Improving Quality of Life with Percutaneous Coronary Intervention in Chronic Coronary Syndrome Patients with SYNTAX Score of More than 22

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1. Introduction

Coronary artery disease (CAD) is a disease characterized by atherosclerotic plaque formation in the epicardial coronary arteries. 1, 2 It is well known as the leading cause of mortality around the world. 2, 3 Annually, in Indonesia, at least 470,000 mortalities are estimated to be caused by CAD or stroke. 4 The various clinical presentations can be caused by the dynamic nature of CAD. Generally, according to the clinical presentation, CAD can be classified into chronic coronary syndromes (CCS) and acute coronary syndromes (ACS). 1 CCS in a new terminology proposed by the European Society of Cardiology (ESC) replacing stable CAD. The CCS is defined as the progressive atherosclerotic plaque accumulation process accompanied by functional alteration in the coronary artery. It has replaced the old terminology stable CAD. 1 The management of CCS includes lifestyle changes, optimal medical treatment (OMT), and myocardial revascularization. 1, 5

Myocardial revascularization strategies in CAD include percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery. 4 The purpose of myocardial revascularization in CCS includes: (1) myocardial ischemia elimination; (2) eliminate clinical manifestations; and (3) major adverse cardiovascular event (MACE) risk reduction. 1, 5 Revascularization strategy by PCI or CABG can be determined using the Synergy Between PCI With Taxus and CABG (SYNTAX) score. 5

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Keywords:
Percutaneous Coronary Intervention; Optimal Medical Treatment; Chronic Coronary Syndrome; Quality of Life; SYNTAX score.

ABSTRACT

Background: The benefit of PCI to improve quality of life (QoL) in chronic coronary syndrome (CCS) is still unclear.

Objectives: This study aimed to assess the benefit of percutaneous coronary intervention (PCI) in improving QoL among CCS patients receiving OMT.

Methods: We conducted a retrospective cohort study. CCS patients who underwent coronary angiography (CAG) and/or PCI were grouped into OMT plus PCI and OMT groups. The SYNTAX score was used to assess the complexity and severity of coronary artery lesions. The outcome measured was QoL assessed using Seattle Angina Questionnaire (SAQ) and rehospitalization.

Results: A total of 57 patients in the OMT plus PCI group and 49 patients in the OMT group were included. The percentage of patients with good QoL was higher in the OMT plus PCI group than OMT group (64.5% vs. 35.5%; p = 0.007). The OMT plus PCI group revealed a better activities of daily living (85.11 ± 12.46 vs. 71.81 ± 27.89; p = 0.014) and angina stability (84.32 ± 23.63 vs. 71.81 ± 27.89; p = 0.014) than OMT group. Among patients with SYNTAX scores of more than 22, achievement of good QoL was greater in the OMT plus PCI group than the OMT group (80.8% vs. 45.5%; p = 0.025).

Conclusion: PCI improved the QoL in CCS patients treated with OMT. Second, OMT plus PCI improves physical limitation and angina stability. For patients with a SYNTAX score of more than 22, OMT plus PCI was correlated with good QoL achievement.

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1. Introduction

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Basically, the SYNTAX score is the assessment tool to evaluate the severity or complexity of coronary artery lesions. Until now, the superiority of OMT plus PCI versus OMT alone based on the SYNTAX score in quality of life (QoL) of CCS patients is still unclear. Therefore, this study purposed to evaluate the benefit of PCI in improving QoL among CCS patients receiving OMT based on the SYNTAX score.

2. Method

2.1. Study design participants

A retrospective cohort study was completed in dr. Saiful Anwar General Hospital Malang, East Java, Indonesia in 2016. This research was approved by the ethical review board and conformed with the principles of the declaration of Helsinki. Before conducting data collection, patients or their family members had signed the informed consent.

We identified patients who had undergone coronary angiography (CAG) and/or PCI from the registry database in the catheterization laboratory of the dr. Saiful Anwar General Hospital. The inclusion criteria include: (1) CCS patients receiving OMT; (2) good compliance to the medical treatment; (3) underwent CAG and had at least 50% stenosis in one or more coronary arteries; and (4) aged more than 40 years old. Patients were excluded because of these reasons: (1) lost to follow-up; (2) psychiatric disorders; and/or (3) disability to conduct physical activities. Patients were classified into “OMT plus PCI group” and “OMT group.” All important information about demographic data, cardiovascular diseases (CVD) risk factors, comorbid diseases, echocardiographic parameters, and treatment regimen were obtained from the direct interview and medical record.

