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# Impact of surgical and non-surgical weight loss on echocardiographic and strain parameters in Asian patients

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Surgical weight loss (SWL) improves myocardial mechanics as measured by speckle-tracking imaging. However non-surgical versus SWL and the subsequent impact on myocardial function in overweight Asian subjects has not been evaluated. 66 patients underwent a 16-week lifestyle intervention (LSI) programme consisting of dietary interventions and exercise prescription. Echocardiography with speckle tracking was performed at baseline and post-intervention. This group was compared against a group of 12 subjects who had undergone bariatric surgery and a control group of 10 lean Asian subjects. A generalised structural equation model (gSEM) was constructed to ascertain the effect of modality of weight loss on strain parameters, adjusting for BMI. Participants attained significant weight loss after LSI ( $28.2 \pm 2.66$  kg/m<sup>2</sup> vs.  $25.8 \pm 2.84$  kg/m<sup>2</sup>,  $p = 0.001$ ). This was associated with a non-significant trend towards improvement in strain parameters. SWL participants had significant improvement in the left ventricular global longitudinal strain ( $-20.52 \pm 3.34$  vs.  $-16.68 \pm 4.15$ ,  $p < 0.01$ ) and left atrium reservoir strain ( $44.32 \pm 14.23$  vs.  $34.3 \pm 19.31$ ,  $p = 0.02$ ). Lean subjects had significantly higher strain parameters than overweight subjects. The gSEM model demonstrated surgical modality of weight loss as an independent predictor of improvement in strain parameters. Significant improvement in echocardiographic parameters were documented in patients who underwent bariatric surgery.

**Keywords** Obesity, Subclinical cardiac dysfunction, Echocardiography, Speckle-tracking strain parameters

Obesity is a major public health hazard and is associated with multiple cardiovascular morbidities<sup>1,2</sup>. Subjects with obesity have dilatation of cardiac chambers, impairment of diastolic filling and subclinical left ventricular systolic dysfunction<sup>3</sup>. For example, although left ventricular ejection fraction (LVEF) appears to remain normal, the echocardiographic strain parameters of the left ventricle can be significantly reduced consistent with subclinical LV dysfunction<sup>4-6</sup>.

In obesity, numerous studies have shown that weight loss after bariatric surgery can lead to improvement in cardiac function and long-term cardiovascular health<sup>6-8</sup>. Many of these studies on bariatric surgery involve morbidly obese Western populations with average body mass index (BMI) of around 50 kg/m<sup>26,9</sup>.

On the other hand, Asians with obesity tend to not have body mass indices that are as markedly elevated<sup>10</sup>. In fact, obesity is defined by a lower cut-off value in Asian populations<sup>11</sup>. In addition, rather than truncal obesity

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and absolute increase in the body mass, in Asians, visceral adiposity accumulates and contributes to adverse cardiovascular outcomes<sup>12,13</sup>.

To our best knowledge, it is unknown if similar improvement in cardiac function can be demonstrated in Asian patients with obesity (who tend to have lower BMI than their Western counterparts), and also in the context of non-surgical weight loss, where the changes in weight is more modest. Therefore, we aimed to report changes in echocardiographic parameters and speckle-tracking strain parameters in Asian patients with obesity, who underwent either surgical or non-surgical weight loss. A secondary aim of our study was to assess if the modality of weight loss (either surgical or non-surgical) had a direct impact on speckle-tracking strain parameters independent of the change in BMI.

## Methodology

### Study population

We prospectively recruited individuals with elevated BMI into a non-surgical weight loss (NSWL) arm and a surgical weight loss (SWL) arm. There was also a control group of lean Asian subjects.

Sixty-six (66) participants were recruited in the NSWL arm. Inclusion criteria were a BMI of 25–32 kg/m<sup>2</sup> and having no known prior cardiovascular disease. We excluded patients with significant changes in their diet or attempts to lose weight for the past 6 months, previous abdominal surgery, or prior psychiatric condition. A cohort of 12 participants who had undergone elective bariatric surgery were recruited into the SWL arm. Inclusion criteria for the SWL arm included a BMI of more than 35 kg/m<sup>2</sup> and scheduled for the bariatric surgery. Exclusion criteria were patients with known cardiovascular disease or prior psychiatric conditions. Subsequently, we compared the NSWL arm with a group of healthy lean subjects, with no prior cardiovascular history, and BMI of between 18 and 23 kg/m<sup>2</sup>.

