Factors Influencing the 99th Percentile of Cardiac Troponin I Evaluated in Community-Dwelling Individuals at 70 and 75 Years of Age

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BACKGROUND: We aimed to investigate the effects of sex, prevalent cardiovascular disease (CVD), and aging on the 99th percentile of cardiac troponin I (cTnI).

METHODS: cTnI was measured using a high-sensitivity assay (Abbott Diagnostics) in 814 community-dwelling individuals at both 70 and 75 years of age. We determined the cTnI 99th percentiles separately using nonparametric methods in the total sample, in men and women, and in individuals with and without CVD.

RESULTS: The cTnI 99th percentile at baseline was 55.2 ng/L for the total cohort. Higher 99th percentiles were noted in men (69.3 ng/L) and individuals with CVD (74.5 ng/L). The cTnI 99th percentile in individuals free from CVD at baseline (n = 498) increased by 51% from 38.4 to 58.0 ng/L during the 5-year observation period. Relative increases ranging from 44% to 83% were noted across all subgroups. Male sex [odds ratio, 5.3 (95% CI, 1.5–18.3)], log-transformed N-terminal pro-B-type natriuretic peptide [odds ratio, 1.9 (95% CI, 1.2–3.0)], and left-ventricular mass index [odds ratio, 1.3 (95% CI, 1.1–1.5)] predicted increases in cTnI concentrations from below the 99th percentile (i.e., 38.4 ng/L) at baseline to concentrations above the 99th percentile at the age of 75 years.

CONCLUSIONS: cTnI concentration and its 99th percentile threshold depend strongly on the characteristics of the population being assessed. Among elderly community dwellers, higher concentrations were seen in men and individuals with prevalent CVD. Aging contributes to increasing concentrations, given the pronounced changes seen with increasing age across all subgroups. These findings should be taken into consideration when applying cTnI decision thresholds in clinical settings.

Current guideline documents recommend the use of the cardiac troponin 99th percentile as the threshold for clinical decision-making in acute coronary syndrome (1–3). This threshold should be defined for each assay individually in a sufficiently large sample of individuals free from cardiovascular disease (CVD)3 (2). However, the implications of CVD on the 99th percentile and what criteria to use in defining a healthy population remain subject to debate. In some analyses, for example, the 99th percentiles have been derived from cohorts of younger ages than the ages commonly seen with acute coronary syndrome patients in the emergency department (4–6). Another area of concern in this context relates to sex-specific issues, because most investigators have noted higher troponin concentrations in men compared to women (4–10).

To further investigate the influence of CVD, sex, and aging on troponin 99th percentiles, we performed an analysis of troponin concentrations in a sample of elderly community dwellers whose cardiac troponin I (cTnI) had been measured with a high-sensitivity assay at the age of 70 and again at the age of 75 years.

Materials and Methods

STUDY DESIGN

All individuals aged 70 years living in Uppsala, Sweden, were eligible for participation in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. Potential study participants were randomly chosen from the registry of community inhabitants. Of the 2025 individuals invited, 1016 participated in the

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3 Nonstandard abbreviations: CVD, cardiovascular disease; cTnI, cardiac troponin I; PIVUS, Prospective Investigation in Uppsala Seniors; NT-proBNP, N-terminal pro-B-type natriuretic peptide; ECG, electrocardiogram; LV, left-ventricular; hsTnI, high-sensitivity troponin I; eGFR, estimated glomerular filtration rate; LVEF, LV ejection fraction; LVMI, LV mass index.

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study. Written informed consent was obtained from all participants. The study protocol was approved by the local ethics committee and complies with the Declaration of Helsinki.

All participants reported their medical history and smoking habits and underwent blood sampling at baseline. Serum and plasma aliquots that were not analyzed immediately were stored frozen at −80 °C. Echocardiography was performed approximately 1 week after the baseline examinations.

Five years after enrolment, all surviving study participants were invited to a reexamination 1 month after their 75th birthday, and 827 individuals (85.8% of all survivors) attended. In total, 814 of these individuals had available cTnI results obtained at both baseline and 5-year follow-up, and formed the cohort for the present analysis.

