Tissue Doppler Echocardiography for assessment of cardiac function in children with type 1 Diabetes Mellitus

Thesis

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Abstract

Background: Impairment of cardiac function in patients with type1 Diabetes represents one of the serious complications. Tissue Doppler echocardiography is a recent modality of echocardiography which proved to have additional value in the evaluation of ventricular filling in diabetic patients. **Objective:** To evaluate the cardiac function in children with T1DM by conventional and tissue Doppler echocardiography. **Method:** In this cross-sectional study, echocardiography for 40 patients aged ≥ 6 years with T1DM for > 5 years was done and compared with that of 20 healthy age and sex matched children. Also comparison between patients according to their glycemic control and dyslipidemia was done. **Results:** RV-DD was found in 12.5% of patients and LV-DD was found in 12.5% of other patients and only one patient had both RV-DD and LV-DD. Subjects showed a significant difference in AO, LVIDd, LVIDs and FS% by M-mode. Tricuspid E wave velocity, tricuspid A wave velocity and mitral E wave velocity were found significantly higher in controls by PW Doppler. IRT of right ventricle, S' of left ventricle showed significant difference by TDI. We did not find any relation between glycemic control, duration of diabetes and dyslipidemia with evidence of cardiac dysfunction. **Conclusion:** Diastolic dysfunctions are present in type 1 diabetic patients and early detection of this dysfunction is of great importance, because in the early stages medical interventions could prevent or delay progression and reduce the risk of developing heart failure in individuals with diabetes mellitus.

Key Words: Type 1 diabetes mellitus, tissue Doppler echocardiography, diastolic dysfunction, glycemic control, children.

Contents

LIST OF ABBREVIATIONS

A'	Late tissue diastolic wave
ACE	Angiotensin converting enzyme
ADA	American Diabetes Association
AGEs	Advanced Glycation End products
AHA	American Heart Association
AO	Aorta
ARBs	Angiotensin Receptors Blockers
A wave	Late diastolic filling velocity (atrial contraction)
BG	Blood Glucose
BMI	Body mass index
BP	Blood pressure
CAD	Coronary Artery Disease
CAN	Cardiac autonomic neuropathy
CHO	Carbohydrate
cIMT	carotid Intima Media Thickness
CO	Cardiac output
CVD	Cardiovascular disease
CW Doppler	Continuous-wave Doppler echocardiography
DBP	Diastolic blood pressure
DCCT	Diabetes Control and Complications Trail
DCM	Diabetic cardiomyopathy
DEMPU	Diabetes, Endocrine and Metabolism Pediatric Unit
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DMD	Diabetic myocardial disease
DR	Diabetic retinopathy
DT	Deceleration time
E'	Early tissue diastolic wave
ECG	Electrocardiography
EF	Ejection fraction
ET	Ejection time
E wave	Early diastolic filling velocity
FBG	Fasting Blood Glucose
FS	Fractional shortening
GAD	Glutamic acid decarboxylase
GFR	Glomerular filtration rate
HbA1c	Glycosylated hemoglobin
HDL	High density lipoprotein
HF	Heart failure
HHS	Hyperglycemic hyperosmolar state

HNF	Hepatocyte nuclear factor
HRV	Heart rate variability
IA	Islet cell auto antibodies
IAAs	Insulin autoantibodies
IFG	Impaired Fasting Glucose
IGT	impaired Glucose Tolerance
INS	Insulin gene
IVCT	isovolumic contraction time
IVRT	isovolumic relaxation time
IVSd	Inter ventricular septal wall at end diastole
LA	Left atrium
LDL	Low density lipoprotein
LV	Left ventricle
LV-DD	Left ventricular diastolic dysfunction
LVH	Left Ventricular Hypertrophy
LVIDd	Left ventricular internal dimensions at end diastole
LVIDs	Left ventricular internal dimensions at systole
MHC	Major histocompatibility complex
MI	Myocardial infarction
MODY	Maturity onset diabetes of the young
MPI	Myocardial performance index
NGSP	National Glycohemoglobin Standardization Program
OGTT	Oral Glucose Tolerance Test
PD	P wave dispersion
PNF	pseudo normal filling
PPBG	Postprandial Blood Glucose
PVD	Peripheral vascular disease
PW Doppler	Pulsed-wave Doppler echocardiography
PWTd	thickness of left ventricular wall at end diastole
QTc	Corrected QT interval
RV-DD	right ventricular diastolic dysfunction
S'	Systolic wave
SBP	Systolic blood pressure
T1DM	Type 1diabetes mellitus
T2DM	Type 2 diabetes mellitus
TDI	Tissue Doppler imaging
TG	Triglycerides
TSCs	Tissue stem cells
USA	United states of America
WHO	World Health Organization
1,25(OH)2D3	1,25 dihydroxy calcitriol

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INTRODUCTION

AIM OF THE WORK

INTRODUCTION

Impairment of cardiac function in patients with type1 Diabetes represents one of the serious complications and if present, may affect the quality of life and prognosis of the disease **(Elshahed et al., 2008)**.

