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ORIGINAL ARTICLE

Cardiac troponin T associates with left ventricular function and synchrony assessed by CMR in the general population: results from the Akershus Cardiac Examination 1950 Study

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Abstract

Background and aim Cardiac troponin T (cTnT) is a blood biomarker of myocardial injury that is associated with future adverse cardiovascular events in the general population. Left ventricular (LV) global longitudinal strain (GLS) and mechanical dispersion (MD) are metrics of systolic function and synchrony that can be obtained from cardiac imaging. Studies suggest an association between cTnT and echocardiographically assessed GLS and MD, but it is unknown whether cTnT relates to these metrics when assessed by cardiac magnetic resonance (CMR). We hypothesized that cTnT associates with GLS and with MD assessed by CMR feature tracking (CMR-FT) in the general population.

Methods and results cTnT and CMR-FT measurements were performed in 186 community dwellers from the Akershus Cardiac Examination 1950 Study. The participants' age ranged from 68 to 70 years. Median cTnT concentration was 7.0 ng/L (interquartile interval 5.0–12.6 ng/L), median absolute value of GLS was 17.3% (interquartile interval 15.7–18.8%), and median MD was 80.7 milliseconds (interquartile interval 61.8–105.0 milliseconds). In multivariable linear regression models adjusted for common clinical risk factors of cardiovascular disease, with GLS and MD as outcome and cTnT as the predictor variable of interest, $\log_{10}$ transformed cTnT was significantly associated with both absolute GLS [β-coefficient −1.65, confidence interval (−2.84, −0.46)] and MD [β-coefficient 28.56, confidence interval (12.14, 44.92)].

Conclusion In older adults from the general population, higher cTnT concentrations are associated with worse systolic function and synchrony assessed by CMR-FT LV GLS and MD, adding information about myocardial function to traditional risk factors.

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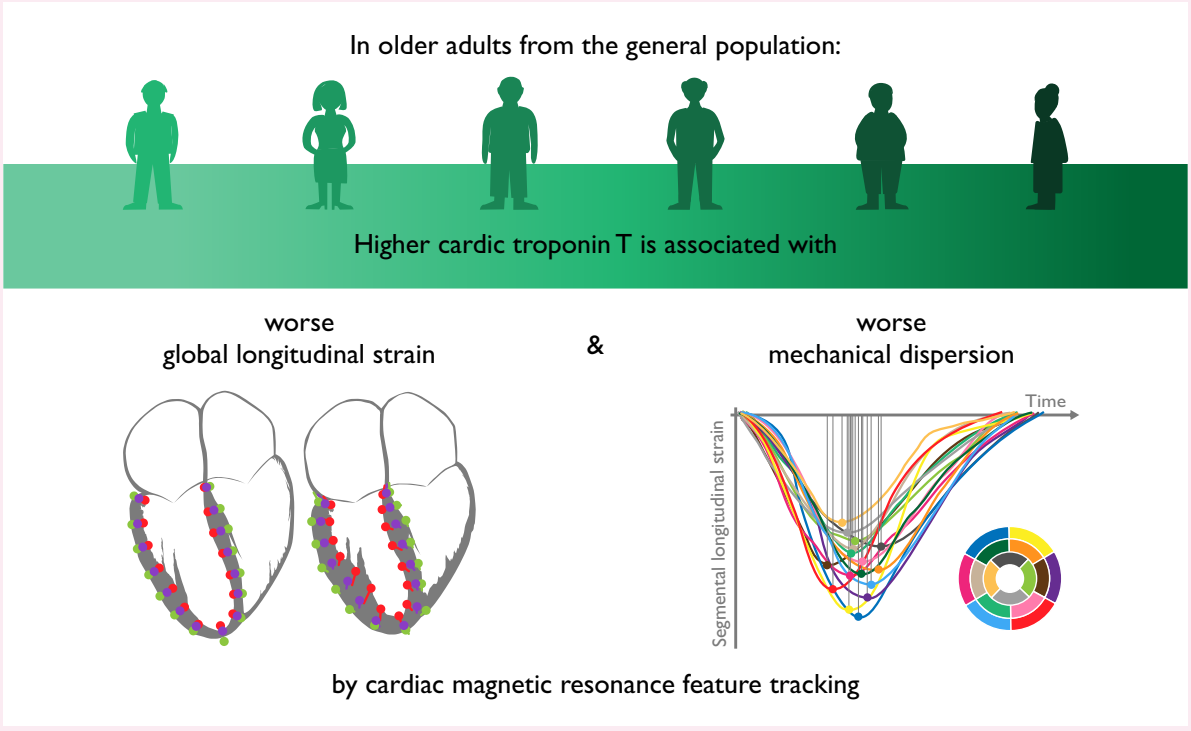
Graphical Abstract



In older adults from the general population, higher cardiac troponin T is associated with worse global longitudinal strain and worse mechanical dispersion as assessed by cardiac magnetic resonance feature tracking.