The cTnI 99th percentiles were calculated for the total cohort and prespecified subgroups: men and women, and individuals with and without prevalent CVD. CVD was defined as previous myocardial infarction, previous stroke, previous coronary revascularization, congestive heart failure [self-reported heart failure or increased N-terminal pro B-type natriuretic peptide (NT-proBNP) concentrations], NT-proBNP >210 pg/mL in men or >250 pg/mL in women, a pathologic 12-lead electrocardiogram (ECG) [ST-segment depression (Minnesota codes 4-1 and 4-2), T-wave inversion (Minnesota codes 5-1, 5-2, or 5-3), pathologic Q waves (Minnesota code 1-1), or left bundle branch block (Minnesota code 7-1)] (14), or ECG evidence of left-ventricular (LV) hypertrophy, if information was available.

LABORATORY ANALYSIS AND OTHER INVESTIGATIONS

Measurements of cTnI were performed in frozen EDTA plasma samples using the ARCHITECT STAT high-sensitivity troponin I (hsTnI) assay (Abbott Laboratories) on an ARCHITECT i2000SR platform. After thawing, the samples were centrifuged at 10 000 g for 30 min before analysis. The same lot of reagents was used for all analyses. The ARCHITECT STAT hsTnI assay is a double chemiluminescent immunoassay utilizing a capture antibody directed against amino acids 24–40 of the cTnI protein, and a chimeric detection antibody directed against amino acids 41–47. The limits of blank and of detection of this assay have been described as 0.9 and 1.2–1.5 ng/L, respectively, and the 99th percentile among healthy individuals has been described as 13.6–23.0 ng/L (9, 10). The imprecision profile of 250 duplicate samples in our internal validation showed a 10% CV at 12.0 ng/L and a 20% CV at <2.0 ng/L. NT-proBNP was measured at baseline and 5-year follow-up using the Elecsys proBNP sandwich immunoassay on an Elecsys 2010 instrument (Roche Diagnostics), and the estimated glomerular filtration rate (eGFR) was calculated according to the 4-variable Modification of Diet in Renal Disease Study equation (15).

Echocardiography was performed by an experienced examiner (L. Lind) blinded to clinical data and using an Acuson XP124 cardiac ultrasound unit, as described previously (16). LV volumes were determined according to the Teichholz method and from that, the LV ejection fraction (LVEF) was determined. The LV mass index (LVMI) was calculated according to the recommendations from the American Society of Echocardiography (17). LV hypertrophy was defined as LVMI >116 g/m2 in men or >104 g/m2 in women (18).

STATISTICAL ANALYSIS

Categorical variables are expressed as frequencies and percentages, and continuous variables as medians (with 25th and 75th percentiles) or mean (SD). The Mann–Whitney U-test was used for between-group comparisons of continuous variables and the Wilcoxon signed-rank test for within-group comparisons.

The cTnI percentiles including their 95% CIs were estimated using 10 000 bootstrap samples from the PIVUS cohort. Bootstrapping is a nonparametric method which resamples a given data set a specified number of times, allowing for the reliable calculation of specific statistics, e.g., percentiles and their distribution characteristics.

Predictors of an increase in cTnI concentrations from below the 99th percentile at baseline to above the 99th percentile at 5-year follow-up were identified by univariate logistic regression. Tested covariates included sex, hypertension, diabetes, body mass index, current smoking, previous smoking, pathologic ECG, previous myocardial infarction, self-reported heart failure, previous coronary revascularization, previous stroke, NT-proBNP, eGFR, LVEF, LVMI, LV hypertrophy, previous CVD, and intercurrent cardiovascular (CV) events (defined as myocardial infarction, stroke or coronary revascularization occurring between baseline and 5-year follow-up). If necessary, continuous variables were logarithmically transformed to achieve a normal distribution.

In all tests, a 2-sided P value <0.05 was considered significant. The software packages SPSS 19.0 (SPSS) and SAS 9 (SAS Institute) were used for the statistical analyses.

