"ESTIMATION AND CORRELATION OF CLINICAL SIGNIFICANCE OF LIPOPROTEIN (A) AS A RISK FACTOR OF ATHEROSCLEROTIC VASCULAR EVENTS IN ELDERLY: A ONE YEAR CROSS-SECTIONAL STUDY IN KLE'S DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI"

BY

REG NO: BG0121013

Dissertation

Submitted to the KLE Academy of Higher Education and Research, Belagavi, Karnataka

In Partial Fulfilment

of the Requirements for the Degree of

M.D.

IN

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE

JAWAHARLAL NEHRU MEDICAL COLLEGE, BELAGAVI, KARNATAKA

DECEMBER 2024 / JANUARY 2025

KLE Academy of Higher Education and Research (Deemed-to-be University) Belagavi, Karnataka

Endorsement

This is to certify that the dissertation entitled

"ESTIMATION AND CORRELATION OF CLINICAL SIGNIFICANCE OF LIPOPROTEIN (A) AS A RISK FACTOR OF ATHEROSCLEROTIC VASCULAR EVENTS IN ELDERLY: A ONE YEAR CROSS SECTIONAL STUDY IN KLE'S DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI"

is a bonafide research work done by **REG NO. BG0121013**.

DR REKHA S PATIL, MD
Professor & Head
Department of Medicine
J N Medical College
KAHER
Belagavi, Karnataka

Date:
Place: JNM, Belagavi

Dr. REKHA S. PATIL
M.D., Gen. Med.
Consultant of General Medicine
KMC Reg. No. 70246
KLES Dr. Prabhakar Kore Hospital & MRC, Belagavi.

DR N S MAHANTASHETTI
Principal
J N Medical College
KAHER
Belagavi, Karnataka

PRINCIPAL
JAWAHARLAL NEHRU MEDICAL COLLEGE
BELAGAVI

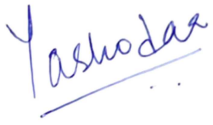
Date:
Place: JNMC, Belagavi

UNDERTAKING

I, **(REG NO: BG0121013),** hereby declare that the information and the data mentioned in my dissertation entitled **"Estimation and correlation of clinical significance of lipoprotein (a) as a risk factor of atherosclerotic vascular events in elderly: A one-year cross-sectional study in "KLE's Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi"** belongs to me and is original. I am aware of the definition of plagiarism as detailed below:

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of another's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the University.



Date:

Place: Belagavi **REG NO: BG0121013**

PLAGERISM CLEARANCE REPORT

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be-University)

(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu rincipal@jnmc.edu

Ref No: MDC/PG/ Date: 19-06-2024

"ACCEPTANCE LETTER"

The softcopy of thesis entitled: **"ESTIMATION AND CORRELATION OF CLINICAL SIGNIFICANCE OF LIPOPROTEIN (A) AS A RISK FACTOR OF ATHEROSCLEROTIC VASCULAR EVENTS IN ELDERLY: A ONE-YEAR CROSS-SECTIONAL STUDY IN KLE'S DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI"** has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **05%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide.

KAHER * BELAGAVI * J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BG0121013
Postgraduate Student,
2021-22 Batch,
Department of General Medicine.
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 122 **Date: 27/09/2022**

To,

REG NO: BG0121013
PG Student in General Medicine,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ESTIMATION AND CORRELATION OF CLINICAL SIGNIFICANCE OF LIPOPROTEIN (A) AS A RISK FACTOR OF ATHEROSCLEROTIC VASCULAR EVENTS IN ELDERLY: A ONE YEAR CROSS-SECTIONAL STUDY IN KLE'S DR PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

LIST OF ABBREVIATIONS

Sr. No.	Abbreviation	Expansion
1	Lp(a)	LIPOPROTEIN (a)
2	LDL	LOW DENSITY LIPOPROTEIN
3	HDL	HIGH DENSITY LIPOPROTEIN
4	TPA	TISSUE PLASMINOGEN ACTIVATOR
5	ASCVD	ATHEROSCLEROTIC CARDIOVASCULAR DISEASE
6	LDLR	LOW DENSITY LIPOPROTEIN RECEPTOR
7	VLDL	VERY LOW DENSITY LIPOPROTEIN
8	ASGPR	ASIALOGLYCOPROTEIN RECEPTOR
9	CHD	CORONARY HEART DISEASE
10	CHF	CONGESTIVE HEART FALIURE
11	NLA	NATIONAL LIPID ASSOCIATION
12	ELISA	ENZYME LINKED IMMUNOASSAY
13	CAD	CORONARY ARTERY DISEASE
14	NEJM	NEW ENGLAND JOURNAL OF MEDICINE
15	BMI	BODY MASS INDEX
16	SBP	SYSTOLIC BLOOD PRESSURE

17	PCSK 9	PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9
18	DBP	DIASTOLIC BLOOD PRESSURE
19	HTN	HYPERTENSION
20	DM	DIABETES MILLETUS
21	TG	TRIGLYCERIDE
22	HBA1C	GLYCATED HEMOGLOBIN
23	LAA	LARGE ARTERY ATHEROSCLEROSIS
24	MACE	MAJOR ADVERSE CARDIOVASCULAR EVENTS
25	SVD	SINGLE VESSEL DISEASE
26	DVD	DOUBLE VESSEL DISEASE
27	TVD	TRIPLE VESSEL DISEASE

ABSTRACT

INTRODUCTION

Lipoprotein (a) was identified as a variant of low-density lipoprotein (LDL) 40 years ago. Lipoprotein (a) consists of one LDL particle containing apoB-100 and one molecule of a large, highly polymorphic glycoprotein known as apo (a). The study aimed to evaluate and correlate the clinical significance of lipoprotein (a) as a risk factor for atherosclerotic vascular events in the elderly population.

METHODOLOGY

This cross-sectional study was conducted among patients admitted in a tertiary care hospital from January 1st to December 31st 2023 for over a period of 1 year. 142 study participants included in the study were divided into 2 groups atherosclerotic vascular event group (2 subgroups: -Cardiovascular atherosclerotic vascular event subgroup and neurological atherosclerotic vascular event subgroup) and no atherosclerotic vascular event group. We excluded those with active infections, neoplasia, renal dysfunction, hepatic dysfunctions.

Detailed history and examination were done on the day of enrolment into the study. Blood sample in fasting was withdrawn from all the study participants for serum lipoprotein (a), serum HDL, LDL, total cholesterol, triglycerides, HBA1C, creatinine.

RESULTS

Among 142 study participants in the study, majority of study participants were male (n=96, 67.6%). The mean age was 71.63 years. High lipoprotein (a) levels noted in 51.41% study participants. High Lp(a) levels were seen in 56% study participants in

cardiovascular atherosclerotic vascular event subgroup, 43.33% study participants in neurological atherosclerotic vascular event subgroup and 51.61% in no atherosclerotic vascular event group .

Our study showed that increased levels of lipoprotein (a) may not be associated with higher risk of development of atheroclerotic vascular events in elderly.

CONCLUSION

Our study concludes that Lipoprotein (a) may not be used to infer any clinical significance nor may have any role to play as a risk factor for atherosclerotic vascular events in elderly (age >65 years).

INDEX

LIST OF FIGURES

LIST OF TABLES

LIST OF GRAPHS

INTRODUCTION

Lipoprotein and its composition

Lipoprotein (a), identified as a type of low-density lipoprotein (LDL) 40 years ago, is composed of a single LDL particle containing apoB-100 and a large, highly polymorphic glycoprotein known as apo(a). A distinctive feature of apo(a) is the presence of loop-like structures called kringles. These kringle domains are triple-loop structures stabilized by three internal disulfide bonds and are also found in other coagulation factors, including plasminogen (PLG), prothrombin, urokinase, and tissue-type plasminogen activators. Liver also produces apoprotein (a). The hepatocyte cell membranes are where they are also constructed. LPA gene controls the major locus of Lp(a) concentration. Lp(a) plasma concentrations are highly heritable.

Plasma levels of Lp(a) exhibit significant individual variability, far surpassing that of other plasma lipoprotein components. Generally, African individuals have Lp(a) plasma levels that are 2 to 3 times higher than those of European and most Asian populations. The population's levels of Lp(a) are often rather variable due to the polymorphisms in the LPA gene (3). They span from less than one mg/dl and up to 1000 mg/ dl. The serum lipoprotein (a) levels up to 30mgdl are taken to be normal. Patients of Asian and White racial backgrounds tend to have lower average Lp(a) levels than those of African origin (3). Lipoprotein (a) value of more than 50 mg/dL are indicative of a higher risk of heart disease in patients (4). Prevalence of individuals with reduced Lp(a) increases or mild-moderate cases increases during the

routine screening. Lp(a) more than 30 and less than 50 has not demonstrated any development of risk of stroke or heart diseases (5).

