Role of Surgical Intervention in The Management of Diabetes Mellitus

Essay

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List of Abbreviations

ADA	:	American Diabetes Association
BMI	:	Body Mass Index
BPD	:	Biliopancreatic Diversion
CIT	:	Clinical Islet Transplantation
DCCT	:	Diabetes Control and Complications Trial
DM	:	Diabetes Mellitus
DPP-4	:	Dipeptidyl peptidase IV
ESCs	:	Embryonic Stem Cells
EWL	:	Excess weight loss
FFA	:	Free Fats Acids
FPG	:	Fasting Plasma Glucose
GAD	:	Glutamic Acid Decarboxylase
GIP	:	Glucose-Dependent Insulinotropic Polypeptide
GIPR	:	Gastric Inhibitory Polypeptide
GLP-1	:	Glucagonlike Peptide-1
HbA1c	:	Glycated Hemoglobin
HDL	:	High Density Lipoprotein
HLA DR	:	Human Leukocyte Antigen - antigen D Related
IA2	:	Islet Antigen 2
IEQ	:	Islet Equivalents Quantification
IFG	:	Impaired Fasting Glucose
IGT	:	Impaired Glucose Tolerance
IL	:	Interleukine
LADA	:	Latent Autoimmune Diabetes of Adults
LSG	:	Laparoscopic Sleeve Gastrectomy
MHC	:	Histocompatibility Complex
NEFAs	:	Nonesterified Fatty Acids

List of Abbreviations (Cont.)

NGSP	:	National Glycohemoglobin Standardization Program
NICE	:	National Institute for Health and Clinical Care Excellence
NPH	:	Neutral Protamine Hagedorn
OGTT	:	Oral Glucose Tolerance Test
OHS	:	Obesity Hypoventilation Syndrome
OSA	:	Obstructive Sleep Apnea
OXM	:	Oxyntomodulin
PAK	:	Pancreas-After-Kidney transplant
PDRI	:	Pancreas Donor Risk Index
PSCs	:	Pluripotent Stem Cells
PTA	:	Pancreas Transplant Alone
PYY	:	Peptide YY
RYGB	:	Roux-En-Y Gastric Bypass
SGLT-2	:	Selective Sodium-Glucose Transporter-2
SNPs	:	Single-Nucleotide Polymorphisms
SPK	:	Simultaneous Pancreas and Kidney transplant
T2DM	:	Type 2 Diabetes Mellitus
TGFb	:	Transforming Growth Factor Beta
TNF	:	Tumour Necrosis Factor
TZDs	:	Thiazolidinediones
WHO	:	World Health Organization

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Introduction

Since its earliest description several thousand years ago, diabetes has remained a chronic progressive disease. Diabetes mellitus is a devastating and complex metabolic disease, expected to affect over 500 million people worldwide by the year 2030 ***(Abu-Rmeileh et al., 2013)***.

This increasing prevalence is a testament to improvement in managing diabetes-related complications, as well as our global "modernization" and the accompanying metabolic derangements. Diabetes is now ranked as the sixth leading cause of death by disease in the U.S, in many places it ranks far higher ***(Francesco et al., 2009)***.

There are two main forms of diabetes. Type 1 diabetes mellitus (T1DM), in which there is insulin deficiency due to autoimmune-mediated destruction of pancreatic β-cell islets, and exogenous insulin is essential for survival and prevention of ketoacidosis. Type 2 diabetes mellitus (T2DM), in which 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 ***(A. Maleckas et al., 2015).***

Diet modification and oral hypoglycemic medications have proven to be inadequate, whereas insulin therapy only solves the problem temporarily. In a U.K. prospective diabetes Study, diabetic patients were treated with diet modification, metformin, sulfonylurea, or insulin. Consistent with the progressive nature of diabetes, monotherapy was

abandoned in 75% of the patients studied in a follow-up of 9 years. Even with the newest pharmaco-therapies, patients continue to develop macro- and microvascular complications, also it is associated with increased cardiac and stroke related deaths, kidney failure, blindness, and 60% of nontrauma lower limb amputations ***(Turner et al., 2009)***.

