Galectin-3 as a candidate upstream biomarker for quantifying risks of myocardial ageing

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Abstract

Aims Galectin-3 (Gal-3) is implicated in the pathogenesis of heart failure and is also influenced by ageing. This study aims to determine the extent to which Gal-3 levels estimate odds of myocardial dysfunction in ageing cohorts, ‘upstream’ prior to clinical disease.

Methods and results Four hundred seventy-five asymptomatic subjects underwent simultaneous assessments of cardiovascular structure and function, with measurements of circulating Gal-3. Myocardial dysfunction was defined as impaired myocardial relaxation (ratio of peak velocity flow in early diastole E (m/s) to peak velocity flow in late diastole by atrial contraction A (m/s) < 0.84) (mean E/A ratio 0.84 in the cohort). Of 475 subjects (mean age 68 ± 12 years, 231 women), 222 (47%) had myocardial dysfunction. Subjects with myocardial dysfunction were older (mean age 73 ± 5 vs. 64 ± 14 years, P < 0.0001), and more had hypertension (59 vs. 40%, P < 0.0001), dyslipidaemia (54 vs. 39%, P = 0.001), diabetes mellitus (25 vs. 14%, P = 0.002), higher body mass index (BMI) (24 vs. 23 kg/m², P = 0.002), and higher heart rate (76 vs. 71 b.p.m., P = 0.0001). Participants with impaired myocardial relaxation had lower peak velocity flow in early diastole E (0.6 ± 0.1 vs. 0.8 ± 0.2 m/s, P < 0.0001), and higher peak velocity flow in late diastole by atrial contraction A (0.9 ± 0.1 vs. 0.7 ± 0.2 m/s, P < 0.0001), and higher mitral valve flow deceleration time (224.7 ± 43.2 vs. 204.8 ± 33.1 m/s, P < 0.0001). Participants with impaired myocardial relaxation had higher Gal-3 levels (17.2 ± 6.2 vs. 15.5 ± 4.1, P = 0.0004) but similar B-type natriuretic peptide (37 ± 4 vs. 34 ± 29, P = 0.37) and high-sensitivity troponin I (21 ± 72 vs. 11 ± 41, P = 0.061) levels and urine microalbumin-to-creatinine ratio (4.6 ± 8.1 vs. 4.2 ± 10.8, P = 0.75) compared with those without impaired myocardial relaxation. After multivariable adjustments, Gal-3 [odds ratio (OR) 1.05, 95% confidence interval (CI) 1.00–1.10, P = 0.039], age (OR 2.60, 95% CI 1.64–4.11, P < 0.0001), BMI (OR 2.16, 95% CI 1.44–3.23, P < 0.0001), and heart rate (OR 1.04, 95% CI 1.02–1.06, P < 0.0001) were associated with impaired myocardial relaxation. Adjusted ORs (95% CI) for myocardial dysfunction were 1.0 (ref), 1.62 (0.92–2.85), 1.92 (1.08–3.41), and 2.01 (1.11–3.66) across consecutive quartiles of Gal-3 after adjustment for age, BMI, risk factors, and heart rate.

Conclusions Among asymptomatic community-dwelling elderly adults, the highest quartile of Gal-3 was associated with twofold increased odds of myocardial dysfunction compared with the lowest quartile of Gal-3. Gal-3 may have a role as an ‘upstream’ biomarker in estimating odds of myocardial ageing prior to clinical disease.

Keywords Galectin-3; Biomarker; Cardiovascular; Ageing

Received: 22 March 2019; Revised: 17 May 2019; Accepted: 14 June 2019

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Introduction

The ageing heart undergoes morphological alterations over time.¹–³ Ageing of the cardiovascular system is exemplified by alterations that include diastolic dysfunction, increased arterial stiffness, and impairments in endothelial functions.²,⁴ These morphological and functional changes contribute to the prevalence of heart failure (particularly heart failure with
preserved ejection fraction) in the ageing population.\textsuperscript{5,6} The prevalence of heart failure in persons aged older than 75 years is approximately 8.4% compared with 0.7% in those aged 45–54 years.\textsuperscript{7} Despite this huge burden of heart failure in older persons, elderly adults are poorly represented in clinical research.\textsuperscript{8–10} To address this burden, tools that predict structural and functional alterations in the heart prior to incident cardiovascular disease are urgently needed to tackle cardiovascular disease risks in older persons.

Current literature and clinical practice emphasize investigations that use biomarkers to understand cardiovascular disease. However, there are hardly any investigations into candidate biomarkers that can represent processes of myocardial ageing that may predate incident cardiovascular disease.

