CARDIOLOGY UPDATES NEWSLETTER

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IN THIS ISSUE

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "Cardiology updates" which contains latest and interesting news in the field of Cardiology

Association of lipoprotein(a) levels on the risk of major adverse cardiovascular events (MACE) and coronary revascularization in individuals with incident atherosclerotic cardiovascular disease

INTRODUCTION

Lipoprotein(a) [Lp(a)] is an isomeric protein made up of apolipoprotein(a), apolipoprotein B-100, and lipids such cholesterol, phospholipids, and triglycerides. Previous study has shown that Lp(a) was an independent risk factor for coronary artery disease (CAD) and can induce atherosclerosis, inflammation, and thrombosis.[1] Atherosclerotic cardiovascular disease (ASCVD) risk was independently and causally correlated with greater levels of Lp(a), according to epidemiological and genetic research. It is yet unclear, though, how higher Lp(a) in a group with secondary prevention relates to the likelihood of later CV events. It is particularly challenging to give risk assessment and secondary preventive measures for newly diagnosed, or incident, ASCVD patients due to the paucity of information about the risk of high Lp(a).[2] As a result, the purpose of this study was to examine and emphasize the increased risk of major adverse cardiovascular events (MACE) in those with elevated vs normal Lp(a) levels in a newly diagnosed ASCVD group representing an acute situation.

METHODS

This was a large-scale prospective cohort study. A total of 32,537 participants, who were recruited to be between the target age range of 40 and 69 years, had baseline biological measurements taken and completed touchscreen questionnaires in accordance with a standard protocol. Adult patients with a valid Lp(a) measurement whose first ASCVD diagnosis (index date) happened after their enrollment date were included in the incident ASCVD cohort for this investigation. To compare the extra risk associated with elevated versus normal Lp(a) levels in an existing high-risk acute patient group, the incident ASCVD cohort was stratified into those with "normal" (<65 nmol/L) and "elevated" (>150 nmol/L) Lp(a) concentrations. The occurrence of MACE was the study's main finding. After an incident ASCVD diagnosis,

researchers looked into the rates of all MACE as well as the time to first MACE. The total number of MACE reported throughout the follow-up period divided by 100 person-years of follow-up was used to compute the incidence rate (IR) of both the composite and disaggregated MACE components. Cox proportional hazard models were used to quantify the risk of MACE resulting from an increase in Lp(a) of 100 nmol/L.

RESULTS

The current study showed that 5204 (16.0%) had increased Lp(a), while 222,257 (68.4%) had normal Lp(a). 41.2% of those with increased Lp(a) and 35.61% of those with normal Lp(a) experienced a subsequent MACE. Patients with increased vs normal Lp(a) had substantially higher ($p < 0.001$) IRs of composite MACE and coronary revascularization within the first year of follow-up (IR difference 6.79 and 4.66). Patients with raised Lp(a) (16.45; 95% CI: 15.97–16.94; IRD = 1.71; IRR = 1.12, $p < 0.001$) had a substantially greater IR of non-fatal MI over the whole follow-up period than those with normal Lp(a) (14.74; 95% CI: 14.51–14.97). Comparing patients with raised Lp(a) (3.78; 95% CI: 3.55–4.02; IRD = 1.23; IRR = 1.48, $p < 0.001$) to those with normal Lp(a) (2.55; 95% CI: 2.45–2.64), the IR of coronary revascularization also increased. Throughout the whole and one-year follow-up period, the IR of MACE was considerably greater in incident MI and IS patients with raised Lp(a), but not in incident coronary revascularization patients. In the one-year and overall follow-up, respectively, patients with elevated Lp(a) and MI (IRD = 5.96 and 1.73) and coronary revascularization (IRD = 3.72 and 1.01) as their incident ASCVD diagnosis had significantly ($p < 0.005$) higher IRs of coronary revascularization, as did incident IS patients (IRD = 0.39; IRR = 2.27, $p = 0.007$) in the overall follow-up. A continuous increase in Lp(a) of 100 nmol/L was linked to a higher risk of composite MACE by 8% (HR = 1.08; 95% CI: 1.06–1.10; $p < 0.001$), non-fatal MI by 3.2%, non-fatal IS by 9.6%, and coronary revascularization by 19% during the whole follow-up period (Figure 1). Regardless of baseline LDL-C or incident ASCVD diagnosis, there was a usually robust correlation between rising Lp(a) and coronary revascularization.