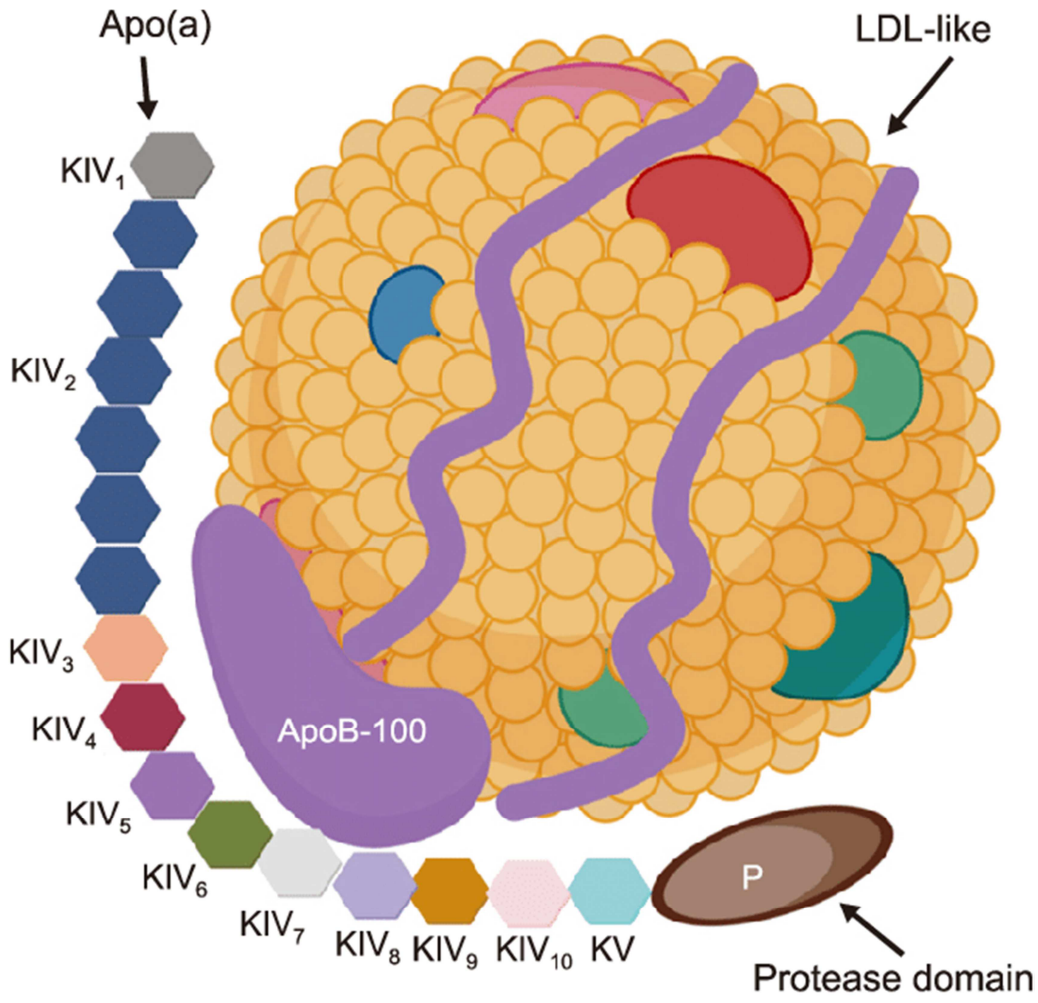


Figure 1: Lipoprotein A Structure

Pathophysiology

It is a well-studied known risk indicator for atherosclerosis, CAD, stroke, thrombosis, and aortic stenosis. Elevated levels of Lp(a) have been linked to stroke and cardiovascular disease (6). This has been linked to this lipoprotein's thrombotic and atherosclerotic characteristics. Generally speaking, lipoprotein(a) promotes thrombosis and atherosclerosis. Because of the way it is structured, Lp(a) causes less

fibrinolysis. More specifically, plasminogen and tissue plasminogen activator (TPA) share structural similarities with apolipoprotein(a) (Figure 2).

This enables to contend with plasminogen over the special binding location, disrupting its functionality, decreasing fibrinolysis. Lp(a) also promotes thrombogenesis by elevating plasminogen activator inhibitor-1 (7). Due to its ability to attach to oxidized phospholipids and carry cholesterol, Lp(a) causes atherosclerosis.

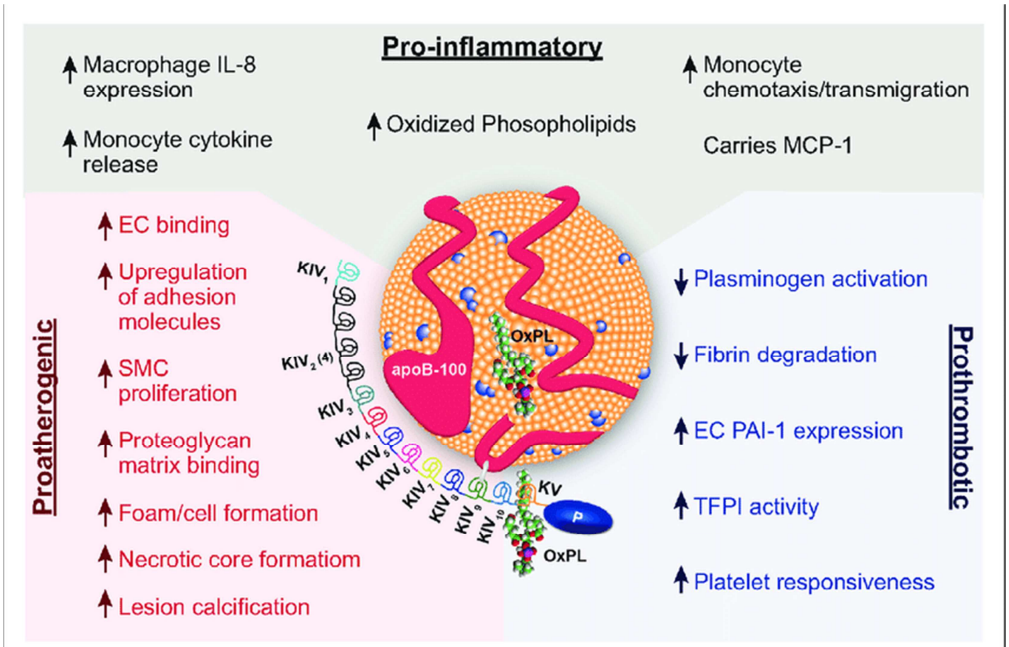


Figure 2: Pathogenesis of Lp (a)

Moreover, it adheres to macrophages causing foam cells to develop. Atherosclerotic plaques eventually accumulate cholesterol as a result of this process. The role of Lp(a) in wound healing has been proposed as one idea (8). On the other

hand, individuals with markedly lower Lp(a) levels do not appear to be linked to any long-term health risks.

Screening

Serum blood tests is the screening method for Lp(a). Main goal for testing Lp(a) is to further identify those who are more likely to develop cardiovascular disease. When there is a substantial family history of early atherosclerotic cardiovascular disease (ASCVD) in first-degree relatives, a personal history of premature ASCVD, and severe primary hyperlipidemia, the NLA advises Lp(a) be taken into consideration for screening. Additionally, for people in the borderline ASCVD risk category, the NLA suggests screening for serum lipoprotein (a) levels to facilitate the process of collaborative decision-making regarding statin therapy (9). There are no formal screening recommendations for Lp(a) from the American College of Cardiology or the American Heart Association (10). Lp(a) screening is generally advised based on criteria established by the European Atherosclerosis Society which includes individuals having more than or equal to ten percent of ten-year risk of CVD, a personal history of early CVD, and recurrent CVD while receiving statin medication. Lp(a) screening is also indicated by familial hypercholesterolemia, high lipoprotein(a) levels, and a family history of early cardiovascular disease. It is generally advised by the European Society of Cardiology that individuals have Lp(a) screened at least once in their lifetime (1).

Epidemiology

Stroke is the second leading cause of death globally. Stroke is the third leading cause of disability in the world. A total of 12.2 million cases of incidence of stroke happens every year. And 6.6 million deaths globally happened in 2019 due to stroke (12). Incidence (cumulative incidence) of stroke range was 105 to 152 per 1,00,000 persons per year in India. The crude prevalence of stroke was 44.29 to 559 per 1,00,000 persons per year across India (13). Prevalence of Myocardial infarction among geriatric (above 60 years) population was estimated as 3.8% (14). Cardiovascular death is the leading cause of death in India. It is responsible for 26.6% of deaths in India and 13.6% of disability-adjusted life years. Most common cause of cardiovascular death is myocardial infarction (15). Cardiovascular events are the leading cause of death in the world. In 2019, 17.9 million people lost life due to cardiovascular events which contributes 32% of the deaths globally (16).

Recommendations need to be improved and recommendations specifically for elderly group has to be developed. This area is still understudied and needs further evaluation. This study helps us to understand the association of lipoprotein (a) and atherosclerotic vascular events especially in the elderly population and whether a raised lipoprotein (a) is a risk factor for these events. This study facilitated the evaluation of whether commonly recognized risk factors for atherosclerotic vascular diseases, such as lipoprotein (a), LDL, HDL, and total cholesterol, differ based on gender and age. Additionally, it contributes to our understanding of the pathophysiological role of lipoprotein (a) in elderly populations, particularly among healthy elderly.

AIMS AND OBJECTIVE

- To estimate and correlate the clinical significance of lipoprotein (a) as a risk factor of atherosclerotic vascular events in elderly.