Informed consent was obtained from all participants. Ethical approval was granted by the Institutional Review Board of the National University Hospital, Singapore. All recruitment methods were carried out in accordance to relevant guidelines and regulations.

### Study design

Participants in the NSWL arm underwent a 16-week lifestyle intervention. The lifestyle intervention consisted of 5 consultations with the dietician, with the duration between visit 2 to 4 weeks apart. During the first visit with the dietician, participants were asked to provide a 24-h recall of their dietary intake and a subsequent analysis was performed. Participants were taught the concepts of meal replacements and a sample meal plan was provided. During the second visit with the dietician, participants were taught on the different types of fat and how to identify fat content in food. Participants were taught on how to measure their caloric needs based on their weight and physical activity level and how to regulate their consumption to achieve weight loss. Subsequent consultations with the dietician entailed analysis of their food consumption and identifying any barriers participants have in being compliant to their weight-loss meal plans. Participants were also provided with exercise prescriptions which advised on exercise and physical activity sessions. Transthoracic echocardiogram was performed at baseline and after 16 weeks of lifestyle intervention.

Patients in the SWL arm underwent either a sleeve gastrectomy or a gastric bypass operation. Transthoracic echocardiogram was performed at baseline and after 24 weeks after surgery.

### Clinical and demographic data

Clinical and demographic data were obtained from the medical records of the clinical encounter within 1 month of the baseline echocardiogram. We also recorded information regarding history of hypertension, hyperlipidaemia and diabetes mellitus. BMI of participants, calculated by dividing weight in kilograms by height in meters squared, was measured both at baseline and after 16 weeks of lifestyle interventions or at 24 weeks after surgery for the NSWL and SWL cohorts respectively.

### Measurement of echocardiographic parameters

All echocardiographic studies were performed using commercially available ultrasound systems, and images were retrospectively analyzed by experienced echocardiographers according to current guidelines<sup>14–16</sup>. From the parasternal long-axis view, left ventricle (LV) dimensions were assessed and LV mass was calculated by the formula of Devereux. LV end-diastolic and end-systolic volumes were assessed from the apical two- and four-chamber views and LV ejection fraction (LVEF) was calculated using the Simpson's biplane method. Left atrium (LA) volumes were calculated using the method of discs at end-systole in the apical two- and four-chamber views. All volumes were indexed for body surface area (BSA), calculated by the formula of Du Bois. Diastolic function was assessed by pulsed-wave Doppler recordings of the transmitral flow to obtain peak early (E) and late (A) diastolic velocities. Tissue Doppler imaging of the mitral annulus on the apical four-chamber view was used to measure  $e'$  at both the lateral and septal side, and  $e'$  was averaged to calculate the  $E/e'$  ratio. Pulmonary artery systolic pressure was calculated from the peak velocity of the tricuspid regurgitant jet using the Bernoulli equation, adding the right atrial pressure determined by the inspiratory collapse and diameter of the inferior vena cava<sup>14–16</sup>.

### Measurement of strain parameters

The TOMTEC™ automated strain analysis software was used to measure strain parameters of the LV, left atrium and right ventricle. Left ventricular strain analysis was based on speckle tracking of apical 4-chamber, apical 3-chamber, and apical 2-chamber views<sup>15</sup>. Right ventricular strain analysis was derived on speckle tracking of right-ventricle focused apical view and left atrial strain analysis was based on the apical 4-chamber view<sup>17</sup>. The

TOMTEC™ auto-strain software utilizes an automated approach to strain analysis. The user identifies the relevant apical images for analysis before an endocardial border is placed on the myocardium. The user can adjust the border placement and check tracking throughout the cardiac cycle to ensure accurate myocardial tracking is achieved.

### Statistical analysis

The data were expressed as mean  $\pm$  standard deviation, median (interquartile range, IQR) and frequencies (%), depending on their nature. Exploratory analyses were performed with independent t-test, Mann–Whitney U-test and Chi Square test. A generalized structural equation model (gSEM) was constructed to ascertain the effect of modality of weight loss on left ventricle strain, right ventricle strain and left atrium strain, while adjusting for change in BMI. Analyzed with Stata MP Version 18 (Stata Corp, Texas, USA), all statistical tests were conducted at 5% level of significance.

