Factors Associated with Arterial Stiffness in Chronic Hemodialysis Patients in Jakarta: The Role of Hemodialysis Frequency and Pentraxin 3

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ABSTRAK

Latar belakang: *kekakuan arteri merupakan prediktor mortalitas pada pasien hemodialisis, hemodialisis menginduksi inflamasi, ditandai dengan peningkatan intradialisis pada penanda inflamasi pentraxin 3 (PTX3). Kekakuan arteri pada pasien hemodialisis dua kali seminggu di Indonesia lebih rendah daripada yang ditemukan dalam studi pasien tiga kali seminggu. Oleh karena itu, penelitian ini bertujuan untuk mengetahui faktor-faktor yang berhubungan dengan kekakuan arteri, dengan fokus pada peran frekuensi hemodialisis dan PTX3.* ***Metode:*** *studi potong lintang dilakukan di RS. Cipto Mangunkusumo, RS. Fatmawati, dan RS. Medistra pada pasien hemodialisis dua kali dan tiga kali seminggu. Kekakuan arteri diukur dengan kecepatan gelombang nadi karotis-femoralis setelah hemodialisis, dan sampel darah untuk pengujian PTX3 diambil sebelum hemodialisis. Analisis bivariat dan multivariat dilakukan dengan menggunakan uji chi-kuadrat dan regresi logistik.* ***Hasil:*** *dari 122 subjek, 82 menjalani hemodialisis dua kali seminggu. Tidak ada perbedaan dalam kekakuan arteri antara subjek dua kali dan tiga kali seminggu. Dalam analisis bivariat, PTX3, penyakit kardiovaskular, dialisis vintage memiliki nilai p <0,05, sedangkan analisis multivariat berikutnya menunjukkan bahwa PTX3>2,3 ng/ml dikaitkan dengan kekakuan arteri (OR 5,18; 95% IK 1,07-24,91), sebagai serta penyakit kardiovaskular (disesuaikan OR 3,67; 95% IK 1,40-10,55), LDL (disesuaikan OR 3,10; 95% IK 1,04-9,24), dan dialisis vintage (disesuaikan OR 2,72; 95% IK 1,001-7,38).* ***Kesimpulan:*** *kadar PTX3 pradialisis di atas 2,3 ng/ml berhubungan dengan kekakuan arteri. Tidak ada perbedaan kekakuan arteri antara pasien hemodialisis dua kali dan tiga kali seminggu.*

Kata kunci: *kekakuan arteri, kecepatan gelombang nadi, pentraxin 3, frekuensi hemodialisis.*

ABSTRACT

Background: *arterial stiffness is a mortality predictor in hemodialysis patients, hemodialysis induces inflammation, marked by an intradialysis increase in the inflammatory marker pentraxin 3 (PTX3). Arterial stiffness in twice-weekly hemodialysis patients in Indonesia is lower than has been found in studies of thrice-weekly patients. This study therefore aims to determine the factors associated with arterial stiffness, focusing on the role of hemodialysis frequency and PTX3.* ***Methods:*** *a cross-sectional study was conducted at Cipto Mangunkusumo*

Hospital, Fatmawati Hospital, and Medistra Hospital involving patients with twice- and thrice-weekly hemodialysis. Arterial stiffness was measured by carotid-femoral pulse wave velocity after hemodialysis, and blood samples for PTX3 testing were taken before hemodialysis. Bivariate and multivariate analyses were performed using chi-squared tests and logistic regression. ***Results:*** *out of 122 subjects, 82 underwent twice-weekly hemodialysis. There was no difference in arterial stiffness between patients with twice- and thrice-weekly hemodialysis. In bivariate analysis, PTX3, cardiovascular disease, dialysis vintage had p values of <0.05, while the subsequent multivariate analysis showed that PTX3>2.3 ng/ml was associated with arterial stiffness (adjusted OR 5.18; 95% CI 1.07–24.91), as well as cardiovascular disease (adjusted OR 3.67; 95% CI 1.40–10.55), LDL (adjusted OR 3.10; 95% CI 1.04–9.24), and dialysis vintage (adjusted OR 2.72; 95% CI 1.001–7.38).* ***Conclusion:*** *predialysis PTX3 levels above 2.3 ng/ml were associated with arterial stiffness. There was no difference in arterial stiffness between patients with twice- and thrice-weekly hemodialysis.*

