Original Article

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Evaluation of QRS Fragmentation and BMI in Obese and Non-Obese Children

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Abstract

Background: Fragmented QRS (fQRS) on electrocardiography is a marker of myocardial fibrosis and scar formation. We aimed to investigate whether the fQRS complex in children with and without obesity correlates with Body Mass Index (BMI).

Methods: In this cross-sectional study, 104 children (5 to 17 years) referred to the pediatric clinic were studied. We divided participants into normal and obese groups. Standard 12-lead ECGs, anthropometric data, and blood pressure were recorded. All ECGs were analyzed blindly by two independent clinicians. Surveyed parameters of the ECG included heart rate, QRS duration, QT interval, presence of Q waves, and fQRS.

Results: Among 104 participants, 52 patients had normal BMI and 52 cases were obese. Systolic blood pressure (p=0.001), pulse pressure (p=0.007), mean blood pressure (p=0.006), and heart rate (p=0.009) were meaningfully different between the two groups. We found fQRS in four children with obesity. The frequency of fQRS was significantly different between children with obesity and children in the control group (p=0.041). We have found that each unit change of weight and BMI at 1.07 and 1.45, respectively, could be useful in prediction of the occurrence of fQRS complex in children.

Conclusion: This study suggested a significant association between the fQRS in children's ECG and their weight and BMI. It would appear that each unit increasing weight and BMI predicts an increasing the occurrence of fQRS. The ECG may consider using fQRS as a cardiac risk marker in children with obesity.

Keywords: Body mass index, Children, ECG, Fragmented QRS, Obesity

Introduction

Fragmented QRS (fQRS) is a suitable marker of myocardial scar that is assessed by 12-lead Electrocardiogram (ECG) evaluation. FQRS is detected when the additional notches in the QRS complex become revealed (1). It is typically defined as the presence of additional notches in the R or S waves in the absence of Bundle Branch Block (BBB) or as an RSR' pattern in the original QRS wave (with a duration of <120 *ms*) (2). Fragmented QRS (fQRS) is a readily available finding on ECG which is available in clinical practice. FQRS develops due to the impaired myocardial perfusion, and electrical activation after disrupted left ventricular dilatation. It is an electrocardiographic marker of myocardial fibrosis or scar tissue and has been associated with a worse prognosis. Additionally, fQRS has been associated with increased arrhythmia and sudden cardiac mortality in patients with idiopathic dilated cardiomyopathy (2).

Various studies have shown an association between obesity and Cardiovascular diseases (CV) such as acute myocardial infarction, heart failure, arrhythmia (heart rhythm disorders), Sudden Cardiac Death (SCD), and Coronary Artery Disease (CAD) (3,4). Excess myocardial fat deposits may develop the ventricular arrhythmias. In addition, free fatty acids, and other bioactive molecules are accumulated nearby myocytes, which accordingly provoke the structural and electrical changes in myocardium and heart function (5). In fact, poor electrical conduction causes delayed impulse transmission and re-entry of the pulses in to the myocardium (6). Investigators declare that *abnormality* of *the heart's electrical functions* and early or delayed depolarization due to the fatty infiltration accounts as an important mechanism of arrhythmogenesis in obesity (7). *FQRS that is recorded* during wavelet *electrocardiogram* (*ECG)* is as a predictor of inhomogeneous conduction and delayed activation of the myocardium (8). Other studies have shown that fQRS and other depolarization abnormalities can predict mortality and SCD. In addition, fQRS is found to be associated with increased risk of mortality and arrhythmic events in patients with cardiovascular disorders (9).

Evaluation of fQRS has significant benefits, since it is a simply available and non-invasive ECG marker which could help identify the high-risk subtypes of arrythmia in the obese and overweight individuals. Given the impact of obesity on the structure of the heart as well as its pathophysiology, we postulated that fQRS could be a useful indicator of the risk of sudden cardiac death in obese and overweight subjects. Therefore, we conducted a study on the potential usage of QRS fragmentation evaluation among obese/overweight individuals in children with obesity.

Prognostic assessment of patients suffering from cardiovascular diseases often requires invasive evaluations (2). The presence of fQRS on a routine 12-lead surface ECG can be detected to determine the severity of heart involvement in various cardiac diseases. In the present study, we aimed to investigate whether an increased high Body Mass Index (BMI) is independently associated with the presence of fQRS on ECG and underlying cardiovascular status.