Studies on adults have reported that patients with type 1 Diabetes show ultra-structural and functional myocardial deterioration **(Eun et al., 2010)**. Similarly, it has been reported that young patients with type1 Diabetes have significant changes in left ventricular dimension and myocardial relaxation **(Suys et al., 2004)**.

Children and young adolescents with type1 diabetes rarely have insight on regarding their disease and their diet is accordingly difficult to control. Therefore, alteration of cardiac function in these patients may begin earlier than is generally thought and these changes may be accelerated when glycemic control is poor.

Echocardiography is a non-invasive method that can be used for the diagnosis of Diabetic cardiomyopathy or Diabetes induced myocardial dysfunction. Tissue Doppler echocardiography is a recent modality of echocardiography which proved to have additional value in the evaluation of ventricular filling in diabetic patients **(Eun et al., 2010)**.

Conventional and tissue Doppler echocardiography can predict early stages and progression of diabetic cardiac changes, so assessment particularly by tissue Doppler is warranted in patients with type1 Diabetes to follow the progression from subclinical to symptomatic ventricular dysfunction **(Elshahed et al., 2008)**.

However, studies which evaluated the use of Tissue Doppler in detection of cardiac dysfunction in children with type1 diabetes are few and conflicting.

AIM OF THE WORK

- Assessment of systolic and diastolic functions of left and right ventricles in patients with Type1 Diabetes by conventional and Tissue Doppler Echocardiography.

REVIEW OF LITRATURE

CHAPTER ONE

TYPE 1 DIABETES MELLITUS (T1DM)

Definition

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels **(American Diabetes Association, 2013a)**.

Etiology

T1DM is a multifactorial disease thought to arise from complex interaction between both genetic susceptibility and environmental insults **(Fowler, 2007)**

Genetic factors

In disorders following a Mendelian pattern of autosomal dominant or recessive transmission the pattern of inheritance of the disease phenotype is usually obvious. It is much more difficult in diabetes to confidently define the reported linkage susceptibility genes **(Moussa et al., 2005).**

Although the genetic aspect of T1DM is complex, with multiple genes involved, there is a high sibling relative risk. Whereas dizygotic twins have a 5-6% concordance rate for T1DM **(Steck et al., 2005**), Monozygotic twins will share the diagnosis more than 50% of the time by the age of 40 years **(Redondo et al., 2008**). The genetic contribution to T1DM is also reflected in the significant variance in the frequency of the disease among different ethnic populations, T1DM is most prevalent in European population, with people from northern Europe more often affected than those from Mediterranean regions **(Borchers et al., 2010)**.

Among the genetic determinant of susceptibility, with more than 18 putative loci identified to date, a region in chromosome 6p21 (IDDM1) containing the major histocompatibility complex (MHC) is the only one consistently associated with T1DM in genome wide screenings. Candidate gene studies also identified the insulin gene (INS) on chromosome 11 (IDDM2) as the second most important genetic susceptibility factor, contributing 10% of genetic susceptibility to T1DM (**Thomson et al., 2007**).

A hierarchy of DR-DQ halotypes associated with increased risk for T1DM has been established. The most susceptible halotypes are as follows **(Erlich et al., 2008)**:

- DRB1*0301 - DQA1*0501 - DQB1*0201 (odds ratio [OR] 3.64)
- DRB1*0405 - DQA1*0301 - DQB1*0302 (OR 11.37)
- DRB1*0401 - DQA1*0301 - DQB1*0302 (OR 8.39)
- DRB1*0402 - DQA1*0301 - DQB1*0302 (OR 3.63)
- DRB1*0404 - DQA1*0301 - DQB1*0302 (OR 1.59)
- DRB1*0801 - DQB1*0401 - DQB1*0402 (OR 1.25)

Other halotypes appear to offer protection against T1DM. These include the following **(Erlich et al., 2008)**:

- DRB1*1501 - DQA1*0102 - DQB1*0602 (OR 0.03)
- DRB1*1401 - DQA1*0101 - DQB1*0503 (OR 0.02)
- DRB1*0701 - DQA1*0201 - DQB1*0303 (OR 0.02)

Environmental factors

Environmental influence is another important factor in the development of T1DM. The best evidence for this influence is the demonstration in multiple population of a rapid increase in the incidence