Original Article

The Effect of Left Atrial Structure and Function on The Atrial Conduction Time in Patients with Paroxysmal Supraventricular Tachycardia

Aalaa Saad Adil[1], Mohammed Ameen Kadhim[2], Ismail Ibrahim Husein[3]

[1]Physiology department, college of medicine, Al-Iraqia University;

[2]Consultant interventional cardiologist and electrophysiologist in Department of Catheterization, Ibn Al-Bitar center for cardiac surgery,

[3]Physiology department, college of medicine, Al-Mustansiriyah University; Baghdad, Iraq.

Abstract

Objectives: To explore the effect of left atrial changes in structure and function on the total atrial conduction time (TACT) and left atrial conduction delay (LACD) in patients with paroxysmal supraventricular tachycardia.

Patients and methods: A cross sectional study, hospital based with analytic element was conducted at Ibn Al-Bitar center for cardiac surgery. Patients were recruited from electrophysiological (EP) lab. The inclusion criteria were the followings: all patients admitted to EP lab for electrophysiological study(EPS) because of episodes of SVT were included. Those patients should: 1) have normal cardiac anatomy and function, 2) be in sinus rhythm and 3) be in a drug-free state. History, general examination and a twelve-lead surface electrocardiography (ECG) were taken. The (EPS) of the heart was conducted. Surface ECG and intracardiac electrograms (EGM) were done simultaneously, and evaluated. (TACT) and (LACD) were recorded. Transthoracic traditional echocardiography was done during one-lead ECG monitoring. All echocardiographic measures were performed, focusing on these parameters: (LA anteroposterior diameter, area and volume). LA functional assessment using the following methods: 1) volumetric method; maximal LA volume (LA V max), minimal LA volume (LA V min), and pre-atrial contraction (LA V pre-A) were measured using apical four- and two-chamber views; and 2) pulsed-wave and tissue Doppler echocardiography methods; late mitral filling (A) velocity and late mitral annular filling (a') velocity measurements.

Results: In our study (110) patients (66 of them were women), 42.22 ± 1.68 years old. We found that there are significant positive correlations of LA V max and LA V min with TACT, and there is a significant negative correlation of (a`) velocity with TACT. Other parameters were having non-significant correlations with TACT and LACD.

Conclusion: Patients with dilated left atrium are more prone for atrial fibrillation due to the prolonged atrial conduction time and dilated atria, in order to take in consideration for the possible risk factors modification.

Keywords: left atrium, electrophysiology, total atrial conduction time, left atrial conduction delay, echocardiography, supraventricular tachycardia.

1. Introduction

The left atrium (LA): is often regarded as a prognostic marker of cardiovascular risk. It carries out three key physiological functions that affect LV filling and performance.

During ventricular systole, it acts as a reservoir for pulmonary venous return; during early ventricular diastole, it serves as a conduit for pulmonary venous return; and

Address for correspondence: Aalaa Saad Adil, Physiology department, college of medicine, Al-Iraqia University

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during late ventricular diastole, it acts as a booster pump to increase ventricular filling. It modulates left ventricular filling and cardiovascular performance in these ways(1). . It is very dynamic and responds to many pathophysiological insults with time-dependent structural, functional, and electrical remodeling. Atrial dilatation, the defining feature of structural remodeling, is typically accompanied with a rise in interstitial fibrosis and structural modifications to the heart (2). A larger LA is associated with poorer cardiovascular outcomes (3).

Increased wall tension brought on by an increase in LA pressure and impairment in LA function related to an atrial myopathy are the most frequent causes of an increase in LA size in the absence of mitral valve disease (6). LA enlargement is a measurement of the severity and recurrence of diastolic dysfunction as well as the magnitude of the increase in LA pressure (4). Electrical and functional continuity of atrial myocytes is necessary for sinus beat transmission through the atria. Atrial conduction time, which is inversely related to atrial conduction velocity, is used to quantify atrial conduction features (5).

