Post-therapeutic Response Evaluation of Patients Receiving Percutaneous Coronary Intervention at the Regional Hospital in Bantul, Yogyakarta

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Abstract: Coronary Artery Disease (CAD) is the main cause of mortality in heart disease. Its treatment involves complex therapies, such as pharmacological Percutaneous Coronary Intervention (PCI) to widen the clogged artery and lifestyle intervention to decrease the severity of CAD and restenosis. The complexity of the pharmacological therapy received by CAD patients may cause Adverse Drug Reaction (ADR) events. Therefore, this study aimed to identify the response of CAD patients after receiving PCI therapy at the Regional Hospital in Bantul, Yogyakarta. This descriptive research used retrospective data and a total population sampling method. The samples were CAD outpatients who had received PCI at this hospital from January to September 2017 and met the inclusion criteria. The sample size was 65 patients. The results showed that the responses of the CAD patients to PCI therapy included restenosis symptoms (70.77%) (namely, one restenosis symptom (43.08%) and two restenosis symptoms (27.69%)), uncontrolled lifestyle intervention (namely, abnormalities in total cholesterol (58.62%), LDL cholesterol (93.10%), HDL cholesterol (72.41%), triglyceride (70.69%), blood pressure (72.22%), and HbA1c (50%)), and adverse drug reaction (4.62%).

1 INTRODUCTION

Coronary Artery Disease (CAD) is the main cause of mortality in heart disease (WHO, 2011). Among the 33 provinces in Indonesia, the Special Region of Yogyakarta has the 15th highest CAD cases that affect 16,663 people according to the basic estimate from doctor's diagnosis and 36,104 people based on doctor's diagnosis on the exhibited symptoms (National Primary Health Research, 2013). The high number of CAD cases is caused by the influencing risk factors (Anwar, 2004).

According to Rilantono (2012), the principle of CAD treatment is generally a long-term effort to improve cardiac function and increase life expectancy. Apart from the use of pharmacological drugs, CAD cases can diminish with mechanical reperfusion using Percutaneous Coronary Intervention (PCI). PCI uses a stent (ring) to reduce the occurrence of sudden occlusion.

Based on the statistical report published by AHA (2014), there is an increase in PCI procedure per 10,000 population. The number raised from 37.2 procedures per 10,000 people (37.2/10,000) in 1990-1992 to 59.2/10,000 in 2002-2004. It reached 135.1/10,000 in men of 65-75 years old and 64.0/10,000 in women from the same age group. On the contrary, the numbers of procedures in men and women aged ≥75 years were 128.7/10,000 and 69.0/10,000, respectively. The revascularization of coronary blood vessels with PCI increased from 264/100,000 in 2002 to 267/100,000 in 2005. Such increase was higher than the rise of the Coronary Artery Bypass Grafting (CABG) procedure in the same years, i.e., from 121/100,000 to 94/100,000.

However, PCI may cause a problem, namely the growth of tissue within the lumen of the arteries due to the biological response of vascular injury that causes the narrowing of arteries and the recurrence of clogs within six months called restenosis (Levine *et al.*, 2011). The incidence of restenosis after PCI is quite high, which is up to 30% six months after the procedure (Aaronson & Ward, 2008).

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Apart from taking medical interventions, the risk of CAD can be managed with obedience to a healthy lifestyle (lifestyle intervention). After receiving a PCI procedure, patients are always advised to apply a healthy lifestyle to reduce future cardiovascular events. Also, lifestyle changes may advance the benefits of the medical therapy and revascularization procedures (Ruß *et al.*, 2009).

Consuming different types of drugs routinely, CAD patients need evaluation and monitoring to achieve effective treatment. Therefore, the comprehension of treatment failure and adverse drug reaction (ADR), especially in chronic diseases such as CAD, is necessary (Depkes RI, 2009). Accordingly, a study identifying the patients' response to PCI procedures, including the occurrence of restenosis symptoms afterward like chest pain and shortness of breath, the risk factor control (namely, total cholesterol level, LDL cholesterol, HDL cholesterol, triglyceride level, blood pressure, and HbA1c), and Adverse Drug Reaction (ADR) at the Regional Hospital in Bantul, Yogyakarta is necessarily interesting.

