



Analysis of Characteristics of Coronary Artery Stenosis Based on the Comorbidities in Coronary Heart Disease Patients Undergoing Coronary Angiography

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ABSTRACT

Background: Comorbid diseases are a risk factor for atherosclerosis in coronary heart disease (CHD). Atherosclerosis causes the narrowing of the coronary arteries so that the heart muscles lack blood supply. Diagnostic coronary angiography is an invasive medical examination performed to determine the presence of coronary artery stenosis and to show the location and the number of coronary artery stenosis.

Objective: This study aimed to analyze the characteristics of coronary artery stenosis based on comorbidities of patients with CHD undergoing coronary angiography.

Methods: This analytical study was conducted using a cross-sectional design of 105 patients with CHD undergoing coronary angiography at the catheterization laboratory at Bahteramas Hospital, Southeast Sulawesi, from January 1 to December 31, 2021. Statistical testing used Chi-square tests with 95% confidence interval and significance set as $p < 0.05$.

Results: Most of the respondents were over 45 years old as many as 87 (82.9%), and most are male as many as 72 (68.6%). The category of the highest number of stenosis was less than two stenosis, namely 70 patients (66.7%) with the most common location as the Left Anterior Descending. The comorbidities category included a history of dyslipidemia in 41 people (39.0%), history of diabetes mellitus (DM) in 28 people (26.7%), and history of hypertension in 75 people (71.4%). The bivariate analysis showed a history of DM was associated with coronary artery stenosis (p -value = 0.007) with an Odds Ratio of 3.111.

Conclusions: Patients with DM have 3.111 times greater possibility of developing stenosis of the coronary arteries. WC:246

KEYWORDS: Arterial stenosis, Coronary angiography, co-morbid diseases, Coronary heart disease, Diabetes mellitus

INTRODUCTION

Coronary Heart Disease (CHD) is the number one cause of death in the world, including Indonesia, which is estimated to reach 23.3 million cases in 2030. CHD is caused by the narrowing of the coronary arteries due to atherosclerosis or spasms of the heart muscles or a combination of both [1]. CHD risk factors include nonmodifiable and modifiable risk factors. The nonmodifiable factors are age, gender, and family history. Meanwhile, modifiable risk factors are dyslipidemia, smoking, hypertension, diabetes mellitus (DM), obesity, and lack of physical activity [2].

Previous research conducted in the United States showed that the average age of patients with CHD was 58.1 years, female sex (24%), family history of CHD (44.8%), smoked (47.7%), and had an average body mass index (BMI) of 27.9 kg/m², as well as other risk factors such as hypertension (46.3%), DM (17.1%) and dyslipidemia (44.1%). The prevalence of CHD based on a doctor's diagnosis or symptoms is 1.5%. Based on the results of the study [3], the most common age of patients with CHD in Indonesia ranges from 65-74 years, female sex (1.6%), smoking (1.2%), obesity (1.7%), hypertension (5.5%), DM (9.2%), and abnormal lipid results (1.8%) [4].

Hyperlipidemia is a major risk factor for atherosclerosis. Decreased high density lipoprotein (HDL)-C levels and increased triglyceride levels cause metabolic disturbances [2]. A higher triglyceride index is a marker of insulin resistance associated with a higher risk of coronary arterial disease (CAD) events, especially in the elderly and postmenopausal women [5].

The most common risk factor considered a strong predictor of cardiovascular events is hypertension. High blood pressure increases the risk of all clinical manifestations of CHD, including angina pectoris, myocardial infarction, and sudden death [6]. High



and persistent blood pressure can cause direct trauma to the walls of the coronary arteries, thereby facilitating the occurrence of atherosclerosis [4].

Diabetes is one of the comorbidities in CHD. Diabetes promotes atherosclerosis by damaging the walls of blood vessels which cause fat to build up on the damaged walls and narrows blood vessels [6]. DM causes a poor prognosis in very old patients undergoing coronary angiography at risk of coronary revascularization and death[7].

Early and advanced stages of CAD can be diagnosed through coronary angiography (CAG). CAG is an invasive medical examination performed to determine the presence of blocked coronary arteries and show the location and amount of coronary artery stenosis. Determination of the degree of obstruction is estimated as a percentage of the arterial lumen by comparing the area of narrowing with the adjacent normal artery [8]. CAG is the gold standard in the diagnosis of patients with suspected CAD based on complaints, electrocardiograph (ECG) recordings, and/or non-invasive imaging examinations or stress tests.

