



## Joint Meeting of Coronary Revascularization(JCR) 2015

# ASSOCIATION OF PLASMA ST2 LEVELS WITH ECHOCARDIOGRAPHIC PARAMETERS OF DIASTOLIC DYSFUNCTION IN DIABETIC PATIENTS AT AN OUTPATIENT CLINIC

**Diana Hui Ping Foo<sup>1</sup>, Alan Yean Yip Fong<sup>1,2</sup>, Salbiah Binti Sindot<sup>1</sup>, Stella Li Li Chan<sup>1</sup>, Ruziah Binti Mat Sa'at<sup>1</sup>, Hasni Adha Binti Ibrahim<sup>1</sup>, Sally Suriani Ahip<sup>3</sup>**

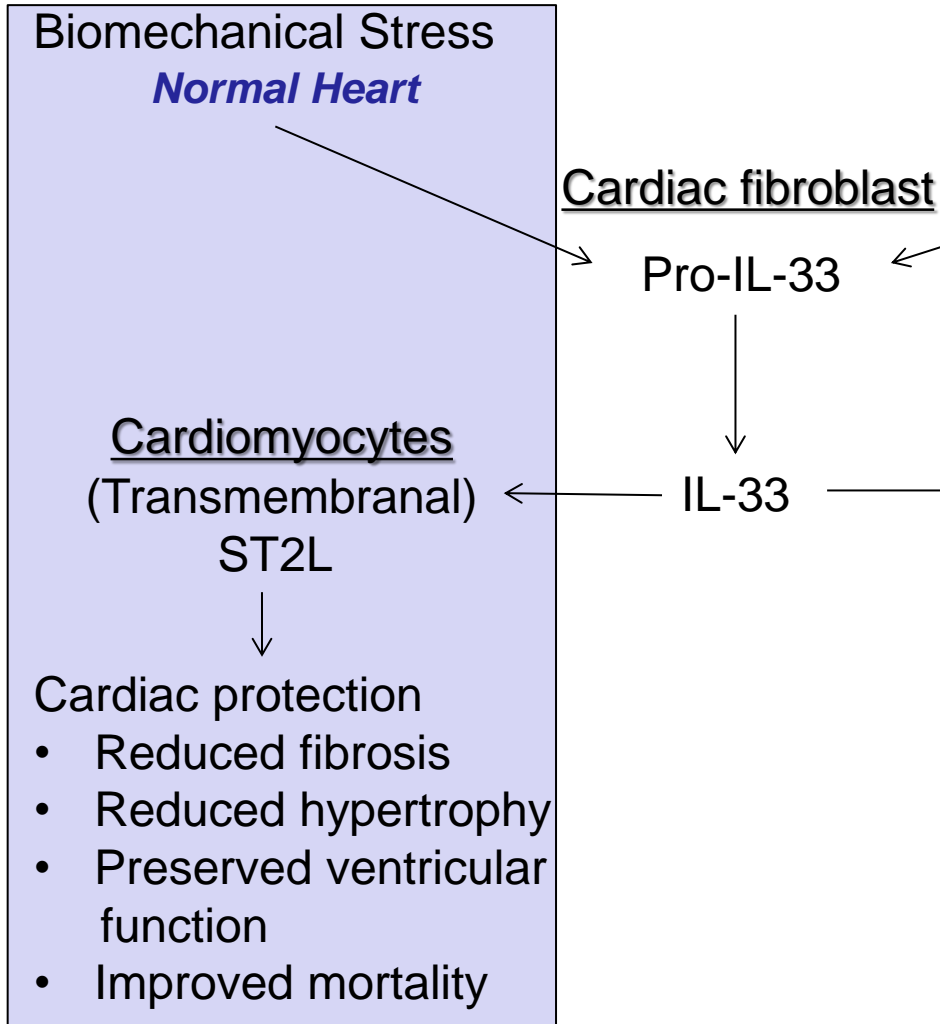
<sup>1</sup> Clinical Research Centre, Sarawak General Hospital, Kuching, Sarawak

<sup>2</sup> Department of Cardiology, Sarawak General Hospital Heart Centre, Kota Samarahan, Sarawak

