Role of cardiac marker troponin I in chronic periodontitis with coronary artery disease

Sanggap Indra Sitompul1,2, Aryati3, Budi Susetyo Pikir4*, Monika Estherlita Sinta5

INTRODUCTION

Periodontitis is a multifactorial persistent inflammatory disease. It relates to microbial pathogens, susceptible hosts, and environmental or systemic risk factors. Additionally, periodontitis is associated with plaque accumulation, which is characterized by progressive destruction of the supporting tissues of teeth, including periodontal ligament and alveolar bone.1 The prevalence of periodontitis is around 20-50% in developing and developed countries.2 This disease can be diagnosed by clinical examination and radiography.3

Coronary atherosclerosis is an inflammatory and complex disease, which is characterized by coronary artery remodeling.4 Atherosclerosis is associated with dysfunction of endothel and impaired Nitric Oxide bioavailability.5 Angina in myocardial ischemia is caused by the reduced oxygenated blood supply to the myocardium. Moreover, it is related to a combination of focal or diffuse (macrovascular) epicardial disease, microvascular dysfunction or both.6 Coronary angiography is a gold standard for examining coronary atherosclerosis.7 It can be evaluated by the anatomy and degree of obstruction of the lumen in the coronary arteries.8

The association between periodontitis and systemic diseases has been reported in cases, including atherosclerosis.9,10 Although there is no causal relationship between periodontitis and cardiovascular disease, periodontitis can be a nontraditional, modifiable risk factor for cardiovascular disease.11 Patients with periodontitis disease have a high risk of obesity, endothelial dysfunction, hypertension, dyslipidemia, platelet hyperreactivity, and prothrombotic state, including bacterial transmission from the oral cavity.12,13 These conditions lead to the development, maturation, and instability of atheroma in the arteries.14

The complex of Troponin plays an important role in regulation of myocyte contractility. Troponin I inhibits actin-myosin interaction, resulting in a higher level of troponin T. The troponin complex regulates the myocyte contraction.
Troponin I inhibits actin-myosin interaction, resulting in a higher level of Troponin T. An increase in Troponin in the blood occurs due to ischemia of the cardiac vessels.18

Several studies reported an essential role of Troponin in cardiovascular diseases, associated with an increased short-term risk of death, acute MI, or hospitalization, complements noninvasive clinical assessment of suspected CAD, and the degree of severity of CAD.16-20 Additionally, Troponin is related to diagnosing and stratification of patients with suspected acute coronary syndrome (ACS).21 It is a gold standard for the diagnosis of acute myocardial infarction (AMI), acute heart failure, and cardiotoxicity detection.15,22,23

A study reported Troponin I and T to have good diagnostic accuracy in CAD, however, Troponin I is a more reliable prognostic marker than creatine kinase, especially in patients with ischemic chest pain.24,25 Troponin I examination and assessment of chest pain can be used to evaluate patients with CAD, especially those with suspected angina pectoris without a history of previous cardiovascular disease. Additionally, it relates to the results of coronary angiography.26

Several previous studies have shown a relationship between periodontitis and Troponin on the extent of AMI and the development of cardiac lesions.27,28 Furthermore, this relationship is more significant in CAD patients than healthy individuals.29 This study analyzes the relationship between Chronic Periodontitis (CP) and Troponin I levels in CAD patients, especially non-AMI.

MATERIAL AND METHODS

Study design
This study was analytical observational and cross-sectional design. A total of 90 CAD patients with CP who underwent coronary angiography participated in the study. This study was conducted from December 2021 until November 2022 at dr. Doris Sylvanus Hospital, Palangka Raya, Central Kalimantan, Indonesia. Data was collected by consecutive sampling.

CP patients with non-AMI CAD and at least had 20 teeth were the inclusion criteria. Use of antibiotics and anti-inflammatory in the last three months, treatment of periodontal disease in the previous six months, pregnancy, fever, pneumonia, kidney failure, and severe liver disease were the exclusion criteria.