2.2. SYNTAX Score assessment

SYNTAX Score was assessed by carefully reading the coronary angiogram. The calculation of the SYNTAX score was completed using the online calculator. The variables of SYNTAX score include: (1) the dominant coronary artery; (2) number of coronary lesions; (3) segment involved; (4) total occlusion; (5) trifurcation; (6) bifurcation; (7) aorto-ostial lesion; (8) tortuosity; (9) lesion length; (10) calcification; (11) thrombus; and (12) diffuse disease. A total SYNTAX score of ≤22, 22-32, and ≥32 are categorized as mild, moderate, and severe lesions, respectively. Two physicians conducted the SYNTAX score assessment. The discrepancy in the SYNTAX score assessment between the two investigators was resolved by the suggestion from the third investigator.

2.4. Outcome

The outcomes assessed were QoL and rehospitalization assessed within 6 to 12 months following CAG and/or PCI. Outcome data were obtained from the direct interview or phone call. QoL was assessed using the Seattle Angina Questionnaire (SAQ). Variables measured in SAQ included activities of daily living (ADL), angina stability, angina frequency, treatment satisfaction, and disease perception. The SAQ >70 was classified as good QoL. On the other hand, patients were classified as having poor QoL if they had SAQ ≤70.

2.4. Statistical Analysis

We used the IBM Statistical Package for Social Science (SPSS version 25.0) for the statistical analysis process. Mean and standard deviation (SD) were used to demonstrate the continuous data. Categorical data were showed using the number and percentage. T-test and Mann Whitney test were used to compare continuous data with typically and not normally distributed data, respectively. The Chi-squared test and Fisher’s exact test were used to compare categorical data. Statistically significant was considered if the p-value was less than 0.05.

3. Result

3.1. Baseline characteristics

Generally, both groups share similar baseline characteristics (p ≥0.05). Male predominated our study population, 83.1% and 74.5% for OMT plus PCI group and OMT group, respectively. The mean age was 58.88 ± 7.56 years old for OMT plus PCI group and 61.55 ± 8.55 years old for the OMT group. In OMT plus PCI group, the most common CVD risk factor was hypertension (69%). While in the OMT group, dyslipidemia (64.4%) was the common CVD risk factor. Heart failure was the most common comorbid disease in OMT plus PCI group (36.8%) and the OMT group (57.4%). The baseline mean left ventricular ejection fraction (LVEF) was 48.72 ± 16.92% in OMT plus PCI group and 50.50 ± 15.78% in the OMT group. All patients in both groups received antiplatelet and statin. The mean syntax score was 19.7 ± 10 and 19.91 ± 12.98 for OMT plus PCI group and OMT group, respectively. SYNTAX score severity distribution between both groups was not significantly different (p = 0.155) (Table 1).

3.1. Clinical outcomes

The mean follow-up duration of all patients was 7.8 ± 0.95 months. The rehospitalization rate between OMT plus PCI group and the OMT group was not significantly different (16.9% vs. 17%; p = 1.00). However, the percentage of patients with good QoL was higher in the OMT plus PCI group than OMT only group (64.5% vs. 35.5%; p = 0.007). We also performed subgroup analysis in each SAQ parameter. The OMT plus PCI group revealed a better ADL (85.11 ± 12.46 vs. 12.46 ± 21.87; p = 0.014) and angina stability (84.32 ± 23.63 vs. 36.8%) and the OMT group (57.4%). The baseline mean left ventricular ejection fraction (LVEF) was 48.72 ± 16.92% in OMT plus PCI group and 50.50 ± 15.78% in the OMT group. All patients in both groups received antiplatelet and statin. The mean syntax score was 19.7 ± 10 and 19.91 ± 12.98 for OMT plus PCI group and OMT group, respectively. SYNTAX score severity distribution between both groups was not significantly different (p = 0.155) (Table 1).

