A Preliminary Study of Left Atrial Function and Left Atrial Stiffness in Type 2 Diabetic Patients with Normotensive Patients Without Symptomatic Cardiovascular Disease

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Research Article

Keywords: Left atrial stiffness index, tow-dimensional speckle tracking imaging, type 2 diabetes mellitus

Posted Date: May 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-511000/v1

Abstract

Background: The purpose of this study was to investigate the relationship between left atrial function and left atrial stiffness in type 2 diabetic patients.

Methods: A total of 41 healthy subjects (controls) and 39 patients with type 2 diabetes mellitus (DM2 patients) were enrolled in this study. The left atrial volume index was measured by biplanar Simpson method. The early and late diastolic velocities (e'and a') were measured by tissue Doppler in lateral and septal boeder of the mitral annulus. Lateral and septal myocardial velocities were averaged. E/e ratio was computed.The peak atrial longitudinal strain (PALS) was analyzed by tow-dimensional speckle tracking imaging (2D-STI) technique.The ratio of E/e ' to PALS was used as an indicator of LASI.

Results: The maximum volume (LAVImax), minimum volume (LAVImin) and pre-contraction volume (LAVIpre) of the left atrium in DM2 patients were significantly higher than those in the control groups, and the differences were statistically significant (P<0.05). The difference between PALS decrease and LASI increase was statistically significant (P<0.05).PALS and LASI were statistically correlated with three phase volume index of left atrial and E/e'ratio. LASI was superior to PALS and left atrial volume index in diagnosing diabetic normotensive patients without symptomatic cardiovascular disease.

Conclusion: Compared with the controls, PALS decreased and LASI increased in DM2. PALS and LASI were significantly correlated with left atrial volume and E/e'. LASI showed the highest diagnostic efficacy in the diagnosis of diabetes. PALS and LASI can be used as indicators for early evaluation of left atrial function in patients with DM2.

Trial registration number:+86-17856931224;date of registration:May 3,2021

Introduction

The prevalence of type 2 diabetes mellitus (DM2) increases with age, obesity epidemic and sedentary lifestyle changes.The risk of cardiovascular disease increases,resulting in significant cardiac morbidity and mortality [1]. In DM2, these patients may have related changes in cardiac function before the onset of clinical symptoms. The early changes of left ventricular function in patients with DM2 have been widely studied[2-7], and the evaluation of left atrial (LA) function has attracted more and more attention.

Left atrial stiffness index ((LASI) is a new index proposed in recent years, which is calculated by two-dimensional speckle tracking imaging (2D-STI), provides an alternative method to explore the function of LA and detect the early changes of myocardial performance in LA.Some studies have shown that LASI increases with atrial remodeling, reflecting the deterioration of reserve function [8, 9]. Therefore, the purpose of this study is to evaluate the abnormality of left atrial function in patients with type 2 diabetes mellitus by 2D-STI, and to explore the correlation between LASI and left atrial function.

Materials And Methods

Selection of the Patients

Thirty-nine patients with DM2 with normal blood pressure in the outpatient or inpatient department of our hospital from October 2020 to October 2021 were selected, including 19 males and 20 females. Inclusion criteria for DM2 [10]: Nüchternglukose (venöses Plasma)≥7.0mmol/L, 2-h-Glukose nach 75g OGTT (venöses Plasma) ≥11.1mmol/L, HbA1c ≥6.5% or Nicht-Nüchtern („Random-Glucose“,venös oder kapillär) ≥11.1mmol/L. All patients with DM2 had normal blood pressure and no related clinical complications. Another 41 healthy subjects matched with the above-mentioned age and sex were selected as the control group, including 18 males and 23 females.

This study was approved by the Medical Ethics Committee of our hospital, and all the participants signed the informed consent form before participating in the study.

Echocardiographic measurements

All patients were examined by the same researcher using PhilipsEPIQ7C (S5-1 probe, frequency 1-5MHz) color Doppler echocardiography. Connect the single-lead ECG during the examination. All patients were in sinus rhythm at the time of examination.