Electrophysiology studies (EPS) of the heart: are carried out to identify arrhythmias and classify patients at risk of sudden cardiac death into different risk categories. An electrophysiological investigation includes the measurement of baseline intervals, incremental and decremental pacing of the atria and ventricles with an extra pharmacologic challenge, mapping, and catheter ablation(7). The assessment of total atrial conduction time (TACT) or left atrial conduction delay (LACD) has provided useful information regarding the likelihood of atrial fibrillation development and recurrence(13). The invasive (EPS) of the heart, is considered the gold standard for TACT and LACD assessment. According to previous research(8), a prolonged TACT is a reliable predictor of new-onset atrial fibrillation(AF)(9). Inadequate LA myocardial deformation and a prolonged TACT may indicate early, subclinical cardiac disease(10). LA remodeling may give some insights for early prevention of AF(11). These echocardiographic remodeling markers have been linked to both electrical conduction slowness and localized atrial fibrosis, according to researches on electrophysiologic mapping(12).

Total atrial conduction time (TACT): “formerly known as the Inter-atrial conduction time (IACT)” was determined as the interval between the high right atrium (where the surface ECG's P wave starts) and the distal coronary sinus (beginning of A wave in strip C1-2 in the intracardiac ECG) (13,14,15).

Left atrial conduction delay (LACD): “formerly known as the intra-left atrial conduction time (ILCT)” the time in the intracardiac ECG between the proximal and distal sections of the coronary sinus was known as the left atrial conduction delay (between the beginnings of A waves in the C9-10 and C1-2 in the intracardiac ECG)(13,14,15).

Patients And Methods

The study population: This cross sectional study, was conducted at Ibn Al-Bitar center for cardiac surgery, Baghdad, Iraq. Patients were recruited from EPS lab. All the patients were subjected to an exhaustive medical examination, routine physical examination, including: blood pressure and pulse rate measurement, a twelve-lead conventional ECG, and an echo-Doppler evaluation. The inclusion criteria were the followings: all patients admitted to the EPS lab for EPS because of episodes of SVT included; 1) having normal cardiac anatomy and function, 2) be in sinus rhythm and 3) be in a drug-free state. The exclusion criteria were: 1)congenital heart diseases, 2)moderate or greater valvular disease, 3)atrioventricular blocks, 4)recent myocardial infarction, 5)bundle branch blocks, 6)medications alter cardiac conduction, 7)history of cardiac surgery and 8)diseases affecting cardiac function or structure (like diabetes mellitus, hypertension or thyroid diseases).

Electrophysiological study (EPS): The EPS of the heart was conducted with the SIEMENS CATH. LAB. system. A computer running the EP Tracer (CardioTek, Maastricht, the Netherlands) program was used to receive intracardiac recordings. Conduction times were evaluated at a rate of 150 mm/s while simultaneously recording surface ECG and intracardiac electrograms (EGM). Three catheters—a quadripolar catheter in the right ventricle, a decapolar catheter in the coronary sinus, and an ablation catheter—were introduced through three venous accesses through the femoral vein.

The time between the start of the P wave in the surface ECG and the start of the A wave in strip C1-2 in the intracardiac EGM was used to define TACT. And the time between the onsets of the A waves in the C9-10 and C1-2 of the intracardiac EGM, was used to define LACD. The suggested formula, corrected time = time 800/R-R interval, was used to adjust TACT and LACD for heart rate. Prior to ablation, all measurements were performed in sinus rhythm.

Echocardiography: Using a commercially available ultrasound transducer and apparatus, transthoracic conventional echocardiography was performed while one-lead ECG monitoring was being done on the patients while they were lying in the left lateral decubitus position (3.5 Mhz or M5S probe, Vivid 7 and Vivid E9, GE-Vingmed, Horten, Norway). Measurements were made of all conventional Doppler and echocardiographic parameters.

I. LA's linear measurements: Utilizing M-mode echocardiography, the LA anteroposterior (AP) diameter was assessed in the parasternal long-axis view. Using the leading-edge to leading-edge protocol, AP diameter of LA was measured in the parasternal long-axis view, perpendicular to the aortic root long axis, at the level of the aortic sinuses. On the basis of tracings of the blood-tissue interface on apical four- and two-chamber views, LA volume was calculated using 2D echocardiography (2DE). By drawing a straight line connecting the two opposing portions of the mitral annulus,

the contour is closed at the mitral valve level. All values were indexed to body surface area (BSA) were reported.