REVIEW OF LITERATURE

Lp (a) Structure

Lipoprotein (a) is identified as a form of low-density lipoprotein (LDL) 40 years ago. It has apolipoprotein (a), which is attached to apolipoprotein B100, and is structurally a variation of LDL. These two are known to cause coronary artery diseases (17) (Figure 2). There is only one disulfide bridge connecting these two components. The hepatocyte cell membranes are where they are constructed. The plasma concentrations of the apolipoprotein (a) isoform and Lp (a) are inversely correlated. The LPA gene's varying amount of Kringle IV repeats causes the isoform variation. The fluctuating amounts of Lp(a) observed in the general population are caused by variations in Kringle units. Lesser Kringle repeats generally result in low serum Lp(a) levels. Additionally, endoplasmic reticulum's intracellular accumulation of apolipoprotein (a) precursor increases with the size of the protein's isoforms. In 1963, Kåre Berg made the discovery of Lp(a) in human serum while researching variations in LDL antigenicity. Additional analysis of Lp(a) revealed that it is made up of an LDL that is covalently attached to an unusual protein known as apo(a). Previous research has demonstrated that there can be anywhere between 12 and 51 Kringle 4 (KIV) domains, resulting in 34 distinct apo(a) isoform sizes. Moreover, there are ten different types (KIV types 1–10) inside the repeating KIV domain. All of these types are in a single copy, with exception of KIV type 2, which appears in varied quantities. Apolipoprotein of LDL and apo(a) were demonstrated to be dissociated from LDL by reducing agents, suggesting the presence of a di-sulphide bond between the two molecules (2). Research has demonstrated that apo(a)Cys4057 and apoBCys4326 are connected via a disulfide link (18, 19 and 20). In electron

microscope research, it revealed that apo(a) has been encased around the LDL molecule, indicating that the apoB and apoA have numerous interactions. Numerous investigations found apo(A) binds with apoB without sharing the electrons or the reverse were observed (22). While a few of these interactions might develop after Lp(a) is assembled to stabilize the structure, others might be engaged in Lp(a) assembly.

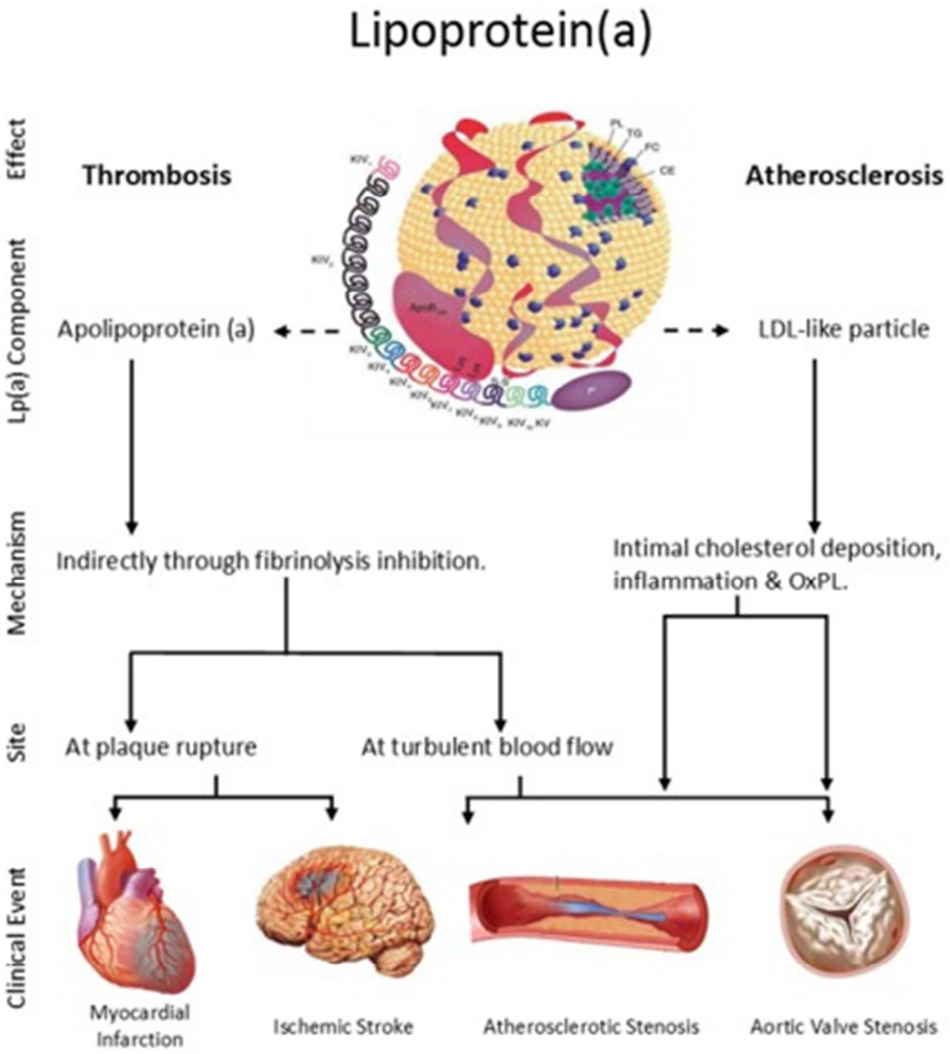


Figure 3: Lipoprotein (a) in thrombosis and atherosclerosis

Lp (a) Assembly

Most evidence points to extracellular Lp(a) assembly, either at the surface of hepatocytes or in circulation. However,studies in humans have provided some support for intracellular assembly (23). Over the past ten years, research has shown that Lp(a) is put together in two steps, with apo(a) and apoB engaging in noncovalent interactions before the di-sulphide bond among apo(a)Cys4057 and apoBCys4326 forms (17, 24). The first non-covalent contact may involve the lysine interaction apoprotein (a) and residues of lysine in apoprotein B accordance with experiment demonstrating that lysine analogues interfere with Lp(a) assembly (25). Additional evidence supporting this has been provided by mutagenesis studies that show impaired lipoprotein (a) following loss of binding of lysine in apo(a) KIV types 6–8 (26). KIV 7 and 8, but not 6 are required for effective assembly of Lp(a) according to a recently published study which utilizes single point mutations to alter the lysing bonding sites in KIV (27). Multiple reports have indicated that apoprotein B sequences can bind to apoprotein (a) noncovalently. According to Becker et al., this noncovalent interaction between an apoprotein B 18 segment and apoprotein A is facilitated by an apoprotein B lysine residue located at the N-terminus, specifically apoBLys680. (28). The non-covalent reaction with apoprotein A has also been linked to regions in the C-terminal part of apoprotein B. Tests utilizing apoprotein B molecules revealed an area crucial for effective Lp(a) assembly, situated among apoprotein B 95 which contains four thousand three hundred and thirty amino acids, apoprotein B 97 with four thousand three hundred and ninety-seven amino acids (29). A 21-amino acid sequence with 4 lysine residues at position which suggested possible binding site of Lp(A) was found after the apoB4330 to 4397 region was further

characterized. It has been demonstrated that a peptide covering this sequence can bind apoprotein A and prevent lipoprotein A production in vitro (30).

In transgenic mice showing full-length apoB mutant, mutations in lysine residues within the apoprotein B 4372 to B 4392 region disrupt Lp(a) assembly (31). The collective research indicates that lipoprotein (a) assembly is complex, requiring multiple interactions between apo(a) and apoprotein B for proper association before forming the disulfide bond. Future investigations in this area may identify new targets for developing lipoprotein (a)-lowering drugs by pinpointing same aminoacid interactions among apoprotein A, apoprotein B crucial for lipoprotein (a) assembly. Recent elucidations of the crystal structures of certain apoprotein A KIV domain will undoubtedly aid in this endeavor.

Lp (a) Metabolism

Metabolic fate of this molecule found to be difficult despite years of investigation. Initially, it is thought that lipoprotein (a) was eliminated by the receptor of low-density lipoprotein due to its resemblance to LDL. This theory has been validated by certain investigations on patients with familial hypercholesterolemia (FH) who have mutant LDLRs, which demonstrate the study participants with familial hypercholesterolemia have greater levels of lipoprotein (a) than the non-familial hypercholesterolemia participants (32, 33). Contrary to these findings, an in-vivo kinetic analysis in individuals with FH revealed receptor of LDL is unnecessary for degradation of Lp(A) (34). Research on animals suggests that the receptor of low-density lipoprotein plays a part in the uptake of Lp(a) since mice that overexpress the receptor of low-density lipoprotein gene have higher Lp(a) clearance, while rabbits with LDLR gene deficiencies have higher Lp(a) levels (35).

