The Correlation between Age and Vascular Calcification in Renal Failure Subject

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***Abstract*- Background:** Cardiovascular disease (CVD) is a major cause of morbidity and mortality in renal failure. The clinical pathology of CVD in renal failure is arteriosclerosis. One of the features of arteriosclerosis in renal failure is vascular calcification. High level of phosphate and calcium in chronic kidney disease (CKD) are the risk factor of vascular calcification. Furthermore, vascular calcification is an aging process which related to calcium deposit and inflammation. Method used to assess vascular calcification is lateral abdominal radiographs which is expressed as score Abdominal Aortic Calcification (AAC).

Objective: To determine the effect of age on the severity of vascular calcification in renal failure subject.

Methods: Observational study with cross sectional design in subjects with renal failure underwent hemodialysis at least 3 months in Wahidin Sudirohusodo Hospital from September until December 2013, aged over 20 years old,. Lateral plain abdominal X-ray was performed in Radiology department of Wahidin Sudirohusodo Hospital. The AAC Score was used to assess vascular calcification by measuring total accumulation of calcium deposits on abdominal aorta showed by calcification score: score 0 (no calcification), 1-6 (moderate calcification), 7-24 (severe calcification).

Result: from 63 subjects, 23 subjects (36,5%) had vascular calcification where 14 subjects (22,2%) have moderate calcification and 9 subjects (14,3%) have severe calcification. There was a significant correlation between AAC score and age ($p<0,001$).

Conclusion: Age is correlated with the severity of vascular calcification in renal failure subjects.

***Index Terms*-** Age, Vascular calcification, Renal failure.

I. BACKGROUND

Cardiovascular disease (CVD) is the mayor cause of mortality and morbidity in renal failure (RF) subjects. Based on United States Renal Data System (URDS) and The European Registry of the Patients on Renal Replacement Therapy, the risk of myocard infarct in renal failure under hemodialysis is 3.5 which is 50 times higher than other population.

There are three pathologies of CVD in Chronic Kidney Disease (CKD): left ventricular hypertrophy, atherosclerosis and arteriosclerosis. The clinical pathology of CVD in renal failure is arteriosclerosis. One of the features of arteriosclerosis in renal failure is vascular calcification (VC). Vascular calcification is a physiologic condition that is related with aging process, which calcium phosphate deposits especially hydroxyapatite in blood vessels.

Several medical conditions such as hypertension, diabetes, and chronic kidney disease became a risk factors for CVD. Higher levels of phosphate in CKD is associated with lower renal function. Hyperphosphatemia plays a role in pathomechanism of VC. Diabetes and CKD will accelerate VC process. Meema HE (1976) reported the incidence of VC in age group of 15–30 is 30% and age group 40-50 is 50% using a skeletal radiology in CKD subject. [6]

Vascular calcification degree can be detected through several imaging technique. One of them is lateral abdominal radiography that classified with Abdominal Aortic Calcification (AAC). Abdominal Aortic Calcification score is the total calcium deposit in aortic abdominal vessel that is measured with lateral abdominal imaging against lumbal vertebra columna (L1-L4).

The objectives of this study is to determine the effect of age on the severity of VC in renal failure subject.

II. METHODS

This study is observational study with cross sectional design in subjects with renal failure who underwent hemodialysis at least 3 months in Wahidin Sudirohusodo Hospital on September-December 2013, aged over 20 years old, with no phosphate binding agent and vitamin D therapy in the last three months. Vascular calcification detected with lateral abdominal imaging.

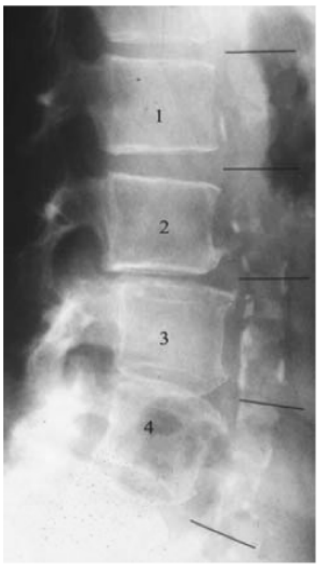
Cummulated score that described with AAC is the total of:

a. Degree of calcification on aorta (L1-L4), either from anterior or posterior wall, with maximum score of 24, classified as :

0 = no calcification deposit anterior vertebra
1 = calcification deposit less than 1/3 of anterior longitudinal aorta
2 = calcification deposit 1/3 – 2/3 of anterior longitudinal aorta
3 = calcification deposit in 2/3 or more of anterior longitudinal aorta

b. Calcified segment with total aorta segment that shows calsification degree with maximum score of 4.

The degree of AAC score classified as 0 (without calcification) , 1-6 (moderate calcification), and 7-24 (severe calcification).[9]



GRADING

0: no calcific deposits in front of the vertebra

1: small scattered calcific deposits filling less than 1/3 of the longitudinal wall of the aorta

2: 1/3 – 2/3 of the wall calcified

3 : 2/3 or more of the wall calcified

Level	Affected segment	Scores for individual segments		Composite score (AAC)
		Posterior Wall Range 0-3	Anterior Wall Range 0-3	Anterior-Posterior severity Range 0-6
L1	1	1	0	1
L2	1	2	1	3
L3	1	3	2	5
L4	1	3	3	6
Total	4	9	6	15
Maximum	4	12	12	24

Figure 1. Abdominal Aortic Calcification (AAC) Score

Collected data analyzed with Stastical Package for Social Science (SPSS). Study results are presented in tables and graphics. The results are considered significant if $p<0.001$.

