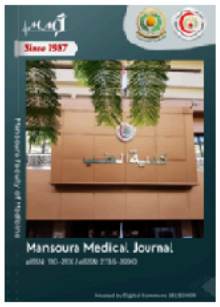
MANSOURA MEDICAL JOURNAL

ISSN - Print: 1110-211X - Online: 2735-3990

journal homepage: mmj.mans.edu.eg



Volume 52 | Issue 3 Article 2

Assessment of Serum Lipoprotein Phospholipase A2 as an Atherosclerotic Risk Factor in Ischemic Stroke Elderly Patients

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Cover Page Footnote

There are some limitations of the current work. 1The sample size was relatively small, and 2the enrolled cases were not representative of all patients with anterior circulation infarction at different time points. Furthermore,3 there was no long-term follow-up. For that, there is a need for multicenter clinical trials with larger sample sizes to explain whether Lp-PLA2 quantification helps determine the risk of ischaemic strokes.

ORIGINAL STUDY

Assessment of Serum Lipoprotein Phospholipase A2 as Atherosclerosis Risk Factor in Ischemic Stroke Elderly Patients

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Abstract

Background: **Significant evidence does exist regarding the significant role of inflammation in the development of atherosclerosis. Lipoprotein phospholipase A2 is a phospholipase A2 enzyme (Lp-PLA2) that is predominantly produced by macrophages and lymphocytes in atherosclerotic plaque. Increased Lp-PLA2 concentrations are significantly linked to atherosclerosis-related diseases which include cardiovascular diseases and ischemic strokes.**

Aim: **This study was conducted to assess the role of serum levels of Lp-PLA2 in cerebral atherosclerosis (CA).**

Methods: **This prospective cross-sectional case−control study enrolled 100 patients aged 60 years old or more with acute ischemic stroke (AIS). Using the TOAST classification, patients were divided into case group 'atherosclerotic' and control group' nonatherosclerotic' including cardioembolism, small vessel occlusion, stroke of other determined etiology, and stroke of undetermined etiology.**

Results: **The median LP2A was significantly higher in atherosclerotic cases as compared with non-atherosclerotic cases (132.5 vs. 49.75, respectively). Significant negative association was found between Glasgow coma scale (GCS) and LP2A in addition to positive correlation between LP2A and the following; National Institutes of Health Stroke Scale (NIHSS) at admission, NIHSS at discharge and modified Rankin scale (mRS) at discharge. A statistically significant relationship was revealed between LP2A and hypercholesterolemia among the atherosclerotic group ($P < 0.05$).**

Conclusion: **This study concluded that Lp-PLA2 was markedly increased among atherosclerotic ischemic stroke subjects. In addition, it could be used as a reliable marker in the context of the differentiation between atherosclerotic ischemic stroke and nonatherosclerotic ones. Higher levels of Lp-PLA2 were associated with higher stroke severity and disability.**

Keywords: Cerebral atherosclerosis, Color coded duplex, Ischemic stroke, Lipoprotein phospholipase A2

1. Introduction

Cerebral atherosclerosis (CA) is the accumulation of cholesterol-laden plaques in the walls of large cerebral vessels. CA can range from minor thickening of the arterial wall to severe luminal stenosis resulting in decreased cerebral flow and metabolic processes. As the age is increased, the prevalence of CA is increased. Also, an increased prevalence is associated with several risk factors including hyperlipidemia, elevated blood pressure (BP), diabetes mellitus (DM) and smoking. CA occurs in 7% of asymptomatic middle-aged subjects and 82% of subjects aged greater than 80 years (Wingo et al., 2020).

Significant evidence does exist regarding the key role of inflammatory process in atherosclerosis (Koenig and Khuseyinova, 2007). Lipoprotein phospholipase A2 (Lp-PLA2) is predominantly produced by macrophages and lymphocytes in the atherosclerotic plaque. Approximately 80% of Lp-PLA2 is bound to the low-density lipoprotein (Tselepis and John Chapman, 2002).