Significant clinical trials demonstrating that statins do not affect Lp(a) levels provide substantial evidence against the involvement of the LDLR in Lp(a) clearance (36). In case, LDLR had a significant role in the removal of Lp(a), statins, which increase LDLR gene expression, would be expected to effectively lower Lp(a) levels. Furthermore, there is limited in vitro evidence supporting the binding of Lp(a) to LDLR, as cell culture studies show that lipoprotein (a) has low affinity for the LDLR (37). Based on animal research, the liver seems to be the primary location of Lp(a) metabolism, but there are reports of modest buildup in the muscle and spleen as well (38). While the kidney is not the primary pathway for Lp(a) catabolism, low levels of apo(a) have been detected in human urine, indicating that the kidney may possibly be involved in Lp(a) clearance (39). While cell culture studies showed interactions between lipoprotein (a) and other LDLR like megalin/gp330 and VLDL receptors, their physiological importance remains uncertain. Recently, Kostner et al. identified an asialoglycoprotein receptor (ASGPR) which binds and internalizes Lp(a) and is highly expressed in the liver (40). ASGPR-knockout mice and hedgehogs have been used in a number of in vivo studies that imply this receptor may be key mechanism in hepatic uptake of lipoprotein (a) (41).

Risk factor for CVD

Elevated lipoprotein (a) were shown in numerous large clinical trials to be a distinct risk factor for the development of cardiovascular disease (42, and 43). Based on a meta-analysis of 5436 participants with coronary heart disease (CHD) from 27 prospective studies, individuals in the highest third of Lp(a) levels had a 70% greater risk of developing CHD compared to those in the lowest third (44). The cut-off point of 30 mg/L is commonly cited as the threshold where Lp(a) becomes a risk factor. In

the majority of big cardiovascular investigations, Lp(a) was found to be a small risk variable, with the probability ratio for those over the cut-off level being approximately 2. However, additional studies indicate that the presence of other risk factors, such as elevated LDL or low HDL cholesterol levels, increases the risk of developing coronary heart disease (CHD) in individuals with elevated Lp(a) levels (45). This remains applicable even when thrombotic conditions like Factor V Leiden, protein C deficiency, and antithrombin III insufficiency coexist with elevated levels of Lp(a) (46).

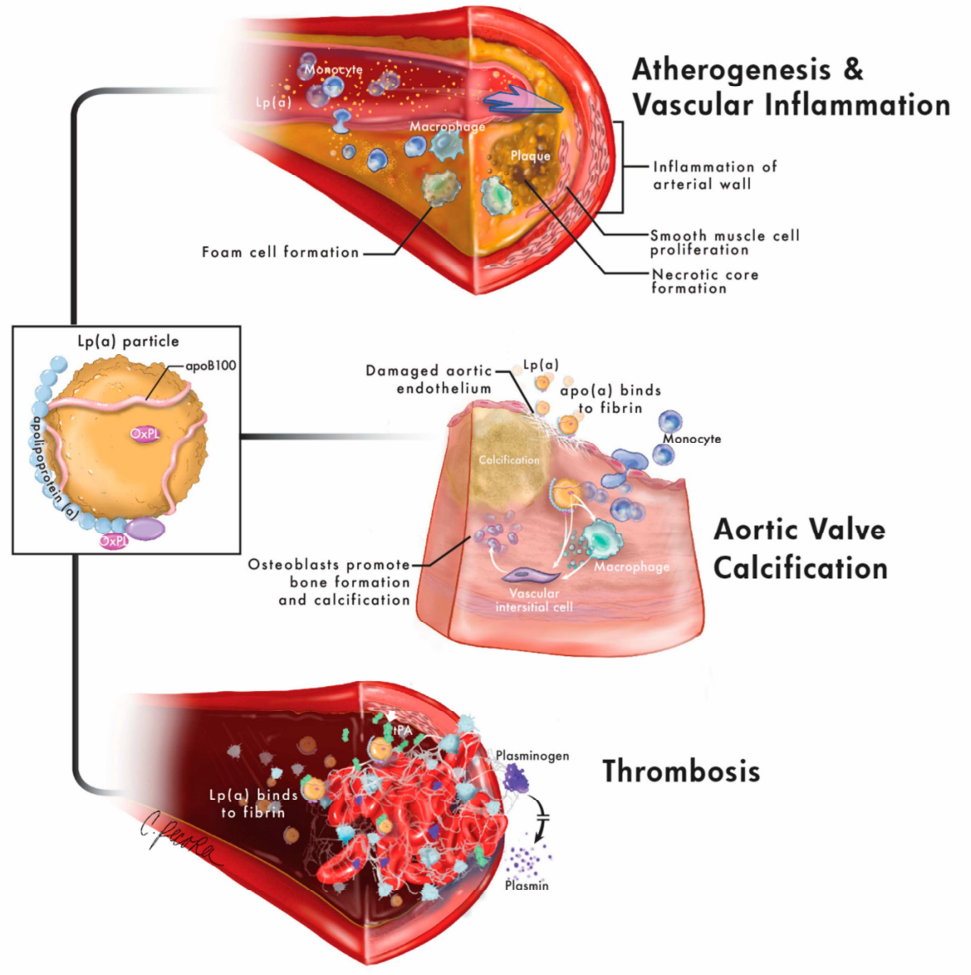


Figure 4: Cardiovascular complications of Lp (a)

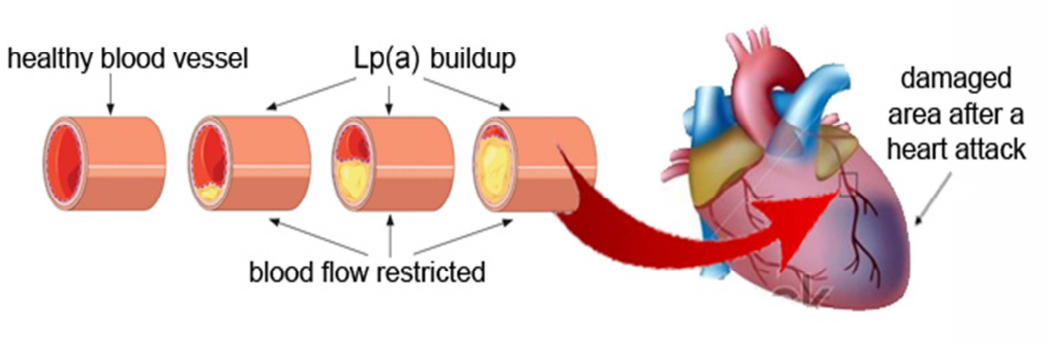
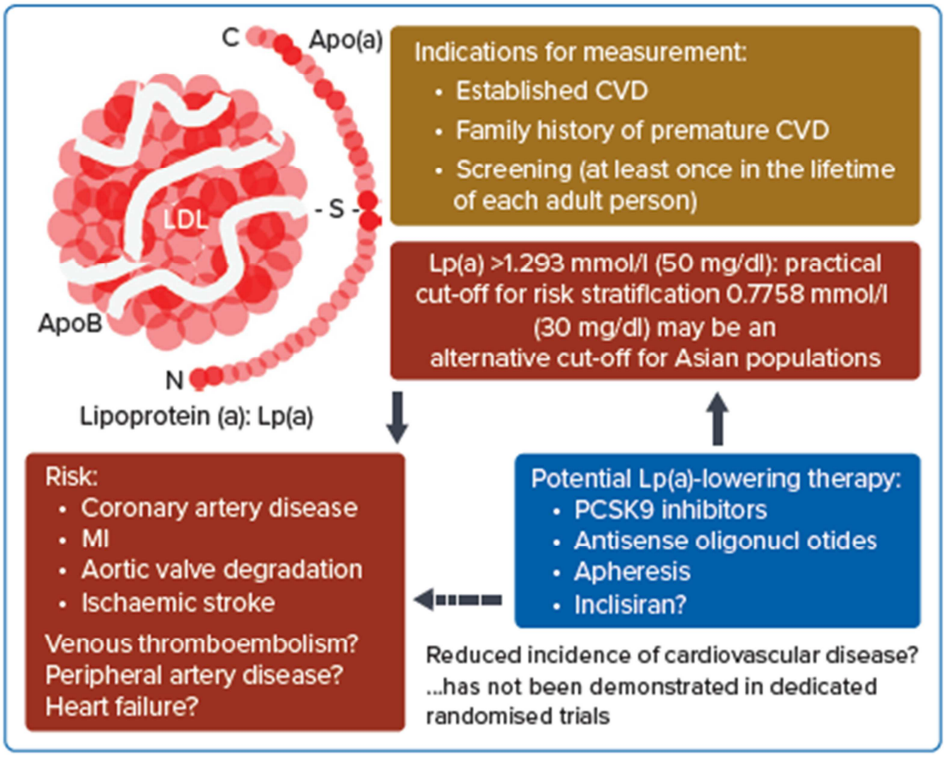


Figure 5: Buildup of Lp (a) in blood vessels

Several studies have observed the accumulation of Lp(a) in the arteries of individuals with atherosclerosis, among those with elevated Lp(a) and those with heart faliure. The aorta (47), coronary (48), cerebral (49), and peripheral arteries (50) have all been shown to exhibit immunohistochemical staining for Lp(a), with the degree of atherosclerosis associated with the relative quantity of Lp(a) deposition. Research conducted on rabbits has also shown that administered human Lp(a) accumulates in atherosclerotic and balloon-damaged arteries (51). The binding capacity of apo(a) for extracellular matrix proteins is probably what keeps Lp(a) in the artery wall (52) (Figure 6).



