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Hypertension as a Determining Factor in the Rupture of Intracranial Aneurysms, Diagnosed by 64-MDCT Angiography

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Abstract

Background: To determine a correlation between risk factors and the rupture of intracranial aneurysms. **Methods**: A cross-sectional study of 29 patients with a saccular intracranial aneurysm was obtained using consecutive sampling and examination of 64-MDCT angiography. Bivariate statistical analysis using Fisher's exact test was arranged using cross-tabulation to determine the correlation between each risk factor of age, sex, hypertension, and smoking with the occurrence of ruptured intracranial aneurysms. **Results**: The highest incidence of ruptured intracranial aneurysms were in patients aged <60 years (70%), male (75%), experienced hypertension (85%), and were smokers (85.7%). Only the risk factor of hypertension had a correlation with the occurrence of a ruptured intracranial aneurysm ($p < 0.05$). The prevalence ratio of age and sex were 1.0 and 0.9, whereas hypertension and smoking were 2.6 and 1.3. **Conclusions**: The risk factor of hypertension leading to a ruptured intracranial aneurysm was 2.6 times higher than non-hypertensive patients, and as such hypertension is a risk factor associated with the occurrence of ruptured intracranial aneurysms.

Keywords: intracranial aneurysm, hypertension, 64-MDCT angiography

Introduction

The most common cause of subarachnoid haemorrhage (SAH), accounting for 85% of cases, is a spontaneous rupture of an intracranial aneurysm. Although there has been extensive development of multimodal support strategies, SAH is still a disease with high morbidity and mortality that has high fatality rates between 25-50%.[1,2] The incidence of SAH in European populations is around 10-15 people in every 100,000 people each year.[3] Around 10% of patients with intracranial haemorrhage, due to an aneurysm, died before hospital admission and only 30% of patients showed positive results to therapy.[4] As imaging techniques have developed the diagnosis of potential intracranial aneurysm ruptures has increased, and as such the development of appropriate management decisions and therapies by considering risk factors and the morphology of intracranial aneurysms is needed.[5,6] Although the rates of morbidity and mortality due to treatment using coiling and clipping is fairly well known, the treatment of unruptured intracranial aneurysms is still unclear.

An intracranial aneurysm is an abnormal dilation of the artery wall, due to weaknesses which are mainly located in the circle of Willis or more rarely in other intracranial regions such as the medium cerebral artery, pericallosal arteries, and the circle of vertebrobasilar. The basic progression of unruptured intracranial aneurysms and its therapeutic indications remain disputable, resulting in a poor prognosis ofthe ruptured intracranial aneurysm. The only prospective study ever conducted was on Japanese and Finnish populations and showed that the size and location of an aneurysm was a more important risk factor for the potential rupture of the intracranial aneurysm when compared to the patients age and sex.[7] However, retrospective studies have published different results in which hypertension, smoking, age, and gender are more important risk factors for a ruptured aneurysm intracranial.[8] Review of population, hypertension, age, size, early SAH, and site (PHASES) based on geography is also related to the risk of a ruptured intracranial aneurysm. Finnish populations appear to have the highest risk of a ruptured intracranial aneurysm whilst, North American and European populations have the lowest risk.[9]

Data on the risk factors of SAH intracranial aneurysms in Indonesian populations is yet to be published. In this study, the risk factors identifed were age, sex, hypertension, and smoking status in patients with saccular intracranial aneurysms and the relationship between these risk factors and the occurrence of intracranial aneurysm rupture. Multidetector computed tomography angiography (MDCTA) has been widely used in neurovas-cular imaging and is a relatively non-invasive diagnostic tool.[10,11]

Table 1. Risk Factors Associated with Patients with Saccular Intracranial Aneurysms

Risk Factors		Number of Patients	%
Age	≥60 y.o.	9	29.03
	<60 y.o.	20	64.52
Sex	Female	21	67.74
	Male	8	25.81
Hypertension Status	Hypertensive	20	64.52
	Non-Hypertensive	9	29.03
Smoking Status	Smoker	7	22.58
	Non-Smoker	22	70.97

The preferred technique in this current study was 64-MDCTA modalities that were used to determine an intracranial aneurysm.

Methods

This study was an observational analytical research structure using across-sectional approach. The study was conducted retrospectively, based on medical records of patients with saccular intracranial aneurysms, by reviewing imaging with 64-MDCTA from July 2012 to June 2016. The study was conducted in the Radiology Department of the Dr. Kariadi Semarang Hospital. The sample size consisted of 29 patients who had a diagnosis of a saccular intracranial aneurysm, that had already been inspected using 64-MDCT angiography. Patients with arteriovenous malformations, a history of post coiling of the intracranial aneurysms or fusiform shape, and those with incomplete medical records were excluded from this study. The sampling technique used was a consecutive sampling technique.

Information regarding the age, sex, hypertension and smoking status were taken from the medical records of patients from the Dr. Kariadi Semarang Hospital. The risk factors were categorised into those aged ≥60 years and <60 years, female and male, those with a history of hypertension or no hypertension, and smokers and non smokers.

