Estimated Glomerular Filtration Rate is a Predictive Factor for High-Sensitivity Cardiac Troponin T in a Community-Based 4.8-year Prospective Study

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Research

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**Abstract**

**Objectives:** Persistent elevation of cardiac troponin T (cTnT), which is considered as a sensitive and specific biomarker of myocardial injury, is frequently observed in patients with renal insufficiency. Meanwhile, estimated glomerular filtration rate (eGFR) is an independent risk factor of cardiovascular diseases. With a highly sensitive assay, the prevalence of detectable highly sensitive cTnT (hs-cTnT) is greatly improved even in general population. The aim of this study was to better understand the relationship between renal function (eGFR) and myocardial injury (hs-cTnT) in a community-based population.

**Methods:** We analyzed the relationship between baseline eGFR and follow-up hs-cTnT, and the change of hs-cTnT in 1354 participants after 4.8 years follow-up.

**Results:** In Pearson's correlation analysis, baseline eGFR showed a negative relationship with follow-up hs-cTnT ($r=-0.439; P < 0.001$). In multiple linear regression analysis, baseline eGFR was independently and negatively associated with follow-up hs-cTnT ($\beta=-0.310, P = 0.005$). Stepwise logistic regression models revealed that baseline eGFR was significantly associated with the change in hs-cTnT after 4.8 years follow-up. However, the change in eGFR was not associated with the change in hs-cTnT.

**Conclusions:** Baseline eGFR levels were independently and negatively associated with follow-up hs-cTnT. Furthermore, baseline eGFR levels were an independent predictor of the change in hs-cTnT 4.8 years follow-up, indicating a relationship between renal function and myocardial injury in a community-based population.

**Introduction**

Cardiac troponin T (cTnT), a 37-kD polypeptide mainly expressed by cardiomyocytes, is a specific and sensitive biomarker of myocardial injury. It has already been used clinically to help diagnosing cardiovascular diseases (CVD) including acute coronary syndromes [1–3], and elevated cTnT levels are proved to correlate with worse prognosis [4–5]. With the development of highly sensitive cardiac troponin T (hs-cTnT) assays, the limit of detection becomes lower than before [6–8], and its diagnostic and prognostic values enhanced [8–10]. Moreover, minimal elevated hs-cTnT levels have also been found in general populations without overt CVD [11]. Although the cause and significance still remain unclear, these minimal elevations seem to indicate worse prognosis as well [11].

CVD is one of the leading causes of morbidity and mortality in patients with chronic kidney disease (CKD). Patients with CKD are more likely to die from CVD than to progress to end-stage renal disease (ESRD) [12]. Previous studies have proved that decreased estimated glomerular filtration rate (eGFR) is an independent risk factor of CVD [13–14]. And persistent elevation of cardiac biomarkers, such as hs-cTnT, are also observed in patients with renal insufficiency [15–16]. Renal function and myocardial injury seem to interact with each other and lead to outcomes together, and the underlying mechanism is not yet clear. Our previous study have demonstrated that low eGFR is independently and positively associated with
elevated hs-cTnT in a community-based population. To better understand the influence of renal function on hs-cTnT, in this study we measured the association between renal function at baseline and hs-cTnT levels at follow-up in the same community-based population.

Material And Methods

Study Population

This cohort study conducted in Pingguoyuan, a community in Shijingshan district, Beijing, China. Through cooperation between People’s Liberation Army (PLA) General Hospital and the community management committee, physicians made a public recruiting announcement within the community. This study operated on the basis of voluntary principle and aimed to recruit community population. We excluded bedridden or mental patients, and patients with severe systemic diseases from this study. At first, after routine physical examinations performed in community medical center, 1680 participants (age ≥ 18 years) were selected between September 2007 and January 2009. Adequate measurements and questionnaires were obtained, and their blood were collected for further detection. These participants were continuous followed. The second visit conducted during February 1 to September 30, 2013. The average follow-up time was 4.8 years. During the second visit, adequate measurements and questionnaires were obtained again in community medical center. 181 participants lost follow-up. The other 1499 participants had integrated data and the follow-up rate was 89.2%. Participants with overt CVD (including myocardial infarction, coronary artery related operation, and cerebrovascular accident) or death were also excluded from study. Finally, 1354 remaining participants were included in this study.

