

BMJ Open Association of serum cardiac troponin I and severity of coronary stenosis in patients with varied renal functions: a retrospective cohort study

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ABSTRACT

Background and objective Recent studies showed cardiac troponin I (cTnI) might be a non-invasive biomarker to estimate the severity of coronary stenosis. However, serum cTnI is also found associated with renal function. The study objective is to analyse the association of serum cTnI and severity of coronary stenosis in patients with varied renal functions.

Design A retrospective cohort study.

Setting The First Affiliated Hospital, College of Medicine, Zhejiang University in Hangzhou, China.

Population A total of 6487 subjects who underwent elective coronary angiography between January 2017 to June 2020 were involved in this study.

Primary outcomes Severity of coronary stenosis was divided into three degrees based on Gensini score, mild coronary stenosis, moderate coronary stenosis and severe coronary stenosis.

Results By using ordinal logistic regression, serum cTnI was associated with severity of coronary stenosis (OR=1.14, $p<0.05$). By construction and comparison of two models for predicting severity of coronary stenosis, the addition of cTnI significantly improved the predictive ability of the model. Differences between areas under the curves were 0.03, 0.03, 0.03, 0.12 (all $p<0.05$). Net reclassification improvements were 0.08, 0.05, 0.05, 0.35, respectively, in varied renal functions. Compared with the participants with normal renal function and without hypertroponinaemia, groups of participants with hypertroponinaemia showed higher ORs. ORs were 3.52, 4.20, 4.45, 6.00, respectively, as renal function decreased (all $p<0.05$).

Conclusions In this cohort of patients with stable coronary artery disease and varied renal functions, cTnI was intensely associated with severity of coronary stenosis which based on Gensini score. The presentation of hypertroponinaemia in patients with impaired renal function always indicates a higher risk of severe coronary stenosis.

INTRODUCTION

Approximately one-third of deaths worldwide are attributed to cardiovascular diseases.¹ Coronary artery disease (CAD) is one of the major cardiovascular diseases,

Strengths and limitations of this study

- This study involved a large number of participants, including more than 3000 stable coronary artery disease (CAD) patients with mildly decreased renal function. Few studies draw the conclusions for patients with mildly decreased renal function like us.
- Coronary angiography was performed for each participant to evaluate the CAD severity.
- Few studies conducted in-depth analysis of the relationship between cardiac troponin and severity of coronary stenosis and the risk of severe coronary stenosis in population with varied renal functions. Ordinal logistic regression was performed to illustrate the association of serum cardiac troponin I and severity of CAD.
- It is a retrospective cohort study so that it cannot confirm the aetiology of CAD.
- Selective bias may exist in this study because the participants were all inpatients who mostly presented clinical symptoms or highly suspected of CAD. They were distinguished from normal healthy people.
- All subjects are Chinese and visited in the First Affiliated Hospital, College of Medicine, Zhejiang University. These results may not represent for other ethnicities.

leading to reduction of blood flow to heart muscle.² Recent studies have shown that patients with chronic kidney disease (CKD) have higher risk and mortality of CAD,^{3 4} while 7.6% of deaths of CAD are attributed to impaired renal function.⁵ The comorbidity raises new challenges in management of CAD patients especially for those with impaired renal function.⁴

Coronary angiography is a golden standard to evaluate the severity of coronary stenosis. However, patients have to undergo the coronary angiography using contrast media and X-ray.⁶ This is an invasive procedure, and the contrast media is

often nephrotoxic and may trigger allergic reactions.⁷ For patients with impaired renal function, indication of coronary angiography is more cautious. A no-invasive index is an urgent need for patients with impaired renal function.

Recent studies focused on cardiac troponin I (cTnI) as a proxy to evaluate the severity of coronary stenosis.^{8,9} However, recent studies showed that serum cTnI was also elevated in CKD patients without CAD and associated with renal function.¹⁰ These studies raised a question that the elevated serum cTnI in CAD patients with impaired renal function attributes to impaired renal function or progression of CAD.

To elucidating the association of serum cTnI and severity of coronary stenosis in patients with different renal functions, we carried out a large-scale study involving a total of 6487 patients. All participants underwent coronary angiography and examined their serum cTnI as well as renal function. This study may provide new sights into the management of CAD in those with impaired renal function.

METHODS

Patient and public involvement

No patient involved.