CAG should be performed if there are spontaneous episodes of myocardial ischemia, ischemia provoked by minimal activity, or non-invasive examinations with moderate or high risk. The results of cardiac catheterization will determine the appropriateness next steps. American Heart Association (AHA) recommends coronary angiography in candidates for Percutaneous Coronary Intervention (PCI) or failed thrombolytic rescue and in patients with cardiogenic shock, structural heart injury, or other major complications [9]. Symptom status with clinical risk factors needs to be emphasized in assessing patient selection for CAG, which will have symptomatic implications for PCI compliance. Appropriate application of CAG can facilitate the selection of the right patient for PCI [10].

The conclusions from CAG are knowing the location and extent of the stenosis that will determine whether PCI is necessary or not. Early recognition of atherosclerotic lesions followed by appropriate revascularization can help reduce mortality in patients with acute coronary syndrome (ACS). CAG indications in this study were patients with complaints of unstable chest pain and ECG findings showing non-ST-elevation myocardial infarction (NSTEMI). PCI is performed if stenosis of >50% in the left main coronary artery or >70% in any other epicardial coronary artery.

The role of comorbidities in determining the incidence of stenosis needs to be further investigated, particularly regarding the location, number, and degree of arterial obstruction based on the type of comorbid disease, so that proper prevention and management can be conducted.

METHODS

This research was a correlation analysis research with a cross-sectional approach. The study used secondary data taken from medical records of 105 patients with CHD who underwent CAG at the catheterization laboratory at Bahteramas Hospital, Southeast Sulawesi Province from January 1 to December 31, 2021. The study was approved by the research ethics committee of the Medicine Faculty, Halu Oleo University (Approval Number 029/UN17.1.3/ETIK/2021) and informed consent had been obtained from the Bahteramas hospital medical record unit.

The checklist sheet was used to collect the demography data (age, gender), the smoking history, and BMI that was calculated by dividing weight in kilograms with the square of the height in meters (kg/m^2). BMI was categorized into two: obese if $\text{BMI} \geq 23 \text{ kg}/\text{m}^2$ and not obese if $\text{BMI} < 23 \text{ kg}/\text{m}^2$. Comorbidity data review included a history of dyslipidemia, hypertension, and DM listed in the medical records based on the doctor's diagnosis. The data were categorized into two, namely patients with less than two comorbidities and patients with more or equal to two comorbidities. Characteristics of vessel stenosis consist the number of vessels involved, the location, and the degree of obstruction. The number of vessel stenosis was categorized into four: no stenosis, one vessel stenosis, two vessel stenosis, and three vessel stenosis. Stenosis is significant if greater than 50% stenosis of the left main coronary artery or greater than 70% of the other epicardial coronary artery.

The data were complemented by information from medical records. Statistical analysis was conducted using SPSS Version 20 (IBM Corp., Armonk, NY). Data were presented as frequency distribution and percentages for categorical variables. Chi-Square test was used to analyze the categorical variables with p -value of $<.05$ considered as statistically significant.



RESULTS

1. Frequency Distribution of Respondent Characteristics

Table 1. Patient Characteristics (n=105)

| Characteristics of Respondent | Total n | % |
|-------------------------------------|------------|--------------|
| Age: | | |
| ▪ > 45 years old | 87 | 82.9 |
| ▪ ≤ 45 years old | 18 | 17.1 |
| Gender: | | |
| ▪ Male | 72 | 68.6 |
| ▪ Female | 33 | 31.4 |
| The Smoking History | | |
| ▪ Yes | 38 | 36.2 |
| ▪ No | 67 | 63.8 |
| Obesity: | | |
| ▪ Yes (BMI ≥ 23 kg/m ²) | 46 | 43.8 |
| ▪ No (BMI < 23 kg/m ²) | 59 | 56.2 |
| Comorbidities Number | | |
| ▪ ≥2 comorbidities | 42 | 40.0 |
| ▪ < 2 comorbidities | 63 | 60.0 |
| History of Dyslipidemia | | |
| • Yes | 41 | 39.0 |
| • No | 64 | 61.0 |
| History of Hypertension | | |
| ▪ Yes | 75 | 71.4 |
| ▪ No | 30 | 28.6 |
| History of Diabetes mellitus | | |
| ▪ Yes | 28 | 26.7 |
| ▪ No | 77 | 73.3 |
| Number of Vessel Stenosis | | |
| ▪ No Stenosis | 15 | 14.3 |
| ▪ 1 vessel | 55 | 52.4 |
| ▪ 2 vessels | 26 | 24.8 |
| ▪ 3 vessels | 9 | 8.6 |
| Total | 105 | 100.0 |

