

## Research Article

# Relationship between lncRNA-Ang362 and prognosis of patients with coronary heart disease after percutaneous coronary intervention

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The severity and complexity evaluation of coronary artery disease in patients with coronary heart disease (CHD) require objective and accurate prognosis indexes. We assessed the relationship between lncRNA-Ang362 and prognosis of CHD patients after percutaneous coronary intervention (PCI). Clinical follow-up data of CHD patients were prospectively collected. lncRNA-Ang362 levels were detected by real-time quantitative polymerase chain reaction. Survival rate was calculated by the Kaplan–Meier method, and risk ratios and 95% confidence intervals were computed using univariate and multivariate COX proportional hazard models. Finally, 434 patients were included in the follow-up cohort. The median follow-up time was 24.8 months (6.7–40). The incidence of adverse cardiovascular events was 13.6%. The high expression group significantly tended to be smoker and higher body mass index, low-density lipoprotein cholesterol, high-sensitivity C-reactive protein, creatinine, and uric acid levels compared with the low expression group. According to the SYNTAX grade, the high-risk and medium-risk groups had significantly higher lncRNA expression levels than the low-risk group. The univariate COX regression analysis indicated that high lncRNA-Ang362 expression significantly increased the risk of adverse cardiovascular events in CHD patients after PCI (hazard risk (HR) = 3.19, 95% confidence interval (CI): 1.29–7.92). Multivariate analysis found high lncRNA-Ang362 expression was independently related to worse prognosis in CHD patients after PCI (HR = 2.83, 95%CI: 1.34–6.02). Plasma lncRNA-Ang362 may be a prognosis factor in CHD patients after PCI. The patients with higher lncRNA-Ang362 expression usually have poor prognosis.

## Introduction

Coronary atherosclerotic heart disease, often referred to as coronary heart disease (CHD), is a heart disease caused by coronary artery stenosis or occlusion, resulting in myocardial ischemia, hypoxia or necrosis [1]. CHD is a middle-aged and elderly disease, since it commonly attacks adults over 40 years old. The incidence of CHD is gradually equal to that in men [2]. However, CHD is becoming more prevalent among younger people in recent years. The morbidity and mortality of CHD are in the first place of chronic non-communicable diseases, which seriously threaten human health and place a huge economy burden for patients and the society [3]. CHD is caused by progressive coronary atherosclerosis and influenced by many factors, including age, gender, obesity, smoking, hyperglycemia, hyperlipidemia, hypertension, hyper-homocysteine, hyper-uric acid, procalcitonin, platelet to lymphocyte, and genetic factors [4–6]. Revascularization is the most effective treatment for CHD. Although it cannot completely cure CHD, it can greatly improve the clinical symptoms of CHD patients and raise their life quality and survival rate [7]. At present, coronary artery revascularization mainly includes coronary artery bypass grafting (CABG)

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and percutaneous coronary intervention (PCI) [8]. With the advent of PCI, its rapid development and the continuous emergence of new anticoagulant and antiplatelet drugs has continuously broken through the restricted area of PCI treatment [9]. Nevertheless, the severity and complexity evaluation of coronary artery disease (CAD) in CHD patients require objective and accurate indexes.

Long non-coding RNA (lncRNA), a new type of non-coding RNA, is more than 200 nucleotides in length and does not encode proteins [10]. The lncRNA expression in the heart or circulation of patients with myocardial infarction may be significantly abnormal [11,12]. As reported, lncRNA-LIPCAR can predict heart failure after myocardial infarction, suggesting that lncRNA is expected to be a new molecular marker of heart disease [13]. lncRNA-Ang362 can up-regulate angiotensin II and is located between miR-222 and miR-221, which both can interact with angiotensin II and regulate the proliferation of vascular smooth muscle cells (VSMCs) [14]. The similar regulating mechanism indicates that lncRNA-Ang362 may impact the development of atherosclerosis through regulating VSMC proliferation. The present study hypothesized that lncRNA-Ang362 may be released into circulation during the procession of CHD. We explored the changes of plasma lncRNA-Ang362 expression during the development of CHD and the feasibility of using lncRNA-Ang362 as a potential prognosis biomarker for CHD after PCI.