Study design

It is a retrospective single-centre study at the First Affiliated Hospital, College of Medicine, Zhejiang University. We included patients who underwent invasive coronary angiography from January 2017 to June 2020 in this hospital.

Participants

Stable CAD is defined as a period of CAD that is asymptomatic with or without using medications or revascularisation therapy.¹¹ Patients with clinically stable state and underwent elective coronary

angiography during the period from January 2017 to June 2020 were included. Demographic characteristics, blood values, medical history and medications were recorded. Patients with maintenance dialysis, acute coronary syndrome, endocarditis, myocarditis, severe lethal arrhythmias, severe anaemia, malignancy, pulmonary embolism, respiratory failure and conducted radiofrequency ablation, coronary artery bypass grafting within 3 months and other situations which lead to elevation of cTnI were excluded.¹² Finally, 6487 patients were remained in the following analysis.

Coronary angiography

Coronary angiography was performed for all participants and they have signed consent forms before the operations. Examinations, such as echocardiography, X-ray, biochemistry, routine blood, urine, stool tests, and coagulation indexes, were conducted before the operation. The surgical procedure was performed complying with the interventional procedure specifications. Severity of coronary stenosis was quantified by Gensini score algorithms.¹³ Gensini score is a widely used scoring system to evaluate the extent of coronary stenosis. The severity of coronary stenosis score is multiplied by the location score of the coronary tree for every lesion, and the sum of all lesions is the Gensini score.¹⁴ It evaluates locations of plaques and numbers of stenotic lesions to determine the severity of coronary stenosis.¹⁵ To discriminate severity of coronary stenosis, we divided all participants into three groups based on tertiles of Gensini score¹⁶: (1) Gensini score ranged from 0 to 9 (mild coronary stenosis; n=2224); (3) Gensini score ranged from 9 to 29 (moderate coronary stenosis; n=2106); and (4) Gensini score \geq 29 (severe coronary stenosis; n=2157) (table 1).

Table 1 Baseline characteristics of participants from different groups divided by Gensini score

	Total n=6487	0-9 n=2224	9-29 n=2106	\geq 29 n=2157	P value
Male (%)	4361 (67.2)	1293 (58.1)	1432 (68.0)	1636 (75.8)	<0.001
Age, years (IQR)	64 (57-71)	63 (58-71)	65 (58-71)	65 (58-71)	<0.001
BMI, kg/m ² (IQR)	24.3 (22.4-26.4)	24.2 (22.1-26.2)	24.3 (22.5-26.4)	24.3 (22.5-26.4)	<0.001
Diabetes (%)	1596 (24.6)	361 (16.2)	541 (25.7)	694 (32.2)	<0.001
Hypertension (%)	4052 (62.5)	1200 (54.0)	1385 (65.8)	1467 (68.0)	<0.001
Smoking (%)	2956 (45.6)	828 (37.2)	1000 (47.5)	1128 (52.3)	<0.001
LDL, mmol/L (IQR)	1.8 (1.4-2.3)	1.9 (1.4-2.4)	1.7 (1.3-2.2)	1.9 (1.4-2.4)	<0.001
TC, mmol/L (IQR)	3.5 (2.9-4.1)	3.6 (3.0-4.2)	3.3 (2.8-4.0)	3.5 (3.0-4.2)	<0.001
eGFR, mL/min/1.73m ² (IQR)	87.3 (74.2-95.9)	89.5 (78.1-97.2)	87.0 (75.0-95.1)	84.8 (69.8-94.7)	<0.001
cTnI, ng/L (IQR)	9 (3-30)	5 (2-16)	7 (3-25)	21 (6-175)	<0.001

IQR was interquartile ranged from the first quartile to the third quartile.

The p value represents the significance of the non-parametric rank sum test (continuous variables) and χ^2 tests (categorical variables).

BMI, body mass index; cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; TC, total cholesterol.