Lp-PLA2 is a vascular-specific inflammatory biomarker which has a significant role in the

Received 18 August 2023; revised 9 September 2023; accepted 13 September 2023.
Available online 16 November 2023

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https://doi.org/10.58775/2735-3990.1394

atherosclerosis, including its formation, progression and rupture of atherosclerosis plaque (Lp et al., 2010). Increased Lp-PLA2 concentrations are significantly linked to atherosclerosis-related conditions, such as cardiovascular diseases and ischaemic strokes (Caslake and Packard, 2005). Furthermore, the high Lp-PLA2 concentrations might contribute to stroke occurrence and recurrence. Nonetheless, few studies investigated predictive role of Lp-PLA2 concentrations in evaluating the severity of cerebrovascular stenosis and neurologic deterioration in acute ischemic stroke (AIS) (Wei et al., 2017). So, we did this work to study the role of serum Lp-PLA2 levels in CA.

2. Patients and methods

This prospective cross-sectional case−control study enrolled 100 patients (aged 60 years old or more) with AIS at the Neurology department at Mansoura University diagnosed with acute ischemic stroke over a period of one year after approval of the Institutional Review Board (IRB). Using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification (Adams et al., 1993), patients were classified into case group 'atherosclerotic' and control group' nonatherosclerotic' including Cardioembolism, small vessel occlusion, stroke of other determined etiology and stroke of undetermined etiology.

3. Methods

Studied patients were subjected to detailed history taking including history of previous TIAs or strokes, thorough neurologic examination, and assessment of the severity of neurologic impairment utilizing the National Institutes of Health Stroke Scale (NIHSS) (Meyer and Lyden, 2009), and modified Rankin scale (mRS) for disability assessment (Nobels-Janssen et al., 2022). Laboratory investigations included complete blood picture, international normalized ratio (INR), random blood sugar, liver function tests and complete lipid profile. Patients had electrocardiography.

3.1. Serum Lp-PLA2 concentration

A fasting blood sample (3 ml) was collected from each patient within 48 h postadmission. The sera were obtained via blood centrifugation at 3000 r/min over 10 min and then kept at −80 °C till analysis. Serum Lp-PLA2 concentrations were quantified utilizing the enzyme linked immunosorbent assay (ELISA) with commercial kits (Lp-PLA2 assay kit, Tianjin Kangerke Biotechnology Co. Ltd., China). In the Lp-PLA2 assay kit, the plate had been precoated with human Lp-PLA2 antibody. Lp-PLA2 present in the serum sample will be bound to antibodies coated on the wells. Addition of enzyme conjugate reveal the degree of this binding by color reaction and consequently concentration of serum Lp-PLA2 after blotting of standard curve.

3.2. Ethical consideration

This work obtained its approval from the IRB of the faculty of medicine, Mansoura University (MS.21.04.1470). A verbal consent was obtained from each patient before participation. Confidentiality and privacy were maintained throughout the study. The data were not and will not be utilized in other purposes rather than the current work.

3.3. Statistical analysis and data interpretation

Data were analyzed using SPSS software, v 25 (SPSS Inc., PASW statistics, Chicago). Qualitative data were presented as utilizing frequencies and percent's. Quantitative data were presented as medians for non-normally distributed data and means±SDs for normal distribution of data after testing normality by Kolmogrov−Smirnov test. Significance was set at P less than or equal to 0.05 level. Mann Whitney U and Kruskal Wallis test were utilized for comparison between two studied groups and more than two studied groups, correspondingly for non-normally distributed data. The Spearman's rank-order correlation determined the strength and direction of a linear relationship among two non-normally distributed continuous variables. Multiple linear regression was utilized assess predictors of continuous normally distributed outcome following log transformation with calculation of R2.

4. Results

The mean age of the patients was 67.74 and standard deviation 10.89 years, 51.0% females, 25% are on ventilator, Median stroke to door time per hours is 6 ranging from 0.5 to 96 h, mean weight was 84.63 kg and median Glasgow coma score (GCS) was 13 ranging from 4 to 15, median NHISS at discharge was 14 ranging from 0 to 28, mRS at discharge was 4 (range = 1−6), 26% known atrial fibrillation (AF), 15% newly detected AF, 41% DM, 75% hypertension, 51% hypercholesterolemia, 26% smokers and 17% RF coronary artery disease. Mean systolic blood pressure at admission was 162.05, mean diastolic blood pressure was 99.15, median

random blood glucose was 110 mg/dl ranging from 70 to 373 mg/dl, median creatinine was 0.8 ranging from 0.6 to 5.2 mg/dl, mean INR is 1.09, mean platelet count is 257.5, 27% have positive history of stroke, 25% anti platelets and 8% anticoagulants. Intracranial hemorrhage was detected among 6% of the studied cases, median LP2A is 73.8 ranging from 4.4 to 2543.