Galectin-3 (Gal-3) is a β-galactoside-binding lectin that plays a role in inflammation, fibrosis, atherosclerosis, and heart failure.\textsuperscript{11–14} High Gal-3 levels are associated with cardiovascular mortality and adverse outcomes,\textsuperscript{15,16} while inhibition of Gal-3 has been found to prevent adverse cardiac remodelling.\textsuperscript{17} Gal-3 levels increase with age and have been shown to be associated with cardiovascular risk factors\textsuperscript{18} and ageing outcomes.\textsuperscript{19} Given these properties, Gal-3 may represent a composite biomarker of age-associated cardiovascular ageing.

In this study, we hypothesize that Gal-3 levels may be associated with cardiovascular ageing among elderly adults, specifically defined by an early phase of myocardial ageing, representative of ‘upstream’ alterations prior to clinical disease. If our hypothesis is true, then Gal-3 levels may be used ‘upstream’ prior to cardiovascular development in ageing, to personalize an individual’s risks of cardiovascular deterioration with age.

**Methods**

The subjects were recruited from the Cardiac Ageing Study (CAS)\textsuperscript{20,21} a prospective study initiated in 2014 that examines characteristics and determinants of cardiovascular function in elderly adults. CAS participants were recruited from the local community and also from the prospective, population-based cohort, the Singapore Chinese Health Study.\textsuperscript{22}

The study sample consisted of men and women who participated in the baseline CAS 2014 examination who had no self-reported history of physician-diagnosed cardiovascular disease (such as coronary heart disease and stroke) or cancer. The study complies with the Declaration of Helsinki. Written informed consent was obtained from participants upon enrolment. The SingHealth Centralised Institutional Review Board (2014/628/C) had approved the study protocol. All methods were performed in accordance with the relevant guidelines and regulations.

All participants were examined and interviewed on one study visit by trained study coordinators. Participants completed a standardized questionnaire that included medical history and coronary risk factors. Hypertension was defined by current use of antihypertensive drugs or physician-diagnosed hypertension. Diabetes mellitus was defined by current use of anti-diabetic agents or physician-diagnosed diabetes mellitus. Dyslipidaemia was defined by current use of lipid-lowering agents or physician-diagnosed dyslipidaemia. Smoking history was defined as ever smokers (former or current smoking) or never smokers. Body mass index was calculated as weight in kilograms divided by the square of height in metres. Sinus rhythm status was ascertained by resting electrocardiogram. Clinical data were obtained on the same day as assessment of echocardiography and serum collection.

**Transthoracic echocardiography imaging**

Echocardiography was performed using ALOKA α10 with a 3.5 MHz probe. In each subject, standard echocardiography, which included two-dimensional, M-mode, pulse Doppler and tissue Doppler imaging, was performed in the standard parasternal and apical (apical four-chamber, apical two-chamber, and apical long) views, and three cardiac cycles were recorded. The left ventricular ejection fraction, left atrial volume, and left atrial volume index were measured. The transmirtal flow E and A waves with the sample volume position at the tip of the mitral valve leaflets from the apical four-chamber view were recorded by Doppler echocardiography. E/A ratio was computed as a ratio of peak velocity flow in early diastole E (m/s) to peak velocity flow in late diastole by atrial contraction A (m/s). Pulsed wave tissue Doppler imaging was performed with the sample volume at the septal and lateral annulus from the apical four-chamber view. The frame rate was between 80 and 100 frames per second. The tissue velocity patterns were recorded and expressed as E’ and A’. All measurements were measured by the same operator, and the measurements were averaged over three cardiac cycles and adjusted by the RR interval.

**Biomarker measurements**

Blood samples were collected on the day of echocardiography acquisition. Plasma levels of Gal-3 (ARCHITECT Galectin-3; produced by Fujirebio Diagnostics Inc for Abbott Laboratories), high-sensitivity troponin I (ARCHITECT STAT High Sensitive Troponin I; Abbott Laboratories), and B-type natriuretic peptide (BNP) (ARCHITECT BNP; produced by Fujirebio Diagnostics Inc for Abbott Laboratories) were measured on the Abbott ARCHITECT i2000SR analyser. Mid-stream urine samples were collected for analysis of random spot urine microalbumin-to-creatinine ratio. Urine microalbumin

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ESC Heart Failure 2019; 6: 1068–1076
DOI: 10.1002/ehf2.12495
(ARCHITECT Microalbumin; Abbott Laboratories) and urine creatinine (ARCHITECT Creatinine; Abbott Laboratories) were measured on the ARCHITECT cSystems.