Patient characteristics
Age, gender, T2DM, smoking, history of percutaneous coronary intervention (PCI), stroke, hypertension, dyslipidemia, body mass index (BMI), hemoglobin, platelets, SGOT, SGPT, urea, serum creatinine, mean PD were measured in this study. Meanwhile, age, smoking, T2DM, dyslipidemia, hypertension, BMI and gender were confounding factors for Troponin I according to previous studies.27

Coronary angiography and echocardiography
The angiographic appearance is considered to be significant if the stenosis is ≥70% of the main coronary artery on one projection or 50% on two projections, and 50% of left main branch coronary artery.6 The Philips Allura FC angiography and quantitative coronary angiography software were used for stenosis calculations. Echocardiographic examination was conducted using the GE Vivid Q Ultrasound Machine, Horten, Norway or Philips Sparq Ultrasound system, Bothell. Left Ventricle Ejection Fraction (LVEF) measurement by Teich method. A cardiologist performed these examinations.

Periodontal examination
CP examination was performed based on dental examination and panoramic x-ray with a mean periodontal probing depth of 4 mm on 6 index teeth (16, 21, 24, 36, 41, 44). Mild CP group for mean periodontal probing depth <4 mm and moderate-severe CP group for mean periodontal probing depth ≥ 4 mm. Additionally, CP examination was also evaluated by the dental probe instrument Hu- Friedy PCPUNC 15 and performed by a periodontist.

Blood evaluation
Blood was collected to determine hemoglobin, platelets, urea, creatinine, SGOT, SGPT and Troponin at the dr. Doris Sylvanus, Palangkaraya, Indonesia.

Troponin examination
Troponin level was measured by sandwich immunodetection using ichroma™ Tn I Plus, which is a quantitative Fluorescence Immunoassay (FIA) of cardiac troponin-I (Tn-I) with values ranging in this study ≤0.01 - <0.30 ng/mL. Boditech Med Incorporated, Dongnae myeon, Chuncheon-si, Gang Won do, Republic of Korea.

Statistical analysis
Statistical analysis was conducted by using SPSS software. The descriptive statistical tests were presented as the median, mean, and SD for quantitative and frequency variables, while percentages for qualitative variables. The normality test was conducted using the T-test if the data had normal distribution or the Mann-Whitney test if the data had no normal distribution before a comparative test between mild CP and moderate-severe CP. Then bivariate analysis was performed on the Troponin I category (with a threshold ROC result) using the Chi-square test. Moreover, multivariate analysis was conducted to determine the independent variables of the major factor of Troponin I, followed by the logistic regression test. An important difference was noted if p < 0.05 with 95% of the confidence interval.

RESULTS
As shown in Table 1, most of the respondents were male (75.6%), followed by 24.4% of females. Seventy-five respondents (83.3%) were less than 60 years old, and 16.7% were over 60. For comorbidities, 77.8% had hypertension, 27.8% had T2DM, 7.8% had a stroke, and 52.2% had dyslipidemia. In addition, 17.8% had a history of PCI, and 51.1% smoked. 43.3% of respondents with a BMI ≥ 25 kg/m² were classified as obese, while 56.7% had BMI <25 kg/m² and were classified as non-obese. Additionally, 47.8% had mild CP, and 52.2% had classified moderate-severe CP.

As shown in Table 2, no significant differences were found in gender, age, T2DM, smoking, history of PCI, stroke, dyslipidemia, obesity, and the group with mild CP and moderate-severe CP.

Table 3 showed no significant differences were found in BMI,
Hemoglobin, urea, creatinine, SGOT, SGPT, LVEF of patients with mild CP and moderate-severe CP. Platelets between mild CP (mean=279.6 $10^3$/uL) were higher than moderate-severe CP (mean=251.91 $10^3$/uL) with a value of $p = 0.030$ ($p < 0.05$). Comparisons of the mean PD between mild CP and moderate-severe were 3.56 mm and 4.46 mm, respectively, with a $p$-value of 0.000 ($p < 0.05$). The mean PD in patients with mild CP was lower than moderate-severe CP. Troponin I in patients with moderate to severe CP was significantly higher than in mild CP. The comparisons of Troponin I between mild CP and moderate-severe CP were 0.02 ng/mL and 0.03 ng/mL, respectively, with a $p$-value of 0.026 ($p < 0.05$).