### Results

Of the 78 participants in the study, 66 (84.6%) participants were in the NSWL group, while the remaining 12 (15.4%) were in the SWL group.

#### Baseline characteristics

Baseline characteristics of all subjects are summarized in Table 1. Participants in both NSWL and SWL arms were similarly matched in age and sex distribution (age:  $38.39 \pm 8.86$  vs.  $39.83 \pm 10.32$  years,  $p = 0.312$ ; female sex: 89.4% vs. 83.3%,  $p = 0.545$ ). Participants in the SWL arm had significantly higher BMI than in the NSWL arm (BMI:  $44.3 \pm 4.96$  kg/m<sup>2</sup> vs.  $28.2 \pm 2.66$  kg/m<sup>2</sup>,  $p < 0.01$ ).

#### Baseline anthropometric and echocardiographic features

The baseline echocardiographic features and speckle-tracking strain parameters of the NSWL and SWL cohort are listed in Table 2. As compared to the NSWL cohort, the SWL group had significantly larger left ventricular diameter in diastole (LVIDD), larger left atrium (LA), higher left ventricular mass index (LVMI) and higher relative wall thickness (RWT). Participants in the SWL cohort also had a significantly lower left ventricular ejection fraction (LVEF).

In terms of tissue Doppler indices and speckle-tracking strain parameters, participants in the SWL cohort had a lower left ventricle septal E'/A' ratio ( $0.993 \pm 0.463$  vs.  $1.20 \pm 0.353$ ,  $p = 0.04$ ), higher left ventricle E/E' ratio ( $10.14 \pm 1.87$  vs.  $8.42 \pm 1.79$ ,  $p < 0.01$ ), lower lateral left ventricle E' velocity ( $10.83 \pm 3.38$  vs.  $13.34 \pm 2.84$ ,  $p = 0.04$ ), lower left ventricle lateral E'/A' ( $1.25 \pm 0.605$  vs.  $1.57 \pm 0.490$ ,  $p = 0.02$ ) and higher left ventricle E/E' ( $7.67 \pm 2.26$  vs.  $6.4 \pm 1.45$ ,  $p < 0.01$ ). Participants undergoing SWL had lower global left ventricular longitudinal strain ( $-16.68 \pm 4.15$  vs.  $-22.05 \pm 2.98\%$ ,  $p < 0.01$ ), right ventricular free wall strain ( $-19.32 \pm 5.35$  vs.  $-21.56 \pm 3.32$ ,  $p = 0.047$ ) and left atrial reservoir strain ( $34.3 \pm 19.31$  vs.  $51.456 \pm 11.24$ ,  $p < 0.01$ ).

#### Changes in anthropometric and echocardiographic features

Table 3 lists the follow-up anthropometric and echocardiographic parameters of the 2 cohorts. At follow-up, both groups achieved a significant decrease in BMI. Participants in the NSWL cohort had an average BMI reduction of 2.4 kg/m<sup>2</sup> ( $p < 0.01$ ) and the SWL cohort had an average reduction of 10.3 kg/m<sup>2</sup> ( $p < 0.01$ ). Participants in the SWL cohort showed significant improvement in average LV fractional shortening ( $36.67 \pm 5.38$  vs.  $37.5 \pm 5.21$ ,  $p = 0.024$ ). There was also a significant increase in mitral E velocity, left ventricle septal E' and left ventricle lateral E'. Additionally, participants in the SWL cohort demonstrated significant improvement in speckle-tracking strain parameters in all 3 chambers measured. Patients who underwent NSWL had significant reductions in mitral A velocity, left ventricle septal A velocity and a significant increase in left ventricle E velocity. Unlike patients in the SWL cohort, patients who underwent NSWL did not have any significant improvement in their strain parameters.