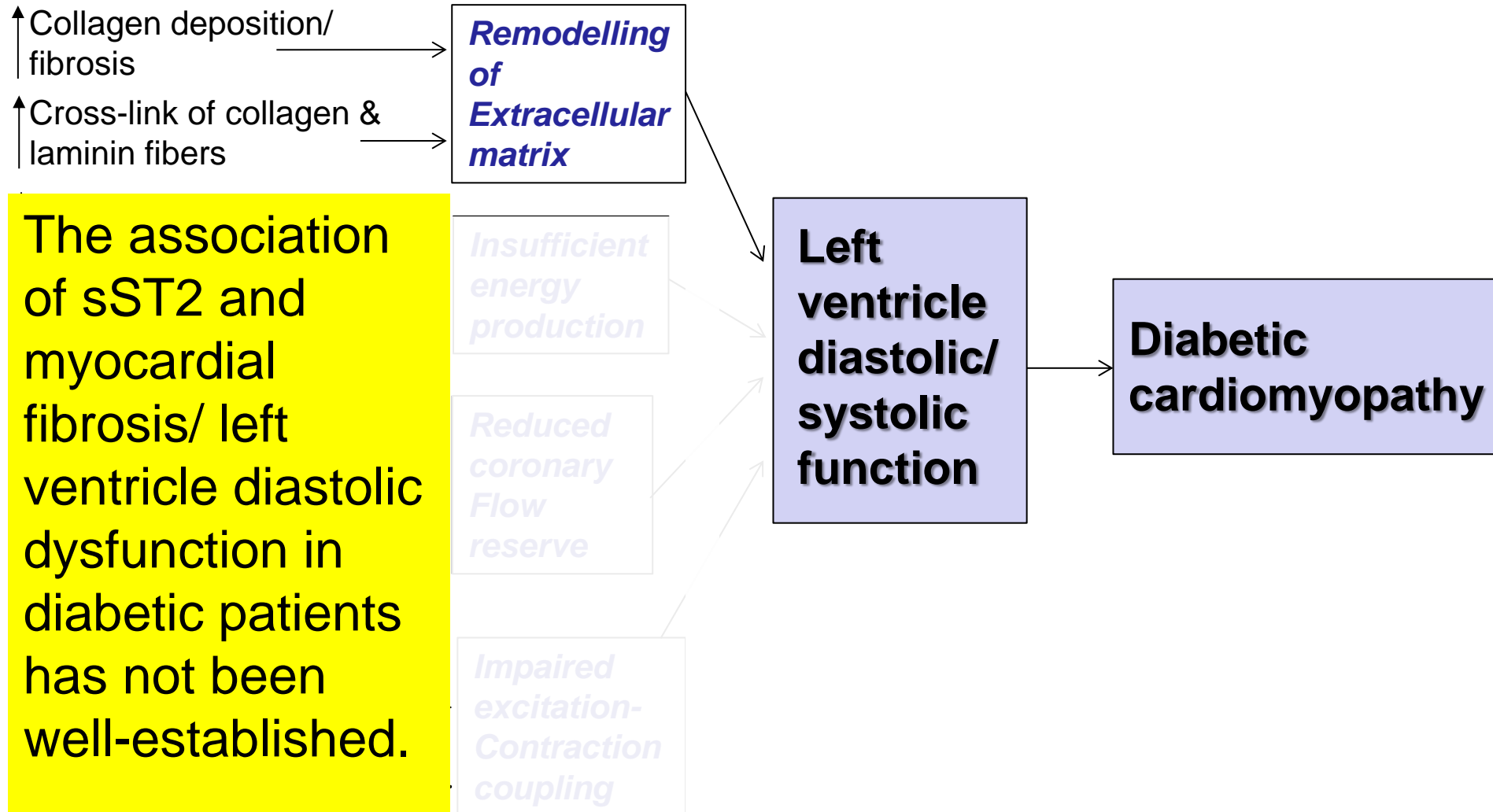
<sup>3</sup> Klinik Kesihatan Kota Sentosa, Kuching, Sarawak



# IL-33/ST2 SIGNALLING PATHWAY



# Mechanisms of contractile dysfunction in diabetic cardiomyopathy



The association of sST2 and myocardial fibrosis/ left ventricle diastolic dysfunction in diabetic patients has not been well-established.



# Where we are...



# Our strength



# Diabetes mellitus is a major health issue in Malaysia

- About 2.6 million (15.2%) adults aged 18 years and above living with diabetes mellitus.