Results

The mean age of the 814 participants with available cTnI results at both baseline and 5-year follow-up was 70.2 (0.2) years, and 403 participants (49.5%) were males. Clinical characteristics are given in Table 1. Table 2 presents the cTnI 99th percentiles in the total
cohort and the assessed subgroups. For the total cohort, the 99th percentile at baseline was 55.2 ng/L, 69.3 ng/L in men and 26.3 ng/L in women, respectively (P = 0.090). The cTnI 99th percentile was 38.4 ng/L in the 498 participants free from CVD at baseline and 74.5 ng/L in the 316 individuals with prevalent CVD at baseline (P = 0.047).

The 99th percentile in the total cohort increased from 55.2 ng/L at baseline to 79.7 ng/L at 5-year follow-up, as demonstrated in Table 2. This corresponds to a relative increase by 44%. The relative increase in 99th percentiles was more pronounced in women compared to men (83% vs 53%) although men consistently had absolute concentrations that were twice as high as those in women. In cohorts with and without CVD at baseline, similar relative increases in the 99th percentiles were noted over time despite absolute concentrations almost 2-fold higher in participants with prevalent CVD. Even in the 382 participants who still remained free from CVD at the age of 75 years, the 99th percentile increased from 31.6 ng/L to 51.3 ng/L, a relative increase of 62%. Again, the relative increase in the 99th percentiles was not substantially different from that of participants with CVD at the age of 75 years despite 2-fold higher absolute concentrations in that cohort.

In an explorative analysis, we assessed the change in median cTnI concentrations in men and women with and without CVD at the age of 75 years (Table 3). Given the small numbers of participants in these subcohorts, we refrained from calculation of the respective 99th percentiles. For participants without CVD, median cTnI concentrations were approximately 25% higher in men compared to women but increased to a similar extent in both sexes. In the cohort with CVD, men had 37% higher median cTnI baseline concentrations, a numerically greater relative increase over time, and 46% higher median concentrations at 5-year follow-up compared to women.

Considering the cTnI 99th percentile derived from participants without CVD at baseline, i.e., 38.4 ng/L, 6 of the 814 individuals (0.6%) had persistently increased concentrations at both 70 and 75 years of age; in 18 individuals (2.2%) cTnI increased from concentrations below the 99th percentile at age 70 years to concentrations above at age 75 years whereas 6 individuals (0.7%) had decreasing cTnI from concentrations above to concentrations below the 99th percentile. On unadjusted logistic regression, male sex [odds ratio 5.3 (95% CI, 1.5–18.3; P = 0.009)], ln(NT-proBNP) [odds ratio 1.9 (95% CI, 1.2–3.0; P = 0.004)] and LVMI [odds ratio per 10 g/m² increase: 1.3 (95% CI, 1.1–1.5; P < 0.001)] were significantly associated with an increase in cTnI concentrations.

Discussion

Our investigation sheds new light on the challenges related to defining the 99th percentile for cardiac troponin concentrations, the biochemical benchmark for clinical decision-making in suspected or confirmed acute coronary syndrome. Guideline documents recommend that this threshold be derived from a reference population that is free from CVD and that is well balanced with respect to age groups, race, and sex (2). However, as illustrated by our results using a high-sensitive assay, several issues need to be considered in this context.

First, our data highlight the importance of sex on cTnI concentrations. Men had 24%–46% higher median concentrations compared to women but increased to a similar extent in both sexes. In the cohort with CVD, men had 37% higher median cTnI baseline concentrations, a numerically greater relative increase over time, and 46% higher median concentrations at 5-year follow-up compared to women.

