Greater carotid intima-media thickness in elderly patients compare to the non-elderly regular hemodialysis patients

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ABSTRACT

Background: Age is a factor contributing to atherosclerosis. The elderly was shown to have a higher atherosclerosis incidence. But the studies in the hemodialysis patients were still limited.

Objective: Through the examination of carotid intima-media thickness (CIMT), we investigated whether the atherosclerosis was more severe in the elderly than the non-elderly on regular hemodialysis.

Methods: A cross-sectional study was conducted at our hemodialysis unit in Sanglah General Hospital from May to June 2016. All regular hemodialysis patients over 18 years old were recruited. But, patients with a malignancy, severe anemia, systemic lupus erythematosus (SLE), an acute infection, a liver function abnormality, a history of long-term steroid therapy, or patients who smoked tobacco were excluded. We examined the CIMT using a grayscale ultrasound. An independent t-test analysis was used to compare the CIMT means of the elderly and the non-elderly patients.

Results: Our sample consisted of 30 elderly and 30 non-elderly hemodialysis patients. It was found that the CIMT mean in the elderly was significantly higher than in the non-elderly (0.73 ± 0.1 mm versus 0.58 ± 0.09 mm, $p<0.001$).

Conclusion: More severe atherosclerosis was found in the regular hemodialysis patients in their late life.

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INTRODUCTION

The proportion of the elderly among the world population has increased because of the healthy lifestyle and the improving life expectancy. The world elderly population in 1990 was 9.2%, 11.7% in 2013, and expected to be 21.1% in 2050.[1] The number of population aged 60 years old or more was predicted to double from 841 million in 2013 to 2 billion in 2050. The elderly proportion increase is quicker in the developing countries than in the developed countries. It was predicted that two third of the elderly population lives in the developing countries.[1] The increase in the elderly population is related to the rising prevalence of the non-communicable diseases. Because the chronic and the degenerative diseases often occur in the elderly.

Old age has become an independent non-traditional risk factor for cardiovascular disease (CVD), mainly atherosclerosis. The risk of CVD may increase if other risk factors, including chronic kidney disease (CKD) and its treatment—hemodialysis or dialysis are present. CVD causes more than half of the total mortality of the elderly patients with CKD.[2]

Old age, CKD, and hemodialysis are the risk factors for atherosclerosis, a frequently found CVD. However, only limited studies can be found about the role of old age in atherosclerosis in patients on hemodialysis. A study showed strong predictor factors of the calcification of the arterial wall lining in CKD were age (OR 1.04, CI 95% 1-1.08, p=0.04) and hemodialysis (OR 8.09, CI 95% 2.67-24.5, p<0,001).[3] However, this study does not compare a group of the elderly to the non-elderly.

Based on the high occurrence of atherosclerosis and its morbidity and mortality, an initial examination was developed for detecting subclinical atherosclerosis in CKD and elderly patients. Carotid intima-media thickness (CIMT) test is useful for evaluating subclinical atherosclerosis on peripheral circulation. Because CIMT test is non-invasive, it becomes one of the ideal modalities for assessing an elderly patient. The increase of the CIMT shows the stiffness of an artery or subclinical atherosclerosis.[4]

The aim of this study is to examine through CIMT test whether an old age has a role in the pathogenesis of atherosclerosis in dialysis patients. The result may contribute to a development of a safer observation and therapy programs.

METHODS

A cross-sectional study was conducted to identify the mean difference of the CIMT between two groups of regular hemodialysis patients in the elderly group (60 years old or over) and the

non-elderly group (patients aged 18 to 59 years old). The study was conducted from May until June 2016 in our hemodialysis unit, Sanglah General Hospital, Bali. Ethical clearance was given by the Research Ethical Committee, Medicine Faculty of Udayana University in conjunction with the teaching hospital, Sanglah General Hospital.

All patients aged 18 years old and more on a regular hemodialysis were included. A patient was on a regular hemodialysis when the patient had been on hemodialysis for at least three months, and the hemodialysis was conducted twice a week for 4.5 hours/session.[5] All of the hemodialysis used a Nipro® hemodialysis machine.