Based on Table 1, it was found that 87 people (82.9%) were over 45 years old; 72 people (68.6%) were male; as many as 38 people (36.2%) had a smoking habit; 46 people (43.8%) had excess BMI (≥ 23 kg/m²); 41 people (39.0%) had a history of dyslipidemia; 75 people (71.4%) had a history of hypertension; and 28 people (26.7%) had a history of DM. Based on sex, the distribution of obesity in men was 69.6% and 30.4% in women. The distribution of dyslipidemia in men was 70.7%, and for women it was 29.3%. The distribution of hypertension was 66.7% for men and 33.3% for women. The distribution of DM was 67.9% men and 32.1% women.

The number of respondents who did not experience coronary artery stenosis were 15 people (14.3%), stenosis in one vessel were 55 people (52.4%), stenosis in two vessels were 26 people (24.8%), and stenosis in three vessels as many as 9 people (8.6%). The most common location was in the left anterior descending (LAD) artery (46.6%), followed by the left circumflex (LCx) (28.6%) and right coronary artery (RCA) (23.3%). Most stenosis locations involving two vessels



together were LAD and LCx (57.7%) followed by LAD and RCA (23.1%). Meanwhile, the most common stenoses involving three vessels together were LAD, LCx, and RCA (55.6%), followed by LM, LCX, and RCA (13.3%). There were 63 patients (60%) with significant stenosis, which were indicated for PCI.

2. Frequency Distribution of Vessel Stenosis Based on Comorbidities

Table 2. Characteristics of Vessel Stenosis Based on Comorbidities

| Comorbidities | Percentage Vessel Stenosis | | | |
|-------------------|----------------------------|----------|----------|----------|
| | No Stenosis | 1 Vessel | 2 Vessel | 3 Vessel |
| No Comorbidities | 30.0 | 60.0 | 0.0 | 0.0 |
| Dyslipidemia | 4.9 | 43.9 | 41.5 | 9.8 |
| Hypertension | 5.3 | 56.0 | 29.3 | 9.3 |
| Diabetes mellitus | 7.1 | 46.4 | 32.1 | 14.3 |

The majority of 60% of patients had single-vessel stenosis in a group without comorbid diseases. In the group of patients with dyslipidemia, 43.9% had one-vessel stenosis, 41.5% had two-vessel stenosis, and 9.8% had three-vessel stenosis. In the hypertension group, 56.0% had one-vessel stenosis, 29.3% had two-vessel stenosis, and only 9.3% had three-vessel stenosis. Whereas in the group of patients with DM, there were 46.4% who had 46.4% one-vessel stenosis, 32.1% two-vessel stenosis, and 14.3% 3-vessel stenosis. The results showed that more patients with diabetes had stenosis in three vessels than those with dyslipidemia and hypertension.

3. Analysis of Coronary Artery Stenosis Based on the Comorbidities

Table 3. Analysis of Coronary Artery Stenosis Based on the Comorbidities

| Comorbidities | Stenosis ≥ 2 vessels | | Stenosis < 2 vessels | | Total | OR | p-value |
|-------------------------------------|--------------------------------|------|----------------------|------|-------|------|----------------|
| | n | % | n | % | | | |
| | History of Dyslipidemia | | | | | | |
| ▪ Yes | | | | | | | |
| ▪ No | 20 | 19.0 | 21 | 20.0 | 41 | 39.0 | 1.761 0.212 |
| | 15 | 14.3 | 49 | 46.7 | 64 | 61.0 | |
| History of Hypertension | | | | | | | |
| ▪ Yes | 24 | 22.9 | 51 | 48.6 | 75 | 71.4 | 0.813 0.647 |
| ▪ No | 11 | 10.5 | 19 | 18.1 | 30 | 28.6 | |
| History of Diabetes mellitus | | | | | | | |
| ▪ Yes | 12 | 11.4 | 16 | 15.2 | 28 | 26.7 | 3.111 0.007 |
| ▪ No | 23 | 21.9 | 54 | 51.4 | 77 | 73.3 | |

