Lipoprotein (a) is a newly validated Biomarker for Large Artery Atherosclerosis Stroke

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BACKGROUND

Lipoprotein(a) (Lp (a)) serum levels are genetically determined and contribute to atherogenesis[1]. High Lp (a) levels are associated with an increased cardiovascular morbidity[2]. Recently, serum Lp (a) levels have been associated with large artery atherosclerosis (LAA) stroke etiology[3]. We aimed to externally validate this association in an independent cohort.

METHODS

We included acute ischemic stroke patients from a prospective cohort study from the University Hospital Bern (Inselspital), Switzerland. Lp (a) serum levels were measured in serum, drawn within 24 hours after symptom onset. We assessed the association of Lp (a) with LAA stroke in univariate and multivariate analysis, adjusting for traditional LAA stroke risk factors.

RESULTS

Overall, 746 patients were included, of which 105 had a LAA stroke (14%). Lp (a) was higher in patients with LAA stroke compared to patients with non-LAA stroke (23.0 nmol/l [IQR:9.8-80.0] versus 16.3 nmol/l [5.8-57.0], p=0.01). In univariate analysis, patients with LAA stroke were significantly more often men, suffered more often from dyslipidaemia, arterial hypertension, diabetes and had a higher BMI than patients with non-LAA stroke. In a multivariable logistic regression model, elevated Log_{10}(Lp (a)) was associated with LAA stroke with a aOR of 1.50 (95%CI 1.02-2.21, p=0.04).

	Total (n=746)	LAA Stroke (n=105)	Non-LAA Stroke (n=641)	p-value
Demographic data				
Age, y, median [IQR]	71 [61-80]	72 [63-79]	71 [60-80]	0.59
Men, n (%)	467 (62.6)	77 (73.3)	390 (60.8)	**0.02**
Dyslipidaemia, n (%)	427 (58.0)	71 (67.6)	356 (56.4)	**0.03**
Previous cerebrovascular event	154 (20.7)	29 (27.6)	125 (19.5)	0.07
Arterial hypertension	510 (68.4)	85 (81.0)	425 (66.3)	**0.002**
Current Smoking	133 (17.8)	26 (24.8)	107 (16.7)	0.05
Ever Smoking	238 (31.9)	37 (35.2)	201 (31.4)	0.43
Coronary heart disease	133 (17.8)	19 (18.1)	114 (17.8)	0.89
Diabetes mellitus	115 (15.4)	25 (23.8)	90 (14.1)	**0.01**
Positive family history	112 (19.9)	12 (16.0)	100 (20.5)	0.44
BMI kg/m^2 , median [IQR]	25.7 [23.1-28.3]	26.4 [24.4-29.1]	25.6 [22.9-28.3]	**0.01**
NIHSS on admission, median [IQR]	6 [3-12.5]	5 [3-12]	6 [3-13]	0.64
Statins	195 (26.2)	35 (33.7)	160 (25.0)	0.07
Platelet inhibitors	280 (37.6)	52 (49.5)	228 (35.6)	**0.009**
Antihypertensive drugs	442 (59.5)	76 (73.1)	366 (57.3)	**0.002**
Laboratory values, median [IQR]				
Lipoprotein (a), nmol/L	16.9 [6.1-60.0]	23.0 [9.8-80.0]	16.3 [5.8-57.0]	**0.01**
LDL, mmol/L	2.6 [2.0-3.3]	2.6 [2.1-3.4]	2.6 [2.0-3.3]	0.33
Apolipoprotein B, g/L	0.95 [0.78-1.13]	0.94 [0.8-1.13]	0.95 [0.77-1.13]	0.74
Cholesterol, mmol/L	4.7 [4.0-5.5]	4.6 [4.1 -5.4]	4.7 [4.0-5.5]	0.75
Triglycerides, mmol/L	1.4 [1.0-2.0]	1.4 [1.1-2.0]	1.4 [1.0-2.0]	0.92
Non-HDL, mmol/L	3.3 [2.7-4.2]	3.3 [2.9-4.2]	3.3 [2.7-4.1]	0.58
HbA1c, %	5.8 [5.6-6.2]	6.0 [5.7-6.3]	5.8 [5.6-6.2]	**0.002**