Questionnaire and anthropometric measurements

Questionnaires and anthropometric measurements were carried out by qualified physicians from PLA General Hospital. Face-to-face questionnaires used in our study was specially developed to collect necessary information. Tape and digital scale were used to measure height and weight. Waist circumference was defined as the middle part between the last rib and the iliac crest. Hip circumference was defined as the widest part of hips. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were detected in sitting after resting for at least 10 minutes. We measured at least twice and then took the average for analyses.

Biomarker variable determination

After fasting for at least 12 h, blood samples of every participants were took in the morning and kept at 4 °C. Samples should be centrifuged and separated within 2 hours and then kept at -80 °C before use. Fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and LDL-C were assessed by Roche enzymatic assays (Roche Diagnostics GmbH, Mannheim, Germany) on a Roche auto-analyzer (Roche Diagnostics, Indianapolis, IN, USA). Creatinine (Cr) was assessed by Roche enzymatic assays (Roche Diagnostics GmbH) on a Hitachi 7600 auto-analyzer.
hs-cTnT was assessed by Elecsys Troponin T high sensitive assays (Roche Diagnostics GmbH) on a Modular Analytics E170 auto-analyzer (Roche Diagnostics).

All blood specimens were measured in the same laboratory according to the criteria of the World Health Organization Lipid Reference Laboratories.

Definition of variables

Hypertension was defined as follows: (1) SBP ≥ 140 mmHg; (2) DBP ≥ 90 mmHg, and/or (3) the use of antihypertensive medication. Current smoking was defined as smoking 1 or more cigarettes per day for at least 1 year. Body mass index (BMI) was defined as weight in kilograms divided by height in meters squared (kg/m²). Waist-hip ratio (WHR) was calculated as waist circumference divided by hip circumference. Renal function was determined by eGFR, calculated by using the following Chronic Kidney Disease Epidemiology Collaboration equations: GFR = 141 × min (Scr/κ, 1)\(^{\alpha}\)×max (Scr/κ, 1\(^{-1.209}\)×0.993\(^{A\text{ge}}\)×1.018 [if female] × 1.159 [if black], where Scr is plasma creatinine levels (mg/dL), κ is 0.7 for females and 0.9 for males, \(\alpha\) is -0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ [15].

Statistical Analyses

Dichotomous variables were expressed as numbers and percentages, and continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range). Continuous variables were tested for normality before being analyzed and were normalized by natural logarithm transformation if necessary. All analyses were performed at a mean follow-up interval of 4.8 years.

Baseline eGFR levels were categorized as: quartile 1 (≤ 86.54 ml/min/1.73 m²), quartile 2 (86.63 to 94.99 ml/min/1.73 m²), quartile 3 (95.08 to 104.54 ml/min/1.73 m²), and quartile 4 (≥ 104.56 ml/min/1.73 m²). All participants were divided into four groups according to their baseline eGFR levels to analyze eGFR as a predictor of follow-up hs-cTnT. One-way ANOVA (continuous variables) or chi-square tests (categorical variables) were performed for statistical comparison between groups. A Pearson’s correlation analysis and a multiple linear regression analysis were performed to evaluate the association between baseline eGFR and follow-up hs-cTnT.