According to Table 1, a nonsignificant difference was found among both groups as regard age and gender. Mean age of control group is 67.88 years versus 67.60 for cases group. Control group are distributed as following 66% females and 44% males versus 46% females and 54% males for cases group. No significant difference was found among both groups regarding need of assisted ventilation, weight, GCS, NIHSS at admission as well as NIHSS and mRS at discharge ($P > 0.05$).

As demonstrated in Table 2, a significant difference was revealed among both groups regarding AF and hypercholesterolemia. Hypercholesterolemia was more frequent among atherosclerotic group than nonatherosclerotic group; 66% versus 36%, respectively. AF was significantly higher in non-atherosclerotic cases while hypercholesterolemia was significantly higher in the atherosclerotic cases. No significant difference was found between studied groups as regard mean systolic and diastolic BP at admission, RBS, creatinine, INR and platelet count ($P > 0.05$).

Table 3 shows a significant difference among both groups regarding the history of prophylactic treatment before the onset. Among atherosclerotic group; 66% have negative history of prophylactic treatment, 32% on antiplatelet and 2% on anticoagulants versus 68%, 18% and 14% for non-atherosclerotic group. No significant difference existed among the two groups as regards ICH. A significantly higher median LP2A was reported in the atherosclerotic group versus the non-atherosclerotic group (132.5 vs. 49.75, respectively).

Table 4 illustrates that presence of hypercholesterolemia and increase in LP2A are statistically significant predictors of disease with the overall % predicted is 85%. Hypercholesterolemia enhanced risk of disease by 3.45 (odds ratio = 3.45; 95% CI:1.52–78.5, every increase one unit in LP2A increase risk by 1.052 (odds ratio = 1.03–1.08). Table 5 shows that ROC curve of L2PA illustrates that cut off point for area under curve in differentiating cases from control group is excellent (AUC = 0.916) with the best estimated cut-off value was 100 achieving 90, 64, and 77% for sensitivity, specificity and accuracy, respectively.

In Table 6, no significant association existed between L2PA and sex, age and weight of the studied cases. A nonsignificant correlation was detected between indication for ventilator and median L2PA ($P = 0.585$). A significant negative association was revealed between GCS and L2PA ($r = -0.785$) ($P < 0.001$*), positive correlation between L2PA and the following; NIHSS at admission ($r = 0.858$) ($P < 0.001$*), NIHSS at discharge ($r = 0.756$) ($P < 0.001$*) and mRS at discharge ($r = 0.484$) ($P < 0.001$*).

As shown in Table 7, a non-significant correlation was found between L2PA and the following; AF, DM, hypertension, smoking and RF coronary artery disease ($P > 0.05$), and shows significant relation

Table 1. Demographics, ventilator use and clinical assessment of the studied groups.

	NonAtherosclerotic ($n = 50$)	Atherosclerotic ($n = 50$)	Test of significance
Age in years			$t = 0.128$
mean ± SD	67.88 ± 11.74	67.60 ± 10.09	$P = 0.898$
Sex	*N* (%)	*N* (%)	
Female	28 (66.0)	23 (46.0)	$\chi^2 = 1.0$
Male	22 (44.0)	27 (54.0)	$P = 0.317$
Ventilator			
No	35 (70)	37 (74)	MC = 0.429
Yes	13 (26)	12 (24)	$P = 0.807$
Not known	2 (4)	1 (2)	
Weight (Kg)			$t = 0.233$
mean ± SD	84.86 ± 9.98	84.40 ± 9.72	$P = 0.816$
GCS			Z = 0.495
Median (minimum -maximum)	13 (4–15)	14 (5–15)	$P = 0.621$
NIHSS at admission			Z = 0.499
Median (minimum -maximum)	13 (3–28)	15 (0–24)	$P = 0.618$
NIHSS discharge			Z = 0.09
Median (minimum -maximum)	10 (3–28)	12 (0–24)	$P = 0.928$
mRS discharge			Z = 0.483
Median (minimum -maximum)	4 (1–6)	4 (1–6)	$P = 0.629$

t:Student *t* test, χ^2 = Chi–Square test, Z:Mann Whitney *U* test, MC: Monte Carlo test, *statistically significant.

