

Association of Risk Factors for Coronary Artery Disease with The Incidence of Abdominal Aortic Calcification on Abdominal CT-Scan Imaging In Haji Adam Malik General Hospital

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ABSTRACT

Introduction: Coronary Artery Disease (CAD) is the one of manifestation for cardiovascular disease and a cause of death and disability. Abdominal aortic calcification (AAC) has been shown to be strongly associated with atherosclerosis and CAD events. This study to investigated the association of risk factors for CAD with the incidence of AAC on abdominal CT Scan.

Method: This study was an observational analytic study with a cross-sectional design on 105 patients who underwent abdominal CT scans with/without intravenous contrast at Radiology Department of H. Adam Malik General Hospital. AAC score was identified calcification on the abdominal aorta (from 1 cm above the origin of the celiac trunk to 1 cm below the iliac bifurcation) use the Agatston method. Analyzing the association CAD risk factors such as gender, age, diabetes mellitus, hypertension, smoking, and alcohol and AAC score.

Results: The results of the analysis using the Chi Square comparative test showed that there was a significant relationship between age ($p=0.000$), hypertension ($p=0.017$), diabetes ($p=0.006$), in othe words there is no significant relationship between gender ($p=0.613$), smoking ($p=0.22$) and alcohol ($p=0.28$) with AAC score.

Conclusion: There is a significant relationship between age, hypertension and diabetes with the AAC score.

Abdominal aorta, Coronary artery disease, Vascular calcification, Atherosclerosis, Agatston score, Computed tomography

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INTRODUCTION

Cardiovascular disease (CVD) is the number one cause of death globally each year, which is a group of disorders of the blood vessels and heart, includes coronary artery disease (CAD) and cerebrovascular disease. In 2019, World Health Organization (WHO) estimated 17.9 million people in the world died caused CVD which is 32% of all deaths in the world. 7.3 million CVD death due to CAD, where 1/3 of these deaths occur in people under 70 years of age.[1] According to the Basic Health Research (Riskesdas) in 2018, the incidence of heart and blood vessel disease is elevated. Individuals in Indonesia suffer from CAD at least 15 out of 1000 people, or around 2,784,064.[2] Atherosclerosis is a pathological process that underlies most cases of CAD, cerebrovascular disease and aortic and peripheral vascular disease. By Multiple Risk Factor Intervention Trial, risk factors for atherosclerosis include age, men, genomic abnormalities, family history, hypertension, smoking, diabetes, obesity, physical inactivity, high cholesterol levels, stress, and drinking alcohol.[3,4]

Since the representatives change in the blood vessels has been known to be a form of calcification due to atherosclerosis, many studies have been widely conducted to evaluate the association of calcification with clinical diseases. Mazziotti G et al, arterial calcification is a marker of CAD, and AAC has been shown to be strongly associated with atherosclerosis and cardiovascular disease events.[5] Iribareen et al, measured the

level of aortic calcification though chest X-ray and reported that the level of calcification was associated with CAD and ischemic heart disease. Oei et al, measures coronary artery calcification (CAC) using a CT scan and correlates it with body mass index (BMI), age, gender, smoking, diabetes, and cholesterol level. Wilson et al, related the prevalence and mortality of CAC and cerebrovascular disease by measuring the AAC using lumbar X-rays. Sun and Jang measured abdominal aortic and iliac artery calcification using CT scan and reported the association with hypertension, diabetes, renal dysfunction, CAD and cerebrovascular disease.⁴ According to Jurgens and Goncalves, AAC is correlated with CAC and asymptomatic coronary artery disease. AAC on CT scan is a strong predictor of future cardiovascular events in adults without cardiovascular symptoms.^[6] This research aims to analyze the association risk factors for CAD with AAC score on abdominal CT scans in the General Hospital. H. Adam Malik Medan.

METHOD

Study Site and Subjects

This research is an observational analytic study with *cross sectional* design in patients who perform CT Scan abdomen with/without intravenous contrast at H. Adam Malik Medan General Hospital period September to November 2022 with a total of 105 patients. Excluded patients were patients with a history of surgery that resulted in changes to the abdominal aorta, conditions that made the abdominal aorta difficult to assess, such as abdominal masses and ascites, and with malignancy.