Table 1. Clinical characteristics.a

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>5-year follow-up</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>70.2 (0.2)</td>
<td>75.3 (0.2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>591 (72.6%)</td>
<td>662 (81.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>84 (10.0%)</td>
<td>116 (14.3%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.1 (4.1)</td>
<td>26.9 (4.4)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>72 (8.8%)</td>
<td>51 (6.3%)</td>
</tr>
<tr>
<td>Previous smoking</td>
<td>339 (41.6%)</td>
<td>326 (42.9%)</td>
</tr>
<tr>
<td>Pathologic ECG findings</td>
<td>129 (15.8%)</td>
<td>180 (22.1%)</td>
</tr>
<tr>
<td>History</td>
<td></td>
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</tr>
<tr>
<td>Myocardial infarction</td>
<td>47 (5.8%)</td>
<td>72 (8.8%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>26 (3.2%)</td>
<td>45 (5.5%)</td>
</tr>
<tr>
<td>PCI/CABGb</td>
<td>40 (4.9%)</td>
<td>67 (8.2%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>25 (3.1%)</td>
<td>51 (6.3%)</td>
</tr>
<tr>
<td>CVD</td>
<td>82 (10.1%)</td>
<td>131 (16.1%)</td>
</tr>
<tr>
<td>Intercurrent CV events</td>
<td>–</td>
<td>49 (6.0%)</td>
</tr>
<tr>
<td>Biochemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP, ng/L</td>
<td>106 (62–173)</td>
<td>125 (73–232)</td>
</tr>
<tr>
<td>eGFR, mL/min/m²</td>
<td>79.1 (66.4–94.9)</td>
<td>79.0 (69.3–89.8)</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, %</td>
<td>66.6 (8.0)c</td>
<td>64.1 (7.0)d</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>91.6 (26.2)c</td>
<td>94.6 (25.3)d</td>
</tr>
<tr>
<td>LV hypertrophy</td>
<td>157 (23.0%)c</td>
<td>169 (25.2%)d</td>
</tr>
</tbody>
</table>

a Categorical data are given as frequencies (with percentages). Continuous data are given as median values (with 25th and 75th percentiles) or mean (SD) as appropriate.
b PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.
c n = 682.
d n = 670.
community-dwellers compared to the 99th percentile of 30 ng/L found in the cohort, the 99th percentile of 55.2 ng/L was much higher than the reference populations. This highlights the importance of appropriate criteria to define healthy individuals.

Men
- cTnI 70 year (n = 403)
  - 25th: 2.0 (2.0–3.1)
  - 50th: 3.0 (2.9–3.1)
  - 75th: 4.1 (3.9–4.3)
  - 97.5th: 7.4 (5.5–10.0)
  - 99th: 22.4 (17.7–30.0)

- cTnI 75 year (n = 403)
  - 25th: 3.6 (3.5–3.7)
  - 50th: 4.9 (4.7–5.1)
  - 75th: 7.0 (6.6–7.6)
  - 97.5th: 11.2 (10.8–11.6)
  - 99th: 24.9 (21.9–37.9)

Women
- cTnI 70 year (n = 411)
  - 25th: 2.2 (2.1–2.3)
  - 50th: 3.0 (2.9–3.1)
  - 75th: 3.9 (3.7–4.2)
  - 97.5th: 7.2 (6.8–7.6)
  - 99th: 27.7 (19.4–37.9)

- cTnI 75 year (n = 411)
  - 25th: 3.2 (3.0–3.4)
  - 50th: 4.2 (4.0–4.4)
  - 75th: 5.6 (5.4–6.0)
  - 97.5th: 12.2 (9.0–14.0)
  - 99th: 48.3 (16.1–90.1)

Study participants without CVD at 70 years
- cTnI 70 year (n = 498)
  - 25th: 2.2 (2.1–2.3)
  - 50th: 3.0 (2.9–3.1)
  - 75th: 4.1 (3.9–4.4)
  - 97.5th: 17.6 (10.7–30.7)
  - 99th: 38.4 (21.8–46.6)

- cTnI 75 year (n = 498)
  - 25th: 3.3 (3.1–3.5)
  - 50th: 4.3 (4.1–4.5)
  - 75th: 5.9 (5.5–6.2)
  - 97.5th: 33.0 (15.2–56.8)
  - 99th: 58.0 (36.5–81.8)

Study participants without CVD at 75 years
- cTnI 70 year (n = 316)
  - 25th: 3.1 (2.9–3.2)
  - 50th: 4.2 (3.9–4.5)
  - 75th: 6.9 (6.0–8.5)
  - 97.5th: 44.1 (20.5–69.5)
  - 99th: 74.5 (43.0–313.7)