Materials and Methods

A descriptive cross-sectional study was conducted on 104 patients, from September 2019 to December 2020 at Amir-Kabir Hospital affiliated with Arak University of Medical Sciences, Arak, Iran. The age range of the participants was between 5 to 17 years old that was divided into two groups: the obese and non-obese according to the BMI. Only those patients were included in the study whom themselves or their legal guardians were informed about the study, and signed the consent form. Ethical principles were considered and followed based on the ethical code approved by the Ethics Committee of Arak University of Medical Sciences (IR.ARAKMU.REC.1399.176).

A sample size of n=52 was estimated for each group according to the study of Kumar Narayanan *et al*, with α and β errors of 0.05 and 0.2, respectively (6,10).

All the participants' weight and height were measured according to standard protocols by well-trained personnel including cardiologists, internal medicine physicians, and pediatricians. Children were barefoot and wore only light underwear during assessment of the variables. Weight and height were sequentially measured to the nearest 0.1 *kg* and 0.5 *cm*.

BMI was calculated using weight and height measurements and application of the formula: weight (*kg*)/height^2 (m^2). Obesity for children

and teens is defined as a BMI at or above the 95th percentile according to the same age and gender. The International Obesity Task Force (IOTF) has also supplied reference for specific values of BMI cut-off for the classification of overweight and obesity (through BMI of 25 and 30 kg/m^2 at 18 years of age). Blood pressure was measured in all the participants by experienced personnel making use of mercury sphygmomanometers and convenient-size cuffs. The participants were advised to avoid caffeine and exercise for ≥30 *min* before evaluations; they had ≥5 *min* rest before the measurement. For all the participants, we measured the blood pressure twice in the right arm whilst lying in the supine position, and it was recorded with all appropriate data. The evaluators used a cuff that was fitted to the child's right arm. The average of the two blood pressure measurements was used in the analysis. Hypertension was defined as having Systolic Blood Pressure (SBP) and/or Diastolic Blood Pressure (DBP) levels greater than or equal to the 95th percentile of height, gender, and age reference levels.

A resting 12-lead surface ECG (with a speed of 25 *mm/s* and an amplitude of 10 *mm/mV*) was obtained from all the patients while lying in the supine position. ECG assessment was performed by two independent cardiologists blinded to the study. ECGs in sinus rhythm before and unrelated to the sudden cardiac death event were used. Parameters assessed from the 12-lead ECG included heart rate, QRS duration, QT interval, presence of Q waves, and fQRS. The QT interval was corrected using Bazett's formula. Taking into consideration, previously determinate criteria for assessing *fQRS*, the present analysis was limited to ECGs with narrow QRS (QRS duration <120 *ms*). Exclusion criteria were the diabetes mellitus, parental discontent, underlying cardiovascular disease, under-treatment medical cardiac therapy, lack of proper ECG, complete or incomplete bundle-branch block, and QRS complex duration ≥120 *ms*.

We compared the mean±standard deviation of data using independent samples t-test whereas the frequency of categorical variables was compared using chi-square test. For calculating odd's ratio, we used risk estimation in chi-square or logistic regression estimation. Stepwise logistic univariate and multivariate regression analyses were performed to identify independent determinants of QRS fragmentation. The p-values less than 0.05 were considered as the statistically significant results. After data collection, we used SPSS software for statistical analysis SPSS 23 (IBM Corp., Armonk, New York, USA).

Results

Table 1 represents the demographic and clinical characteristics of cases and controls. Out of 104 children studied, between 5 to 17 years old, 49 children (47.11%) were boys and 55 children (52.89%) were girls. Both case and control groups were matched for the gender. The average age of the children was 9 years old and due to terms of age matching, the

Table 1. Baseline and demographic characteristics of the participants in case and control groups

Variables	Control group (n=52)	Case group (n=52)	p-value *
Age	8.65±2.72	8.63±2.70	0.999
Gender (%)			
Female	26 (50.0)	26 (50.0)	0.999
Male	26 (50.0)	26 (50.0)	
Weight (*kg*)	29.95±10.18	42.76±17.15	0.0001
Height (*cm*)	131.36±16.01	130.69±16.01	0.583
BMI	16.74±1.45	23.91±3.55	0.0001
BSA	1.03±0.23	1.23±0.31	0.0003

* p-value calculated by independent t-test and chi2 test at 95% of CI. SD: Standard Deviation, BMI: Body Mass Index, BSA: Body Surface Area.

average age of both groups was completely same. Systolic blood pressure, pulse pressure, mean blood pressure, and heart rate were significantly different between the case and control groups (Table 2).

QRS fragmentation in any territory was detected in 4 (7.69%) cases and any (0%) controls. Four fQRS patients were in the case group and had a BMI above 95%. The frequency of fQRS complex between children with and without obesity was significantly different (p=0.041).

