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Smoking Parameters in Coronary Heart Disease Patients Treated at Dr. Hasan Sadikin General Hospital Bandung, Indonesia

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Abstract

The association between smoking and coronary heart disease (CHD) has been studied extensively, though smoking parameters that contribute to the development of CHD may still need to be studied further. This cross-sectional study aimed to describe the characteristics of smoking parameters, including the number of cigarettes smoked, age when started smoking, duration of smoking, and cessation of smoking, in CHD patients treated at Dr. Hasan Sadikin General Hospital, Indonesia. CHD patients aged ≥18 years were included from the cardiology outpatient clinic and hospital wards. Smokers (current smokers/quit smoking <6 months) and ex-smokers (quit smoking ≥6 months) were considered patients who had a history of smoking. The Brinkman index, i.e., duration of smoking x number of cigarettes/day, was used to measure the degree of smoking that were categorized into mild, moderate, and severe smokers. Eighty-seven subjects diagnosed with CHD were recruited in this study. Seventy-seven percent of the subjects were male, and the mean age of subjects studied was 58.5±10.4 years. Among all subjects, a history of smoking was found in 66.7% (37.9% smokers and 28.7% ex-smokers), with all composed of male subjects. The age of subjects who had a history of smoking was 20 (15–35) years. Most were moderate smokers (74.1%) from Brinkman Index measurement. Smoking history has a significant association with male sex, lower total cholesterol, and lower LDL levels (p-value<0.05).

Keywords: Brinkman Index, coronary heart disease, coronary heart disease risk factor, smoking, smoking parameter

Introduction

Coronary heart disease (CHD) is still the number one cause of death in the world. Epidemiological data in Indonesia showed that 26.4% of deaths were caused by CHD. Based on the National Basic Health Research (*Riset Kesehatan Nasional*/ Riskesdas) data in 2018, CHD prevalence in all ages was 1.5%. In overcoming this problem, primary prevention has become an obligation and has been implemented as policy by the Indonesian Ministry of Health, including better control of modifiable risk factors of CHD, such as control of associated diseases like hypertension, diabetes mellitus, and dyslipidemia; changing sedentary behavior, weight reduction, and smoking cessation.[1–4]

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As a preventable risk factor of CHD, smoking cessation and avoiding secondhand smoke exposure have been strongly encouraged for patients and their families. Active smoking and secondhand smoke exposure cause more than 30% of CHD. Indonesia has the highest prevalence of smoking among Southeast Asian countries and even, according to the Global Adults Tobacco Survey (GATS) in 2011, has the highest number of active smokers, consisting of 67% male (±57.6 million people) and 2.7% female (±2.3 million people) with the prevalence of 33.8% in the ≥15 years old population.[2,3,5,6]

The exact mechanism of cardiovascular damage due to smoking is not well established. It is thought to be related to the effect of smoking on endothelial function, where smoking causes oxidative processes and negatively affects platelet function, fibrinolysis, inflammation, and vasomotor function, which can lead to CHD. Framingham's study provides evidence regarding the cardiovascular effect of cigarette smoking which states it is estimated that cigarette

smokers have a two-fold risk of developing CHD in comparison to non-smokers. The risk also multiplies with the increasing amount of smoking among smokers. The study also identified cigarette smoking as an independent risk factor for sudden cardiac death.[5–7]

In comparison to the age of smoking initiation, smoking at age 12 or younger than 12 years had an increased risk of all-cause mortality in the CHD, MI, and angina pectoris.[8]Compared to never-smokers, regardless of initiation age, ever-smokers had significantly higher risk of all atherosclerotic diseases. There is a statistically significant trend between younger initiation and higher risk for CHD (p for trend <0.001). According to the previous study, people who smoked ≤ 9, 10–19, and ≥20 cigarettes per day had a substantially higher risk of dying from all causes, CVD and cancer, regardless of the specific type of CVD. The risk of dying from CVD and cancer has returned similar to that of never smoker after 20 and 30 years since quitting.[8,9]

The Framingham study also includes important findings regarding the benefit of smoking cessation from a cardiovascular perspective. Filion et al.[7] mentioned that the risk of CHD in participants who continue to smoke after their baseline exam is twice higher than participants who quit. Galluci et al.[3] found that cessation at an early age (40 years) has a 90% reduction in the risk of death. Though the association between smoking and CHD has been studied extensively, smoking parameters that may be beneficial for patient education strategies, such as the duration of smoking, amount of smoking, and initiation of smoking, which contributes to the development of CHD, may still need to be studied further, especially in Indonesia where such study has not been conducted. This study describes the characteristics of smoking parameters of CHD patients in our hospital outpatient clinics.[3,4,7,8]

