(>6 points), the median survival was 18 months, the 1-year survival was 60%, and the 5-year survival was 8%. One month after MitraClip implantation, only 51% of these patients were in NYHA functional class I or II. For comparison, among the low-risk patients (<3 points), the median survival was 47 months, the 1-year survival was 97%, and the 5-year survival was 76%. One month after MitraClip implantation, 78% of the patients were in NYHA functional class I or II. The C-statistic of the risk model against the 1-year survival was 0.71 (95% confidence interval: 0.65 to 0.77).

Survival and symptom reduction after clip implantation is highly variable. According to the current risk model, low- and intermediate-risk patients have an excellent outcome. In contrast, patients with multiple risk factors carry a poor prognosis and have a limited reduction in symptoms. In the latter patients, the limited benefit of mitral valve implantation should be taken into account in clinical decision making for a percutaneous mitral valve repair procedure.

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http://dx.doi.org/10.1016/j.jacc.2017.03.602

Please note: Dr. Van der Heyden has served as a proctor for Abbott Vascular MitraClip and Boston Lotus Valve. Dr. Baan has served as a proctor for Abbott Vascular MitraClip; and has received an unrestricted research grant from Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Obesity-Related Changes in Cardiac Structure and Function Among Asian Men and Women

Obesity is a global public health problem and major risk factor for cardiovascular disease and heart failure. Due to the high prevalence of diabetes and cardiovascular risk factors in Asians with relatively normal body mass index (BMI) defined by international standards, the World Health Organization (WHO) has recommended lower BMI thresholds for clinical prevention among Asians (1). However, the influence of these chosen cutoffs on cardiac structural and functional changes has not been comprehensively assessed in a large Asian population.

We aimed to investigate the influence of BMI and waist circumference (WC) on cardiac structural remodeling and functional alterations in >4,000 consecutive asymptomatic Asian participants undergoing cardiovascular health screening from 2009 to 2012 at a tertiary medical center in Taipei, Taiwan. The setting, design, and exclusion criteria have been previously published (2). All participants underwent comprehensive Doppler echocardiography including left ventricular (LV) deformation assessment by speckle tracking (version 10.8, EchoPAC, GE Vingmed Ultrasound, Horten, Norway) to define global longitudinal strain (GLS) (expressed as absolute values), global circumferential strain (GCS) (expressed as absolute values), and cardiac torsion. LV mass index (LVMi) was calculated as LV mass/height$^{2.7}$. BMI cutoffs were used to classify participants according to Public Health Action Trigger Points recommended by 2004 WHO Expert Consultation (**Table 1**) (1). The final cohort included a total of 4,031 participants with complete data.

In the entire cohort (mean age 49.8 ± 10.8 years, 65.2% men, mean BMI 24.3 ± 3.6 kg/m^2), higher BMI

TABLE 1 Associations Between Obesity and Changes in Cardiac Structures and Functions