Keywords: *arterial stiffness, pulse wave velocity, pentraxin 3, hemodialysis frequency.*

INTRODUCTION

Cardiovascular diseases are the leading cause of death in the chronic hemodialysis population.[1] Previous studies have shown that the increased cardiovascular risk may be due to early vascular structure changes toward a stiffer vasculature, and arterial stiffness is an independent predictor of mortality in hemodialysis patients.[2]

CKD is a proinflammatory condition in which there is an increase in the production of prooxidant molecules, disruption of oxidative product clearance, and antioxidant deficiency. Along with traditional cardiovascular risk factors, inflammation can accelerate arterial stiffness, which is also exacerbated by vascular calcification as a manifestation of bone mineral disorders in CKD.[3] The gold standard for arterial stiffness measurement is pulse wave velocity (PWV) in the carotid-femoral axis,[2] and a PWV value of 10 m/s or greater has been recommended as a suitable cut-off for an increased risk of cardiovascular mortality.[4]

Hemodialysis is a process that cleans various uremic toxins and withdraws excess fluid, but the exposure of blood to an artificial dialyzer membrane during hemodialysis can induce inflammation.[5-8] Pentraxin 3 (PTX3), a marker of inflammation, starts to increase 30 minutes after hemodialysis begins and continues increasing until hemodialysis ends.[9] This prompts the presumption that, if hemodialysis is done more frequently or for longer periods, the patient will have increased risk of inflammation due to more frequent exposure to the dialyzer. PTX3 is closely associated with cardiovascular disease and a mortality predictor in hemodialysis patients,[10,11] but there are to date no published studies regarding PTX3 and arterial stiffness in the hemodialysis population.

At present, most hemodialysis in Indonesia is done twice weekly for a total of 10 hours, whereas the hemodialysis recommendations according to KDOQI are thrice weekly for a total of 12 hours.[12] Sari et al. found that arterial stiffness in twice-weekly hemodialysis patients is lower than has been found in studies done in thrice-weekly hemodialysis patients.[13,14] Inflammation due to hemodialysis has a strong role in the pathophysiology of arterial stiffness, and this study was therefore conducted to assess the association of hemodialysis frequency and PTX3 with arterial stiffness in hemodialysis patients, adjusted for other known risk factors.

METHODS

This was a cross-sectional study conducted in hemodialysis units in Cipto Mangunkusumo National General Hospital, Fatmawati General Hospital, and Medistra Hospital in December 2019. Subjects with a hemodialysis vintage of more than 1 year gave informed consent to participate in the study, which was approved by the local ethical committee. Exclusion criteria were conditions that prevented neck examination, hemodynamic disorders, fluid overload, malignancy, pregnancy, using immunosuppressant drugs, acute infections, and lack of cooperation. This study has been

approved by the Ethics Committee of Faculty of Medicine Universitas Indonesia (Ref. Number KET-1318/UN2.F1/ETIK/PPM.00.02/2019).

Measurement of PWV

Vascular studies were performed with subjects resting in a supine position after the hemodialysis session ended. PWV was measured in the carotid and femoral arteries using a PWV machine (Syphgmocor XCEL, AtCor Medical) in accordance with the manufacturer's recommendations. PWV was automatically calculated by measuring the time for the pulse wave to travel between the carotid and femoral arteries.

Clinical Examination

Clinical parameters, including BMI, gender, age, smoking status, and history of cardiovascular diseases, were collected from medical records. Interdialytic weight gain (IDWG) was operationalized as the mean IDWG over one month.