Table 1 The Sample Characteristics

Characteristics	Elderly (n=30) f (%)	Elderly (n=30) median (min-max) or mean ± SD	Non-elderly (n=30) f (%)	Non-elderly (n=30) median (min-max) or mean ± SD
Sex				
Male	20 (66.7%)		13 (43.3%)	
Female	10 (33.3%)		17 (56.7%)	
Ethnicity				
Bali	28 (93.3%)		24 (80.0%)	
Java	2 (6.7%)		3 (10.0%)	
Other	0 (0%)		3 (10.0%)	
Length of regular hemodialysis (in month)		41.6 ± 25.2		58.3 ± 39.3
Diabetes	9 (30.0%)		6 (20.0%)	
Coronary artery disease	7 (23.3%)		2 (6.7%)	
Stroke history	6 (20.0%)		2 (6.7%)	
Peripheral artery disease	1 (3.3%)		1 (3.3%)	
Statin consumption	5 (16.7%)		1 (3.3%)	
Systolic blood pressure (mmHg)				
Lying down		150.3 ± 26.9		148.7 ± 22.6
Sitting		147.8 ± 27.4		148.7 ± 22.2
Standing		148.3 ± 26.9		148.7 ± 22.2
Diastolic blood pressure (mmHg)				
Lying down		80 (60-110)		90 (70-110)
Sitting		81.7 ± 13.9		88.0 ± 9.6
Standing		81.0 ± 13.2		88.0 ± 9.6
Body mass index (kg/m^2)		22.3 ± 3.3		22 ± 5.0
Body mass index category				
Underweight	3 (10.0%)		7 (23.3%)	
Normal	21 (70.0%)		18 (60.0%)	
Overweight	6 (20.0%)		4 (13.3%)	
Obesity	0 (0%)		1 (3.3%)	
Waist circumference (cm)		86.2 ± 9.1		83.4 ± 15.3
Lipid profile (mg/dl)				
Total cholesterol		162.2 ± 39.7		165.2 ± 40.5
Low-density lipoprotein		101.4 ± 35.6		107.5 ± 32.9
High-density lipoprotein		41.4 ± 15.0		37.1 ± 11.8
Triglycerides		135.4 ± 81.8		172.8 ± 98.1
Dyslipidemia	21 (70.0%)		24 (80.0%)	
Calcium-phosphate product >55mg^2/dl^2	20 (66.7%)		16 (53.3%)	

Table 2 CIMT Mean Difference

Group	CIMT mean (in millimeter)	p-value
Elderly	0.73 ± 0.1	<0.001
Non-elderly	0.58 ± 0.09	

Patients with a malignancy, severe anemia, tobacco smoking, a systemic lupus erythematosus (SLE), an acute infection, a liver function abnormality, a history of long-term steroid therapy were excluded. Malignancy was defined as a group of abnormalities identified by the growth and spread of abnormal cell. Severe anemia was defined as a persistent condition of hemoglobin level less than 6 g/dl even though it had been corrected.[6] A patient was defined as smoker if he or she smoked at least 2 cigarettes a day for more than 1 month or had stopped smoking for less than three months before the study.[7] Systematic lupus erythematosus is an autoimmune disease which fulfills the American College Rheumatology (ARA) criteria in 1997.[8] A long-term corticosteroid therapy is a medical treatment using glucocorticoid for more than 5 years.

Our study recorded the age, sex, ethnicity, nutritional status based on the waist circumference and body mass index. Furthermore, we recorded the duration of the regular hemodialysis, the presence of hypertension, diabetes, lipid profile, dyslipidemia, the history of a coronary heart disease, stroke, peripheral artery disease, calcium-phosphate product >55 mg^2/dL^2, statin consumption, and the mean of CIMT. CIMT is the thickness of tunica intima and media of carotid artery measured by a grayscale ultrasound (Medison®, 7.5MHz linear probe). The measurement was done by a radiologist who had been trained and appointed by the hospital radiology unit. The participants were examined in the supine position, the neck extended, and the head tilted slightly (45°-50°) towards the opposite of the observed side. The measurement of the tunica intima and media thickness was done on three points on both sides of the carotid artery. The three points were on the common carotid artery (10 mm proximal to bifurcation), the bifurcation, and the internal carotid artery (10 mm distal to bifurcation). The mean of CIMT was the mean of the six measured points.

The data were analyzed using a computer statistical software program. The numerical data were tested for distribution normality using Kolmogorov-Smirnov test. A student t-test was done to compare the mean of the CIMT between the elderly and the non-elderly group, α=0.05.

RESULTS

Our sample consisted of 60 patients. Each group consisted of 30 patients. The sample characteristics were shown in Table 1. The elderly group comprised of twenty males and ten females, The non-elderly group consisting of 13 males and 17 females. Most of the characteristics showed no difference between the elderly and the non-elderly group. But, the elderly group had a lower sitting diastolic (p=0.05) and standing diastolic blood pressure (p=0.02) than the non-elderly group.

The CIMT mean of the elderly group was significantly higher than the non-elderly (0.73±0.1mm vs. 0.58±0.09mm, p<0.001) as shown in Table 2.