Keywords cardiac troponin T • global longitudinal strain • mechanical dispersion • LV systolic function • LV synchrony • cardiac magnetic resonance feature tracking

Lay summary

- People who at first glance look similar can have very different risks of developing heart disease. Identifying people at risk who could benefit from treatment may reduce the number of individuals suffering from heart disease.
- Troponin T is a protein indicating heart muscle damage that can be measured in blood. It is used to diagnose heart attacks amongst people with acute heart symptoms but can also be detected in people without acute symptoms. In this setting, even a small increase, well within what is considered normal, has been shown to be linked to a higher risk of future heart disease.
- Cardiac magnetic resonance allows us to appreciate even subtle changes in the heart muscle contraction. Reduced shortening of the heart, called 'global longitudinal strain' (GLS), and decreased coordination, called 'mechanical dispersion' (MD), are considered indicators of impaired heart function and potential warning signs of heart disease.
- This study, examining 186 people aged 68–70 from the general population, showed that people with higher troponin T levels had poorer heart motion, indicated by worse GLS and MD. The link between higher troponin T and worse heart motion was also present amongst those who had troponin T levels within normal range, and even after accounting for differences in sex, age, kidney function, hypertension, obesity, diabetes, and smoking. This increases our understanding of heart disease development, strengthens our knowledge of risk factors for future heart disease and opens the possibility for prevention.

Introduction

Cardiac troponin T (cTnT) is a readily available biomarker of myocardial injury. Although routinely used to diagnose acute myocardial infarction,[1] it is frequently detectable in asymptomatic individuals.[2] Previous studies have shown that even within the normal range, cTnT concentrations in the general population are independently associated with a higher risk of future cardiovascular events and mortality, providing additional prognostic information to traditional risk factors.[2–4]

Alterations of left ventricular (LV) contractility may precede cardiovascular events.[5] These alterations can be described by global longitudinal strain (GLS), which represents myocardial deformation from end-diastole in the longitudinal direction, and by mechanical dispersion (MD), a measure of spread in time to maximal deformation of the LV segments, thereby reflecting the synchrony of the LV contraction.[6–8] Even though more commonly evaluated by echocardiography, GLS and MD can also be assessed by cardiac magnetic resonance (CMR) feature tracking (CMR-FT).[9] GLS has emerged as an imaging biomarker

providing significant diagnostic and prognostic value across cardiac diseases when assessed by echocardiography or by CMR-FT.[5,9,10] Importantly, GLS has also been shown to predict all-cause mortality, heart failure, and coronary artery disease in the general population when assessed by echocardiography.[11] MD is an imaging biomarker in its earlier stages, which up to now almost exclusively has been evaluated by echocardiography. When derived by speckle tracking echocardiography, MD has shown superior predictive value over ejection fraction (EF) and GLS for risk stratification of ventricular arrhythmias in a number of cardiac diseases.[7] Additionally, MD has also been reported to provide incremental prognostic information for cardiovascular events in the general population, surpassing the prognostic value of GLS and established risk factors.[8]

Previous studies have demonstrated an association between cTnT and echocardiographically assessed GLS and MD in the general population.[12,13] However, these associations have been less studied by CMR, which offers a higher signal-to-noise ratio but a lower temporal resolution compared with echocardiography.[14] Only one study has reported on the association between cTnT and GLS evaluated by CMR in the general population,[5] and none has addressed the association between cTnT and MD by CMR. Accordingly, this cross-sectional observational study of older adults from the general population tested the hypothesis that cTnT levels are associated with worse LV systolic function and synchrony assessed by CMR-FT GLS and MD.

Methods

Study population and design

The current investigation is a sub-study of the previously described prospective population-based Akershus Cardiac Examination (ACE) 1950 Study,[15] comprising 3706 community dwellers born in 1950 and residing in Akershus County, Norway. The baseline examination was conducted between 2012 and 2015 at Akershus University Hospital and Bærum Hospital/Vestre Viken Hospital Trust. The present cross-sectional sub-study consists of 201 participants examined by CMR in 2019. Stratified by sex, ACE 1950 participants from quartiles having the lowest and the highest cardiac troponin at baseline were included. Only participants who at baseline had no overt angina or coronary artery disease, defined as self-reported history of myocardial infarction or coronary artery interventions, and an estimated glomerular filtration rate (eGFR) > 60 mL/min/1.73 m^2 were eligible for inclusion. A total of 364 participants were contacted for potential inclusion. At the time of CMR, a self-reported medical history was obtained alongside clinical and biochemical investigations. Comprehensive descriptions of obtained variables can be found in Supplementary data online, *Table S1*. The ACE 1950 Study complies with the Declaration of Helsinki and is approved by the Regional Committee for Medical Research Ethics. All participants provided informed written consent before participation in both ACE 1950 and the current sub-study.

Blood sampling and biochemical analyses

Venous blood samples were collected within a week before CMR, centrifuged at room temperature, and frozen at −80°C. cTnT was measured from venous blood using troponin T high-sensitivity STAT assay on a Cobas e801 analyser (Roche Diagnostics, Rotkreuz, Switzerland). The limit of detection for cTnT was 3.0 ng/L.[16] Undetectable concentrations were assigned the value of 1.5 ng/L.