2 MATERIALS AND METHOD

2.1 Materials

This study used the medical records of the outpatients at Panembahan Senopati Regional Hospital in Bantul, Yogyakarta as the research materials.

2.2 Methods

This descriptive study relied on the collection of retrospective data. These data were acquired from the medical record of the research subjects, namely 65 CAD outpatients who had received PCI procedures at Panembahan Senopati Regional Hospital from January to September 2017. The research subjects were selected with a total population sampling technique.

Table 1: The characteristics of patients by sex

Sex	Number of patients (n)	(%)
Male	51	78.46
Female	14	21.54
Total	65	100

(Source: Primary data analysis, 2018)

2.3 Data Analysis

The response of the CAD patients after receiving PCI procedures at the hospital was analyzed descriptively. The data were presented qualitatively and quantitatively in percentage. The assessed response included restenosis symptoms (i.e., chest pain and shortness of breath), controls over the risk factor (i.e., total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, blood pressure, and HbA1c), and adverse drug reaction. These responses were identified using in-depth analysis with references to related literature.

3 RESULTS AND DISCUSSION

3.1 Patients' Characteristics

3.1.1 The Characteristics Of Patients by Sex

The characteristics of patients by sex (Table 1) were analyzed to determine the ratio of male to female patients. The samples consisted of 51 male outpatients (78.46%) and 14 female outpatients (21.54%). Compared with women, men have a higher risk of CADs with earlier occurrences. However, the risk of COD in women increases after menopause. Women produce estrogen as natural protection against hypercholesterolemia and CAD. Also, unhealthy lifestyles, such as smoking habit, can also increase the risk factors for men (Sallam & Watson, 2013).

The results showed that all female CAD patients receiving PCI had reached menopause. According to AHA (2014), the prevalence of PCI therapy for CAD was higher in men (83.0/10,000) than in women (38.7/10,000) because women have more stable angina and fewer blockages in their blood vessels (Lundberg & King, 2012; Nowakowska *et al.*, 2008).

3.1.2 The Characteristics of Patients by Age

The age grouping of the CAD patients in this research is presented in Table 2. It shows that the incidence of CAD is dominant in the age group of ≥ 45 years. This finding is in line with the theory that states that the risk level of CAD is higher at the age of 40 years and over (AHA, 2014).

The results of this study are in line with the National Primary Health Research (2013), which

Table 2: The characteristics of patients by age

Age (years old)	Number of patients (n)	(%)
35-44	3	4.62
45-54	13	20.00
55-64	25	38.46
65-74	17	26.15
≥75	7	10.77
Total	65	100

(Source: Primary data analysis, 2018)

indicates that the prevalence of CAD based on doctor's diagnosis and patient's symptoms increase with age. The highest group found at age 65-74 years that is 2.0% and 3.6 % but decreased slightly in the age group ≥75 years that is 1.7% and 3.2%.

This research only found seven (7) CAD patients aged ≥75 years (10.77%). This number is probably attributable to the life expectancy in Indonesia, which makes the population size of the CAD patients at this group age seem small. Based on the Statistics Indonesia (BPS, 2016), the life expectancy of the Indonesian population increases from one year to another. For instance, it extended from 69.8 years in 2010 to 70.6 years. However, it has not reached 75 years.

3.1.3 The Characteristics of Patients Based on Comorbidities

The data obtained from the medical history showed that all patients in this study had comorbidities, namely dyslipidemia, hypertension, dyspepsia, Congestive Heart Failure (CHF) and hyperuricemia (Table 3). Some of which are identified as the risk factors of CAD. According to Karikaturijo (2010), CHF is one of the complications of CAD. This condition occurs when the arterial blood vessels narrow and, therefore, decrease the oxygen supply to the heart. Consequently, the heart muscle weakens.