Furthermore, the relationship between baseline eGFR levels and the change in hs-cTnT from baseline to follow-up and the relationship between the change in eGFR and the change in hs-cTnT were also investigated. Change in eGFR levels was expressed as eGFRΔ (eGFR\(_{\text{follow-up}}\)−eGFR\(_{\text{baseline}}\)) and eGFR\(_{\Delta}\) was categorized as eGFR\(_{\Delta}\)I (eGFR\(_{\text{follow-up}}\)−eGFR\(_{\text{baseline}}\)<0) and eGFR\(_{\Delta}\)II (eGFR\(_{\text{follow-up}}\)−eGFR\(_{\text{baseline}}\)≥0). Change in hs-cTnT was expressed as hs-cTnT\(_{\Delta}\) (hs-cTnT\(_{\text{follow-up}}\)−hs-cTnT\(_{\text{baseline}}\)). hs-cTnT\(_{\Delta}\) was categorized as hs-cTnT\(_{\Delta}\)I (hs-cTnT\(_{\text{follow-up}}\)−hs-cTnT\(_{\text{baseline}}\)<0) and hs-cTnT\(_{\Delta}\)II (hs-cTnT\(_{\text{follow-up}}\)−hs-cTnT\(_{\text{baseline}}\)≥0). A forward stepwise multivariable logistic regression analysis was used to investigate the associations between different groups of baseline eGFR and hs-cTnT\(_{\Delta}\), and the associations between eGFR\(_{\Delta}\) and hs-cTnT\(_{\Delta}\).
All analyses were conducted using SPSS software for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA). A 2-sided value of P < 0.05 was considered significant.

**Results**

**Baseline characteristics of participants**

Our study included 1354 participants. The number of males and females were 558 (41.21%) and 796 (58.79%) respectively, and mean age at baseline was 61.28 ± 11.27 years old. There were 356 current smokers (26.29%), 707 hypertensive (52.22%), and 28 subjects with an eGFR < 60 ml/min/1.73 m$^2$ (2.07%).

The baseline characteristics of participants were shown in Table 1. They were divided into four groups based on quartile levels of baseline eGFR (≤ 86.54, 86.63–94.99, 95.08-104.54, and ≥ 104.59 ml/min/1.73 m$^2$). Age, sex, WHR, current smoking, hypertension, SBP, TC, TG, HDL-C, LDL-C, Cr, and hs-cTnT across the baseline eGFR quartiles were significantly different (P < 0.05).
Table 1
Baseline characteristics of the participants according to baseline eGFR

| Characteristic | Overall (n = 1354) | Quartile 1 (n = 337) | Quartile 2 (n = 298) | Quartile 3 (n = 380) | Quartile 4 (n = 339) | P-value |
|----------------|--------------------|---------------------|---------------------|---------------------|---------------------|---------|
| eGFR (ml/min/1.73 m²) | 94.41 ± 14.19 | 75.05 ± 9.56 | 91.16 ± 2.20 | 99.70 ± 2.68 | 110.61 ± 5.01 | < 0.001 |
| Age (years) | 61.28 ± 11.27 | 68.57 ± 9.09 | 63.50 ± 8.89 | 56.55 ± 7.82 | 49.36 ± 8.92 | < 0.001 |
| Male sex [n (%)] | 558 (41.21) | 171 (50.74) | 118 (39.60) | 163 (42.89) | 106 (31.27) | < 0.001 |
| BMI (kg/m²) | 25.50 ± 3.41 | 25.61 ± 3.30 | 25.39 ± 3.55 | 25.55 ± 3.41 | 25.44 ± 3.39 | 0.863 |
| WHR | 0.82 ± 2.44 | 0.74 ± 0.34 | 0.74 ± 0.33 | 0.78 ± 0.27 | 1.0251 ± 0.85 | < 0.001 |
| Current smoking [n (%)] | 356 (26.29) | 107 (31.75) | 76 (25.50) | 105 (27.63) | 68 (20.06) | < 0.001 |
| Hypertension [n (%)] | 707 (52.22) | 230 (68.25) | 188 (63.09) | 176 (46.32) | 113 (33.33) | < 0.001 |
| SBP (mm Hg) | 128.43 ± 18.27 | 134.52 ± 19.81 | 130.87 ± 17.58 | 126.50 ± 17.13 | 122.36 ± 16.21 | < 0.001 |
| DBP (mm Hg) | 76.84 ± 10.33 | 76.46 ± 11.25 | 75.84 ± 9.76 | 77.61 ± 10.36 | 77.23 ± 9.81 | 0.173 |
| TC (mmol/L) | 5.00 ± 0.03 | 4.98 ± 0.94 | 5.15 ± 0.96 | 5.03 ± 0.89 | 4.85 ± 0.88 | 0.001 |
| TG (mmol/L) | 1.85 ± 1.30 | 1.84 ± 1.21 | 1.90 ± 1.49 | 1.89 ± 1.35 | 1.75 ± 1.17 | < 0.001 |
| HDL-C (mmol/L) | 1.39 ± 0.36 | 1.33 ± 0.36 | 1.42 ± 0.38 | 1.39 ± 0.37 | 1.40 ± 0.34 | 0.037 |

