

HYPERGLYCEMIA IS THE MAIN DETERMINANT OF CARDIAC AUTONOMIC DYSFUNCTION IN YOUTH WITH OBESITY ACROSS THE SPECTRUM OF GLYCEMIC REGULATION.

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Background: Heart Rate Variability (HRV) results from the autonomic nervous system activity, it is a non-invasive marker of cardiac autonomic function. Loss of parasympathetic function and sympathetic override, reflected in decreased HRV, is one of the earliest subclinical manifestations of cardiac autonomic dysfunction. Lower HRV is associated with increased risk of cardiac events in adults. We aim to characterize HRV in normal weight and overweight children with and without dysglycemia and to investigate the determinants of HRV in these youth, including body composition, glycemia measures and inflammatory markers.

Materials/Methods: We evaluated 94 adolescents (50 males/44 females), age 15 ± 2.1 yrs; 21 normal weight with normal glucose tolerance (NW-NGT), 23 overweight with NGT (OW-NGT) and 50 overweight with impaired glucose regulation (OW-IGR) including prediabetes ($n=27$) and type 2 diabetes ($n=23$, diabetes duration 18.2 ± 18 mon). They underwent assessment of anthropometrics, body composition (DXA scan), inflammatory markers (hs-CRP and TNF- α), fasting labs and 2-hour oral glucose tolerance test (OGTT) with determination of glucose and insulin concentrations. HRV indices were measured using EndoPat. The frequency-domain index: LF/HF (ratio of low frequency (LF) to high frequency (HF) power), estimates the ratio between sympathetic and parasympathetic activity. A higher LF/HF is indicative of loss of parasympathetic activity and decreased HRV.

Results: LF/HF was higher in the OW-IGR group compared with NW and OW-NGT ($p=0.005$). After controlling for sex, race and Tanner stage, LF/HF was positively related to fasting glucose (FBG) ($r=0.39, p<0.001$), 2hr-glucose ($r=0.31, p=0.004$) and HbA1c ($r=0.22, p=0.04$), negatively correlated with the insulinogenic index ($r=-0.27, p=0.02$), but not to fasting insulin or HOMA-IR; LF/HF also correlated with percent body fat ($r=0.22, p=0.04$), hs-CRP ($r=0.33, p=0.002$) and TNF- α ($r=0.38, p=0.006$). In a linear regression model with LnLF/HF as the dependent variable and percent body fat, hs-CRP, FBG, and HOMA-IR as the independent variables, FBG ($\beta=0.39, p=0.003$) and hs-CRP ($\beta=0.21, p=0.09$) were the significant determinants of LnLF/HF independent of age, sex, race and Tanner stage as covariates ($R^2=0.23, p=0.013$).

Conclusions: Youth with impaired glucose metabolism have evidence of early subclinical cardiac autonomic dysfunction with loss of parasympathetic function and sympathetic overdrive as reflected by higher LF to HF ratio, related to glycemia and systemic inflammation.

Images / Graph / Table

	NW N=23	OW-NGT N=25	OW-HGR N=51	P-value
Age (SD) years	35.1 (2.3)	34.3 (2.4)	35.3 (1.8)	0.206
AAHIC (%)	145/2 (67/24/9)	11/75 (4/74/22)	17/112 (14/62/4)	<0.001
Male (%)	14 (67)	10 (44)	26 (52)	0.303
BMI (SD) kg/m ²	20.8 (2.8)	29.6 (5.0)	35.7 (5.6)	<0.001
BMI Z-score (SD)	0.21 (0.69)	1.84 (0.53)	2.29 (0.38)	<0.001
Waist (SD) cm	70.4 (7)	94.8 (15.1)	107 (14.7)	<0.001
Percent body fat (SD) %	17.9 (6.2)	37.2 (5.1)	38.8 (6)	<0.001
HbA1c (SD) %	5.55 (0.25)	5.44 (0.24)	5.99 (0.35)	<0.001
Fasting BG (SD) mg/dL	90.6 (5.9)	92.3 (5.0)	107.6 (14.0)	<0.001
2-hr OGTT BG (SD) mg/dL	118.1 (18.3)	114.9 (16.2)	183.6 (48.6)	<0.001
HS-CRP (SD) mg/dL	0.55 (0.69)	1.53 (1.53)	3.5 (1.24)	<0.001
Fasting Insulin (SD) mIU/L	11.37 (12.8)	31.08 (25.84)	38.64 (25.10)	<0.001
Insulinogenic Index (SD)	1.43 (0.68)	4.99 (3.13)	2.72 (2.12)	<0.001
LDL (SD) mg/dL	76.2 (21)	77.9 (24)	90.7 (23.1)	0.019
Trig w HDL ratio (SD)	1.06 (0.54)	2.16 (1.41)	3.11 (2.21)	<0.001
SBP (SD) mmHg	113.2 (11.4)	114.6 (10.8)	120.4 (9.2)	0.012
DBP (SD) mmHg	69.1 (8.2)	71.8 (7.1)	74.5 (6.2)	0.096
MAP (SD) mmHg	83.8 (7.3)	84.8 (9.1)	89.8 (6.2)	0.002
Heart Rate (SD) beats/min	65.9 (11.2)	70.5 (8)	71.6 (9.06)	0.067
LF Power (SD) ms ²	128.1 (44.8)	134.2 (59.3)	160.2 (63.9)	0.062
HF Power (SD) ms ²	240.5 (85.1)	295.1 (73.3)	242.6 (93.1)	0.044
LF to HF ratio (SD)	0.6 (0.29)	0.45 (0.26)	0.87 (0.66)	0.005