

The appropriate troponin T level associated with coronary occlusions in chronic kidney disease patients

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Background: High-sensitivity troponin T (HS Trop T) plays an important role as a diagnostic marker for acute coronary syndrome. It is also related to cardiovascular outcomes. HS Trop T levels may be varied in individuals with renal dysfunction. This study aimed to find the appropriate HS Trop T cutoff points in chronic kidney disease (CKD) patients who had coronary artery occlusion.

Patients and methods: The study was conducted at the Emergency Department, Ramathibodi Hospital, Mahidol University, Thailand. CKD patients stage 3–5 who had HS Trop T levels after 2 hours of chest pain and had coronary angiographic results were enrolled. Patients were divided into two groups: those who had significant occlusion of more than 70% of a coronary artery as the coronary artery disease (CAD) group and the non-CAD group.

Results: In total, 210 patients met the study criteria. There were 132 patients (62.86%) who had significant stenosis of coronary arteries by coronary angiograms. The average age (standard deviation) of all patients was 71.02 (9.49) years. HS Trop T levels were significantly higher in all CKD patients with CAD than the non-CAD group (0.4973 versus 0.0384 ng/mL). Sex and HS Trop T levels were significantly associated with CAD by multivariate logistic regression analysis. The HS Trop T level of 0.041 ng/mL gave sensitivity and specificity of 65.91% and 75.65%, respectively, for CAD.

Conclusion: The HS Trop T level of 0.041 ng/mL provided diagnostic properties for established coronary artery occlusion in CKD patients.

Keywords: high-sensitivity troponin T, acute coronary syndrome, coronary artery occlusion, chronic kidney disease, sensitivity, specificity, coronary angiogram

Introduction

Acute coronary syndrome (ACS) is a common disease at emergency departments, and has high morbidity and mortality.¹ Cardiac biomarkers are a useful diagnostic tool for ACS.^{2–4} High-sensitivity troponin T (HS Trop T) is very specific to myocardial tissue, and a level of more than 0.014 ng/mL has specificity to acute myocardial infarction in normal renal function patients.⁵

Chronic kidney disease (CKD) is a common disease in clinical practice and increases risk for ACS. Serum Trop T levels of renal dysfunction patients may be higher than the normal population, resulting in higher cutoff points.⁶ The cutoff point of HS Trop T for ACS with renal dysfunction may be higher than normal population.^{7,8} The diagnosis of ACS may need to be confirmed by coronary angiogram, but some studies have used clinical diagnosis of ACS.^{7,8} This study aimed to find the appropriate HS Trop T cutoff points in CKD patients who presented with ACS and had coronary

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artery occlusion by coronary angiogram. Factors associated with coronary occlusion in CKD patients who are suspected to have ACS were also studied.

Patients and methods

The study was conducted at the Department of Emergency, Ramathibodi Hospital, Mahidol University, Thailand. CKD patients stages 3–5 who had HS Trop T levels (Hoffman-La Roche Ltd, Basel, Switzerland) after 2 hours of chest pain and had coronary angiographic results were enrolled. Patients who had received hemodialysis therapy or who had been diagnosed with non-coronary artery disease (non-CAD) by coronary angiogram were excluded. The study period was between June 1, 2010 and June 30, 2013.

Eligible patients were identified by using International Classification of Diseases 9 code 88.5 (clinical medication procedure code). Charts of eligible patients were retrospectively reviewed. Baseline characteristics, comorbid diseases, medications, history of smoking, HS Trop T levels, serum creatinine, and coronary angiographic results were recorded. CKD was classified by estimated glomerular filtration rate (eGFR) as stages 3–5 with eGFR of 31–60, 15–30, and <5 mL/min/1.73 m². eGFR was calculated by the Chronic Kidney Disease Epidemiology Collaboration formula. Serum creatinine on the date of the emergency room visit was used to calculate eGFR.

ACS was diagnosed by clinical findings of chest pain, HS Trop T, and ECG.³ The thrombolysis in myocardial infarction (TIMI) risk score was calculated.⁹ Significant CAD was defined by the presence of coronary artery occlusion of more than 70% of the culprit coronary artery or arteries.

Statistical analyses

Patients were divided into two groups by significant occlusion of more than 70% of a coronary artery as CAD and non-CAD. Baseline and clinical characteristics of patients in both groups were compared using descriptive statistics. Univariate logistic regression analyses were applied to calculate the crude odds ratios (ORs) of individual variables for CAD. All clinically important variables or results of univariate analyses with a *P*-value less than 0.10 were included in subsequent multivariate logistic regression analyses. Analytical results were presented as adjusted ORs and 95% confidence intervals. Various cutoff points of HS Trop T were calculated by using receiver operating characteristic (ROC) analysis. The areas under ROC curves, sensitivity, specificity, and predictive values of all cutoff points were also executed. The association of HS Trop T levels and various factors were also calculated by multivariate logistic

regression analyses. All data analyses were performed with Stata software (StataCorp LP, College Station, TX, USA). The study protocol was approved by the Ethics Committee in Human Research, Mahidol University.