Analyses of the extent of changes in echocardiographic and speckle-tracking strain parameters between the SWL and NSWL cohort are listed in Table 4. Participants who underwent SWL had significantly greater reduction

Variables	Non-surgical weight loss N = 66	Surgical weight loss N = 12	P-value
Demographics and Comorbidities			
Age, years	$38.39 \pm 8.86$	$39.83 \pm 10.32$	0.312
Female sex, (%)	59 (89.4)	10 (83.3)	0.545
Hypertension, (%)	0 (0)	6 (50)	N.A
Hyperlipidaemia, (%)	3 (4.56)	7 (58.3)	N.A
Diabetes Mellitus, (%)	1 (1.52)	5 (41.67)	N.A
Type of Bariatric Surgery			
Sleeve Gastrectomy, (%)	N.A	10 (83.3)	N.A
Gastric Bypass, (%)		2 (16.7)	
Body Mass Index, kg/m <sup>2</sup>	$28.20 \pm 2.66$	$44.3 \pm 4.96$	<0.01
Reduction in Body Mass Index, kg/m <sup>2</sup>	$-2.4 \pm 1.12$	$-10.30 \pm 2.74$	<0.01

**Table 1.** Baseline clinical characteristics.

Variables	Non-surgical weight loss N = 66	Surgical weight loss N = 12	P-Value
Echocardiographic Parameters			
Left Ventricular Internal Diameter diastole, mm	45.94 ± 3.01	50.25 ± 5.17	< 0.01
Left Ventricular Internal Diameter systole, mm	30.58 ± 5.64	32.42 ± 5.32	0.151
Left Ventricular Mass Index, g/m <sup>2</sup>	66.74 ± 12.085	80.83 ± 22.99	< 0.01
Left Atrium, mm	34.0 ± 4.13	39.67 ± 6.27	< 0.01
Left Ventricular Ejection fraction, visual, %	65.31 ± 3.93	62.67 ± 5.33	0.02
Mitral Deceleration Time, msec	170 ± 27.44	171.92 ± 19.12	0.409
Mitral E Velocity, cm/s	82.89 ± 14.87	78.42 ± 19.00	0.183
Mitral A Velocity, cm/s	55.80 ± 10.52	67.17 ± 22.04	< 0.01
Mitral E/A	1.53 ± 0.378	1.35 ± 0.716	0.10
Left Ventricle Septal E' Velocity, cm/s	10.28 ± 2.19	7.75 ± 1.76	0.109
Left Ventricle Septal E/E'	8.42 ± 1.79	10.14 ± 1.87	< 0.01
Left Ventricle Lateral E, cm/s	13.34 ± 2.84	10.83 ± 3.38	0.04
Left Ventricle Lateral E/E'	6.40 ± 1.45	7.67 ± 2.26	< 0.01
Right Ventricle E', cm/s	12.86 ± 2.71	11.17 ± 2.44	0.02
Pulmonary Artery Systolic Pressure, mmHg	24.02 ± 4.015	23 ± 2.37	0.274
Speckle-Tracking Strain Parameters			
Left ventricular global longitudinal strain, %	-22.05 ± 2.98	-16.68 ± 4.15	< 0.01
Right ventricular free wall strain, %	-21.56 ± 3.32	-19.32 ± 5.35	0.047
Left atrium reservoir strain, %	51.456 ± 11.24	34.3 ± 19.31	< 0.01