**Statistical methodology**

We first examined bivariable association of subject clinical characteristics, cardiac function, and biomarkers with impaired myocardial relaxation. Impaired myocardial relaxation was defined as ratio of peak velocity flow in early diastole E (m/s) to peak velocity flow in late diastole by atrial contraction A (m/s) less than 0.84 (mean E/A ratio was 0.84 in our study sample).

Clinical characteristics, cardiac function, and biomarkers were compared between preserved and impaired myocardial relaxation using t-test or \( \chi^2 \) test as appropriate. Continuous variables are reported as a mean with standard deviation.

Logistic regression models were constructed to assess the association of Gal-3 with impaired myocardial relaxation. The initial univariable logistic regression model examined the individual association with demographic variables and clinical covariates. Those variables associated in the univariable analysis with a \( P < 0.05 \) were candidate confounding factors associated with Gal-3. These candidates were then adjusted via multivariable logistic regression. We further fitted a logistic regression to estimate relative risks of impaired myocardial relaxation across Gal-3 quartiles controlled for potential confounding factors. To explore the shape of the association, we fitted restricted cubic splines with four knots at the 10th, 36.7th, 63.4th, and 90th, using the 12th percentile of Gal-3 as the reference. Odds ratios (ORs) for impaired myocardial relaxation and the 95% confidence intervals (CIs) are shown in the graph. A Wald-type test for non-linearity yielded a \( P \)-value \(<0.0001\), suggesting that a non-linear curve was the best fit for the data. The association between Gal-3 quartiles and E/A ratio is shown in age groups (<65, 65–75, and >=75 years). The association between Gal-3 and other echocardiographic parameters is explored using linear regression (Supporting Information, Table S1).

All statistical analyses were performed using STATA 15 (College Station, TX, USA). For all analysis, a two-tailed \( P \)-value of <0.05 was considered significant.

**Results**

**Baseline characteristics of the study population**

A total of 475 participants (mean age 68 ± 12 years, 231 women) were included in the analysis. All completed clinical assessment, transthoracic echocardiography, and blood sampling on the same day.

The baseline characteristics of the study sample are shown in Table 1. There were 222 (47%) participants with impaired myocardial relaxation. Participants with impaired myocardial relaxation were older (mean age 73 ± 5 vs. 64 ± 14 years, \( P < 0.0001 \)), and more had hypertension (59 vs. 40%, \( P < 0.0001 \)), dyslipidaemia (41 vs. 39%, \( P = 0.001 \)), diabetes mellitus (25 vs. 14%, \( P = 0.002 \)), higher body mass index (24 ± 3 vs. 23 ± 4 kg/m², \( P = 0.002 \)), higher systolic blood pressure (138 ± 20 vs. 148 ± 27 mmHg, \( P < 0.0001 \)), and higher pulse rate (76 vs. 71 b.p.m., \( P = 0.0001 \)). Participants with impaired myocardial relaxation had higher Gal-3 levels (17.2 ± 6.2 vs. 15.5 ± 4.1, \( P = 0.0004 \)) but similar BNP (37 ± 4 vs. 34 ± 29, \( P = 0.37 \)) and high-sensitivity troponin I (21 ± 72 vs. 11 ± 41, \( P = 0.061 \)) levels and urine microalbumin-to-creatinine ratio (4.6 ± 8.1 vs. 4.2 ± 10.8, \( P = 0.75 \)) compared with those with preserved myocardial relaxation.

