



Effect of Single Anastomosis Duodeno-ileal Bypass (SADI) on Type 2 Diabetes Mellitus

A Meta-Analysis

*Submitted For Partial Fulfillment of Master Degree in
General Surgery*

By

Moataz Taha Gomaa Abdelgawad

MB.B.Ch

Faculty of Medicine – Ain-Shams University

Under supervision of

Prof. Dr. Ahmad Helmy Ali Youssuf

Professor of General Surgery

Faculty of Medicine - Ain Shams University

Prof. Dr. Islam Hossam El-Din El-Abbassy

Assistant Professor of General Surgery

Faculty of Medicine - Ain Shams University

Dr. Mohamed Gamal El-Fouly

Lecturer of General Surgery

Faculty of Medicine - Ain Shams University

***Faculty of Medicine
Ain Shams University
2019***

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبَّحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

First, thanks are all due to Allah for Blessing this work until it has reached its end, as a part of his generous help throughout my life.

I would like to express my deepest respect, thanks and gratitude to Prof. Dr. Ahmad Helmy Ali Youssuf, Professor of General Surgery, Ain Shams University, who devoted much of his precious time, kind guidance and meticulous supervision.

I would like to Sincerely thank Prof. Dr. Islam Hossam El-Din El-Abbassy, Assistant Professor of General Surgery, for his advice, kind assistance and guidance.

Thanks are due to Dr. Mohamed Gamal El-Fouly, Lecturer of General Surgery, Ain Shams University, for his continous guidance, correction and explanation.

Last but not least, I would like to thank my family and friends for their constant support and encouragement.

List of Contents

Title	Page No.
List of Abbreviations	5
List of Tables	7
List of Figures	8
Introduction	1
Aim of the Work.....	12
Type 2 Diabetes Mellitus	13
Surgical Treatment of Type 2 Diabetes Mellitus	23
Bariatric Surgery Overview	37
Single Anastomosis Duodeno-Ileal Bypass With Sleeve Gastrectomy (SADI-S).....	44
Methodology and Meta-analysis	58
Results	87
Summary	90
Conclusion.....	92
References	93
Arabic Summary	—

List of Abbreviations

Abb.	Full term
ADA	American Diabetes Association
AGB	Adjustable Gastric Banding
ASMBS	The American Society of Metabolic and Bariatric Surgery
BA	Bile Acids
BMI	Body Mass Index
BpD	Bilio-pancreatic Diversion
BPD-DS	Bilio-Pancreatic Diversion and Duodenal Switch
CCTs	Clinical Controlled Trials
CDC	Center for Disease Control and Prevention
CNS.....	Central Nervous System
CRR.....	Complete Remission Rate
DIOS	Distal loop Duodeno-Ileostomy
DJBS.....	Duodeno-Jejunal Bypass Sleeve
DM	Diabetes Mellitus
DOD	Duration of Disease
EASD	European Association for the Study of Diabetes
EWL.....	Expected Weight Loss
FBS	Fasting Blood Sugar
fGf19	plasma fibroblast growth factor 19
FPG/fpG.....	Fasting Plasma Glucose
fXR	Farnesoid X Receptor
GLp-1	glucagon-like peptide-1
GLUT-2.....	Glucose Transporter 2
IDF.....	International Diabetes Foundation
IGT.....	Impaired Glucose Tolerance
JIB	Jejuno-Ileal Bypass
LDL.....	Low Density Lipoproteins

List of Abbreviations Cont...

Abb.	Full term
LSG	Laparoscopic Sleeve Gastrectomy
MeSH	Medical Subject Headings
MGB.....	Mini-Gastric Bypass
oGTT	Oral Glucose Tolerance Test
PG	Plasma Glucose
POSE	Primary Obesity Surgery, Endoluminal
Postop.	Postoperatively
PPrBS	Post-prandial Blood Sugar
pyy	peptide yy
RCTs	Randomized Controlled Trials
RyGB	Roux-en-y gastric bypass
SADI-S.....	Single Anastomosis Duodeno-ileal bypass with Sleeve Gastrectomy
SG	Sleeve Gastrectomy
SoS	Swedish Obese Subjects Study
T2DM.....	Type 2 Diabetes Mellitus
UK.....	United Kingdom
USA.....	United States of America
VBG	Vertical Banded Gastroplasty