The left ventricular end-diastolic diameter (LVEDd), left atrial anterior-posterior diameter(LAAD), interventricular septum thickness(IVSd) and left ventricular posterior wall thickness(LVPWd) were routinely measured on the long-axis view of the left ventricle. Mitral flow patterns were recorded in apical four-chamber view. Peak early diastolic filling velocity(E), peak late diastolic filling velocity (A) and E/A ratio were measured by Pulsed Doppler blood flow spectrum. The early and late diastolic velocities (e'and a') were measured by tissue Doppler in lateral and septal boeder of the mitral annulus. Lateral and septal myocardial velocities were averaged. E/A and E/e′ ratios were computed.The left ventricular ejection fraction (LVEF) was measured by Simpson method in apical four-chamber and two-chamber view.The maximum, minimum and before atrial contraction volumes of left atrium were measured at the end of T wave, the peak of R wave and the beginning of P wave. Each parameter shoule be measured at least three times continuously, and then the average value was be calculated. Left atrial maximum volume index (LAVImax),before atrial contraction volume index (LAVIp) and left atrial minimum volume index (LAVImin) were obtained by body surface area (BSA) to exclude individual differences.Left atrial passive emptying volume (LAVIp)), left atrial active emptying volume(LAVIa),total left atrial emptying volume (LAVIt),total left atrial emptying fraction (LAVtEF),left atrial passive emptying fraction (LAVpEF) and left atrial active emptying fraction (LAVaEF) were calculated.

Measurement of left atrial stiffness (LASI)[11]

The two-chamber and four-chamber dynamic two-dimensional cardiac cycle data were collected and analyzed by Qlab10.5 workstation software,and PALS was measured by2D-STI,E/e' ratio to PALS was obtained to calculate LASI.

All above measurements were calculated from three consecutive cycles at least. Average of the three measurements was recorded.

Statistical methods

SPSS22.0 software was used for statistical analysis.All the parameters are tested by normal test, and the continuous variables in accordance with the normal distribution are expressed in the form of mean ±standard deviation. The independent samples' t-test was used to compare the differences between the two groups,and the chi-squared test was used to classify variables. The correlation was evaluated by Pearson correlation coefficient, and the diagnostic efficiency was analyzed by ROC curve. The difference was statistically significant ($P < 0.05$).

Results

In the evaluation of basic clinical characteristics, there was no significant difference in age, sex, BMI and blood pressure between the two groups. HbAlc and blood lipids in the diabetic group were significantly higher than those in the control group. (all $P<0.05$).(Table 1)

There was no significant difference in LAAD,LVEDd,IVSd,LVPWd and LVEF between the two groups. E,E/A ratio and e' in DM2 group were lower than those in normal control group, but A was higher than that in normal control group, and the difference was statistically significant (all $P < 0.05$). Compared with the normal control group, E/e' of DM2 patients was higher, and the difference was statistically significant ($P < 0.05$).(Table 2)

The levels of LAVImax(26.76±5.44vs. 23.23±5.01 ml/□), LAVImin(12.26±2.22vs. 9.10±2.28 ml/□) and LAVIpre(19.58±2.89vs. 16.86±2.87 ml/□) in DM2 group were significantly higher than those in normal control group($P < 0.05$ for all). There was no significant difference in LAVIp, LAVIa, LAVIt and LAVpEF($P >0.05$ for all). Compared with the normal control group, PALS(30.19±4.96vs. 38.00±4.23 %) decreased and LASI(0.33±0.82vs. 0.21±0.05 ml/□) increased in DM2 patients, and the difference was statistically significant($P < 0.05$ for all).(Table 3)

Figure 1 illustrates the correlation between PALS and left atrial volume index and E/e'. There was a significant negative correlation between PALS and LAVImax($r=-0.425$□$P<0.001$), LAVImin($r=-0.582$□ $P<0.001$), LAVIpre($r=-0.544$□$P<0.001$) and E/e' ($r=-0.255$□$P=0.022$) in the whole study population.(Figure 1)

Figure 2 illustrates the correlation between LASI and left atrial volume index and E/e'. There was a significant positive correlation between LASI and LAVImax($r=0.610$□$P<0.001$), LAVImin($r=0.651$□$P<0.001$), LAVIpre($r=0.613$□$P<0.001$) and E/e' ($r=0.804$□$P<0.001$) in the whole study population.(Figure 2)

We conducted a subgroup analysis to evaluate the effects of HbAlc on left atrial volume index, PALS and LASI. The results showed that there was no significant difference of HbAlc on left atrial volume index, PALS and LASI between normal control group and DM2 group($P>0.05$).