Malnutrition was assessed with a subjective global assessment, on the basis of which patients' nutritional status was graded as A, B, or C. In this study, grades B and C were combined and considered as malnourished.

Biochemical Analysis

Peripheral blood was collected before hemodialysis on Wednesday or Thursday for thrice-weekly subjects and on Thursday, Friday, or Saturday for twice-weekly subjects. Blood samples were placed in an EDTA tube and centrifuged at 1,000 g (approximately 3,000 rpm) for 15 minutes. The analysis was carried out with the Quantikine® ELISA Human Pentraxin 3/ TSG-14 Immunoassay (R&D systems) reagent in the Prodia laboratory. Measurements were performed using routine laboratory methods for serum parameters such as hemoglobin, creatinine, calcium, phosphate, and low-density lipoprotein. Hyperphosphatemia was defined as serum phosphate above 4.6 mg/dl. Hypercalcemia was defined as serum calcium above 10 mg/dl.

Statistical Analysis

The data was processed using IBM SPSS 25. Numerical data with normal distributions is expressed as mean (SD), while data with abnormal distributions is expressed as median (min–max). Bivariate analysis was conducted with chi-squared tests, and multivariate analysis was performed with logistic regression.

RESULTS

Of the 122 subjects, 80 were twice-weekly hemodialysis patients. The mean age was 52.7 years old, and 54.9% were male. Diabetes was found in 32.8% of subjects, hypertension in 82.8%, and arterial stiffness in 21.3%. No

Table 1. Baseline characteristics of the study population.

Parameters	HD twice weekly (n=82)	HD thrice weekly (n=40)	Total (n=122)
Gender–male, n (%)	45 (54.8)	22 (55.0)	67 (54.9)
Age, years, mean (SD)	49.79 (14.58)	58.73 (14.97)	52.72 (15.24)
Dialysis vintage, months, median (range)	72 (12–236)	32.5 (13–119)	54 (13–236)
Diabetes mellitus, n (%)	22 (26.8)	20 (50)	40 (32.8)
Hypertension, n (%)	71 (86.5)	30 (75)	101 (82.8)
Cardiovascular disease, n (%)	18 (21.9)	12 (30)	30 (24.6)
LDL cholesterol, mg/dl, median (range)	101 (25–189)	110 (41–219)	105 (25–219)
Phosphate, mg/dl, median (range)	5.55 (1.2–10.8)	4.55 (2.2–9.3)	5.25 (1.0–10.8)
Hyperphosphatemia, n (%)	61 (74.4)	17 (42.5)	78 (63.9)
Hypercalcemia, n (%)	9 (10.9)	1 (2.5)	10 (8.2)
Hemoglobin, g/dl, mean (SD)	9.74 (1.60)	10.05 (1.63)	9.84 (1.60)
Malnutrition, n (%)	4 (4.8)	8 (20)	12 (9.8)
Albumin, g/dl, mean (SD)	3.98 (0.35)	3.87 (0.41)	3.95 (0.37)
IDWG, kg, mean (SD)	3.30 (0.90)	1.78 (0.80)	2.80 (1.11)
IDWG > 5%, n (%)	55 (67.1)	1(2.5)	56 (45.9)
PWV, m/s, mean (SD)	8.72 (2.04)	8.79 (1.71)	8.75 (1.93)
PTX3, ng/ml, mean (SD)	1.14 (0.83)	1.05 (0.61)	0.93 (0.05–4.65)
PTX3 > 2.3 ng/ml, n (%)	6 (7.3)	3 (7.5)	9 (7.4)

Table 2. Bivariate analysis between dependent variables and arterial stiffness.