Dyslipidemia had the highest proportion in this research. Dyslipidemia, as well as hypertension, is the risk factor of CAD. The results showed that after receiving PCI procedures, the CAD outpatients at the Regional Hospital in Bantul, Yogyakarta who had dyslipidemia also showed the symptoms of hypertension. Dyslipidemia and hypertension are both known to have a close relationship with the incidence of CAD because continuous high blood pressure in CAD patients would result in damaged blood vessels, allowing the accumulation of fatty

Table 3: The characteristics of patients based on comorbidities

Comorbidities	N= 65	(%)
Dyslipidemia	58	89.23
Hypertension	17	26.15
Dyspepsia	16	24.62
Congestive Heart Failure (CHF)	10	15.38
Hyperuricemia	10	15.38

(Source: Primary data analysis, 2018)

plaque and eventually the blockage of the blood vessels (Budiman *et al.*, 2015).

The other coexisting disease in CAD patients after the PCI therapy was dyspepsia. Suspected polypharmacy in CAD management may cause upper gastrointestinal disorders. Aspirin as an antiplatelet in CAD patients can cause gastrointestinal disturbances. Dyspepsia, nausea, and vomiting occur in 2-6% of patients after taking aspirin (Meylers, 2006).

The association of uric acid with the incidence of cardiovascular disease is still controversial and under investigation (Torpy *et al.*, 2009). An experimental study reveals that uric acid stimulates the release of chemo-attractant protein-1, interleukin-1b (IL-1b), interleukin-6 (IL-6), and tumor necrosis factor-a (TNF-a). Therefore, uric acid may contribute to the development of vascular disease and atherosclerosis through pro-inflammatory pathways (Ruggiero *et al.*, 2006).

3.2 The Effect of Drug Use Profile on The Cardiovascular System

Table 4 shows that the CAD patients who have received PCI therapy take acetylsalicylic acid, clopidogrel, bisoprolol fumarate, candesartan, and simvastatin. In this study, acetylsalicylic acid or aspirin was quite largely used by the CAD patients after receiving the therapy. For patients without resistance or allergic to aspirin, or without bleeding tendency, aspirin has to be given immediately to continue their lifetime (AHA, 2011). The clinical trials in Aaronson & Ward (2008) reveal that aspirin at low doses can decrease infarcts and mortality by more than 50%.

Clopidogrel has been proven as effective as aspirin in the prevention of ischemic events in at-risk patients. Clopidogrel and aspirin affect different

Table 4: The drug use profile

Type of drugs	N= 493	(%)
Acetylsalicylic acid	59	11.97
Clopidogrel	47	9.53
Bisoprolol fumarate	55	11.16
Candesartan	45	9.13
Simvastatin	60	12.17
Others	227	46.04

(Source: Primary data analysis, 2018)

pathways in the coagulation process. Therefore, their combination can be administered to patients undergoing stenting, and it has been proven to reduce ischemic events by 20% in patients with NSTEMI or unstable angina compared with the single use of aspirin (Yusuf *et al.*, 2001).

Beta blockers are used to treat hypertension, angina, supraventricular heart arrhythmias, myocardial infarction, and chronic heart failure (Aaronson & Ward, 2008). A meta-analysis of 147 randomized controlled trials with 464,000 patients proposes beta-blockers as the first-line therapy in CAD patients. In the first two years after myocardial infarction, beta blockers can reduce cardiovascular events twice than other antihypertensive agents (Law *et al.*, 2009).

Besides beta-blockers, another widely prescribed antihypertensive drug found in this research was candesartan from the Angiotensin Receptor Blocker class (ARB). Sakamoto *et al.* (2016) develop a randomized controlled trial involving 1,145 patients who received different treatments after the PCI procedures, namely (1) candesartan plus standard medical treatment and (2) conventional medical treatment during the follow-up in the succeeding three years. They prove that the administration of candesartan soon after PCI treatment does not improve the prognosis, but it reduces some cardiac events for three (3) years.