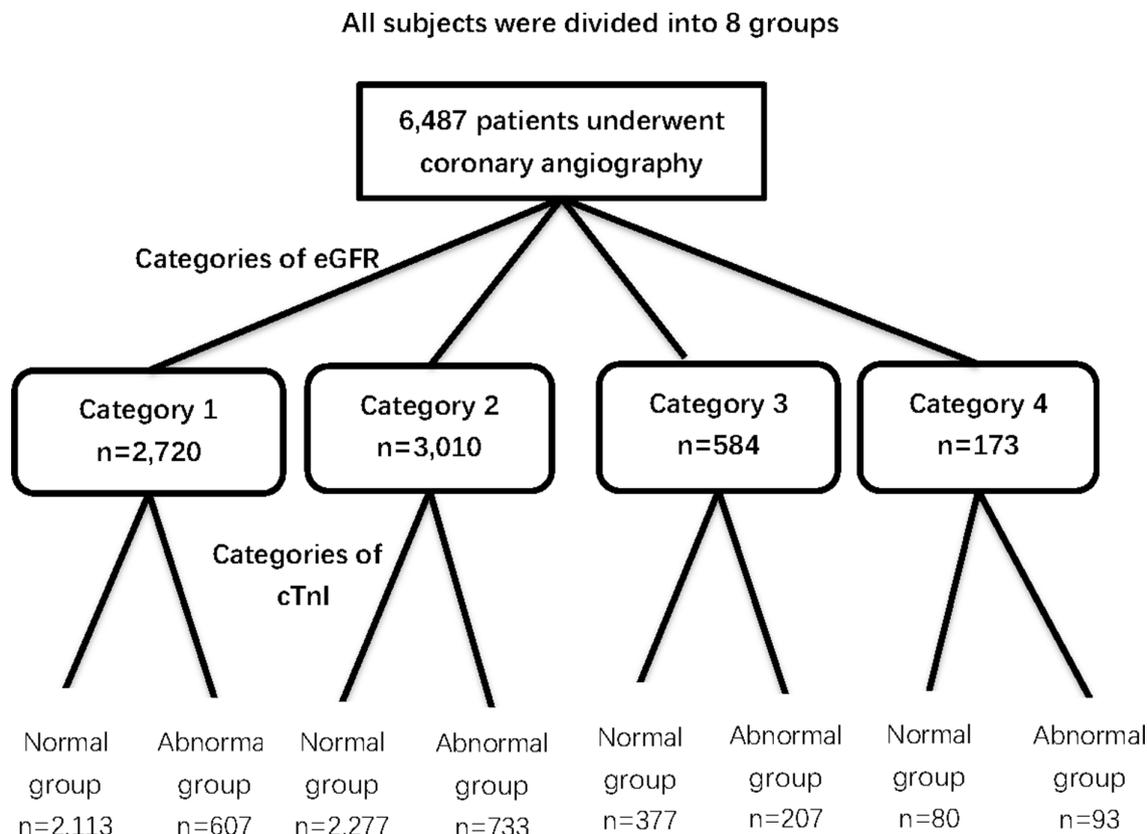


Figure 1 Details of category in all participants. Categories of eGFR: category 1: eGFR ≥ 90 mL/min/1.73 m² (normal renal function); category 2: eGFR ranged from 60 to 90 mL/min/1.73 m² (mildly decreased renal function); category 3: eGFR ranged from 30 to 60 mL/min/1.73 m² (moderately decreased renal function); category 4: eGFR < 30 mL/min/1.73 m² (severely decreased renal function). Categories of cTnI: no hypertroponinaemia (normal group): level of cTnI ranged from 0 to 33 ng/L; hypertroponinaemia (abnormal group): level of cTnI greater than 33 ng/L. cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate.

Blood tests

Blood sample for each participant was drawn to quantify level of serum cTnI and estimated glomerular filtration rate (eGFR). All the tests were conducted within 1 hour after blood withdrawal. The level of serum cTnI was measured by fluorescent enzyme immunoassay (ST AIA-PACK cTnI third-Gen) produced by Tosoh AIA-360 automated enzyme immunoassay analyzer, with a reference range from 0 to 33 ng/L.¹⁷ The calculated limits of quantitation at 20% CV and 10% CV were 30 and 100 ng/L, respectively.¹⁸ These tests were conducted within 7 days before the operation of coronary angiography. Participants with serum cTnI level greater than 33 ng/L were defined as hypertroponinaemia. Renal function was evaluated by eGFR that was calculated by CKD-Epidemiology Collaboration equation.¹⁹ Based on the Kidney Disease Improving Global Outcomes,²⁰ all participants were divided into four categories: (1) eGFR ≥ 90 mL/min/1.73 m² (normal renal function; category 1, n=2720); (2) eGFR ranged from 60 to 90 mL/min/1.73 m² (mildly decreased renal function; category 2, n=3010); (3) eGFR ranged from 30 to 60 mL/min/1.73 m² (moderately decreased renal function; category 3, n=584); and

(4) eGFR < 30 mL/min/1.73 m² (severely decreased renal function; category 4, n=173) (figure 1).

