Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2021; 38(3): 246-250
doi: 10.52142/omujecm.38.3.7

Relationship between arylesterase activity and pulse pressure index in patients with an acute ischemic stroke

Pinar AYDIN OZTRUK[1], Unal OZTURK[2], Onder OZTURK[3,*]

[1]Department of Neurosurgery, Diyarbakır Gazi Yasargil Education and Research Hospital, University of Health Sciences, Diyarbakir, Turkey
[2]Department of Neurology, Diyarbakır Gazi Yasargil Education and Research Hospital, University of Health Sciences, Diyarbakir, Turkey
[3]Department of Cardiology, Diyarbakır Gazi Yasargil Education and Research Hospital, University of Health Sciences, Diyarbakir, Turkey

Received: 11.10.2020 • **Accepted/Published Online:** 07.02.2021 • **Final Version:** 23.04.2021

Abstract

Stroke is a multifactorial disease. Arylesterase (ARE) activities have been considered as an anti-atherosclerosis factor. Increased pulse pressure (PP) may lead to a high risk of coronary artery disease and neurovascular morbidity and mortality. Nevertheless, there are limitations for PP as an evaluation index. In order to overcome the defects of PP, there is a novel parameter, "pulse pressure/systolic pressure" named "pulse pressure index (PPI)" for evaluation of cardiovascular effect. We researched the relationship between ARE activities and pulse pressure index (PPI) in acute ischemic stroke patients. We evaluated and compared the ARE activity and PPI in 87 ischemic stroke patients and 48 control patients. ARE activity was measured with the ultraviolet (UV) spectrophotometric method by using "Rel Assay Diagnostic" kits. Pulse pressure was measured by subtraction of diastolic blood pressure from systolic blood pressure. PPI was calculated as "pulse pressure / systolic pressure". Hypertension, age, diabetes mellitus, dyslipidemia importantly higher in ischemic stroke patients than the control group ($p<0.05$). PPI was significantly higher in ischemic stroke patients than the control group (0.486±0.075 and 0.417±0.051, $p<0.05$). ARE activity was significantly lower in ischemic stroke patients than in the control group (511.59 ± 68.51 and 584.16 ± 81.74 $p=0.019$). This study demonstrated that ARE activity is lower and PPI is higher in acute ischemic stroke patients than control subjects. Our results suggested that, ARE activity and PPI are important risk factors in acute ischemic stroke patients.

Keywords: arylesterase, pulse pressure, index, stroke

1. Introduction

The relationship between neurological disease and free radical activity have been researched in clinical trials. Cerebrovascular diseases are a multifactorial etiology originating from genetic and environmental predisposing factors (Kim et al., 2007). The pathophysiology of acute neurovascular diseases is carotid arter atherosclerosis (Aydin et al., 2019). Free radical activity and hypertension were associated with atherosclerotic neurovascular and coronary heart diseases. The generation of free oxidant activity is a significant pathophysiologic mechanism of causing to cerebral damage in the ischemic neurovascular disease (Michalak et al., 2011). Oxidized low density lipoproteins (LDL) in the arterial vascular wall are a significant pathophysiology of neurovascular atherosclerosis. ARE is a carboxylesterase. ARE enzyme catalyzes of fatty acids. ARE has got antioxidant property. This enzyme prevents oxidation of blood lipids. ARE has got an anti-atherosclerotic property (Mackness et al., 1991). ARE is preventing the oxidation of lipoproteins (Rozenberg et al., 2003). Therefore, ARE can decrease the progression of atherosclerotic disease. Also, ARE activity can influence atherosclerotic cerebrovascular disease. Increased vascular free radical activity is an important pathophysiology of arterial hypertension (Miyajima et al., 2007). In arterial hypertension, reactive oxygen radicals (ROR) can influence the antioxidant activity of enzymes. The importance of ROR in arterial vascular endothelial function and the pathophysiology of arterial hypertension have been lately investigated (Touyz and Schiffrin, 2004).