64-MDCT angiography were obtained for all patients with a 64 channel CT scanner (Siemen, Germany) with a slice thickness of 0.5 mm x 64 mm. Rotation time was 0.4 seconds and a standard dose exposure factor was selected. An antecubital vein of the arm was connected to an automatic injector (Double Head MedradStellant, USA) with an 18–20 G needle and 80 mL of 350 mgI/mL of non-ionic contrast media (Iomeron 350, Bracco, Milan, Italy), at a flow-rate of 4 mL/s, was then injected. Furthermore, 30 mL of saline solution was injected at the same

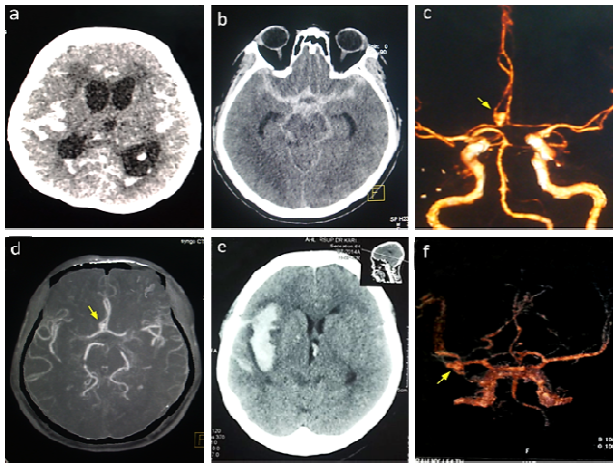

Figure 1. a) Imaging of Subarachnoid Haemorrhage and Intraventricular Haemorrhage on a CT Scan; b) Imaging of Subarachnoid Haemorrhage on a CT Scan Confirmed by 64-MDCTA; c) and d) Imaging Showing a Ruptured Intracranial Aneurysm of an Anterior Communicating artery; c) Volume Rendered Image and d) Maximum Intensity Projection image; e) Imaging of an Intracranial Haemorrhage on a CT Scan Confirmed by 64-MDCTA;f) Imaging Showing a Ruptured Intracranial Aneurysm of the Right Middle Cerebral Artery; f) Volume Rendered Image

flow-rate (4 mL/s) to push the previously introduced contrast media.[10,11] Two radiologists evaluated the results of the 64-MDCTA images to determine the form of the intracranial aneurysms and their SAH status due to the ruptured intracranial aneurysm.

Data was analysed using univariate analysis to understand the characteristics of the variables studied. The prevalence ratio was then calculated with a 95% confidence level and bivariate analysis was performed using Fisher's exact test. This information was then arranged using cross-tabulation to determine whether there was a correlation between the independent variables of age, sex, hypertension, and smoking status with a ruptured intracranial aneurysm. This research was approved by The Ethical Review Committee of our Hospital with a reference number of 805/EC/FK-RSDK/2016.

Results

The break down of risk factors for patients with saccular intracranial aneurysms were as follows, there were 20 patients aged less than 60 years (64.52%) with the ratio between those aged <60 years compared with those aged ≥60 years being 2.2:1. There were 21 female patients (67.74%), and the ratio of female patients versus male patients was 2.6:1. There were 20 hypertensive patients (64.52%), with the ratio of those with hypertension compared to those who were non-hypertensive being 2.2:1. Finally, there were 22 non-smoking patients

(74.19%), and the ratio between non-smoking patients and smoking patients was 3.1:1 (Table 1). The majority of patients who experienced ruptured intra-cranial aneurysms, based on the risk factors studied, were less than 60 years of age (70%), male (75%), had a history of hypertension (85%), and were smokers (85.7%) (Table 2). The 64-MDCTA imaging of subarachnoid, intraparenchymal, or intraventricular haemorrhages caused by a ruptured intracranial aneurysm can be seen in Figure 1. Statistical analysis using Fisher's exact test was at a 95% confidence level. The magnitude of the possibility of a ruptured intracranial aneurysm based on risk factors was calculated using prevalence ratio. The correlation between risk factors and intracranial aneurysm rupture status can be seen in Table 2.

As outlined in Table 2, it can be seen that the risk factor of age, either ≥60 or <60, have almost the same percentage for a ruptured intracranial aneurysm, at 66.7% and 70% respectively. Similarly, the risk factor of gender also has a comparable percentage, with female being 66.7% and male being 75%. The risk factors of a diagnosis of hypertension compared to patients who are non hypertensive have a different percentage for a ruptured intracranial aneurysm at 85% and 33.3% ($p < 0.05$). Additionally, the risk factor of smoking versus non-smoking have a different percentage at 85.7% and 63.6%, however it was not statistically significant ($p > 0.05$).

Statistical analysis using Fisher's exact tests howed that the risk factors of age, sex, and smoking are not associated with the occurrence of a ruptured intracranial aneurysm ($p > 0.05$). However, hypertension did have a correlation with the occurrence of a ruptured intracranial aneurysm ($p < 0.05$). The prevalence ratio for age and sex were 1.0 and 0.9 respectively, indicating they are not a risk factor for a ruptured intracranial aneurysm. The risk factors of hypertension and smoking have a prevalence ratio of 2.6 and 1.3 respectively. These results indicate that hypertensive patients are 2.6 times more likely to experience a ruptured intracranial aneurysm than non hypertensive patients, and patients who smoke are 1.3 times more likely than non-smokers.