Based on the Troponin I ROC curve for predicting mild CP and moderate-severe CP, it showed an AUC diagnostic value of 0.589 (Figure 1). Furthermore, the curve was above the 50% line, with a value of $p=0.148$ (95% CI: 0.471-0.706). The cut-off point for Troponin I was 0.015 ng/mL. Therefore, it was classified into two categories: Troponin I <0.015 ng/mL and Troponin I category > 0.015 ng/mL.

We found that in 75 patients with Troponin I <0.015 ng/mL, 42.7% had no dyslipidemia, and 57.3% had dyslipidemia with a $p=0.030$ ($p < 0.05$). Patients with Troponin I < 0.015 ng/mL tend to have more dyslipidemia than patients with troponin I > 0.015 ng/mL. The effect of CP on Troponin I showed 15 patients with Troponin I > 0.015 ng/mL, 80% had moderate CP, and 20% had mild CP. Of the 75 patients with Troponin I <0.015 ng/mL, there was 46.7% with moderate to severe CP and 53.3% with mild CP with a $p$-value of 0.018 ($p < 0.05$). Our results showed a significant difference in the patients with mild CP and moderate-severe CP. Patients with Troponin I < 0.015 ng/mL tend to have mild CP, while patients with Troponin I > 0.015 ng/mL tend to be more moderate-severe CP (Table 4).

According to the logistic regression analysis (Table 5), CP was the most significant effect on Troponin I. Patients with moderate-severe CP tended to have Troponin I > 0.015 ng/mL. In contrast, patients with mild CP tended to have Troponin I <0.015 ng/mL with an OR value of 5.528. Dyslipidemia significantly affected Troponin I, with an OR value of 4.52. We found the possibility of the patient without dyslipidemia with a probability of 4.52 times (95% CI: 1.247 – 16.389) compared to a patient with dyslipidemia if Troponin I > 0.015 ng/mL.

**DISCUSSION**

In the present study, CAD patients were dominated by moderate to severe CP, male, and aged < 60 years. Additionally,
there were no significant differences in gender, age, T2DM, smoking, history of PCI, stroke, dyslipidemia, or BMI in groups with mild CP and moderate-severe CP. Our results are supported by the previous study showing that the incidence of atherosclerosis of the coronary arteries is higher in patients with periodontitis or poor periodontal status than in those without periodontitis. Another study showed that the distribution of periodontitis reached 66.7% at the ages of 45–59 years and was dominated by men (61.5%).

A study conducted in Korea shows periodontitis has an OR of CAD reaching 1.34 (95% CI = 1.22–1.48, p <0.001). Therefore, periodontitis is related to the risk factor of CAD. In the current study, the platelet count in patients with mild CP was significantly higher than in moderate-severe CP. Troponin levels are associated with CAD and can predict the presence of obstructive CAD in patients with suspected stable angina with a 5-fold increase regardless of known cardiovascular risk factors.

We found an effect of CP severity and dyslipidemia on Troponin I. There were significant differences in the mild CP and moderate-severe CP groups. Patients with Troponin I <0.015 ng/mL tended to have mild CP, whereas patients with troponin I > 0.015 ng/mL tended to have severe CP. In addition, patients with Troponin I < 0.015 ng/mL had more dyslipidemia than patients with troponin I > 0.015 ng/mL. Furthermore, based on logistic regression analysis, we observed that periodontitis had a stronger effect on Troponin I than dyslipidemia. CP had a significant effect on Troponin I. If Troponin I levels are > 0.015 ng/mL, then the patient may have a risk of moderate-severe CP 5.528 times compared to mild CP (95% CI: 1.373 – 22.247, p= 0.016).