Variables		Arterial stiffness		p	OR
		PWV ≥10 m/s n = 26 n (%)	PWV<10 m/s n = 96 n (%)		
HD frequency	Twice weekly	19 (23.2)	63 (76.8)	0.473	1.32 (0.60–2.8)
	Thrice weekly	7 (17.5)	33 (82.5)		
PTX3	>2.3 ng/ml	5 (55.6)	4 (44.4)	0.021	2.98 (1.48–6.02)
	≤2.3 ng/ml	21 (18.6)	92 (81.4)		
Age	>60 years	8 (20.5)	31 (79.5)	0.883	0.94 (0.45–1.98)
	≤60 years	18 (21.7)	65 (78.3)		
Diabetes mellitus	Yes	10 (23.8)	32 (76.2)	0.625	1.19 (0.59–2.38)
	No	16 (20.0)	64 (80.0)		
Hypertension	Yes	22 (21.8)	79 (78.2)	1.0	1.14 (0.44–2.97)
	No	4 (19.0)	17 (81.0)		
LDL cholesterol	>100 mg/dl	20 (26.3)	56 (73.7)	0.11	2.01 (0.87–4.65)
	≤100 mg/dl	6 (13.0)	40 (87.0)		
Malnutrition	Yes	3 (25.0)	9 (75.0)	0.718	1.19 (0.42–3.40)
	No	23 (20.9)	87 (79.1)		
Cardiovascular disease	Yes	12 (40.0)	18 (60.0)	0.004	2.62 (1.37–5.0)
	No	14 (15.2)	78 (84.8)		
Dialysis vintage	>54 months	18 (28.6)	45 (71.4)	0.043	2.1 (0.99–4.47)
	≤54 months	8 (13.6)	51 (86.4)		
Serum calcium	Hypercalcemia	2 (20.0)	8 (80.0)	1.0	0.93 (0.25–3.38)
	Not hypercalcemia	24 (21.4)	88(78.6)		
Serum phosphate	Hyperphosphatemia	18 (23.1)	60 (76.9)	0.526	1.27 (0.60–2.67)
	Not hyperphosphatemia	8 (18.2)	36 (81.8)		
IDWG	>5% dry weight	12 (21.4)	44 (78.6)	0.97	1.01 (0.51–2.00)
	≤5% dry weight	14 (21.2)	52 (78.8)		

Table 3. Multivariate analysis of arterial stiffness and Pentraxin 3, cardiovascular disease, dialysis vintage, and LDL cholesterol.

Variables	Adjusted OR	95% CI	p value
PTX3	5.18	1.07–24.91	0.04
Cardiovascular disease	3.67	1.40–10.55	0.009
Dialysis vintage	2.72	1.001–7.38	0.05
LDL cholesterol	3.10	1.04–9.24	0.042

subjects were smoking at the time of the study. (**Table 1**) Compared to the thrice-weekly hemodialysis subjects, the twice-weekly subjects were younger and had longer dialysis vintage, lower LDL cholesterol, and higher IDWG. There were no differences in PWV and PTX3 between patients with twice- and thrice-weekly hemodialysis.

In the bivariate analysis (**Table 2**), PTX3, cardiovascular disease, and dialysis vintage were found to be associated with arterial stiffness. The multivariate analysis (**Table 3**) showed the same, in addition to an association with LDL cholesterol.

DISCUSSION

Arterial stiffness was found in 21.3% of subjects. This proportion is lower than found by Sari et al.[13], at 30%, and by Utescu et al.[14], at 43%; the mean PWV in this study was also lower than found by Sari et al.[13] in twice-daily hemodialysis patients, at 9.0 (SD 2.2) m/s. The mean PWV in thrice-weekly subjects was 8.79 (SD 1.71) m/s, lower than found in thrice-weekly subjects by Utescu et al. (13.1 (SD 3.7) m/s), lower than in a study conducted by Wang et al. in stage 5 non-dialysis CKD subjects (11.6 (SD 3.3) m/s), and lower than in a study conducted by Krishnasamy et al. in stage 4 and 5 CKD subjects (9.7 m/s [7.6–11.7]).[14-16] Previous studies have

shown that arterial stiffness in hemodialysis patients is higher than in the normal population. This is due to traditional cardiovascular risk factors; vascular calcification, which is a manifestation of bone mineral disorders in CKD; and inflammations that accelerate changes in the blood vessel structure. The low PWV and lower proportion of arterial stiffness in this study need to be compared with the average PWV in the healthy population in Indonesia, but there have so far been no studies of arterial stiffness in this population.