Results

There were 1,550 patients who had HS Trop T results and coronary angiographic results. Of those, 282 patients met the study criteria. We excluded 72 patients due to hemodialysis (42 patients), inappropriate time of HS Trop T level (22 patients), stress-induced cardiomyopathy (five patients), and pulmonary embolism (three patients). In total, 210 patients were included in the analysis. There were 132 patients (62.86%) who had significant coronary artery stenosis by coronary angiogram. Triple-vessel disease was the most common CAD (83 patients); double-vessel disease and single-vessel disease were found in 26 and 23 patients, respectively.

The average age (standard deviation) of all patients was 71.02 (9.49) years. Being of male sex, having diabetes mellitus, and significantly higher TIMI risk scores were found in the CAD group (Table 1). The mean eGFR of CAD was significantly lower in the CAD group than the non-CAD group: 38.91 versus 42.81 mL/min/1.73 m² (*P*=0.031). HS Trop T levels were significantly higher in all CKD patients with CAD than in the non-CAD group (0.4973 versus 0.0384 ng/mL, *P*=0.008), and when classified by stage in CKD 3 but not in 5 (Table 1). Two factors were significantly associated with CAD by multivariate logistic regression analysis (Table 2). Female sex and HS Trop T levels had adjusted ORs (95% confidence interval) of 0.51 (0.26–0.98) and 5.92 (3.02–11.60).

For all CKD patients, the cutoff points for HS Trop T and CAD are shown in Table 3 and Figure 1. The area under the ROC curve was 77.15%, giving sensitivity and specificity of 65.91% and 75.65%, respectively, for the cutoff point of 0.041 ng/mL. The cutoff point of HS Trop T at 0.041 gave sensitivity and specificity of 67.31% and 79.03% (CKD stage 3; Table 4 and Figure 2) and 71.43% and 56.25% (CKD stages 4 and 5; Table 5 and Figure 3), respectively.

Discussion

Third-generation Trop T has been shown to be a predictor of future CAD and associated with mortality in CKD patients.^{10,11} This study added the correlation of HS Trop T and significant coronary occlusion with an adjusted OR of 5.92 in CKD patients (Table 2). Sex is another significant factor (Table 2). As in previous reports, males were at higher

Table 1 Characteristics of all patients categorized by presence of coronary artery disease (CAD) from coronary angiograms

	All patients n=210	CAD n=132	Non-CAD n=78	P-value
Mean age, years \pm SD	71.02 \pm 9.49	71.17 \pm 9.59	70.76 \pm 9.37	0.766
Male sex, n (%)	127 (60.48)	89 (67.42)	38 (48.72)	0.007
Comorbid diseases, n (%)				
Hypertension	160 (76.19)	103 (78.03)	57 (73.08)	0.415
Diabetes mellitus	103 (49.05)	74 (56.06)	29 (33.18)	0.008
Dyslipidemia	90 (42.86)	57 (43.18)	32 (42.31)	0.902
Pulmonary disease	28 (13.33)	16 (12.12)	12 (15.38)	0.501
Connective tissue disease	3 (1.43)	2 (1.52)	1 (1.28)	1.000
Stroke	25 (11.90)	17 (12.88)	8 (10.26)	0.571
Cirrhosis	3 (1.43)	3 (2.27)	0	0.296
Cancer	13 (6.15)	6 (4.55)	7 (8.97)	0.240
Post-PTCA	54 (25.71)	31 (23.48)	23 (29.49)	0.336
Previous CAD	35 (16.67)	24 (18.18)	11 (14.10)	0.443
Other factors				
Family history of CAD	2 (0.95)	2 (1.52)	0	0.531
Chest pain more than twice in 24 hours	75 (37.29)	51 (38.64)	21 (26.92)	0.084
Smoking	13 (6.19)	8 (6.06)	5 (6.41)	1.000
Aspirin use	135 (64.29)	87 (65.91)	48 (61.51)	0.523
TIMI risk score				
Mean \pm SD	2.74 \pm 1.29	2.90 \pm 1.31	2.46 \pm 1.22	0.015
TIMI categories				
Low risk (TIMI 1, 2)	101 (48.10)	60 (45.45)	41 (52.56)	0.290
Moderate risk (TIMI 3, 4)	87 (41.43)	55 (41.67)	32 (41.03)	
High risk (TIMI 5, 6)	22 (10.48)	17 (12.88)	5 (6.41)	
Electrocardiographic findings				0.004
Non-myocardial infarction	136 (64.76)	75 (56.82)	61 (78.21)	
ST-elevation myocardial infarction	18 (8.57)	16 (12.12)	2 (2.56)	
Non-ST-elevation myocardial infarction	56 (26.67)	41 (31.06)	15 (19.23)	
eGFR (mL/min/1.73 m ²)				0.031
Mean \pm SD	40.36 \pm 0.87	38.91 \pm 1.13	42.81 \pm 1.32	
eGFR by category				
CKD stage 3	166 (79.05)	104 (78.79)	62 (79.79)	0.094
CKD stage 4	37 (17.62)	21 (15.91)	16 (20.51)	
CKD stage 5	7 (3.33)	7 (5.30)	0	
HS Trop T (ng/mL)				0.008
Mean \pm SD		0.4973 \pm 1.5186	0.0384 \pm 0.0534	
HS Trop T (ng/mL) by CKD category				
CKD stage 3		0.5152 \pm 1.6712	0.0304 \pm 0.0307	0.023
CKD stages 4 and 5		0.4306 \pm 0.7272	0.0693 \pm 0.0976	0.055