Participants with impaired myocardial relaxation had greater interventricular septum thickness at end diastole (0.81 ± 0.1 vs. 0.78 ± 0.1 cm, \( P = 0.013 \)), greater interventricular septum thickness at end systole (1.3 ± 0.2 vs. 1.2 ± 0.2 cm, \( P = 0.0009 \)), greater left ventricular posterior wall at end diastole (0.8 ± 0.1 vs. 0.7 ± 0.1 cm, \( P = 0.0002 \)), greater left ventricular posterior wall at end systole (1.5 ± 0.2 vs. 1.4 ± 0.2 cm, \( P = 0.018 \)), greater left ventricular mass index (77.7 ± 32.3 vs. 71.5 ± 20.0 g/m², \( P = 0.029 \)), greater isovolumic relaxation time (107.3 ± 19.8 vs. 95.2 ± 16.3 ms, \( P < 0.0001 \)), lower peak velocity flow in early diastole (0.6 ± 0.1 vs. 0.8 ± 0.2 m/s, \( P < 0.0001 \)), higher peak velocity flow in late diastole by atrial contraction A (0.9 ± 0.1 vs. 0.7 ± 0.2 m/s, \( P < 0.0001 \)), and higher mitral valve flow deceleration time (224.7 ± 43.2 vs. 204.8 ± 33.1 m/s, \( P < 0.0001 \)). Notably, participants with impaired myocardial relaxation did not have other features of diastolic dysfunction: mean ratio of peak velocity flow in early diastole to peak early diastolic septal mitral annular velocity was 9.9 ± 2.8, mean peak early diastolic septal mitral annular velocity was 0.07 ± 0.02, mean pulmonary artery systolic pressure was 26.7 ± 7.5 mmHg, and mean left atrial volume index was 21.1 ± 7.1 (ml/m²). All participants had preserved left ventricular systolic function. These results are presented in Table 1.

**Galectin-3 and its relationship with age and myocardial function**

Participants were divided into age subgroups (<65, 65–75, and >=75 years) and quartiles of Gal-3 (Figure 1). In tandem with reductions in E/A ratio seen between the age groups, we observed increases in Gal-3 levels with age.

The univariable associations between Gal-3 and echocardiographic parameters are displayed in Supporting Information, Table S1. There was an association between Gal-3 and
isoventricular relaxation time (β = 0.41, P = 0.032), peak velocity flow in late diastole by atrial contraction (β = 0.008, P < 0.0001), mitral valve flow deceleration time (β = 0.88, P = 0.01), pulmonary artery systolic pressure (β = 0.13, P = 0.038), pulmonary vein systolic velocity (β = 0.27, P = 0.012), pulmonary vein flow at atrial contraction (β = 0.14, P = 0.001), peak early diastolic septal mitral annular velocity (β = -0.001, P < 0.0001), peak early diastolic lateral mitral annular velocity (β = -0.001, P < 0.0001), and ratio of peak velocity flow in early diastole E to peak early diastolic septal mitral annular velocity (β = 0.07, P = 0.007).

**Determinants of impaired myocardial relaxation**

At the univariate level, Gal-3 levels (OR 1.09, 95% CI 1.04–1.14, P < 0.0001), age (OR 2.57, 95% CI 1.69–3.90, P < 0.0001), body mass index (OR 1.96, 95% CI 1.35–2.84, P < 0.0001), hypertension (OR 2.17, 95% CI 1.50–3.13, P < 0.0001), and diabetes mellitus (OR 1.94, 95% CI 1.46–2.58, P < 0.0001) were associated with impaired myocardial relaxation.
In a prospective cohort study of elderly adults pre-specified to study alterations in cardiovascular structure and function with ageing, our results suggest that Gal-3 may be used to predict odds of myocardial dysfunction associated with myocardial ageing.

In this cross-sectional analysis, we observed impairments in myocardial relaxation, typically seen with ageing when left ventricular filling decreases in early diastole, leading to reductions in the mitral peak early-to-late diastolic filling velocity ratio. In contrast to studies that have reported associations between Gal-3 and cardiovascular conditions within clinical cohorts, our studied cohort consisted of community-dwelling elderly adults who did not have clinical heart failure, further supported by relatively low BNP levels. Notably, BNP levels were similar among those with or without impaired myocardial relaxation. Besides, levels of high-sensitivity troponin I assays in the cohort were low and below upper reference limits suggested in other studies and those that rule out coronary artery disease.

Age-associated changes in Gal-3 have been reported in other cohorts, and our findings confirm these previous observations. In fact, we provide new findings by demonstrating changes in Gal-3 within age subgroups that correlated with reductions in myocardial function. Our large sample size had allowed depictions of exact quartiles of Gal-3 to be studied in relation to both age and myocardial ageing. This allows future studies to reference their findings in relation to similar reference quartiles. Prior studies among clinical cohorts

### Table 3: Odds ratio (95% CI) for impaired myocardial relaxation by quartile of galectin-3

| Quartiles of galectin median (range) | Number of cases | Odds ratio (95% CI) |
|-------------------------------------|-----------------|---------------------|
| Low: 12.1 (6.4–13.6)                | 121             | 1.00                |
| 14.6 (13.7–15.6)                    | 123             | 1.62 (0.92–2.85)    |
| 16.7 (15.7–18.3)                    | 115             | 1.92 (1.08–3.41)    |
| High: 20.9 (18.4–83)                | 116             | 2.01 (1.11–3.66)    |

CI, confidence interval.