National Diabetes Registry  
Report

NATIONAL HEALTH  
AND

- The primary healthcare settings in the Ministry of Health (MOH) bear a much higher diabetic patient load (56%) compared to other healthcare institutions.

Non-Communicable Disease Section  
Disease Control Division  
Ministry of Health Malaysia

# Study rationale (1)

## Framingham Risk Score for Cardiovascular Disease

### Risk Factor

Age

Sex

Systolic Blood pressure

Total cholesterol

HDL

Smoking

Diabetes mellitus

# Study rationale (2)

## Renal assessment

- Proteinuria
- Serum creatinine
- Glomerular filtration rate (GFR)
- Ultrasound

## Cardiovascular risk assessment

- Assessment of risk factors
- **Limited assess to echocardiography facilities**

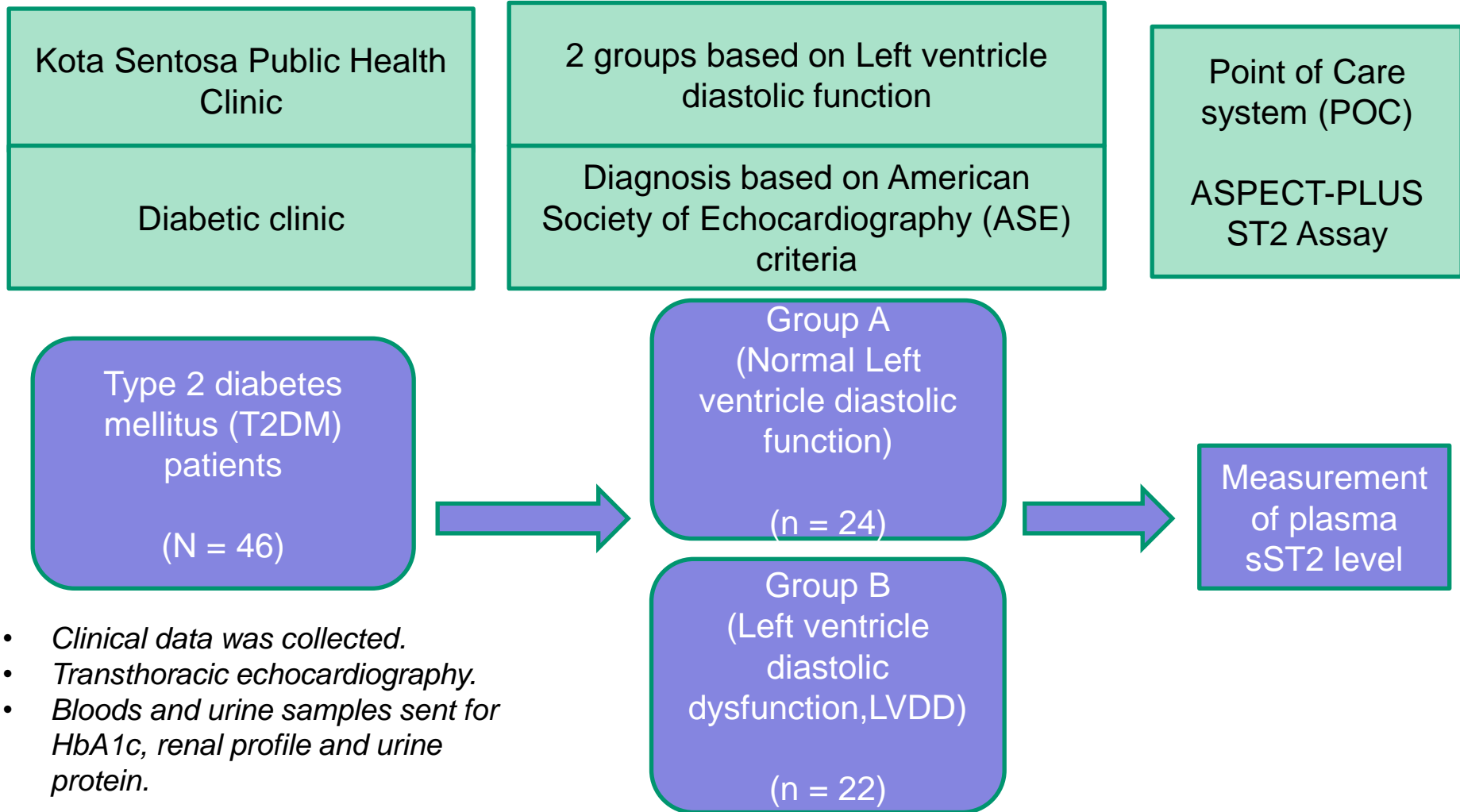
**Can ST2 detect left ventricle diastolic dysfunction early in asymptomatic diabetic patients at an ambulatory setting?**