CMR acquisition and post-processing

The participants were examined with a 1.5 T Phillips Achieva MRI scanner (Philips Medical Systems, Best, The Netherlands). The CMR protocol included breath-hold balanced steady-state free precession (SSFP) sequences with contiguous short-axis slices covering the ventricles, four-chamber view, LV outflow tract view, and two-chamber view. The temporal resolution was 30 frames per cardiac cycle. Image analyses were performed using the post-processing software CVI42 (Version 5.13.5, Circle Cardiovascular Imaging Inc.). Ventricular volumes and mass were quantified using short-axis SSFP images. Trabeculations and papillary muscles were included in the LV volume and excluded from both contours for LV mass estimation and feature tracking. LV GLS and MD were obtained by CMR-FT. All measurements were derived from 2D analyses. LV GLS and segmental time to peak longitudinal strain were obtained from the long-axis views. As MD is barely researched by CMR-FT and there is no standardized way of calculating it, we a priori decided to adopt the same calculation method that is applied by echocardiography. MD was calculated as the standard deviation of the time to peak longitudinal strain of the 16 American Heart Association (AHA) segments that prior to the analyses were adjusted for heart rate. The adjustment was done by standardizing the time to peak longitudinal strain to a heart rate of 60 [(time to peak longitudinal strain * 60)/heart rate at CMR] prior to calculating the standard deviation. A more in-depth method description along with image acquisition parameters can be found in the Supplementary data. Furthermore, in our supplementary analyses, we have incorporated alternative methods for calculating MD, consistent with previous CMR-FT studies. These methods express MD as a percentage of the cardiac cycle in both the circumferential and longitudinal directions.

Statistical analyses

The study population was divided into sex-specific cTnT quartiles. Continuous variables were described as median with interquartile intervals and categorical as number and percent of quartile group. Quartile differences were compared using Mann–Whitney *U* test for continuous and the χ^2 test for categorical variables. Participants with missing data were excluded from the analyses, and this is reported along with the results. Spearman rank correlation analyses were performed to compare the association between cTnT, GLS, and MD. Correlation analyses were also performed using MD obtained in comparable ways to previous CMR-FT publications (Supplementary methods).

Associations between continuous cTnT and both GLS and MD were examined using multivariable linear regression. Due to the heavily skewed distribution of cTnT and non-normally distributed model residuals, a logarithmic transformation with base 10 was applied prior to regression. Multivariable linear models were created, considering a priori–selected potential confounders known to influence cardiovascular risk and cTnT concentrations.[9,17–19] The 'basic model' included cTnT, sex, and age, while the 'clinical risk factor model' was additionally expanded by eGFR, hypertension, body mass index (BMI), diabetes mellitus, and daily smoking. An 'extended clinical model' was also obtained that in addition adjusted for LVEF and end-diastolic volume indexed by body surface area (LVEDVI). An overview of variables in each model along with definitions is presented in Supplementary data online, *Table S1*. Multicollinearity between features was assessed using variance inflation factor. Homoscedasticity was examined using White test. All analyses were done using Python 3.8.5.

Subgroup analyses were performed for participants with cTnT levels within the sex-specific normal range (i.e. < 9.0 ng/L for women and < 16.0 ng/L for men[16]) and comprised multivariable linear regression of the same covariable models as for the main analyses.

Study reporting and quality assessment

Reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies. Natural language processing tools driven by artificial intelligence have been used for proofreading the manuscript and have not been utilized for generating content.

Results

Participants

Among the 364 ACE 1950 participants who were contacted, 201 were included in the current sub-study and underwent CMR (*Figure 1*). A total of 186 (93%) of the 201 who underwent CMR had valid CMR-FT measurements of GLS and MD and were included in the analyses. The 15 excluded participants comprised five with missing/deficient images, six with imprecise long-axis image planning resulting in lack of coverage of one or more AHA segment, and four had artefacts resulting in inadequate feature tracking. All 186 participants were included in