## Materials and methods

### Study population

We enrolled CHD patients who received coronary arteriography in the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine between June 2011 and July 2014. CHD diagnosed by referring to the American College of Cardiology Coronary Scoring [15]. All patients were confirmed by two experienced clinicians. Criteria for inclusion were: stable angina pectoris, unstable angina pectoris or acute myocardial infarction with ischemic evidences (including electrocardiograph, treadmill test, coronary computed tomography angiography or radionuclide myocardial perfusion imaging), interfered stenotic plaque, vessel diameter  $\geq 1.5$  mm and stenosis  $\geq 70\%$  by angiography. Criteria for exclusion were: history of PCI, coronary artery bypass grafting (CABG) and valve replacement valvular dyslipidemia, severe congenital dyslipidemia, dilated cardiomyopathy, severe pulmonary hypertension and ventricular septal perforation, severe liver, kidney and lung diseases, definite bacterial and fungal infections, severe anemia, severe malnutrition and terminal malignant tumor, unmedicated rheumatic diseases, hyperthyroidism, and hypothyroidism. The present study was approved by the ethics committee of The Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine. The research has been carried out in accordance with the World Medical Association Declaration of Helsinki, and that all subjects provided informed consent.

### Clinical data collection and relevant definition

Clinical data were collected by questionnaire. The data source was from medical records. From each subject, the following data were collected: age (year), gender (male vs. female), history of diabetes, hypertension (systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg) [16], smoking (at least five cigarettes a day for more than one year), drinking (2–4 times a month) [17], body mass index (BMI = body weight/height<sup>2</sup> kg/m<sup>2</sup>; normal: 18.5–24; overweight: 24–28; obesity:  $\geq 28$ ) [18]. All patients were graded on SYNTAX ([www.syntaxscore.com](http://www.syntaxscore.com)), and the CAD patients were again divided into three groups: a low-risk group (SYNTAX score  $< 23$ ), a medium-risk group (SYNTAX score 23–32) and a high-risk group (SYNTAX score  $> 32$ ) [19]. The biochemical parameters were detected by a biochemical analyzer (Hitachi, Japan), including blood glucose, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), high-sensitivity C-reactive protein (hs-CRP), creatinine, and uric acid. The type of CHD, lesion count, and left ventricular ejection fraction (LVEF) were collected by medical records.

### Plasma lncRNA level

Fasting blood samples were collected before coronary angiography from each subject. In the morning, ethylenediaminetetraacetic acid dipotassium salt was used for anticoagulation. The samples were centrifuged at 3000 r/min and 4°C for 15 min and were immediately separated to collect plasma. lncRNA-Ang362 levels were detected by real-time quantitative polymerase chain reaction (qRT-PCR) as follows: total RNA from the plasma to be tested was extracted using a TRIzol reagent, and isopropanol was replaced by 75% ethanol for RNA precipitation. RNA quality was measured using a NanoDrop 1000 spectrophotometer. A total of 1  $\mu$ g RNA was reversed into cDNA using a DBI Bestar qPCR RT kit (DBI Bioscience, Ludwigshafen, Germany). The qRT-PCR conditions performed on a 7500 Fast real-time PCR instrument were: incubation at 95°C for 2 min, and then annealing at 95°C for 15 s and 60 s for 40 cycles. lncRNA-Ang362 PCR primers were designed by Raybo Biotechnology Co., Ltd. The

F and R sequences were as follows: 5' -TGAGGGCAAGATGACAAAGA-3', 5'-GCCCTTGCCTTGTATGGTAT-3' (lnc-Ang362); 5'-CTCGCTTCGGCAGCACAT ATACT-3', 5'-ACGCTTCACGAATTTGCGTGTC-3' (U6 as internal reference). MicroRNAs were quantitatively analyzed by the  $2^{-\Delta\Delta Ct}$  method. The process was repeated three times and the average value was used.

## Follow-up

Regular telephone follow-up or outpatient follow-up after discharge was conducted at least once a month to record major adverse cardiovascular events of the patients after discharge, including death, nonfatal myocardial infarction, and revascularization (from the post-operation to occurrence of events). Myocardial infarction was defined as chest pain persisting for more than 20 min or abnormal changes of electrocardiogram accompanied by increased troponin anomaly. Revascularization was defined as retreatment of previous diseased vessels by surgery or interventional surgery or the treatment of new vascular stenosis.