Statistical methods

Continuous variables were described by median and IQR. Discontinuous variables expressed as numbers and percentages. Statistical comparison of groups was undertaken by non-parametric rank sum test (continuous variables) or χ^2 tests (categorical variables). Ordinal logistic regression was used to define the association of serum cTnI level and severity of coronary stenosis. Receiver operating characteristic (ROC) analysis was performed to detect the ability of discriminating severe coronary stenosis in model 1 (combined age, body mass index (BMI), diabetes, hypertension, gender, smoking status, low-density lipoprotein (LDL), total cholesterol (TC)) and model 2 (add cTnI to model 1). Pairwise comparison of ROC curves, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were calculated to compare the predictive ability of these two models. ORs of hypertroponinaemia and severe coronary stenosis were analysed by logistic regression (the presence of hypertroponinaemia as a binary

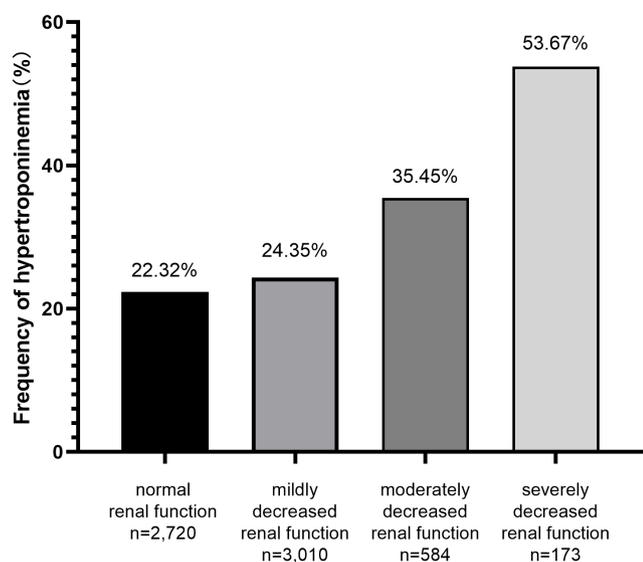


Figure 2 Frequency of hypertroponinaemia in patients with different renal function. normal renal function: eGFR ≥ 90 mL/min/1.73 m²; mildly decreased renal function: eGFR ranged from 60 to 90 mL/min/1.73 m²; moderately decreased renal function: eGFR ranged from 30 to 60 mL/min/1.73 m²; severely decreased renal function: eGFR < 30 mL/min/1.73 m². Hypertroponinaemia was defined as level of cTnI greater than 33 ng/L. cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate.

variable). A two-sided $p < 0.05$ was considered statistically significant. All statistical methods were complicated in IBM SPSS Statistics V.26 and R statistical software, V.4.0.3.

RESULTS

Baseline characteristics

A total of 6487 participants were involved in this analysis, including 2126 females (32.8%) and 4361 males

(67.2%). Among them, 2956 (45.6%) participants are smokers or have ever smoked. A total of 1596 (24.6%) participants and 4052 (62.5%) participants suffered from diabetes²¹ and hypertension, respectively. Table 1 shows the classical risk factors of CAD and level of cTnI and eGFR in different severity of coronary stenosis.

Frequency of participants with varied renal functions having hypertroponinaemia

The distribution of serum cTnI level in patients with different renal functions has been shown in figure 2. The medians (IQR) of serum cTnI level were 6 (3–27) ng/L, 8.5 (4–31) ng/L, 20 (7–69.3) ng/L, 88 (26–722) ng/L, respectively, in participants with normal renal function, mildly decreased renal function, moderately decreased renal function, severely decreased renal function. The frequencies of having hypertroponinaemia were 22.32%, 24.35%, 35.45%, 53.76%, respectively. Increased frequency of having hypertroponinaemia was observed associated with worsening renal function.