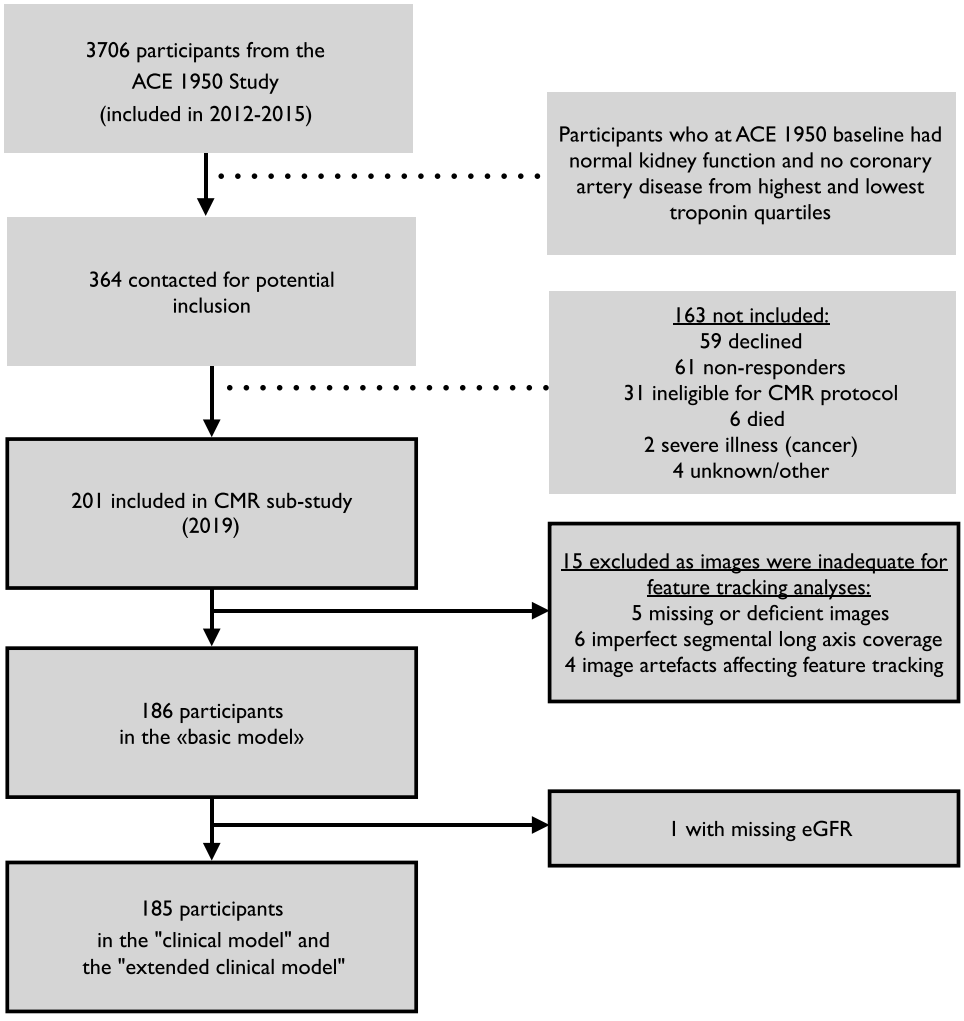


Figure 1 Flow diagram of study population selection.

the basic multivariable linear regression model. One participant had missing eGFR and was excluded from the clinical risk factor model.

Clinical and CMR characteristics according to cTnT quartiles

Table 1 presents the participants' clinical and biochemical characteristics, categorized into quartiles of cTnT levels. In quartile 3, participants were slightly older with a higher prevalence of hypertension compared with the lowest quartile. Participants in quartile 4 had worse kidney function compared with quartile 1.

Participants in quartiles 3 and 4 had significantly worse GLS and worse MD compared with quartile 1 (*Table 2*). They also had worse MD compared with quartile 2. Quartile 4 had worse GLS compared with quartile 2 (*Figure 2*).

Correlations between cTnT, GLS, and MD

cTnT correlated positively with MD ($rho = 0.41$, $P < 0.001$) and negatively with absolute value GLS ($rho = -0.31$, $P < 0.001$), as shown in *Figure 3*.

Absolute value of GLS and MD showed a significant negative correlation ($rho = -0.36$, $P < 0.001$). There was a significant correlation between cTnT and MD calculated as the percentage of the cardiac cycle for longitudinal but not circumferential strain (see Supplementary data online, *Figure S1*).

Linear associations between cTnT and CMR outcomes of GLS and MD

Higher cTnT concentrations were independently associated with worse GLS and worse MD in the basic model, the model additionally adjusting for common clinical risk factors of cardiovascular disease and the most extensive model additionally adjusting for LVEF and LVEDVI (*Figure 4*; Supplementary data online, *Table S5*). Results from assumption tests are shown in Supplementary data online, *Tables S2–S4*.

A subgroup analysis among the participants with sex-specific normal range cTnT (median 5.6 ng/L and interquartile interval of 4.7–7.3 ng/L) also showed significant associations between higher cTnT concentrations and both worse GLS and MD for both the basic ($n = 131$) and the clinical risk factor ($n = 132$) models (see Supplementary data online, *Table S5*).