Table 2. Comparison of medical history, blood pressure, and laboratory findings between the studied groups.

	NonAtherosclerotic ($n = 50$)	Atherosclerotic ($n = 50$)	Test of significance
AF			
No	11 (22.0)	48 (96.0)	MC = 56.62
Known	25 (50.0)	1 (2.0)	$P < 0.001$[a]
Newly-detected	14 (28.0)	1 (2.0)	
Diabetes	18 (36.0)	23 (46.0)	$\chi^2 = 1.03$ $P = 0.309$
Hypertension	36 (72.0)	39 (78.0)	$\chi^2 = 0.480$ $P = 0.488$
Hypercholesterolemia	18 (36.0)	33 (66.0)	$\chi^2 = 9.0$ $\boldsymbol{P = 0.003}$[a]
Smoking	11 (22.0)	15 (30.0)	$\chi^2 = 0.832$ $P = 0.362$
RF coronary artery disease	9 (18.0)	8 (16.0)	$\chi^2 = 0.071$ $P = 0.790$
Systolic BP at admission (Hg/mm)			$t = 0.695$
mean ± SD	163.6 ± 21.45	160.5 ± 23.13	$P = 0.489$
Diastolic BP at admission (Hg/mm)			$t = 0.029$
mean ± SD	99.20 ± 18.28	99.10 ± 15.54	$P = 0.977$
RBS mg/dl			Z = 0.912
Median (minimum–maximum)	101 (70–347)	125.5 (77–373)	$P = 0.362$
Creatinine (mg/dl)			Z = 1.63
Median (minimum–maximum)	0.8 (0.6–3.1)	0.8 (0.6–5.2)	$P = 0.103$
INR			$t = 0.0$
Mean ± SD	1.089 ± 0.12	1.089 ± 0.122	$P = 1.0$
Platelet count			$t = 0.128$
Mean ± SD	258.46 ± 72.17	256.54 ± 77.66	$P = 0.898$

[a] Statistically significant.

Table 3. Comparison of stroke history, history of prophylactic treatment, intracranial hemorrhage and Lipoprotein phospholipase2A.

	NonAtherosclerotic ($n = 50$)	Atherosclerotic ($n = 50$)	Test of significance
History of prior stroke	10 (20)	17 (34)	$\chi^2 = 2.48$ $P = 0.115$
History of prophylactic treatment before the onset			
None	34 (68)	33 (66)	
Anti platelets	9 (18)	16 (32)	MC = 6.48
Anticoagulants	7 (14)	1 (2)	$P = 0.039$*
ICH	2 (4.0)	4 (8.0)	FET = 0.709 $P = 0.678$
LP2A	49.75 (4.4–97)	132.5 (30.2–2543)	Z = 7.17 $P < 0.001$*

χ^2, Chi–Square test; FET, Fischer exact test; MC, Monte Carlo test; Z, Mann Whitney *U* test *statistically significant.

Table 4. Predictors of atherosclerotic stroke in the study groups.

	B	*P* Value	Odds ratio (95%CI)
Hypercholesterolemia	1.24	0.003[a]	3.45 (1.52–78.5)
LP2A	0.051	<0.001[a]	1.052 (1.03–1.08)
Overall% predicted = 85%			

[a] Statistically significant.

between L2PA and Hypercholesterolemia among the atherosclerotic group ($P < 0.05$). A nonsignificant relationship existed between L2PA and the following; history of stoke, history of prophylactic treatment before the onset, and ICH ($P > 0.05$).

5. Discussion

Lp-PLA2 is an inflammatory factor which has a role in the pathogenetic process of atherosclerotic plaques and is linked to a high risk of AIS (Wang et al., 2022). Therefore, the current study aimed at assessing the role of serum level of Lp-PLA2 in CA.