Elevated pulse pressure (PP) is a major clinical risk factor for the coroner and neurovascular morbidity and mortality (Assmann et al., 2005). Cardiovascular factors are affecting PP. Prior clinical trial findings on PP demonstrated that PP is a major risk factor for coronary artery disease, and mortality, genes may affect PP and gender may affect PP, cardiovascular disease and mortality (Lynch et al., 2007). Nevertheless, there is drawback for PP as an assessment for the index. On account of to get over the drawbacks of PP, there is

* Correspondence: droozturk@hotmail.com

a novel parameter, "pulse pressure/systolic pressure" termed "pulse pressure index (PPI)" for evaluation of cardiovascular consequences (Cai et al., 2015). We investigated the association between ARE activities and pulse pressure index (PPI) in acute ischemic stroke patients.

2. Materials and methods

This cross-sectional study included 87 adult patients (Females, 51; males, 36; mean age, 67.5 ± 12.7 years; range 40–89 years) with acute ischemic stroke (≤ 24 hours of symptom onset) admitted to the neurology care unit, between November 2013 and December 2014 and 48 control patients. They were classified into 2 groups: Ischemic stroke patients (Group 1, n=87), control patients (Group 2, n=48). Demographic, clinical characteristics, laboratory parameters of patients, including stroke severity assessment with National Institutes of Health Stroke Scale (NIHSS) on admission to the neurology care unit were recorded. Patient clinical data, history of cardiac and vascular predisposing risk factors, and the onset of acute stroke were established, and neurological physical examination was conducted at the time of admission to the care unit.

The diagnosis of acute ischemic stroke was made to attribute the neurological physical examination and cranial imaging within 24 hours of symptom onset. Patients with a well-defined time of symptom onset of acute ischemic stroke were included in this study. Patients who have any prior history of transient ischemic attack or cerebrovascular disease, intracranial hemorrhage were excluded. Exclusion criteria from the study are diseases that affect ARE activities. These diseases are chronic heart disease, diabetes mellitus, chronic renal disorder and malignancy. Admission stroke severity was determined using the NIHSS score (Lyden, 2017).

All patients taken immediate cranial computed tomography (Philips Brilliance 64, Royal Philips, Netherlands) after admission to the emergency care unit. Troponin values were calculated, and the electrocardiogram (ECG) was taken after admission to the neurology care unit. Echocardiographic examination (Vivid system 5, GE, Horten, Norway) was performed within the first 48 hours of admission to the neurology clinic. The NIHSS assessment and echocardiographic analysis were performed by blinded investigators. The study was accepted by the Ethics Committee of Dicle University Faculty of Medicine (the committee's date: 30-10-2013, Reference number: 411). Informed written consent to participate in this study was obtained from participants or their parents. The study was performed in proper with the guideline of the Helsinki Declaration.

Venous blood samples were obtained from the patients in admission to the neurology care unit. Blood samples were taken from the antecubital vein into blood tubes. Then blood samples were separated from the cells by centrifugation at 5000 rpm for 5 min. Serum samples were aliquoted and stored at -70°C until analysis. ARE activities were calculated with the UV spectrophotometric method by using "Rel Assay Diagnostic" kits. Arterial blood pressure calculations were performed in all stroke patients within 10 minutes after admission to the neurology care unit. Blood pressure was measured with a digital blood pressure measuring device after five minutes of rest, as recommended by the Joint National Committee-7 report (Chobanian et al., 2003). Patients were seated or lying on the bed with their arm bared and supported at heart level. Two readings, separated by 2 minutes, were obtained and averaged. Additional blood pressure measurements were obtained if these measurements differed by > 5 mm Hg. Pulse pressure was measured by subtraction of diastolic blood pressure from systolic blood pressure. PPI was calculated by "pulse pressure / systolic pressure".

Statistical analysis was carried out with the SPSS statistical package (Version 12.0; SPSS Inc., Chicago, IL, USA). All baseline clinical parameters were analyzed. Continuous variables were expressed as the mean ± SD; and categorical variables were expressed as percentages. Independent Sample T-Test, Mann-Whitney U test and Chi-square test, Pearson's Correlation test and regression analysis were used for comparison of data as appropriate. p values of < 0.05 were considered statistically significant.