Abbreviations: SD, standard deviation; PTCA, percutaneous transluminal coronary angioplasty; TIMI, thrombolysis in myocardial infarction; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; HS Trop T, high-sensitivity troponin T.

Table 2 Factors associated with coronary artery disease by coronary angiogram using multivariate logistic regression analysis

Factors	Adjusted odds ratio	95% confidence interval	P-value
Female sex	0.51	0.26–0.98	0.044
Diabetes mellitus	1.53	0.79–2.98	0.204
Frequent chest pain	1.39	0.57–3.41	0.462
eGFR	0.98	0.96–1.01	0.422
TIMI score	1.20	0.85–1.68	0.289
HS Trop T	5.92	3.02–11.60	<0.001

Note: Frequent chest pain: chest pain more than two times in 24 hours.

Abbreviations: eGFR, glomerular filtration rate; TIMI, thrombolysis in myocardial infarction; HS Trop T, high-sensitivity troponin T.

Table 3 Diagnostic properties of various high-sensitivity troponin T (HS Trop T) levels and coronary artery disease in all patients with chronic kidney diseases (n=210; area under ROC curve =0.7715)

HS Trop T (ng/mL)	0.014	0.030	0.036	0.041	0.100
Sensitivity	92.42%	76.52%	68.94%	65.91%	43.94%
Specificity	28.21%	58.97%	71.79%	75.64%	91.03%
Positive predictive value	68.54%	75.94%	80.53%	82.08%	89.23%
Negative predictive value	68.75%	59.74%	57.73%	56.73%	48.97%

Abbreviation: ROC, receiver operating characteristic.

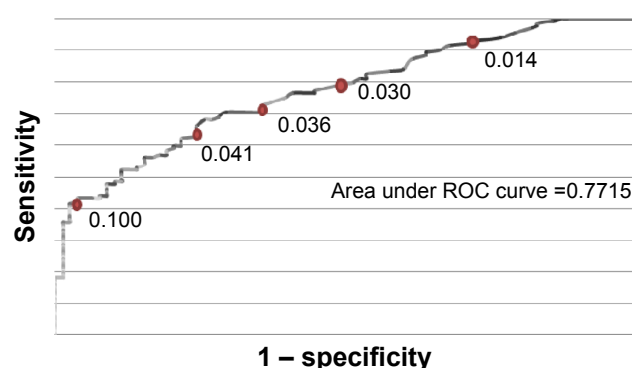


Figure 1 Receiver operating characteristic (ROC) curve of high-sensitivity troponin T levels and coronary artery disease in all patients (n=210).

risk for CAD than females. After adjustment by multivariate logistic regression analysis, TIMI score and GFR became non-significant factors for coronary occlusion (Tables 1 and 2). These results may indicate that sex and HS Trop T levels were the only two independent factors associated with significant coronary occlusion, but not GFR level or disease severity.

A study from France suggested using an HS Trop T cutoff point at 0.0358 ng/mL for acute myocardial infarction in patients with CKD. Its sensitivity and specificity were 94% and 86%, respectively.¹² Another study conducted in the US compared HS Trop T levels in 51 CKD patients with 112 normal renal function patients who had ACS.⁷ The sensitivity of ACS diagnosis increased from 63% to 87% if the cutoff point of HS Trop T increased from 0.1 to 0.5 ng/mL. For a Thai population, the Trop T level of 0.1 ng/mL gave sensitivity of 90.90% and specificity of 84.50% in CKD patients with suspected ACS compared with CKD patients without ACS symptoms.¹³ Other studies also showed that the cutoff point for HS Trop T to diagnose acute myocardial infarction needs to be adjusted by the GFR.^{14–16}