ROC curves demonstrating the predictive power of the five LA parameters are presented in Figure 3. LASI showed the highest diagnostic efficiency in the diagnosis of diabetes, and the area under the ROC curve was 0.904.LASI with the cutoff value of 27.5% showed a high specificity(90.2%) in the diagnosis of diabetes,with a sensitivity of 74.4%.

Table1. Comparison of clinical basic parameters between DM2 patients and controls.

	DM2 patients（n=39）	Controls（n=41）	p vaule
Age(years)	48.03±6.69	45.41±7.52	0.106
Sex(n,%)males	19(48.7%)	18(43.9%)	0.666
BMI（kg/㎡）	22.72±3.00	23.87±2.57	0.7
HbAlc（%）	8.04±2.33	4.82±0.35	<0.001
SBP(mmHg)	119±10	120±11	0.562
DBP(mmHg)	75±10	74±10	0.828
TC(mmol/L)	5.23±1.14	4.50±0.61	0.001
TG(mmol/L)	1.56±0.49	1.33±0.45	0.033
HDL(mmol/L)	1.38±0.26	1.51±0.24	0.033
LDL(mmol/L)	3.27±0.80	2.48±0.50	<0.001

BMI: body mass index; HbA1c: glycosylated hemoglobin; SBP:systolic blood pressure,DBP: diastolic blood pressure; TC: total cholesterol; TG: triglyceride;HDL:High density lipoprotein; LDL:Low density lipoprotein

Table2. Comparison of parameters between DM2 patients and controls of conventional echocardiography

	DM2 patients（n=39））	Controls（n=41）	p vaule
LAAD（mm)	34.62±3.61	33.31±3.42	0.102
LVEDd（mm)	45.38±3.54	44.85±3.57	0.507
IVSd（mm)	8.76±0.82	8.72±0.83	0.808
LVPWd（mm)	8.54±0.78	8.49±0.79	0.803
LVEF（%)	61.48±2.63	62.48±3.05	0.123
E（cm/s)	80.31±14.21	91.45±12.20	<0.001
A（cm/s)	72.92±8.17	57.07±10.12	<0.001
E/A	1.07±0.25	1.63±0.28	<0.001
Averaged e'(cm/s)	8.35±1.55	11.94±2.02	<0.001
Averaged a'(cm/s)	10.31±1.76	10.34±1.73	0.927
E/e'	9.80±1.89	7.91±1.88	0.006

LVEDd:left ventricular end-diastolic diameter;LAAD:left atrial anterior-posterior diameter;IVSd:interventricular septum thickness; LVPWd:left ventricular posterior wall thickness; E: peak early diastolic filling velocity, A: peak late diastolic filling velocity, e': peak early diastolic velocity of the mitral annulus, a': peak late diastolic velocity of the mitral annulus.

Table3. Comparison of left atrial volume, PALS and LASI between DM2 patients and controls.

	DM2 patients（n=39）	Controls（n=41）	p vaule
LAVImax（ml/㎡）	26.76±5.44	23.23±5.01	0.003
LAVImin（ml/m²）	12.26±2.22	9.10±2.28	<0.001
LAVIpre（ml/m²）	19.58±2.89	16.86±2.87	<0.001
LAVIp（mL）	7.18±3.84	6.37±3.49	0.328
LAVIa（mL）	7.32±2.12	7.76±2.08	0.353
LAVIt（mL）	14.50±4.46	14.13±3.92	0.695
LAVtEF（%）	53.29±8.63	60.38±8.31	<0.001
LAVpEF（%）	25.45±10.46	26.05±10.94	0.803
LAVaEF（%）	37.18±8.52	46.06±9.84	<0.001
PALS（%）	30.19±4.96	38.00±4.23	<0.001
LASI	0.33±0.08	0.21±0.05	<0.001