An alternative option to achieve near normoglycaemia in diabetic patients type I is transplantation of the whole pancreas (vascularised pancreas transplantation). Some would argue that this is perhaps a complicated approach when only the islet cells are needed to restore physiological levels of blood glucose, but perhaps more importantly pancreas transplantation has an appreciable high rate of morbidity and mortality compared with kidney transplantation alone .With these factors in mind investigators have tried to isolate and transplant individual islet of Langerhans cells ***(Kimber et al., 2011)***.

Stem cells hold great promise for pancreatic beta cell replacement therapy for diabetes. The proof-of-principle that cellular transplants of pancreatic islets, which contain insulin-secreting beta cells, can reverse the hyperglycemia of type 1 diabetes has been established, and there is now a need to find an adequate source of islet cells. Human embryonic stem cells can be directed to become fully developed beta cells and there is expectation that induced pluripotent stem (iPS) cells can be similarly directed. iPS cells can also be generated from patients with diabetes to allow

studies of the genomics and pathogenesis of the disease. Some alternative approaches for replacing beta cells include finding ways to enhance the replication of existing beta cells, stimulating neogenesis (the formation of new islets in postnatal life), and reprogramming of pancreatic exocrine cells to insulin-producing cells ***(Weir GC et al., 2011).***

Type 2 diabetes is a multifactorial disorder and obesity is considered the most important risk factor. The prevalence of obesity among adults with diagnosed diabetes is over 50 %, and the prevalence of overweight is over 80 %. It has been estimated that the risk for developing type 2 diabetes is increased 93-fold in women and 42-fold in men who are severely obese (BMI ≥35) in coparison with those who have healthy weight ***(Karen Meyvis et al., 2013)***.

Given this information, weight loss is one of the most important treatment strategies to obtain good glycemic control (glycated hemoglobin [HbA 1c] <7 %). Intentional weight loss of at least 5 % to 10 % of bodyweight has repeatedly been shown to improve glycemic control, lipid profile, blood pressure and cardiovascular risk profiles in obese subjects with type 2 diabetes ***(Wing et al., 2011).***

Weight loss has influence on control of T2DM. Despite weight loss, short-term (7 days) 50% caloric restriction can increase insulin sensitivity and insulin secretion. Moreover, it was observed that metabolic control worsens with increasing total calorie amount even if weight loss is maintained**.** Caloric restriction may partially explain rapid improvement in blood glucose after bariatric surgery, but other proposed mechanisms may also play an important role ***(A. Maleckas et al., 2015)***.

Studies have shown that after bariatric surgery, blood glucose may return to normal without medication in up to three out of four people with type 2 diabetes. Others are able to reduce their diabetes medication. Improvement in blood glucose is likely to be greatest in people who have only had type 2 diabetes for a short time, before insulin production is significantly reduced.With combination procedures which operate on the small intestine, such as gastric bypass, there appear to be hormonal effects apart from weight loss that result in a rapid decrease in blood glucose levels and improved diabetes control within days of surgery. A return to normal blood glucose levels is more likely with these procedures than with gastric banding, however, they also have a higher risk of complications and nutritional deficiencies (***Zimmet P et al., 2011)***.

Aim of the work

The aim of this essay is to review the role of different surgical procedures as a new modality in treatment of both types of diabetes mellitus, and to assess their outcome.

Anatomical Facts

STOMACH

The stomach is the widest part of the alimentary tract and lies between the oesophagus and the duodenum. The stomach is situated in the upper abdomen, extending from the left upper quadrant downwards, forwards and to the right, lying in the left hypochondrium, epigastrium and umbilical regions. It occupies a recess beneath the diaphragm and anterior abdominal wall bounded by the upper abdominal viscera on either side. The peritoneal surface of the stomach is interrupted by the attachments of the greater and lesser omenta, which define the greater and lesser curvatures and separate the anteriorand posterior surfaces ***(Csendes and Burgos, 2010)***.

PARTS OF THE STOMACH (Fig. 1)

For descriptive purposes, the stomach can be divided into a fundus, body, pyloric antrum and pylorus by artificial lines drawn on its external surface. The internal appearance and microstructure of these regions vary. The fundus is dome-shaped and projects above and to the left of the oesophageal opening (cardiac (cardial) orifice) to lie in contact with the left dome of the diaphragm; it lies above a horizontal line from the cardiac notch to the greater curvature ***(Didio and Anderson, 2011)***.