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Figure 1. Good quality of life outcome among patients with SYNTAX score of more than 22. OMT = optimal medical treatment; PCI = percutaneous coronary intervention; SYNTAX = Synergy Between PCI With Taxus and CABG.
71.81 ± 27.89; p = 0.014) than OMT group. However, the angina frequency (82.79 ± 20.75 vs. 73.43 ± 23.99; p = 0.033) and treatment satisfaction (82.77 ± 15.27 vs. 80.19 ± 16.24; p = 0.401) in both groups were not significantly different (Table 2).

We also conducted a further subgroup analysis. In the OMT plus PCI group, the SYNTAX score in the patients who suffered from rehospitalization was not significantly different from those who did not suffer from rehospitalization (19.86 ± 9.50 vs. 19.90 ± 12.70; p = 0.967). However, in this group, patients with good QoL revealed a lower SYNTAX score than patients with poor QoL (18.50 ± 9.07 vs. 25.60 ± 12.63; p = 0.040).

In the OMT group, the SYNTAX score between rehospitalized and non-rehospitalized patients was not significantly different (19.79 ± 13.61 vs. 20.50 ± 12.92; p = 0.691). The SYNTAX score in good QoL and poor QoL patients was also not significantly different (17.51 ± 12.07 vs. 23.15 ± 13.76; p = 0.143) (Table 2). Moreover, among patients with SYNTAX score of more than 22s, achievement of good QoL was greater in OMT plus PCI group than the OMT group (80.8% vs. 45.5%; p = 0.025) (Figure 1).

Table 1. Baseline characteristics of patients included in this study

<table>
<thead>
<tr>
<th>Variable</th>
<th>OMT + PCI (n = 59)</th>
<th>OMT (n = 47)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Demographic Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years old</td>
<td>58.88 ± 7.56</td>
<td>61.55 ± 8.55</td>
<td>0.091</td>
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<tr>
<td>Body height, cm</td>
<td>163.63 ± 5.71</td>
<td>161.96 ± 5.47</td>
<td>0.234</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>66.39 ± 9.55</td>
<td>66.21 ± 10.26</td>
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<tr>
<td>Male, %</td>
<td>49 (83.1)</td>
<td>35 (74.5)</td>
<td>0.400</td>
</tr>
<tr>
<td>CVD risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active smoker</td>
<td>13 (22.0)</td>
<td>10 (21.3)</td>
<td>0.705</td>
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<tr>
<td>Diabetes mellitus</td>
<td>23 (39.0)</td>
<td>10 (21.7)</td>
<td>0.094</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>34 (57.6)</td>
<td>29 (64.4)</td>
<td>0.568</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>12 (23.5)</td>
<td>11 (27.5)</td>
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<tr>
<td>Hypertension</td>
<td>40 (69.0)</td>
<td>27 (57.4)</td>
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<td>Comorbid diseases</td>
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<tr>
<td>CKD</td>
<td>1 (1.8)</td>
<td>0 (0.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (1.8)</td>
<td>0 (0.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Heart failure</td>
<td>21 (36.8)</td>
<td>27 (57.4)</td>
<td>0.057</td>
</tr>
<tr>
<td>PAD</td>
<td>1 (1.9)</td>
<td>3 (6.7)</td>
<td>0.327</td>
</tr>
<tr>
<td>Stroke</td>
<td>7 (11.9)</td>
<td>6 (12.8)</td>
<td>1.000</td>
</tr>
<tr>
<td>Echocardiographic parameter</td>
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<tr>
<td>LVEF</td>
<td>48.72 ± 16.92</td>
<td>50.50 ± 15.78</td>
<td>0.709</td>
</tr>
<tr>
<td>Treatment</td>
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<tr>
<td>ACE inhibitors</td>
<td>31 (52.5)</td>
<td>31 (67.4)</td>
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<tr>
<td>Antiplatelet</td>
<td>59 (100)</td>
<td>47 (100)</td>
<td>-</td>
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<tr>
<td>ARBs</td>
<td>17 (28.8)</td>
<td>7 (14.9)</td>
<td>0.142</td>
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<tr>
<td>Beta-blockers</td>
<td>30 (50.8)</td>
<td>18 (38.3)</td>
<td>0.274</td>
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<td>Nitrates</td>
<td>33 (55.9)</td>
<td>25 (53.2)</td>
<td>0.932</td>
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<tr>
<td>Statins</td>
<td>59 (100)</td>
<td>47 (100)</td>
<td>-</td>
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<tr>
<td>SYNTAX score</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>19.70 ± 10.00</td>
<td>19.91 ± 12.98</td>
<td>0.927</td>
</tr>
<tr>
<td>Mild (SS ≤22)</td>
<td>33 (57.6)</td>
<td>25 (53.2)</td>
<td>0.155</td>
</tr>
<tr>
<td>Moderate (SS = 22-32)</td>
<td>21 (33.9)</td>
<td>12 (25.3)</td>
<td></td>
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<tr>
<td>Severe (SS &gt;32)</td>
<td>5 (8.5)</td>
<td>10 (21.3)</td>
<td></td>
</tr>
</tbody>
</table>