Table 3 shows the association between fQRS with BMI, weight, height, and BSA. It was found that there is a statistically significant correlation between the presence of fQRS complex in children's ECG and their weight and BMI. It was also found that each unit weight and BMI at 1.07 and 1.45, respectively, could predict the occurrence of fQRS complex in children. According to our findings, with each increment in BMI value, the risk of fQRS increases 1.45, and with each increment of weight unit (*kilogram*), the chance of having fQRS increases by 1.07. Further, with each increment in BSA unit, the chances of having fQRS increase to 49.04. However, the odds ratio for height was not significant, statistically. Table 4 shows the demographic and clinical characteristics of four obese children with fQRS.

Discussion

The global BMI averages, as well as overweight and obesity, with different patterns, are increasing

Table 2. Variables of comparison between case and control groups

Variables	Control group (n=52)	Case group (n=52)	p-value *
FQRS (%)			
No	52 (100.0)	48 (92.31)	0.041
Yes	0 (0.0)	4 (7.69)	
SBP (*mmHg*)	96.73±13.05	103.55±8.36	0.001
DBP (*mmHg*)	70.38±6.99	72.01±6.28	0.106
HR	90.96±9.90	95.63±10.07	0.009
QTc	394.13±11.01	395.26±10.75	0.298
Pulse pressure	26.34±11.96	31.53±8.71	0.007
BP mean	79.16±7.58	82.53±5.72	0.006

* p-value calculated by independent t-test and chi2 test at 95% of CI.
FQRS: Fragmented QRS, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate, QTc: QT corrected, BP means: Blood Pressure Mean.

Table 3. Association between fQRS with BMI, weight, height, and BSA

Variables	Crud OR	95% CI	Adjusted OR *	95% CI
BMI	1.45	(1.11-1.90)	1.5	(1.09-2.07)
Weight	1.07	(1.01-1.12)	1.07	(1.01-1.14)
Height	1.05	(0.99-1.12)	1.05	(0.97-1.14)
BSA	49.04	(2.76-974.0)	82.12	(2.12-5868.19)
SBP	1.11	(0.92-1.32)	-	-
DBP	0.99	(0.88-1.21)	-	-

* Adjust for SBP and DBP and calculated by logistic regression. CI: Confidence Interval, BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate.

Table 4. Demographic and clinical characteristics of four obese children with FQRS

Case	Gender	Age (year)	Weight (*kg*)	BMI (kg/m^2)	Location fQRS	Q-wave	QTC	HR	SBP	DBP
1	Female	8	46	29.4	Lateral/inferior	N	415	101	105	85
2	Female	9	43	24.2	Inferior	N	400	96	105	80
3	Male	13	68	25.5	Lateral	N	405	95	125	80
4	Male	14	90	34.2	Lateral/inferior	N	410	88	130	80

in different countries. Even in developing countries, being overweight is a growing problem in the pediatric age group. Epidemiological changes, lifestyle changes, and the significant prevalence of obesity have made the Middle East face the highest global burden of non-communicable diseases, especially diabetes and cardiovascular disease (11).

A fragmentation in QRS on 12-lead ECG reflects the abnormality of heterogeneous depolarization of ventricular myocardium, around the infarction zone or scar caused by myocardial damage. The fQRS may predict major adverse cardiac pathologies or cardiac involvement. The fQRS determination is a simple, inexpensive, readily available, and easily applied in ECG parameter that can be identified by clinicians.

In the ECG of the studied children, only 4 children with fQRS complex were identified, all belong to case group and had a BMI above 95% of the reference value. The frequency of fQRS complex between children with obesity and whom without obesity was statistically significant (p=0.041). Therefore, it can be concluded that childhood obesity can cause myocardial damage, which is observed as an fQRS complex in the ECG.

This study also found a significant association between the presence of fQRS complex in children's ECG and their weight and BMI. It was also found that obesity and BMI at 11.2% and 10.2%, respectively, could predict the occurrence of fQRS complex in children. In our study, there was a Q wave in any patients but in inferior and lateral leads, there were fQRS in two very obese children.

Metabolic syndrome is associated with the deterioration of the left ventricular (LV) systolic and diastolic functions. One of the factors for this impairment is myocardial fibrosis. The fQRS complexes are found to be associated with myocardial fibrosis. Ender Oner *et al* suggested that fQRS is more common among metabolic syndrome patients compared to non-metabolic syndrome patients. The presence of fQRS is associated with pronounced subclinical LV systolic and diastolic dysfunctions in metabolic syndrome patients (6).