Association of serum cTnI level and severity of coronary stenosis in participants with varied renal functions

To evaluate the association of serum cTnI level and severity of coronary stenosis in participants with varied renal functions, we performed ordinal logistic regression using level of serum cTnI as a continuous variable and severity of coronary stenosis as an ordinal categorical variable. The result was presented in table 2. After adjusted by sex, age, BMI, diabetes, hypertension, smoking status, LDL and TC, serum cTnI level was associated with severity of coronary stenosis. The ORs were 1.11, 1.18, 1.10, 1.56 (all $p < 0.001$) in the participants with normal renal function, mildly decreased renal function, moderately decreased renal function and severely decreased renal function, respectively.

Table 2 Association between level of serum cTnI and Gensini score in patients with varied renal function

	eGFR (mL/min/1.73 m ²)				
	Overall n=6487	≥ 90 n=2720	60–90 n=3010	30–60 n=584	< 30 n=173
Univariable model					
OR	1.15	1.12	1.14	1.10	1.57
95% CI	1.12 to 1.18	1.08 to 1.15	1.13 to 1.24	1.02 to 1.18	1.12 to 2.20
P value	< 0.001	< 0.001	< 0.001	0.009	0.008
Multivariable model					
OR	1.14	1.11	1.18	1.10	1.56
95% CI	1.11 to 1.17	1.08 to 1.15	1.13 to 1.23	1.02 to 1.18	1.10 to 2.19
P value	< 0.001	< 0.001	< 0.001	0.01	0.01

Multivariable model was adjusted by age, sex, body mass index, diabetes, hypertension, smoking status, low-density lipoprotein and total cholesterol.

cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate.

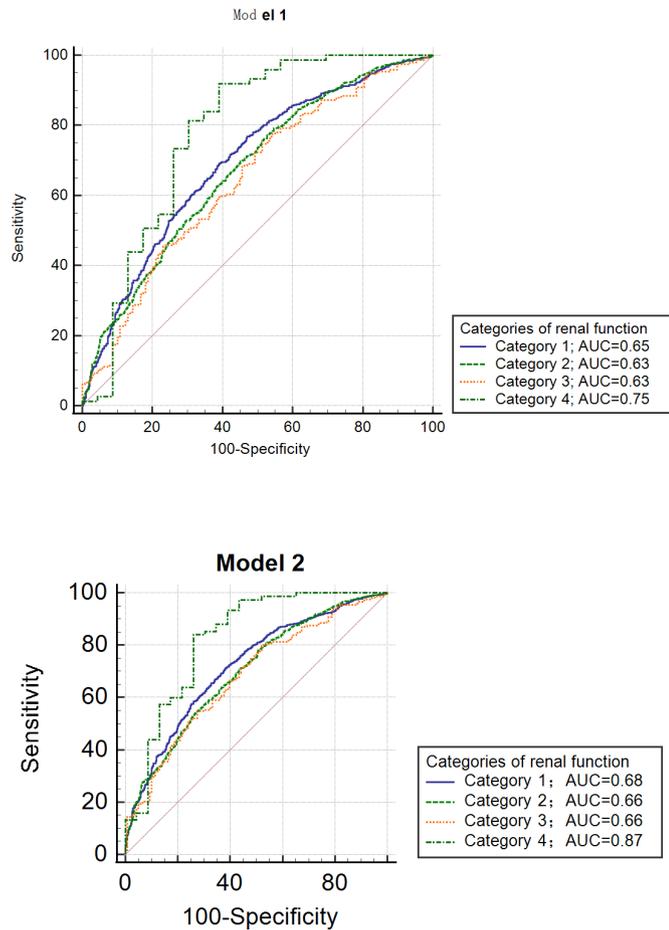


Figure 3 Receiver operating characteristic curves of cTnI in discriminating severe coronary stenosis note: model 1 combined age, body mass index, diabetes, hypertension, gender, smoking status, low-density lipoprotein, total cholesterol. Model 2 was based on model 1 with the addition of cTnI. Categories of eGFR: category 1: eGFR ≥ 90 mL/min/1.73 m² (normal renal function); category 2: eGFR ranged from 60 to 90 mL/min/1.73 m² (mildly decreased renal function); category 3: eGFR ranged from 30 to 60 mL/min/1.73 m² (moderately decreased renal function); category 4: eGFR < 30 mL/min/1.73 m² (severely decreased renal function). AUC, area under the curve; cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate.