The Lp(a) molecule consists of an apolipoprotein (Apo) B-containing LDL-like segment and a plasminogen-like glycoprotein Apo(a) segment connected to each other by a disulphide bridge (-S-). CVD = cardiovascular disease; Lp(a) = lipoprotein (a); PCSK9 = proprotein convertase subtilisin/ kexin type 9.

Figure 6: Lipoprotein (a) and cardiovascular diseases

According to Hughes et al., apo(a) lysine binding sites enhance Lp(a)'s affinity for extracellular matrix which envelops cells, altering these sites decreases Lp(a) deposition in the vascular wall (53). Both whole and fragmented apo (a) can be deposited with Lp(a). It is probable that elastases or metalloproteinases released by cells in the artery walls cleave proteins to generate apo(a) fragments (54). Following deposition, both intact Lp(a) and apo(a) fragments can initiate various biological processes that contribute to the advancement of atherosclerosis (Figure 7, Figure 8and Figure 9).

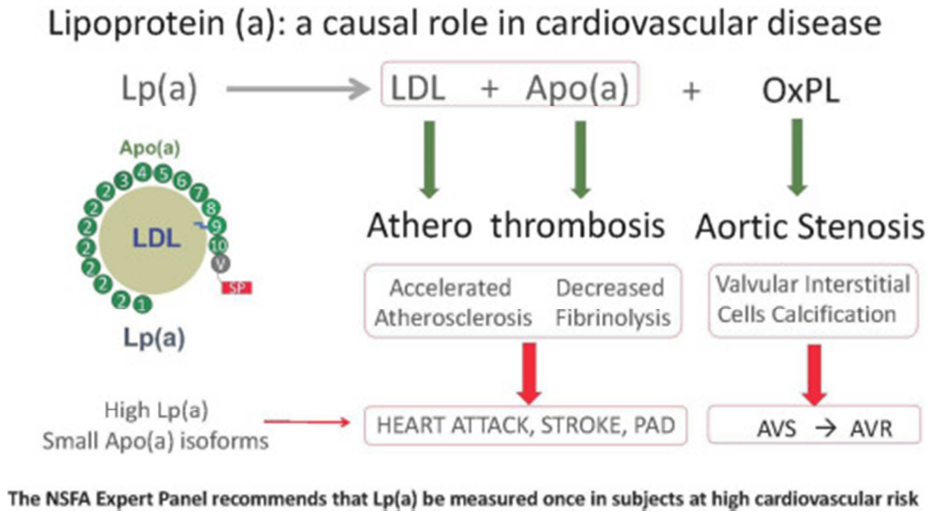


Figure 7: Role of Lp (a) in CVD

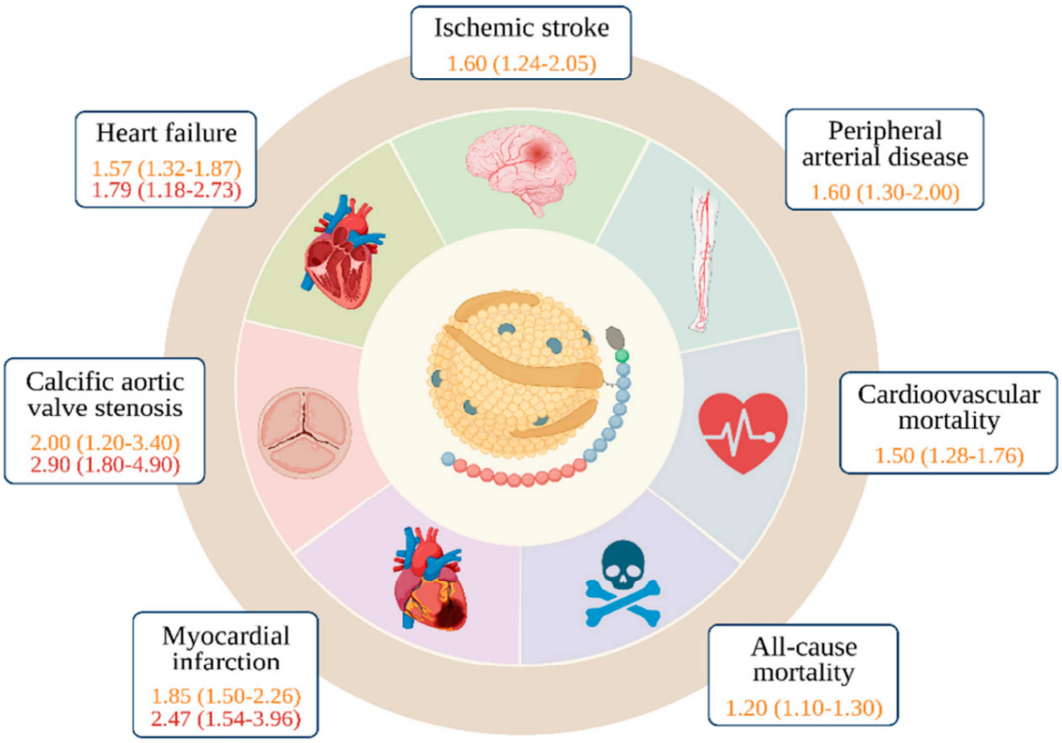


Figure 8: Impact of Lp (a)

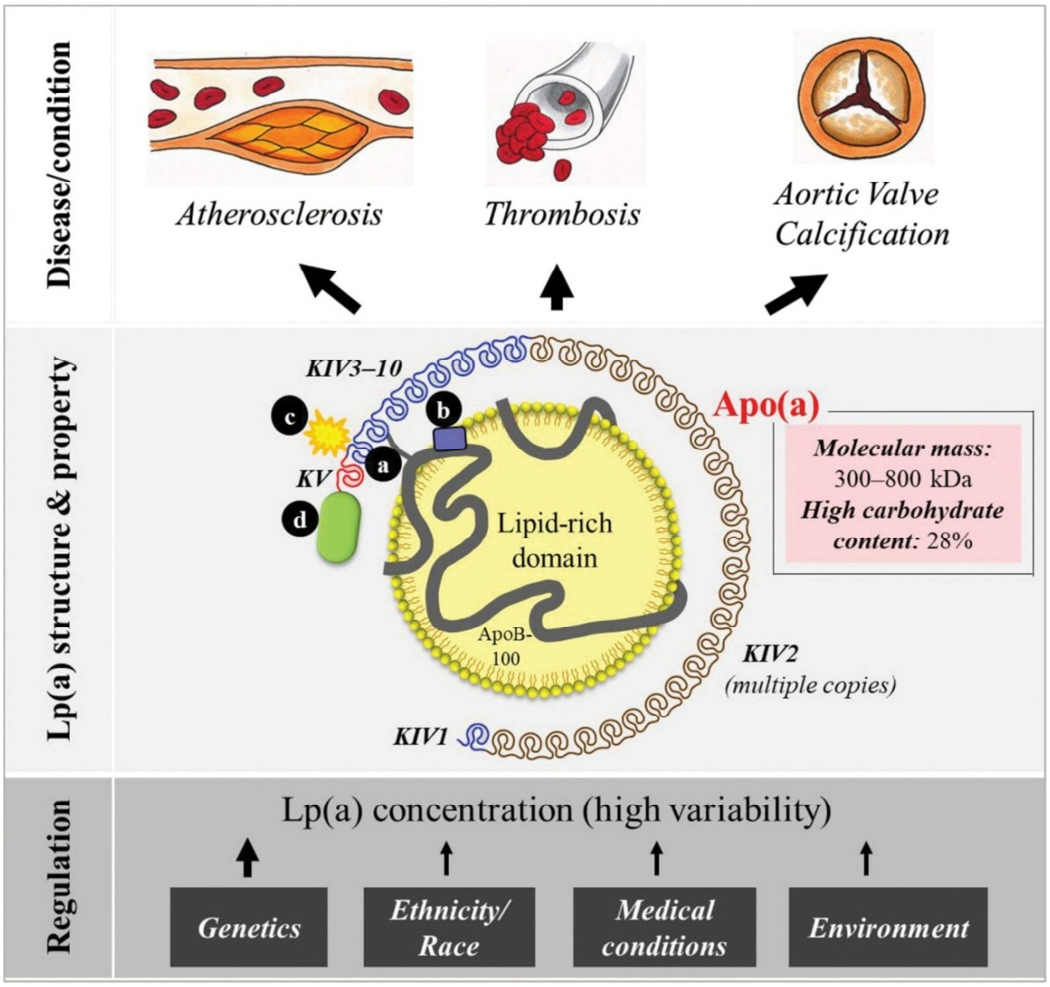


Figure 9: Lp (a) and cardiac diseases

Diagnosis of Lp(a)

One method of screening for Lp(a) is a serum blood test. The main goal of Lp(a) screening is to find those who are more likely to develop cardiovascular disease. Current expert recommendations on testing for elevated levels of lipoprotein (a) are diverse. The National Lipid Association (NLA) suggests considering Lp(a) testing for individuals with severe primary hyperlipidemia, a history of premature atherosclerotic cardiovascular disease, or a significant family history of the condition among first-degree relatives. NLA also recommends considering Lp(a) testing to

support shared decision-making on statin therapy for those in the risk category for borderline atherosclerotic cardiovascular disease. There are no formal Lp(a) screening guidelines from the American College of Cardiology or the American Heart Association. Guidelines from Canada suggest screening everyone for Lp(a). The circumstances in which screening for Lp(a) is usually recommended are outlined in guidelines that have been issued by the European Atherosclerosis Society (EAS). Patients meeting specific criteria, including a history of premature CVD, recurrent cardiovascular events despite statin therapy, and a 10-year cardiovascular disease risk of ≥10%, should undergo Lp(a) screening. People with elevated lipoprotein (a), familial hypercholesterolemia, and a family history of CVD are additionally recommended to get screened. European Society of Cardiology (ESC), advised the individuals to undergo lipoprotein (a) testing minimum once during their lifetime (5) (Figure 10).