LAVImax: left atrial maximum volume index; LAVImin: left atrial minimum volume index; LAVIpre: atrial pre-systolic left atrial volume index; LAVIp: left atrial passive emptying volume; LAVIa: left atrial active emptying volume; LAVIt: left atrial total emptying volume; LAVtEF: total left atrial emptying fraction; LAVpEF: left atrial passive emptying fraction; LAVaEF: active left atrial emptying fraction; PALS: peak atrial longitudinal strain; LASI: left atrial stiffness index

Discussion

Our study mainly found that LASI increased and PALS decreased in patients with DM2 compared with normal controls. LASI and PALS were significantly correlated with left atrial volume index and E/e'. LASI is superior to PALS and left atrial volume index in diagnosing left atrial function parameters in patients with diabetes.

The standard LASI calculation formula is：LASI=LAP/PALS, LAP refers to left atrial pressure, which needs to be measured by catheter in the left atrium. It is an invasive measurement, which can not be promoted because of limited clinical application, and there are few related clinical studies. In the course of the study, Mahfouz et al.[12] used E/A and E/e’to replace LAP, and found that E / e’/ PALS had the highest correlation with LAP/PALS, which could be used for the non-invasive determination of LASI.So in our research, we use E/e'/PALS to calculate LASI. Previous studies have shown that impaired left atrial mechanical function is associated with atrial fibrillation, and LASI is significantly increased in patients with atrial fibrillation, which is positively correlated with left atrial volume index [13, 14]. Similarly, in our study, we found that PALS decreased and LASI increased in patients with DM2, which may be related to

long-term disturbance of blood glucose metabolism in diabetic patients, leading to microvascular fibrosis, local myocardial interstitial fibrosis, and later atrial arrhythmias and strokes are more common in these patients. It is well known that patients with type DM2 have a higher risk of atrial fibrillation, and a significant correlation between higher HbAlc and the future development of atrial fibrillation has been confirmed [15].

There was no significant correlation between HbAlc and left atrial volume index, PALS and LASI, suggesting that the changes of left atrial volume and functional parameters were not affected by blood glucose control in the near future. Previous studies have confirmed that LA function is impaired and left atrial volume is increased in DM2 patients with normal blood pressure and asymptomatic cardiovascular disease. Although the mechanism of this damage is unclear, atrial myocardial damage caused by persistent hyperglycemia and LA fibrosis has been considered to be a pathogenic factor[16, 17]. Compared with the control group, the left atrial volume index of DM2 patients increased, the difference was statistically significant, while the LAAD value of the two groups changed little, the difference was not statistically significant. This may be due to the fact that the left atrium is a three-dimensional structure, and when the left and right diameters increase at the same time, there will be a significant difference in volume. In addition, we also found that in patients with DM2, the ratio of Eram An and the early diastolic filling velocity of mitral annulus by tissue Doppler decreased, while the ratio of E/e'mean increased, suggesting that the left ventricular diastolic function was impaired to some extent.

In our study, we compared the diagnostic efficacy of left atrial volume index, PALS and LASI in predicting changes in left atrial function parameters in DM2 patients with normal blood pressure and asymptomatic cardiovascular disease. Our data show that LASI has a high positive predictive value, showing sensitivity (74.4%) and high specificity (90.2%) when the cutoff value is 27.5%. Although the area under the curve of LASI and PALSROC is similar, the difference between the enlarged sample size of LASI is higher than that of PALS, may be more obvious.

This study has some limitations:1.the sample size is small, so we can only do a preliminary study, and we still need to expand the sample size to further verify different taxonomic groups;2.the independent predictors of LA function changes in DM2 patients cannot be determined;3our study is not prospective and there is no follow-up of arrhythmias in patients. 4.At present, there is no 2D-STI analysis software for left atrial strain, but the accuracy of PALS, results calculated by left ventricular analysis software is affected to some extent.