The proportions of arterial stiffness in patients with twice- and thrice-weekly hemodialysis were not statistically different. The similarity in arterial stiffness between the two groups may be caused by differences in dialysis vintage. Patients with twice-weekly hemodialysis had higher dialysis vintage—almost twice that of thrice-weekly subjects (72 months [12–236] vs. 32.5 months [13–119]; p = 0.000)—so the twice-weekly subjects experienced longer inflammatory exposure due to hemodialysis.

PTX3 is an inflammation marker that increases during hemodialysis; the median PTX3 in this study was 0.93 ng/ml (0.05–4.65), lower than found by Suliman et al. (10.6 ng/ml [2.4–75.1]), El Sebai et al. (2.3 ng/ml (0.9–33)), and Oglio et al. (2.4 (SD 0.6) ng/ml).[9,17,18] PTX3 in this study was taken predialysis, similar to the other studies, so the median value of PTX3 may have been lower in this study due to differences in the subject selection criteria; for example, El Sebai et al. did not exclude subjects with malignancies. In the bivariate and multivariate analysis, PTX3 was found to be associated with arterial stiffness, which suggests that inflammation is an independent factor related to arterial stiffness. This study is the first to find an association between PTX3 and arterial stiffness in hemodialysis patients.

The proportions of PTX3 >2.3 ng/ml in patients with twice- and thrice-weekly hemodialysis were similar, despite differences in the characteristics of the two groups. The increasing value of PTX3 might have returned to baseline value intradialysis, similar to as Sjöberg et al.[19], who found in a sub-analysis of seven hemodialysis patients that baseline predialysis PTX3 values in three consecutive hemodialysis sessions with intervals of 1 or 2 days did not differ.

The proportion of arterial stiffness was higher in subjects with cardiovascular disease (40% vs 15.2%; p = 0.004). This was in line with previous studies, which found that PWV is an independent predictor of cardiovascular mortality.[20-23] PTX3 is an acute phase reactant released by neutrophil granules in response to a stimulus that triggers inflammation,[24] and its expression in macrophages and endothelial cells has been found to be stronger in mice with advanced atherosclerotic lesions than those without. Oglio et al.[9] found an increase in intracellular PTX3 expression in neutrophils at the end of hemodialysis, and intracellular PTX3 concentration is correlated with endothelial dysfunction, which contributes to the pathophysiology of cardiovascular disease.

We found dialysis vintage to be one of the determinants of arterial stiffness, as the proportion of arterial stiffness was higher in subjects with longer dialysis vintage. This is in line with a cohort study by Goldsmith et al.[25], which found that the proportion of vascular calcification increased from 49% at the onset of hemodialysis to 92% after hemodialysis for 9.7 years; dialysis vintage was also a determining factor for the severity of vascular calcification, which is one of the contributing factors for arterial stiffness.