The body extends from the fundus to the angular incisure (incisura angularis), a constant external notch at the

lower end of the lesser curvature. The cardia is the region of the stomach adjacent to the oesophageal opening. A line drawn from the angular incisure to an inconstant indentation on the greater curvature defines the lower boundary of the body. The pyloric antrum extends from this line to where the stomach narrows to become the pyloric canal (1–2 cm long), which terminates at the pyloric orifice ***(Didio and Anderson, 2011)***.

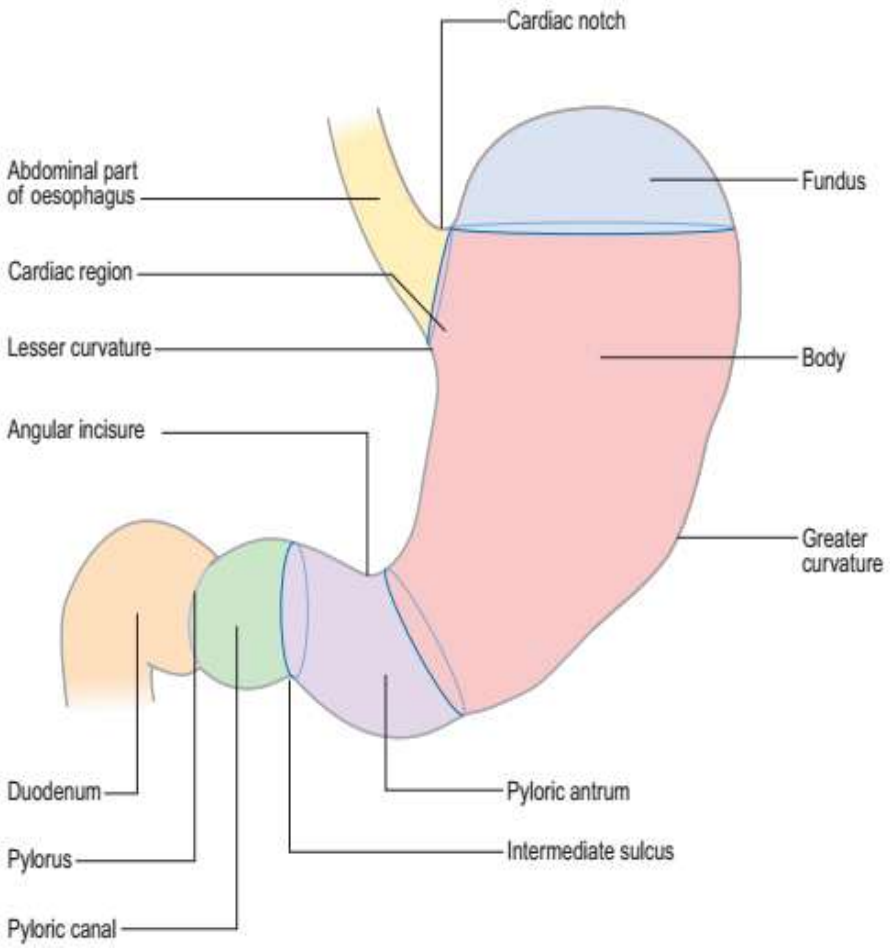

Figure 1: Parts of stomach ***Didio and Anderson, 2011***

GASTRIC RELATIONS (Fig. 2)

Gastric curvatures

- ***Lesser curvature***

The lesser curvature extends between the cardiac and pyloric orifices and forms the medial border of the stomach. It descends from the medial side of the oesophagus in front of the decussating fibres of the right crus of the diaphragm, curves downwards and to the right, and lies anterior to the superior border of the pancreas. It ends at the pylorus, just to the right of the midline. In the most dependent part, there is typically a notch, the angular incisure, whose position and appearance vary with gastric distension. The lesser omentum is attached to the lesser curvature and contains the right and left gastric vessels ***(Csendes and Burgos, 2010)***.

- ***Greater curvature***

It starts from the cardiac notch, formed between the lateral border of the abdominal oesophagus and the fundus of the stomach, and arches upwards, posterolaterally and to the left. Its highest convexity, the apex of the fundus, is approximately level with the left sixth rib anteriorly but varies between individuals and with respiration. From this point, it sweeps inferiorly and anteriorly, slightly convex to the left, almost as far as the tenth costal cartilage in the supine position, where it turns medially to end at the pylorus in the transpyloric plane at the lower border of the