Data Collection

The basic data on subjects age, gender, history of hypertension, diabetes mellitus, smoking and alcohol consumption were obtained through medical records and anamnesis (a questionnaire). Hypertension and diabetes were defined as history of taking medication or identified as the diseases in the medical record or known through anamnesis. Smoking and alcohol consumption were identified by anamnesis (a questionnaire).

Abdominal aortic calcification measurement

Calcification was assessed by 2 readers (a Radiologist and a Radiology Resident, Kappa score >80%) at the abdominal aorta site using multidetector CT scans (Philips Ingenuity 128 and GE Brightspeed) 1 cm over the celiac trunk (proximal) to 1 cm under the iliac bifurcation (distal) quantitatively on axial sections using the Agatston method, where lesions with HU 130 in the area will be automatically calculated. The calcification score was categorized into 0 for no calcification, 1 for 1-99, 2 for 100-399 and 3 for >400 [7] (Fig. 1).

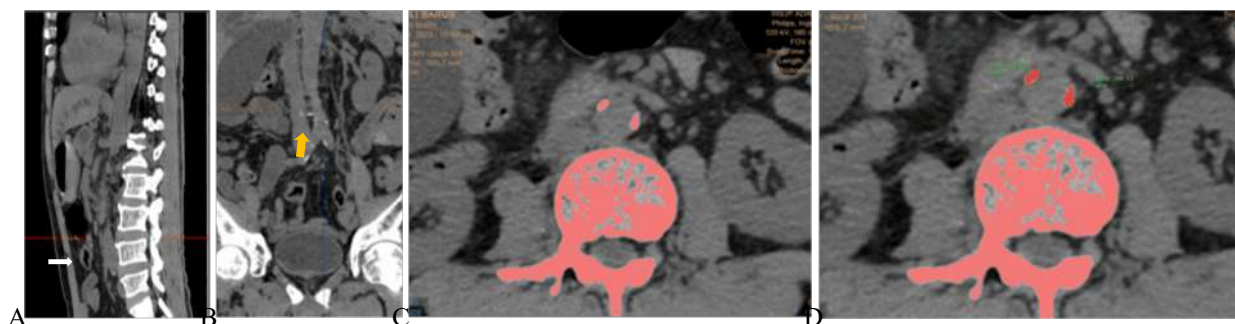


Figure 1. Abdominal Aortic Calcification Scoring by thr Agatston Method axial unenhanced abdominal CT image. A) Sagittal view, to assessed celiac trunk (white arrow), B) Coronal view, to assessed iliac bifurcation (yellow arrow), C) The calcification with attenuation greater than 130 HU level area colour-code pink. A region of interest in abdominal aortic is manually drawn so that only calcification are selected. D).Calcification within the region of interest are selected, and calcium score is automatically calculated according to the Agatston method.

Statistical Analysis

Data will be analyzed descriptively to determine the frequency distribution of each variable demographic characteristics and risk factors. Then continued with inferential analysis to analyze the association between the four independent variables with the incidence of calcification using the Chi Square test. The results of the study were declared meaningful with p value <0.05.

RESULTS

General Characteristics of the Subjects

The characteristics of all the study subjects (n=105) are provided in Table 1. Male composed 56 people (53.3%) of the study sample. More than 25% of the sample was in range 46-55 years old, 20% had hypertension, 17.1% had diabetes mellitus, 38.1% had smoked and 21.9% had consumption alcohol.

Table 1 Characteristics of the subjects

Variable	Frequency	Percentage
Gender		
- Male	56	53.3
- Female	49	46.7
Age		
- 17-25	12	11.4
- 26-35	11	10.5
- 36-45	25	23.8
- 46-55	27	25.7
- 56-65	18	17.1
- >65	12	11.4
Hypertension		
- Yes	21	20
- No	84	80
Diabetes mellitus		
- Yes	18	17.1
- No	87	82.9
Smoking		
- Yes	40	38.1
- No	65	61.9
Drinks alcohol,		
- Yes	23	21.9
- No	82	78.1

Table 2 shows characteristics divided by gender, the greatest age in the male group with age range of 36-45 years, was 15 people (26.8%) while the female group in the age range 46-55 years was 13 people (26.5%). The subjects with hypertension were mostly in the male group with 12 people (21.4%), DM were mostly in the female group with 10 people (20.4%), who smoked the most in the male group with 39 people (69.9%), drink alcohol were all in the male group with a total of 23 people (41.1%), and prevalence of AAC most were found in the male group with 35 people (62.5%) (Table 2).

