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EFFECT OF FASTING AND POSTPRANDIAL CONDITION ON LEFT ATRIAL ELECTROMECHANICAL DELAY IN HEALTHY NON DIABETIC SUBJECTS

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ABSTRACT

Background: atrial electromechanical delay (AEMD), which is defined as the time interval between the atrial electrical depolarization and the initiation or peak of atrial mechanical contraction, is associated with atrial remodeling that finally leads to atrial fibrillation (AF).

Objective: to assess the effect of fasting and postprandial condition on intra-atrial electromechanical coupling in healthy non-diabetic subjects

Patients and methods: 55 subjects were enrolled in this descriptive observational cross sectional study, (mean age was 33.27±7.49 years, 33 males), all patients were assessed by thorough history taking, clinical examination, 12 lead surface ECG, ECG gated Echocardiography with measurement of atrial electromechanical coupling (PA), left atrial intra-AEMD over a period of 1 year from July 2017 to July 2018 in Mansoura specialized medical hospital

Results: it was found that PA lateral (50.98±8.07 vs. 50.38±7.47 ms, p 0.026), PA Septal (34.87±6.33 vs. 34.16±6.32 ms, p 0.003) and, left intra-AEMD (PA lateral–PA Septal) (16.72±7.34 vs. 16.21±6.57 ms, p 0.01), values were higher in post prandial condition than in fasting state

Conclusion: Determining electromechanical events including the atrial conduction time with transthoracic echocardiography is a simple, noninvasive method to be assessed. PA lateral, PA septal and left atrium EMD are prolonged in postprandial condition than during fasting.

KEY WORDS : electromechaincal delay ; left atrial remodeling.

INTRODUCTION

Atrial electromechanical delays (AEMDs) are defined as the time intervals between the atrial electrical depolarization and the initiation or peak of atrial mechanical contraction. It has been shown that prolonged AEMDs can be used as markers to discriminate patients with paroxysmal atrial fibrillation (PAF) from controls without PAF or to predict the occurrence of PAF in case-control or observational studies ***(1).*** The clinical evidence supports the notion that prolonged AEMDs reflect left atrial electrical remodeling, which is essential for the maintenance of atrial fibrillation ***(2).***

Studies showed that postprandial glucose level (PPG) may be considered a marker rather than a risk factor for cardiovascular disease (CVD) ***(3).*** Postprandial hyperglycemia (PPH) better predicts future CVD morbidity and mortality compared with fasting hyperglycemia in both diabetics and normo-glycemic individuals ***(4)***

Oxidative stress is a central implicating factor for vascular endothelial dysfunction during post prandial hyperglycemia (PPH). This is attributed to its multifaceted role in decreasing nitric oxide (NO) bioavailability and by inducing pro-inflammatory responses that exacerbate the magnitude of oxidative stress. That PPH increases CVD risk, even in healthy individuals, suggesting a critical need to better define the mechanisms ***(5).***

Oxidative stress contributes significantly to vascular dysfunction by reducing NO bioavailability through several overlapping mechanisms. Extensive knowledge indicates that oxidative stress is enhanced by chronic hyperglycemia and some data indicate that even transient postprandial glucose excursions also increase oxidative stress ***(6).***

There was significant EMD in patients with diabetes mellitus (DM) as compared with healthy volunteers. Inflammation and oxidative stress have been implicated in the pathogenesis of both the DM and AF ***(7,8)***.

Atrial conduction abnormalities were evaluated with noninvasive techniques by using electrocardiography (ECG) and tissue Doppler imaging (TDI) in previous studies ***(9,10).***

AEMD has also been demonstrated to be longer in many diseases that affect heart tissue ***(11,12,13,14,15)***

The aim of this study was to assess the effect of fasting and postprandial condition on intra-atrial electromechanical coupling in healthy non-diabetic subjects.

PATIENTS AND METHODS

- **Study population**

55 middle aged healthy subjects were enrolled in this descriptive cross sectional study, (mean age was 33.27±7.49 years, 33 males), All patients were assessed by thorough history taking, clinical examination, 12 lead surface ECG, ECG gated Echocardiography with measurement of atrial electromechanical coupling (PA), left atrial intra-AEMD over a period of 1 year from July 2017 to July 2018 in department of cardiovascular medicine, Faculty of medicine, Mansoura University.

- **Exclusion Criteria**

Exclusion Criteria include History of chronic medical disease including: Diabetes mellitus and hypertension, history of structural cardiac disease including valvular heart disease, arrhythmia, left ventricular systolic or diastolic dysfunction and ischemic heart disease, History of chronic renal failure, history of chronic liver disease, persons with abnormal ECG changes as conduction abnormalities and arrhythmia, Obese persons with body mass index (BMI) more than 30 kg/m2.

- **Ethics statement**

The study was explained to all patients and they gave oral informed consent. Besides, the study was approved by the ethics committee of the Faculty of medicine, Mansoura University.

- **Methodology**

All subjects were assessed by thorough history taking including;

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age and gender, special habits and past medical history.