## Statistical analysis

Statistical analysis was performed on SPSS 20.0 and Graphpad 8.0, and normality test was carried out for quantitative data first. The study population was divided into a high expression group and a low expression group according to the median lncRN-Ang362 level. Data with normal distribution were expressed as mean  $\pm$  standard deviation, and compared between groups by two independent sample *t*-test. Data of skewness distribution were represented by median, and compared between groups through nonparametric rank sum test. Categorical data were expressed by counts and percent and compared between groups via the Chi-square test. Survival rate was calculated using the Kaplan–Meier method, and risk ratio (HR) and 95% confidence intervals (CIs) were computed through univariate and multivariate COX proportional hazard models. The adjusted factors for multivariate analysis included age, gender, smoking, drinking, hypertension, diabetes mellitus, BMI, TC, TG, LDL-C, HDL-C, hs-CRP, creatinine, uric acid, vessel lesions, and LVEF.  $P < 0.05$  was considered as statistically significant.

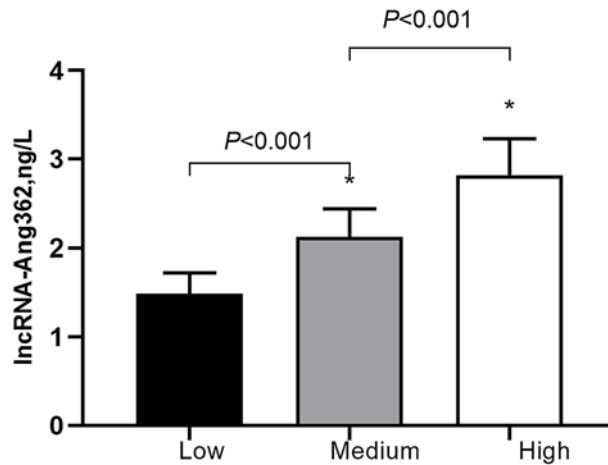
## Results

### General characteristics

Initially, we obtained data from 612 CHD patients who received PCI. According to the inclusion and exclusion criteria, we excluded 178 patients owing to the history of CABG ( $n=22$ ), history of PCI ( $n=56$ ), valve replacement ( $n=13$ ), severe congenital dyslipidemia ( $n=12$ ), dilated cardiomyopathy ( $n=9$ ), tumor ( $n=12$ ), severe liver and kidney dysfunction ( $n=23$ ), and incomplete follow-up data ( $n=31$ ). Finally, 434 patients including 218 males and 216 females were included in the follow-up cohort. Their mean age was  $66.0 \pm 5.9$  years old. The ratios of hypertension and diabetes were 29.0% ( $n=126$ ) and 26.5%, respectively. The ratios of history of smoking and drinking were 36.6% ( $n=159$ ) and 30.0% ( $n=130$ ), respectively. The ratios of acute myocardial infarction, unstable angina pectoris and ischemic cardiomyopathy were 35.7%, 39.9%, and 24.4%, respectively. About 82.3% of patients had more than one lesion vessel. The median follow-up time was 24.8 months (6.7–40.0). After more than 3-year follow-up, 59 (13.6%) patients had adverse cardiovascular events, including 6 deaths, 21 patients with revascularization and 22 patients with myocardial infarctions.