Arterial stiffness was also found to be associated to LDL cholesterol in the multivariate analysis. One of the mechanisms that may explain the relationship between LDL and arterial stiffness is the formation of atherosclerotic plaque. Dyslipidemia is closely related to oxidative stress and inflammation, and, in hyperlipidemic conditions, lipoprotein is more susceptible to oxidation, and the oxidized form is more atherogenic. Oxidized LDL will therefore enter arterial wall macrophages faster.[26]

The proportion of subjects with arterial stiffness was not different between subjects aged 60 years and older, and those younger than 60 years. Previous studies suggested age as risk factor for arterial stiffness, but this study found no association between age and arterial stiffness. In CKD patients, arterial stiffness occurs at

an earlier age, which is called early vascular aging.[27] The lack of difference in arterial stiffness between the two age groups was probably due to differences in dialysis vintage; the dialysis vintage of subjects under 60 years was almost twice that of those older than 60 (83.2 (SD 53.3) months vs 46.8 (SD 32.1) months; $p < 0.001$). Therefore, younger subjects experienced longer exposure to inflammation due to hemodialysis. The effect of longer dialysis vintage in arterial stiffness probably outweighed the effect of older age.

The proportion of arterial stiffness did not differ between subjects with IDWG above 5% of dry body weight and those below. The similarity in arterial stiffness in both IDWG groups caused by PWV in this study was examined post-dialysis, thereby eliminating the overhydration factor.

We found no association between diabetes mellitus, hypertension, serum calcium, or phosphate and arterial stiffness, despite all of them playing important roles in the pathology of arterial stiffness. This is one of our study limitations, in that we did not consider the duration, severity, and long-term control of diabetes and hypertension. Our study only involved a one-time examination of serum calcium and phosphate, so it might not reflect their long-term control.

This study has other limitations. It was a cross-sectional study, so we were not able to assess long-term metabolic control. We were also unable to achieve similar proportions of patients with thrice- and twice-weekly hemodialysis with similar dialysis vintages, and we could not achieve a balanced proportion of patients with thrice- and twice-weekly hemodialysis overall, even though the number of subjects had already met the minimum sample size. We also did not examine post-dialysis PTX3, so we were unable to see the role of hemodialysis in increasing the inflammatory response. All variables that had a significant association with arterial stiffness in the multivariate analysis had wide confidence intervals; this could be narrowed if the study sample were larger.

CONCLUSION

In summary, predialysis PTX3 above 2.3 ng/ml was associated with arterial stiffness, as was cardiovascular disease, dialysis vintage, and LDL cholesterol level. This study found no association between hemodialysis frequency and arterial stiffness.

REFERENCES

1. Perhimpunan Nephrologi Indonesia. 11th report of Indonesian Renal Registry 2018. Jakarta: Pernefri; 2019.
2. Georgianos PI, Pikilidou MI, Liakopoulos V, Balaskas E V, Zebekakis PE. Arterial stiffness in end-stage renal disease—pathogenesis, clinical epidemiology, and therapeutic potentials. Hypertens Res. 2018;41(5):309–19.
3. Liakopoulos V, Roumeliotis S, Zarogiannis S, Eleftheriadis T, Mertens PR. Oxidative stress in hemodialysis: causative mechanisms, clinical implications, and possible therapeutic interventions. Semin Dial. 2019;32(1):58–71.
4. Williams B, Mancia G, Spiering Wi, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Eur Heart J. 2018;39:3021–104.
5. Canaud B, Cristol J, Morena M, Moragues H, Vaussenat F, Bosc J. Imbalance of oxidants and antioxidants in haemodialysis patients. Blood Purif. 1999;17:99–106.
6. Nguyen A, Lethias C, Zingraff J, Herbelin A, Naret C, Descamps-latscha B. Hemodialysis membrane-induced activation of phagocyte oxidative metabolism detected in vivo and in vitro within microamounts of whole blood. Kidney Int. 1985;28:158–67.
7. Galli F, Canestrari F, Bellomo G. Pathophysiology of the oxidative stress and its implication in uremia and dialysis. Contrib Nephrol. 1999;127:1–31.
8. Lakshmi BS, Devi NH, Suchitra MM, Rao PVLNS, Kumar VS. Changes in the inflammatory and oxidative stress markers during a single hemodialysis session in patients with chronic kidney disease. Ren Fail. 2018;40(1):531–40.
9. Oglio M, Simone S, Ciccone M, et al. Neutrophil-dependent pentraxin-3 and reactive oxygen species production modulate endothelial dysfunction in haemodialysis patients. Nephrol Dial Transp. 2017;32(9):1540–9.
10. Xu Y, Ding X, Zou J, et al. Plasma pentraxin 3 is associated with cardiovascular disease in hemodialysis patients. Ren Fail. 2011;33(10):998–1004.