	Unadjusted Means				Adjusted Means				Multivariate Linear Regression (BMI)		Multivariate Linear Regression (Waist Circumference)	
	Group 1	Group 2	Group 3	p for	Group 1	Group 2	Group 3	p for				
BMI, kg/m²	18.5–22.9	23.0–27.49	≥27.5	Trend	18.5–22.9	23.0–27.49	≥27.5	Trend	Beta (SE)	p Value	Beta (SE)	p Value
Conventional echocardiography												
IVS, mm	8.5 ± 1.1	9.2 ± 1.0*	9.6 ± 1.0*†	<0.001	8.8 ± 0.5	9.1 ± 0.4*	9.3 ± 0.4*†	<0.001	0.25 (0.005)	<0.001	0.24 (0.002)	<0.001
LVEDV, mL	69.9 ± 13.3	77.9 ± 12.2*	82.8 ± 11.3*†	<0.001	73.3 ± 6.4	77.4 ± 5.8*	78.2 ± 5.2*†	<0.001	0.10 (0.06)	<0.001	0.17 (0.02)	<0.001
LVEF, %	63.0 ± 5.1	62.3 ± 5.0*	61.8 ± 5.3*	<0.001	62.9 ± 0.9	62.3 ± 0.8*	62.2 ± 0.8*†	<0.001	−0.08 (0.03)	<0.001	−0.08 (0.01)	<0.001
LVMi, g/height$^{2.7}$	32.8 ± 7.4	37.3 ± 7.3*	41.8 ± 8.3*†	<0.001	35.0 ± 3.9	36.8 ± 3.6*	38.1 ± 3.8*†	<0.001	0.39 (0.04)	<0.001	0.25 (0.02)	<0.001
LAV (max), ml	25.1 ± 8.1	31.2 ± 10.3*	37.4 ± 12.0*†	<0.001	28.1 ± 3.7	30.7 ± 3.3*	32.2 ± 3.5*†	<0.001	0.34 (0.06)	<0.001	0.31 (0.02)	<0.001
Diastolic indices or deformation/torsion measures*												
e', cm/s	10.1 ± 2.5	9.1 ± 2.3*	8.3 ± 2.0*†	<0.001	9.8 ± 1.7	9.2 ± 1.5*	8.9 ± 1.6*†	<0.001	−0.12 (0.01)	<0.001	−0.13 (0.004)	<0.001
E/e'	7.5 ± 2.3	7.9 ± 2.5*	8.7 ± 2.7*†	<0.001	7.7 ± 1.3	7.9 ± 1.2*	8.1 ± 1.4*†	<0.001	0.10 (0.01)	<0.001	0.09 (0.005)	<0.001
GLS, %	20.8 ± 2.0	19.9 ± 1.7*	19.2 ± 1.7*†	<0.001	20.6 ± 0.8	20.0 ± 0.6*	19.7 ± 0.6*†	<0.001	−0.15 (0.01)	<0.001	−0.18 (0.004)	<0.001
GCS, %	18.5 ± 2.3	18.2 ± 2.3*	18.0 ± 2.2*†	<0.001	18.4 ± 0.4	18.3 ± 0.4*	18.1 ± 0.5*†	<0.001	−0.11 (0.01)	<0.001‡	−0.11 (0.005)	<0.001‡
Torsion, °/cm	2.23 ± 0.96	2.21 ± 0.89	2.16 ± 0.82	0.41	2.23 ± 0.24	2.20 ± 0.22*	2.11 ± 0.22*†	<0.001	−0.06 (0.005)	0.03‡	−0.07 (0.002)	0.02‡

Values are mean ± SD unless otherwise indicated. Group 1: acceptable risk (n = 1,473), Group 2: increased risk (n = 1,858), Group 3: high risk (n = 700); body mass index (BMI) cutoffs were based on 2004 World Health Organization Expert Consultation for Asians. Adjusted for age, blood pressure, heart rate, fasting glucose, total cholesterol, high-density lipoprotein cholesterol, estimated glomerular filtration rate, histories of hypertension, diabetes, and active smoking or cardiovascular disease in multivariate analysis. *p < 0.05 vs. Group 1. †p < 0.05 vs. Group 2 for analysis of variance post hoc analysis; global circumferential strain and global longitudinal strain were expressed as absolute values; further adjusted for left ventricular mass index for diastolic indices and deformation or torsion measures. ‡Interaction p for sex <0.05.

e' = tissue Doppler early-diastolic mitral annulus relaxation velocity; E = mitral inflow Doppler early-diastolic velocity; GCS = global circumferential strain; GLS = global longitudinal strain; IVS = interventricular septal thickness; LAV (max) = maximum left atrial volume; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; M/V = mass-to-volume ratio; RWT = relative wall thickness.

and larger WC were associated with greater LV mass, left atrial dilatation, lower tissue Doppler early-diastolic mitral annulus relaxation velocity (e′), higher early-diastolic mitral inflow-to-tissue Doppler velocity ratio (E/e′); more pronounced contractile dysfunction in terms of decreased GLS, GCS, and lower torsion after adjusting for age, sex, LVMi, heart rate, biochemical data, active smoking, histories of hypertension, diabetes, or cardiovascular disease (all $p < 0.05$) (Table 1). Important sex differences were observed, wherein women had a more pronounced functional decline in GCS (for women, adjusted $\beta = -0.14$, $p < 0.001$; for men, adjusted $\beta = -0.08$, $p = 0.004$) and torsion (for women, adjusted $\beta = -0.08$, $p = 0.02$; for men, adjusted $\beta = -0.01$, $p = 0.17$) with greater BMI than men (all $p_{interaction} < 0.05$).