3. Results

Clinical characteristics of patients are summarized in Table 1. Age, hypertension, systolic blood pressure (BP), diastolic BP (DBP), heart rate, PP, PPI, diabetes mellitus, dyslipidemia, glucose, creatinine, LDL cholesterol were significantly higher in ischemic stroke patients than control group ($p < 0.05$). ARE activity and HDL cholesterol being significantly lower in acute ischemic stroke patients than control group ($p < 0.05$).

Table 1. Clinical characteristics of patients

Variables	Group 1 (Ischemic Stroke) n=87	Group 2 (Control Group) n=48	p
Age (years)	67.5±12.7	44.3±17.2	0.023
Gender (F/M), n	51 / 36	26 / 22	0.321
Hypertension, n %	54 (63%)	10 (20%)	0.027
SBP (mmHg)	161.4 ± 18.7	122.8 ± 12.5	0.042
DBP (mmHg)	95.6 ± 11.9	71.9 ± 8.6	0.039
Heart Rate (bpm)	119.2 ± 19.5	85.1 ± 11.7	0.029
PP, mm-Hg	62.4±17.2	45.1±11.9	0.036
PPI	0.486±0.05	0.417±0.051	0.043
Diabetes Mellitus, %	28 (32 %)	3 (7 %)	0.014
Smoking, n %	19 (22 %)	4 (8 %)	0.627
Dyslipidemia, n %	23 (27%)	2 (4 %)	0.006
Glucose (mg/dl)	165.3 ± 35.6	103.4 ± 24.3	0.029
HbA1c	9.8 ± 2.5	5.7 ± 1.8	0.039
Creatinine (mg/dL)	1.7±0.6	0.8±0.2	0.029
ARE activity	511.59 ± 68.51	584.16 ± 81.74	0.019
LDL cholesterol (mg/dL)	141.4 ± 28.7	105.8 ± 15.9	0.029
HDL cholesterol (mg/dL)	33.8 ± 8.1	41.3 ± 8.3	0.041

F: Female, M: Male, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, PP: Pulse Pressure, PPI: Pulse Pressure Index, ARE: Arylesterase, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein

Echocardiographic findings are summarized in Table 2. Left ventricle (LV) septal thickness, LV diastolic diameter, LV posterior wall thickness, and E/e' values were significantly higher in Group 1 patients than in Group 2 patients ($p < 0.05$). LVEF was significantly lower in Group 1 patients than in Group 2 patients ($p < 0.05$).

Table 2. Echocardiographic parameters of patients

Variables	Group 1 (Ischemic Stroke) n=87	Group 2 (Control Group) n=48	p
LV septal thickness	12.1±1.3	10.4±0.8	0.024
LVDd (mm)	54.8±6.3	49.1±4.3	0.045
LV posterior wall thickness, mm	11.4±1.2	10.6±0.7	0.032
LVDs (mm)	43.2±4.2	38.3±3.5	0.367
LAD (mm)	42.4±3.9	37.1±3.6	0.645
RAD (mm)	34.1±3.1	32.4±2.7	0.692
RVDd (mm)	29.8±2.6	27.9 ± 2.2	0.451
LVEF (%)	51.5±6.2	59.6±5.7	0.036
E/e'	10.3±3.6	7.1 ±2.75	0.027

LV: Left ventricle, LVDd: Left ventricular diastolic diameter, LVDs: Left ventricular systolic diameter, LAD: Left atrial diameter, RAD: Right atrial diameter, RVDd: Right ventricular diastolic diameter, LVEF: Left ventricular ejection fraction

Correlation analysis was performed to research the relationship between PPI and clinical parameters showed a negative correlation between the PPI and LVEF (left ventricular ejection fraction), ARE. In addition, there was a positive correlation between the PPI and E/e', age, heart rate, systolic blood pressure (SBP) (Table 3).