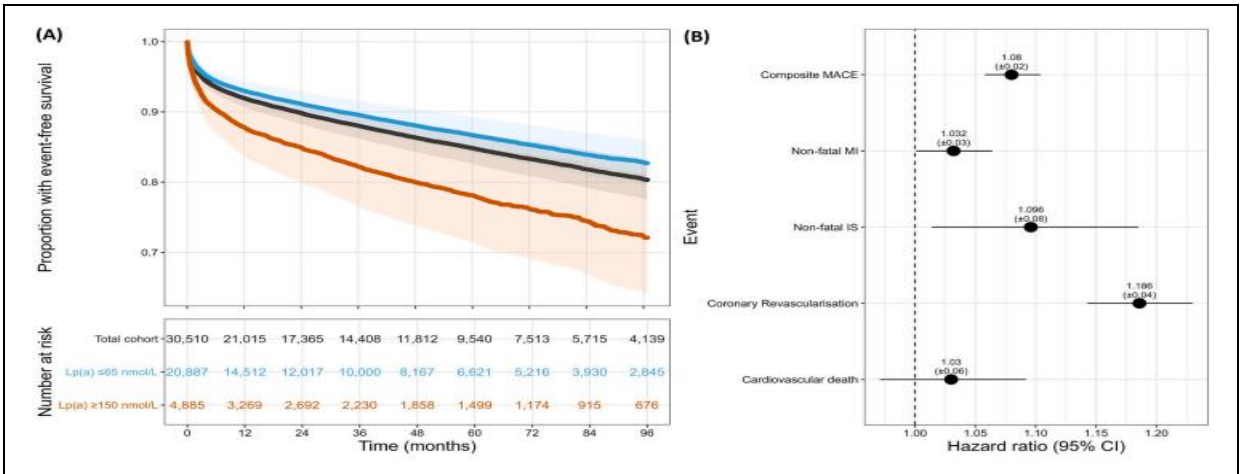

Figure 1 . (A) Association of normal and elevated Lp(a) with first composite MACE over the full available follow-

up time. (B) Adjusted association (hazard ratio) of 100 nmol/L Lp(a) with first composite and disaggregated MACE over the full available follow-up period

DISCUSSION

The current investigation found that higher Lp(a) was related with an increased risk of future MACE and coronary revascularization.[2] Similarly, Zhu L et al. found that Lp(a) increases were related with recurrent cardiovascular events when LDL-C levels were high, although this relationship could change when LDL-C levels were extremely low. Patients with CAD who have elevated LDL-C levels (≥1.4 mmol/L) and Lp(a) levels were considered high-risk and need additional medication to lower their levels.[1]

CONCLUSION

This study concluded that elevated Lp(a) was associated with a higher risk of future MACE and coronary revascularization, indicated a group that might benefit from early and more focused management for cardiovascular risk, including Lp(a), particularly within the first year following ASCVD diagnosis. Proactive Lp(a) testing as part of standard clinical practice could help identify and manage these high-risk patients.

Elevated Lp(a) is associated with a higher risk of future MACE and coronary revascularization.