Statins are the drug of choice for lowering LDL cholesterol, and they are used up to the highest tolerable dose to achieve targeted LDL cholesterol concentrations (PERKI, 2013). According to Cerit *et al.* (2016), patients who have stable CAD after PCI and receive a long-term statin therapy are associated with increased epicardial perfusion.

The description of the response of patients to Percutaneous Coronary Intervention therapy is as follows:

3.3 Restenosis Symptoms

The results showed that after PCI, CAD patients could experience re-blockage (restenosis). The restenosis symptoms observed in this research included chest pain and dyspnea (Table 5).

Not every sampled patient in this research exhibited the symptoms of restenosis. Nineteen (19) patients (29.23%) had no symptoms of restenosis, 28 patients (43.08%) showed one symptom of restenosis, and the remaining 18 patients (27.69%) had two symptoms of restenosis. According to Aaronson & Ward (2008), restenosis can occur in 30% of CAD patients within six months after the PCI procedure. The results of this research showed that CAD patients experienced the symptoms of restenosis within ≤6 months (23.08%) and >6 months (76.92%) after the procedure.

3.4 Lifestyle Intervention

The goal of lifestyle intervention is to prevent cardiovascular complications in patients with DM, cholesterol, and hypertension to improve their

Table 5: The incidence of restenosis

The incidence of restenosis	Number of patients (n)	(%)
No restenosis	19	29.2
1 symptom (chest pain or dyspnea)	28	43.1
2 symptoms (chest pain and dyspnea)	18	27.7
Total	65	100

(Source: Primary data analysis, 2018)

Table 6: The distribution of CAD patients with dyslipidemia disease according to total cholesterol levels post PCI therapy

Total cholesterol	N= 58	(%)
Normal (<200 mg/dL)	24	41.38
Abnormal (≥200 mg/dL	34	58.62

(Source: Primary data analysis, 2018)

Table 7: The distribution of CAD patients with dyslipidemia disease according to LDL cholesterol levels post PCI therapy

LDL cholesterol	N= 58	(%)
Normal (<100 mg/dL)	4	6.9
Abnormal (≥100 mg/dL)	54	93.1

(Source: Primary data analysis, 2018).

Table 8: The distribution of CAD patients with dyslipidemia disease according to HDL cholesterol levels post PCI therapy

HDL cholesterol	N= 58	(%)
Normal (≥40 mg/dL)	16	27.59
Abnormal (<40 m/dL)	42	72.41

(Source: Primary data analysis, 2018)

Table 9: The distribution of CAD patients with dyslipidemia disease according to triglycerides post PCI therapy

Triglycerides	N= 58	(%)
Normal (<150 mg/dL)	17	29.31
Abnormal (≥150 mg/dL)	41	70.69

(Source: Primary data analysis, 2018)

Table 10: The distribution of CAD patients with hypertension according to blood pressure levels post PCI therapy

Blood pressure levels	N= 18	(%)
Normal	5	27.78
Abnormal	13	72.22

(Source: Primary data analysis, 2018)

glycemic control and reduce the occurrence of dyslipidemia and hypertension (Blumenthal *et al.*, 2011). The following tables show the results of the laboratory analysis of CAD patients with the comorbidities of dyslipidemia, hypertension, and diabetes mellitus (DM).

Table 11: The distribution of CAD patients with diabetes mellitus disease according to HbA1c post PCI therapy

HbA1c	N= 8	(%)
Normal (<7.0 %)	4	50
Abnormal (≥7.0 %)	4	50

(Source: Primary data analysis, 2018)

Tables 6, 7, 8, and 9 show that after receiving the pharmacological and PCI procedures, the number of patients with abnormal cholesterol levels is higher than the normal ones. This condition indicates that not every sampled patient in this research adheres to the suggested pharmacological therapy and lifestyle.