Clinical examination included: BP, pulse, general examination and local cardiac examination.

Investigations included: 12 lead surface electrocardiogram, Echocardiography, liver function tests, kidney function tests, fasting and 2 hour post-prandial blood glucose levels.

- **Echocardiography**

Conventional echocardiography for assessment of cardiac chamber, left ventricular thickening and ejection fraction according to American Society of Echocardiography (ASE) recommendation for exclusion of cardiac anomaly.

Assessment of Atrial electromechanical coupling:

ECG gated Tissue Doppler echocardiography was performed Using General electric System Vivid –E9 machine with tissue Doppler imaging capability using (2.5-5) MHZ probe.

In apical four-chamber view, the pulsed Doppler sample volume was placed at the level of the LV lateral mitral annulus, and subsequently at the septal mitral annulus. The time interval from the onset of the P wave on surface ECG to the beginning of the late diastolic wave on TDI, which is named PA, was obtained from the lateral mitral annulus (lateral PA), septal mitral annulus (septal PA), the difference between lateral PA and septal PA (lateral PA-septal PA) was defined as intra-left atrial EMD. All measurements were recorded over an average of three cardiac cycles ***(16)***, These measurements were calculated in fasting and 2 hours post prandial.

- **Statistical analysis**

Data were analyzed with SPSS version 21. The normality of data was first tested with one-sample Kolmogorov-Smirnov test to obtain:

DESCRIPTIVE DATA:

Descriptive statistics were calculated for the anthropometric measurements and laboratory data in the form of:

- Mean ± Standard deviation (SD).
- Median and range (Minimum – Maximum).
- Frequency (Number-percent)

A P value <0.05 was considered statistically significant.

RESULTS

The mean age among all subjects was 33.27±7.49 years, with their age ranging from 21 to 47 years. The ratio of subjects with age <30 y was 38.2%, subjects with age 30-40 y was 36.4%, subjects with age >40 y was 25.4% there was 33 male and 22 female with male/female ratio (60%) versus (40%) (Table1).

Among the study population, there was 9 smokers and 46 non-smoker with smoker/non-smoker ratio (16.4%) versus (83.6%) (Table1).

Table (1): Demographic data of the studied group

Variables	Study group (n=55)	
	No	%
Gender		
Male	33	60.0%
Female	22	40.0%
Age/years		
<30 y	21	38.2%
30-40 y	20	36.4%
>40 y	14	25.4%
Mean ± SD	33.27±7.49	
Min-Max	21.00-47.00	
Smoking		
yes	9	16.4%
No	46	83.6%

Table (2): relation between fasting, post prandial PA lateral

PA lateral (ms)	Fasting PA lateral	Postprandial PA lateral	Paired t-test	p-value
Mean ± SD	50.38±7.47	50.98±8.07	2.29	0.026*
Min-Max	39.00-63.00	39.00-65.00		

As shown in table (**2**) the PA lateral is significantly prolonged in post prandial state than in fasting.

Table (3): Comparison between fasting and post prandial PA septum

PA septum (ms)	Fasting PA septum	Post prandial PA septum	Paired t-test	p-value
Mean ± SD	34.16±6.32	34.87±6.33	3.16	0.003*
Min-Max	22.00-50.00	22.00-50.00		

As shown in table **(3)** the PA septum is significantly prolonged in ost prandial state than in fasting.

Table (4): Comparison between fasting and post prandial Left intra-atrial EMD

Left intra-atrial EMD (ms)	Fasting Left intra-atrial EMD	Post prandial Left intra-atrial EMD	Paired t-test	p-value
Mean ± SD	16.21±6.57	16.72±7.34	2.67	0.01*
Min-Max	9.00-31.00	9.00-35.00		

As shown in table **(4)** the left atrial EMD is significantly prolonged in post prandial state than in fasting.

Table (5): Relation between fasting, post prandial Left intra-atrial EMD and smoking

EMD (ms)	Smoking		t-test	p-value
	Yes (n=9)	No (n=46)		
Fasting Left intra-atrial EMD	28.55±2.87	13.80±3.73	11.18	<0.001**
Post prandial Left intra-atrial EMD	30.88±3.10	13.95±3.89	12.27	<0.001**

As shown in table (**5**) smoking prolong left atrium EMD , in smoker subjects the fasting EMD was 28.55±2.87,post prandial EMD was 30.88±3.10 ,while in non-smoker subjects the fasting EMD was 13.80±3.73,post prandial EMD was 13.95±3.89

Table (6): Relation between fasting, post prandial Left intra-atrial EMD and sex

EMD (ms)	Sex		t-test	p-value
	Male (n=33)	Female (n=22)		
Fasting Left intra-atrial EMD	17.72±7.38	13.95±4.34	2.155	0.036*
Post prandial Left intra-atrial EMD	18.45±8.38	14.13±4.46	2.210	0.031*