Note: data were presented in mean ± SD or n(%); ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; CABG = coronary artery bypass graft; CAD = coronary artery disease; CCBs = calcium channel blockers; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular diseases; LVEF = left ventricular ejection fraction; OMT = optimal medical treatment; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; SS = SYNTAX score; SYNTAX = Synergy Between PCI With Taxus and CABG.
4. Discussion

Our study revealed several important findings. First, PCI could improve the QoL in CCS patients. Second, OMT plus PCI improved physical limitation and angina stability. The last, in patients with SYNTAX score of more than 22, OMT plus PCI was associated with good QoL achievement.

The pathogenesis mechanisms in CCS start with atherosclerosis, which develops and progress slowly for several decades. The several risk factors for CVD such as aging, diabetes mellitus, dyslipidemia, genetics, hypertension, obesity, or lack of physical activity will lead a low-grade inflammation and accelerate the atherosclerosis process. In CCS, this slow atherosclerotic plaque progression causes gradual thickening of the inner layer of the coronary arteries, which can narrow the arterial lumen in various severity. In most cases, the lesion severity evaluation is conducted using CAG. However, to determine the structure of the vessel wall and the morphology of atherosclerotic plaque, imaging tools such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT) are needed. The blood flow restriction due to obstructive lesions in the coronary arteries cannot compensate for increased myocardial oxygen demand in certain conditions. This oxygen supply and demand mismatch leads to myocardial ischemia. In general, if the lesion is greater than 80% of lumen diameter, compensatory vasodilatation will not be helpful. Vascular spasm or endothelial injury may increase the severity of stenosis due to atherosclerotic plaque. Current practice guidelines strongly recommend lifestyle changes, OMT, and myocardial revascularization such as PCI or CABG as the backbone treatment of CCS.

Our study revealed that OMT plus PCI was associated with good QoL. Our results supported the findings from prior studies such as COURAGE trial and TIME trial. The COURAGE trial results gave us an important lesson that among CCS patients receiving OMT, PCI had small but significant advantages in improving QoL, especially in the three years following the PCI procedure. The TIME trial that included elderly patients aged ≥75 years old demonstrated that PCI and CABG improved the QoL and symptom relief. On the other hand, myocardial revascularization successfully reduced the incidence of MACE.

In the subgroup analysis of the SAQ, our results demonstrated that PCI was associated with better ADL and angina stability. In CCS, the underlying coronary lesion is the stable plaque with significant stenosis. The stable coronary plaque contains (1) low lipid accumulation; (2) greater smooth muscle cell; (3) more extracellular matrix; and (4) thick fibrous cap. When coronary artery stenosis reaches more than 80% of lumen diameter, adequate oxygen supply to the myocardial tissue cannot be provided. In this condition, PCI is reasonable because it can provide a wider vessel lumen diameter close to the normal vessel lumen diameter. Therefore, an adequate oxygen supply can be restored. Moreover, the balance between oxygen demand and oxygen supply can be achieved, and angina symptoms can be relieved.

SYNTAX score is the assessment tool to evaluate the severity or complexity of coronary artery lesions. A greater SYNTAX score indicates a more severe and more complex coronary lesion as well as poor prognosis in patients receiving PCI. In patients with complex lesions such as left main coronary artery disease or three-vessel disease, the SYNTAX score could predict the incidence of mortality or MACE. Our studies revealed that patients with good QoL in the OMT plus PCI group revealed a lower SYNTAX score than patients with poor QoL. According to this finding, we could learn that PCI would be effective if applied in patients with low complexity of coronary lesions. Moreover, the current myocardial revascularization guideline strongly recommends CABG over PCI for CCS patients with: (1) left main disease with moderate or high SYNTAX score without diabetes mellitus; (2) three-vessel disease with diabetes mellitus; and (3) three-vessel disease with moderate or high SYNTAX score without diabetes mellitus. However, the recommendation for PCI is higher than CABG in one or two-vessel disease without proximal left anterior descending (LAD) stenosis.