Discussion

Results from this study revealed that the female subjects were 2.6 times more likely to experience an intercranial aneurysm than their male counterparts, and those aged below 60 years were 2.2 times more likely than those aged ≥60 years old. These results are inline with several other studies that suggest that the prevalence of intracranial aneurysms was higher in females over males. However, whilst these other studies have also found a correlation between ruptured intracranial aneurysms and women, results from the present study were not statistically significant as a risk factor.[7,12-14]

There was a correlation shown between hypertension and a ruptured intracranial aneurysm in this study,a finding that is not consistent with other studies which found that hypertension was only a risk factor for intracranial aneurysms, not a rupture.[2,7,15] Results suggest that the increased blood pressure became a triggering factor for a ruptured intracranial aneurysms. In the present study, blood pressure was checked at the time of rupture and may be a result of a sudden blood pressure increase, leading to different results to previous studies. Hypertension can lead to aneurysm formation, however the current treatment from hypertension reduces the further development of intracranial aneurysms, thus minimising the long term risk of rupture despite a sudden increase in blood pressure.[16]

Previous studies reported that smoking was an independent risk factor for developing an intracranial aneurysm and subsequent rupture of intracranial aneurysms, however the present study found that smoking is not a risk factor for a ruptured intracranial aneurysm. Whilst smoking increases the risk of rupture, it is not a triggering factor for a ruptured intracranial aneurysm. These results suggest that smoking debilhitates the walls of blood vessels, making them more vulnerable to rupture. The weakened walls of an aneurysm may be caused by the growth of the aneurysm or be due to an inflammation of the blood vessel walls.[17-19] The present study did not account for the risk of passive smoke, which is highly likely in many Indonesian female patients, and may explain why female patients experienced a rupture despite not smoking.

Based on the scoring of PHASES, sex and smoking are not included as a risk factor or a predictor, however age, hypertension, and geographic factors are included as predictors of the risk of a ruptured intracranial aneurysm.[9,20] In the present study, gender and smoking were not statistically significant as a risk factor for a ruptured intracranial aneurysm. The risk factor of age did not match with the criteria of PHASES, where increasing age increases the risk of ruptured intracranial aneurysms. However, the risk factor ofhypertension in this present study was in accordance to the PHASES criteria. Geographical location, as a criteria of PHASES, was different between Indonesian and North American, European, Japanese, and Finnish populations. Ethnicities and tribes in Indonesia are very diverse and as such may show different results.

This research may be usefulas a reference for treatment to decrease the prevalence of ruptured intracranial aneurysms. Due to results that suggest that most aneurysms occur in patients aged <60 years of age,early detection is vital and appropriate treatment interventions. Furthermore, females should be more vigilant to the symptoms of intracranial aneurysms and passive

Table 2. Analysis of Ruptured Intracranial Aneurysms Based on Risk Factor

Risk Factor		Ruptured IA	%	Unruptured IA	%	PR	*p-value*
Age	≥60 y.o.	6	66.7	3	33.3	1.00	$p = 1.0$
	<60 y.o.	14	70.0	6	30.0		
Sex	Female	14	66.7	7	33.3	0.90	$p = 1.0$
	Male	6	75.0	2	25.0		
Hypertension	Hypertensive	17	85.0	3	15.0	2.60	$p = 0.01$
	Non-Hypertensive	3	33.3	6	66.7		
Smoking	Smoker	6	85.7	1	14.3	1.30	$p = 0.38$
	Non-Smoker	14	63.6	8	36.4		

smoking habits. Additionally, hypertensive patients with intracranial aneurysms require tight control of their blood pressure as well as smoking cessation.

Subarachnoid haemorrhage due to a ruptured intracranial aneurysm has been associated with high morbidity and mortality. Unruptured intracranial aneurysm therapy, intended to prevent the occurrence of intracranial haemorrhage, was affected by risk factors associated with intracranial aneurysm therapy. The study of International Study of Unruptured Intracranial Aneurysms (ISUIA) reported that patients who had completed un ruptured intracranial aneurysm therapies of clipping or coiling, had morbidity and mortality risks of about 10% per year.[5,16] However, the therapies themselves are not without risks, as it necessary to determine the high-risk groups using rupture risk profiles to determine who will benefit from the therapy.

The Author's of this study recognise there were certain limitations including a small sample size due to the rarity of cases of intracranial aneurysms. Additionally, this study utilised secondary data resulting in a lack of data regarding the history of hypertension, a history of medications, and uncontrolled hypertension.

Conclusions

The risk factor of hypertension can potentially increase the likelihood of a ruptured intracranial aneurysm by 2.6 times when compared to non-hypertensive patients.

Conflict of Interest Statement

The Authors declare that there is no conflict of interest regarding the publication of this paper.

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