List of Tables

Table No.	Title	Page No.
Table (1):	Epidemiologic Determinants and Risk Factors of Type 2 D.M.	16
Table (2):	Criteria for the Diagnosis of Diabetes.	17
Table (3):	Collective-Analysis of The Effect of Single Anastomosis Duodeno-ileal Bypass (SADI) on Type 2 Diabetes Mellitus From published Papers Up to Date.	62
Table (4):	Detailed analysis of mean age and sex among patients in the included studies & country of origin of each study.	69
Table (5):	Meta-analysis of HbA1c (%) ≤ 1 year postoperatively.	70
Table (6):	Meta-analysis for postoperative (1 and half - 2 year) HbA1c (%).	72
Table (7):	Meta-analysis for postoperative (3 year) HbA1c (%).	74
Table (8):	Meta-analysis for glycemia (≤ 1 year) HbA1c (%).	76
Table (9):	Meta-analysis for postoperative remission.	78
Table (10):	Meta-analysis for needing anti-diabetic therapy post-operatively.	80
Table (11):	Meta-analysis for needing oral anti-diabetic therapy post-operatively.	83
Table (12):	Meta-analysis for needing insulin therapy post-operatively.	85

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Scopinaro biliopancreatic diversion.....	40
Figure (2):	Sleeve gastrectomy	41
Figure (3):	Port application in SADI-S.....	46
Figure (4):	Dissecting the greater curvature of the stomach.	47
Figure (5):	Performing a sleeve gastrectomy using a linear stapler.	48
Figure (6):	Creation of sleeve over a bougie.....	49
Figure (7):	Duodenal division using linear stapler.....	49
Figure (8):	Performing a duodeno-jeujenal anastomosis.....	50
Figure (9):	Creation of hand-sewn duodenoileal anastomosis.....	51
Figure (10):	Port removal of stomach.	52
Figure (11):	Final aspect of the duodeno-ileal bypass.....	52
Figure (12):	SADI-S. A sleeve gastrectomy is followed by a duodeno-ileal diversion at 200 cm from the ileocecal junction	57
Figure (13):	SADI-S patients/ year.....	57
Figure (14):	Forest plot for postoperative (≤ 1 year) HbA1c.....	71
Figure (15):	Funnel plot for postoperative (≤ 1 year) HbA1c.....	71
Figure (16):	Forest plot for postoperative (1 and half - 2 year) HbA1c.....	73
Figure (17):	Funnel plot for postoperative (1 and half - 2 year) HbA1c.	73
Figure (18):	Forest plot for postoperative (3 year) HbA1c.....	75

List of Figures Cont...

Fig. No.	Title	Page No.
Figure (19):	Funnel plot for postoperative (3 year) HbA1c.....	75
Figure (20):	Forest plot for postoperative (≤ 1 year) glycemia.....	77
Figure (21):	Funnel plot for postoperative (≤ 1 year) glycemia.....	77
Figure (22):	Forest plot for postoperative remission.....	79
Figure (23):	Funnel plot for postoperative remission.....	80
Figure (24):	Forest plot for needing anti-diabetic therapy post-operatively.....	81
Figure (25):	Funnel plot for needing anti-diabetic therapy post-operatively.....	82
Figure (26):	Forest plot for needing oral anti-diabetic therapy post-operatively.....	84
Figure (27):	Funnel plot for needing oral anti-diabetic therapy post-operatively.....	84
Figure (28):	Forest plot for needing insulin therapy post-operatively.....	86
Figure (29):	Funnel plot for needing insulin therapy post-operatively.....	86
Figure (30):	Flow chart of literature selection.....	87

Introduction

Several conventional and novel methods of bariatric surgery — termed metabolic surgeries — induce long-term remission of type 2 diabetes mellitus (T2DM) and dramatically improve other metabolic abnormalities, such as hyperlipidemia and hypertension, independent of the patients' weight (*Buchwald et al., 2004; Cohen et al., 2006; O'Brien et al., 2006; Lee et al., 2008*). Some studies demonstrated that these metabolic effects are not only attributable to drastic weight loss and diminished caloric intake, but also to endocrine changes that result from surgical manipulation of the gastrointestinal tract (*Suter et al., 2009; Thaler and Cummings, 2009*).

Duodenal switch has proved to be the most effective procedure in terms of the long-term weight loss outcome and comorbidity resolution (*Sanchez-Pernaute et al., 2007*). Single-anastomosis duodeno-ileal switch (SADIS) is a modification of the original biliopancreatic diversion with duodenal switch (BPDDS) (*Sanchez-Pernaute et al., 2010*). Due to its simpler technique and reduced number of anastomosis, SADIS has shown potentials in bariatric surgery (*Sanchez-Pernaute et al., 2013*).

The interest for single-loop techniques is increasing because of its theoretical advantages on operative time and postoperative complications. A novel technique combining the physiological advantages of pylorus preservation and the

technical benefits of single-loop reconstruction was introduced into bariatric surgery by Sanchez-Pernaute, who described the single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S) (*Sanchez-Pernaute et al., 2007*).