Cohort	Indications for Lp(a) Measurement
Universal screening at least once in the lifetime of each adult person	Should be considered[18,19] Elevated Lp(a) is associated with an increased risk of future cardiovascular events. The Lp(a) level is mostly consistent throughout an individual's lifetime
People with a family history of premature CVD	Recommended[17–19] Elevated Lp(a) might facilitate shared decision-making for initiation of treatment
Patients with established CVD	Should be considered[19] Elevated Lp(a) is associated with recurrent cardiovascular events
Serial measurement of Lp(a)	Not recommended[17–19] Lp(a) level is mostly consistent through an individual's lifetime. Its role as a treatment target has not been established

CVD = cardiovascular disease; Lp(a) = lipoprotein(a).

Figure 10: Screening for Lp (a)

To quantify Lp(a), multiple kinds of immunoassays are utilized, including the enzyme-linked immunosorbent assay, immunoturbidometric, and immunonephelometric tests. All of these assays involve polyclonal antibodies from different animal species, with the exception of ELISA. Direct-binding, sandwich-type ELISAs that are available generally incorporate both monoclonal and polyclonal antibodies. The structural variability of lipoprotein (a) resulting from apo(a) size heterogeneity has a major impact on the accurate determination of lipoprotein (a) in human plasma. Amount of repetitive antigenic determinants present in different lipoprotein (a) molecules varies, and size of the apo(a) particle affects how sensitive the antibodies are to these repeated epitopes. Because of this, immunoassays that employ polyclonal or monoclonal antibodies that specifically target Kringle IV type 2 epitopes will typically overestimate the apo(a) concentration in samples with larger apo(a) and underestimate the apo(a) concentration in samples with smaller apo(a) relative to the apo(a) in the assay calibrator. To overcome these difficulties, scientists have created isoform-independent assays that seek to quantify Lp(a) precisely while excluding the influence of apo(a) size polymorphism. For instance, an ELISA that precisely measures Lp(a) without considering the effects of apo(a) size polymorphism have been developed using a monoclonal antibody (a-40) that targets distinct epitope found in KIV 9 of apo(a). To summarize, the fluctuating antibody immunoreactivity towards distinct apo(a) size isoforms which leads to imprecise quantification of Lp(a) levels, potentially causing an overestimation or underestimation of the actual values. This emphasizes how crucial it is to interpret Lp(a) results using standardized assays and considering the effects of apo(a) size variation (5).

The accuracy of the results may be impacted by the use of aspirin, ethanol, niacin supplements, and oral estrogen supplements. The length of time that a person should cease taking drugs or supplements that can affect the findings of a Lp(a) analysis can vary. You should adhere to the detailed instructions supplied by the testing laboratory (5).

Lp(a) is commonly tested in mg/dL, but because of the significant inter-individual size variation brought on by Kringle IV type 2, it is preferably assessed in nmol/L. The range of desired and ideal Lp(a) test results is less than 14 mg/dL. >50 mg/dL is the highest risk range. Individuals who have a Lp(a) between 14 and 30 mg/dL are categorized as borderline risk, whereas those who have a Lp(a) between 31 and 50 mg/dL are high risk. Because Lp(a) particles contain low-density lipoprotein particles, Lp(a) levels directly influence serum low-density lipoprotein levels. Lipoprotein-X (LpX) levels are often presented as a separate result in laboratory testing for Lp(a). Elevated levels, are linked to hyper viscosity syndromes and cholestasis. Given that Lp(a) is genetically transmitted, screening should be undertaken for children whose parents have high levels of Lp(a); in contrast, reverse cascade screening should be considered when a child has an elevated level of Lp(a) (5).

A study done in Japanese population by Kario K showed a close association between Lp(a) as an acute phase reactant in old Japanese. Subjects with higher level may develop cardiovascular disease later in life, whereas healthy old individuals may develop vascular disease later in life, whereas the remaining healthy old individuals have lower Lp(a) (55).

A study published by K Heinimann showed that the Lp(a) concentration did not differ between male and female. Higher value of Lp(a) was associated with the history of MI and anticoagulant medication. There is low statistical significance of low Lp(a) and regular intake of vitamin pills. Results confirm the association of longer life and low Lp(a) concentration which are longer extent independent of external risk factors. Thus Lp(a) could be a true longevity gene (56).

A study done by Hulya Cicek showed that for middle aged men elevated Lp(a) is an independent risk factor for premature CAD and importance of Lp(a) as a risk factor appears to decrease with age. The data suggests that the utility of Lp(a) in predicting the risk of CAD is low in older men (57).

Lp (a) - Cerebrovascular events

A study conducted in Netherlands (58) among patients admitted for acute cerebral ischemia were followed up for a period of minimum 1.5 years. The study aimed to understand whether Lp(a) is a prognostic factor in high-risk individuals with acute ischemic stroke. Increased Lp (a) was reported in 35% of the study population with cerebral ischemia. Lp(a) and stroke severity or occurrence of vascular events were not significantly associated in the study.

A meta-analysis was conducted to assess the link among Lp(a) and ischemic stroke risk from 20 relevant studies. The findings indicate that elevated Lp(a) is independently associated with an increased risk of ischemic stroke. This suggests that higher values of lipoprotein(a) show increased likelihood of experiencing ischemic stroke, highlighting its role as an independent risk factor in this context (59).

Another meta-analysis tried to understand whether Lipoprotein(a) is a stroke risk factor. In this meta-analysis, 31 studies were included based on the inclusion and exclusion criteria. Among case-control studies included in above metanalysis, unadjusted mean Lp(a) was elevated in patients with stroke. In nested case-control studies Lp (a) was not a risk factor for occurrence of stroke. According to prospective cohort studies, patients in the highest quartile of the Lp(a) distribution had incident strokes more frequently than patients in the lowest quartile. This meta-analysis concluded that elevated Lp(a) as a risk factor for incidence of stroke (60).

Compared to coronary artery disease (CAD), the role of Lp(a) as a risk factor for stroke is less firmly established, and findings from multiple major population-based cohort studies on stroke were inconsistent. However, a recent systematic review and meta-analysis, encompassing seven studies involving 871 cases of intracerebral hemorrhage and 41 studies involving 7,874 patients with ischemic stroke, demonstrated a strong association between elevated Lp(a) levels and the risk of ischemic stroke compared to controls. Furthermore, the analysis revealed significant correlations between Lp(a) levels and both the likelihood of intracerebral hemorrhage and the subtype of ischemic stroke related to large artery atherosclerosis (61).

A study conducted in the United States examined Lp(a) as a risk factor for ischemic stroke with consideration for racial differences. The research involved 30,239 adults aged 45 and older, both Black and White, recruited between 2003 and 2007 as part of the REGARDS (Reasons for Geographic and Racial Differences in Stroke) project, which investigates stroke mortality variations across races and regions. Using an immunonephelometric technique, researchers assessed baseline Lp(a) levels in 572 incident ischemic stroke cases and a random sample of 967

participants from the cohort. Cox proportional hazards models, stratified by race and gender, were employed to calculate stroke hazard ratios based on baseline Lp(a) quartiles adjusted for age, sex, and other stroke risk factors. The study found that being in the highest Lp(a) quartile compared to the lowest was moderately associated with ischemic stroke. Specifically, the HR was 1.14 for White individuals and 1.96 (95% CI, 1.10–3.46) for Black individuals, with a p-value for interaction of 0.12. Although men had lower Lp(a) levels than women, the study showed no gender difference in association between lipoprotein (a) and stroke risk. The study concluded that Lp(a) is indeed a risk factor for ischemic stroke (62).

A study conducted in Denmark investigated the link between Lp (a) and stroke. This research included over ten thousand participants from the "Copenhagen City Heart Study" and 49,699 participants from the Copenhagen General Population Study, all of whom had measurements of plasma Lp(a), LPA Kringle-IV type 2 number of repeats, and LPA rs10455872. After adjusting for multiple variables, the study found that individuals with lipoprotein(a) levels above 93 mg/dl (>199 nmol/L; 96th to 100th percentile) had a significantly higher risk of ischemic stroke compared to those with levels below 10 mg/dl (<18 nmol/L; first to 50th percentile), with a multivariable-adjusted hazard ratio of 1.60 (95% CI: 1.24 to 2.05). Observational analyses also showed that higher levels of lipoprotein(a) were associated with increased genetic causal risk ratios for LPA Kringle-IV type 2 number of repeats and LPA rs10455872 with hazard ratio of 1.2 and 1.27 respectively. Additionally, every 50 mg/dl (105 nmol/L) increase in lipoprotein(a) level was associated with a multivariable-adjusted hazard ratio of 1.20 (95% CI: 1.13 to 1.28) for ischemic stroke. Among individuals over 70 years of age who smoke regularly and have hypertension along with elevated lipoprotein(a) levels (>93 mg/dl; 96th to 100th percentile), the

absolute 10-year risk of ischemic stroke was highest at 17%. Risk estimates from the Copenhagen City Heart Study showed a similar trend, although statistical significance was not reached. The study concluded that elevated plasma levels of lipoprotein (a) are linked to a higher risk of ischemic stroke, as demonstrated by both observational data and genetic causal analyses in a large, modern general population study (63).