11. Krzanowski M, Krzanowska K, Gajda M, et al. Pentraxin 3 as a new indicator of cardiovascular-related death in patients with advanced chronic kidney disease. Polish Arch Intern Med. 2017;127(3):170–7.
12. KDOQI. Clinical practice guidelines and clinical practice recommendations for 2006 updates: hemodialysis adequacy, peritoneal dialysis adequacy and vascular access. Am J Kidney Dis. 2006;48:S1–322.
13. Sari CMY, Nainggolan G, Marbun M. Correlation between central arterial stiffness and handgrip strength in chronic hemodialysis patients. Saudi J Kidney Dis Transpl. 2019;30:891–7.
14. Utescu MS, Couture V, Mac-way F, et al. Determinants of progression of aortic stiffness in hemodialysis patients: a prospective longitudinal study. Hypertension. 2013;62:154–60.
15. Krishnasamy R, Tan S, Hawley CM, et al. Progression of arterial stiffness is associated with changes in bone mineral markers in advanced CKD. BMC Nephrol. 2017;18(1):281.
16. Wang M, Tsai W, Chen J, Huang J. Stepwise increase in arterial stiffness corresponding with the stages of chronic kidney disease. Am J Kidney Dis. 2005;45(3):494–501.
17. El Sebai AA, El Hadidi ES, Abdel Al H, El Sayed EY. Pentraxin-3 in hemodialysis patients: relationship to comorbidities. Saudi J Kidney Dis Transpl. 2016;27(4):701–9.
18. Suliman M, Qureshi A, Carrero J, et al. The long pentraxin PTX-3 in prevalent hemodialysis patients: associations with comorbidities and mortality. Q J Med. 2008;101:397–405.
19. Sjöberg B, Snaedal S, Stenvinkel P, Qureshi AR, Heimbürger O, Bárány P. Three-month variation of plasma pentraxin 3 compared with C-reactive protein, albumin and homocysteine levels in haemodialysis patients. Clin Kidney J. 2014;7:373–9.
20. London GM, Safar ME, Pannier B. Aortic aging in ESRD: structural, hemodynamic, and mortality implications. J Am Soc Nephrol. 2016;27:1837–46.
21. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. Circulation. 1999;99(18):2434–9.
22. Shoji T, Emoto M, Shinohara K, Kakiya R, et al. Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. J Am Soc Nephrol. 2001;12:2117–24.
23. Verbeke F, Van Biesen W, Honkanen E. Prognostic value of aortic stiffness and calcification for cardiovascular events and mortality in dialysis patients: outcome of the Calcification Outcome in Renal Disease (CORD) Study. Clin J Am Soc Nephrol. 2011;6:153–9.
24. Rolph MS, Zimmer S, Bottazzi B, Garlanda C, Mantovani A, Hansson GK. Atherosclerosis and lipoproteins rapid communication production of the long pentraxin PTX3 in advanced atherosclerotic plaques. Arter Thromb Vasc Biol. 2002;22:e10–4.
25. Goldsmith D, Covic A, Sambrook P, Ackrill P. Vascular calcification in long-term haemodialysis patient in a single unit: a retrospective analysis. Nephron. 1997;77:37–43.
26. Aviram M. Hyperlipidaemia and cardiovascular disease: inflammation and oxidative stress in diabetic patients. Curr Opin Lipidol. 2009;20:258–9.
27. Mikael LDR, Machado A, De Paiva G, et al. Vascular aging and arterial stiffness. Arq Bras Cardiol. 2017;109(3):253–8.