The surgical options for management of Type 1 Diabetes mellitus

Essay

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Ahmed Fathy Elabd Dlal

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List of Abbreviations

A1C	**:**	Glycated hemoglobin
ADA	**:**	American Diabetes Association
Anti-GAD	**:**	Antibodies to glutamic acid decarboxylase
ARCFH	**:**	Arbor Research Collaborative For Health
ASCs	**:**	Adult stem cells
BM	**:**	Bone Marrow
BM	**:**	Bone marrow
BMCs	**:**	Bone marrow cells
BMSCs	**:**	Bone marrow stem cells
BMT	**:**	Bone marrow transplantation.
CB-SCs	**:**	Human cord blood-derived stem cells
CCK	**:**	Cholecystokinin
CHD	**:**	Coronary heart disease
CITR	**:**	Collaborative Islet Transplant Registry
CLI	**:**	Diabetic critical limb ischemia
CT	**:**	Computed tomography
CVD	**:**	Macrovascular disease
DF	**:**	Diabetic foot
DR	**:**	Diabetic retinopathy
EPCs	**:**	Endothelial progenitor cells
ES	**:**	Embryonic stem
ESC	**:**	Embryonic stem cell

FSCs	**:**	Foetal stem cells
GVHD	**:**	Graft-versus-host disease
Hb	**:**	Hemoglobin
HBMMSCs	**:**	Human bone marrow MSCs
hES	**:**	Human embryonic stem cells
HLA	**:**	Human leukocyte antigen
HSC	**:**	Adult hematopoietic stem cells
HSC	**:**	Haemopoietic stem cell
HSCs	**:**	Hematopoietic stem cells
HSCT	**:**	Hematopoietic stem cell transplantation
hSCT	**:**	Haemopoietic stem cell transplantation
HTRs	**:**	Gastrin-releasing peptide
ICA	**:**	Islet-cell antibodies
ICM	**:**	Inner cell mass
IDDM	**:**	Insulin-dependent diabetes mellitus
IDDM	**:**	Insulin-dependent diabetes mellitus
IPCs	**:**	Insulin-producing cells
Ips	**:**	Induced pluripotent stem
iPS	**:**	Induced pluripotent stem cells
IVF	**:**	In vitro fertilization
LDs	**:**	Living donors
MODY2	**:**	Maturity-onset diabetes of the young
MRI	**:**	Magnetic resonance imaging
MSCs	**:**	Mesenchymal stem cells

MSCs	**:**	Mesenchymal Stem Cells
MSCs	**:**	Mesenchymal stem cells
NEPECs	**:**	Non endocrine pancreatic epithelial cells
PAK	**:**	pancreas after kidney
PET	**:**	Positron-emission tomography
PET	**:**	Positron emission tomography
PP	**:**	Pancreatic polypeptide
PTA	**:**	pancreas transplant alone
PVD	**:**	Peripheral vascular disease
SC	**:**	Stem Cell
SCNT	**:**	Somatic cell nuclear transfer
SCT	**:**	Stem cell transplantation
SDF-1	**:**	Stromal cell-derived factor 1
SPK	**:**	Simultaneous pancreas and kidney transplantation
T1D	**:**	Type 1 diabetes
UCB	**:**	Umbilical cord blood
UCB-SCs	**:**	Umbilical cord blood stem cells
VIP	**:**	Vasoactive intestinal peptide
WHO	**:**	World Health Organization

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Introduction

Diabetes mellitus is metabolic disorder characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both ***(American Diabetes Association, 2009)***.

Diabetes mellitus (DM) is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance, as changing lifestyles lead to reduced physical activity, and increased obesity. The global prevalence of DM in the year 2010 among adults has been estimated to be 6.4%. It is estimated that by the year 2030, Egypt will have at least 8.6 million adults with diabetes ***(Shaw et al., 2010)***.

Diabetes is the eleventh most important cause of premature mortality in Egypt, and is responsible for 2.4% of all years of life lost (YLL). Similarly, diabetes is the sixth most important cause of disability burden in Egypt ***(NICHP, 2004)***.

The recent WHO Stepwise survey of non-communicable diseases in Egypt, showed the prevalence of known diabetes to be 6.0% ***(Ellabany et al., 2006).***

While hyperglycemia is the defining characteristic of diabetes, the underlying pathogenesis leading to hyperglycemia differs significantly among the various forms of the disease.