Conclusions

Patiens with DM2 have increased left atrial volume index.LASI can accurately reflect the early changes of left atrial structure and function in DM2 patients with normal blood pressure and asymptomatic cardiovascular disease, which provides a reliable basis for early clinical intervention.

Declarations

The fund project is the special project fund for the central government to guide local science and technology development in Anhui Province (No. 2017070802D152).

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.Our materials and data are true and reliable. This study was approved by the Medical Ethics Committee of our hospital, and all participants signed informed consent before participating in the study.In this study, 80 patients agreed to participate in the study and agreed to publish their datas in journal articles.

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Figures

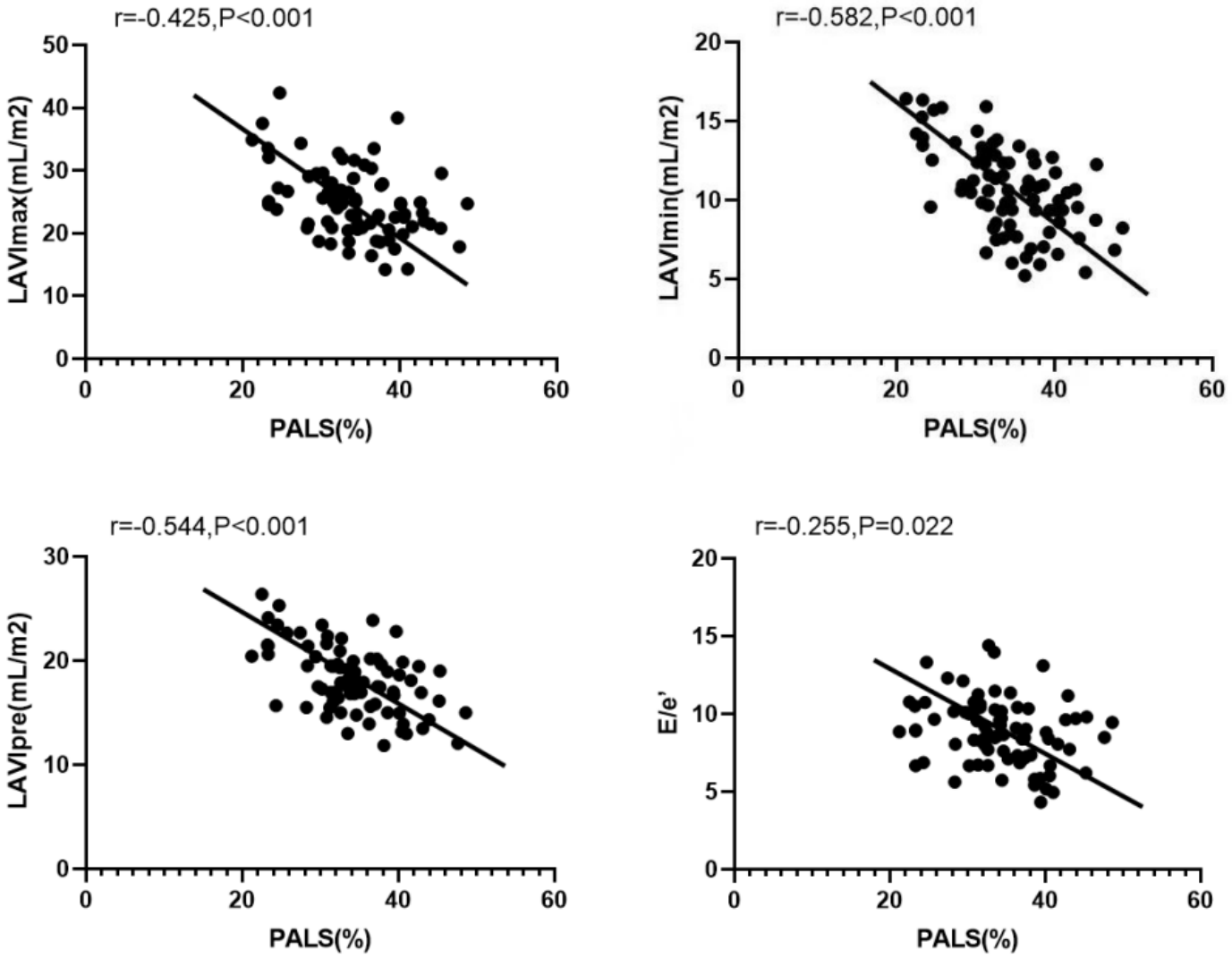

Figure 1

Correlation of PALS and LAVImax , LAVImin ,LAVIpre and E/e'

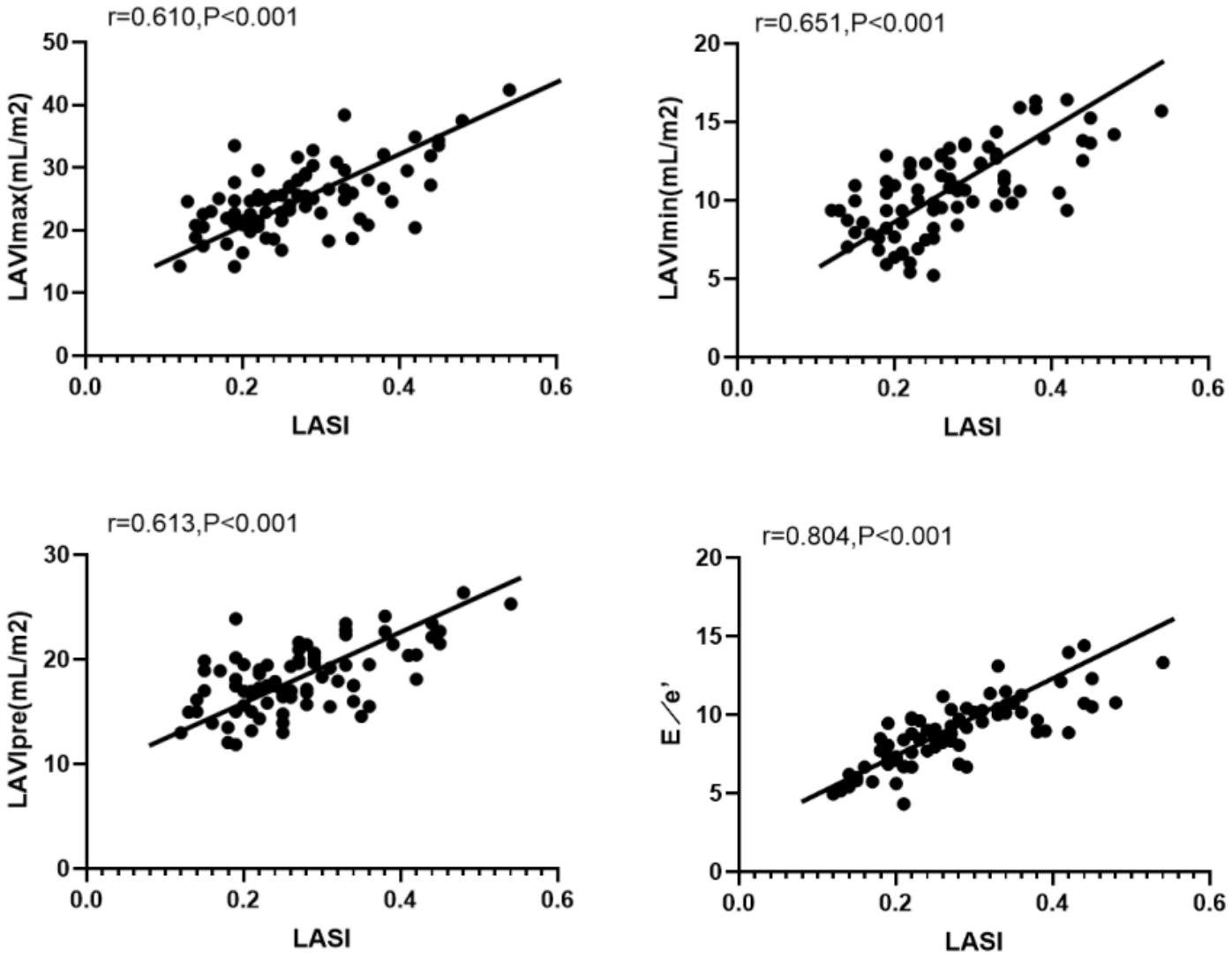

Figure 2

Correlation of LASI and LAVImax, LAVImin ,LAVIpre and E/e'