Table 1 Clinical and biochemical characteristics according to cTnT quartiles

	Quartile 1 ($n = 48$)	Quartile 2 ($n = 47$)	Quartile 3 ($n = 45$)	Quartile 4 ($n = 46$)	ALL ($n = 186$)
Range cTnT, ng/L					
Women	1.5–4.6	4.6–5.6	5.6–10.9	11.1–23.6	1.5–23.6
Men	3.4–6.1	6.1–8.1	8.1–17.7	18.7–74.4	3.4–74.4
cTnT, ng/L	4.4 (3.8–5.0)	6.3 (5.1–6.9)‡	8.7 (7.4–11.9)‡	20.4 (15.3–27.8)‡	7.0 (5.0–12.6)
Women	3.8 (3.4–4.4)	5.0 (4.8–5.4)‡	7.3 (6.2–8.4)‡	14.9 (12.1–17.7)‡	5.6 (4.6–10.9)
Men	4.9 (4.2–5.4)	6.8 (6.7–7.4)‡	11.9 (9.8–14.7)‡	27.4 (21.9–31.5)‡	8.1 (6.1–17.5)
Female sex	23 (47%)	22 (46%)	22 (49%)	22 (47%)	89 (48%)
Age, years	68.9 (68.6–69.2)	68.9 (68.6–69.2)	69.1 (68.9–69.4)*	68.9 (68.7–69.2)	69.0 (68.6–69.2)
Caucasians	48 (100%)	47 (100%)	45 (100%)	45 (98%)	185 (99%)
Higher education	26 (54%)	22 (46%)	28 (62%)	23 (51%)[a]	99 (53%)[a]
Inclusion site Ahus (vs. Bærum)	32 (66%)	31 (66%)	29 (64%)	30 (65%)	122 (66%)
eGFR, mL/min/1.73 m^2	93.7 (86.0–96.4)	93.2 (86.9–95.7)	90.9 (85.9–95.8)[a]	89.2 (82.1–94.1)*	92.6 (85.2–95.5)[a]
Hypertension	22 (45%)	24 (51%)	31 (69%)*	28 (61%)	105 (56%)
Diabetes mellitus	1 (2%)	2 (4%)	2 (4%)	4 (9%)	9 (5%)
Body mass index, kg/m^2	25.7 (23.3–27.2)	26.4 (24.1–28.3)	24.7 (22.3–29.4)	27.3 (23.7–29.7)	26.2 (23.5–28.5)
Daily smokers	2 (4%)	1 (2%)	6 (13%)	1 (2%)	10 (5%)
Coronary artery disease	3 (6%)	1 (2%)	3 (7%)	3 (6%)	10 (5%)
Heart failure	0 (0%)	0 (0%)[a]	3 (7%)[a]	3 (7%)[a]	6 (3%)[b]
Systolic blood pressure, mmHg	132 (123–146)	133 (121–149)	139 (128–145)	138 (127–149)	136 (124–148)
Diastolic blood pressure, mmHg	74 (70–80)	73 (68–81)	76 (71–82)	77 (71–84)	75 (70–82)
Heart rate, bpm.	66 (61–72)	64 (58–73)	65 (57–69)	64 (56–69)	65 (58–71)
HbA1c, mmol/mol	38.0 (36.0–39.0)	38.0 (35.5–40.4)	36.0 (35.0–39.0)[a]	37.1 (35.0–39.8)	37.2 (35.0–40.0)[a]
Total cholesterol, mmol/L	5.6 (5–6.2)	5.5 (4.8–6.0)	5.2 (4.6–5.9)[a]	5.3 (4.7–6.1)	5.4 (4.8–6.0)[a]
High-density lipoprotein, mmol/L	1.7 (1.3–2.0)	1.5 (1.3–1.7)	1.9 (1.3–2.2)[a]	1.6 (1.2–1.9)	16 (13–2.0)[a]
Triglycerides, mmol/L	1.1 (0.9–1.6)	1.4 (0.9–1.6)	1.1 (0.8–1.4)[a]	1.2 (0.9–1.6)	1.2 (0.9–1.6)[a]

Participants grouped according to sex-specific cTnT quartiles from lowest to highest. cTnT values below the limit of detection (3.0 ng/L) were set to 1.5 ng/L. Continuous variables described with median and interquartile interval, categorical as number and percent of quartile. Two-sided Mann–Whitney *U* and χ^2 tests were employed to compare group differences with the lowest quartile as the reference.
cTnT, cardiac troponin T.
[a]Missing data for one participant.
[b]Missing data for three participants
*$P < 0.05$, †$P < 0.01$, ‡$P < 0.001$.

Table 2 LV CMR characteristics according to cTnT quartiles

	Quartile 1 ($n = 48$)	Quartile 2 ($n = 47$)	Quartile 3 ($n = 45$)	Quartile 4 ($n = 46$)	ALL ($n = 186$)
Range cTnT, ng/L	1.5–6.1	4.6–8.1	5.6–17.5	11.1–74.4	1.5–74.4
GLS (absolute value), %	17.6 (16.9–19.3)	17.5 (16.3–19.1)	16.7 (15.5–18.3)*	16.2 (14.8–18.1)†	17.3 (15.7–18.8)
MD, milliseconds	68.0 (57.8–86.6)	77.7 (60.3–90.0)	86.8 (68.9–115.7)†	98.5 (76.5–110.4)‡	80.7 (61.8–105.0)
Ejection fraction, %	61 (57–63)	61 (56–65)	59 (53–65)	58 (54–64)	58.9 (55.1–64.2)
LV mass indexed by BSA, g/m^2	37.8 (32.8–45.5)	41.6 (34.6–48.0)	44.0 (37.1–51.7)*	52.9 (37.6–61.7)‡	41.8 (34.9–52.5)
End-diastolic volume, mL/m^2	64.9 (53.9–72.9)	68.8 (58.8–74.9)	71.9 (59.8–86.0)*	78.5 (61.9–85.5)†	69.7 (58.4–80.0)
End-systolic volume, mL/m^2	25.6 (20.5–30.8)	25.4 (20.6–33.0)	26.2 (22.9–38.7)	29.9 (24.6–36.6)†	26.7 (21.5–34.7)

Participants grouped according to sex-specific cTnT quartiles from lowest to highest. Continuous variables described with median and interquartile interval, categorical as number and percent of quartile. GLS reported as absolute value and MD in milliseconds. There was no missing data. Two-sided Mann–Whitney *U* and χ^2 tests were employed to compare group differences with the lowest quartile as the reference.
cTnT, cardiac troponin T; GLS, global longitudinal strain; MD, mechanical dispersion; BSA, body surface area.
*$P < 0.05$, †$P < 0.01$, ‡$P < 0.001$.