**Table 2.** Differences in baseline echocardiographic parameters and speckle strain parameters.

Parameters	Non-surgical weight loss, N = 66		Surgical weight loss, N = 12		P-value <sup>1</sup>	P-Value <sup>2</sup>
	Baseline	Post-Intervention (4 months)	Baseline	Post-intervention (6-months)		
Body Mass Index, kg/m <sup>2</sup>	28.20 ± 2.66	25.8 ± 2.84	44.3 ± 4.96	34.0 ± 2.22	< 0.01	< 0.01
Left Ventricular Internal Diameter diastole, mm	45.94 ± 3.01	46.20 ± 3.31	50.25 ± 5.17	49.83 ± 4.06	0.288	0.807
Left Ventricular Internal Diameter systole, mm	30.58 ± 5.64	30.72 ± 5.31	32.42 ± 5.32	30.17 ± 3.41	0.133	0.140
Left Atrium, mm	34.0 ± 4.13	33.85 ± 3.53	39.67 ± 6.27	39.5 ± 5.09	0.447	0.897
Left Ventricular Ejection fraction, visual, %	65.31 ± 3.93	65.11 ± 3.53	62.67 ± 5.33	65.9 ± 4.08	0.759	0.067
Mitral Deceleration Time, ms	170 ± 27.44	171.98 ± 30.64	171.92 ± 19.12	174.08 ± 21.91	0.373	0.792
Mitral E Velocity, cm/s	82.89 ± 14.87	82.06 ± 19.14	78.42 ± 19.00	85.92 ± 17.89	0.279	0.04
Mitral A Velocity, cm/s	55.80 ± 10.52	54.0 ± 11.82	67.17 ± 22.04	63.25 ± 25.0	0.0277	0.305
Mitral E/A	1.53 ± 0.378	1.56 ± 0.422	1.35 ± 0.716	1.68 ± 1.05	0.201	0.121
Left Ventricle Septal E' Velocity, cm/s	10.28 ± 2.19	10.43 ± 2.10	7.75 ± 1.76	10.08 ± 2.87	0.424	< 0.01
Left Ventricle Septal E/E'	8.42 ± 1.79	8.01 ± 2.10	10.14 ± 1.87	8.83 ± 1.66	0.230	0.045
Left Ventricle Lateral E, cm/s	13.34 ± 2.84	14.20 ± 3.42	10.83 ± 3.38	12.92 ± 3.50	< 0.01	< 0.01
Left Ventricle Lateral E/E'	6.40 ± 1.45	5.93 ± 1.41	7.67 ± 2.26	7.0 ± 1.88	0.061	0.331
Right Ventricle E', cm/s	12.86 ± 2.71	12.59 ± 2.84	11.17 ± 2.44	12.83 ± 2.25	0.129	0.107
Pulmonary Artery Systolic Pressure, mmHg	24.02 ± 4.015	22.86 ± 4.51	23 ± 2.37	26 ± 7.46	0.140	0.406
Speckle-Tracking Strain Parameters						
Left ventricular global longitudinal strain, %	-22.05 ± 2.98	-22.77 ± 3.21	-16.68 ± 4.15	-20.52 ± 3.34	0.125	< 0.01
Right ventricular free wall strain, %	-21.56 ± 3.32	-22.02 ± 3.59	-19.32 ± 5.35	-23.49 ± 6.42	0.404	0.03
Left atrium reservoir strain, %	51.456 ± 11.24	48.78 ± 19.09	34.3 ± 19.31	44.32 ± 14.23	0.190	0.02

**Table 3.** Echocardiographic and speckle strain parameters at baseline and follow-up. 1: P-value comparing Non-Surgical Weight Loss at baseline and post intervention. 2: P-value comparing Surgical Weight Loss at baseline and post-intervention.

Variables	Non-surgical weight loss N = 66	Surgical weight loss N = 12	P-value
Anthropometric			
Reduction in BMI, kg/m <sup>2</sup>	-2.4 ± 1.12	-10.30 ± 2.74	< 0.01
Echocardiographic Parameters			
Left Ventricular Internal Diameter diastole, mm	0.184 ± 2.52	-0.417 ± 5.78	0.362
Left Ventricular Internal Diameter systole, mm	0.345 ± 2.28	-2.25 ± 4.90	< 0.01
Left Atrium, mm	-0.0566 ± 3.07	-0.167 ± 4.37	0.459
Left Ventricular Ejection fraction, visual, %	-0.316 ± 4.02	3.25 ± 5.53	< 0.01
Mitral Deceleration Time, ms	1.46 ± 32.32	2.17 ± 27.71	0.472
Mitral E Velocity, cm/s	-2.94 ± 11.77	7.5 ± 11.45	< 0.01
Mitral A Velocity, cm/s	-2.53 ± 9.40	-3.92 ± 12.62	0.333
Mitral E/A	0.0393 ± 0.342	0.147 ± 0.250	0.163
Left Ventricle Septal E' Velocity, cm/s	0.0547 ± 2.08	2 ± 1.90	< 0.01
Left Ventricle Septal E/E'	-0.369 ± 1.73	-1.31 ± 2.0	0.0513
Left Ventricle Lateral E, cm/s	0.858 ± 2.28	2.08 ± 1.44	0.04
Left Ventricle Lateral E/E'	-0.615 ± 1.63	-0.671 ± 2.29	0.461
Right Ventricle E', cm/s	-0.451 ± 2.87	-1.67 ± 3.29	0.101
Speckle-Tracking Strain Parameters			
Left ventricular global longitudinal strain, %	-1.13 ± 3.39	-3.84 ± 2.90	0.011
Right ventricular free wall strain, %	-1.24 ± 6.01	-4.17 ± 5.83	0.09
Left atrium reservoir strain, %	1.35 ± 13.96	10.02 ± 13.44	0.0386

**Table 4.** Differences in extent of changes at follow-up between non-surgical weight loss and surgical weight loss cohort.

in LVIDD and a significant improvement in fractional shortening and left ventricle ejection fraction. Participants in the SWL cohort also had significant improvement in mitral E velocity, mitral annular tissue Doppler septal and lateral E' velocities. The SWL cohort had also significant improvement in left ventricular global longitudinal and left atrium reservoir strain.