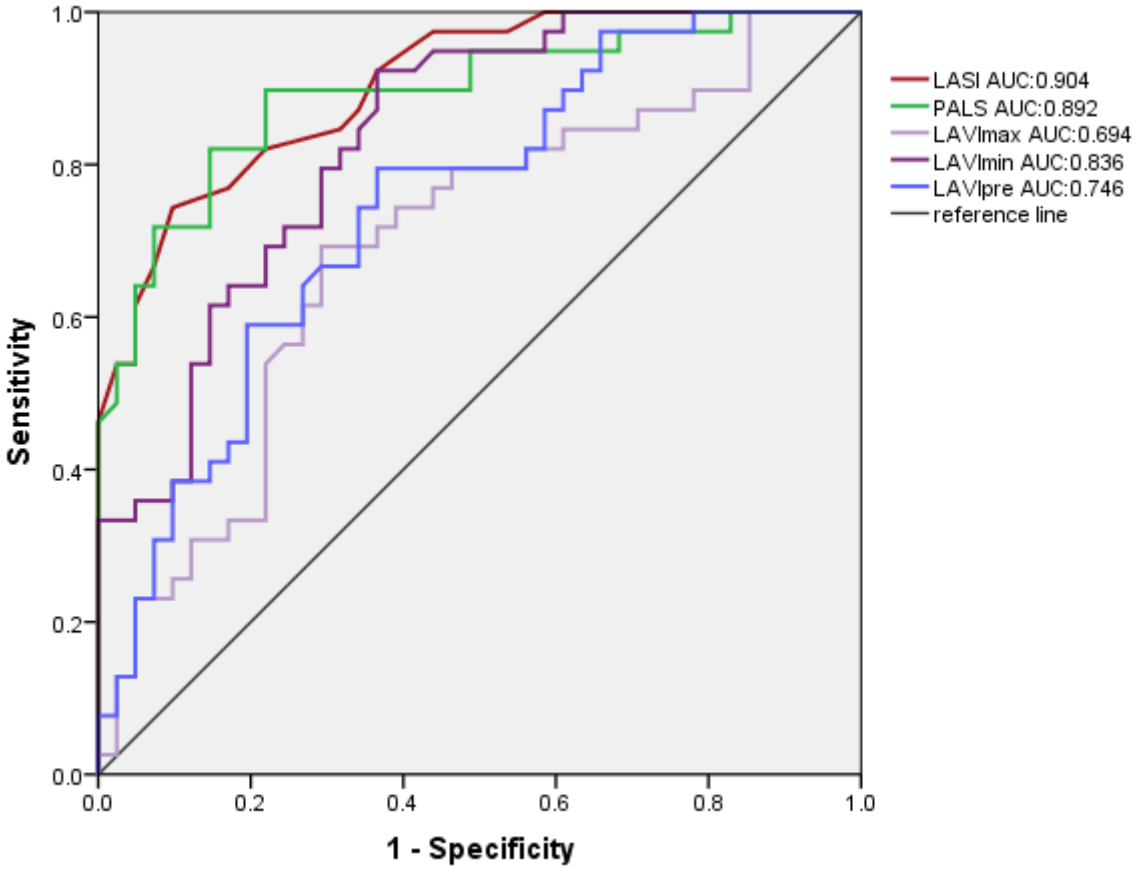

Figure 3

ROC curves for LAVImax, LAVImin ,LAVIpre,PALS and LASI for the prediction of DM2

Supplementary Files

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