The analysis showed that most of the respondents did not have a history of dyslipidemia with stenosis of fewer than two vessels, in as many as 49 people (46.7%). Based on a history of hypertension, it was found that most of the respondents had a history of hypertension with stenosis of fewer than two vessels, in as many as 51 people (46.7%). Meanwhile, based on the history of DM, it was found that most of the respondents did not have a history of DM with stenosis of fewer than two vessels, in as many as 54 people (51.4%).



The results of bivariate analysis using chi-square with a significance level = 0.05 obtained p -value = 0.212 for a history of dyslipidemia (OR: 1.761), p -value = 0.647 for a history of hypertension (OR: 0.813), and p -value = 0.007 for a history of diabetes mellitus (OR: 3.111). Thus, there is a significant relationship between a history of DM and the risk of stenosis. Patients with DM have a 3.111 times greater possibility of stenosis.

DISCUSSION

The age factor is related to the prevalence of coronary artery disease (CAD) and is an independent predictor of side effects after acute coronary syndrome (ACS) [7]. ACS can occur at a younger age but is rarely accompanied by comorbidities, so the coronary lesions experienced tend not to be extensive and complex [11]. In this study, most respondents were over 45 years old, 26.7% in the two or more vessel stenosis category, and 56.2% in the less than two vessel stenosis category.

Most of the respondents in this study were male, both in stenosis of less than two vessels (42.9%) and stenosis of two or more vessels (25.7%). CHD was more common in men and the risk increases with age, but the increase is sharper in women. Among younger subjects, overall risk factor levels were more favorable. However, with age, this advantage noticeably decreases. The risk of CHD increases at age above 55 years in men and over 65 years in women.

One study on female patients undergoing CAG in Bangladesh found that CAD is increasingly prevalent among the female population of age group 41-60 years, especially in South Asia. The increased risk of CAD in post-menopause is related to the incidence of hypertension at the age of 65 years and over, and also changes in lipid profile such as low HDL and high triglycerides. Endothelial dysfunction, small vessel size, diffuse atherosclerosis, microvascular disease, and endothelial dysfunction play an important role in ischemic events, rather than coronary artery obstruction in the female population [12]. Increases in CHD incidence and age-related mortality in both sexes are associated with increases in total serum cholesterol, blood pressure, BMI, and prevalence of diabetes but are higher in women. In women, BMI and DM have a stronger relationship with coronary death.

The most common risk factors in patients with CHD undergoing revascularization are diabetes mellitus, dyslipidemia, and obesity [11]. The proportion of patients with non-ST-elevation acute coronary syndrome increases with increasing BMI. The data showed that most patients with CHD are classified as type I obesity. Obesity is associated with numerous adverse health outcomes including coronary artery disease, stroke, heart failure, and DM. In this study, 46 respondents (43.8%) had excess BMI (>23 kg/m²). The most common comorbid disease was hypertension with 75 respondents (71.4%), followed by dyslipidemia with 41 respondents (39.05%), and the least was DM with 28 respondents (26.7%). The most common comorbidities were found in males compared to females. In line with other studies the results showed that there was a linear relationship between BMI and the prevalence of comorbidities such as DM, hypertension, and dyslipidemia [13]. Meanwhile, patients in the high BMI group were on average 4.6 years younger ($p < 0.0001$), and there was a lower proportion of women in this group [14]. This study found that there were more obese sufferers at the age of less than 45 years (55.6%), and more in men (70%).

A person with high BMI or largewaist circumference is at high risk for CVD. It is related to altered intermediary risk factors (atherogenic dyslipidemia, hypertension, and DM). The amount of adipose tissue located in the abdominal cavity, also called visceral adipose tissue (VAT), is a major correlate of health risk predicting increased risk of type 2 DM and poor cardiovascular outcomes [15].