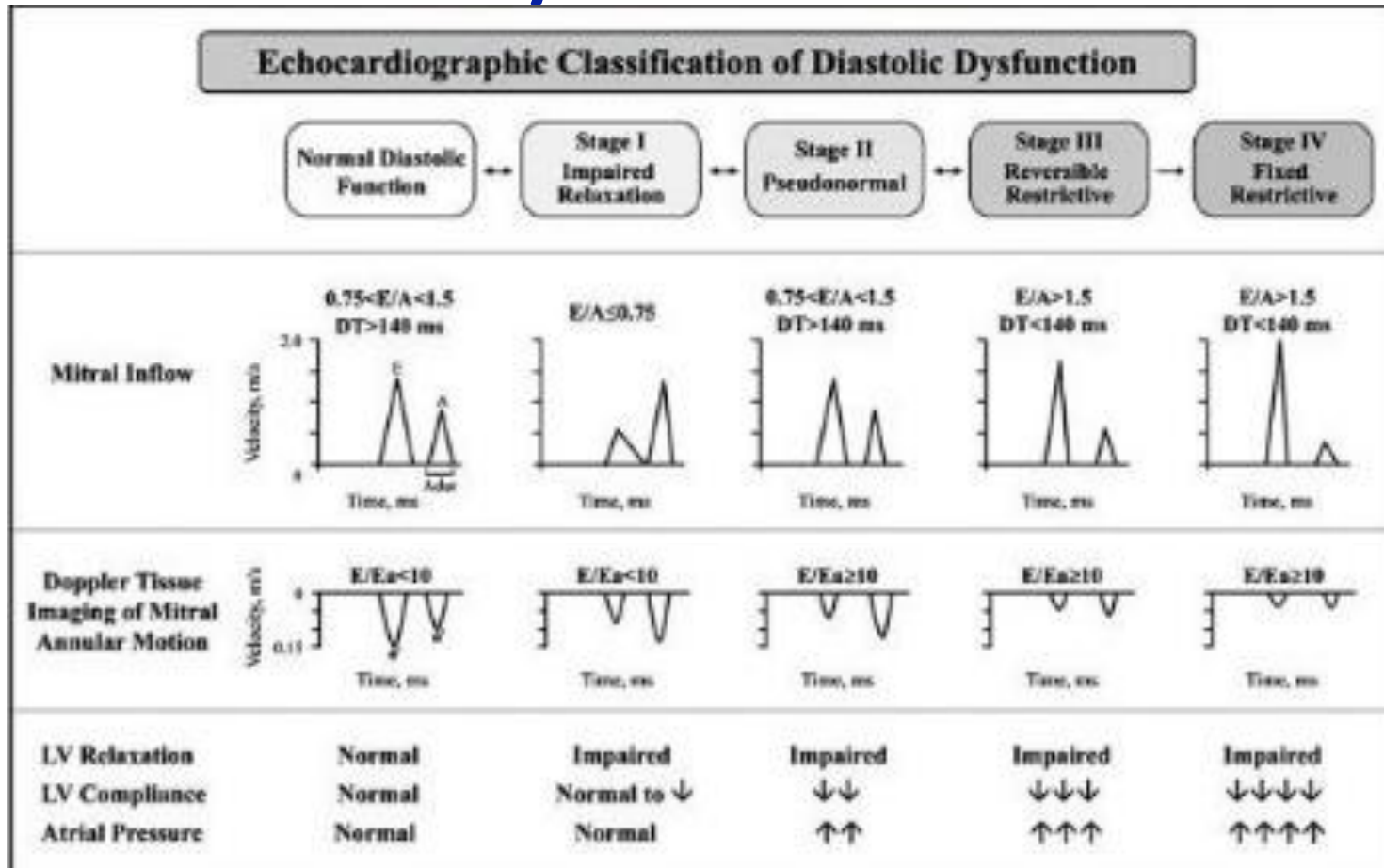
# Objective

- To investigate the association between plasma ST2 levels and left ventricle diastolic dysfunction diagnosed by echocardiography in patients with Type 2 diabetes mellitus