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Relationship between impaired cardiovascular fitness and the triglyceride-glucose index in non-diabetic young population

INTRODUCTION- Cardiorespiratory fitness (CRF) is commonly regarded as the best indicator of overall body health and function since it was closely linked to the integrated functioning of many physiological systems, such as the cardiovascular, musculoskeletal, and respiratory systems. A low estimated cumulative risk factor is one of the best indicators of non-communicable diseases, such as cancer and cardiovascular disease (CVD), and has been linked

to an increased risk of traditional cardiovascular risk factors.[1] It has been demonstrated that the triglyceride-glucose (TyG) index was linked to the incidence of CVD. Individuals with the highest TyG index had a nearly twofold increased risk of coronary heart disease in comparison to those with the lowest TyG index. In middle-aged and older people, the triglyceride-glucose index has been associated with the development, progression, and prognosis of cardiovascular disease. However, in the young, non-diabetic population, the link between the TyG index and poor cardiovascular function (CVF) was yet unknown.[2] The aim of the study was to investigate the link between the TyG index and impaired CVF in a non-diabetic young population.

METHODS-This was a cross sectional study, included a total of 3364 participants who completed CVF examination and had fasting blood samples taken. Only survey participants aged 12 to 49 were eligible for the CVF assessment. Participants in CVF tests were frequently asked to conduct aerobic exercise on a treadmill. Impaired CVF was defined as low to moderate CVF levels assessed by estimated maximum oxygen consumption (Vo2max) using sex and age-specific parameters. The TyG index was computed as Ln [TG (mg/dL) × FPG (mg/dL)/2]. This study's statistical analysis was performed using R version 4.3.1 (R Foundation). The study population was grouped into quartiles using population-weighted descriptive statistics and the TyG index. The study used restricted cubic splines (RCS) with weight to investigate the correlation between the TyG score and impaired CVF.

RESULTS-The study results showed that the TyG index (median±standard deviation) was 8.36±0.52, and the study population's age (median with interquartile range) was 28 (19–37) years. Impaired CVF was positively correlated with non-Hispanic Black individuals' BMI, waist circumference, SBP, DBP, metabolic syndrome, HbA1c, FPG, TG, and TyG index. Impairment in CVF was negatively correlated with Hb and level 6 physical activity. Whether elevated by one unit or one standard deviation, the TyG index showed a strong positive correlation with reduced CVF in three weighted multivariable logistic models. The TyG index was further divided into quartiles, with the Q1 group serving as a standard for assessing the relationship between impaired CVF and other quantile groups. In model 3, Q3 (OR: 1.61; 95% Cl 1.21–2.13) and Q4 (OR: 1.55; 95% Cl 1.06–2.26) showed a significant rise in odds ratios (OR) when compared to Q1, and the p-value for the trend was 0.009 (Table 1). Multivariable logistic regression analysis indicated a significant relationship between the TyG index and impaired CVF (per 1-unit increase in the TyG index: OR, 1.46; 95% Cl 1.13–1.90). Restricted cubic splines (RCS) demonstrated a dose-response association between the TyG index and impaired CVF. In individuals under the age of 20, a significant interaction (p=0.027) was seen between the TyG score for impaired CVF and sex.

TyG index	HR (95%CI)		
	Model 1	Model 2	Model 3
Per 1 unit increase	1.60 (1.31–1.94)**	1.39 (1.11–1.74)*	1.46 (1.13–1.90) *
Per 1 SD increase	4.46 (2.38–8.35)**	2.84 (1.38–5.83)*	3.38 (1.47–7.76) *
Q1	Reference	Reference	Reference
Q2	1.26(0.99–1.60)	1.22(0.94–1.57)	1.24 (0.96–1.60)
Q3	1.80 (1.35–2.38)**	1.53 (1.17–2.00)*	1.61 (1.21–2.13)*
Q4	1.81 (1.34–2.44)**	1.45 (1.02–2.06)*	1.55 (1.06–2.26)*
p for trend	**< 0.001**	**0.011**	**0.009**

Table 1. Relationship in various logistic models between the TyG index and impaired cardiovascular fitness

DISCUSSION-The current study identified a link between the TyG index and poor CVF in young non-diabetic individuals. This study also discovered a significant sex interaction between the TyG index and poor CVF in individuals under the age of 20.[2] Lu YW et al. and Wu S et al. have found that the TyG index was linked with subclinical atherosclerosis, and arterial stiffness.[3,4]

CONCLUSION-The current study concluded that those with higher TyG index values among young people without diabetes were more likely to have impaired CVF. Furthermore, sex may have an impact on CVF, with men more likely to experience reduced CVF in settings with similar TyG index values.