As shown in table (**6**) the left atrium EMD is more prolonged in males than in females, in male subjects the fasting EMD was 17.72±7.38 ,post prandial EMD was 18.45±8.38,while in female subjects the fasting EMD was 13.95±4.34 ,post prandial EMD was 14.13±4.46

Table (7): Relation between fasting, post prandial Left intra-atrial EMD and age

EMD	Age / y			ANOVA test	p-value
	<30y (n=21)	30-40 y (n=20)	>40y (n=14)		
Fasting Left intra-atrial EMD	13.00±3.97 a	15.15±5.20 b	22.57±7.31ab	13.72	<0.001**
Post prandial Left intra-atrial EMD	13.00±4.32 a	15.50±5.39 b	24.07±8.38 ab	15.21	<0.001**

ab: similar letters indicate significant difference between groups by post hoc LSD test.

As shown in table **(7)** direct correlation between left atrium EMD and increasing age, in subjects <30 years old the fasting EMD was 13.00±3.97, post prandial EMD was 13.00±4.32, while in subjects 30-

40 years old the fasting EMD was 15.15±5.20, post prandial EMD was 15.50±5.39, in subjects >40 years old the fasting EMD was 22.57±7.31, post prandial EMD was 24.07±8.38.

DISCUSSION

Electro-Mechanical Delay (EMD) has been defined as the temporal interval between the onset of cardiac electrical activity and myocardial contraction. The delay between the electrical stimulation and mechanic contraction results from structural changes in the atria ***(9).***

Atrial conduction disorders are frequent in elderly subjects and/or those with structural heart diseases, mainly mitral valve disease, dilated cardiomyopathy, coronary slow flow, and hypertension ***(17,18,19,20).***

Atrial Electro-Mechanical Delay(AEMD) has been shown as a marker of new onset AF **(21)**

Chao et al., 2011 have shown that atrial electromechanical interval is associated with atrial remodeling that finally leads to AF, so the measurement of atrial EMD may be used to determine who is prone to AF***(2).***Atrial fibrillation (AF) is one of the most frequently sustained cardiac arrhythmias seen in clinical practice, and is associated with an increased risk of ischemic stroke, heart failure, and overall mortality ***(8).***

To our knowledge, there is no study had evaluated atrial conduction abnormalities using both tissue Doppler imaging (TDI) and electrocardiography (ECG) to assess effect of fasting and post prandial condition on left atrium electromechanical delay in healthy non diabetic subjects. In this descriptive cross sectional study we aimed to determine the correlation of atrial conduction abnormalities between the surface electrocardiographic and TDI measurements in healthy non diabetic subjects in fasting, postprandial conditions.

In this study the PA septum, PA lateral, left atrium EMD were prolonged in postprandial state compared with the fasting state, also the postprandial EMD is directly proportional to the level of post prandial blood glucose level.

To our best knowledge no previous studies had shown the effect of fasting and post prandial condition on left atrium electromechanical delay in healthy non diabetic subjects ,however, ***Ayhan et al.,2012*** found that left atrial electromechanical delays was significantly higher in patients with glucose intolerance than in controls **(22)**

In accordance with previous studies ***(Rachid et al., 2017)*** that found that increasing age, the LA conduction becomes slower and the LA compliance reduces, suggesting the presence of age related fibrotic changes of the LA wall ***(23),*** also ***(Rosca et al., 2011)*** showed that Age is a known cause of atrio-ventricular conduction delay as well as the increased incidence of atrial fibrillation ***(24),*** we found direct correlation between left atrium EMD and increasing age

We also found that left atrium EMD is more prolonged in males than in females, and this may explains why male sex is a risk factor atrial fibrillation as showed by ***(Benjamin et al.,1994).(25)***

The study also showed that smoking prolong left atrium EMD, this goes with a study consisting of 50 smokers and 40 non-smokers, it was found that inter- and intra-atrial electromechanical delay was significantly higher in cigarette smokers compared with non-smokers, and the amount of smoking was strongly correlated with inter-atrial electromechanical delay***(Akturk et al.,2012)(26)***

- **Study limitations**
- Being a cross-sectional study is the major limitation of our study. subjects were not followed prospectively for atrial arrhythmic episodes.
- Our study was conducted in a single center with a relatively small number of participants. This was also a cross-sectional study.
- All subjects were in sinus rhythm during the study, we did not perform Holter examination to investigate presence of atrial arrhythmias in our study population.
- conduction times were determined with tissue Doppler echocardiography, and the gold standard technique, electrophysiological study, was not performed.

CONCLUSION

we found that

- left atrium EMD is prolonged during postprandial condition than during fasting.
- left atrium EMD is prolonged in smokers than in non-smokers.
- Left atrium EMD is prolonged in males more than in females.
- left atrium EMD is prolonged in older age than in younger.

Determining electromechanical events including the atrial conduction time with transthoracic echocardiography is a noninvasive and simple method to measure. Large-scale and long-term follow-up prospective studies are required to establish the predictive value of atrial conduction parameters for the future development of AF in subjects in whom AEMD is found to be prolonged.

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