### lncRNA-Ang362 and clinical parameters

The study population was divided by the median lncRN-Ang362 level into a high expression group ( $n=217$ ) and a low expression group ( $n=217$ ). The high expression group versus the low expression group tended to be smokers (50.8% vs. 45.8%,  $P=0.024$ ) and had higher BMI ( $27.2 \pm 3.2$  vs  $24.2 \pm 3.3$ ,  $P < 0.001$ ), LDL-C ( $3.1 \pm 0.8$  vs  $2.6 \pm 0.7$ ,  $P < 0.001$ ), hs-CRP, creatinine ( $7.8 \pm 1.7$  vs.  $5.2 \pm 0.6$ ,  $P < 0.001$ ), and uric acid levels ( $371.4 \pm 79.1$  vs.  $327.4 \pm 68.2$ ,  $P < 0.001$ ), but significantly smaller LVEF ( $53.1 \pm 8.9$  vs.  $58.7 \pm 7.2$ ,  $P < 0.001$ ). We compared the lncRNA-Ang362 levels among different SYNTAX grades and found the high-risk and medium-risk groups had significantly higher lncRNA expression levels than the low-risk group ( $P < 0.05$ ; Figure 1). No significant differences were observed in age ( $P=0.098$ ), male ratio ( $P=0.701$ ), hypertension ratio ( $P=0.057$ ), diabetes ratio ( $P=0.328$ ), drinking ratio ( $P=0.209$ ), or several biochemical parameters, including blood glucose level ( $P=0.565$ ), TC ( $P=0.547$ ), TG ( $P=0.388$ ), and HDL-C ( $P=0.898$ ). The ratios of acute myocardial infarction, unstable angina pectoris and ischemic cardiomyopathy were 33.2%, 35.5%, and 21.7%, respectively, in the low expression group and 38.32%, 44.2%, and 27.2%, respectively, in the high expression group, without significant differences between groups ( $P=0.270$ , 0.063, and 0.180, respectively). We also did not observe significant difference in the lesion count of vessel ( $P=0.102$ ). The detailed information is presented in Table 1.



**Figure 1. Histogram of IncRNA-Ang362 expression**

Relationship between IncRNA-Ang362 expression and SYNTAX grade (high vs. low:  $P < 0.05$ ; Medium vs. low:  $P < 0.05$ ; High vs. Medium:  $P < 0.05$ ). \* $P < 0.05$ .

**Table 1 Baseline demographics of study population by IncRNA-Ang362**

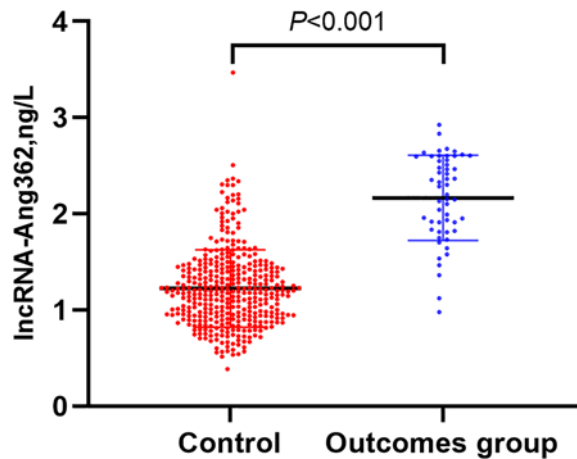
Factors	Low expression (n=217)	High expression (n=217)	$\chi^2/t$	P
Age (year)	65.7 ± 5.8	66.3 ± 6.1	1.043	0.298
Male (n, %)	107 (49.3%)	111 (51.2%)	0.147	0.701
Hypertension (n, %)	54 (24.9%)	72 (33.2%)	3.623	0.057
Diabetes (n, %)	53 (24.4%)	62 (28.6%)	0.958	0.328
Smoking (n, %)	96 (45.8%)	63 (50.8%)	5.104	0.024
Drinking (n, %)	59 (27.2%)	71 (32.7%)	1.581	0.209
BMI, kg/m <sup>2</sup>	24.2 ± 3.3	27.2 ± 3.2	9.614	0.000
Blood glucose, mmol/l	6.3 ± 1.6	6.4 ± 2.0	0.575	0.565
TC, mmol/l	4.5 ± 2.0	4.6 ± 1.4	0.603	0.547
TG, mmol/l	1.6 ± 1.3	1.7 ± 1.1	0.865	0.388
LDL-C, mmol/l	2.6 ± 0.7	3.1 ± 0.8	6.929	0.000
HDL-C, mmol/l	1.1 ± 0.2	1.0 ± 0.2	0.128	0.898
Hs-CRP, mg/l	5.2 ± 0.6	7.8 ± 1.7	21.245	0.000
Creatinine, mmol/l	64 (52–76)	75 (62–86)	14.78	0.000
Uric acid, mmol/l	327.4 ± 68.2	371.4 ± 79.1	6.206	0.000
AMI (n, %)	72 (33.2%)	83 (38.2%)	1.214	0.270
UAP (n, %)	77 (35.5%)	96 (44.2%)	3.470	0.063
Ischemic cardiomyopathy	47 (21.7%)	59 (27.2%)	1.797	0.180
Lesion count			2.668	0.102
Single vessel (n, %)	32 (14.7%)	45 (20.7%)	6.201	
Multiple vessel (n, %)	185 (85.3%)	172 (79.3%)	1.657	
LVEF (%)	58.7 ± 7.2	53.1 ± 8.9	7.206	0.000