Methods

This cross-sectional study was carried out between September and December 2019 in the Cardiology and Vascular Medicine Department of Dr. Hasan Sadikin General Hospital Bandung, West Java, Indonesia. This study has been approved by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital with the exemption number LB.02/02/X.6.5/339/2021. Established CHD patients or patients who had acute coronary syndrome (ACS) episodes aged ≥18 years from the outpatient clinic and hospital ward were included in this study. Participation was voluntary, and informed consent was obtained before data collection. Patients with a primary diagnosis of non-cardiac diseases who did not receive any CHD therapy were excluded. Demographical data, such as sex, age, educational degree, risk factors of CHD, and smoking parameters, were obtained through interviews. Patients who had a history of smoking but lack of smoking parameters data were excluded. Risk factors of CHD, such as hypertension, family history of coronary heart disease (CHD), diabetes mellitus, dyslipidemia, low physical activity, and smoking status, were obtained through interviews. Low physical activity was defined as subjects who exercised <30 minutes/day or <3.5 hours/week. The smoking status of the subjects was classified as smokers, ex-smokers, and non-smokers. Smokers were defined as subjects who were still smoking by the time of data collection, ex-smokers were smokers that who had smoking ≥6 months, and non-smokers were those who had never routinely smoked in their lifetime. Smokers and ex-smokers were considered patients who had a history of smoking.

For subjects who had a history of smoking, further interviews regarding smoking parameters were done. Smoking parameters in this study include the amount of smoking, duration of smoking, initiation of smoking, duration of smoking cessation, and the Brinkman Index. The amount of smoking was defined by how many cigarettes the subject smoked per day. The smoking duration was how long subjects were smokers, initiation of smoking was the age subjects started smoking, and duration of smoking cessation was defined by the amount of time subjects had quit smoking, if ever. The Brinkman index was used to measure the degree of smoking, which was composed of the duration of smoking in years multiplied by the number of cigarettes per day. Based on the Brinkman Index, the degree of smoking was categorized as mild smokers (1–199), moderate smokers (200–599), and severe smokers (>600). Physical examination, i.e., blood pressure measurement, heart rate measurement, and BMI calculation, was carried out. Laboratory examination such as lipid profile (total cholesterol, LDL, HDL, triglycerides) and fasting blood glucose (FBG) was taken from medical records.

Statistical analysis was conducted using IBM SPSS Statistic Version 26. Normality test was conducted on numerical data using Shapiro-Wilk or Kolmogorov-Smirnov test. Categorical data were presented in percentages, and numerical

data was presented in mean and standard deviation if the distribution was normal and in median and range if not. Bivariate analysis comparing two groups, i.e., patients who had a history of smoking and those who did not, was conducted using an independent t-test or Mann-Whitney for numerical data and Chi-square or Fisher test for categorical data.

Results

Eighty-seven subjects diagnosed with CHD were recruited in this study as shown in Table 1. Seventy-seven percent of the subjects were male, and the mean age of the subjects was 58.5 ± 10.4 years. Most of the subjects had a secondary school level of education, composed of 48.3% of the total population. Among all subjects, a history of smoking was found in 66.7% (37.9% smokers and 28.7% ex-smokers) of subjects, followed by low physical activity (59.8%), hypertension (56.3%), diabetes (31%), and dyslipidemia (11.4%). Male sex had a significant association with a history of smoking (p-value<0.05) as shown in Table 2.

Subjects who had a history of smoking, as shown in Table 1. The average age of subjects