- cTnI 75 year (n = 316)
  - 25th: 4.4 (4.1–4.7)
  - 50th: 6.1 (5.6–6.5)
  - 75th: 9.4 (8.6–11.1)
  - 97.5th: 60.8 (40.3–106.8)
  - 99th: 112.3 (60.8–291.0)

Study participants with CVD at 70 years
- cTnI 70 year (n = 382)
  - 25th: 2.2 (2.1–2.3)
  - 50th: 3.0 (2.8–3.1)
  - 75th: 4.0 (3.7–4.2)
  - 97.5th: 12.0 (8.3–23.4)
  - 99th: 31.6 (12.9–68.2)

- cTnI 75 year (n = 382)
  - 25th: 3.2 (3.0–3.3)
  - 50th: 4.1 (3.9–4.4)
  - 75th: 5.5 (5.2–6.0)
  - 97.5th: 32.9 (13.1–42.6)
  - 99th: 51.3 (34.0–68.2)

Study participants with CVD at 75 years
- cTnI 70 year (n = 432)
  - 25th: 2.9 (2.7–3.0)
  - 50th: 3.8 (3.7–4.2)
  - 75th: 5.9 (5.4–7.0)
  - 97.5th: 38.5 (20.6–56.7)
  - 99th: 62.9 (39.3–174.2)

- cTnI 75 year (n = 432)
  - 25th: 4.2 (4.0–4.4)
  - 50th: 5.7 (5.4–6.0)
  - 75th: 8.7 (8.3–9.6)
  - 97.5th: 60.9 (37.8–93.1)
  - 99th: 106.1 (63.8–173.7)

* Data given with 95% CIs. Bootstrap results are based on 10 000 bootstrap samples. Δ1, Relative change in median cTnI concentrations; P values refer to comparisons using the Wilcoxon signed-rank test. Δ2, Relative change in cTnI 99th percentiles.

This sex-related difference has been ascribed to intrinsic differences in the amount of troponin between the male and female myocardium (22). Second, the cTnI 99th percentile in study participants free from CVD was 38.4 ng/L. Participants with prevalent CVD, in contrast, had twice as high 99th percentiles, which reflects the association of troponin concentrations to chronic cardiac afflictions (i.e., impaired LV systolic function, LV hypertrophy, or coronary artery disease) in the general population (23) and highlights the importance of appropriate criteria to define reference populations (2).

Third, the 99th percentile in the 70-year old study participants free from CVD was considerably higher compared to the previously described 99th percentiles as determined in younger reference populations, ranging from 13.6–23.0 ng/L (9, 10). Even for the total study cohort, the 99th percentile of 55.2 ng/L was much higher compared to the 99th percentile of 30 ng/L found in the Gutenberg Health Study investigating middle-aged community-dwellers (24). These data emphasize the relationship of increasing age with higher troponin concentrations (6, 8). Notably, Apple et al. did not find a difference in the cTnI 99th percentiles (Singulex assay) in healthy individuals <20 and >50 years of age (20). We therefore assume that the relative importance of age on circulating troponin concentrations increases exponentially with more advanced age, as supported by data from Australian patients without myocardial infarction (25), and a recent Swedish study that found highly age-dependent hsTn 99th percentiles that increased sharply at a breakpoint around 60–65 years (19).