Notes: Continuous variables (age, BMI, WHR, SBP, DBP, TC, TG, HDL-C, LDL-C, FBG, Cr, hs-cTnT and eGFR) were expressed as mean (± SD) or median (interquartile range), and categorical variables (male, current smoking, and hypertension) were expressed as counts and percentages.

Abbreviations: estimated glomerular filtration rate (eGFR); body mass index (BMI); waist-hip ratio (WHR); systolic blood pressure (SBP); diastolic blood pressure (DBP); total cholesterol (TC); triglyceride (TG); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); fasting blood glucose (FBG); highly sensitive cardiac troponin T (hs-cTnT).
|                | Overall     | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 |
|----------------|-------------|------------|------------|------------|------------|
| LDL-C (mmol/L) | 2.94 ± 0.71 | 2.94 ± 0.72 | 3.04 ± 0.73 | 2.93 ± 0.70 | 2.86 ± 0.70 | 0.043 |
| FBG (mmol/L)   | 5.40 ± 1.66 | 5.31 ± 1.35 | 5.29 ± 1.41 | 5.44 ± 1.69 | 5.56 ± 2.05 | 0.184 |
| Cr (mmol/L)    | 65.78 ± 16.05 | 82.18 ± 14.67 | 66.38 ± 10.59 | 62.29 ± 11.15 | 52.87 ± 11.43 | < 0.001 |
| hs-cTnT (pg/mL)| 7.43 ± 9.29 | 9.22 ± 8.27 | 7.42 ± 9.96 | 6.86 ± 8.89 | 5.53 ± 10.83 | < 0.001 |

Notes: Continuous variables (age, BMI, WHR, SBP, DBP, TC, TG, HDL-C, LDL-C, FBG, Cr, hs-cTnT and eGFR) were expressed as mean (± SD) or median (interquartile range), and categorical variables (male, current smoking, and hypertension) were expressed as counts and percentages.

Abbreviations: estimated glomerular filtration rate (eGFR); body mass index (BMI); waist-hip ratio (WHR); systolic blood pressure (SBP); diastolic blood pressure (DBP); total cholesterol (TC); triglyceride (TG); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); fasting blood glucose (FBG); highly sensitive cardiac troponin T (hs-cTnT).

Distribution characteristics of hs-cTnT

Among all participants, hs-cTnT concentrations ranged from 3.03 to 176.40 pg/mL, and its median concentration is 7.43 ± 9.29 pg/mL. 614 (45.35%) had undetectable hs-cTnT (< 3 pg/mL), 577 (42.61%) had hs-cTnT concentrations range from 3 to 13.2 pg/mL, and 163 (12.04%) had hs-cTnT concentrations ≥ 13.3 pg/mL.