Table 3. Correlation of patients' characteristics and pulse pressure index

Parameters	Pearson's correlation coefficient (r value)	p
LVEF	-0.459	0.034
E/e'	0.376	0.038
ARE	-0.457	0.029
Age	0.435	0.045
SBP	0.483	0.038
Heart rate	0.324	0.041

LVEF: Left ventricular ejection fraction, ARE: Arylesterase, SBP: Systolic Blood Pressure

Logistic regression analysis was performed to identify the potential predictors for PPI. Results of the multivariate analysis revealed that age, SBP, LVEF, ARE and heart rate were a powerful predictor of PPI (Table 4).

Table 4. Multivariate logistic regression analysis between PPI and clinical parameters

Parameters	OR	95 % CI	p
SBP	0.647	0.523-0.614	0.028
LVEF	0.789	0.651-0.915	0.036
ARE	0.562	0.376-0.829	0.043
Age	0.482	0.287-0.792	0.037
Heart rate	0.381	0.256-0.691	0.035

SBP: Systolic Blood pressure, ARE: Arylesterase, LVEF: Left ventricular ejection fraction

4. Discussion

Acute stroke is identified as one of the significant reasons for mortality and morbidity (Feigin et al., 2014). Stroke is a multifactorial disease. This may account for why the incidence of acute stroke demonstrates racial and regional variations. There is a proof for ROR relevance in the pathogenesis of a lot of diseases, with a specific point on those related to atherosclerosis, such as diabetes, cardiovascular disease, acute stroke, and chronic renal diseases. ARE acts as a significant component of the enzymatic antioxidant system with PON-1, which has the same functions. Moreover, both PON-1 and ARE interact to form a significant component of the enzymatic plasma antioxidant system (Sahin et al., 2019). Shenhar TS and colleagues found that ARE was significantly lower in acute stroke patients who had any degree of white matter lesion (WML) than WML-free patients (Shenhar-Tsarfaty et al., 2013). Strokes are associated with changes in serum ARE activity (Can Demirdöğen et al., 2008). The present study is the first study in the literature that evaluates the relationship between ARE activity and PPI in acute ischemic stroke patients. The main finding of our study is that ARE activity is significantly decreased in acute ischemic stroke patients than in control subjects. Also, Chawhan and colleagues (2015) suggested that ARE enzyme activity is substantially reduced in ischemic stroke patients compared to healthy controls. They are suggested that, ARE is a risk factor for ischemic stroke. Demirdogen and colleagues demonstrated that the arylesterase activities of acute ischemic stroke patients were lower than those of control subjects, regardless of the genotype group they belong to (Can Demirdöğen et al., 2008). In the opinion of Wannamethee and colleagues, low HDL-C value is a significant predisposing component for the initiation of stroke (Wannamethee et al., 2000). In this research, we observed that HDL is importantly lower in acute ischemic stroke patients than in healthy controls. Also, we observed that LDL cholesterol was importantly higher in acute ischemic stroke patients than in healthy controls.

Acute stroke is characterized by profound autonomic dysregulation, including changes in the autonomic reflex pathways, central autonomic neuroanatomical locations and hormonal factors. According to prior investigations on BP changes during the early period of stroke, there is higher increase of SBP than DBP during the acute stroke (Morfis et al., 1997). The acute stress response to stroke events increased sympathetic tone, and compensatory response to cerebral ischemia might account these evidences (Castillo et al., 2004). As a result, an increase of PP could have occurred if there was a more prominent elevation of SBP than DBP during the acute ischemic stroke period. In this study, we found that SBP, DBP, heart rate, PP, PPI were significantly higher in acute ischemic stroke patients than in healthy controls. Lee and colleagues suggested that PP when calculated in the early period of acute ischemic stroke has relationships with major cerebrovascular and cardiovascular events and recurrent stroke. Also, they are

suggested that PP has an important predictive power than other usually used BP parameters (Lee et al., 2018). For ischemic stroke events, other analyses based on the REGARDS population demonstrated that PP was an independent predictor of stroke event after adjusting for DBP or mean arterial pressure, but not after adjusting for SBP (Glasser et al., 2015). A meta-analysis of 16 cohort clinical studies in Japan suggested that a substantial association between PP and ischemic stroke in men (Miura et al., 2009). On the other hand, SBP and DBP were not compared with PP in this meta-analysis. Recently, Chang JJ and colleagues reported that PP as an independent predictor for in hospital mortality in patients with spontaneous intracerebral hemorrhage (Chang et al., 2017).