In the current study, we found Troponin I cut-off point was 0.015 ng/mL to predict mild and moderate-severe CP in CAD patients. Meanwhile, Ramasamy's research showed that a troponin I value > 0.52 ng/L had a sensitivity of 100%, and a value > 11.6 ng/L had a specificity of 100% for CAD. Severity and degree of periodontitis have been reported to associate with the extent of AMI. Another study showed a relationship between CP and Troponin I level. A disturbance of endothelial function in CP patients was also reported based on an assessment of flow-mediated dilation. Troponin I increased significantly in smoking and non-smoker CP patients compared to healthy subjects. Several theories showed the role of Troponin between CP and CAD. Additionally, periodontal infection has direct or indirect effects and triggers Troponin I levels in periodontitis. This condition indicates a potential risk of developing heart lesions in patients with chronic inflammation. The primary mechanism is the spread of oral pathogens through blood vessels.

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**Table 3. Comparison of parameter data (numerical scale) between mild CP and moderate-severe CP**

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Mild CP</th>
<th>Moderate-Severe CP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age (year)</td>
<td>50.67</td>
<td>52.91</td>
<td>7.56</td>
</tr>
<tr>
<td>2. BMI (Kg/m^2)</td>
<td>24.72</td>
<td>25.21</td>
<td>4.16</td>
</tr>
<tr>
<td>3. Hemoglobin (gr%)</td>
<td>13.95</td>
<td>14.02</td>
<td>1.55</td>
</tr>
<tr>
<td>4. Platelets (10^3/µL)</td>
<td>279.60</td>
<td>251.91</td>
<td>56.82</td>
</tr>
<tr>
<td>5. Urea (mg/dL)</td>
<td>34.07</td>
<td>33.38</td>
<td>13.04</td>
</tr>
<tr>
<td>6. Creatinine (mg/dL)</td>
<td>1.053</td>
<td>1.048</td>
<td>0.26</td>
</tr>
<tr>
<td>7. SGOT (U/L)</td>
<td>20.47</td>
<td>24.72</td>
<td>14.93</td>
</tr>
<tr>
<td>8. SGPT (U/L)</td>
<td>28.60</td>
<td>31.17</td>
<td>14.93</td>
</tr>
<tr>
<td>9. LVEF (by Teich) %</td>
<td>58.40</td>
<td>54.12</td>
<td>17.75</td>
</tr>
<tr>
<td>10. Mean PD (mm)</td>
<td>3.56</td>
<td>4.46</td>
<td>0.51</td>
</tr>
<tr>
<td>11. Troponin I (ng/mL)</td>
<td>0.02</td>
<td>0.03</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Significant p<0.05

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**Figure 1.** Result of ROC with area under the curve (AUC) for Troponin I.
Bacteremia, endotoxia, and microbial invasion have been reported to be associated with periodontitis and atherosclerotic disease. Increased subgingival pathobionts and overexpression of virulence factors in periodontitis are markers of increased acute myocardial injury and the severity of underlying plaques in coronary arteries. Simultaneous extraction of periodontal pathobiont DNA from intracoronary thrombus and subgingival plaque in patients with AMI promotes bacterial transfer from the oral cavity. Besides, CP triggers a vascular response and increases the pro-inflammatory cytokines and adhesion molecules. This condition causes endothelial dysfunction. Inflammation by periodontal-pathogenic bacteria in the periodontal pocket causes endothelial dysfunction.

Endothelial dysfunction occurs at the beginning of atherogenesis, leading to impaired coronary artery perfusion and plaque rupture. Endothelial dysfunction and CAD cause ischemia, cell death, breakdown of contractile proteins, increased membrane permeability in cardiomyocytes, and troponin expression in the blood. Endotoxin or lipopolysaccharides (LPS) levels stimulate apoptosis in myocardial tissue through proinflammatory acute phase proteins and also cytokines, causing contractile dysfunction and sarcomer destruction. This condition increases troponin levels in the peripheral blood. Proliferation of vasa vasorum and atherosclerosis can be accelerated by LPS-induced systemic inflammation. Other studies have shown a relationship between periodontitis and increased D Dimer.