Relationship between baseline eGFR and follow-up hs-cTnT

The relationship between baseline eGFR and follow-up hs-cTnT as continuous variables (after natural logarithm transformation) was analyzed and the results were shown in Table 2. Baseline eGFR showed a negative relationship with follow-up hs-cTnT (r = -0.439; P < 0.001) in Pearson's correlation analysis. In multiple linear regression analysis, baseline eGFR was independently and negatively associated with follow-up hs-cTnT (β = -0.310; P = 0.005). Additionally, baseline age (β = 0.025; P < 0.001), sex (β = 0.296; P < 0.001), BMI (β = 0.010; P = 0.026), and FBG (β = 0.026; P = 0.002) were also independently and positively associated with follow-up hs-cTnT.
Table 2
Pearson's correlation and multiple linear regression analysis for the association between baseline eGFR and follow-up hs-cTnT.

| Pearson Correlation | Multiple Linear Regression |
|---------------------|---------------------------|
| r                   | P-value       | β               | P-value       |
| Age (years)         | 0.554         | < 0.001        | 0.025         | < 0.001       |
| Male sex            | 0.304         | < 0.001        | 0.296         | < 0.001       |
| Hypertension        | 0.228         | 0.521          | 0.039         | 0.295         |
| Current smoking     | 0.173         | < 0.001        | 0.008         | 0.834         |
| BMI (kg/m^2)        | 0.060         | 0.037          | 0.010         | 0.026         |
| WHR                 | 0.012         | 0.685          | 0.004         | 0.463         |
| SBP (mm Hg)         | 0.233         | < 0.001        | 0.001         | 0.575         |
| DBP (mm Hg)         | 0.015         | 0.605          | -0.002        | 0.379         |
| TC (mmol/L)         | 0.011         | 0.715          | 0.046         | 0.248         |
| TG^a (mmol/L)       | 0.045         | 0.124          | -0.026        | 0.480         |
| HDL-C^a (mmol/L)    | -0.147        | < 0.001        | -0.110        | 0.193         |
| LDL-C (mmol/L)      | 0.024         | 0.417          | -0.049        | 0.283         |
| FBG (mmol/L)        | 0.083         | 0.005          | 0.026         | 0.002         |
| eGFR^a (ml/min/1.73 m^2) | -0.439 | < 0.001 | -0.310 | 0.005 |

Abbreviations: r, Pearson correlation coefficient; β, stepwise multiple linear regression coefficient. Covariates in the multiple-adjusted models included age; sex; hypertension; current smoking; body mass index (BMI); waist-hip ratio (WHR); systolic blood pressure (SBP); diastolic blood pressure (DBP); total cholesterol (TC); triglyceride (TG); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); fasting blood glucose (FBG); and estimated glomerular filtration rate (eGFR).

^aNatural logarithm-transformed.

Relationship between baseline eGFR and hs-cTnT

Stepwise logistic regression models were performed to evaluate the relationship between different quartiles of baseline eGFR and hs-cTnT, and Quartile 4 was used as the reference. The results were shown in Table 3. In unadjusted models, hs-cTnT was significantly associated with baseline eGFR in quartile 1 (OR, 3.452; 95% CI, 2.443–4.878; P < 0.001), quartile 2 (OR, 1.508; 95% CI, 1.054–2.158; P =
0.024), and quartile 3 (OR, 1.554; 95% CI, 1.107–2.180; P = 0.011). Furthermore, after adjusting for age and sex (model 1) and for hypertension, current smoking, BMI, eGFR, FBG, and plasma levels of TG, TC, HDL-C, LDL-C (model 2), hs-cTnTδ maintained association with baseline eGFR in quartile 1 (OR, 4.447; 95% CI, 2.279–8.678; P < 0.001), quartile 2 (OR, 1.818; 95% CI, 1.124–2.941; P = 0.015), and quartile 3 (OR, 1.831; 95% CI, 1.068–3.138; P = 0.028).

| Table 3 |
| Logistic regression analysis for the association between baseline eGFR and hs-cTnTδ |

| Quartile 1 vs Quartile 4 | Quartile 2 vs Quartile 4 | Quartile 3 vs Quartile 4 |
|--------------------------|--------------------------|--------------------------|
| ≤ 86.54 vs ≥ 104.56      | 86.63–94.99 vs ≥ 104.56  | 95.08–104.54 vs ≥ 104.56 |

| hs-cTnTδ |
|----------|
| Unadjusted | 3.452(2.44–4.878) | < 0.001 | 1.508(1.05–2.158) | 0.024 | 1.554(1.10–2.180) | 0.011 |
| Model 1   | 3.166(2.20–4.539) | < 0.001 | 1.498(1.04–2.151) | 0.029 | 1.567(1.11–2.210) | 0.010 |
| Model 2   | 4.447(2.27–8.678) | < 0.001 | 1.818(1.12–2.941) | 0.015 | 1.831(1.06–3.138) | 0.028 |