Hypertension, age, hyperlipidemia and Diabetes Mellitus are major risk factors for atherosclerotic cerebrovascular disease (Wu et al., 2010). In our study, hypertension was importantly more common in acute ischemic stroke patients. Age was significantly higher in acute ischemic stroke patients than in healthy controls. Stroke-related sympathetic activation is high in patients with acute ischemic stroke. Irrespective of prior cardiovascular status, an acute phase of stroke markedly influences LV function, and biochemical parameters (Glucose, troponin, creatinine) (Ripoll et al., 2018). In this research, we observed that LVEF was importantly lower in acute ischemic stroke patients than in healthy controls. Öztürk and Ozturk (2019) found that the severe acute ischemic stroke patients had lower LVEF.

Hendrix and colleagues (2019) found that diabetes mellitus history is an important predictor of stroke severity. Lindsberg and colleagues suggested that increased blood glucose is frequent in the acute period of stroke (Lindsberg and Roine, 2004). In our study blood glucose and HbA1c levels were significantly in acute ischemic stroke patients than in healthy controls. Lindsberg and Roine (2004) reported that diabetes is frequent in severe acute ischemic patients. But, stress related hyperglycemia is more common in these patients. In this research, we observed that E/é value was importantly higher in severe stroke patients. Ryu and colleagues (2018) suggested that E/e' ratios were associated with carotid arterial occlusion in AF-related stroke and may play a role in identifying patients at high risk of severe stroke. In this research, we observed that creatinine levels were importantly higher in acute ischemic stroke patients. Mostofsky and colleagues (2009) suggesting that shared risk factors underlying vascular diseases including age, diabetes mellitus, hypertension, left ventricular hypertrophy may indicate vascular pathogenesis resulting from reduced renal clearance. Renal function predicts survival in patients with acute ischemic stroke.

In conclusion, this study demonstrated that ARE activity is lower and PPI is higher in acute ischemic stroke patients than control subjects. Our results suggested that, ARE activity and PPI are important risk factors in acute ischemic stroke patients.

Conflict of interest

None to declare.

Acknowledgments

None to declare.