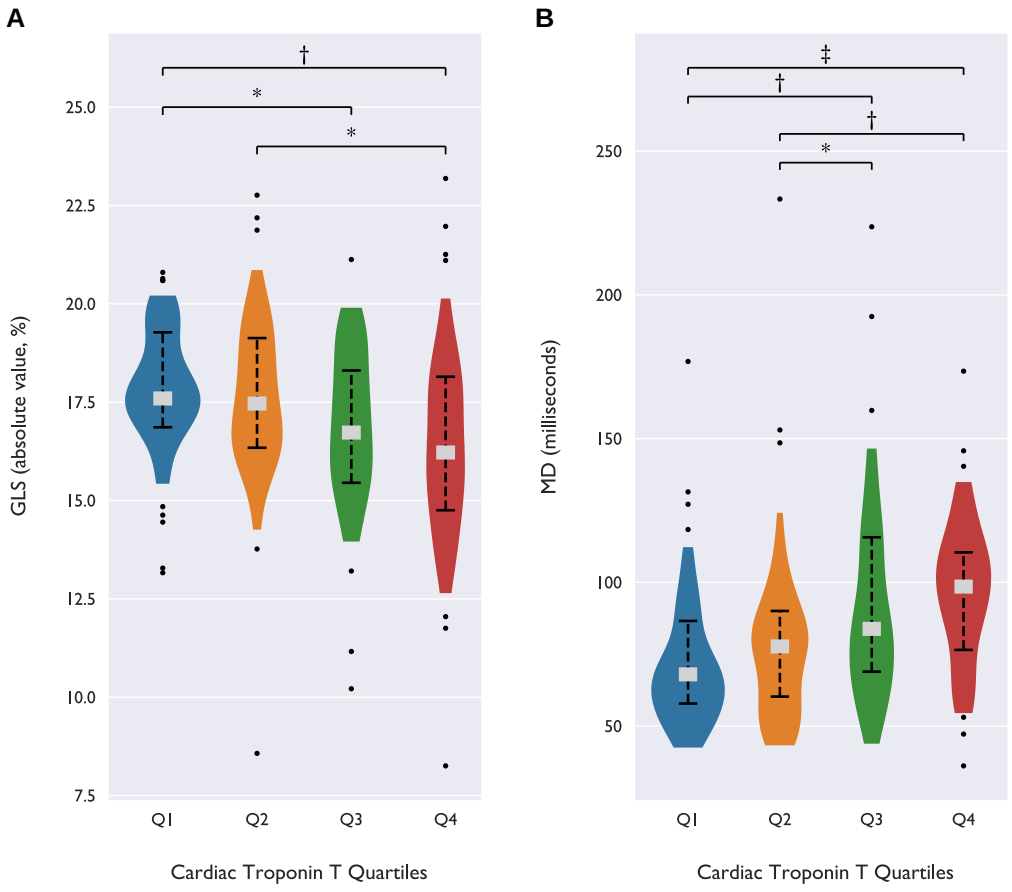


Figure 2 Violin plots depicting distribution of *A*) GLS and *B*) MD across sex-specific cTnT quartiles from lowest (Q1) to highest (Q4) concentrations. Dots represent observations further than 1.5 SD from the mean. Differences between groups were compared using the two-sided Mann–Whitney *U* test. Level of confidence is denoted as **P* < 0.05, †*P* < 0.01, and ‡*P* < 0.001. GLS, global longitudinal strain; MD, mechanical dispersion; cTnT, cardiac troponin T.

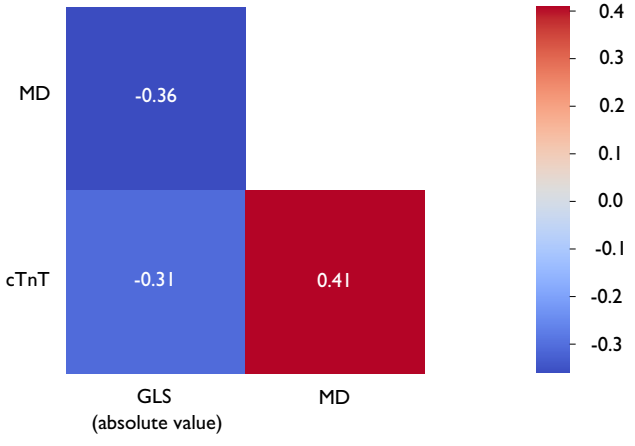


Figure 3 Spearman rank correlation coefficients between cTnT, GLS, and MD. All correlation coefficients had *P* < 0.001. cTnT, cardiac troponin T; GLS, global longitudinal strain; MD, mechanical dispersion.