Abbreviations: Data are presented as odds ratios and corresponding 95% confidence intervals (CIs). Model 1: adjusted for age, sex; model 2: adjusted for age, sex, hypertension, current smoking, body mass index (BMI), waist-hip ratio (WHR), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), and estimated glomerular filtration rate (eGFR).

**Relationship between eGFRδ and hs-cTnTδ**

No significant association between eGFRδ and hs-cTnTδ was shown after a stepwise logistic regression analysis. The results were shown in Table 4.
Table 4
Logistic regression analysis for the association between eGFRδ and hs-cTnTδ

| eGFRδ          | hs-cTnTδ          | OR (95%CI) | P-value |
|----------------|-------------------|------------|---------|
| Unadjusted     |                   | 1.095(0.679–1.767) | 0.709   |
| Model 1        |                   | 1.288(0.772–2.149) | 0.332   |
| Model 2        |                   | 1.241(0.726–2.122) | 0.431   |

Abbreviations: Data are presented as odds ratios and corresponding 95% confidence intervals (CIs). Model 1: adjusted for age, sex; model 2: adjusted for age; sex; hypertension; current smoking; body mass index (BMI); waist-hip ratio (WHR); systolic blood pressure (SBP); diastolic blood pressure (DBP); total cholesterol (TC); triglyceride (TG); high-density lipoprotein cholesterol (HDL-C); low-density lipoprotein cholesterol (LDL-C); fasting blood glucose (FBG); and estimated glomerular filtration rate (eGFR).

Discussion

In the present cohort study based on community population, we aimed to further investigate the association between eGFR and hs-cTnT. We found that baseline eGFR were independently and negatively associated with follow-up hs-cTnT. Furthermore, baseline eGFR was an independent and positively predictor of the change in hs-cTnT (hs-cTnTδ) after 4.8 years of follow-up. However, we couldn’t prove the association between eGFRδ and hs-cTnTδ. Together with the results from our present study, we confirmed that renal function was related to myocardial injury, and decreased renal function could lead to increased myocardial injury in community-based population without overt CVD.

Troponins are thin myofilament proteins including three isoforms: cardiac troponin I, C and T (cTnI, cTnC and cTnT). They are coded by separate genes differed in structure, and cTnT is cardio-specific. They form a complex to regulate the contraction of striated muscles, and release quickly from cytoplasm when cardiomyocytes get injured [17–19]. The measurement of circulating cTnT assists in diagnosing myocardial injury including acute coronary syndromes and acute myocardial infarction, facilitating risk stratification, and evaluating treatment strategies [20–22]. However, with the development of highly sensitive assays, the detection limit of hs-cTnT is much lower than before, and the prevalence of detectable hs-cTnT is greatly improved in general population without overt CVD [23–24]. In our current study, among 1354 participants aged 61.28 ± 11.27 years old, 740 (54.65%) of them had detectable hs-cTnT concentrations above 3 pg/mL. The prevalence of hs-cTnT concentrations above 13.3 pg/mL was approximately 12.0%, which is similar to the prevalence in another study conducted in the majority of community-dwelling older adults [24].