	Lean subjects (N = 10)	Overweight subjects (N = 66)	P-value
Age, years	33.92 ± 7.6	38.39 ± 8.9	0.112
Female sex, %	7 (70%)	59 (89.4)	0.09
Body Mass Index, kg/m <sup>2</sup>	19.4 ± 3.04	28.2 ± 2.66	< 0.01
Echocardiographic Parameters			
Left Ventricular Internal Diameter diastole, mm	44.4 ± 5.36	45.94 ± 3.01	0.184
Left Ventricular Internal Diameter systole, mm	28.2 ± 4.08	30.58 ± 5.64	0.204
Left Atrium, mm	32.4 ± 6.17	34.0 ± 4.13	0.291
Left Ventricular Ejection fraction, visual, %	63.6 ± 2.63	65.31 ± 3.93	0.188
Mitral Deceleration Time, ms	186.9 ± 26.18	170 ± 27.44	0.0720
Mitral E Velocity, cm/s	77.01 ± 17.14	82.89 ± 14.87	0.257
Mitral A Velocity, cm/s	54.01 ± 11.73	55.80 ± 10.52	0.623
Mitral E/A	1.47 ± 0.395	1.53 ± 0.378	0.643
Left Ventricle Septal E' Velocity, cm/s	9.85 ± 2.23	10.28 ± 2.19	0.566
Left Ventricle Septal E/E'	7.81 ± 2.78	8.42 ± 1.79	0.357
Left Ventricle Lateral E', cm/s	12.78 ± 1.80	13.34 ± 2.84	0.548
Left Ventricle Lateral E/E'	6.18 ± 1.90	6.40 ± 1.45	0.684
Right Ventricle E', cm/s	12.77 ± 3.94	12.86 ± 2.71	0.927
Pulmonary Artery Systolic Pressure, mmHg	24.29 ± 8.77	24.02 ± 4.015	0.870
Speckle-Tracking Strain Parameters			
Left ventricular global longitudinal strain, %	-24.4 ± 2.5	-22.05 ± 2.98	0.02
Right ventricular free wall strain, %	-28.8 ± 5.5	-21.6 ± 3.3	< 0.01
Left atrium reservoir strain, %	75.24 ± 9.174	51.46 ± 11.2	< 0.01

**Table 5.** Speckle-tracking strain parameters between lean versus overweight subjects.

Table 5 compares the baseline echocardiographic and speckle-trackings strain parameters between lean subjects and mildly overweight subjects in the NSWL cohort. Baseline echocardiographic parameters between lean and overweight subjects were similar in terms of systolic function, structural parameters and doppler indices. Lean subjects, however, had significantly higher strain parameters in all 3 chambers measured – left ventricle ( $-24.4 \pm 2.5$  vs.  $-22.05 \pm 2.98$ ,  $p = 0.02$ ), right ventricle ( $-28.8 \pm 5.5$  vs.  $-21.6 \pm 3.3$ ,  $p < 0.01$ ), and left atrium ( $75.24 \pm 9.174$  vs.  $51.46 \pm 11.2$ ,  $p < 0.01$ ).

### Predictors of improvement in strain parameters with gSEM

Using the gSEM model (Table 6) there was evidence supporting surgical modality of weight loss as an independent and significant predictor of improvement in strain parameter, after adjusting for the respective baseline strain parameters and change in BMI. Cardiovascular risk factors of hypertension, diabetes and hyperlipidemia were included into the gSEM model initially for exploratory purposes. Owing to the fact that the variables were statistically not significant ( $p > 0.05$ ) in analyzing the outcomes of strain parameters, we decided to exclude them in the final analysis on parsimonious grounds. Patients undergoing surgical weight loss had a significantly lower average follow-up GLS LV by about 4 units when compared with non-surgical subjects ( $p < 0.001$ ), after adjusting for baseline GLS LV and BMI. In the surgical cohort, patients had a significantly higher average follow-up GLS RV by about 12.6 units when compared with non-surgical subjects, after adjusted for baseline GLS RV and BMI ( $p < 0.001$ ). However, the impact of surgical weight loss on left atrium strain parameter was statistically non-significant ( $p: 0.364$ ).