Table 1 Baseline Characteristics by Smoking Status

Variable	n=87	Overall (n,%)	Non-smokers (n=29)	Smokers (n=33)	Ex-smokers (n=25)
Male	67	67 (77)	9 (31)	33 (100)	25 (100)
Age, years	67	58.5±10.4	58.3 ± 11.6	57.2 ± 10.3	60.2 ± 9.2
Education	87				
Primary school		19 (21.8)	8 (27.6)	7 (21.2)	4 (16)
Secondary school		42 (48.3)	13 (44.8)	16 (48.5)	13 (52)
College		26 (29.9)	8 (27.6)	10 (30.3)	8 (3)
Modifiable risk factors					
Low physical activity	52	52 (59.8)	14 (50)	17 (51.5)	21 (84)
Hypertension	49	49 (56.3)	17 (58.6)	17 (51.5)	15 (60)
Diabetes mellitus	27	27 (31)	10 (34.5)	9 (27.3)	8 (32)
Dyslipidemia	10	10 (11.4)	4 (13.8)	3 (9.1)	3 (12)
Physical examination					
Systolic blood pressure, mmHg	87	118 (90–160)	120 (90–160)	110 (90–150)	120 (90–160)
Diastolic blood pressure, mmHg		78 (60–100)	80 (60–90)	70 (60–100)	77 (60–90)
Body mass index (BMI), kg/m^2	80	23.4 (16.6–38)	23.4 (16.6–38)	22.6 (16.6–31.2)	23.4 (19–28.9)
Laboratory measurement					
Fasting blood glucose (FBG), mg/dL	65	124 (77–487)	129 (93–487)	124 (77–365)	129.5 (95–318)
Total cholesterol, mg/dL	62	173.6 ± 37.6	190.8 ± 40.2	162.5 ± 28.5	169.9 ± 42.7
LDL, mg/dL	62	114.2 ± 32.4	128.3 ± 35.8	107.4 ± 22	106 ± 39.7
HDL, mg/dL	62	38 (20–116)	41 (21–97)	37.5 (24–116)	36 (20–51)
Triglycerides, mg/dL	59	132 (70–845)	149 (70–439)	131.5 (73–314)	144 (71–845)

Table 2 Differences in Characteristics by History of Smoking

Variable	(n=87)	History of Smoking		p-value
		Yes (n=58)	No (n=29)	
Male	67	58 (100)	9 (31)	<0.001
Age, years	87	58.5±9.9	58.3±11.6	0.914
Education	87			0.656
Primary school		11 (19)	8 (27.6)	
Secondary school		29 (50)	13 (44.8)	
College		18 (31)	8 (27.6)	
Modifiable risk factors				
Low physical activity	52	38 (65.5)	14 (50)	0.168
Hypertension	49	32 (55.2)	17 (58.6)	0.760
Diabetes mellitus	27	17 (29.3)	10 (34.5)	0.623
Dyslipidemia	10	6 (10.3)	4 (13.8)	0.635
Physical Examination				
Systolic blood pressure, mmHg	87	118 (90–160)	120 (90–160)	0.388
Diastolic blood pressure, mmHg	87	72.5 (60–100)	80 (60–90)	0.587
Body mass index (BMI), kg/m^2	80	23 (16.6–31.3)	23.4 (16.6–38)	0.285
Fasting blood glucose (FBG), mg/dL	65	124 (77–365)	129 (93–487)	0.779
Total cholesterol, mg/dL	62	164.8 ± 33.3	190.8 ± 40.2	<0.01
LDL, mg/dL	62	107 ± 28.3	128.3 ± 35.8	0.01
HDL, mg/dL	62	37 (20–116)	41 (21–97)	0.096
Triglycerides, mg/dL	59	132 (71–845)	149 (70–439)	0.785

was similar, with the oldest average age being 60.2±9.2 years in the ex-smoker population. Most subjects, regardless of their smoking status, had hypertension, with the highest number in the ex-smoker population. Both dyslipidemia and diabetes were most commonly found in

Table 3 Smoking Parameters of Subjects

Variable	n	Description (n,%)
Age of started smoking, years	58	20 (15–35)
Amount of smoking, cigarette/day	58	12 (3–36)
Duration of smoking, years	58	32.5 (18–54)
Duration of smoking cessation, years	25	5 (1–30)
Brinkman index classification, %	58	
Mild smokers		6 (10.3)
Moderate smokers		43 (74.1)
Severe smokers		9 (15.5)

the non-smoker population, 11.4% and 31%, respectively. The median BMI in the smoker population was 22.6 (16.6–31.2), making it lower compared to the other two groups. From laboratory measurement, non-smokers had the highest average for total cholesterol, LDL, and HDL; the mean and median were 190.8±40.2 mg/dL, 128.3±35.8 mg/dL, and 41 (21–97) mg/dL, respectively. As for triglycerides and FBG, ex-smokers had the highest mean and median, which were 144 (71–845) and 129.5 (95–318), respectively. Smoking history has a significant association with total cholesterol and LDL (p-value <0.05) as shown in Table 2.