As is well known, CVD accounts for nearly half of the deaths in patients with ESRD, and patients with renal insufficiency also have a high risk for CVD and progress early to CVD before reaching dialysis [25]. The mutual effect between renal function and CVD is evident. As a specific and sensitive biomarker of
myocardial injury, hs-cTnT elevation was found in patients with renal insufficiency, and associated with increased risk for mortality, even in the absence of clinically suspected ischemic heart disease [26–28]. Thus, in the current study we sought to further explore the relationship between renal function and myocardial injury, and the predictive value of eGFR on hs-cTnT in a community-based population after 4.8 years of follow-up. Pearson's correlation analysis revealed that baseline eGFR showed a negative association with follow-up hs-cTnT (r=-0.439; P < 0.001), and this association remained independently and negatively in multiple linear regression analysis (β=-0.310, P = 0.005). Additionally, after stepwise adjusting for conventional cardiovascular prognostic indicators, such as plasma lipid levels, hypertension, BMI, and FBG, baseline eGFR was independently and positively associated with hs-cTnT (quartile 1: OR, 4.447; 95% CI, 2.279–8.678; P < 0.001, quartile 2: OR, 1.818; 95% CI, 1.124–2.941; P = 0.015, and quartile 3: OR, 1.831; 95% CI, 1.068–3.138; P = 0.028). These results implied that impaired renal function could lead to increased myocardial injury, and the worse the renal function at baseline, the more serious the myocardial injury as time progressed.

The pathophysiologic mechanisms responsible for the release of hs-cTnT in patients with renal insufficiency still need further exploration. Several reasons that may help explain this correlation are provided below. Firstly, except for some major clinical presentations of CVD like acute coronary syndromes [25], patients with renal insufficiency also suffer from repeated episodes of clinically silent myocardial necrosis, which could result in elevated hs-cTnT [29–30]. Secondly, some studies proposed a theory that cTnT could resolve into small immunoreactive fragments and be cleared by kidney. This may partly illustrate the high prevalence of elevated hs-cTnT in patients with reduced renal excretion [31–32]. Thirdly, uremic-induced myocardial ischemia or injury is another factor that should be taken into consideration [16].

Conclusions

Taken together, by analyzing data from a community-based population, we found that baseline eGFR levels were independently and negatively associated with follow-up hs-cTnT. Furthermore, baseline eGFR levels were an independent predictor of the change in hs-cTnT 4.8 years follow-up, indicating a relationship between renal function and myocardial injury in a community-based population.

Declarations

Ethical Approval and Consent to participate

The protocol of this study was under supervision of the Ethics Committee of PLA General Hospital, and written consents were provided by every participant.

Consent for publication
We give our consent for publication.

**Availability of data and materials**

The data and materials in our study are available.

**Competing interests**

We declare no competing interests.

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**Authors' contributions**

Conceived and designed the experiments: PY. Performed the experiments: JH XW RC HW. Analyzed the data: JH XW. Contributed reagents/materials/analysis tools: JH WX HW. Contributed to the writing of the manuscript: JH. Designed the software used in analysis: JH XW YB.

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**References**

1. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. Circulation 2007;116:2634–2653.
2. Aviles RJ, Askari AT, Lindahl B, et al. Troponin T levels in patients with acute coronary syndromes, with or without renal dysfunction. N Engl J Med 2002;346:2047–2052.
3. Apple FS, Wu AH, Mair J, et al. Future biomarkers for detection of ischemia and risk stratification in acute coronary syndrome. Clin Chem 2005;51:810–824.
4. Sato Y, Yamada T, Taniguchi R, et al. Persistently increased serum concentrations of cardiac troponin t in patients with idiopathic dilated cardiomyopathy are predictive of adverse outcomes. Circulation
5. Lindahl B, Toss H, Siegbahn A, et al. Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. N Engl J Med 2000;343:1139-1147.

6. Omland T, de Lemos JA, Sabatine MS, et al. A sensitive cardiac troponin T assay in stable coronary artery disease. N Engl J Med 2009;361:2538–2547.

7. Mingels A, Jacobs L, Michielsen E, et al. Reference population and marathon runner sera assessed by highly sensitive cardiac troponin T and commercial cardiac troponin T and I assays. Clin Chem 2009;55:101–108.

8. Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. N Engl J Med 2009;361:858–67.

9. Keller T, Zeller T, Peetz D, et al. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. N Engl J Med 2009;361:868–877.

10. Latini R, Masson S, Anand IS, et al. Prognostic value of very low plasma concentrations of troponin T in patients with stable chronic heart failure. Circulation 2007;116:1242–1249.