Classical risk factors combined with cTnI to discriminate severe coronary stenosis

To detect the predictive value of cTnI in discriminating severe coronary stenosis (Gensini score ≥ 29 ; n=2157) for patients with different renal functions, we performed ROC curves in model 1 and model 2. Combining age, BMI, diabetes, hypertension, gender, smoking status, LDL, TC in model 1. Model 2 was based on model 1 with the addition of cTnI. It has been shown in figure 3 and table 3 that areas under the curve (AUCs) and 95% CIs were 0.65 (0.62 to 0.67) vs 0.68 (0.66 to 0.70), 0.63 (0.60 to 0.65) vs 0.66 (0.64 to 0.68), 0.63 (0.59 to 0.68) vs 0.66 (0.61 to 0.71), 0.75 (0.66 to 0.83) vs 0.87 (0.79 to 0.93), respectively, in model 1 and model 2 in patients with decreasing renal function. By pairwise comparison of

ROC curves, the difference between AUCs were 0.03, 0.03, 0.03, 0.12 (all $p < 0.05$); NRI were 0.08, 0.05, 0.05, 0.35 (all $p < 0.05$), IDI were 0.04, 0.03, 0.02, 0.17 (all $p < 0.05$), respectively, as renal function decreased. By adding serum cTnI to the model, the ability of discriminating severe coronary stenosis could be significantly improved.

Risk of severe coronary stenosis in participants with hypertropoanaemia and worsening renal function

Participants with serum cTnI level greater than 33 ng/L were defined as hypertropoanaemia (abnormal group), while participants with serum cTnI level ranged from 0 to 33 ng/L were defined as no hypertropoanaemia (normal group). The details of categories in all participants were shown in figure 1. In this ordinal logistic regression, severity of coronary stenosis was used as an ordinal variable, and presence of hypertropoanaemia was set as a binary variable. Sex, age, BMI, diabetes, hypertension, smoking status, LDL, TC were adjusted in this analysis. A group of participants having normal renal function (eGFR ≥ 90 mL/min/1.73 m²) and without hypertropoanaemia (cTnI < 33 ng/L) were set as baseline (OR=1). In every category of renal function, the group of participants having hypertropoanaemia (≥ 33 ng/L) showed a higher odd ratio than those without hypertropoanaemia (table 4). Compared with the baseline group, the odd ratios were 3.52, 4.20, 4.45, 6.00, respectively, in participants with normal renal function, mildly decreased renal function, moderately decreased renal function and severely decreased renal function (figure 4). In the subgroup of hypertropoanaemia, the risk of severe coronary stenosis was higher as renal function worsening.

DISCUSSION

CAD is often caused by coronary artery obstruction due to the formation of atherosclerotic plaque. As the disease progresses, the rupture of atherosclerotic plaques could lead to angina pectoris and results in acute cardiovascular events. The period before acute cardiovascular events happens is known as the stable status. It is also an important window of time to monitor the disease severity so that the secondary prevention can be performed promptly. Moreover, evaluating severity of coronary stenosis in this period by no-invasive index is more significant for patients with impaired renal function.

Cardiac troponin was one of standards in diagnosing myocardial infarction.⁸ The potential predictive value of cardiac troponin for patients with stable CAD begun to be explored. Samman *et al* found cTnI was independently associated with severity of coronary stenosis.²² The studies of Korosoglou *et al*²³ and Oemrawsingh *et al*²⁴ showed that cardiac troponin level was associated with vulnerable plaque in patients with stable CAD. And cardiac troponin level could predict coronary event for patients with stable CAD.

**Table 3** Receiver operating characteristic curves of cardiac troponin I (cTnI) in discriminating severe coronary stenosis

eGFR (mL/min/1.73m ²)	≥90	60–90	30–60	<30
Model 1				
AUC	0.65	0.63	0.63	0.75
95% CI	0.62 to 0.67	0.60 to 0.65	0.59 to 0.68	0.66 to 0.83
Model 2				
AUC	0.68	0.66	0.66	0.87
95% CI	0.66 to 0.70	0.64 to 0.68	0.61 to 0.71	0.79 to 0.93
Pairwise comparison of ROC curves				
Difference between areas	0.03	0.03	0.03	0.12
95% CI	0.02 to 0.04	0.02 to 0.04	0.02 to 0.05	0.04 to 0.21
P value	<0.001	<0.001	<0.001	0.006
NRI	0.08	0.05	0.05	0.35
95% CI	0.04 to 0.13	0.03 to 0.11	0.02 to 0.19	0.03 to 0.72
P value	0.02	0.04	0.006	0.041
IDI	0.04	0.03	0.02	0.17
95% CI	0.03 to 0.04	0.02 to 0.04	0.01 to 0.03	0.11 to 0.23
P value	<0.001	<0.001	<0.001	<0.001

AUC was the area under receiver operating characteristic curves.