References

1. Assmann, G., Cullen, P., Evers, T., Petzinna, D., Schulte, H., 2005. Importance of arterial pulse pressure as a predictor of coronary heart disease risk in PROCAM. Eur. Heart. J. 26(20), 2120-2126.
2. Aydin, O.P., Yilmaz, T., Ozturk, U., 2019. Effects of Bemiparin Sodium Versus Dabigatran Etexilate After Anastomosis in Rat Carotid Arteries on the Development of Neointima and Thrombolytic Efficacy. World. Neurosurg. 126, e731-e735.
3. Cai, A., Mo, Y., Zhang, Y., Li, J., Chen, J., Zhou, Y., Chen, R., Wei, R., Huang, Y., Tang, S., Feng, Y., 2015. Relationship of pulse pressure index and carotid intima-media thickness in hypertensive adults. Clin. Exp. Hypertens. 37(4), 267-270.
4. Demirdogen, C., Türkanoğlu, B.A., Bek, S., Sanisoğlu, Y., Demirkaya, S., Vural, O., Arinc, E., Adali, O., 2008. Paraoxonase/arylesterase ratio, PON1 192Q/R polymorphism and PON1 status are associated with increased risk of ischemic stroke. Clin. Biochem. 41(1-2), 1-9.
5. Castillo, J., Leira, R., García, M.M., Serena, J., Blanco, M., Dávalos, A., 2004. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. Stroke. 35(2), 520-526.
6. Chang, J. J., Khorchid, Y., Dillard, K., Kerro, A., Burgess, L.G., Cherkassky, G., Goyal, N., Chapple, K., Alexandrov, A.W., Buechner, D., Alexandrov, A.V., Tsivgoulis, G., 2017. Elevated Pulse Pressure Levels Are Associated With Increased In-Hospital Mortality in Acute Spontaneous Intracerebral Hemorrhage. Am. J. Hypertens. 30(7), 719-727.
7. Chawhan, S. S., Mogarekar, M.R., Wagh, R.V., Das, R.R., Pramanik, S.S., Sonune S.M., Chawhan, S.M., 2015. Relation of Paraoxonase1, Arylesterase and Lipid Profile in Ischemic Stroke Patients. J. Clin. Diagn. Res. 9(11), Bc01-03.
8. Chobanian, A. V., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo, J.L., Jones, D.W., Materson, B.J., Oparil, S., Wright, J.T., Roccella, E.J., 2003. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 42(6), 1206-1252.
9. Feigin, V. L., Forouzanfar, M.H., Krishnamurthi, R., Mensah, G.A., Connor, M., Bennett, D.A., Moran, A.E., Sacco, R.L., Anderson, L., Truelsen, T., O'Donnell, M., Venketasubramanian, N., Barker-Collo, S., Lawes, C.M., Wang, W., Shinohara, Y., Witt, E., Ezzati, M., Naghavi, M., Murray, C., 2014. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet. 383 (9913), 245-254.
10. Glasser, S. P., Halberg, D.L., Sands, C.D., Mosher, A., Muntner, P.M., Howard, G., 2015. Is Pulse Pressure an Independent Risk Factor for Incident Stroke, REasons for Geographic And Racial Differences in Stroke. Am. J. Hypertens. 28(8), 987-994.
11. Hendrix, P., Sofoluke, N., Adams, M.D.,Kunaprayoon, S., Zand, R., Kolinovsky, A.N., Person, T.N., Gupta, M, Goren, O, Schirmer, C.M., Rost, N.S., Faber, J.E., Griessenauer, C.J., 2019. Risk Factors for Acute Ischemic Stroke Caused by Anterior Large Vessel Occlusion. Stroke. 50(5), 1074-1080.
12. Kim, N. S., Kang, K., Cha, M.H., Kang, B.J., Moon, J., Kang, B.K., Yu, B.C., Kim, Y.S., Choi, S.M., Bang, O.S., 2007.

Decreased paraoxonase-1 activity is a risk factor for ischemic stroke in Koreans. Biochem. Biophys. Res. Commun. 364(1), 157-162.

13. Lee, H.W., Kim, K.J., Han, B.J., Kim, M.K., Cho, J.T., Shin, K.H., Yeo, D.I., Cha, M.J., Kim, J.K., Nah, D.H., Kim, D.E., Ryu, W.S., Park, J.M., Kang, K., Lee, S.J., Oh, M.S., Yu, K.S., Lee, B.C., Hong, K.S., Cho, Y.J., Choi, J.C., Sohn, S.I., Hong, J.H., Park, T.H., Park, S.S., Kwon, J.H., Kim, W.J., Lee, J., Lee, J.S., Lee, J., Gorelick, P.B., Bae,H.J., 2018. Predictive Value of Pulse Pressure in Acute Ischemic Stroke for Future Major Vascular Events. Stroke. 49(1), 46-53.

14. Lindsberg, P. J., Roine, R.O., 2004. Hyperglycemia in acute stroke. Stroke. 35(2), 363-364.

15. Lyden, P., 2017. Using the National Institutes of Health Stroke Scale: A Cautionary Tale. Stroke. 48(2), 513-519.

16. Lynch, A. I., Arnett, D.K., Pankow, J.S., Miller, M.B., North, K.E., Eckfeldt, J.H., Hunt, S.C., Rao D.C., Djoussé, L, 2007. Sex-specific effects of ACE I/D and AGT-M235T on pulse pressure: the HyperGEN Study. Hum. Genet. 122(1), 33-40.

17. Mackness, M. I., Arrol, S., Durrington, P.N., 1991. Paraoxonase prevents accumulation of lipoperoxides in low-density lipoprotein. FEBS. Lett. 286(1-2), 152-154.