II. LA functional assessment: 1. Volumetric method: At various times during the cardiac cycle, LA volumes were measured in order to evaluate the phasic functions using the volumetric method: On an ECG, the maximal LA volume (LA V max) occurs at the end of the T wave, just before the mitral valve opens; the minimal LA volume (LA V min) occurs at the QRS complex, just as the mitral valve closes; and the pre-atrial contraction (LA V pre-A) occurs at the start of the P wave. Biplane length area method was depended which employ apical four- and two-chamber views.

2. Pulsed-wave Doppler study method: From the apical four-chamber view, pulsed wave Doppler is utilized to record the mitral inflow. Early (E) and late diastolic (A) peak velocities, or "A velocity" that indicates atrial contraction," were determined, along with their ratio, from the LV inflow.

3. Tissue Doppler imaging method: Early (e') and late diastolic (a') velocities at the mitral lateral and medial annulus were measured. Calculations were made to determine the ratio of the E-wave velocity to the average early mitral annular (e') velocity (E/e'). From the four-chamber view, the sample volume is located on the annulus, near to the mitral valve's insertion point. Both lateral and septal (medial) sites were noted. Sweep velocity was 66 cm/s.

Statistical Analysis: To identify the impact of various factors on study parameters, the Statistical Analysis System- SAS (2012) application was employed. To significantly compare between means, the T-test and Least Significant Difference (LSD) test (Analysis of Variation, ANOVA) were utilized (0.05 and 0.01 probability). Estimation of correlation coefficient between the study's variables was done (16).

RESULTS

The total sample size was (110) patients (66 of them were women), 42.22 ± 1.68 years old were enrolled in the study. All parameters examined were in table (1) and (2). In our study we found significant positive correlations of LA maximal and minimal volumes with TACT, and there is a significant negative correlation with a` velocity. Other parameters were having non-significant correlations with TACT and LACD, table (3) and (4).

Table 1: electrophysiological parameters

Parameters	*Gender*		*T-test*
	Male	*Female*	
TACT(msec.)	82.88 ±2.42	80.60 ±1.64	5.23 NS
LACD (msec.)	30.22 ±1.52	26.75 ±0.88	3.16 *
TACT (corr.) (msec.)	107.72 ±4.89	101.96 ±3.01	10.58 NS
LACD (corr.) (msec.)	39.42 ±2.35	33.65 ±1.22	4.84 *

* (P≤0.05), ** (P≤0.01), NS: Non-Significant.

TACT: total atrial conduction time, LACD: left atrial conduction delay, Corr.: corrected, , ind: indexed to surface area.

Table 2: echocardiographic parameters

Parameters	*Gender*		*T-test*
	Male	*Female*	
EF (%)	63.43 ±0.69	61.78 ±0.89	2.44 NS
LA D (cm)	2.93 ±0.09	2.92 ±0.06	0.202 NS
LA D Ind (cm/m2)	1.48 ±0.04	1.55 ±0.02	0.101 NS
LA V (max)(ml)	36.47 ±1.91	34.68 ±1.49	4.39 NS
LA V max ind (ml/m2)	18.26 ±0.86	18.33 ±0.74	2.21 NS
LA V (min) (ml)	15.56 ±0.90	15.80 ±0.88	2.41 NS
LA V (min) Ind (ml/m2)	7.82 ±0.42	8.38 ±0.46	1.27 NS
LA V (PreA) (ml)	23.54 ±1.10	23.95 ±1.11	2.96 NS
LA V (PreA) Index (ml/m2)	11.84 ±0.52	12.64 ±0.56	1.55 NS
Doppler flow parameters:			
E velocity (m/sec)	0.739 ±0.02	0.747 ±0.02	0.054 NS
A velocity (m/sec)	0.623 ±0.03	0.690 ±0.02	0.058 *
E/A ratio	1.27 ±0.07	1.12 ±0.03	0.106 *
Tissue Doppler parameters:			

e` velocity (m/sec)	0.132 ±0.01	0.128 ±0.01	0.011 NS
e`/a` ratio	1.61 ±0.12	1.35 ±0.06	0.221 *
E/e ratio	5.78 ±0.21	6.09 ±0.23	0.637 NS

* (P≤0.05), ** (P≤0.01), NS: Non-Significant.