Several mechanisms may be to explain the independent association between BMI and fQRS. First, raised body fat induces a wide variety of metabolic dysfunctions before the development of obesity-related cardiovascular risk factors and cardiac disorders. These metabolic changes include autonomic nervous system dysfunction, an increase in thrombogenic factors, inflammation, and fat infiltration into the myocardium that may trigger fibrosis within the myocardium (12). Second, obesity may also increase sympathetic excitability by altering sensitivity; it affects ventricular conduction and causes disturbances in this process (13). Third, high BMI-related increased epicardial adipose tissue thickness may directly have adverse effects on the myocardium. Increased epicardial fat has endocrine and paracrine activity and secretes inflammatory cytokines and chemokines that might influence coronary atherosclerosis and myocardial fibrosis independently (14,15). When these adverse effects of body fat on the metabolism are taken into account, the subclinical atherosclerosis should be taken into consideration by evaluating the BMI and fQRS.

Aryanejad *et al* claimed the obesity can have adverse impacts on the ECG of children compared to normal-weight persons. These changes are related to an increased risk of arrhythmias. Considering these changes can be corrected with weight control, the families should be warned about the overweight and

obesity; they should be educated for prevention of the comorbid risk factors (16).

Yaman *et al* have reported that the presence of fQRS on the admission ECG is associated with increased epicardial adipose tissue thickness and pronounced subclinical LV systolic and diastolic dysfunction in healthy individuals (10).

Binu *et al* suggested that changing in ECG patterns in patients with morbid obesity, the predominant changes included tachycardia, atrial enlargement, ventricular hypertrophy, conduction defects, LAD, features of ischemia or old infarction and repolarization abnormalities. Furthermore, a greater prevalence in morbid obesity without any case of death were reported in Binu *et al*'s study. Anyhow, further studies are needed to evaluate the effect of weight reducing measures on the reversibility of these changes and determining their association with outcomes in obese individuals. In addition, this research team found an increased frequency of tachycardia, atrial enlargement, ventricular hypertrophy, conduction defects (LBBB/RBBB), LAD, features of ischemia or old infarction (pathological Q-waves, poor R-wave progression, ST-segment depression and inverted T-waves), and repolarization abnormalities (prolonged QTc interval) in patients suffering from morbid obesity (17).

Ultimately, increased body fat related to increased transthoracic resistivity may be another factor affecting ventricular conduction disorders on ECG. fQRS provides prognostic information on multifarious cardiovascular diseases, however, it may not always be related to coronary artery disorders. Accordingly, the definition of independent predictors of fQRS such as BMI may provide better predictive risk stratification and could be helpful to assign the exact prognostic value of fQRS when considering it as a prognostic factor.

However, our primary goal was to find a useful diagnostic tool to detect heart complications in early stage. A prevalence of fQRS in obese children suggests the need for an additional biomarker to clarify them as a cardiac side effect. Our results demonstrated that a close correlation can be observed between myocardial complications and obesity. Subjects with fQRS in the study were low (4.7%), but there was a predicted circumstance of fQRS in children.

Therefore, according to the results, obesity during childhood can be associated with heart damage and cause cardiovascular complications. Children who have obesity are more likely to have high blood pressure and high cholesterol, which are risk factors for cardiovascular disease. Despite the increasing prevalence of obesity among children, paying attention to this issue can increase their cardiovascular health and prevent its complications at an older age.

Limitations

Our study had several limitations: first, we coronary angiography was not performed to identify coronary artery disease. Secondly, we cannot measure lipid profiles and glucose tests. Thirdly, we did not demonstrate the presence of cardiac fibrosis histopathological or with other imaging modalities. We did not perform a cardiac MRI, which is considered to be a gold standard in myocardial fibrosis and a meaningful tool to evaluate cardiac function and myocardial damage. Further studies with larger patient groups are needed to clarify the exact evaluation fQRS and these findings in children's obese populations. The current study lacked a clinical follow-up; therefore, we could not conclude whether or not the presence of fQRS was clinically significant in patients obese.

Conclusion

This study found a significant association between the presence of fQRS complex in children's ECG and their weight and BMI. The presence of fQRS on conventional ECG is advantageous in suspecting cardiac involvement in obese children, that each unit increasing weight and BMI predicts an increasing occurrence of fQRS in obese children. Importantly, our results provide evidence that fQRS could be a biomarker for obesity with the probability of increased myocardial scar. It seems that complications of obesity can be reduced by changing lifestyle and increasing the sports activity and healthy diet.

Competing interests

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Conflict of Interest

The authors declare that they have no conflict of interest.

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