III. RESULT

During the study period, we found 63 subjects, 21-67 years, which consisted of 38 (60.3%) male subjects and 25 (39.7%) female subjects. Based on the classification, we found 50 (79.3%) subjects are <60 years old and 13 (20.7%) subjects are ≥60 years old. Vascular classification found in 23 (36.5%) subjects, whereas 40 (63.5%) subjects did not experience VC. From the 23 subjects who had obtained VC, 14 (60.8%) subjects with moderate calcification and 9 (39.2%) subjects with severe calcification. (Table 1)

Tabel 1. Subjects characteristic

	n	%
Age		
<60 years	50	79,3
≥60 years	13	20,7
Sex		
Male	38	60,3
Female	25	39,7
Calcification Score		
No VC (score 0)	40	63,5
Moderate VC (score 1-6)	14	22,2
Severe VC (score 7-24)	9	14,3

VC = vascular calcification

Subjects then divided into two age groups: <60 years and ≥60 years. In the ≥60 years group, we found subjects with severe VC (46.2%) are more than the moderate VC (38.5%) and no calcification (15.4%). Subjects with severe VC are more common in the ≥60 years group (46.2%) compared with <60 years group (6.0%). In <60 years group, 76.0% subjects are not experiencing VC, compared with ≥60 years group (15.4%), p <0.001. (Table 2)

Tabel.2 Correlation of age with vascular calcification degree

			Vascular Calcification			Total
			No	Moderate	Severe	
Age	<60 years	n	38	9	3	50
		%	76,0%	18,0%	6,0%	100,0%
	≥60 years	n	2	5	6	13
		%	15,4%	38,5%	46,2%	100,0%
Total		n	40	14	9	63
		%	63,5%	22,2%	14,3%	100,0%

Chi Square test (p<0,001)

IV. DISCUSSION

Cardiovascular disease is a major cause of morbidity and mortality in RF subject. One form of pathology CVD at RF is arteriosclerosis. Critical overview of arteriosclerosis is VC. Vascular calcification is a part of the aging process and is associated with deposits of calcium and phosphate. On CKD espescially RF stage, occurance of hyperphosphatemia is a risk factor for CVD.

Decreasing of glomerular filtration rate in CKD will make a decline in urinary phosphate excretion which will cause hyperphosphatemia. Chronic kidney disease also cause hypocalcemia due to impaired synthesis of 1,25-dihydroxyvitamin D of the kidney which is the active metabolite of vitamin D in the body. Low calcium concentrations activate the calcium-sensing receptors on the parathyroid glands that will increase the secretion of parathyroid hormone (PTH) that causes secondary hyperparathyroidism. Giving vitamin D to secondary hyperparathyroidism will increase serum calcium and phosphate, which in turn increases the calcium phosphate product that causes vascular calcium deposition in which a major cause of vascular calcification.

In this study from 63 VC subjects, 23 (36.5%) subjects with VC, whereas 40 (63.5%) subjects did not experience VC (Table 1). Of the 23 subjects who had obtained VC, 14 (60.8%) subjects with moderate calcification and 9 (39.2%) subjects with severe calcification.

In this study (Table 2) is known subject to the age group ≥60 years experiencing higher VC {(moderate (38.5%) and severe (46.2%)} compared with age <60 years {(moderate (18.0%) and severe (6.0%)}, p <0.001. This is consistent with the study by Honkanen et al., From subjects with RF who found that age is an independent predictor factor of the incidence and severity of VC measured using AAC assessment scores. Similar research by Moe et al., 10 (2003) on the subject of RF who underwent transplantation and dialysis showed that by using spiral CT technique found only increasing age correlate with aortic calcification in subjects with RF.

Research by Biel et al. (2011) reported that the prevalence of VC increases with age. On the whole the study population, 12% of men and women, with age group of 28-40 years, had evidence of VC examined using electrone-beam computed tomography (EBCT). However, Simon et al. (1995) reported that approximately 63% of the population is male, with a mean age of 48 years. Another study by Newman et al (2011) showed that the male population and 90% of women aged over 70 years. These studies reported a strong correlation between age and VC.[8]

Naves et al (2005) in the study of European Union-supported European Vertebral Osteoporosis Study (EVOS) to subjects of > 50 years, with same sex and region of residence, reported that the prevalence of VC in subjects with normal renal function or mild renal insufficiency due to aging, found to be significantly lower than in subjects who undergo dialysis. The study by Russo et al. (2004) found that 40% of CKD patients (mean age 52 years and mean GFR 33 mL / min) showed VC compared with 13% at the same age without impaired renal function. [16]

The involvement of some of the risk factors and the number of VC will increase the severity of VC and mortality. In patients with CKD, VC severity figure is almost 20 times higher than the general population. [16]

Along with aging, changes in the structure and the compliance of the vascular where the vascular has increased levels of collagen, elastin damage and decreased production elastin.11 Calcium deposits increased along with the increasing age.[12] High levels of minerals in vascular followed by passive degeneration process of crystal hidrosiapatit leads to vascular calcification is more common with increasing age.13 On RF subject this situation is exacerbated by the state of uremia which resulted in increased levels of phosphate, calcium-phosphate product, and PTH, all of which can increase the incidence of VC.

V. CONCLUSION

Increased age is associated with severity of VC on RF subject.

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