Common to all is the presence of defects in insulin secretion and/or insulin action ***(Gruessner et al., 2006).***

Type 1 diabetes occurs when the pancreatic beta cells are destroyed and the patient develops profound or absolute insulin deficiency. Nearly all cases are autoimmune in origin. This form of diabetes accounts for approximately 5% to 10% of diabetes. The disease most often appears in childhood, but patients of any age may present with type 1 diabetes. A mixture of genetic and environmental factors are believed to lead to the autoimmune destruction that causes type 1diabetes. Over the past 10 years the incidence of type 1 diabetes has increased ***(Nghiem et al., 2008).***

Type 2 diabetes occurs as the result of defects in both insulin secretion and insulin action. This form of the disease represents about 90% of prevalent cases of diabetes ***(Zehrer et al., 2008).***

Accordingly, the significant population already afflicted with this disease compounded by the increasing incidence worldwide will have a tremendous impact on future healthcare both domestically and globally. Estimates show that patients with T1DM treated with intensive medical management have six- to seven fold higher direct cost than age-matched nondiabetics ***(Nakache et al., 2006).***

Diabetes mellitus is generally treated with oral diabetic drugs and/or insulin. However, the morbidity and mortality associated with this condition increases over time, even in patients receiving intensive insulin treatment, and this is largely attributable to diabetic complications or the insulin therapy itself ***(Nakache et al., 2006).***

Diabetes mellitus is associated with devastating complications that increase both the mortality and morbidity of those suffering from the disease ***(Nghiem et al., 2008).***

Acute complications of the diabetis mellitus are Diabetic ketoacidosis: It is life threatening complication, it is called diabetic coma ***(Kitabchi et al., 2004)*** and, Hypoglycemia: one of the most common complications for Diabetic patient receiving insulin or oral hypoglycemic agents ***(Tattersall, 2001)***.

Chronic complications of diabetes are best considered in three separate categories:

1- Microvascular (small vessel) disease, the clinical manifestations of which are diabetic retinopathy and diabetic nephropathy.
2- Neuropathy (involvement of both the peripheral and autonomic nervous system), the clinical manifestations of which can lead to various problems.

3- Macrovascular (larg vessel or atherosclerotic disease, the clinical manifestations of which are angina and myocardial infarctions, cerebrovascular accidents, and peripheral vascular disease ***(Harmel and Mather, 2004).***

Diabetic neuropathy it is the most common neuropathy in developed countries and accounts for more hospitalizations than all the other diabetic complications combined ***(Vinik and Mehrabyan, 2004).***

Foot ulcers that occur as a result of diabetic neuropathy are estimated to affect about 15% of all patients with diabetes at some point during their lifetime. In addition, approximately 85% of lower extremity amputations are preceded by a foot ulcer ***(Zehrer et al., 2008).***

The quest for a surgical treatment for T1DM first began more than a century ago with the likes of Oskar Minkowski and Josef von Mering at the University of Strasburg. It was not until 1966 when success was achieved by Kelly, who completed the first whole-organ pancreatic transplant at the University of Minnesota ***(Kelly et al., 1966).***

The goal of pancreas transplantation is to safely restore normoglycaemia by the provision of sufficient β cell mass. Transplantation of a pancreas, unlike liver, lung, and heart, is not a life-saving operation but it improves quality of life

because patients do not need to inject insulin on a daily basis or regularly monitor glucose concentrations with finger sticks, and hypoglycaemic unawareness is no longer a problem. The long-term advantages of this surgical procedure have to be balanced against the potential morbidity and mortality associated with diabetes, and the side effects from the long-term immuno-suppression that is needed to prevent alloimmunity and autoimmune recurrence. The risk of immunosuppression is particularly relevant for recipients of pancreas transplant alone), since the only benefit of immune-suppression in this category is insulin free euglycaemia ***(Latta, 2005).***

Technical refinements and the development of better immunosuppressants and better postoperative care have brought about marked improvements in patient and graft survival and a reduction in postoperative morbidity. Consequently, pancreas transplantation has become the curative treatment modality for diabetes, particularly for type I diabetes ***(Hellerstrom et al., 2009).***

Islet cell transplantation subsequently was initiated by Ballinger and Lacy, who, in 1972, were the first to report that isolated islets could reverse the effects of experimentally induced diabetes in rate ***(Brillinger et al., 1972).***