EF:ejection fraction, LA D: left atrial diameter, LA V max: left atrial maximal volume, LA V min: left atrial minimal volume, LA Pre A V: left atrial pre-atrial volume, ind: indexed to surface area, E velocity: early filling velocity A velocity: late filling velocity, E/A ratio: early to late filling velocities ratio, a` velocity: late annular velocity, e`/a` ratio: early to late annular velocities ratio, E/e` ratio: early filling to early annular velocities ratio.

Table 3: Correlation coefficient between some left atrial changes in structures with TACT and LACD.

Parameters	*Correlation coefficient-r*			
	TACT	*Corr. TACT*	*LACD*	*Corr. LACD*
LA D	0.13 NS	-0.02 NS	0.009 NS	-0.09 NS
LA D index	0.06 NS	0.06 NS	-0.04 NS	-0.03 NS
LA V max	0.19 *	0.05 NS	0.04 NS	-0.03 NS
LA V max index	0.15 NS	0.07 NS	0.02 NS	-0.02 NS
LA V min	0.20 *	0.07 NS	0.04 NS	-0.02 NS
LA min. V Ind.	0.16 NS	0.09 NS	0.02 NS	-0.01 NS
LA Pre A V	0.16 NS	0.12 NS	0.04 NS	0.04 NS
LA V PreA Ind	0.13 NS	0.15 NS	0.01 NS	0.06 NS

* (P≤0.05), NS: Non-Significant.

TACT: total atrial conduction time, LACD: left atrial conduction delay, Corr.: corrected, LA D: left atrial diameter, LA V max: left atrial maximal volume, LA V min: left atrial minimal volume, LA Pre A V: left atrial pre-atrial volume, ind: indexed to surface area,

Table 4: Correlation coefficient between some left atrial changes in function with TACT and LACD.

Parameters	*Correlation coefficient-r*			
	TACT	*Corr. TACT*	*LACD*	*Corr. LACD*
A velocity	0.07 NS	0.09 NS	-0.11 NS	-0.07 NS
E/A ratio	-0.14 NS	-0.12 NS	-0.004 NS	-0.02 NS
a` velocity	-0.21 *	-0.17 NS	-0.17 NS	-0.17 NS
e`/a` ratio	0.08 NS	0.14 NS	0.11 NS	0.14 NS
E/e` ratio	-0.04 NS	-0.04 NS	0.03 NS	0.03 NS

* (P≤0.05), NS: Non-Significant.

TACT: total atrial conduction time, LACD: left atrial conduction delay, Corr.: corrected, A velocity: late filling velocity, E/A ratio: early to late filling velocities ratio, a` velocity: late annular velocity, e`/a` ratio: early to late annular velocities ratio, E/e` ratio: early filling to early annular velocities ratio.

Discussion

There are significant positive correlations of LA maximal and minimal volumes with TACT, these results agree with Ramanathan Parameswaran who revealed that electrophysiologic abnormalities, such as global and regional conduction slowing and changes in refractoriness that predispose to the formation of atrial arrhythmias, emerge concurrently with structural change(17). Also agree with Jan-Thorben Sieweke, et al. who reported that echocardiographic measures indicating LA dysfunction and remodeling have a remarkable potential to predict subclinical AF in patients with embolic stroke of unknown source(18).

Acute atrial stretch increases the likelihood of arrhythmias via modulating atrial electrophysiology through stretch-activated channels(19). Acute atrial dilatation lowered both the atrial effective refractory period and the atrial post-repolarization refractoriness, favoring the onset and maintenance of AF(20). Despite the changes in electrophysiological characteristics stated, the triggered

activity and atrial arrhythmias increased in the presence of acute atrial stretch. This demonstrates the multifactorial impact of atrial stretch on atrial electrophysiology(22).