Our study also demonstrated that among patients with SYNTAX score of more than 22s, achievement of good QoL was greater in OMT plus PCI group than the OMT group. The higher the SYNTAX score is associated with, the more complex and the more severe coronary lesion. The ischemic burden and mortality risk also higher in those populations indeed. In those population, revascularization is the mandatory to restore optimal coronary perfusion, reduce angina symptom, and improve QoL.
Current guidelines strongly recommend CABG than PCI for patient with more complex lesion.\textsuperscript{1,5,6} However, in several circumstances such as: (1) the existence of comorbid disease; (2) advanced age; (3) frailty; (4) low life expectancy; (5) mobilization restriction that impede the rehabilitation program; (6) low-quality graft; (7) severe spine and chest deformity; (8) porcelain aorta; or (9) chest radiation sequelae, CABG may be not appropriate.\textsuperscript{6} Stress, fear, or anxiety about the CABG procedure may be the reason for several patients to refuse that procedure.\textsuperscript{20} In those kinds of patients, PCI in CCS patients with SYNTAX score of more than 22 is reasonable because the restoration of optimal coronary is warranted. Our study was the first study assessing the benefit of OMT plus PCI over PCI alone in improving QoL in patients with SYNTAX score of more than 22s to the best of our knowledge. Prior studies such as the COURAGE trial and TIME trial did not use the SYNTAX score in their data analysis.\textsuperscript{17,18}

In this study, we did not find loss to follow-up because the patients who had lost to follow-up patients were excluded. Our study had several limitations. First, the SAQ assessment was conducted only in the end of study. Second, the small number of participants. Third, our study follow-up period duration was not similar among the study participants. Due to those limitations, the randomized controlled trial (RCT) with larger participants, better design, and longer follow-up is needed.

5. Conclusion
Several important lessons could be obtained from our study. Myocardial revascularization by PCI improved the QoL in CCS patients treated with OMT. Second, OMT plus PCI improves physical limitation and angina stability. For patients with SYNTAX score of more than 22, OMT plus PCI was correlated with good QoL achievement.

6. Declarations
6.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involve in the study.

6.2. Consent for publication
Not applicable.

6.3. Availability of data and materials
Data used in our study were presented in the main text.

6.4. Competing interests
Not applicable.

6.5. Funding source
Not applicable.

6.6. Authors contributions
Idea/concept: WK, MSR. Design: MSR. Control/supervision: MSR, PS, DS. Data collection/processing: WK, WKA. Extraction/Analysis/interpretation: WK, WKA. Literature review: WK, WKA, MSR, PS, DS. Writing the article: WK, WKA, MSR, PS, DS. Critical review: WK, WKA, MSR, YW. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

6.7. Acknowledgements
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References


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Results: A total of 57 patients in the OMT plus PCI group and 49 patients in the OMT group were included. The percentage of patients with good QoL was higher in the OMT plus PCI group than OMT only group (64.5% vs. 35.5%; p = 0.007). The OMT plus PCI group revealed a better activities of daily living (85.11 ± 12.46 vs. 12.46 ± 21.87; p = 0.014) and angina stability (84.32 ± 23.63 vs. 71.81 ± 27.89; p = 0.014) than OMT group. Among patients with SYNTAX scores of more than 22, achievement of good QoL was greater in the OMT plus PCI group than the OMT group (80.8% vs. 45.5%; p = 0.025).
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Myocardial revascularization strategies in CAD include percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery.4 The purpose of myocardial revascularization in CCS includes: (1) myocardial ischemia elimination; (2) eliminate clinical manifestations; and (3) major adverse cardiovascular event (MACE) risk reduction.1,5 Revascularization strategy by PCI or CABG can be determined using the Synergy Between PCI With Taxus and CABG (SYNTAX) score.5

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