In this study, the cutoff point of HS Trop T at 0.041 ng/mL gave sensitivities from 65.91% to 71.45% and specificities of

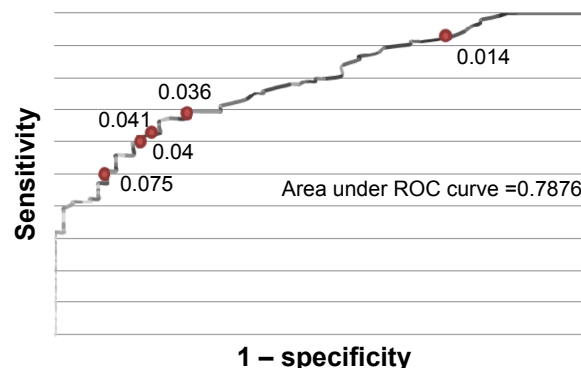


Figure 2 Receiver operating characteristic (ROC) curve of high-sensitivity troponin T levels and coronary artery disease in chronic kidney disease stage 3 (n=166).

71.43% and 79.03% overall and CKD stage 3, respectively. Specificity dropped to 56.25% in CKD stage 4 and 5 (Table 4 and 5). The decreasing of sensitivities by GFR may explain by the high baseline HS Trop T level in low GFR.^{14–16} Note that these diagnostic properties were indications of coronary occlusion by coronary angiogram, not for diagnosis of acute myocardial infarction as in previous studies.^{12–16}

The strength of this study is that all subjects had coronary angiograms performed to confirm the CAD. There are some limitations in this study, including small sample size, retrospective data collection, and generation of HS Trop T. The results therefore may not be applicable for the newer generations of Trop T or another cardiac marker (troponin I). The study population was limited, due to the use of newer-generation HS Trop T in this hospital. Finally, due to the retrospective study design, the study population in the CAD and non-CAD groups may not have been equally distributed. The numbers of patients with high TIMI score, CKD stage 4, and CKD stage 5 were higher in the CAD group than the non-CAD group (12.88% versus 6.41%; 15.91% versus 20.51%; 5.30% versus 0%), as shown in Table 1. However, after controlling of these factors by using multivariate logistic

Table 4 Diagnostic properties of various high-sensitivity troponin T (HS Trop T) levels and coronary artery disease in patients with chronic kidney disease stage 3 (n=166; area under ROC curve =0.7876)

HS Trop T (ng/mL)	0.014	0.036	0.041	0.046	0.075
Sensitivity	90.38%	69.23%	67.31%	64.42%	50.96%
Specificity	33.87%	75.81%	79.03%	80.65%	88.71%
Positive predictive value	69.63%	82.35%	85.19%	84.81%	88.33%
Negative predictive value	67.74%	58.02%	58.82%	57.47%	51.89%

Abbreviation: ROC, receiver operating characteristic.

Table 5 Diagnostic properties of various high-sensitivity troponin T (HS Trop T) levels and coronary artery disease in patients with chronic kidney disease stages 4 and 5 (n=44; area under ROC curve =0.7188)

HS Trop T (ng/mL)	0.036	0.041	0.075	0.100	0.150	0.200
Sensitivity	75.00%	71.43%	57.14%	50.00%	50.00%	46.43%
Specificity	56.25%	56.25%	75.00%	87.50%	93.75%	93.75%
Positive predictive value	75.00%	72.00%	80.00%	87.50%	93.33%	92.86%
Negative predictive value	56.25%	47.37%	50.00%	50.00%	51.72%	50.00%

Abbreviation: ROC, receiver operating characteristic.

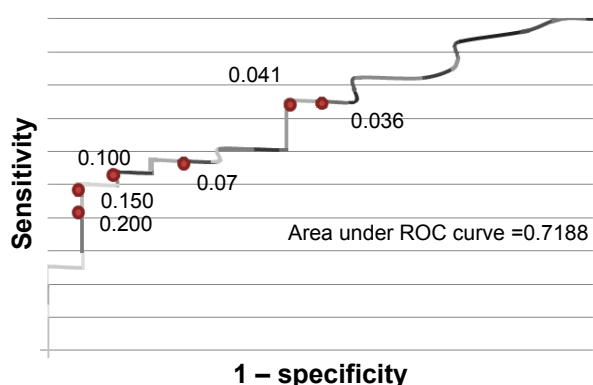


Figure 3 Receiver operating characteristic (ROC) curve of high-sensitivity troponin T levels and coronary artery disease in chronic kidney disease stages 4 and 5 (n=44).

regression analysis, both TIMI score and CKD stage were not an independent factor for having CAD.

Conclusion

The HS Trop T level of 0.041 ng/mL provided diagnostic properties for established coronary artery occlusion in chronic kidney disease patients.

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Disclosure

The authors report no conflicts of interest in this work.

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