### Discussion

Our study evaluated the difference of echocardiographic parameters and speckle-tracking strain parameters between Asian patients who were overweight undergoing NSWL and obese patients undergoing SWL. We also compared the differences in strain parameters between overweight patients undergoing NSWL and healthy lean subjects. Additionally, we evaluated the independent impact of modality of weight loss on speckle-tracking strain parameters. We found that obese participants in the SWL cohort had greater chamber enlargement in the left ventricle and left atrium as well as a lower LVEF. Patients who were obese had lower speckle-tracking strain parameters than overweight patients in the NSWL cohort. Therefore, these findings are consistent with prior studies showing that obesity is associated with chamber dilatation, diastolic dysfunction, and cardiac dysfunction<sup>18–20</sup>. Furthermore, the SWL cohort showed significant improvement in fractional shortening, diastolic dysfunction indices and speckle-tracking strain parameters. Patients in the NSWL group had a trend towards improvement in cardiac function.

Multiple studies have analyzed the association of obesity and cardiovascular co-morbidities including the development of cardiomyopathy and diastolic dysfunction<sup>21–23</sup>. The mechanisms with which obesity leads to cardiac dysfunction are likely multifactorial. For example, obesity is seen in association with hypertension as well as obstructive sleep apnea, which can lead to pathological LV remodeling when it is uncontrolled<sup>24,25</sup>. In addition, high levels of adiposity can also directly lead to fatty infiltration of the myocardium as well as a myocardial toxic effect, where the fatty infiltration may adversely affect myocardial elasticity and contractility<sup>26,27</sup>. Furthermore, persons living with obesity have chronically increased sympathetic response and decreased vagal tone which can result in pathological LV remodeling<sup>28</sup>. Obesity may also be linked to a pro-inflammatory state and suppressed B-type Natriuretic Peptide (BNP) that results in the clinical syndrome of heart failure over time, even in the context of preserved LVEF<sup>29,30</sup>. The confluence of these factors results in adverse cardiac remodeling leading to cardiac dysfunction. Our results demonstrate that subclinical cardiac dysfunction was already present in patients with BMI of  $28 \text{ kg/m}^2$ . Cardiac magnetic resonance (CMR) imaging evaluation uncomplicated obese patients support our findings of early adverse cardiac remodeling. A CMR study conducted by Liu et al. demonstrated increased LV size, thickness, and impaired myocardial contractility in Asian patients with uncomplicated obesity with a similar BMI profile of  $28 \text{ kg/m}^2$ <sup>31</sup>. These findings suggest adverse remodeling starts to occur at lower levels of BMI than previously thought.

To counter these adverse effects of obesity, bariatric surgery has been shown to be an effective method to cause a large reduction in BMI leading to an improvement in speckle-tracking strain parameters<sup>32,33</sup>. These studies had shown significant improvements following bariatric surgery in Western patients with markedly elevated BMI around  $50 \text{ kg/m}^2$ <sup>6,9</sup>. To date, there remained a scarcity of evidence showing similar benefits in Asians who do that have such high BMI and if bariatric surgery has a direct impact on speckle-tracking strain parameters. We demonstrated that despite body mass indices that were lower than their Western counterparts<sup>6,9</sup>, there were still significant improvements in the echocardiographic assessment of cardiac function following bariatric surgery in Asians. Our results also indicate that bariatric surgery was a significant predictor of improvement in speckle-tracking strain parameters, independent of change in BMI. To our knowledge, this is the first study analyzing the

Variable	Coefficient	95% Confidence interval	P value
Left Ventricle Strain	-4.01	-6.46-- -1.56	0.001
Right Ventricle Strain	12.56	5.67-19.44	<0.001
Left Atrium Strain	-3.3	-10.4 - 3.82	0.364

**Table 6.** Impact of Surgical Weight Loss on Strain Parameters – Structural Equation Model<sup>1</sup>. <sup>1</sup> Structural Equation Model has been adjusted for body mass index.

direct impact of surgical weight loss on strain parameters independent of BMI change. Further studies are needed to elucidate pathophysiological mechanism of the direct impact bariatric surgery has on strain parameters.