*Adjusted for age, body mass index, pulse, hypertension, dyslipidaemia, and diabetes.

### Table 2: Univariate and multivariate association with impaired myocardial relaxation

|                               | Unadjusted OR (95% CI) | P-value | Adjusted OR (95% CI) | P-value |
|-------------------------------|------------------------|---------|----------------------|---------|
|                               | Univariate             |         | Multivariate         |         |
| Galectin-3                    | 1.09 (1.04–1.14)       | <0.0001 | 1.05 (1.00–1.10)     | 0.039   |
| Age ≥75 years                 | 2.57 (1.69–3.90)       | <0.0001 | 2.60 (1.64–4.11)     | <0.0001 |
| BMI ≥ 23 kg/m²                | 1.96 (1.35–2.84)       | <0.0001 | 2.16 (1.44–3.23)     | <0.0001 |
| Hypertension                  | 2.17 (1.50–3.13)       | <0.0001 | 1.42 (0.91–2.22)     | 0.120   |
| Dyslipidaemia                 | 1.86 (1.29–2.68)       | 0.001   | 1.39 (0.90–2.16)     | 0.139   |
| Diabetes mellitus             | 2.10 (1.32–3.36)       | 0.002   | 1.37 (0.79–2.36)     | 0.263   |
| Heart rate                    | 1.03 (1.01–1.05)       | <0.0001 | 1.04 (1.02–1.06)     | <0.0001 |

BMI, body mass index; CI, confidence interval; OR, odds ratio.

### Discussion

In prospective cohort study of elderly adults pre-specified to study alterations in cardiovascular structure and function with ageing, our results suggest that Gal-3 may be used to predict odds of myocardial dysfunction associated with myocardial ageing.

In this cross-sectional analysis, we observed impairments in myocardial relaxation, typically seen with ageing when left ventricular filling decreases in early diastole, leading to reductions in the mitral peak early-to-late diastolic filling velocity ratio. In contrast to studies that have reported associations between Gal-3 and cardiovascular conditions within clinical cohorts, our studied cohort consisted of community-dwelling elderly adults who did not have clinical heart failure, further supported by relatively low BNP levels. Notably, BNP levels were similar among those with or without impaired myocardial relaxation. Besides, levels of high-sensitivity troponin I assays in the cohort were low and below upper reference limits suggested in other studies and those that rule out coronary artery disease.

Age-associated changes in Gal-3 have been reported in other cohorts, and our findings confirm these previous observations. In fact, we provide new findings by demonstrating changes in Gal-3 within age subgroups that correlated with reductions in myocardial function. Our large sample size had allowed depictions of exact quartiles of Gal-3 to be studied in relation to both age and myocardial ageing. This allows future studies to reference their findings in relation to similar reference quartiles. Prior studies among clinical cohorts

**P < 0.0001**, dyslipidaemia (OR 1.86, 95% CI 1.29–2.68, P = 0.001), diabetes mellitus (OR 2.10, 95% CI 1.32–3.36, P = 0.002), and heart rate (OR 1.03, 95% CI 1.01–1.05, P < 0.0001) were associated with impaired myocardial relaxation. After multivariable adjustments, Gal-3 (OR 1.05, 95% CI 1.00–1.10, P = 0.039), age (OR 2.60, 95% CI 1.64–4.11, P < 0.0001), body mass index (OR 2.16, 95% CI 1.44–3.23, P < 0.0001), and heart rate (OR 1.04, 95% CI 1.02–1.06, P < 0.0001) remained independently associated with impaired myocardial relaxation. These results are presented in Table 2.

In a multivariable adjusted model, the highest quartile of Gal-3 was associated with two-fold higher odds of impaired myocardial relaxation compared with the lowest quartile (OR 2.01, 95% CI 1.11–3.66) (Table 3).

Data fitting using cubic splines revealed that the magnitude of the association between Gal-3 and impaired myocardial relaxation increased substantially as Gal-3 increased (Figure 2).
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Figure 2 Cubic splines showing association of galectin-3 with impaired myocardial relaxation. The solid dark line represents the odds ratio, and the dotted lines represent 95% confidence intervals. We fitted restricted cubic splines with four knots at the 10th, 36.7th, 63.4th, and 90th percentile in a logistic regression model adjusted for age, body mass index, hypertension, dyslipidaemia, diabetes mellitus, and heart rate.