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; EATV, epicardial adipose tissue volume; HDL, high density lipoprotein; Hs-CRP, high-sensitivity C-reactive protein; LDL, low density lipoprotein; LVEF, left ventricular ejection fraction; TC, total cholesterol; TG, triglyceride; UAP, unstable angina pectoris.

$\chi^2$ : Chi-square test; t: two independent t test.

## IncRNA-Ang362 and prognosis of CHD after PCI

These patients with follow-up outcomes (major adverse cardiovascular events) group had higher IncRNA expression level than that without cardiovascular events (Figure 2). The univariate COX regression analysis (Table 2) indicated that high IncRNA-Ang362 expression increased the risk of adverse cardiovascular events in CHD patients after PCI (HR = 3.19, 95%CI: 1.29–7.92,  $P < 0.001$ ). Poor prognosis in CHD patients after PCI was positively associated with smoking (HR = 2.65, 95%CI: 1.61–3.67,  $P < 0.001$ ), overweight/obesity (1.66, 1.25–3.29,  $P < 0.001$ ), high LDL-C (1.85,



**Figure 2.** Comparison of lncRNA-Ang362 expression between outcomes and control group

**Table 2** Univariate Cox regression analysis to assess independent correlated of adverse events following PCI for CHD during follow-up

Factors	B	SE	Wald $\chi^2$	P	HR (95%CI)
Age $\geq$ 60	0.342	0.018	1.854	0.253	1.41 (0.87–3.15)
Male	0.118	0.385	0.871	0.432	1.13 (0.96–2.69)
Hypertension	0.426	0.396	0.862	0.501	1.53 (0.90–1.49)
Smoking	0.501	0.462	12.983	0.000	2.65 (1.61–3.67)
Drinking	0.384	0.518	0.895	0.469	1.46 (0.49–2.26)
BMI $\geq$ 28 kg/m <sup>2</sup>	0.509	0.148	15.114	0.000	1.66 (1.25–3.29)
Blood glucose $\geq$ 6.1 mmol/l	0.051	0.021	1.612	0.113	1.05 (0.17–1.69)
TC $\geq$ 5.18 mmol/l	0.563	0.793	0.533	0.665	1.52 (0.47–2.89)
TG $\geq$ 1.7 mmol/l	-0.287	0.858	0.212	0.865	0.75 (0.32–2.52)
LDL-C $\geq$ 3.37 mmol/l	0.616	0.476	20.658	0.000	1.85 (1.31–2.76)
HDL-C < 1.04 mmol/l	-0.215	0.434	0.563	0.521	0.81 (0.41–2.02)
Hs-CRP, mg/dl	1.324	0.141	14.875	0.000	3.75 (1.26–4.13)
Creatinine, $\mu$ mol/l	0.224	0.112	21.512	0.000	1.86 (1.24–2.75)
Uric acid, $\mu$ mol/l	0.026	0.101	9.623	0.010	1.22 (1.18–2.12)
Multiple vessel (n, %)	0.713	0.301	10.210	0.005	2.04 (1.13–6.21)
LVEF (%)	0.102	0.081	1.268	0.193	1.11 (0.78–2.22)
lncRNA-Ang362 (high vs. low)	1.160	0.464	16.25	0.000	3.19 (1.29–7.92)

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; EATV, epicardial adipose tissue volume; HDL, high density lipoprotein; Hs-CRP, high-sensitivity C-reactive protein; LDL, low density lipoprotein; LVEF, left ventricular ejection fraction; TC, total cholesterol; TG, triglyceride; UAP, unstable angina pectoris.