Table 3 shows the age-adjusted in patient had AAC and risk factors. In general, calcification begins in the age range of 36-45 for all risk factors, both in gender, hypertension, DM, smoking and alcohol consumption. Male who had AAC was 35 people, female 25 people, had hypertension was 18 people, had DM was 16 people, had smoked was 27 people and had drink alcohol was 16 people.

Univariate Analysis

Table 4 shows the Chi Square comparative test showed that there was a significant relationship (p<0.05) between age, hypertension and DM with the incidence of AAC. While between gender, smoking and alcohol showed no significant relationship (p>0.05).

Table 2. Characteristics of the subjects divided by gender

Variable	Male	Female
Age, n (%)		
- 17-25	6 (10.7)	6 (12.2)
- 26-35	4 (7.1)	7 (14.3)
- 36-45	15 (26.8)	10 (20.4)
- 46-55	14 (25)	13 (26.5)
- 56-65	12 (21.4)	6 (12.2)
- >65	5 (8.9)	7 (14.3)
Hypertension, n (%)		
- Yes	12 (21.4)	9 (18.4)
- No	44 (78.6)	40 (81.6)
Diabetes mellitus, n (%)		
- Yes	8 (14.3)	10 (20.4)
- No	48 (85.7)	39 (79.6)
Smoking, n (%)		
- Yes	39 (69.9)	1 (2)
- No	17 (30.4)	48 (98)
Drinks alcohol, n (%)		
- Yes	23 (41.1)	0 (0)
- No	33 (58.9)	49 (100)
AAC		
- Yes	35 (62.5)	25 (51)
- No	21 (37.5)	24 (49)

Table 3 Characteristics of the subjects divided age-adjusted in patient had AAC and risk factors

Variable	Age group						Total
	17-25	26-35	36-45	46-55	56-65	>65	
Gender							
- Male			6 (17.1)	13 (37.1)	11 (31.4)	5 (14.3)	35
- Female			4 (16)	8 (32)	6 (24)	7 (28)	25
Hypertension			1 (5.6)	8 (44.4)	4 (22.2)	5 (27.8)	18
Diabetes Mellitus			1 (6.3)	8 (50)	3 (18.8)	4 (25)	16
Smoking			5 (18.5)	10 (37)	7 (25.9)	5 (18.5)	27
Drink Alcohol			4 (25)	4 (25)	7 (43.8)	1 (6.3)	16

Table 4 Tabel Chi Square comparative with AAC score

Variable	Total N= 105	AAC Score				P value
		0	1-99	100-399	>400	
Gender, n (%)						
- Male	56	21 (37.5)	12 (21.4)	9 (16.1)	14 (25)	0.613
- Female	49	24 (49)	7 (14.3)	6 (12.2)	12 (24.5)	
Age, n (%)						
- 17-25	12	12 (100)	0 (0)	0 (0)	0 (0)	0.000
- 26-35	11	11 (100)	0 (0)	0 (0)	0 (0)	
- 36-45	25	15 (60)	7 (28)	2 (8)	1 (4)	
- 46-55	27	6 (22.2)	6 (22.2)	10 (37)	5 (18.5)	
- 56-65	18	1 (5.6)	6 (33.3)	3 (16.7)	8 (44.4)	
- >65	12	0 (0)	0 (0)	0 (0)	12 (100)	
Hypertension, n (%)						
- Yes	21	3 (14.3)	4 (19)	5 (23.8)	9 (42.9)	0.017
- No	84	42 (50)	15 (17.9)	10 (11.9)	17 (20.2)	
Diabetes, n (%)						
- Yes	18	2 (11.1)	3 (16.7)	6 (33.3)	7 (38.9)	0.006
- No	87	43 (49.4)	16 (18.4)	9 (10.3)	19 (21.8)	
Smoking, n (%)						
- Yes	40	13 (32.5)	7 (17.5)	6 (15)	14 (35)	0.222
- No	65	32 (49.2)	12 (18.5)	9 (13.8)	12 (18.5)	

Table 4 (continuous)

Variable	Total N= 105	AAC Score				P value
		0	1-99	100-399	>400	
Drink alcohol, n (%)						
- Yes	23	7 (30.4)	3 (13)	5 (21.7)	8 (34.8)	0.282
- No	82	38 (46.3)	16 (19.5)	10 (12.2)	18 (22)	