Model 1 combined age, body mass index, diabetes, hypertension, gender, smoking status, low-density lipoprotein, total cholesterol to discriminate severity of coronary stenosis. Model 2 was based on model 1 with addition of cTnI.

AUC, area under the curve; eGFR, estimated glomerular filtration rate; IDI, integrated discrimination improvement; NRI, net reclassification improvement.

Nephrologists and cardiologists often encounter with the elevated level of serum cTnI in patients with CKD. It is a controversial question that the elevated serum cTnI in CAD patients with impaired renal function attributes to impaired renal function or progression of CAD. On the one hand, as renal clearance plays a role in excretion of cTnI, the elevated cTnI could be due to impaired renal function. Previous study conducted in rats suggested that poor renal clearance could be the reason making elevated serum cTnI in patients with CKD.²⁵ On the other

hand, the cardiac and kidney diseases were intensely linked. The concept ‘cardiorenal syndrome’ has been proposed.²⁶ Impaired renal function induced cardiomyocytes to release more cardiac troponin into circulation. For example, impaired blood flow such as lower coronary flow reserve and disorder of microcirculation in patients with CKD may cause damage of cardiomyocytes.²⁷ As renal function deteriorates, some inflammatory cytokines (like interleukin-6, tumour necrosis factor- α , monocyte chemotactic protein-1) and inflammatory biomarkers

Table 4 Association of hypertroponinaemia and severity of coronary stenosis in patients with varied renal function

eGFR (mL/min/1.73 m ²)	cTnI (ng/L)	OR	95% CI	P value
≥90	<33 (n=2113)	1	—	—
	≥33 (n=607)	3.52	2.78 to 3.80	<0.001
60–90	<33 (n=2277)	1.19	1.17 to 1.23	0.012
	≥33 (n=733)	4.2	2.08 to 4.35	<0.001
30–60	<33 (n=377)	1.82	1.56 to 2.12	<0.001
	≥33 (n=207)	4.45	2.88 to 4.58	<0.001
<30	<33 (n=80)	1.7	0.72 to 3.54	0.09
	≥33 (n=93)	6	3.96 to 7.27	<0.001

IQR was from the first quartile to the third quartile. Patients with cTnI level range from 0 to 33 ng/L and eGFR ≥90 mL/min/1.73m² was set as baseline, OR=1. Sex, age, BMI, diabetes, hypertension, smoking status, low-density lipoprotein and total cholesterol were adjusted in this analysis. Serum cTnI level greater than 33 ng/L was defined as hypertroponinaemia.

BMI, body mass index; cTnI, cardiac troponin I; eGFR, estimated glomerular filtration rate.

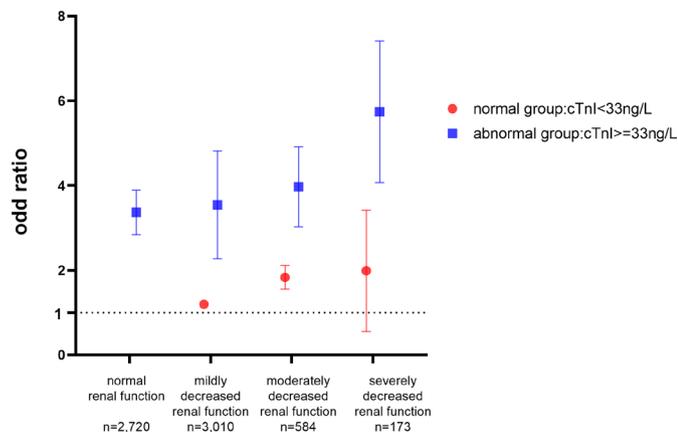


Figure 4 ORs in patients with hypertroponinaemia as renal function decreased. Patients with cTnI level range from 0 to 33 ng/L and eGFR ≥ 90 mL/min/1.73 m² were set as baseline, OR=1. Sex, age, BMI, diabetes, hypertension, smoking status, low-density lipoprotein and total cholesterol were adjusted in this analysis. cTnI, cardiac troponin I; BMI, body mass index; eGFR, estimated glomerular filtration rate.