1.31–2.76,  $P < 0.001$ ), hs-CRP elevation (3.75, 1.26–4.13,  $P < 0.001$ ), elevated creatinine (1.86, 1.24–2.75,  $P < 0.001$ ), uric acid level (1.22, 1.18–2.12,  $P = 0.010$ ), and multiple vessel lesion (2.04, 1.13–6.21,  $P = 0.005$ ). The Kaplan–Meier analysis indicated the high expression group of lncRNA-Ang362 had poorer overall survival rate compared with the low expression group ( $P = 0.011$ , Figure 3).

The multivariate analysis found that high lncRNA-Ang362 expression was independently related to worse prognosis in CHD patients after PCI (HR = 2.83, 95%CI: 1.34–6.02,  $P = 0.007$ ) (Table 3). Poor prognosis in CHD patients after PCI was also positively related to high BMI, LDL-C, hs-CRP, and creatinine.



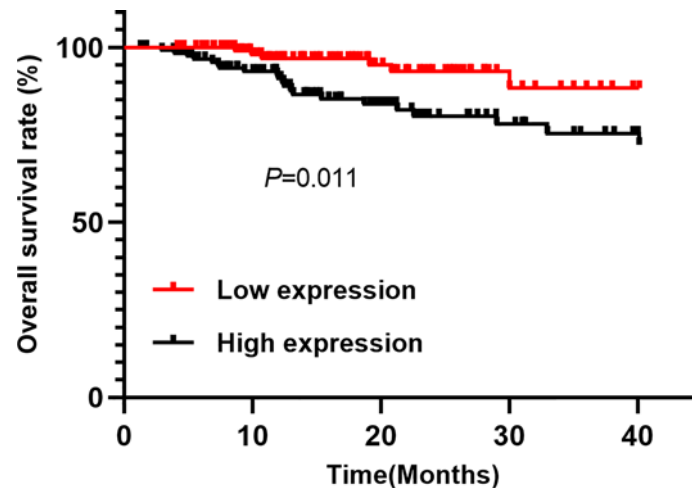


Figure 3. Kaplan–Meier survival curve of lncRNA-Ang362 high expression and low expression group

Table 3 Multivariate COX regression analysis to assess independent correlated of adverse events following PCI for CHD during follow-up

Factors	B	SE	Wald $\chi^2$	P	HR (95%CI)
Smoking	0.221	0.331	11.283	0.021	1.24 (1.17–2.31)
BMI $\geq$ 28 kg/m <sup>2</sup>	0.340	0.461	10.814	0.026	1.40 (1.19–2.74)
LDL-C $\geq$ 3.37 mmol/l	0.523	0.236	12.369	0.011	1.69 (1.22–3.45)
Hc-CRP, mg/dl	1.197	0.393	20.124	0.000	3.31 (1.24–3.89)
Creatinine, $\mu$ mol/l	0.528	0.213	11.478	0.010	1.71 (1.17–2.65)
lncRNA-Ang362 (high vs low)	1.043	0.384	13.025	0.007	2.83 (1.34–6.02)

Adjusting for potential confounding factors, including age, gender, smoking, drinking, hypertension, diabetes mellitus, BMI, TC, TG, LDL-C, HDL-C, hs-CRP, creatinine, uric acid, vessel lesions, and LVEF.

## Discussion

lncRNA-Ang362 was found to be highly expressed in CHD patients with adverse outcomes. The high expression group of lncRNA-Ang362 had better overall survival rate compared with the low expression group. The multivariate analysis indicated high lncRNA-Ang362 expression was independently associated with poor prognosis in CHD patients after PCI. Our study provided a potential prognosis biomarker of CHD after PCI.

Cardiovascular diseases, especially CHD, are still the major cause of death worldwide, causing a major socio-economic burden. Although therapeutic methods such as medications, PCI and CABG have improved the prognosis of CHD, the mortality rate remains high [20]. Therefore, it is necessary to detect CHD in its earlier stage, especially before the development of left ventricular dysfunction. Early identification of CHD patients at high risk of adverse cardiovascular events using circulating or imaging biomarkers may help in this regard [21]. However, the lack of available CAD biomarkers has limited risk prediction [22].