Northern Manhattan study done showed that elevated Lp(a) levels are significantly and independently associated with increased risk, suggesting that Lp(a) is a risk factor for ischemic stroke across White, Black and Hispanic race/ethinic groups. Lp(a) levels >30mg/dl is associated with almost a 2-fold increase in ischemic stroke. Limitations in the study include small sample size, the processing time from taking the blood sample and processing the sample was 1- 2 weeks which may hamper the reliable measurements because of instability of the low molecular weight isoforms, measurement performed after the stroke may not accurately reflect its pretest value and also the study design (64).

According to G. Baggio's study on Lipoprotein(a) and lipid profile in healthy individuals, it was found that the lipoprotein(a) value didn’t change significantly across different age groups. Interestingly, one fourth of the study participants showed elevated lipoprotein (a) values despite not experiencing any atherosclerotic events. Unlike younger and older individuals, group with higher lipoprotein (a) also exhibited elevated levels of IL6, suggesting that genetic regulation of Lp(a) may weaken with age, while variables like chronic inflammation could influence its levels. The study identified some limitations, notably that median and mean log serum Lp(a) levels did not show age-related changes. Additionally, a significant proportion of healthy centenarians had Lp(a) levels that placed them at risk for atherosclerosis and its

complications. These findings challenge the notion that Lp(a) is solely an independent risk factor for atherosclerotic vascular events. To further explore these findings, longitudinal studies are necessary to determine if study participants with increased lipoprotein (a) have maintained these levels throughout their lives (65).

A prospective study that was published in the New England Journal of Medicine revealed that an elevated level of lipoprotein (a), which is an independent predictor of stroke, death from vascular disease, and mortality from all causes, was present in males but not in women. The information is consistent with using Lp(A) levels to forecast older men's risk of occurrences. This study has several limitations- Firstly, the analysis of lipoprotein(a) outcomes may differ based on age, race, and ethnic background. Secondly, the study data was restricted to individuals aged 65 years and older, predominantly of white ethnicity, thus the findings may not generalize to the broader population. Another limitation is that the study was primarily planned in assessing risk for vascular disease, not mortality, and as such, it may not adequately control for various factors that could influence mortality outcomes (66).

Lipid profile and Lp(a)

A study conducted in Pakistan to ascertain the local population's serum lipoprotein(a) levels, as well as the drug's reaction to lipoprotein(a) and its correlation with other lipid profile factors. The Pak-Emirates Military Hospital and Army Medical College in Rawalpindi, Pakistan hosted the cross-sectional analytical study from March 2018 to March 2019. The study's participants were divided into three groups: group I consisted of healthy controls, group II consisted of people with hyperlipidemia who were not taking medication, and group III consisted of diagnosed cases of hyperlipidemia who were receiving statin therapy. For the purpose of

estimating lipoprotein(a) and lipid profile, the samples were analyzed using an automated chemistry analyzer and an enzyme-linked immunosorbent assay. Thirty of the ninety subjects (30.3%) (mean age 43±5 years) were divided into the three groups. There were notable differences between the groups in terms of mean body mass index, total cholesterol, triglycerides, and low-density lipoprotein. The amount of lipoprotein(a) showed a statistically positive correlation with low-density lipoprotein but no correlation with statins. It was discovered that lipoprotein(a) was elevated even in the absence of dyslipidemia, and statin medication was found to controversially raise lipoprotein(a).Lp(a) may also be viewed as a separate risk factor for every known consequence of hyperlipidemia. (67). The study aimed to determine associations between clinical features and dyslipidemias in Pakistani patients with T2DM by analyzing Lp(a) values. 68 patients from Pakistan confirmed with T2DM and 40 healthy individuals, fasting blood samples were analyzed for levels of Lp(a), TC, TG, LDL, HDL, glucose, and HbA1c. The results showed that diabetic patients had markedly elevated levels of Lp(a) compared to the control group. Age, BMI, SBP, DBP and fasting hyperglycemia did not correlate with Lp(a). The relationship between BMI and SBP and DBP was positive. A noteworthy positive association was observed among Lp(a),TC and LDL. There was no discernible relationship between Lp(A), HDL, TG, HbA1c. It was concluded from this study that serum Lp(a) levels are positively correlated with serum total and LDL-c levels and are significantly elevated in type 2 diabetes (68).

Lipoprotein (a) and its impact in young population

A study conducted among children between age 5 and 18 in Germany to evaluate whether Lp (a) levels are affected by BMI. It was conducted among 248 children with obesity and 264 healthy children. The median Lp(a) was 9.7 mg/dL. There was no significance between BMI and Lp(a). However, Lp(a) in youth may be beneficial to identify increased lifetime risk of ASCVD (69).

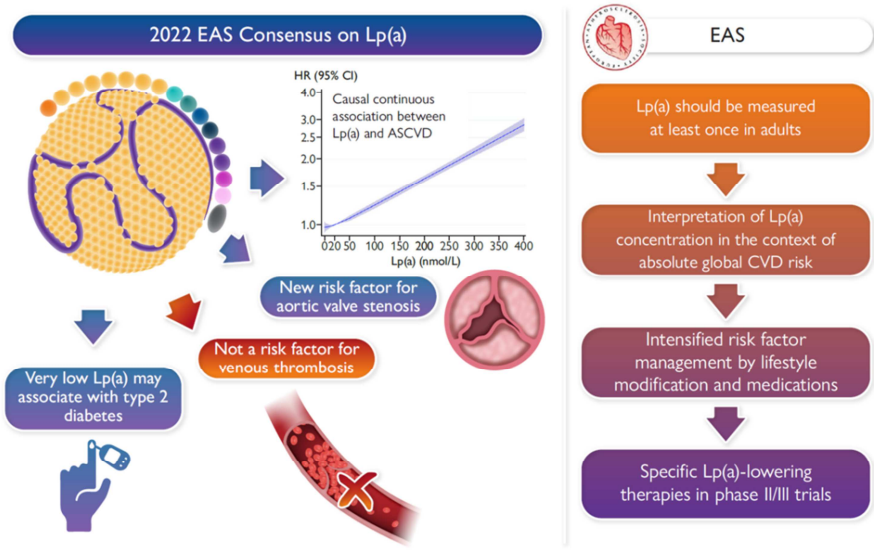


Figure 11: Association between Lp(a) and ASCVD

In CVD risk in Young Finns Study, 95 out of the 3596 patients (2.7%) recruited as children were diagnosed with ASCVD. The median age at diagnosis was 47. Levels of Lp(a) measured among youth aged 9 to 24 years were found to be associated with adult ASCVD and carotid intima-media thickness. Data from BHS (Bogalusa Heart Study) involving White participants was used to replicate these findings from the YFS. The BHS data included measurements of Lp(a) during youth (ages 8–17 years) and adult ASCVD events (15 cases and 572 controls) in 587 individuals. Cox proportional hazard regression analysis was employed to conduct the

assessments. According to the YFS results, individuals exposed to high levels of Lp(a) as children, with a value of 30mg/dl or more, has approximately twice the risk of developing adult ASCVD compared to those with lower levels. Lipoprotein (a), LDL, BMI, and smoking are identified as independent risk factors associated with youth that increase the risk of developing adult ASCVD. In the BHS (Bogalusa Heart Study), White individuals exposed to high Lp(a) levels had a 2.5-fold higher chance of developing adult ASCVD compared to those not exposed, after adjusting for age and sex. This risk remained consistent even after accounting for LDL and BMI. The pooled analysis using a multivariable model showed that individuals exposed to raised Lipoprotein(a) levels were twice as likely to develop adult ASCVD compared to those with lower levels, regardless of cohort or pooled data. However, statistical significance was not found in Lp(a) levels in adolescence and adult carotid artery thickness. Elevated Lp(a) levels during adults represent significant risk factor for future ASCVD development (70).

Treatment and management of Lp(a)

A number of medications have been shown to possibly significantly lower plasma Lp(a). Elevated Lp(a) may be regarded as a risk factor to begin statin medication for primary prevention in individuals with intermediate risk, which is defined as a cardiovascular disease risk of 7.5–20% determined using the Framingham risk score in individuals. It may be justified to consider more rigorous treatment based on higher Lp(a) in high-risk or very-high-risk patients on maximally tolerated statin treatment if their LDL cholesterol is ≥6.98 mmol/l. High Lp(a) levels are highly predictive of recurrent cardiovascular events in the context of secondary prevention and indicate a need for more intensive therapy, such as PCSK9 inhibitors (71) (Figure 12 and Figure 13).