However, in some cases, the typical course of cardiac impulse is disrupted and can start re-entry and result in "circus motions," which then result in fibrillation (e.g. dilated hearts have a typically long journey; interatrial blockage, muscle ischemia usually cause a slowed pace of conduction; and a shorter refractory period). Re-entry can result in abnormal heart rhythms or improper cardiac contraction patterns in many cardiac disorders(23).

Another explanation is that the participants may be in a condition of prediabetes, which puts them at a relatively higher risk for cardiovascular disease, similar to diabetes mellitus(24). Another factor causing this association is the impact of hyperglycemia on atrial tissue(25). Interstitial fibrosis, which results from extracellular protein deposition and inflammatory responses, may eventually cause atrial refractoriness and heterogeneity in atrial conduction(26). Hyperglycemia activates the glycosylation end products-receptor system, raising the levels of circulating tissue growth factors and augmenting atrial structural remodeling(27).

Chronic changes in atrial tissue thought to result from the hyper or hypoglycemias are what lead to heterogeneity in atrial conduction time and atrial refractoriness(28). Prediabetics had considerably longer TACT and LACD than non-diabetics, which are predictors of the onset of AF. This finding raises the possibility that prediabetic people may be more susceptible to AF even before diabetes manifests itself. Before the onset of overt diabetes, LA mechanical functions and conduction times were deteriorated(29).

In our study; there is a significant negative correlation of the a` velocity with the TACT this result disagree with Necla Özer, et al. However, they utilized a different non-invasive echocardiographic technique to detect TACT. Another difference is that the study population consisted of patients with mitral stenosis, which may have contributed to the positive correlation between TACT with a` velocity and other doppler parameters. The previous study shows that TACT gets longer in patients with mitral stenosis and TACT is related with left atrial size, but not with severity of mitral stenosis(30).

Our findings could be explained by the fact that in response to the excessive volume burden, the left atrium engages in a variety of adaptive and maladaptive phases. These may include myocyte growth, hypertrophy, and then necrosis and apoptosis, as well as changes in the extracellular matrix's composition, such as excessive fibroblast proliferation that causes myolysis and, as a result, the loss of the contractile apparatus(31).

There are non-significant correlations of E/A and e`/a` ratios with TACT. e`/a` ratio was found to be useful in the estimation of LV end-diastolic pressure(32). Atrial conduction delay was linked to higher left atrial pressure and worsened LV relaxation. Left atrial dilatation, elevated left atrial pressure, and poor LV relaxation were all evident in patients with paroxysmal AF, and these conditions were linked to significantly prolonged TACT(33).

Rosenberg MA, et al. revealed a greater LA diameter in the prediabetic group compared with the control group. They also detected a weak correlation between (TACT) with E/A and e`/a` ratios, although it was weak(38).

But our results disagree with Eftal Murat Bakirci, et al. who concluded that TACT had negative correlations with the E velocity and E/A ratio. This explained by that the population for that study was on type 2 diabetic patients and when combined with poor left atrial myocardial deformation, subclinical atherosclerosis and inflammation may be a result of prolonged TACT and early subclinical cardiac involvement in people with type 2 diabetes mellitus (10). Additionally, people with type 2 diabetes may have a normal E/e' ratio but an abnormal e'/a' ratio. The diastolic dysfunction of the left ventricle can be detected by significant increases in a' velocity and significant decreases in the E velocity, E/A, and e'/a' ratio. Diastolic left ventricular dysfunction is more common in asymptomatic diabetes patients, who also have wider necks and bigger abdomens than control group(34,35,36). Although there is a non-significant positive correlation of A velocity with TACT, so this may explain the prolonged TACT in obese patients with higher A velocity whose may have asymptomatic left ventricular diastolic dysfunction. So there may be a development of obesity, which has been linked to the growing adipose tissue's hypoxia, leading to adipose tissue fibrosis. (37).