However, for patients who had NSWL, with lower pre-morbid BMI and less reductions in BMI following intervention, we could not similarly demonstrate an improvement in these echocardiographic parameters. It is worth noting that despite modest elevation of BMI, these patients already have subclinical cardiac dysfunction, as evidenced by having significantly lower speckle-tracking strain parameters than healthy lean subjects. This suggests that the onset of subclinical cardiac dysfunction occurs at a lower BMI than previously thought. Our findings further reinforce the need for patients to have aggressive weight management to be within the healthy BMI range. Our study adds to the growing body of evidence leading to the renewed focus of weight loss in the management of cardiovascular disease<sup>34</sup>. This is reflected in the growing prominence of Glucagon-like-peptide-1 receptor agonists (GLP-1 RAs). GLP-1 RAs have demonstrated robust and significant reductions in major adverse cardiac events in cardiovascular outcome trials<sup>35–37</sup>. This has prompted for the inclusion of GLP-1 RAs in the prevention of and treatment of ischemic heart disease<sup>38,39</sup>. It is thought that the weight loss – inducing properties of GLP-1 RAs is a key mediator in its cardiovascular benefits<sup>38</sup>. To the best of our knowledge, this is the first study to comprehensively evaluate the effect of non-surgical weight loss on echocardiographic parameters and speckle-tracking strain parameters in the overweight Asian population.

## Limitations

Overall, we examined a relatively small, single-center cohort of patients undergoing SWL or NSWL. The small cohort may compromise the statistical power of the study. Furthermore, we compared two heterogeneous cohorts, as they had different baseline BMI and underwent two different forms of weight loss – non-surgical versus surgical. As such, although we had only demonstrated improvement in echocardiographic parameters and speckle-tracking strain parameters in the SWL group, it could be the modest changes in BMI in the NSWL group as well as the lower baseline BMI that obscured the trends. We also did not measure the difference in the magnitude of lifestyle changes and exercise, which may also contribute to changes in cardiac function<sup>40</sup>. Furthermore, we did not adjust for the changes in dietary habits between the two groups, as certain component of diet may contribute to changes in myocardial strain<sup>41</sup>. Additionally, we have not elucidated the exact mechanism of how bariatric surgery directly improves myocardial performance independent of weight loss. Nevertheless, our findings show that the likelihood that excess weight loss resulted in the improvement in cardiac parameters, and this is consistent with obesity being associated with significant cardiovascular comorbidities.

## Future directions

Our study raises an interesting point regarding whether bariatric surgery should be performed earlier to prevent the onset of myocardial dysfunction. Various Asian bariatric and metabolic societies have proposed bariatric surgery to be performed for obese patients with a BMI range between 35 and 37 kg/m<sup>2</sup><sup>24</sup>. As indicated in Table 5, myocardial dysfunction, as assessed by speckle-tracking strain parameters, is already apparent in overweight patients. However, our study, with its small cohort does not test the ideal BMI threshold where bariatric surgery would prevent myocardial dysfunction. It is however an important topic to be investigated in the future.

Additionally, further studies are needed to assess if, changes in echocardiographic parameters between and after SWL or NSWL, are translated to improvement symptoms or in longer-term cardiovascular outcomes.

## Conclusion

In conclusion, we find that subclinical cardiac dysfunction is present in Asian patients with obesity and even in patients who are mild overweight. These suggest that the onset of subclinical cardiac dysfunction occurs at a lower level of BMI than previously thought. There was significant improvement in echocardiographic and strain parameters following SWL, with surgical modality being an independent predictor of improvement in strain parameters.

## Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Received: 31 March 2024; Accepted: 6 August 2024

Published online: 15 October 2024

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## Author contributions

Vinay Bahadur Panday, Jinghao Nicholas Ngiam, Siew Pang Chan, Sik Yin Tan and Kian Keong Poh were involved in the data collection, data analysis and writing of the manuscript. Asim Shabbir, Arthur Mark Richards, William K.F. Kong, James D. Thomas, Ching Hui Sia and Kian Keong Poh were involved in the conception and writing of the main manuscript text. All authors reviewed the manuscript.



## Funding

The study was funded in part by the National Medical Research Council (NMRC) Singapore, Transition Award (TA14nov017) and by the National University Health System Clinician Scientist Program (NCSP) award to Kian-Keong Poh.

## Competing interests

The authors declare no competing interests.

## Additional information

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