The Effect of Albumin:Creatinine Ratio on Standard Echocardiographic Parameters in Adolescent Type 1 Diabetes

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INTRODUCTION

Adolescents with type 1 diabetes (T1D) are at increased risk of early adult-onset cardiovascular disease. This study compared standard echocardiographic parameters in patients screened for the Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT) with healthy controls.

METHODS

Study Design

Single center prospective cross-sectional study

Patient Population

The AdDIT study is a multi-centre, randomized, double-blind, placebo-controlled, 2x2 factorial design trial of angiotensin-converting enzyme inhibitor and statin therapy vs. placebo in 500 high-risk (>1.2 mg/mmol) T1D adolescents, defined on the basis of albumin excretion.[1] It also includes a parallel observational study based on longitudinal follow-up of 400 low-risk (<0.8 mg/mmol) and medium-risk (0.8-1.2 mg/mmol) T1D adolescents who were screened but did not qualify for randomization. Subjects recruited in the current study were low- and medium-risk from the parallel observational study and high-risk T1D adolescents that declined participation in the randomized controlled trial. All 199 T1D were compared with 178 adolescents recruited as healthy volunteers, who were not on any vasoactive medications, had no previous history of familial hyperlipidemia, diabetes, obesity, hypertension, or any other significant cardiac, renal or systemic disease and normal cardiac anatomy and function by screening echocardiogram. In subgroup analysis, 68 low-, 78 medium-and 53 high-risk were compared with 65 controls that underwent the same baseline clinical assessment.

Anthropometric Assessment

Height was measured by stadiometer to the nearest 0.1 cm and weight by electronic balance to the nearest 0.1 kg. Resting heart rate and right brachial blood pressure was measured using an age-appropriate cuff and averaging 3 readings with an automated DINAMAP® sphygmomanometer (Critikon, Tampa, Florida, USA).

Echocardiographic Assessment

Using a Vivid 7 ultrasound system (GE, General Electric Corp., Wisconsin, USA) with appropriate transducers ranging from frequencies 4-12 MHz depending on subject age and size, a standardized functional imaging protocol, including subcostal, parasternal, apical and suprasternal views, was performed according to published guidelines.[2] Modalities employed in this study included M-mode, 2D and pulse Doppler blood flow measurements.

Laboratory Assessment

Glycemic control was measured by fasting blood glucose and haemoglobin A1c. Serum lipids including total, low-density lipoprotein and high-density lipoprotein cholesterol and triglycerides were measured. Serum creatinine was used to estimate glomerular filtration rate.[3]

Statistical Analysis

Between groups comparisons were performed using Student's t-tests. Relationships were tested using Pearson's correlations. Statistical significance was considered at p<0.05.

References

1. Adolescent type 1 Diabetes Cardio-renal Intervention Trial Group. Adolescent type 1 Diabetes Cardio-renal Intervention Trial (AdDIT). *BMC Pediatr* 2009; 9: 79.
2. Lopez L, Colan SD, Frommelt PC, et al. Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. *J Am Soc Echocardiogr* 2010; 23: 465-95.
3. Schwartz GJ, Munoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 2009; 20: 629–637.

CONCLUSIONS

Adolescent T1D of short to intermediate disease duration, have early suggestion of blood pressure, diastolic dysfunction and left ventricular geometric changes, which may contribute to increased risk of early adult-onset cardiovascular disease.

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RESULTS

Table 1: Anthropometric Measurements

	T1D n=199	Controls n=178	*p value*
Sex, M:F	98:101	84:94	*0.3759*
Age, years	14.4±1.6	14.4±2.1	*0.7999*
Height, cm	163±10	162±11	*0.2477*
Weight, kg	**60.7±14.3**	54.7±13.8	***<0.0001***
BSA, m^2	**1.65±0.22**	1.57±0.23	***0.0006***
BMI, kg/m^2	**22.6±4.3**	20.6±3.7	***<0.0001***
SBP mmHg	**113±10**	110±9	***0.0005***
DBP, mmHg	**62±7**	58±7	***<0.0001***
MBP, mmHg	**77±7**	75±7	***0.0053***
PP, mmHg	51±9	52±8	*0.4771*
HR, bpm	**66±9**	68±12	***0.0357***