1. Dyslipidemia and vessel stenosis

Dyslipidemia is a major independent risk factor for CAD, that is routinely assessed for the purpose of assessing cardiovascular risk, an especially important determinant of atherosclerosis leading to CVD. Atherogenic dyslipidemia is associated with an increased risk of Silent Myocardial Infarction and CAD in patients with type 2 diabetes and LDL cholesterol levels <3.35 mmol/L [16].

The research of [17] showed that prevalence of hypercholesterolemia, hypertriglyceridemia, high levels of LDL-C, and low levels of high density lipoprotein (HDL)-C are reported to be 41.6, 46.0, 35.5, and 43.9%, respectively in both sexes in the Iranian population. Among men, total cholesterol baseline level was significantly associated with the risk of myocardial infarction (MI). Similarly, this study found that more men (70.7%) have dyslipidemia than women (29.3%). As many as 43.9% of dyslipidemic patients had one-vessel stenosis, 41.5% had two-vessel stenosis, 9.8% had three-vessel stenosis, and 4.9% had no stenosis. This is consistent with other studies that hyperlipidemia, modest hypercholesterolemia, metabolic syndrome, and low HDL-c are co-associated with multivessel CAD regardless of CVD risk factors [18].



Hypertriglyceridemia and low HDL cholesterol are more common in patients with CAD than those with hypercholesterolemia [19]. Hyperlipidemia in atherosclerotic plaques results in the recruitment and migration of monocytes and other immune and inflammatory cells into the vascular subendothelial layer. Activated macrophages express scavenger receptors to facilitate engulfment of native and oxidized low-density lipoproteins, forming foam cells which, along with other inflammatory cells, promote the production of chemokines and cytokines. These mechanisms operate in a feed-forward cycle, promoting the development of atherosclerotic lesions in an inflammatory environment [20].

Dyslipidemia is also associated with an increase in other co-morbidities. The percentage of patients with type-2 DM, hypertension, and a family history of CVD was higher in subjects with atherogenic dyslipidemia [17] [19]. In this study, 50% of patients had one co-morbidity, 34.3% had two co-morbidities, and 5.7% had three co-morbidities. There were 12.4% of patients who were recorded as having no comorbidities. There were 34.1% of patients who had dyslipidemia with DM, and 65.9% had dyslipidemia with hypertension. These findings are related to endothelial dysfunction, small vessel size, diffuse atherosclerosis, microvascular disease, and endothelial dysfunction, which play an important role in ischemic events.

2. Hypertension and vessel stenosis

Hypertension is an atherosclerosis factor and associated with several malfunctions in the cardiovascular system such as malignant ventricular arrhythmias, development of atherosclerosis, and sudden cardiac death after MI [6]. Hypertensive patients experience an increased presence, extent, and severity of coronary atherosclerosis and are likely to experience an increased risk of major adverse cardiac events compared with patients without hypertension, regardless of other clinical risk factors and the presence of obstructive CHD or CHD grade [21].

Previous studies have shown T2DM duration (> 10.5 years) and systolic blood pressure (≥ 140 mmHg) are clinically relevant predictors of CAD, while serum HDL-C level offers negative predictive value. Age, male sex, BMI, and HDL-C were noted as clinically relevant univariate predictors of CAD [22]. The lowest systolic (decreased to 90-114 mmHg) and lowest diastolic (decreased to 60-74 mmHg) pressure in people without cardiovascular disease were associated with the lowest risk for developing CAD.

Hypertensive patients showed greater plaque expansion and stenosis severity, as well as a lower plaque prevalence compared to patients without hypertension. In this study, 56.0% of hypertensive patients had one-vessel stenosis, 29.3% had two-vessel stenosis, and 9.3% had three-vessel stenosis. This number is more than in patients with DM and dyslipidemia. In line with a previous study about relationship of hypertension to coronary atherosclerosis and cardiac events show that hypertensive patients had a greater prevalence of obstructive lesions in 1, 2, or 3 vessels ($p < 0.001$). Hypertensive patients have stenosis of more than $\geq 50\%$ of the proximal and middle coronary arteries and their side branches. In terms of plaque characteristics, any non-calcified or calcified plaques were found more in hypertensive patients than in non-hypertensive patients [21]. Complicated and diffuse coronary artery lesions are seen in patients with CHD-HT, and arterial hypertension can be considered a risk factor for complex coronary lesions in patients with ischemic heart disease. The combination of hypertension and CHD can increase the occurrence of coronary atherosclerosis through mechanisms such as affecting the shear forces of blood flow, the coronary endothelial function, the permeability of the blood vessel walls, the adhesive characteristics of platelets, and remodeling of the blood vessel walls [23].