Higher TyG index values in the young, non-diabetic population increase the risk of experiencing impaired CVF.

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Investigation of the association between symptomatic intracranial hemorrhage occurrence and glial fibrillary acidic protein levels in the bloodstream

INTRODUCTION- Intracranial hemorrhage (ICH) is a common consequence of endovascular treatment (EVT), with rates as high as 46.1% in clinical trials. Asian individuals may have an even higher risk of ICH following endovascular therapy for acute ischemic stroke (AIS) due to the higher prevalence of cerebral atherosclerosis. Hemorrhagic consequences have the potential to reduce or eliminate the benefit-risk ratio of endovascular treatment, particularly in cases of symptomatic ICH (sICH). Consequently, it was critical to determine the predictors of sICH following endovascular therapy in real-world settings in order to continually enhance the effectiveness of this novel therapeutic approach.[1] It has recently been shown that glial fibrillary acidic protein (GFAP) serves as a valid biomarker to differentiate intracerebral hemorrhage from acute internal shock. In addition, individuals with major artery blockage who had endovascular therapy had an adverse prognosis at 90 days if their GFAP levels were increased. Moreover, patients' risk of parenchymal bleeding was 2.51 times higher in those with greater GFAP levels 24 hours after the stroke. However, no research has been done on the connection between GFAP and sICH in AIS patients receiving EVT.[2] The purpose of this study was to determine whether GFAP and sICH were related in AIS patients receiving EVT.

METHODS- This was a retrospective cohort study, included 142 patients diagnosed with AIS and treated with endovascular therapy were initially screened. Patients who presented with major artery blockage in the anterior circulation and received EVT using contemporary thrombectomy procedures were eligible. Patients having concurrent disorders such as aneurysms, vasculitis, arterial dissection, arteriovenous malformation, Moyamoya syndrome, or hematological system abnormalities were not eligible for the study. The control group was made up of Physical Examination Center members who never had a stroke. GFAP levels in the bloodstream were measured using an enzyme linked immunosorbent assay before endovascular therapy (T1) and 24 hours later (T2). sICH was identified using the Heidelberg Bleeding Classification. To evaluate independent risk factors for sICH, multivariable logistic regression models were adjusted for age, gender, and variables with a p-value <0.1 in the univariate analysis. Furthermore, the C-statistic, net reclassification index (NRI), and integrated discrimination improvement (IDI) were calculated to assess the discriminatory and predictive power of GFAP when used in conventional models.

RESULTS- The study showed that patients that were included had an average age of 70.9 ± 10.1 years, with 64.1% of them being male. The baseline median ASPECTS score was 9 (IQR 8–9) while the baseline median NIHSS score was 15 (interquartile range [IQR], 12–18). Of the

patients, 118 (83.1%) had effective recanalization, whereas 77 (54.2%) had poor collateral status. There was a notable increase in serum GFAP levels at T2 compared to T1 (3.813 [1.474, 5.876] versus 0.249 [0.150–0.576] ng/mL, p=0.001). Serum GFAP levels in AIS patients were considerably higher at T1 than in the controls (0.249 [0.150–0.576] versus 0.065 [0.041–0.110] ng/mL, p = 0.001). Following EVT, 18 (14.5%) of the 142 AIS patients experienced sICH. Both the multivariable adjusted model (OR 1.518, 95% CI 1.153–2.000, p = 0.003) and the unadjusted model (OR 1.513, 95% CI 1.269–1.805, p = 0.001) demonstrated significant correlations between serum GFAP levels at T2 and sICH. The violin plot of serum Log GFAP levels in controls and AIS patients was shown in Figure 1. In the control group, the average Log GFAP levels were 4.2 ± 0.6 pg/mL. Patients with AIS showed a substantial rise at T1 (5.7 ± 1.0 pg/mL) or T2 (8.0 ± 0.9 pg/mL) when compared to controls. Additionally, Log GFAP levels at T2 were greater than T1 (p = 0.001). Additionally, GFAP at T2 significantly improved risk categorization for sICH when added to the conventional model (integrated discrimination improvement [IDI] 0.183, 95% CI 0.070–0.295, p = 0.001).