Smoking parameters are shown in Table 3. The mean age of smoking is 20 years old, mean amount of smoking is 12 cigarette/day. The mean duration of smoking is 32.5 years and mean duration of smoking cessation is 5 years. The degree of smoking measured by the Brinkman Index, it was found that most were moderate smokers (74.1%), followed by severe smokers (15.5%) and mild smokers (10.3%)

Discussion

One of the observations made by Cheezum et al.[9] regarding the gender of smokers revealed male population smokes more than the female population, which may be caused by the increasing trend of cigarette smoking beginning first in the male population. This observation is consistent with the result of this study which found that the subjects who had a history of smoking were all male. From bivariate analysis, it was found that the male sex was significantly associated with a history of smoking (*p-value* <0.001). A report by the U.S. Surgeon General in 2002 regarding women and smoking discussed that for women younger than 50 years, smoking is the cause of the majority of CHD, which in this study comprised 5% of the total population. In 2001, Huxley and Woodward[10] reported a pooled adjusted female-to-male relative risk ratio (RRR) of smoking compared to no smoking for CHD was 1.25. Although cardiovascular risk factors affect young, healthy female smokers earlier compared to young, healthy male smokers, other risk factors also must be explored in the women population, including those related to pregnancy or autoimmune disorders, as smoking was a prominent risk factor for the male population.[3,9,11]

According to the smoking parameter, this study was in line with the previous study. People who smoked ≤ 9, 10–19, and ≥20 cigarettes per day had a substantially higher risk of dying from all causes, CVD and cancer, regardless of the specific type of CVD, as seen in this study with the mean amount of smoking was 12 cigarette/day. Differing from the previous study, initiation of smoking at 12 years old or younger had an increased risk of all-cause mortality in the CHD, meanwhile, this study showed that the mean age of started smoking is 20 years old. In addition, compared to never-smokers, regardless of initiation age, ever-smokers had a significantly higher risk of all atherosclerotic diseases. The risk of dying from CVD and cancer causes returned similar to that of never smoking after 20 and 30 years since quitting. Meanwhile, this study showed the mean of smoking cessation duration was only 5 years.[8,9]

The influence of smoking on blood pressure is still conflicting. In a study by Virdis et al.[12] in 2010, although cigarette smoking has an acute hypertensive effect, the consequences of chronic smoking directly inducing hypertension are not yet available. Furthermore, it was stated that smoking cessation does not necessarily reduce blood pressure values. In this study, the ex-smoker population had the highest prevalence of hypertension, as much as 60%, if compared to the two other populations. The median of both systolic and diastolic blood pressure was within the normal range, which was 118 (90-160) and 78 (60-100) mmHg, respectively. Smoking and its effect in activating the sympathetic nervous system and increasing insulin resistance may elevate blood pressure, thus causing arterial stiffness, which elevates hemodynamic stress and damaged vascular endothelium.[3,13]

The multifactorial etiology and molecular mechanism of T2DM were already linked to smoking due to the increased incidence of both insulin resistance and T2DM itself in smokers, though the exact mechanism is still ill-defined. Chemical products and free oxidative radicals of cigarettes may be responsible for processes that lead to smoke-related insulin resistance. Hence diabetes or smoking was also thought to have an epigenetic mechanism related to insulin sensitivity or hypothesized to have a direct impact on the pancreatic beta-cell function. Interestingly, in this study, the diabetes population was the highest in the non-smoker population. These findings may be explained because the non-smoker population may have more non-smoking risk factors compared to the smoker population; thus, CHD may be caused by these other modifiable risk factors.[3]

Aside from the direct effect of smoking on endothelial function, smoking also has an indirect effect on endothelial damage via serum lipids which can enhance it. In this study, dyslipidemia was the highest in non-smokers, making up 13.8% of the non-smoker population. The lipid profile of the subjects in this study was the highest in the non-smoker population. From the mean of LDL and triglycerides of subjects, regardless of their smoking status, they haven't reached the ideal LDL target (<70 mg/dL) and have a triglyceride level >150 mg/dL. The overall mean of LDL and triglycerides was 114.2±32.4 and 173.6±37.6 mg/dL, respectively. In this study, smoking history has a significant association with total cholesterol and LDL (p-value<0.05), though the highest level was in the non-smoker population. More or less the same with the findings regarding the diabetic population, higher lipid profile results, that the non-smokers population in this study may have more non-smoking risk factors compared to the smoker population. Another theory was maybe patients who had a history of smoking had more aggressive treatment by statins compared to those in the non-smoker population and thus had better lipid profile measurements. There was no significant association between smoking history with HDL and triglyceride levels. Pathophysiologically, smoking induces the oxidation of lipids and oxidative modified LDLs captured by macrophages and become foam cells, which later on are the initiators of plaque formation processes. In another study, passive smoking was also linked to negative effects on glucose and lipid parameters, increasing the risk of diabetes and cardiovascular disease. Furthermore, it was observed that smoking cessation improves HDL-cholesterol though this was not what we found in the study as the HDL level in the ex-smoker population was lower than in non-smokers and smoker population. Results of some other studies also revealed that regarding total cholesterol, LDL, and triglycerides levels, there was no significant association.[3,14]