# Materials & Methods



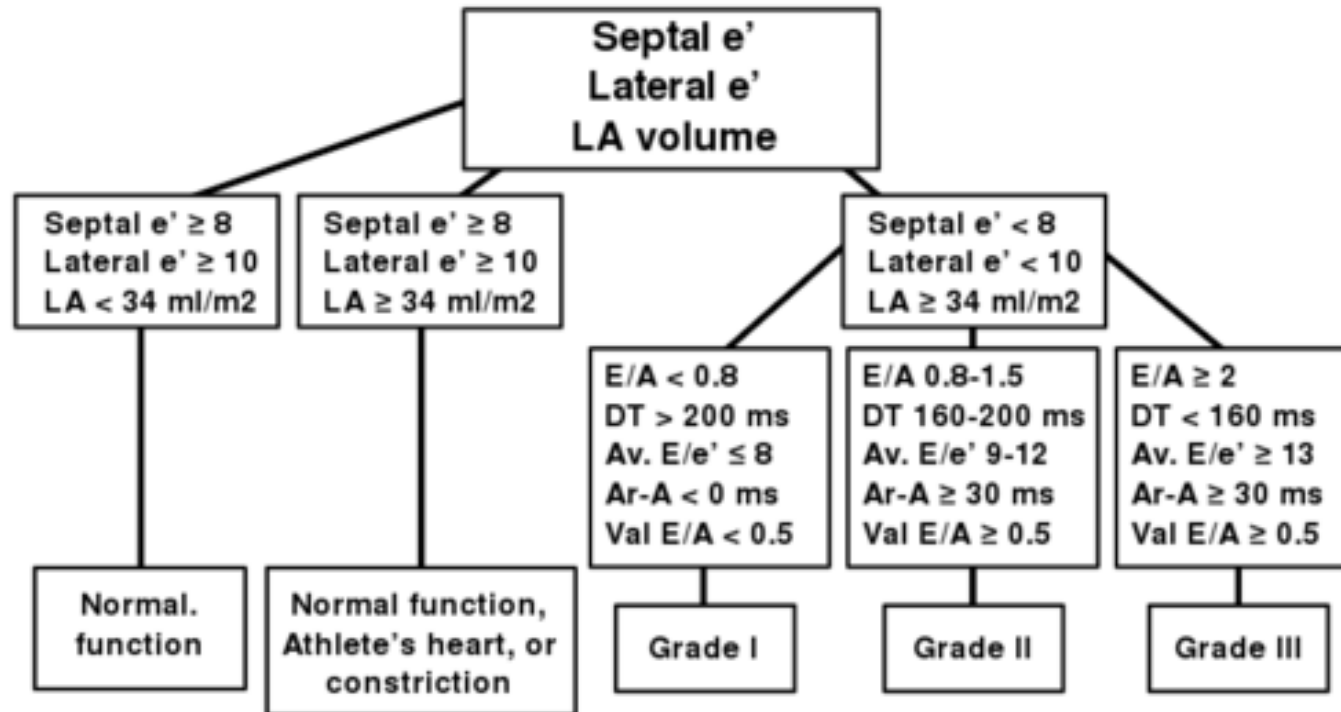
# Echocardiographic criteria of Left ventricle diastolic dysfunction



Nagueh, S.F., et al., *Recommendations for the evaluation of left ventricular diastolic function by echocardiography*. Eur J Echocardiogr, 2009. **10**(2): p. 165-93.