Conclusion

There are significant positive correlations of left atrial maximal and minimal volumes with the total atrial conduction time (TACT), and there is a significant negative correlation with the late mitral annular (a`) velocity. Patients with dilated left atrium are more prone for atrial fibrillation due to the prolonged atrial conduction time and enlarged stiff atria, in order to take in consideration for the possible risk factors modification.

Compliance with Ethical Standards statements

Ethical approval: Physiology department, college of medicine, Al-Iraqia University, Funding details (In case of Funding): I am responsible for paying the financing, Conflict of interest: There is no conflict of interest, Informed Consent: Physiology department, college of medicine, Al-Iraqia University Agreed

References

Blume GG, McLeod CJ, et al. Left atrial function: physiology, assessment, and clinical implications. 2011 Eur J Echocardiogr 2 421–430.

Kallergis EM, Manios EG, et al. Extracellular matrix alterations in patients with paroxysmal and persistent atrial fibrillation: biochemical assessment of collagen type-I turnover. 2008 J Am Coll Cardiol 52 211–215.

Bouzas-Mosquera A, Broullon FJ, et al. Left atrial size and risk for all-cause

mortality and ischemic stroke 2011 Can Med Assoc J 183 E657 – E664.

Geske JB, Sorajja P, et al. The Relationship of Left Atrial Volume and Left Atrial Pressure in Patients With Hypertrophic Cardiomyopathy: An Echocardiographic and Cardiac Catheterization Study 2009 J Am Soc Echocardiogr 22 961–966.

Guron CW, Hartford M, et al. Usefulness of atrial size inequality as an indicator of abnormal left ventricular filling. 2005 Am J Cardiol 95 1448–1452.

Ersboll M, Anderson MJ, et al. The prognostic value of left atrial peak reservoir strain in acute myocardial infarction is dependent on left ventricular longitudinal function and left atrial size 2013 Circ Cardiovasc Imaging 6 26-33.

Hafsa Majeed; Yasar Sattar. Electrophysiologic Study Indications And Evaluation 2022 In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

Den Uijl DW, Gawrysiak M, et al. Prognostic value of total atrial conduction time estimated with tissue Doppler imaging to predict the recurrence of atrial fibrillation after radiofrequency catheter ablation 2011 Euro-pace 13 1533–40.

De Vos CB, Weijs G, et al. Atrial tissue Doppler imaging for prediction of new onset atrial fibrillation 2009 Heart 95 10 835–40

Eftal Murat Bakirci, et al. Relationship of the total atrial conduction time to subclinical atherosclerosis, inflammation and echocardiographic parameters in patients with type 2 diabetes mellitus 2015 CLINICS 70 2 73-80.

Hsiang-Chun Lee, Shyi-Jang Shin, et al. The role of postprandial very-low-density lipoprotein in the development of atrial remodeling in metabolic syndrome 2020 Lipids in Health and Disease 19 210.

Nattel S, Burstein B, Do, et al. Atrial remodeling and atrial fibrillation: mechanisms and implications 2008 Circ Arrhythm Electrophysiol 1 62–73.

Ali Deniz, Levent Sahiner, et al. Tissue Doppler echocardiography can be a useful technique to evaluate atrial conduction time 2012 Cardiology Journal 19 5 487–493

Fatma Hizal Erdem, Alim Erdem, et al. Electrophysiological validation of total atrial conduction time measurement by tissue doppler echocardiography according to age and sex in healthy adults 2016 Journal of Arrhythmia 232 127–132.

Ali Bozorgi, Maryam Khoshnevis, et al. Agreement Between Electrophysiology Study and Tissue Doppler Imaging Regarding the Measurement of Total Atrial Conduction Time and Left Atrial Conduction Delay 2020 Ultrasound in Medicine & Biology 46 3 544-556.

SAS. 2012. Statistical Analysis System, User's Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.

Ramanathan Parameswaran, et al. Left Atrium and Cardiovascular Risk: Does Functionality Matter More Than Size 2018 Journal of the American Heart Association 7 7.

Jan-Thorben Sieweke, Saskia Biber, et al. Septal total atrial conduction time for prediction of atrial fibrillation in embolic stroke of unknown source: a pilot study 2020 Clinical Research in Cardiology 109 205–214.