According to Sari & Husna (2016), there is a relationship between lifestyle and the ability to control cholesterol in patients with hypercholesterolemia. Unhealthy lifestyles may induce high cholesterol levels. The choice of lifestyle is influenced by the prominent development of the era, such as the emergence of an environment that somehow enables excessive consumption of junk food, low physical activity, and lack of health awareness. According to the ESC/EAS Guidelines for the Management of Dyslipidaemias (ESC, 2011), lifestyle interventions, including a dietary plan that reduces saturated fatty acids, have a major impact on LDL levels. An additional of 1% energy from the saturated fat increases LDL levels by 0.02-0.04 mmol/L or 0.8-1.6 mg/dL.

The recommendations of the Eighth Joint National Committee (JNC 8) on the blood pressure targets for hypertensive patients without diabetes mellitus and Chronic Kidney Disease (CKD) aged <60 years and ≥60 years are <140/90 mmHg and <150/90 mmHg, respectively. Meanwhile, in hypertensive patients with diabetes mellitus or CKD, the targeted blood pressure is different, that is <140/90 mmHg (James *et al.*, 2013).

In this research, there were 17 patients with hypertension and 1 patient with Hypertensive Heart Disease (HHD). Among these 18 patients, 13 (72.22%) had blood pressure above the target. Meanwhile, the remaining five patients had normal blood pressure (27.78%) (Table 10). This finding indicates that not every patient in this research adheres to the suggested pharmacological therapy and lifestyle.

Lifestyle interventions for hypertensive patients include weight loss for overweight or obese patients, the reduction of salt intake to 1,5 grams per day, and

regular physical activity. They also advise more consumption of fruits and vegetables (300 grams) and the reduction of saturated fat and cholesterol intake (ESC, 2016).

Based on the results of this research, eight CAD patients had Diabetes Mellitus (DM) after PCI therapy. Half of them had normal HbA1c (hemoglobin glycate) level, whereas the remaining 50% had abnormal HbA1c levels (Table 11). This finding indicates that not every patient in this research adheres to the recommended pharmacological therapy and lifestyle.

According to the consensus PERKENI (2015), physical exercise is one of the pillars in the management of DM if not accompanied by nephropathy. It is useful for maintaining the body's fitness and improving insulin sensitivity. It is not the only factor that controls the HbA1c levels of DM patients, but a good dietary intake (as recommended) and oral hypoglycemic drugs or insulin also play a role in shaping blood sugar levels.

3.5 Pharmacological Management

In this study, three (3) patients experienced the side effects of Adverse Drug Reactions (ADRs) (Table 12), namely cough, as induced by the administration of captopril and ramipril.

Captopril and ramipril are from the class of Angiotensin Converting Enzyme Inhibitor (ACEi) drug that inhibits Renin-Angiotensin System (RAS). ACE is an important enzyme in the renin-angiotensin system that converts angiotensin I to angiotensin II on the surface of endothelial cells. Angiotensin II is proven to cause vasoconstriction in blood vessels. The inhibition of this enzyme can lead to vasodilation and, consequently, decreased blood pressure (Herman & Bhimji, 2017).

In addition to lowering blood pressure with the inhibition of angiotensin II formation, ACEi also inhibits bradykinin degradation and stimulates the synthesis of other vasodilators, such as prostaglandin E2 and prostacyclin. Bradykinin increases in the body, accumulates in the respiratory tract, and then stimulates the incidence of a dry cough (Zamora & Parodi, 2010; Nishio *et al.*, 2011).

Table 12: The incidence of ADR

The incidence of ADR	Number of patients (n)	(%)
No side effects	62	95.38
Side effects	3	4.62
Total	65	100

(Source: Primary data analysis, 2018)

4 CONCLUSIONS

Based on the results of this research, several responses of CAD patients to PCI therapy include restenosis symptoms (70.77%)—consisting of 1 restenosis symptom (43.08%) and 2 restenosis symptoms (27.69%), uncontrolled lifestyle intervention—such as abnormalities in total cholesterol (58.62%), LDL cholesterol (93.10%), HDL cholesterol (72.41%), triglyceride (70.69%), blood pressure (72.22%), and HbA1c (50%), and adverse drug reaction (4.62%).

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