18. Michalak, S., Kazmierski, R., Hellmann, A., Wysocka, E., Kocialkowska-Adamczewska, D., Wencel-Warot, A., Nowinski, W.L. ,2011. Serum paraoxonase/arylesterase activity affects outcome in ischemic stroke patients. Cerebrovasc. Dis. 32(2), 124-132.

19. Miura, K., Nakagawa, H., Ohashi, Y., Harada, A., Taguri, M., Kushiro, T., Takahashi, A., Nishinaga, M., Soejima, H., Ueshima, H., 2009. Four blood pressure indexes and the risk of stroke and myocardial infarction in Japanese men and women: a meta-analysis of 16 cohort studies. Circulation. 119(14), 1892-1898.

20. Miyajima, K., Minatoguchi, S, Ito, Y., Hukunishi, M., Matsuno, Y., Kakami, M., Kawasaki, M., Nishigaki, K., Takemura, G., Fujiwara, H., 2007. Reduction of QTc dispersion by the angiotensin II receptor blocker valsartan may be related to its anti-oxidative stress effect in patients with essential hypertension. Hypertens. Res. 30(4), 307-313.

21. Morfis, L., Schwartz, R.S., Poulos, R., Howes, L.G., 1997. Blood pressure changes in acute cerebral infarction and hemorrhage. Stroke. 28(7), 1401-1405.

22. Mostofsky, E., Wellenius, G.A., Noheria, A., Levitan, E.B., Burger, M.R., Schlaug, G., Mittleman, M.A., 2009. Renal function predicts survival in patients with acute ischemic stroke. Cerebrovasc. Dis. 28(1), 88-94.

23. Öztürk, Ü., Ozturk, O., 2019. Assessment of Myocardial Function by Myocardial Performance Index in Patients with Acute Ischemic Stroke. Dicle Med. J. 46, 715-723.

24. Ripoll, J. G., Blackshear, J.L., Díaz-Gómez, J.L., 2018. Acute Cardiac Complications in Critical Brain Disease. Neurosurg. Clin. N. Am. 29(2), 281-297.

25. Rozenberg, O., Shih, D.M., Aviram, M., 2003. Human serum paraoxonase 1 decreases macrophage cholesterol biosynthesis: possible role for its phospholipase-A2-like activity and lysophosphatidylcholine formation. Arterioscler. Thromb. Vasc. Biol. 23(3), 461-467.

26. Ryu, W. S., Bae, E.K., Park, S.H., Jeong, S.W., Schellingerhout, D., Nahrendorf, M., Kim, D.E., 2018. Increased Left Ventricular Filling Pressure and Arterial Occlusion in Stroke Related to Atrial Fibrillation. J. Stroke. Cerebrovasc. Dis. 27(5), 1275-1282.

27. Sahin, M., Bobusoglu, O., Yetim,A., Ates, F., 2019. Paraoxonase-1 and arylesterase levels in patients with ulcerative colitis. Arab. J. Gastroenterol. 20(1), 14-18.

28. Shenhar-Tsarfaty, S., Waiskopf, N., Ofek, K., Shopin, L., Usher, S., Berliner, S., Shapira, I., Bornstein, N.M., Ritov, Y., Soreq, H., Ben Assayag, E., 2013. Atherosclerosis and arteriosclerosis parameters in stroke patients associate with paraoxonase polymorphism and esterase activities. Eur. J. Neurol. 20(6), 891-898.

29. Touyz, R. M., Schiffrin, E.L., 2004. Reactive oxygen species in vascular biology: implications in hypertension. Histochem. Cell. Biol. 122(4), 339-352.

30. Wannamethee, S. G., Shaper, A.G., Ebrahim, S., 2000. HDL-Cholesterol, total cholesterol, and the risk of stroke in middle-aged British men. Stroke. 31(8), 1882-1888.

31. Wu, C. Y., Wu, H.M., Lee, J.D., Weng, H.H., 2010. Stroke risk factors and subtypes in different age groups: a hospital-based study. Neurol. India. 58(6), 863-868.