(like C reactive protein) will be significantly upregulated.²⁸ Excessive oxidative stress^{29,30} and inflammation could result in the dysfunction of endothelial cell and then promote cardiomyocytes to release more cardiac troponin.³¹

Elucidating the relationship among serum cTnI, renal function and severity of coronary stenosis may help address this question. In this study, we observed the higher frequency of having hypertroponinaemia in patients with worsening renal function. It indicated that patients with worsening renal function were more likely to get cTnI level higher than normal people.

This study showed that the serum cTnI level was associated with severity of coronary stenosis in patients with different renal functions. In the presented study, the ORs in table 2 were significant in every group of renal function, so we could draw the conclusion that cTnI was intensely associated with severity of coronary stenosis. In addition, we also quantified the severity of coronary stenosis by CAD classification. CAD classification was defined as no CAD, one-vessel, two-vessel or three-vessel disease according to the number of affected major epicardial vessels by $\geq 50\%$ diameter stenosis. The association of cTnI and CAD classification was consistent with Gensini score. Brunner *et al* also found this association in patients with CKD.³²

To further proved the association of cTnI and severity of coronary stenosis, we did ROC analysis, respectively, in two models (with or without cTnI) to detect the ability of cTnI in discriminating severe coronary stenosis for patients with different renal functions. The result showed that serum cTnI level had a quite significant value in discriminating severe coronary stenosis, especially in patients with severely decreased renal function. It means elevated serum cTnI level is an index to discriminate severe coronary stenosis in patients with different degree of impaired renal function.

What's more, we performed the ordinal logistic regression analysis to assess the association of presence of hypertroponinaemia and the severity of coronary stenosis for patients with varied renal functions. Compared with baseline, patients with hypertroponinaemia had a higher risk to develop severe coronary stenosis than those without hypertroponinaemia in every stage of renal function. Moreover, this association was consistently increased in patients with hypertroponinaemia as renal function decreased. It reminded clinicians to be more cautious when hypertroponinaemia presented in patients with impaired renal function.

Previous studies in this field usually focused on those patients with CKD (eGFR < 60 mL/min/1.73 m²).^{32,33} Compared with previous studies, this study enrolled more than 3000 patients with mildly decreased renal function (60 mL/min/1.73 m² \leq eGFR < 90 mL/min/1.73 m²). We observed the higher OR in these patients than patients with normal renal function, suggesting that clinicians should be alert when hypertroponinaemia presents even in patients with mildly decreased renal function.

Hypertroponinaemia presents more frequently in patients with impaired renal function. This situation often encounters with nephrologists, emergency physicians and cardiologists. Clinicians are always hesitant to the next medications. To do coronary angiography or not. This study may provide new insights into the clinical practices. According to this study, cTnI makes sense in estimating the severity of CAD for patients with varied renal functions. Moreover, hypertroponinaemia indicated a higher risk of severe CAD in patients with impaired renal function than those with normal renal function. Therefore, when patients having impaired renal function (even in patients with mildly decreased renal function) present hypertroponinaemia, more careful evaluation and more active therapeutic measures (like coronary angiography) should be taken.

There are some limitations in our study. First of all, it is a retrospective cohort study so that it can't confirm the aetiology of CAD. All subjects are Chinese and visited in the First Affiliated Hospital, College of Medicine, Zhejiang University. These results may not represent for other ethnicities. And selective bias may exist in this study because the participants were all inpatients who mostly presented clinical symptoms or highly suspected of CAD. They were distinguished from normal healthy people. The level of cTnI was dynamically changed, but we only took the most recent result before the coronary angiography.

CONCLUSIONS

In this cohort of patients with stable CAD and varied renal functions, cTnI was intensely associated with severity of coronary stenosis which based on Gensini score. The presentation of hypertroponinaemia in patients with impaired renal function always indicates a higher risk of severe coronary stenosis.

Contributors YY contributed to the idea of the study. All authors contributed to the planning, design and implementation of the study. QZ and Y-FW contributed to the writing and shared the first authorship. JC contributed to the statistical analysis. QZ and Y-JT made the tables and figures. XH provided the information and methods of clinical laboratory. CG and QZ contributed to the data collection and management. YY, FH and JC supervised the project and the final version. All authors have approved of the final version. YI acts as the guarantor of this study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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Data availability statement Data are available on reasonable request. Data that support the findings of this study are available from the corresponding author on reasonable request.

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