Physical inactivity has been identified as an important risk factor in the development of CHD. As a primary prevention, regular physical activity decreased the incidence of cardiovascular diseases (CVDs) because at the endothelial level, regular physical activity attributed to higher expression and phosphorylation of NO synthase, which made more effective radical scavenger system, endothelial rejuvenation by circulating progenitor cells (CPCs), and promotes the growth of preexisting coronary vessels by angiogenesis. As a secondary prevention, exercise training improves endothelial function and stops coronary stenosis progression by an atherosclerosis effect on platelets and leukocytes. Myocardial perfusion also may be improved by vasculogenesis on the capillary level. Most of the subjects in this study exercised less than 30 minutes per day or 3.5 hours per week, which is still less ideal than what the exercise guidelines recommend. Interventional studies showed that exercise training might reduce cardiovascular event rate in patients with CHD and reduce its mortality, which raises the urgency to promote physical activity after CHD. In this study, most subjects, regardless of their smoking status, still had a low physical activity.[15]

The adverse effects of cigarette smoking suggest a dose-response relationship between cardiovascular disease which means that the risk of developing CAD increases with the increase of smoking parameters, such as duration of smoking and number of cigarettes smoked. Risk Estimator Plus also distinguishes between smokers and never-smokers, and it was found that after 5 years, the cardiovascular risk of "ex-smokers" is equivalent to the risk of persons who have never smoked. About 52% of ex-smokers in the study had quit smoking more than 5 years, and the median was 5 (1–30) years, which means the risk of this population may be the same as those in the non-smoker population. Nevertheless, this statement is not well proven, and the time frame of the cardiovascular risk following cessation is still not well defined. In the National Health Interview Survey in the United States, smoking was related even to young people; thus, the main recommendation is abstinence from a very early age. Speaking in generality, a significant number of Indonesians tried smoking for the first time before 18 years old, and the number is increasing with the age of first-time smokers getting younger. According to the National Basic Health Research in Indonesia, the prevalence of smoking in the 10–18 years old population in 2018 was 9.1%, with the percentage keep increasing from 2013 and 2016, which was 7.2% and 8.8%, respectively.[2, 6,16]

A study that explored the impact of smoking behavior on the echocardiographic measure of the heart revealed that an increased duration of smoking was associated with worse left ventricle (LV) structure, i.e., increased mass and relative-wall thickness (RWT), worse LV diastolic function, and worse right ventricle (RV) function. Increased amounts of cigarettes smoked per day were also associated with increased left ventricle

mass (LVM), worse diastolic function, worse LV geometry, and worse RV function. Lifetime pack-years, or in this study as measured by the Brinkman Index, were associated with increased LV, worse LV geometry, and worse RV function. According to the Brinkman Index, most smokers in this study were moderate smokers (74.1%). According to a study by Salehi et al.,[17] who aims to investigate the extent of smoking to the number of occluded arteries and the severity of CAD, found that smoking was not significantly associated with the number of damaged coronary arteries, though it was associated with the severity of CAD in a way that smoking was associated with the occlusion of the left anterior descending (LAD) artery and smokers may be more likely to have non-proximal coronary artery occlusion which may be owing to the effect of cigarette and nicotine of the vascular epithelium. A study by Cheezum et al.[9] also revealed that current smokers were associated with the presence, extent, and severity of CAD if compared to non-smokers. Subjects that quit smoking 12 years before CTA had a lower risk of non-calcified plaque, calcified plaque, and obstructive CAD compared to current smokers if compared to current smokers. Quitting smoking is associated with a reduced risk of total mortality with a pooled relative risk (RR) of 0.64 (95% CI, 0.58–0.71). Furthermore, smoking cessation is also associated with a decreased incidence of second cardiac events, including cardiac death and non-fatal myocardial infarction (MI) in patients with a previous history of MI.[18]

Firstly, the limitation of this study was a cross-sectional study with small sample sizes. Secondly, data was collected from interviews which might cause recall bias, and some laboratory findings were missing from medical records. For example, the degree of smoking was measured subjectively from the Brinkman Index and was not further confirmed by laboratory measurements, such as CO_2 level or nicotine levels in the blood. Thirdly, statin dosage was not included in this study thus patients who had high-intensity or moderate-intensity statin which may affect the result of their lipid profile measurements. Lastly, the history of secondhand smoke, an important parameter, was not interviewed in this study.

In conclusion, male population smokes more than the female population. Those who had a history of smoking started smoking at a relatively young age and were moderate smokers, whereas those who never smoked had higher LDL and total cholesterol levels. Those who had quit smoking on average had quit smoking for more than a year. Further prospective studies may be needed to determine smoking parameters associated with morbidities and mortalities.

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