Relatively, the Cardiovascular Health Study, a community study of older living adults, had demonstrated associations between circulating fibrosis-related biomarkers with future risks of incident cardiovascular disease. Taken together, our data support the notion that detection of preclinical myocardial dysfunction in community-dwelling elderly adults using circulating biomarkers such as Gal-3 may be used as a preventative strategy against incident heart failure with preserved ejection fraction among elderly adults.

Our cross-sectional observations preclude causal and biological inferences. However, impaired relaxation is a common characteristic of the aged heart with increasing recognition that myocardial fibrosis may be a contributing factor. Specifically, interventional studies involving disease models suggest that excess collagen, and not myocyte hypertrophy, contributes to myocardial fibrosis in ageing. Gal-3 binds to extracellular proteins and contains collagen-like domains that are substrates for cleavage by matrix metalloproteinases — a group of endopeptidases responsible for matrix protein degradation. In rats, intrapericardial infusion of Gal-3 resulted in left ventricular collagen accumulation and reduction in left ventricular ejection fraction. Given that ageing leads to alterations in the cardiac interstitium, higher circulating levels of Gal-3 may reflect increased cell proliferation and collagen production in the myocardium.

Several limitations of this study deserve mention. First, plasma levels of biomarkers were measured at a single time point, and it is possible that the longitudinal trajectory of change in biomarkers may provide additional causal inferences, independent of baseline levels, on future risks of cardiovascular disease in this cohort. Second, we evaluated myocardial function by conventional echocardiography. Imaging modalities such as magnetic resonance imaging may detect myocardial fibrosis with greater sensitivity and specificity, but their use is not easily replicated in large-scale community studies particularly if intravenous administration of imaging contrast is required. Plasma biomarkers such as Gal-3 are readily available and provide a non-invasive assessment of ageing-related fibrosis appropriate for cohort studies. Given current developments in antifibrotic agents, clinical trials targeting fibrosis may use plasma Gal-3 to determine effects on fibrosis-related myocardial function, extending upstream as a preventive strategy in preclinical cohorts such as high-risk older adults, identified by Gal-3 levels. Third, we acknowledge that our sample size is limited, consisting of mainly older adults. A control group of younger middle-aged adults, matched for gender, may further strengthen our observations regarding myocardial ageing. Fourth, we had focused on left heart assessment in this analysis only. We did not report information about the right heart. Right heart assessment such as right ventricular strain and right ventricular systolic pressure has been previously associated with Gal-3. Importantly, Gal-3 has also been associated with preclinical metabolic heart disease among young obese patients.
who had abnormalities in right ventricular coupling.\textsuperscript{51} Thus, right heart assessment may have added important insights into right heart ageing as a preclinical manifestation of age-related heart dysfunction. Fifth, our study sample consisted of older adults of ethnic Asian Chinese descent, for which results may not be applicable to participants of different ethnic origins within Asia. Given that Gal-3 may be associated with cardiovascular outcomes differentially by race,\textsuperscript{52} future studies incorporating different Asian ethnic groups may be necessary to qualify our observations better among Asians. Finally, while we observed no association between microalbuminuria and myocardial dysfunction in this cohort, we acknowledge that renal clearance of plasma Gal-3 may be impaired in certain populations\textsuperscript{25,53} and more specific measures of kidney function could have been useful for further multivariable adjustments.

However, our study has several strengths. We conducted our study in a large well-characterized community-based population. The large sample size contributed to statistical power and adjustments for confounders. The collection of biomarkers occurred simultaneously with clinical assessment, reducing likelihood of misclassification bias.

In conclusion, Gal-3, in the setting of elderly adults, is associated with impairments in myocardial function related to ageing. Our findings provide support for future research into pathways represented by circulating biomarkers such as Gal-3 to detect cardiovascular disease upstream in order to reduce cardiovascular disease downstream in populations. In the setting of clinical trials, Gal-3 could potentially be used to identify target populations for early interventions.

Acknowledgements

We thank the staff of the imaging and biomarker laboratories for participating in the conduct of the study and Abbott for providing the reagents and kits for biomarker measurements.

Conflict of interest

None declared.

Funding

The Cardiac Aging Study has received funding support from the National Medical Research Council of Singapore (NMRC/TA/0031/2015 and MOH-000153), Hong Leong Foundation, Duke-NUS Medical School, Estate of Tan Sri Khoo Teck Puat, and SingHealth Foundation. Those participants recruited from the Singapore Chinese Health Study were supported by the US National Institutes of Health (NIH R01 CA144034 and UM1 CA182876). The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Associations between galectin-3 and echocardiographic parameters.

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