As regards the demographic features, no significant difference was revealed among the both regarding age and sex. Thus, both groups were comparable and the demographics did not interfere with study's results. With regard to LP2A level, the current study revealed a significantly higher median LP2A among atherosclerotic group than non-atherosclerotic group (132.5 ranging from 30.2 to 2543 and 49.75 ranging from 4.4 to 97, respectively).

This comes along the results reported by Wei et al. (2017), who reported that the serum Lp-PLA2 concentrations in large artery atherosclerosis (LAA) was significantly higher as compared with other subtypes of AIS and the nonacute cerebral infarction group. Such results indicated that Lp-PLA2 levels were significantly correlated with the pathogenesis of LAA. Lp-PLA2 levels were significantly high among cases with LAA and CE subtypes than the nonacute cerebral infarction group. Therefore, Lp-PLA2 can act as a marker for AIS.

Table 5. Validity of lipoprotein phospholipase2A in discriminating atherosclerotic group from nonatherosclerotic group.

	Area under curve (95% CI)	*P* -Value	Cut off level	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy %
LP2A	0.916 (0.859–0.973)	<0.001*	100	90.0	64.0	71.4	86.5	77.0

Also, Jia et al. (2022), reported significantly higher Lp-PLA2 concentrations among LAA cases in comparison to non-atherosclerotic cases and Lp-PLA2 levels had a positive association with the diagnosis of the acute phase of LAA. They concluded that Lp-PLA2 had a close relationship with LAA occurrence and was an independent predictor of the acute phase of LAA.

Additionally, in urban multiethnic population-based sample, it was reported that Lp-PLA2 mass concentrations were linked to risk of atherosclerotic stroke (Katan et al., 2014).

Our results also came along with the results achieved by Zhou et al. (2018), who found that the combination of C-reactive protein (CRP) and Lp-PLA2 was linked to carotid stenosis. They proposed that such combination might be useful for vascular risk assessment and could be a possible therapeutic target for carotid atherosclerosis.

This was supported by meta-analysis that provided significant evidence that Lp-PLA2 activity and mass might have a significant relationship with ischemic heart disease and IS risks in general population. They suggested that Lp-PLA2 might be a useful marker for stratifying those at an enhanced risk of CHD and IS, and Lp-PLA2 might be a potential therapeutic target to prevent atherosclerosis (Li et al., 2017).

Also, Huang et al. (2020), demonstrated that atherosclerosis can be associated with the release of many inflammatory factors including Lp-PLA2, which in turn contribute to the development of atherosclerotic plaque. Arterial thrombosis related to ruptured atherosclerotic plaque can lead to obstruction of intracranial arteries and cerebral infarction. Our study showed that IMT and the Lp-PLA2 concentrations were higher among atherosclerotic cases compared with others.

Regarding outcomes, our study demonstrated that a significant negative association existed between GCS and LP2A (r = −0.785), positive correlation between LP2A and the following; NIHSS at admission (*r* = 0.858), NIHSS at discharge (r = 0.756) and mRS at discharge (r = 0.484).

The same idea was adopted by Wang et al. (2019), who reported that elevated Lp PLA2 mass concentrations were linked to early neurological deterioration (END) in first AIS cases with TOAST subtype of

Table 6. Relation between lipoprotein phospholipase2A and demographics, indication for assisted ventilation and clinical parameters of the studied cases.

	LP2A Median (min–max)	Test of significance
Sex		
Female	152 (44.9–2527)	Z = 1.0
Male	122 (30.2–2543)	*P* = 0.316
Ventilator		
No	124.4 (30.2–2543)	KW = 0.299
Yes	155.15 (44.9–2527)	*P* = 0.585
Not known	404 (404–404)	
	R	***P***
Age (y)	−0.247	0.084
Weight (Kg)	−0.015	0.918
GCS	**−0.785**	**<0.001***
NIHSS at admission	**0.858**	**<0.001***
NIHSS discharge	**0.756**	**<0.001***
mRS discharge	**0.484**	**<0.001***

Z:Mann Whitney *U* test, r:Spearman correlation coefficient, *statistically significant.

Table 7. Correlation between lipoprotein phospholipase2A and medical history and stroke characteristics in the case 'atherosclerotic' group.

