates after Kausch-Whipple procedures, any suggestion of possible tumour multicentricity supported a role for TP as a means of achieving R0 resection, Subsequent studies demonstrated no improvement in postoperative outcome and major metabolic problems were found to occur. These were difficult to address and the procedure fell out of favour. However, recent studies have demonstrated progress regarding postoperative outcomes of TP. In addition new pancreatic tumour entities have been identified in the past decade and these require total rather than partial pancreatectomy ***(Nathan et al., 2009).***

Total pancreatectomy has been used to treat both benign and malignant disease of the pancreas, but its use has been limited by concerns about management of the apancreatic state with its attendant total endocrine and exocrine insufficiency. It