In current study, Troponin I examination was performed in CHD patients without AMI. A study reported that elevated troponin T might be related to ischemia due to increased cell membrane permeability and cardiomyocyte necrosis in ACS. Furthermore, CAD also causes low-grade necrosis or ischemic strain, and troponin leakage from the cytosol. The composition of coronary atherosclerotic plaques is related to troponin T levels which cause atherosclerotic and thrombotic microembolization into the microcirculation and lead to an increase in troponin.

### Table 4. Cross table between confounding factors against the Troponin I category

<table>
<thead>
<tr>
<th>Confounding factor</th>
<th>Troponin I &gt;0.015 ng/mL</th>
<th>Troponin I &lt;0.015 ng/mL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>12</td>
<td>80.0%</td>
<td>63</td>
</tr>
<tr>
<td>≥ 60 years</td>
<td>3</td>
<td>20.0%</td>
<td>12</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>73.3%</td>
<td>57</td>
</tr>
<tr>
<td>female</td>
<td>4</td>
<td>26.7%</td>
<td>18</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>46.7%</td>
<td>37</td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>53.3%</td>
<td>38</td>
</tr>
<tr>
<td>T2DM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12</td>
<td>80.0%</td>
<td>53</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>20.0%</td>
<td>22</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>20.0%</td>
<td>17</td>
</tr>
<tr>
<td>Yes</td>
<td>12</td>
<td>80.0%</td>
<td>58</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>73.3%</td>
<td>32</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>26.7%</td>
<td>43</td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI ≥ 25 kg/m²</td>
<td>6</td>
<td>40.0%</td>
<td>33</td>
</tr>
<tr>
<td>BMI &lt; 25 kg/m²</td>
<td>9</td>
<td>60.0%</td>
<td>42</td>
</tr>
<tr>
<td>CP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CP Moderate-severe</td>
<td>12</td>
<td>80.0%</td>
<td>35</td>
</tr>
<tr>
<td>CP Mild</td>
<td>3</td>
<td>20.0%</td>
<td>40</td>
</tr>
</tbody>
</table>

*Significant p<0.05

### Table 5. Result of logistic regression test

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>p</th>
<th>OR</th>
<th>95.0% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Periodontitis</td>
<td>1.710</td>
<td>0.016</td>
<td>5.528</td>
<td>1.373</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.509</td>
<td>0.022</td>
<td>4.520</td>
<td>1.247</td>
</tr>
<tr>
<td>Constant</td>
<td>0.373</td>
<td>0.384</td>
<td>1.452</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Overall Percentage= 85.1%; Nagelkerke R square = 0.208

Our study showed that age, gender, obesity, hypertension, smoking, and T2DM did not affect the troponin level. In contrast, age, gender, hypertension, smoking, T2DM, dyslipidemia, and BMI have been reported not to affect the troponin level. The previous study revealed that STEMI and periodontitis elevate the troponin level. Our study is concerned with the effect of dyslipidemia on the Troponin I level, although the multivariate analysis showed that CP had a stronger effect on Troponin. Further study is needed to investigate the role of dyslipidemia.

The limitation of this study is analytic observational study with cross-sectional study design and small number of samples.
CONCLUSIONS

There was an effect of CP on increasing Troponin I levels in CAD patients. Further study is needed with a larger sample and more complete parameters to establish this study.

ACKNOWLEDGMENTS

We want give our thank to doctors and nurses at Doris Sylvanus Hospital, Palangka Raya, Indonesia who helped us with this study.

DISCLOSURE

The author reports no conflicts of interest in this work.

ETHICAL CLEARANCE

The ethics committee of dr approved this study. Doris Sylvanus Hospital, Palangka Raya, Indonesia (Number: 5641/ UM-TU/RSUD/11-2021). Participants received consent from the corresponding author.

AUTHOR CONTRIBUTION

All authors contributed to manuscript writing and agreed for the final version of manuscript for publication.

REFERENCES

3. Ayşmāl A, Astuti ER, Devijanti R. Changes in manuscript for publication. All authors had contributed to manuscript in this study. and signed a consent form to participate in this study.