	LP2A Median (min–max)	Test of significance
Atrial fibrillation		
No	132.5 (30.2–2543)	KW = 2.89
Known	42.8 (42.8–42.8)	*P* = 0.236
Newly-Detected	203 (203–203)	
Diabetes		
No	124.4 (30.2–2543)	Z = 0.574
Yes	138 (44.9–404.5)	*P* = 0.566
Hypertension		
No	102 (42.8–2527)	Z = 1.09
Yes	138 (30.2–2543)	*P* = 0.276
Hypercholesterolemia		
No	103 (30.2–404.5)	Z = 1.99
Yes	145.9 (42.8–2543)	***P* = 0.04***
Smoking		
No	138 (42.8–2527)	Z = 0.286
Yes	124.8 (30.2–2543)	*P* = 0.775
RF Coronary Artery Disease		
No	124.6 (30.2–2543)	Z = 1.42
Yes	232.5 (74.6–404.5)	*P* = 0.157
History Of Stroke		
No	127 (30.2–2543)	Z = 0.512
Yes	138 (42.8–404.5)	*P* = 0.609
History Of Prophylactic Treatment Before The Onset		
No	120 (30.2–2543)	KW = 3.41
Anti-Platelets	141.95 (74.6–404)	*P* = 0.182
Anti-Coagulants	404.5 (404.5–404.5)	
ICH		
No	138 (30.2–2543)	Z = 0.930
Yes	94.35 (51.8–2527)	*P* = 0.352

KW:Kruskal Wallis test; Z:Mann Whitney *U* test *statistically significant.

LAA. They conducted their study on a total of 181 patients; early neurologic deterioration was diagnosed in 30 cases within 10 days postadmission. The odds ratio for early neurologic deterioration have increased with increased Lp-PLA2 concentrations ($P = 0.023$). Thus, they concluded that intermediate and high Lp-PLA2 concentration could independently predict early neurologic deterioration in multivariate analysis. In these cases, the END might be because of the progression of atherosclerosis in the atherosclerotic artery, which could decrease the blood supply to ischemic lesions. Moreover, detached fragments from the unstable plaque obstruct other small vessels, thus worsening blood flow to the former ischemic area or result in new lesions. The aggravated inflammatory process in the atherosclerotic plaque mediated by Lp-PLA2 will make then more susceptible to be ruptured. These mechanisms mediate the relation between Lp-PLA2 and the END in AIS cases with TOAST subtype of LAA.

Likewise, Jiang et al. (2021), demonstrated that cases in the higher Lp(a) group showed higher incidences of worse outcomes at three months. Subgroup analysis demonstrated that in the lower Lp-PLA2 group, Lp(a) levels were not correlated with functional outcomes, however the opposite is true for the higher Lp-PLA2 group. After grouped by different concentrations of Lp(a) and Lp-PLA2, the Lp(a) high/Lp-PLA2 high group revealed the highest incidence of worse outcomes at three and twelve months.

This was supported by Zhou et al. (2018), who reported that Lp-PLA2 had an independent correlation with admission severity in AIS cases, indicating its predictive value for those with severe stroke. Also, elevated Lp-PLA2 concentrations were not only correlated with worse outcomes at three and twelve months AIS (Jiang et al., 2021) but also independently predicted the all-cause mortality within twelve months after AIS (Han et al., 2017).

5.1. Conclusion

Our study concluded that; Lp-PLA2 was markedly increased in atherosclerotic ischemic stroke subjects. In addition, it could be used as a reliable marker in the context of the differentiation between atherosclerotic ischemic stroke and non-atherosclerotic ones. Higher levels of Lp-PLA2 were associated with higher stroke severity and disability.

5.2. Limitations

There are some limitations of the current work. The sample size was relatively small. Furthermore, there was no long-term follow-up. For that, there is a need for multicenter clinical trials with larger sample sizes to explain whether Lp-PLA2 quantification helps determine the risk of ischemic strokes.

Funding

This study did not receive any grant from funding agencies.

Conflicts of interest

None.

References

Adams, H.P., Bendixen, B.H., Kappelle, L.J., Biller, J., Love, B.B., Gordon, D.L., Marsh, E.E., 1993. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 24, 35–41.