3. DM and vessel stenosis

DM besides metabolic disease is a vascular disease, associated with extensive atherosclerosis and complications, which the process commences earlier in age, progresses faster, and is associated with more complications. It can also accelerate the development of stable plaques into unstable plaques or plaque rupture, leading to thrombosis and triggering acute coronary syndrome and even death [24].

DM increases the risk of ACS because atherosclerotic plaques in DM patients have a different composition and facilitate rupture and ACS. Evidence from imaging studies in patients with T2DM indicates a high prevalence of CAD [22]. Besides that, patients with DM show an increase in long-term mortality compared to non-diabetic patients who experience ACS [7].

DM was also associated with higher rates of obesity, hypertension and hyperlipidemia. Bad lesions that occur are associated with risk factors such as DM, dyslipidemia, and decreased kidney function [11]. Another study showed there are



significant differences between diabetic and non-diabetic patients in men with myocardial infarction regarding certain risk factors such as age, hypertension, and hypertriglyceridemia in patients with DM whereas smoking and family history are dominant factors in non-diabetic patients [2].

The result of this study showed that DM was associated with vascular stenosis, but not dyslipidemia and hypertension. DM sufferers have a 3.11 times greater chance of experiencing coronary artery stenosis. Consistent with research conducted by [8], the significant predictors of CAD were male gender, age 45 years or older, history of DM, and history of current/previous smoking. Prior hypertension, prior dyslipidemia, and family history of CVD were not significantly associated with CAD.

Diabetes can increase the risk of multi-vessel coronary disease, chronic total occlusion, and can cause severe stent thrombosis, stroke, silent myocardial infarction, and other major side effects after PCI [6]. In this study, 46.4% of diabetic patients had one-vessel stenosis, 32.1% had two-vessel stenosis, and 14.3% had three-vessel stenosis. The percentage of diabetes mellitus patients who have three-vessel stenosis is higher than dyslipidemia and hypertension. There were 63 patients (60%) with significant stenosis, i.e. > 50% stenosis of the left main coronary artery or >70% of the other epicardial coronary artery, which was indicated for PCI. Coronary intervention can be performed during the same laboratory session as the diagnostic catheterization [25]. In line with a study that investigated the duration of T2DM as a determinant of severity of coronary stenosis found that score of zero was observed in 62 (24%) subjects, while 64 (24.7%) subjects had mild coronary calcification, and severe coronary calcification was observed in 57 (22%) patients [22].

The number and stenosis of coronary arteries can be influenced by the course of comorbidities, and the more the number of coronary artery blockages, the wider the possibility of infarct locations. The high-risk lesions are lesions that affect the three coronary and left main arteries. More frequent injury to the left coronary artery is influenced by the presence of elastic fibers in the intima tunica of the left coronary artery, which is less than that of the right coronary artery. Elastic fibers are associated with weak resistance to stress [26].

CONCLUSIONS AND SUGGESTIONS

Comorbid disease is one of the modifiable risk factors for coronary heart disease. Comorbid diseases contribute to the atherosclerotic process leading to coronary artery stenosis. Stenosis can occur in one vessel or multi vessels, whereas stenosis in one vessel is more common than stenosis in two or more vessels. Stenosis mainly occurs in LAD, followed by LCx and RCA.

Among comorbidities, hypertension is the most common disease, followed by dyslipidemia and DM. Meanwhile, DM sufferers have a 3.11 times greater chance of experiencing coronary artery stenosis.

The results of this study are expected to have implications for improving cardiovascular nursing care by increasing promotion and prevention of cardiovascular risk through lifestyle modifications and pharmacological management, such as antihypertensive and cholesterol-lowering drugs in high-risk individuals, to prevent the onset of future CAD.

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ETHICAL CONSIDERATIONS

I. FUNDING STATEMENT

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II. CONFLICT OF INTEREST STATEMENT

There is no conflict of interest in this study.

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