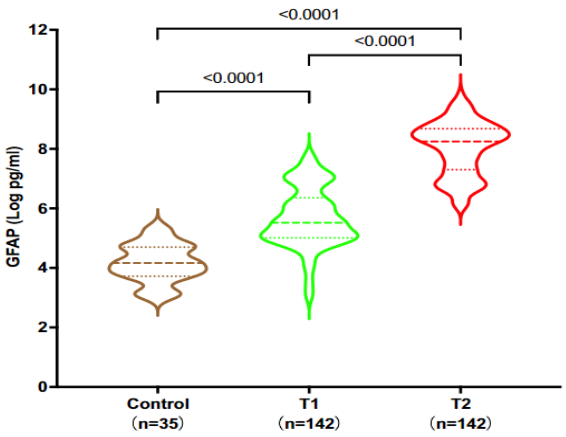

Figure 2 Serum Log GFAP levels in AIS patients and controls plotted using a violin plot.

DISCUSSION- The current study indicated that an increased risk of sICH was connected with greater GFAP levels.[2] Similar to this, Chen CH et al. shown that a higher risk of parenchymal bleeding was associated with elevated GFAP.[3]

CONCLUSION-The current study concluded that in AIS patients, serum GFAP levels significantly increased 24 hours after EVT. An increased risk of sICH was connected with greater GFAP levels.

GFAP may function as a reliable marker for sICH in AIS patients receiving EVT treatment.

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Case report on massive pulmonary embolism in a patient with heart failure due to stress cardiomyopathy

INTRODUCTION

Venous thromboembolism (VTE) is a vasculature-related illness that poses a serious risk to the health, well-being, and occasionally even life of a great number of individuals across the globe. Clinical manifestations include deep vein thrombosis (DVT), which is the formation of a thrombus in the deep vein, usually in the pelvis and lower extremities, and pulmonary embolism (PE), which is the embolization of a thrombus that obstructs a portion of the pulmonary artery vasculature. The most serious and potentially fatal clinical indication of VTE is PE. After cerebrovascular stroke and coronary artery disease (CAD), it is the third most common cause of death from cardiovascular diseases (CVD). The most deadly type of PE, known as massive PE (MPE), is characterized by a substantial blockage of a portion of the pulmonary vasculature, which causes persistent arterial hypotension and cardiogenic shock.[1] Stress cardiomyopathy (SC) is a transient cardiovascular disease that manifests as acute coronary syndrome symptoms and indications following an emotional or physical stressor. In addition to serious side effects such as cardiac failure, arrhythmias, left ventricular outflow blockage, and thromboembolic episodes, SC's pathophysiological mechanisms are yet unknown.[2] This case study draws attention to the possible pathogenic function of the relationship between PE and SC.

CASE PRESENTATION

A 65-year-old female denied having substantial chronic degenerative diseases, displaying only a BMI of 32.1 and a history of thromboembolism episodes (PE and DVT). Her first episode started in August 2021. Following an emotional occurrence (laboral talk), she experienced intense chest discomfort with irradiation to the left arm. She proceeded to the Emergency Department (ED), where the ECG revealed ST-segment elevation in the anterior leads and augmented vector left (aVL), as well as elevated cardiac biomarkers (troponin I 24 ng/ml). Tenecteplase was used for fibrinolysis, and there was no sign of reperfusion. Transthoracic echocardiogram (TTE) revealed apical, anteroseptal, and anterolateral akinesia with a left ventricular ejection fraction (LVEF) of 67%. Angiographically, normal coronary arteries were shown by percutaneous transluminal coronary angioplasty (PTCA), and left ventriculography (LVG) revealed apical dyskinesia using the octopus pot (Figure 1) as well as an increase in the left ventricle's end-diastolic pressure. After a week, the patient was released from the hospital with beta-blockers prescribed for treatment (bisoprolol 1.25 mg QD). When acute dyspnea of New York Heart Association (NYHA) functional class IV, tachycardia, tachypnea, hypotension, and syncope occurred in November 2021, the patient's clinical conditions worsened and led to another ED visit with elevated biomarkers (dimer D 1598 ng/ml, troponin