Caslake, M.J., Packard, C.J., 2005. Lipoprotein-associated phospholipase A2 as a biomarker for coronary disease and stroke. Nat. Clin. Pract. Cardiovasc. Med. 2, 529–535.

Han, L., Zhong, C., Bu, X., Xu, T., Wang, A., Peng, Y., et al., 2017. Prognostic value of lipoprotein-associated phospholipase A2 mass for all-cause mortality and vascular events within one year after acute ischemic stroke. Atherosclerosis 266, 1–7.

Huang, F., Wang, K., Shen, J., 2020. Lipoprotein-associated phospholipase A2: the story continues. Med. Res. Rev. 40, 79–134.

Jia, W., Li, X., Lei, F., Hu, F., Li, F., Zhang, X., et al., 2022. Diagnostic predictive value of tryptase, serum amyloid A and lipoprotein-associated phospholipase A2 biomarker groups for large atherosclerotic cerebral infarction. Emerg. Med. Int. 2022, 5784909.

Jiang, X., Xu, J., Hao, X., Xue, J., Li, K., Jin, A., et al., 2021. Elevated lipoprotein (a) and lipoprotein-associated phospholipase A 2 are associated with unfavorable functional outcomes in patients with ischemic stroke. J. Neuroinflam. 18, 1–8.

Katan, M., Moon, Y.P., Paik, M.C., Wolfert, R.L., Sacco, R.L., Elkind, M.S., 2014. Lipoprotein-associated phospholipase A2 is associated with atherosclerotic stroke risk: the Northern Manhattan Study. PLoS One 9, e83393.

Koenig, W., Khuseyinova, N., 2007. Biomarkers of atherosclerotic plaque instability and rupture. Arterioscler. Thromb. Vasc. Biol. 27, 15–26.

Li, D., Wei, W., Ran, X., Yu, J., Li, H., Zhao, L., et al., 2017. Lipoprotein-associated phospholipase A2 and risks of coronary heart disease and ischemic stroke in the general population: a systematic review and meta-analysis. Clin. Chim. Acta 471, 38–45.

Lp, P.L.A.S.C., Thompson, A., Gao, P., Orfei, L., Watson, S., et al., 2010. Lipoprotein-associated phospholipase A(2) and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. Lancet (London, England) 375, 1536–1544.

Meyer, B.C., Lyden, P.D., 2009. The modified national Institutes of Health stroke scale: its time has come. Int. J. Stroke 4, 267–273.

Nobels-Janssen, E., Postma, E., Abma, I., van Dijk, J., Haeren, R., Schenck, H., et al., 2022. Inter-method reliability of the modified Rankin Scale in patients with subarachnoid hemorrhage. J. Neurol. 269, 2734–2742.

Tselepis, A.D., John Chapman, M., 2002. Inflammation, bioactive lipids and atherosclerosis: potential roles of a lipoprotein-associated phospholipase A2, platelet activating factor-acetylhydrolase. Atherosclerosis Suppl. 3, 57−68.

Wang, Y., Hu, S., Ren, L., Lei, Z., Lan, T., Cai, J., Li, C., 2019. Lp-PLA2 as a risk factor of early neurological deterioration in acute ischemic stroke with TOAST type of large arterial atherosclerosis. Neurol. Res. 41, 1−8.

Wang, Y., Liu, G., Song, H., Cao, C., Ji, X., Cao, G., 2022. Elevated lipoprotein-associated phospholipase A2 is associated with intracranial atherosclerosis. Front. Neurol. 13, 4.

Wei, L., Ke, Z., Zhao, Y., Cai, Z., 2017. The elevated lipoprotein-associated phospholipase A2 activity is associated with the occurrence and recurrence of acute cerebral infarction. Neuroreport 28, 325−330.

Wingo, A.P., Fan, W., Duong, D.M., Gerasimov, E.S., Dammer, E.B., Liu, Y., et al., 2020. Shared proteomic effects of cerebral atherosclerosis and Alzheimer's disease on the human brain. Nat. Neurosci. 23, 696−700.

Zhou, F., Liu, Y., Shi, H., Huang, Q., Zhou, J., 2018. Relation between lipoprotein-associated phospholipase A 2 mass and incident ischemic stroke severity. Neurol. Sci. 39, 1591−1596.