Table 1: Baseline Characteristics of Patients with acute Ischemic Stroke

Variable	aOR	95%-CI	p-value
Log_{10} (Lp (a))	1.50	1.02-2.21	**0.04**
Arterial Hypertension	1.98	1.07-3.68	**0.03**
Women	0.59	0.34-1.02	0.06
Diabetes mellitus	1.72	0.95-3.13	0.08
BMI	1.03	0.98-1.09	0.18
Dyslipidaemia	1.34	0.79-2.29	0.28
Platelet Inhibitor	1.34	0.82-2.21	0.24

Legend: aOR = adjusted odds ratio, CI = confidence interval, Lp(a) = Lipoprotein (a)

Table 2: Multivariable logistic regression model for the association with large artery atherosclerotic stroke and lipoprotein (a)

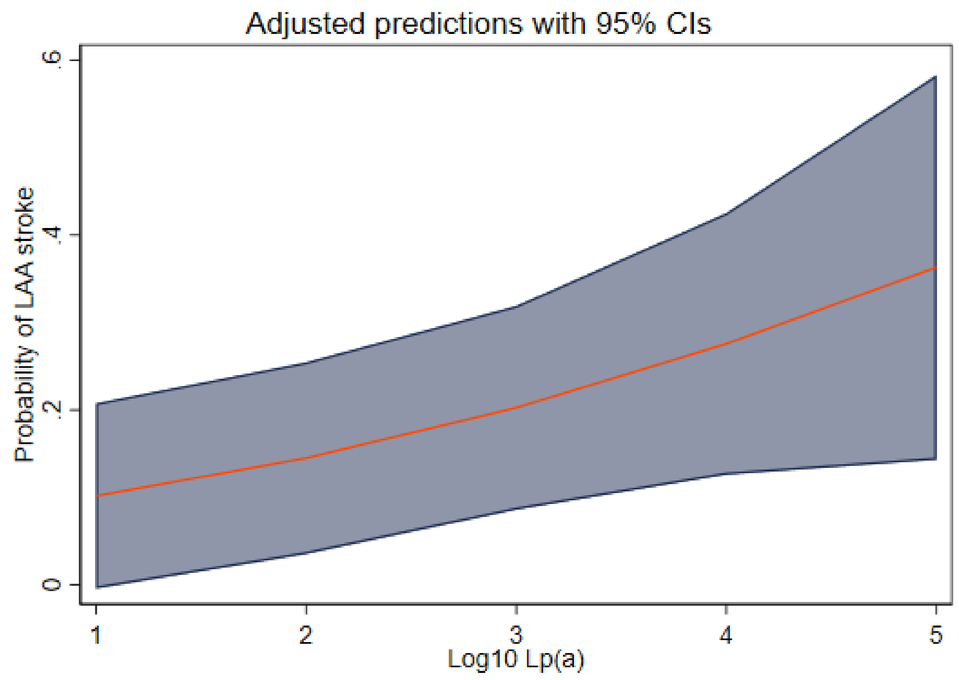

Figure 1: Estimated Probability of Large Artery Atherosclerosis as stroke etiology in multivariable regression analysis
Estimated model for a woman with Arterial Hypertension, Dyslipidemia, Diabetes and BMI of 25.7kg/m^2

CONCLUSIONS

Among ischemic stroke patients, we could validate the independent association of higher Lp (a) levels with LAAS etiology, also after adjusting for traditional cardiovascular risk factors. Independent validation of biomarkers, especially with the aim to guide secondary prevention, is essential. These findings are relevant in view of randomised clinical trials, investigating the effect of specific Lp (a) lowering agents in reducing major adverse cardiovascular events.

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