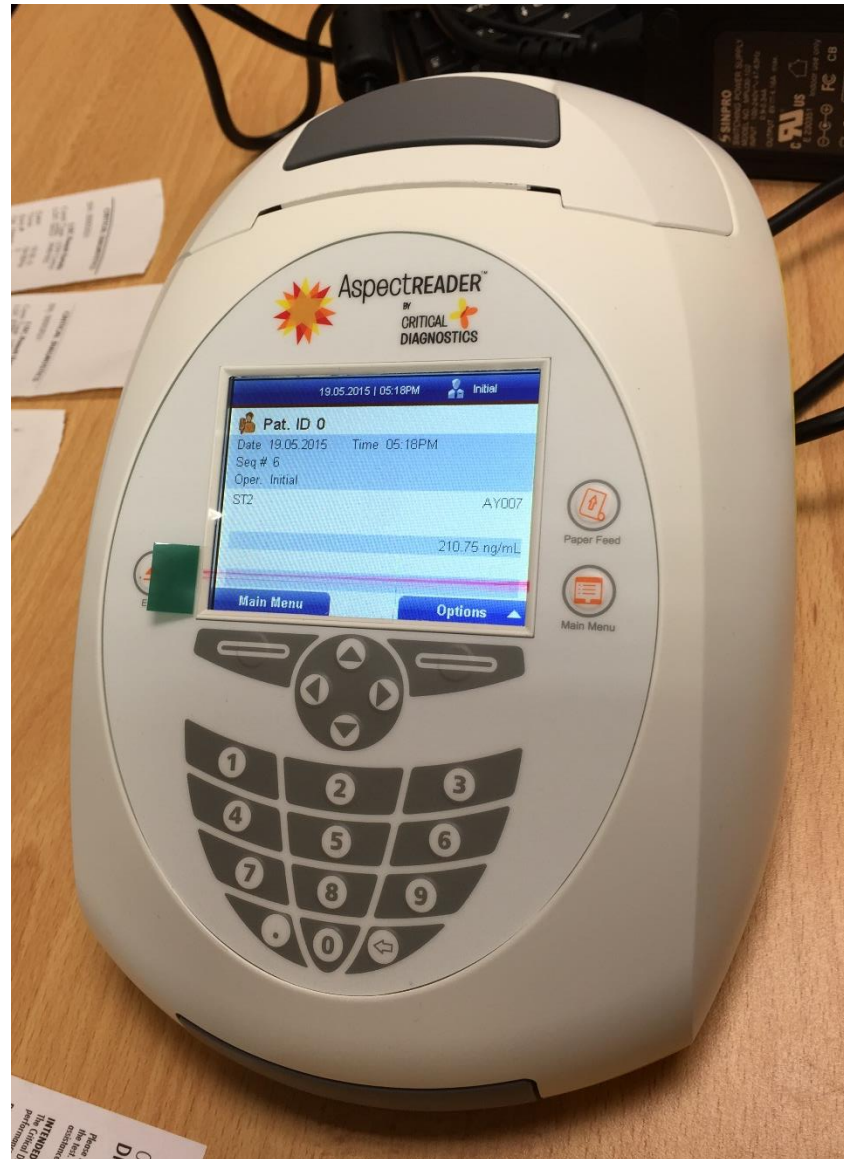
# Echocardiographic criteria of Left ventricle diastolic dysfunction

## Practical Approach to Grade Diastolic Dysfunction



Nagueh, S.F., et al., *Recommendations for the evaluation of left ventricular diastolic function by echocardiography*. Eur J Echocardiogr, 2009. **10**(2): p. 165-93.