DISCUSSION

Our study showed the elderly patients had a higher mean of CIMT than the non-elderly (0.73±0.1mm vs. 058±0.09mm). It is consistent with a study by Pourafkari et al. showing the general population without any CVD risk factor, the 60 years old or more had the greatest mean of tunica intima-media thickness (0.645±0.125mm), while the least (0.305±0.045mm) was in the 20 to 29 years old (p<0.02).[9] The regular hemodialysis may contribute the greater mean of tunica intima-media thickness in our study.

An ultrasonography examination of the carotid, femoral, and brachial in 232 patients who underwent hemodialysis and 208 healthy people, showed a carotid calcification was more frequent on those who have hemodialysis compared to the control (85.3% vs. 20.3%; p<0.001).[3] The study included variables related with vascular calcification, such as age, sex, coronary heart disease history, smoking status, c-reactive protein, carotid plaque, statin and acenocoumarol therapy, calcium-phosphate product, parathyroid hormone concentration, and diabetes.[3] Based on the multivariate analysis, it was identified that age related to the calcification of the arterial inner lining (OR 1.04, CI 95% 1-1.08, p<0.04).[3] We determined the vascular thickening based on carotid ultrasound only. Indeed, we did not examine the femoral and brachial arteries. A carotid ultrasound represents the general vascular condition.

Patel et al. showed a correlation between CIMT and age (r=0.327; p<0.001).[10] The multiple regression models and the covariate analysis showed there were significant relationships between CIMT and age (β=0.34; p<0.01), albumin (β=0.35; p<0.01), and serum calcium-phosphate product (β=0.32, p<0.01).[10] Our study did not have a significant difference in the high calcium-phosphate product (>55 mg^2/dl^2).

Another study by Patel et al., involving 100 patients on regular hemodialysis, showed the elderly patients on regular hemodialysis had a higher mean of CIMT than the younger group (p=0.023). It revealed the pathophysiological process of atherosclerosis and arterial stiffness was related to the aging process.[11] and carotid and coronary vessels are at comparable risk for developing pathologic changes. For this reason, increase in the thickness of the intima-media layers of carotid arteries can be a harbinger of coronary atherosclerosis and also a prognostic factor for cardiovascular accidents. In this study, we evaluated the status of carotid intima-media thickness (CIMT Moreover, a study conducted by Paul et al. showed a positive correlation between age and CIMT (p=0.047).[12] In the study, smokers were excluded, while hypercholesterolemia and hypertension did not show a significant correlation with CIMT.[12]

Vascular aging is a part of an aging process. Together with the aging process, the vascular stiffness process takes place and becomes a predisposition to atherosclerosis. Age itself involves in the vascular aging process through the exposure of the physical and metabolic stresses, the accumulation of metabolic byproducts, and the attrition of the basic arterial constituent and the adaptive and the reparative mechanisms of the arteries.[4]

A chronic shear stress takes place in the vascular bifurcations and curves. Oxidative stress is also considered to be the most common stress leading to atherogenesis. Metabolic byproducts accumulation can cause recurrent inflammation process promoting a vascular fibrosis. An advanced glycation product is one of the metabolic byproducts which furthers vascular aging.[4] Another component of vascular aging was the decrease of reparative ability for adapting to structural changes, such as telomere dysfunction, DNA improvement fault, insulin pathway dysregulation, and angiotensin II signaling change.[4,13]

Non-invasive modality is the choice of diagnostic testing on the elderly to determine atherosclerosis. Arterial ultrasound is a non-invasive technique performing as a CVD risk predictor.[14] The carotid is examined because it has a bifurcation which gets more shear stress.[4]

Our study showed the sitting diastolic blood pressure (t=-2.05, p=0.05) and standing diastolic blood pressure (t=-2.32, p=0.02) in the elderly were lower than the non-elderly. The result can be explained by the higher blood pressure fluctuation occurred as the increase in age, as a consequence of the arterial stiffness in the elderly. An arterial stiffness can manifest as an orthostatic hypotension or an isolated systolic hypertension.[4,15] In the elderly population, atherosclerosis can worsen the arterial stiffness resulted from a change of elastin with collagen and other protein.[16]

An atherosclerosis process monitoring is recommended for the elderly on regular hemodialysis. We recommend a further research in the elderly patients on regular hemodialysis to evaluate the femoral and brachial atherosclerosis and evaluate its dynamic functions (the flow velocity such as pulse wave velocity) to examine the age as atherosclerosis risk factor in the regular hemodialysis patients.

CONCLUSION

More severe atherosclerosis was found in the elderly patients on regular hemodialysis when compared to the non-elderly on regular hemodialysis.

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CONFLICT OF INTEREST

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