I 7.8 ng/ml, and BNP 281 pg/ml). In addition to increasing the oxygen requirement and starting double inotropic medicine (dobutamine and norepinephrine), a computed tomography pulmonary angiography (CTPA) was performed with PE detected at the pulmonary artery bifurcation level. After receiving alteplase for fibrinolysis, she was hospitalized to the Intensive Care Unit and received therapy there until her condition improved. After one week of stay, the patient was discharged with improved symptoms and a NYHA class II. An outpatient follow-up appointment was arranged with rivaroxaban 20 mg QD, a direct oral anticoagulant (DOAC). The hematological and rheumatological etiologies were found to be within normal limits when diagnostic laboratories were called in for a follow-up. Following a year, the decision was made to stop using anticoagulants due to their adequate evolution and after these disorders were ruled out. Following a month-long medication cessation, the patient returned to the ED in January 2023 with an acute bout of dyspnea (NYHA class III) and tachypnea. The patient's increased D-dimer was 9480 ng/ml, and their troponin I level was less than 0.05 ng/ml. TTE was carried out within typical bounds. PE was detected by CTPA at the anterobasal and latero-basal segments of the left pulmonary artery and the posterior-basal segment of the right pulmonary artery. Enoxaparin anticoagulation was started again. After five days of admission, the patient's symptoms had improved, and he was discharged with a NYHA class II, new anticoagulation with DOACs (rivaroxaban 20 mg QD), and extra oxygen needed to keep his oxygen saturation level over 92%. A post-hospitalization outpatient follow-up appointment was set up.

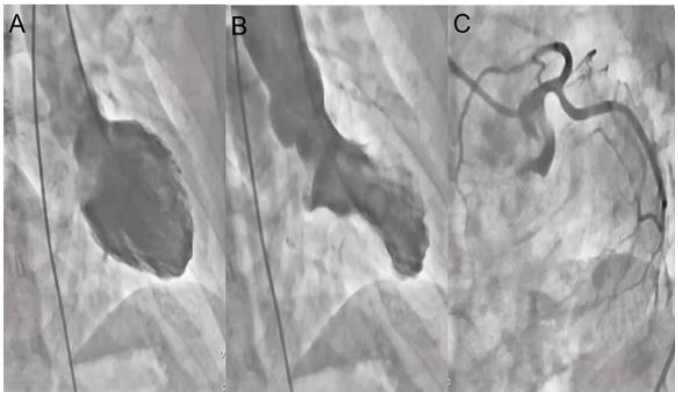

Figure 1. Coronary angiography (CAG) and left ventriculography (LVG). Diastolic phase (A) and systolic phase (B) showed apical dyskinesia. CAG (C) showed normal coronary arteries.

DISCUSSION

The current case report showed the possible pathogenic function of the relationship between PE and SC.[2] Similar to this, Jin Q et al. showed that there was little evidence that Takotsubo syndrome(TTS) and PE were related, and PE may act as a trigger for TTS.[3]

CONCLUSION

This case report concluded with an interesting case of significant PE associated with cardiac failure after SC, which may have pathophysiological significance. There are currently reports of instances where PE precipitated SC, which suggests that the pathophysiology of SC may have resulted in a heart failure with preserved EF in our patient. This decreased the functional class and consequently created an indirect favorable state for VTE.

The ideal duration of anticoagulation after the first three months following a PE episode is still unknown; decisions regarding anticoagulation beyond this time frame should be customized based on the likelihood of recurrent VTE and balanced against bleeding risk.

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