# ASPECT-PLUS ST2 Assay



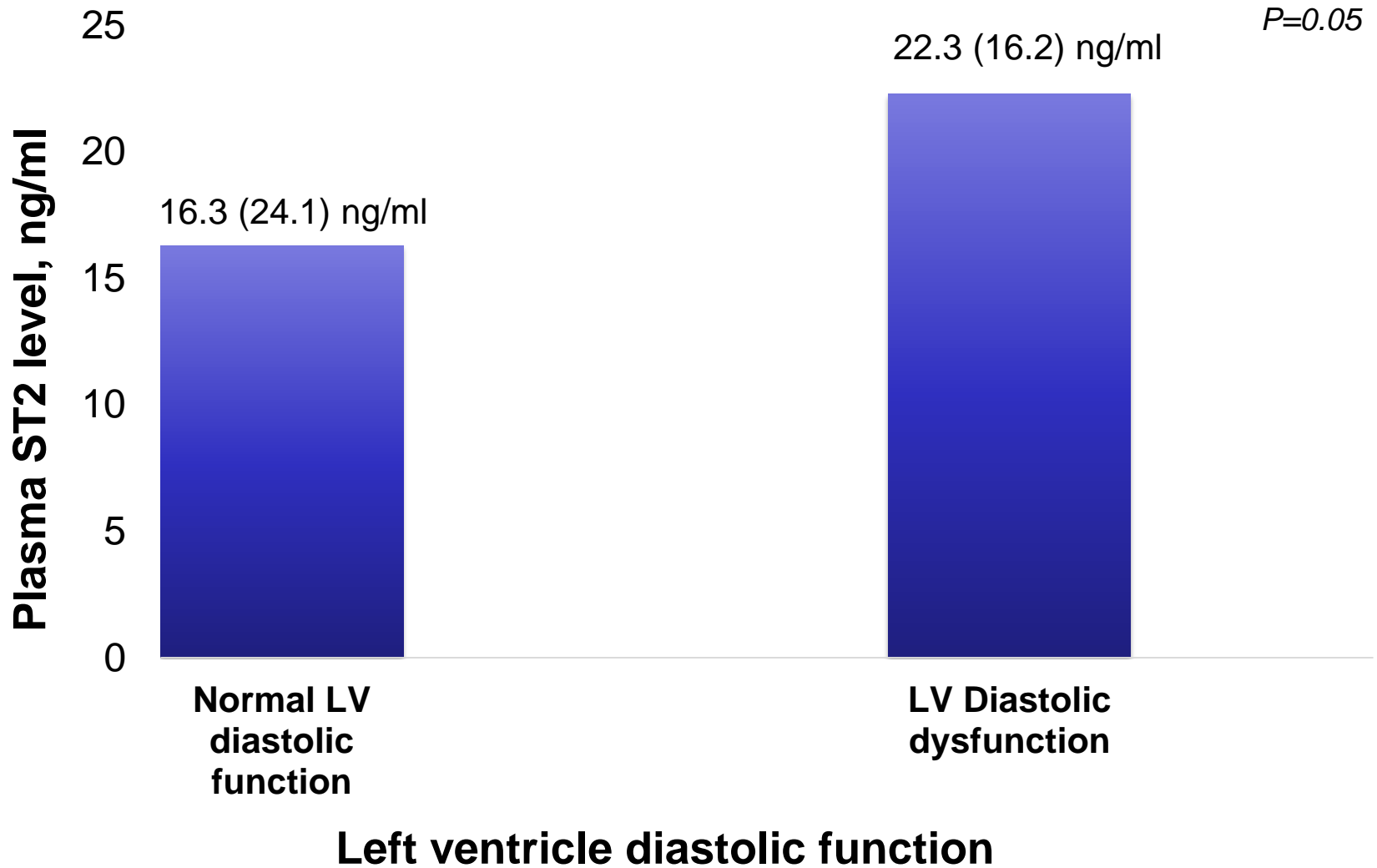
# Clinical Characteristics of Patients

	Overall (N=47)	Group A (Normal) n=24	Group B (LVDD) n=22	P value
<b>Age</b>	55.4±11.3	<b>56±18</b>	<b>62±13</b>	<b>0.043</b>
Male, %	40	55.6	44.4	0.713
Race(Malay:Chinese:Bumiputra)	8:17:21	3:11:10	5:6:11	0.380
<b>Hypertension, %</b>	<b>62.2</b>	<b>44.4</b>	<b>55.6</b>	<b>0.046</b>
Dyslipidemia, %	83	52.6	47.4	0.892
Coronary artery disease, %	4	50.0	50.0	0.950
Heart Rate	77.2±7.1	80±9	75±11	0.225
Systolic blood pressure	131±12.9	<b>130±20</b>	<b>130±13</b>	<b>0.437</b>
Diastolic blood pressure	76.4±8.1	80±10	58.7±10	0.700
BMI	28.6±3.9	27.5±6.3	28.7±5.4	0.516
<b>Proteinuria, %</b>	<b>16</b>	<b>12.5</b>	<b>87.5</b>	<b>0.013</b>
HbA1C	7.5±2.4	<b>7.5±2.6</b>	<b>7.5±2.7</b>	0.562
Glomerular filtration rate	71.5±35.4	76.1±20.4	60.5±45.3	0.068
Serum Creatinine	93±29	89±23	99±34	0.379