BSA=body surface area, BMI = Body Mass Index; SBP =systolic blood pressure; DBP = diastolic blood pressure; MBP=mean blood pressure, PP=pulse pressure, HR=heart rate

Table 2: Echo Measurements – M-Mode

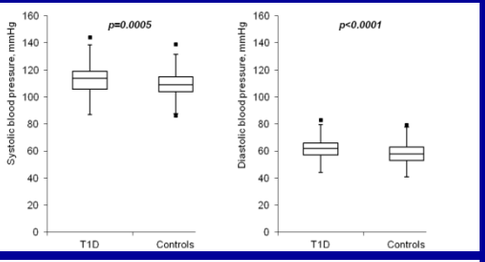
	T1D n=199	Controls n=178	*p value*
IVSD, cm	0.74±0.12	0.73±0.12	*0.4165*
LVPWD, cm	**0.66±0.11**	0.64±0.11	***0.0374***
LVEDD, cm	4.69±0.39	4.66±0.43	*0.4799*
LVESD, cm	2.90±0.32	2.95±0.33	*0.1648*
LVmass$_{ht}$, g/m^2	63±13	63±13	*0.7691*
LVSF, %	**38±4**	37±4	***0.0013***
LVEF, %	**68±5**	66±5	***0.0011***
LVVCFC, circ/sec	**1.18±0.18**	1.14±0.16	***0.0143***

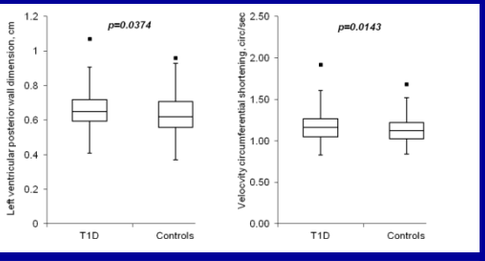
IVSD=interventricular septal dimension diastole, LVPWD=left ventricular posterior wall thickness dimension, LVEDD=left ventricular end-diastolic dimension, LVESD=left ventricular end-systolic dimension, LVmass$_{ht}$ =left ventricular mass indexes to BSA, LVSF=left ventricular shortening fraction, LVEF=left ventricular ejection fraction, LVVCFC= mean velocity of circumferential shortening

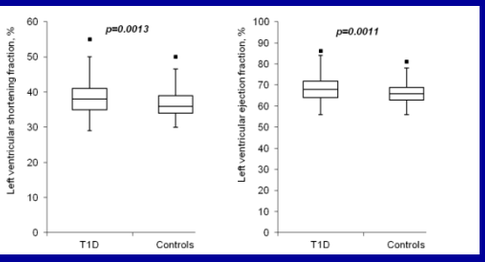
Table 3: Echo Measurements – Pulse Doppler

	T1D n=199	Controls n=178	*p value*
MV-E, cm/s	100±15	99±17	*0.6485*
MV-A, cm/s	41±9	42±11	*0.5977*
MV-E/A	2.5±0.7	2.5±0.7	*0.8100*
MV-AD, msec	122±18	119±20	*0.2231*
MV-DT, msec	**154±17**	149±20	***0.0129***
IVRT, msec	**76±8**	74±7	***0.0077***
PVS, cm/s	41±10	43±11	*0.0813*
PVD, cm/s	61±10	61±12	*0.9851*
LV-MPI	0.30±0.10	0.30±0.09	*0.5983*

MVE=mitral valve E velocity, MVA=mitral valve A velocity, MVE/A=mitral valve E/A ratio, MVAD=mitral valve a wave duration, MVDT=mitral valve deceleration time, IVRT=isovolumic relaxation time, PVS=pulmonary vein systolic velocity, PVD=pulmonary vein diastolic velocity, LVMPI=left ventricular myocardial performance index