The subjects both male and female had the greatest AAC Score = 0, 21 people (37.5%) and 24 people (49%), where statistically $p = 0.613$ ($p > 0.05$) shows that there is no significant relationship between gender and the incidence of AAC. For age characteristics, the greatest age group was found in the age range of 46-55 years was 27 people, with increasing calcification score as the getting old, this shows that there is a significant relationship between age and AAC ($p = 0.000$). While for other characteristics such as hypertension, DM, smoking and alcohol, were found that more patient didn't have these risk factors, but who had risk factors, the greatest calcification score was at score 3 (>400), and patient who did not have risk factors, the greatest calcification score was at score 0 (no calcification of the abdominal aorta). Table 4 shows a significant relationship ($p < 0.05$) between hypertension ($p = 0.017$), DM ($p = 0.006$), but smoking and alcohol where each value is $p = 0.222$ and $p = 0.282$, which indicates that there is no significant relationship ($p > 0.05$) between smoking and alcohol variables on the incidence of AAC.

DISCUSSION

Arterial calcification is a marker of CAD that is associated with in cardiovascular risk factors and the risk of subsequent cardiovascular event in asymptomatic personally. A metaanalysis showed that the incidence and AAC score increased the risk of cerebrovascular events, death and CAD ($p < 0.0001$) for all groups. Factors such as accumulation of phosphate, hormonal changes, inflammation, metabolic disorders and oxidative stress are involved in the differentiation of vascular smooth muscle cells from osteoblasts leading to mineral deposits in the vessel wall. Multifactorial interactions of these factors contribute to the formation and progression of AAC.[3,8,9]

The research aims to assess the association of risk factors such as hypertension, DM, smoking, alcohol consumption age and gender with AAC. In general, the greatest age group was found in the age range of 46-55 years was 27 people, the female group was at the age of 46-55 years was 13 people (26.5%) and the male group in the age range of 36-45 years was 15 people (26.8%). According to theory, risk factors for atherosclerosis occur in women aged >55 years and men aged >45 years.[10]

This study also showed that with getting old, AAC will be formed ($p < 0.001$) in accordance with previous studies.[3,4,8,11,12] This is attributed to the cumulative role of oxidative stress in the pathogenesis of KAAb. Oxidative stress on vascular smooth muscle cells leads to signaling of osteogenetic differentiation in the vascular wall which will cause calcium deposits thus leading to vascular calcification. Increasing age is also a risk factor for diseases associated with chronic kidney disease, coronary heart disease, neurodegenerative diseases and cancer where increased free radical production also shows a major role in the pathogenesis and development of AAC.[9] In the literature search, no studies were found that showed a negative correlation with age, indicating that age is an important risk factor for AAC.[8]

In this study, there was a difference of males and females in the incidence of AAC, 35 (58.3%) vs 25 (41.7%), but, this difference was not statistically significant. The incidence of AAC in males and females appeared together in the age range of 36-45 years. This is similar with Kim ED et al. which shows the incidence of AAC most often occurs in the middle age group.[4] Chuang ML et al. also showed the prevalence of AAC increased with age in both gender. As a risk factor for atherosclerosis, male have a higher risk than female, therefore gender would be expected as an important determinant in the incidence of AAC.[13] Dixon et al. show female more significantly to had calcification ($p < 0.05$) than male for 60-80 years old. This could be due to changes in hormone levels after menopause in women, where a decrease in estrogen is associated with an increase in LDL-C which can induce vascular calcification.[8]

In this study showed that hypertension has an association with the incidence of AAC ($p = 0.017$), which was also found in previous studies.[4,11,14] Like the study by Kim ED et al. found that hypertension in female was associated with AAC scores, but not in male.[4] Hypertension is an independent risk factor in the progression of atherosclerosis and is associated with intimal calcification as a trigger factor for disease. Much of the prevention of cardiovascular disease, especially coronary heart disease, lies in controlling blood pressure. Calcification of the tunica media and hypertension are closely related, where calcification of the tunica media can decrease the elasticity of the media which contributes to the mechanism of hypertension. Decreased elasticity leads to hardening of the arteries which widening pulse pressure, accelerates pulse velocity, and causing hypertension. Meanwhile, hypertension is an independent risk factor for the progression of atherosclerosis and is associated with intimal calcification as a precipitating factor for cardiovascular disease.[15]