# Echocardiographic characteristics of Patients

Echo characteristics (IQR)	Overall (N=47)	Group A (Normal) n=24	Group B (LVDD) n=22	P value
LV end-diastolic volume	43.6±20.9	44.7±16.2	42.5±26.3	0.524
LV end-systolic volume	12.4±9.4	10.9±11.5	14.5±8.1	0.198
LV mass index	100.9±29.4	99.1±44.2	101.3±32.5	0.129
<b>Left ventricular hypertrophy, %</b>	<b>54</b>	<b>40</b>	<b>60</b>	<b>0.071</b>
LV ejection fraction	70±12	72±12	69±11	0.198
Transmitral E peak velocity	71±26	74±23	67.5±29	0.116
Transmitral A peak velocity	73±22	71±18	76±27	0.296
<b>E/A ratio</b>	<b>1.0±0.3</b>	<b>1.0±0.3</b>	<b>0.8±0.3</b>	<b>0.011</b>
<b>E deceleration time</b>	<b>197±40</b>	<b>191±51</b>	<b>204±57</b>	<b>0.036</b>
<b>e' peak velocity</b>	<b>12±8</b>	<b>13.3±6.0</b>	<b>7.5±6.0</b>	<b>0.000</b>
<b>E/e' ratio</b>	<b>6.3±3.6</b>	<b>5.0±1.9</b>	<b>8.6±5.9</b>	<b>0.003</b>
<b>Left atrial volume index</b>	<b>22.2±12.4</b>	<b>19.9±7.6</b>	<b>28.7±15.3</b>	<b>0.034</b>

# Plasma Level of ST2 According to Left Ventricle Diastolic Function by Echo





# Factors influencing plasma ST2 level

## Left ventricle diastolic dysfunction

Variables	SLR <sup>a</sup>	
	b <sup>c</sup> (95% CI)	P value
Age	0.44 (-1.37,0.49)	0.330
HTN	-6.03 (-39.30, 27.25)	0.710
Proteinuria	8.89 (-11.30, 29.08)	0.369
E/A ratio	22.29(-19.60,64.18)	0.280
E Decel time	0.01 (-0.25, 0.24)	0.951
<b>e'</b>	<b>1.01 (0.45,1.57)</b>	<b>0.001</b>
LAVI	0.90 (-0.19, 1.97)	0.102
E/e'	1.61 (-0.01, 3.24)	0.052
LVH	13.39 (-6.26, 33.03)	0.171

<sup>a</sup> Simple linear regression <sup>b</sup> Multiple linear regression <sup>c</sup> Crude regression coefficient <sup>d</sup> Adjusted regression coefficient

# Limitations

- ❖ Single centre study
- ❖ Small sample size
- ❖ Hypothesis generating
- ❖ Therefore, a larger study is required.

# One size fits all?

- Do ACE-inhibitors and ARBs truly benefit **ALL** Type 2 diabetic patients?
- Echocardiography for early detection of subtle changes in left ventricle diastolic function and monitoring of the progression – **Is this still practical in the real situation?**
- ST2 levels were associated with worsening diastolic dysfunction in patients with Type 2 diabetes mellitus. Larger studies should be warranted.



**Acknowledgement**  
**Team (SGHHC/ CRC SGH)**  
**Critical Diagnostics**  
**Kota Sentosa Public Health Clinic**

# Study rationale (2)

## Eye assessment

- Referral to an ophthalmologist

## Renal assessment

- Albuminuria
- Serum creatinine
- Glomerular filtration rate (GFR)
- Ultrasound

## Cardiovascular risk assessment

- Assessment of risk factors
- **Limited assess to echocardiography facilities**

**Can ST2 detect left ventricle diastolic dysfunction early in asymptomatic diabetic patients at an ambulatory setting?**

# Factors influencing plasma ST2 level

## Left ventricle diastolic dysfunction

Variables	SLR <sup>a</sup>		MLR <sup>b</sup>		
	b <sup>c</sup> (95% CI)	P value	Adj.b <sup>d</sup> (95% CI)	t-stat	P value
Age	0.44 (-1.37,0.49)	0.330			
HTN	-6.03 (-39.30, 27.25)	0.710			
Proteinuria	8.89 (-11.30, 29.08)	0.369			
E/A ratio	22.29(-19.60,64.18)	0.280			
E Decel time	0.01 (-0.25, 0.24)	0.951			
<b>e'</b>	<b>1.01 (0.45,1.57)</b>	<b>0.001</b>	<b>1.02 (0.51,1.52)</b>	<b>4.18</b>	<b>0.001</b>
LAVI	0.90 (-0.19, 1.97)	0.102			
E/e'	1.61 (-0.01, 3.24)	0.052			
LVH	13.39 (-6.26, 33.03)	0.171			

<sup>a</sup> Simple linear regression <sup>b</sup> Multiple linear regression <sup>c</sup> Crude regression coefficient <sup>d</sup> Adjusted regression coefficient