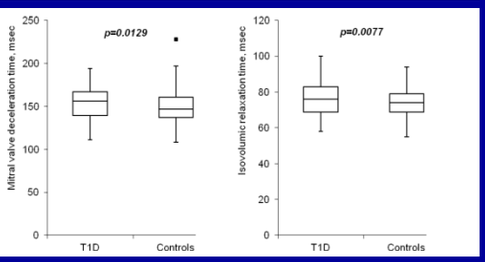


Table 4: Anthropometric Measurements

	Low-Risk n=68	Medium-Risk n=78	High-Risk n=53	Controls n=65
Sex, M:F	27:41	45:33	26:27	28:37
Age, years	14.6±1.6	14.0±1.7	**14.7±1.6***	14.0±2.0
Height, cm	165±8	162±11	164±11	162±12
Weight, kg	**62.7±13.2****	**59.9±16.0***	**59.7±12.6***	53.9±12.5
BSA, m^2	**1.68±0.19****	1.63±0.24	**1.64±0.21***	1.56±0.21
BMI, kg/m^2	**23.0±4.2****	**22.4±4.8***	**22.1±3.7***	20.4±3.8
SBP mmHg	113±9	113±11	114±9	111±8
DBP, mmHg	62±6	62±7	62±7	62±7
MBP, mmHg	77±6	78±8	78±7	77±7
PP, mmHg	51±8	51±10	52±9	49±6
HR, bpm	67±9	65±9	65±9	67±10

*p<0.05 vs. controls, **p<0.001 vs. controls
BSA=body surface area, BMI = Body Mass Index; SBP =systolic blood pressure; DBP = diastolic blood pressure; MBP=mean blood pressure, PP=pulse pressure, HR=heart rate

Table 5: Echo Measurements – M-Mode

	Low-Risk n=68	Medium-Risk n=78	High-Risk n=53	Controls n=65
IVSD, cm	0.72±0.12	0.74±0.12	0.75±0.12	0.71±0.11
LVPWD, cm	**0.66±0.12***	**0.66±0.10***	**0.67±0.11***	0.62±0.10
LVEDD, cm	4.71±0.41	4.71±0.39	4.62±0.38	4.61±0.39
LVESD, cm	2.91±0.33	2.93±0.33	2.85±0.30	2.88±0.31
LVmass$_{ht}$, g/m^2	61±12	65±14	63±14	61±13
LVSF, %	38±5	38±4	38±5	37±4
LVEF, %	68±6	68±5	68±6	67±5
LVVCFC, circ/sec	1.18±0.19	1.18±0.17	1.18±0.18	1.16±0.14

*p<0.05 compared with controls
IVSD=interventricular septal dimension diastole, LVPWD=left ventricular posterior wall thickness dimension, LVEDD=left ventricular end-diastolic dimension, LVESD=left ventricular end-systolic dimension, LVmass$_{ht}$ =left ventricular mass indexes to BSA, LVSF=left ventricular shortening fraction, LVEF=left ventricular ejection fraction, LVVCFC= mean velocity of circumferential shortening

Table 6: Echo Measurements – Pulse Doppler

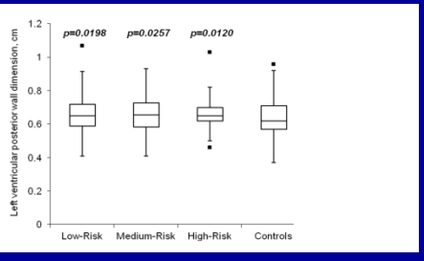
	Low-Risk n=68	Medium-Risk n=78	High-Risk n=53	Controls n=65
MV-E, cm/s	99±15	100±15	100±15	99±17
MV-A, cm/s	42±10	42±9	40±9	42±11
MV-E/A	2.5±0.7	2.5±0.6	2.6±0.7	2.6±0.8
MV-AD, msec	120±17	125±19	120±15	125±21
MV-DT, msec	155±17	153±17	154±17	152±22
IVRT, msec	77±7	76±8	75±8	76±7
PVS, cm/s	41±10	40±11	41±10	42±11
PVD, cm/s	60±10	63±11	61±10	62±11
LV-MPI	0.31±0.10	0.29±0.11	0.28±0.08	0.29±0.08