Kannel WB, Abbott RD, et al. Epidemiologic features of chronic atrial fibrillation: the Framingham study 1982 N Engl J Med 306 1018–22.

Peter Milberg, Gerrit Frommeyer, et al. Sodium channel block by ranolazine in an experimental model of stretch-related atrial fibrillation: prolongation of interatrial conduction time and increase in post-repolarization refractoriness 2013 Europace 15 761–769.

Calkins H, el-Atassi R,et al. Effects of an acute increase in atrial pressure on atrial refractoriness in humans. 1992 Pacing Clin Electrophysiol 15 1674–80.

Chen YJ, Chen SA, et al. Role of atrial electrophysiology and autonomic nervous system in patients with supraventricular tachycardia and paroxysmal atrial fibrillation 1998 J Am Coll Cardiol 32 732–8.

Guyton and Hall 2020 Textbook of Medical Physiology, 14 edition CH. 13 161-162.

American Diabetes Association. Diagnosis and classification of diabetes mellitus 2013 Diabetes Care 36 1 S67-S74.

Lip GY, Varughese GI. Diabetes mellitus and atrial fibrillation: perspectives on epidemiological and pathophysiological links 2005 Int J Cardiol 105 319-321.

Kato T, Yamashita T, et al. What are arrhythmogenic substrates in diabetic rat atria? 2006 J Cardiovasc Electrophysiol 17 890-894.

Kato T, Yamashita T, et al. AGEs-RAGE system mediates atrial structural remodeling in the diabetic rat 2008 J Cardiovasc Electrophysiol 19 415-420.

Karabag T, Aydin M, et al. Prolonged P wave dispersion in pre-diabetic patients 2011 Kardiol Pol 69 566-571.

Naile Eris Gudul, Turgut Karabag, et al. Atrial conduction times and left atrial mechanical functions and their relation with diastolic function in prediabetic patients. 2017 Korean J Intern Med. 32 2 286–294

Necla Özer, BünyaminYavuz, et al. Doppler Tissue Evaluation of Intra-atrial and Interatrial Electromechanical Delay and Comparison with P-wave Dispersion in Patients with Mitral Stenosis 2005 Journal of the American Society of Echocardiography 18 9 945-948

M. Cameli, M. Lisi, et al. Usefulness of atrial deformation analysis to predict left atrial fibrosis and endocardial thickness in patients undergoing mitral valve operations for severe mitral regurgitation secondary to mitral valve prolapse 2013 Am. J. Cardiol. 111 4 595–601.

Dagdelen S, Eren N, Karabulut H, et al. Estimation of left ventricular end-diastolic pressure by color M-mode Doppler echocardiography and tissue Doppler imaging 2001 J Am Soc Echocardiogr 14 951-8.

Ivan Vranka, Peter Penz, et al. Atrial conduction delay and its association with left atrial dimension, left atrial pressure and left ventricular diastolic dysfunction in patients at risk of atrial fibrillation 2007 Exp Clin Cardiol 12 4 197-201.

Aalaa S. Adil. The left ventricular diastolic dysfunction in asymptomatic type 2 diabetes mellitus patients. A Master thesis, Al-Mustansiryah university, 2015.

Abbas N Al Sharify, Ismail I Hussain, Aalaa S Adil. The detection of left ventricular diastolic dysfunction in patients with type 2 diabetes mellitus by tissue Doppler imaging 2016 IRAQI JOURNAL OF COMMUNITY MEDICINE, 29 3 158-167.

SM Ghazi, II Hussain, AS Adil Cholesterol and Triglyceride Indices Are Linked to the Left Ventricle Diastolic Dysfunction: An Echocardiography and Tissue Doppler Study 2019 Indian Journal of Public Health Research and Development 10 4 1485-1490.

Sun K, Halberg N, Khan M, et al. Selective inhibition of hypoxia-inducible factor 1a ameliorates adipose tissue dysfunction 2013 Mol Cell Biol 33 904–17.

Rosenberg MA, Manning WJ. Diastolic dysfunction and risk of atrial fibrillation: a mechanistic appraisal. Circulation 2012;126:2353-2362.