The importance of age is also emphasized by the increase in cTnI 99th percentiles we observed over a 5-year time period in all assessed cohorts, including the most healthy study participants, i.e., those without CVD at the age of 75 years. Male sex, higher NT-proBNP concentrations, and higher LVMI were associated with changes in cTnI concentrations from below to above the 99th percentile. Notably, the increase in the 99th percentile in women from our study population was more pronounced that that in men. Given the similar increases of median cTnI concentrations in both men and women, we assume that this difference is driven by lower baseline 99th percentiles in women and, possibly, by some outliers.
The results from the present analysis raise the question whether sex- and/or age-specific troponin thresholds should be used for clinical decision making in patients with chest pain rather than a single cutoff. Previous investigations, however, have not been able to substantiate a superior diagnostic utility of sex-specific 99th percentiles in chest pain patients (28) or better risk prediction in patients with a recent acute coronary syndrome (26). To the best of our knowledge, the value of age-specific 99th percentiles has not been assessed. Notably, findings from recent studies in elderly chest pain patients demonstrated considerably higher ROC-optimized diagnostic cutoffs compared to established 99th percentiles (27, 28). One of these studies also noted a lower diagnostic accuracy of high-sensitivity troponin T in the elderly (28), which likely reflects higher baseline concentrations and, possibly, a higher prevalence of noncoronary causes of troponin increases (i.e., type 2 infarctions). The choice of appropriate decision thresholds is thus a delicate issue, because the application of “false-low” troponin cutoffs derived from younger reference populations inevitably will increase the rate of diagnosed infarctions in the elderly. Although there is an associated increased risk of exposure of an often frail patient group to potentially hazardous treatments, any lowering of troponin thresholds in chest pain patients has also been shown to improve prognosis because of the concomitant identification of greater proportions of individuals at risk (29). This phenomenon likely applies also to individuals with chronic cardiac diseases and stable low level troponin elevations (26, 30). Consequently, our data underscore the importance of a significant change in troponin concentrations to distinguish acute troponin increases from higher baseline concentrations in the elderly, and of a careful examination of the history, symptoms, and ECG findings in each individual patient to identify those with a coronary event as the most likely cause of troponin leakage (i.e., type 1 infarction) as opposed to type 2 infarction or myocardial afflictions caused by other etiologies.

Some limitations of this analysis need to be acknowledged. The PIVUS study included white individuals aged 70 years. We are reluctant to generalize conclusions from this study to other ethnic or age groups. As typically seen in community populations, the renal function in our study participants was fairly good. We therefore did not dichotomize the eGFR to define renal dysfunction, and instead used it as a continuous variable. Owing to the stringent selection criteria, the sample size was too small to allow for a reliable calculation of the 99th percentiles in men and women with and without CVD, respectively. Finally, this analysis was based on participants attending both the visits at baseline and 5-year follow-up. This selection strategy introduces a survival bias which likely leads to an underestimate of the degree of cTnI change otherwise occurring in the elderly population.

In conclusion, our data demonstrate that cTnI concentrations measured by a high-sensitivity assay and their 99th percentiles strongly depend on the characteristics of the population being assessed. Male sex, prevalent CVD, and, in particular, increasing age contribute to higher 99th percentiles in community-dwelling individuals aged ≥70 years, and these factors need to be taken into consideration when interpreting troponin results in clinical situations.

Table 3. Median cTnI concentrations (ng/L) in men and women and in relation to prevalent CVD.a

<table>
<thead>
<tr>
<th></th>
<th>50th percentile</th>
<th>Δ</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>Men without CVD at 75 years</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>cTnI 70 year (n = 163)</td>
<td>3.4 (3.1–3.6)</td>
<td>+40%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnI 75 year (n = 163)</td>
<td>4.7 (4.3–5.1)</td>
<td></td>
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<tr>
<td><strong>Women without CVD at 75 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnI 70 year (n = 219)</td>
<td>2.7 (2.4–2.8)</td>
<td>+41%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnI 75 year (n = 219)</td>
<td>3.8 (3.5–4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Men with CVD at 75 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnI 70 year (n = 240)</td>
<td>4.6 (4.3–5.0)</td>
<td>+47%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnI 75 year (n = 240)</td>
<td>6.8 (6.3–7.4)</td>
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<tr>
<td><strong>Women with CVD at 75 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cTnI 70 year (n = 192)</td>
<td>3.4 (3.1–3.6)</td>
<td>+39%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnI 75 year (n = 192)</td>
<td>4.7 (4.3–5.2)</td>
<td></td>
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</tbody>
</table>

*a Data given with 95% CIs. Bootstrap results are based on 10 000 bootstrap samples. Δ, Relative change in median cTnI concentrations; P values refer to comparisons using the Wilcoxon signed-rank test.

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