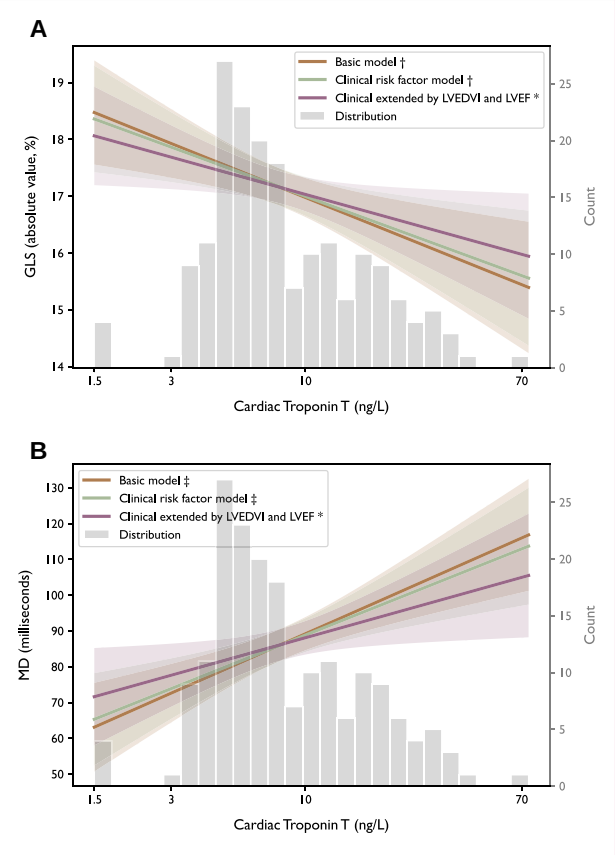


Figure 4 *A*) GLS and *B*) MD, each modelled by three multivariable linear regression models with 95% confidence interval bands. Frequency of observations depicted as a count histogram corresponding to the right vertical axis. Cardiac troponin T is logarithmically transformed using base 10, with annotations reverted to the original, non-transformed values. The 'basic model' includes cardiac troponin T, age, and sex. The 'clinical risk model' additionally adjusts for eGFR, BMI, diabetes mellitus, hypertension, and smoking status. The 'extended clinical model' additionally encompasses LVEDVI and LVEF. Significant associations are denoted with $*P < 0.05$, $\dagger P < 0.01$, and $\ddagger P < 0.001$. GLS, global longitudinal strain; MD, mechanical dispersion; LVEDVI, left ventricular end-diastolic volume indexed by body surface area; LVEF, left ventricular ejection fraction.

In this subgroup, the association between higher cTnT and GLS remained in the clinical model extended by LVEDVI and LVEF, while the association between cTnT and MD was attenuated.

Discussion

The main finding of this study is that higher cTnT concentrations in the general population are associated with worse GLS and worse MD as assessed by CMR-FT, adding information to traditional risk factors for cardiovascular disease. The association holds independently of sex, age, eGFR, hypertension, BMI, diabetes mellitus, and smoking habits and were also evident in a subgroup of participants with cTnT concentrations within the normal range. These findings support and extend previous research documenting a relationship between cTnT and both GLS and MD as assessed by echocardiography.[12,13] The consistency across imaging modalities strengthens the position of cTnT as a marker of decreased systolic function and synchrony.

A recent publication from the Dallas Heart Study demonstrated significantly higher concentrations of cTnT in the population quartile with worst GLS evaluated by CMR-FT, but no association between cTnT and GLS when GLS was modelled by logistic regression using a cut-off at the 80th percentile of the study population.[5] While this provides insight focused on a specific dichotomization of GLS, our investigations modelled GLS continuously for a population with higher median concentrations and greater range of cTnT (reported median from the Dallas Heart Study of 1.5 ng/L vs the current median of 7.0 ng/L). Even in the subgroup of the current population having cTnT within the sex-specific normal range (median 5.6 ng/L interquartile interval of 4.7–7.3 ng/L), the association remained. The investigations done in the present study by linear regression can capture associations that dichotomization potentially obscures and allow for an understanding across a wider range of values. We believe our findings may offer a more holistic view on how cTnT corresponds to changes in GLS across a wider spectrum of measurements.

There is growing evidence that worse GLS, evaluated both by echocardiography and CMR-FT, is associated with a higher risk of adverse cardiovascular events in community dwellers.[5,11] Further, in the Copenhagen City Heart Study, MD by echocardiography demonstrated prognostic ability beyond established risk factors for predicting cardiovascular disease and even outperformed GLS for this task.[8] The current findings of cTnT being associated with both GLS and MD support previous observations of cTnT as an indicator of cardiovascular risk in the general population.[3]

Advantages and challenges of CMF-FT compared with speckle tracking echocardiography

Although CMR is considered reference standard for assessing cardiac volumes and mass, providing reliable information across cardiovascular diseases[20] with superior signal-to-noise ratio,[14,21] it is unclear whether it outperforms deformation metrics obtained by echocardiography.[14] Even though some studies show good agreement between CMR-FT and echocardiographic GLS,[22] concerns are raised regarding limited validation[21] and systematic differences.[23] Additionally, CMR-FT displays variability due to field strength and inter-vendor differences in both software and hardware, leading to a complex array of normal ranges.[19] The lower temporal resolution of CMR-FT compared with echocardiography has also raised concern.[9,14,21,23,24] However, a recent study demonstrated that a temporal resolution of 30 frames per heartbeat, as used in the current study, offers consistent GLS measurements compared with higher temporal resolutions.[25] Any systematic difference in strain values compared to echocardiography should not alter our findings as this applies to deformation metrics of all participants equally.