MVE=mitral valve E velocity, MVA=mitral valve A velocity, MVE/A=mitral valve E/A ratio, MVAD=mitral valve a wave duration, MVDT=mitral valve deceleration time, IVRT=isovolumic relaxation time, PVS=pulmonary vein systolic velocity, PVD=pulmonary vein diastolic velocity, LVMPI=left ventricular myocardial performance index

Table 7: Clinical and Laboratory Measurements

	Low-Risk n=68	Medium-Risk n=78	High-Risk n=53	Controls n=65
T1D duration, years	8.0±3.4	6.9±3.0	6.7±2.9	-
Glucose, mmol/l	**8.5±3.5****	**10.5±4.8****	**10.1±4.5****	4.7±0.7
HbA1c, %	**0.084±0.012****	**0.085±0.013****	**0.086±0.013****	0.054±0.002
Cholesterol, mmol/L	4.35±0.85	4.36±0.97	4.24±0.77	4.24±0.83
HDL, mmol/L	**1.66±0.40***	**1.61±0.33***	**1.65±0.34***	1.46±0.28
LDL, mmol/L	2.32±0.72	2.36±0.77	2.20±0.60	2.36±0.74
Triglycerides, mmol/L	0.83±0.35	0.85±0.41	0.84±0.32	0.93±0.40
Creatinine, mmol/L	55±9	53±9	53±10	56±11
GFR, mL/min/1.73 m^2	111±17	114±17	**115±18***	108±17

*p<0.05 vs. controls, **p<0.0001 vs. controls
T1D duration=type 1 diabetes duration, HbA1c=haemoglobin A1c, LDL=low-density lipoprotein cholesterol, HDL=high-density lipoprotein cholesterol, GFR=glomerular filtration rate



Pearson's correlations

Significant positive correlations: SBP with BMI for low-, medium- and high-risk T1D and controls; DBP with BMI for medium-risk T1D; HR with BMI for high-risk T1D; LVPWD with BMI for low- and medium-risk T1D and controls; DBP with HbA1c for high-risk T1D; and HR with HbA1c for controls.
Significant negative correlations: HR with BMI for controls; SBP with HbA1c for high-risk T1D; HR with HbA1c for high-risk T1D.

Variable	Low-Risk	Medium-Risk	High-Risk	Controls
SBP : BMI	r=+0.24 p=0.0456	r=+0.39 p=0.0004	r=+0.29 p=0.0345	r=+0.31 p<0.0001
DBP: BMI	r=+0.23 p=0.0548	r=+0.24 p=0.0359	r=+0.06 p=0.6540	r=+0.04 p=0.5544
HR : BMI	r=-0.21 p=0.0615	r=+0.19 p=0.1827	r=+0.35 p=0.0038	r=-0.40 p=0.0003
LVPWD : BMI	r=+0.25 p=0.0389	r=+0.31 p=0.0050	r=+0.22 p=0.1137	r=+0.30 p<0.0001
SBP : HbA1c	r=-0.15 p=0.2350	r=+0.21 p=0.0617	r=-0.29 p=0.0361	r=-0.06 p=0.6541
DBP: HbA1c	r=-0.00 p=0.9893	r=+0.10 p=0.3748	r=+0.32 p=0.0214	r=-0.10 p=0.4103
HR : HbA1c	r=+0.11 p=0.1313	r=-0.12 p=0.3172	r=-0.20 p=0.0198	r=+0.24 p=0.0007
LVPWD : HbA1c	r=-0.13 p=0.3066	r=-0.01 p=0.9268	r=+0.02 p=0.8657	r=+0.13 p=0.3178