11. Otsuka T, Kawada T, Ibuki C, et al. Association between high-sensitivity cardiac troponin T levels and the predicted cardiovascular risk in middle aged men without overt cardiovascular disease. Am Heart J 2010;159:972-978.

12. Keith DS, Nichols GA, Gullion CM, et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med 2004;164:659-663.

13. Foley RN, Collins AJ. End-stage renal disease in the United States: an update from the United States Renal Data System. J Am Soc Nephrol 2007;18:2644–2648.

14. Best PJ, Lennon R, Ting HH, et al. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. J Am Coll Cardiol 2002;39:1113–1119.

15. Apple FS, Murakami MM, Pearce LA, et al. Predictive value of cardiac troponin I and T for subsequent death in end-stage renal disease. Circulation 2001;106:2941–2945.

16. Freda BJ, Tang WH, Van Lente F, et al. Cardiac troponins in renal insufficiency: review and clinical implications. J Am Coll Cardiol 2002;40:2065–2071.

17. Coats CJ, Heywood WE, Mills K, et al. Current applications of biomarkers in cardiomyopathies. Expert Rev Cardiovasc Ther 2015;13:825-837.

18. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60:1581-1598.

19. Kociol RD, Pang PS, Gheorghiade M, et al. Troponin elevation in heart failure prevalence, mechanisms, and clinical implications. J Am Coll Cardiol 2010; 56:1071-1078.

20. Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined: a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959-969.
21. Morrow DA, Cannon CP, Rifai N, et al. Ability of minor elevations of troponins I and T to predict benefit from an early invasive strategy in patients with unstable angina and non-ST elevation myocardial infarction: results from a randomized trial. JAMA 2001;286:2405-2412.
22. Heidenreich PA, Alloggiamento T, Melsop K, et al. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. J Am Coll Cardiol 2001;38:478-485.
23. Wallace TW, Abdullah SM, Drazner MH, et al. Prevalence and determinants of troponin T elevation in the general population. Circulation 2006;113:1958-1965.
24. Daniels LB, Laughlin GA, Clopton P, et al. Minimally elevated cardiac troponin T and elevated N-terminal pro-B-type natriuretic peptide predict mortality in older adults: results from the Rancho Bernardo Study. J Am Coll Cardiol 2008;52:450-459.
25. Tomas Berl, William Henrich. Kidney-heart interactions: epidemiology, pathogenesis, and treatment. Clin J Am Soc Nephrol 2006;1:8-18.
26. McLaurin MD, Apple FS, Voss EM, et al. Cardiac troponin-I, cardiac troponin-T, and creatine kinase MB in dialysis patients without ischemic heart disease: evidence of cardiac troponin-T expression in skeletal muscle. Clin Chem 1997;43:976-982.
27. Bhayana V, Gougoulias T, Cohoe S, et al. Discordance between results for serum troponin T and troponin I in renal disease. Clin Chem 1995;41:312-317.
28. Croitoru M, Taegtmeyer H. Spurious rises in troponin T in end-stage renal disease. Lancet 1995;346:1558.
29. Aronow WS, Ahn C, Mercando AD, et al. Prevalence of coronary artery disease, complex ventricular arrhythmias, and silent myocardial ischemia and incidence of new coronary artery events in older persons with chronic renal insufficiency and with normal renal function. Am J Cardiol 2000;86:1142-1143.
30. Nakamura S, Uzu T, Inenaga T, et al. Prediction of coronary artery disease and cardiac events using electrocardiographic changes during hemodialysis. Am J Kid Dis 2000;36:592-599.
31. Sharma R, Gaze DC, Pellerin D, et al. Cardiac structural and functional abnormalities in end stage renal disease patients with elevated cardiac troponin T. Heart 2006;92:804-809.
32. Wang F, Zheng J, Ye P, et al. Association of high-density lipoprotein cholesterol with the estimated glomerular filtration rate in a community-based population. PLoS One 2013;8:e79738.