This review systematically examines randomized controlled trials (RCTs) and controlled clinical trials (CCTs) that evaluated the role of single anastomosis duodeno-ileal bypass (SADI) with sleeve gastrectomy on type 2 diabetes mellitus.

Aim of the Work

The aim of work is to assess the effect of single anastomosis duodeno-ileal bypass (SADI) on type 2 diabetes mellitus patients and the magnitude of their metabolic benefit from undergoing surgery, to help both surgeons and patients make their decisions through giving them a realistic and neutral clearer picture of the expected postoperative outcome.

Type 2 Diabetes Mellitus

There are two main forms of diabetes (*WHO, 1999*). Type 1 diabetes results in insulin deficiency due to autoimmune-mediated destruction of pancreatic β -cell islets, and exogenous insulin is essential for survival and prevention of ketoacidosis. In type 2 diabetes mellitus (T2DM), either insulin resistance or abnormal insulin secretion may predominate, and if diet alone or oral hypoglycemic agents is not enough for control of blood glucose levels, exogenous insulin may be used. The T2DM accounts for over 90% of all cases. The prevalence of diabetes increases worldwide both in developed and in developing nations, and most of the cases are of T2DM, which is strongly associated with decreased physical activity and obesity (*Zimmet, 1999*).

The IDF estimated in 2014 that 387 million people have diabetes worldwide and that by 2035 this number will rise to 592 million. Of those with diabetes currently, 77% live in low- and middle-income countries and 179 million are undiagnosed. These estimates are substantially greater than predicted even a decade ago, suggesting that the global epidemic is still progressing. In the United States, the Centers for Disease Control and Prevention (CDC) estimated in 2014 that 29.1 million people, or 9.3% of the population, had diabetes and that 8.1 million of them (27.8%) were undiagnosed. In 2012, they estimated based on fasting glucose or hemoglobin A_{1c} levels that

86 million people (37% of adults over age 20) had prediabetes and thus were at high risk of developing diabetes (*CDC, 2014; Zimmet et al., 2001; Shaw et al., 2010; IDF, 2014*).

According to 2014 data, the World Health Organization (WHO) region with the highest diabetes prevalence, 13.7%, is the Eastern Mediterranean Region, where Egypt resides. The diabetes prevalence in all other WHO regions is less than 9% (*WHO 2016*). Egypt is 8th of the top 10 countries for the number of adults with diabetes, and with the current figure of 8.2 million predicted to double to 16.7 million by 2045, Egypt will climb to number 6 in the list. Yet the diabetes prevalence figure for Egypt may be an underestimate (*IDF, 2017*).

Few studies have examined the prevalence of diabetes in Egypt. One review of the prevalence of type 2 diabetes in Egypt relied solely on data published by the International Diabetes Federation (IDF) (*Hegazy et al., 2015*), and a population-based survey conducted in the governorate of Qena (in the south of Egypt) relied on a screening questionnaire to identify people with diabetes; blood glucose was evaluated only in “suspected cases” (*Khedr et al., 2016*). The reported prevalence of 8.99% in this population is therefore questionable and probably well below the true prevalence. Furthermore, Egypt lacks the population-based data on diabetes prevalence that are needed to identify factors related to the development and natural history of the disease (*Diabetes Epidemiology Research, 1987*). The lack of a registration system means that diabetes may be one of the

most under-estimated public health problems in Egypt and other low- or middle-income countries (*Krall L.P., 1986*).

The economic burden of diabetes is enormous. The IDF estimates that in 2014 diabetes-related health expenditures amounted to 11% of total health spending on adults (*IDF, 2014*). The CDC suggests that diabetes costs in the United States were \$245 billion with average expenditures per person, adjusted for age and gender, 2.3-fold higher than in the non-diabetic population. The increases in cost are driven by complications, comorbid conditions, and increasing complexity of care driving prescription costs and the frequency of visits (*Zhuo et al., 2015*).

Considerable information is available on the factors that are responsible for the development of T2DM (Table 1) (*Zimmet et al., 2001*). T2DM is thought to occur in genetically predisposed persons who are exposed to a series of environmental influences that precipitate the onset of clinical disease. The syndrome consists of monogenic and polygenic forms that can be differentiated both on clinical grounds and in terms of the genes that are involved in the pathogenesis of these disorders. T2DM has been viewed in the past as a disorder of aging, and this remains true today. However, the prevalence of obesity and T2DM in children has risen dramatically. Recent reports suggest that as many as 20% to 25% of children in the United States with newly diagnosed diabetes have non-immune-mediated forms of the disease (*Hamman et al., 2014*).