To define subclinical LV contractile dysfunction, we examined the lower 95th percentile cutoff values for GLS in a subset of 2,798 healthy participants (1,757 men and 1,041 women) free of hypertension, diabetes, hyperlipidemia, or cardiovascular disease, and with estimated glomerular filtration rate >60 ml/min/1.73 m^2. This provided the lower reference values of normal GLS of 17.6% and 18.3% for men and women, respectively. Sex-specific optimal BMI and WC cutoffs for detecting subclinical LV contractile dysfunction were 26.4 kg/m^2 and 87.5 cm in men and 23.4 kg/m^2 and 83 cm in women.

In this first and largest study assessing obesity-related changes in cardiac structure and function, including LV deformation, among asymptomatic Asian adults, we found that obesity was associated with unfavorable LV remodeling and worse global myocardial deformation, indicating subclinical LV contractile dysfunction despite preservation of chamber ejection fraction. Importantly, sex-specific optimal cutoffs for identifying subclinical LV contractile dysfunction were substantially lower than the current established WHO criteria for Asians (1), especially in women. Furthermore, women showed steeper declines in GCS and torsion with increasing BMI and WC. As the LV may display gender-specific differential remodeling patterns in response to noxious stimuli (3), we speculated that such differences may contribute to the observed functional alterations with excessive BMI by gender.

Our study is limited by its retrospective cross-sectional design, and we cannot draw conclusions regarding causality. Nonetheless, these data add to prior data on obesity-related cardiac changes by providing comprehensive analysis of LV systolic mechanics across a broad range of BMI in a large

Asian population. Importantly, our findings support the use of lower BMI cutoffs to define obesity in Asian adults, by demonstrating the presence of LV structural and functional changes even at these lower cutoffs. Furthermore, lower BMI thresholds may be needed for public health action (e.g., encouraging weight loss and exercise) in Asian communities, and particularly among Asian women who have a lower BMI threshold for subclinical LV contractile dysfunction and steeper decline in LV mechanics with increasing BMI and WC. The implications of our findings for the development of future heart failure deserve further study, particularly heart failure with preserved ejection fraction, which is increasingly recognized to include an obesity-related phenotype (4).

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http://dx.doi.org/10.1016/j.jacc.2017.04.016

Please note: Dr. Lam was supported by a Clinical Scientist Award from the National Medical Research Council; has received research support from Boston Scientific, Bayer, Thermo Fisher, Medtronic, and Vifor Pharma; and has served as a consultant for Bayer, Novartis, Takeda, Merck, AstraZeneca, Janssen Research & Development, LLC, Menarini, Boehringer Ingelheim, and Abbott Diagnostics. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Collapse of the Aspirin Empire

Is it Diabetic Gastroparesis or Cardioprotective Paresis?

I have read with great interest the paper recently published in the *Journal* by Bhatt et al. (1). The investigators reported that a high proportion of patients treated with enteric-coated (EC) aspirin failed to achieve complete inhibition of thromboxane B2 generation due to incomplete absorption. Reduced bioavailability may contribute to "aspirin resistance" in patients with diabetes (1).

Diabetic gastroparesis (DG) is a clinical syndrome characterized by delayed gastric emptying in the absence of mechanical obstruction of the stomach. DG has been generally attributed to autonomic neuropathy and poorly controlled hyperglycemia. The prevalence of gastroparesis is reported to be 20% to 40% of patients with type 2 diabetes mellitus (T2DM) (2). DG can result in many consequences such as impaired glucose regulation, hypoglycemia, decrease drug absorption, nutritional compromise, and a high rate of hospitalizations and poor quality of life (3). DG is associated with coronary artery disease, cardiovascular autonomic dysfunction, and microvascular complications such as peripheral neuropathy and retinopathy. Poor long-term glycemic control, such as elevated hemoglobin A_{1c} and body mass index, were independent predictors of DG (4). Recently, Saito et al. (5) reported that low-dose aspirin irrespective of EC did not affect the risk for cardiovascular events but increased the risk for gastrointestinal bleeding in patients with T2DM in a primary prevention setting.

Growing evidence has demonstrated that EC aspirin therapy fails in primary prevention in patients with T2DM. On account of DG prevalence and adverse effect on drug absorption, DG should be considered as a part of aspirin resistance in patients with T2DM.

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http://dx.doi.org/10.1016/j.jacc.2017.02.074

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.