In the present study, 93% of the obtained CMR images were deemed adequate for analysis of GLS and MD, compared with only 68% of obtained echocardiography images in a previous publication from the ACE 1950 Study.[26] Reasons for this higher rate may include high-resolution images and independence of acoustic window. However, despite its higher yield, CMR remains less accessible. Additionally, there is a likely selection bias of participants able to undergo CMR, and the rate of success may be lower in an unselected clinical setting.

MD assessed by CMF-FT

The current study is the first to calculate MD by CMR-FT using the same approach as adopted for echocardiography, i.e. the standard deviation of segmental time to peak longitudinal strain expressed in milliseconds. The calculation of MD from CMR is not standardized, and previous studies assessing MD by CMR have defined MD as the standard deviation of time to peak segmental strain expressed as percent of cardiac cycle from circumferential[27] or both circumferential and longitudinal measurements.[28]

In this study, we adopted the approach for calculating MD used in echocardiography to make our results comparable to large population studies like the ACE 1950 Study[26] and the Copenhagen City Heart Study.[8] Despite this strategy, MD obtained by CMR-FT in this study was, with a median of 81 milliseconds, substantially higher compared with both a median of 38 milliseconds in the ACE 1950 Study,[26] and the middle tertile between 31 and 51 milliseconds in the Copenhagen City Heart Study.[8] Although the present population is older with higher cTnT, it is unlikely that the population differences are large enough to explain this discrepancy, and the higher MD is more likely explained by differences in imaging modalities, temporal resolution, calculation of deformation from myocardium vs endocardium or post-processing software.

Although a temporal resolution of 30 frames per heartbeat seems sufficient for GLS,[25] the same is not investigated for MD. The lower temporal resolution of CMR compared with echocardiography can impact the variance of time to peak segmental longitudinal strain that forms the basis of MD calculations. On the other hand, the superior tissue contrast and tracking of the whole thickness of the myocardium in CMR could offer a more precise time to peak strain identification for myocardial segments and thereby provide a more sensitive expression of dispersion. We encourage further studies comparing MD obtained with different frame rates and the head-to-head comparison of MD assessed by CMR-FT and echocardiography. It is also noteworthy that the correlation between cTnT and MD evaluated by CMR-FT is substantially higher than the very weak correlation between cTnT and echocardiographic MD previously reported by our group (rho = 0.41 vs. rho = 0.08).[13] More research and long-term follow-up are clearly needed to define the best methodology, normal range, and predictive value of this emerging imaging biomarker.

Interestingly, there also was a correlation between cTnT and MD calculated as percentage of the cardiac cycle from longitudinal segmental strain, but not from circumferential segmental strain (see Supplementary data online, *Figure S1*). As the absolute value of MD calculated as percent from the longitudinal direction also was higher than that from the circumferential, it seems that more pronounced differences in segmental time to peak strain can be obtained from the longitudinal rather than the circumferential direction. It can be hypothesized that by CMR the spread of segmental time to peak longitudinal strain is a more sensitive imaging marker of left ventricular synchrony compared with segmental time to peak circumferential strain. We hope to explore this further in a future study.

Strengths and limitations

Strengths of this study include sex-stratified selection of participants from a well-characterized general population age cohort and a high-sensitivity cTnT assay. However, as all the participants were in their late sixties and mainly European Caucasian, the results might be less generalizable to other age groups and ethnicities. Further, the participants had no overt coronary artery disease 4–7 years prior to CMR and normal eGFR, leaving the findings less generalizable to populations with more prevalent coronary artery disease and impaired renal function.

There are no validated and standardized methods for calculation of MD from CMR, and MD in this study is not directly comparable to other publications. The lower temporal resolution reduces the precision of the segmental time to peak longitudinal strain, which is the basis of calculating MD. Whether or not this is the reason behind the higher values of MD obtained in this study population by CMR-FT compared with what is reported by echocardiography remains to be elucidated by future studies.

This sub-study included participants who 4–7 years prior had cTnT levels in the upper and lower quartiles of the entire ACE 1950 population, and community dwellers with mid-range troponin level may be underrepresented in the current study population. However, at the time of CMR, also mid-range cTnT values were prevalently represented in this study, and although the current study population may be enriched by lower and higher cTnT values, the regression analyses should nevertheless reflect valid associations between cTnT and both GLS and MD.

Conclusion

In a non-acute setting in the general population, higher cTnT concentrations are associated with worse LV systolic function and synchrony evaluated as GLS and MD by CMR-FT and provide additional information to traditional cardiovascular risk factors. The association holds true even when cTnT concentrations are within the normal range. These findings substantiate the role of cTnT in risk stratification for cardiovascular disease in the general population.

Supplementary data

Supplementary data are available at *European Heart Journal - Imaging Methods and Practice* online.

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Data availability

The data underlying this article cannot be publicly shared because of the risk for violating privacy, as regulated by the institutional data protection officer.

Lead author biography

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