Genome-wide analysis has identified that almost all of the human genome is transcribed, with a large amount of lncRNAs [23,24]. lncRNAs range over 200 nucleotides in length [25], and, through epigenetic, transcriptional, or post-transcriptional regulatory mechanisms, are involved in specific physiological and pathological processes of a wide range of human diseases and disorders [26], such as cancers [27] and neurological disorders [28]. As reported recently, some lncRNAs are involved in the development of various cardiovascular diseases [29], including heart failure [30,31], cardiac hypertrophy [32], and myocardial infarction [33]. The plasma levels of some lncRNAs, such as ANRIL, lincRNA-p21 and myocardial infarct-associated transcript-1, markedly increase in atherosclerosis and may be important in its pathogenesis. lncRNAs are stable in plasma and other body fluids and therefore, can serve as biomarkers for some diseases [34]. For example, a prostate-specific lncRNA PCA3 in urine has been identified as the most specific biomarker for detection of prostate cancer with higher specificity than the widely-used prostate-specific antigen test [35]. Other lncRNA biomarkers in plasma include the lncRNA LIPCAR for heart failure post-myocardial

infarction and CHD [36–38]. Moreover, miRNA-221 and miRNA-222 are involved in VSMC proliferation and are elevated in response to Ang II in endothelial cells to promote inflammation and migration. LncRNA-Ang362 is an Ang II-upregulated lncRNA proximal to these two miRNAs, which means that lncRNA and these two miRNAs have a synergistic effect on VSMC proliferation [39]. CHD is mainly caused by atherosclerosis, in which phenotypic transformation and aggregation migration of VSMCs play an important role [40]. These findings suggest that lncRNA-Ang362 is involved in the development of CHD. Our results indicate the lncRNA-Ang362 expression is the severity of CHD and is positively associated with SYNTAX grade, suggesting lncRNA-Ang362 can be a potential prognosis biomarker. Furthermore, the high expression of lncRNA-Ang362 corresponds to a higher incidence of adverse cardiovascular events. This result can be also explained by the synergistic effect of lncRNA with miRNA-221 and miRNA-222. The minichromosomal maintenance protein (MCM) 7 is a key molecule of the lncRNA-Ang362 regulation group that promotes cell proliferation and regulates cell cycle [41]. Excessive activation of MCM7 can lead to excessive proliferation and activity of VSMCs, which often indicates accelerated atherosclerotic process and unstable atherosclerotic plaques in patients [42]. This finding may partly explain why lncRNA-Ang362 can affect the prognosis of CHD patients.

We found that high lncRNA-Ang362 expression was associated with elevated hc-CRP, a marker of inflammation status, which indicates lncRNA-Ang362 is involved in the process of inflammation response. As reported, lncRNA-Ang362 regulates the biological function of angiotensin II that is necessary in regulating VSMC proliferation via promoting inflammation response [43]. The levels of creatinine and uric acid, two kidney function markers, were also positively associated with lncRNA-Ang362. The creatinine and uric acid elevation mean a decreased kidney function, indicating lncRNA-Ang362 may be related to kidney function. Nevertheless, further research is required.

The present study has several limitations. First, this is a single-center study with limited sample size, and further subgroup analysis cannot be obtained. Second, we did not collect data of medicine treatments from some hypertensive or diabetic patients who may be taking medicine, but these treatments may affect the final estimation. Third, we did not explore the molecular mechanisms of the relationship between lnc-Ang362 and CHD severity, which should be tested by research *in vivo* and *in vitro*. Finally, the present result was based on short-term follow-up and thus must be extended by long-term follow-up data.

In conclusion, lncRNA-Ang362 is an independent prognosis biomarker of CHD patients after PCI. Our results provide evidences for the prognosis outcome improvement because lncRNA-Ang362 may be a potential treatment target for CHD after PCI. Studies with larger sample size and longer time follow-up are required to confirm our finding. Future research should also focus on the molecular mechanism.

## Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

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## Author Contribution

F.L.M. and W.H. participated in the design of the study and data collection. G.H.C. performed the statistical analysis. L.Y.W. and W.H. conceived of the study and participated in its design as well as coordination and helped to write and revise the manuscript. All authors read and approved the final manuscript.

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## Abbreviations

aRT-PCR, real-time quantitative polymerase chain reaction; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CHD, coronary heart disease; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; HR, hazard risk; hs-CRP, high sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TC, total cholesterol; TG, triglyceride; VSMC, vascular smooth muscle cell.

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