In patients with DM, the presence of AAC may be a risk factor for CAD. This is in accordance with several previous studies showing that DM is a risk factor in the progression of vascular calcification, especially intima and media calcification. This may be due to multifactors such as increased LDL, Vascular Smooth Muscle Cell (VSMC, and Advanced Glycogen End-Products (AGE). In this study, there was a significant association between DM and the incidence of AAC ($p=0.006$). Just like some previous studies that also showed a significant relationship.[8,11,16] This is not like study of Toussanit et al, no significant correlation was found between AAC and DM ($p=0.84$) where the sample used was hemodialysis patients.[16]

Smoking is a risk factor for CAD and atherosclerosis. Further observations showed more calcification in the abdominal aorta than the thoracic aorta, which increased with amount of cigarettes consumed. Several previous studies have shown the effect of smoking on the occurrence of AAC.[3,4,8,11,16] The study by Kim ED et al. there is a weak positive correlation between AAC and smoking in male samples ($r = 0.349$, $p < 0.001$), but not in female samples ($r = -0.006$, $p = 0.934$).[4] The study of Jee et al. also showed similar results where AAC in female smokers was less than male smokers. This could be because the sample of women who smoked was too low, making it difficult to prove the relationship with AAC. In theory, increasing amount and duration of smoking will increase heart rate and blood pressure and stimulate the sympathetic nervous system continuously. Cigarette-induced oxidative stress also contributes to several mechanisms of cardiovascular disease, including endothelial dysfunction, inflammation, and lipid abnormalities. Radiologic studies on the relationship of smoking to vascular calcification have shown that smoking large amounts of cigarettes contributes to calcium formation in the aorta and coronary arteries. In middle-aged male smokers calcification in the coronary arteries will appear 10 years earlier.[17]

The last risk factor discussed in my study was alcohol consumption. The mechanism alcohol causes atherosclerosis is not fully known. Heavy alcohol consumption reduces nitric oxide (NO) production by reducing endothelial NO synthesis against lipoproteins and other plasma components causing endothelial inflammation/oxidative. In response to endothelial dysfunction, the endothelium will follow various humoral changes by depositing calcium in the area. Previous studies have shown that the relationship between alcohol and CAD forms a J curve, where light to moderate drinkers show a reduced risk of coronary heart disease while heavy drinkers and non-drinkers will actually increase the risk of coronary heart disease but the pathophysiologic mechanism remains unexplained. Studies describe various patterns of association between alcohol use and atherosclerosis, namely no significant association, U or J curves, and dose response.[18]

In my study, it showed that all samples who consumed alcohol were in the male group (23 people), where there were 16 people (64%) with the incidence of AAC that appeared in the age range of 36-45 years and most in the age range of 56-65 years. However, there was no statistically significant association between alcohol consumption and the incidence of AAC ($p = 0.282$). All samples who consumed alcohol were tuak. Tuak is a type traditional alcohol beverage made from fermented palm. This study did not divide alcohol consumption into light, medium and heavy due to the difficulty of measuring alcohol levels in the samples studied. Yang et al. showed no association between alcohol consumption and coronary artery calcification in both men and women aged ≥ 45 years.[18]

The limitations of this study are as follows. First, this study is a cross-sectional study that looks at the relationship of AAC incidence with CAD risk factors, not a case-control or cohort study that looks at the impact of calcification on the emergence of CAD. Secondly, the assessment and measurement of AAC was only in patients who were going to have an abdominal CT scan due to certain diseases, not in the healthy population. Third, the variables of hypertension and diabetes were assessed only based on the history of the disease from both history and medical records, no blood pressure measurement and blood sampling were conducted. Fourth, alcohol consumption and smoking were only assessed using history, which the sample may have reported as none to avoid embarrassment. Fifth, this study was conducted in one hospital center with a small sample size.

CONCLUSION

Abdominal aortic calcification is associated with cardiovascular events and mortality, might be mediated through the effect of calcification on vascular functioning and arterial stiffness. AAC is quantified on CT according to the The Agatston method was a strong predictor of cardiovascular event in adults without cardiovascular symptoms. Non-contrast abdominal CT scan used for other indications can provide information about AAC. Accidental findings of AAC can alert clinicians to a potential risk of cardiovascular disease that should be investigated further. There is a significant relationship ($p < 0.05$) between age, hypertension and DM with the incidence of AAC.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and H. Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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