Potential Therapy	Lp(a) Level	Risk Reduction by Lp(a) Lowering
Statin	9–20% increase	–
Niacin	20–30% decrease	Unknown
PCSK9 inhibitors	23–30% decrease	Further risk reduction independently from LDL cholesterol reduction was reported in sub-analyses[6]
Inclisiran	14–26% decrease (NS)	Unknown
Mipomersen (ASOs)	24–32% decrease	Unknown
Apo(a)-L_{Rx} (ASOs)	35–91% decrease	Ongoing trial (NCT04023552) in patients with a history of CVD and Lp(a) >1.81 mmol/l (70 mg/dl)
Lipoprotein apheresis	70% decrease	94% reduction in an observational study[79]

ASO = antisense oligonucleotide; CVD = cardiovascular disease; Lp(a) = lipoprotein(a); NS = not significant; PCSK9 = proprotein convertase subtilisin/kexin type 9.

Figure 12: Treatment for lowering Lp(a)

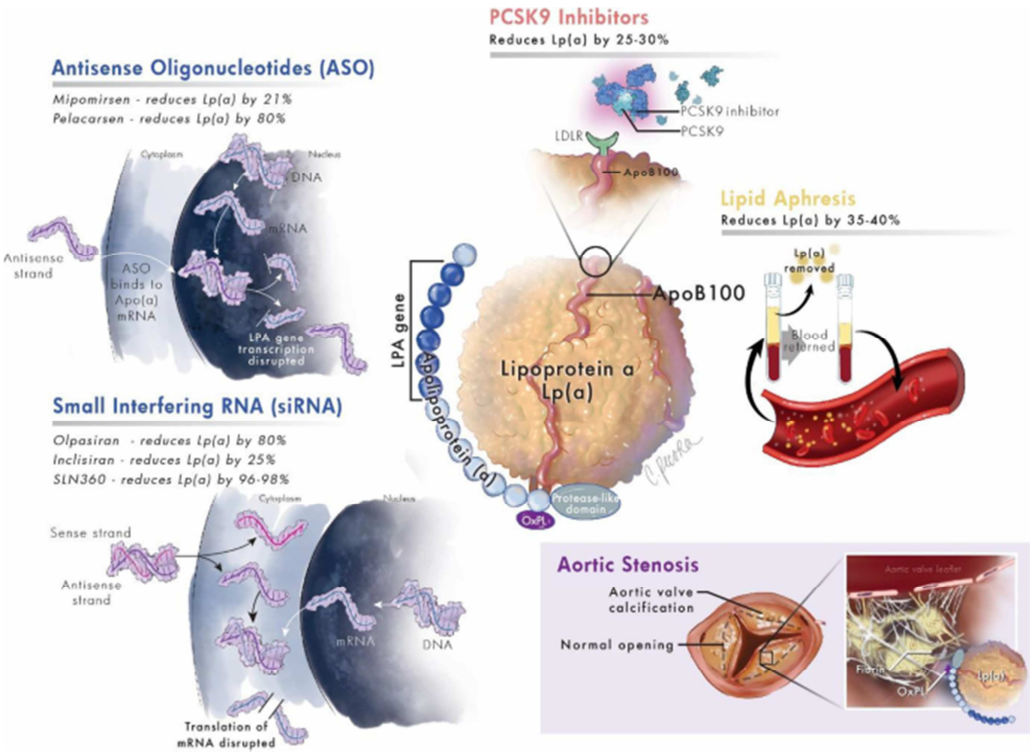


Figure 13: Lp(a) and lowering drugs

MATERIALS AND METHODS

Source of Data: Patients admitted in the department of medicine, cardiology and neurology at "KLEs Dr. Prabhakar Kore Hospital and Medical Research Centre", Belagavi Between 1st January 2023 and 31st December 2023 over a period of 1 year.

Study Design: Cross Sectional Study

Study Period: January 2023 to December 2023

Sample Size: 142

Sample size formula: The minimum sample size formula based on mean and standard deviation is "n =where zα"s linked with the level of significance and zβ is linked with the power of the test. For 5% level of the significance zα =1.96 and zβ=0.84 for 80% power of the test. Ref: Lipoprotein(a) and lipoprotein profile in healthy centenarians: a reappraisal of vascular risk factors by Baggio G, Donazzan S, Monti D, Mari D, Martini S, Gabelli C, Dalla Vestra M, Previato L, Guido M, Pigozzo S, Cortella I, Crepaldi G, Franceschi C. The parameter considered in the calculation is LP(a) low is the mean of the first group (5.0) and is the mean of the second group (5.4). s1 is the standard deviation (SD) of the first group (0.58) and s2 is SD of the second group (0.9).

Sampling technique: Cross sectional study, all consecutive patients fulfilling the inclusion criteria will be included in the study, statistical analysis will be done by SPSS using descriptive analysis and chi-square test.

Inclusion criteria: Study participants are divided into 2 groups:

Group A:

- Participants with age more than 65years
- Participants who had Atherosclerotic vascular event (neurological or cardiovascular)
- The participants in this group were further sub grouped based on the type of atherosclerotic vascular event as:
    1. Cardiovascular atherosclerotic vascular event subgroup
    2. Neurological atherosclerotic vascular event subgroup

Group B:(CONTROL GROUP)

- Participants with age more than 65 years
- Participants with no atherosclerotic vascular events

Exclusion criteria:

Participants with:

1. Active infections
2. Neoplasia
3. Renal dysfunction
4. Liver dysfunction

Study protocol:

A one-year hospital based cross-sectional study from January 2023 to December 2023 at KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

- Informed consent will be taken from all the participants of the study.
- Elderly individuals included in the study are those who are more than or equal to 65years of age.
- At the time of admission, a detailed history and a detailed examination will be performed. The study participant will be asked a history of any atherosclerotic vascular event he has suffered in this lifetime.
- The atherosclerotic vascular event studied includes
    1. **Stroke** which we defined as-"either a cerebrovascular accident or a transient ischemic attack".
    2. **Coronary heart disease** we defined as- "occurrence of angina, myocardial infarction or coronary angioplasty or bypass surgery"

The following details would be recorded for each participant:

1. Hypertension
2. Diabetes mellitus
3. Use of contraceptive pill
4. Current statin therapy
5. Current or former smoker
6. Alcohol consumption
7. ischemic heart disease
8. Chronic obstructive pulmonary disease
9. History of cancer
10. Family history of any cerebrovascular accident, or myocardial infarction or early cardiac death
11. History of any atherosclerotic
12. vascular event
13. History of any regular drug intake

Definition of the above terms:

1. Hypertension: current intake of antihypertensive medication
2. Diabetes mellitus: current intake or oral hypoglycaemic drugs or insulin injections
3. Current smoker is one who consumes at least one cigarette a day

Blood samples will be taken from each participant of the study on the next day of admission after 10 hours of fasting.

The following blood investigation will be performed:

1. Serum lipoprotein(a)
2. Serum LDL cholesterol
3. Serum HDL cholesterol
4. Serum Triglyceride
5. Serum total cholesterol
6. Random Plasma glucose
7. Serum creatinine

Data collection procedure: A one-year hospital based cross-sectional study from January 2023 to December 2023 at "KLE's Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi".

1. Informed consent will be taken from all the participants of the study. Elderly individuals included in the study are those who are more than or equal to 65years of age. At the time of admission, a detailed history and a detailed examination will be performed. The study participant will be

asked a history of any atherosclerotic vascular event he has suffered in this lifetime.

2. The following details would be recorded for each participant:
    1. Hypertension
    2. Diabetes mellitus
    3. Use of contraceptive pill
    4. Current statin therapy
    5. Current or former smoker
    6. Alcohol consumption
    7. Ischemic heart disease
    8. Chronic obstructive pulmonary disease
    9. History of cancer
    10. Family history of any cerebrovascular accident, or myocardial infarction or early cardiac death
    11. History of any atherosclerotic vascular event
    12. History of any regular drug intake
    13. Blood samples will be taken from each participant of the study on the next day of admission after 10 hours of fasting in via venepuncture

Data processing and analysis/statistical analysis:

Data is analysed using statistical software R version 4.4.0. and Microsoft Excel. Categorical variables given in the form of frequency tables. Continuous variables given in Mean ± SD / Median (Min, Max) form. Chi square test is used to check the association of categorical variables with groups. Normality of variable is checked by Shapiro Wilk test and QQ plot. If data follows normal distribution,

parametric tests will be used. Otherwise, non-parametric tests will be used. Spearman's rank correlation test is used to check the correlation of variables. Kruskal Wallis, Dunn test, and Mann Whitney were used. P-value less than or equal to 0.05 indicates statistical significance.

RESULTS

Data contains measurements on 142 subjects which are divided into 2 groups: Group-A:- Atherosclerotic Vascular Event Group (2 subgroups: Cardiovascular Atherosclerotic vascular event subgroup and Neurological Atherosclerotic vascular event subgroup) and Group-B No Atherosclerotic vascular Event Group (CONTROL GROUP) with 80 (50 and 30 in each subgroup respectively) and 62 subjects respectively. The following table gives the comparison of demographic variables over groups.

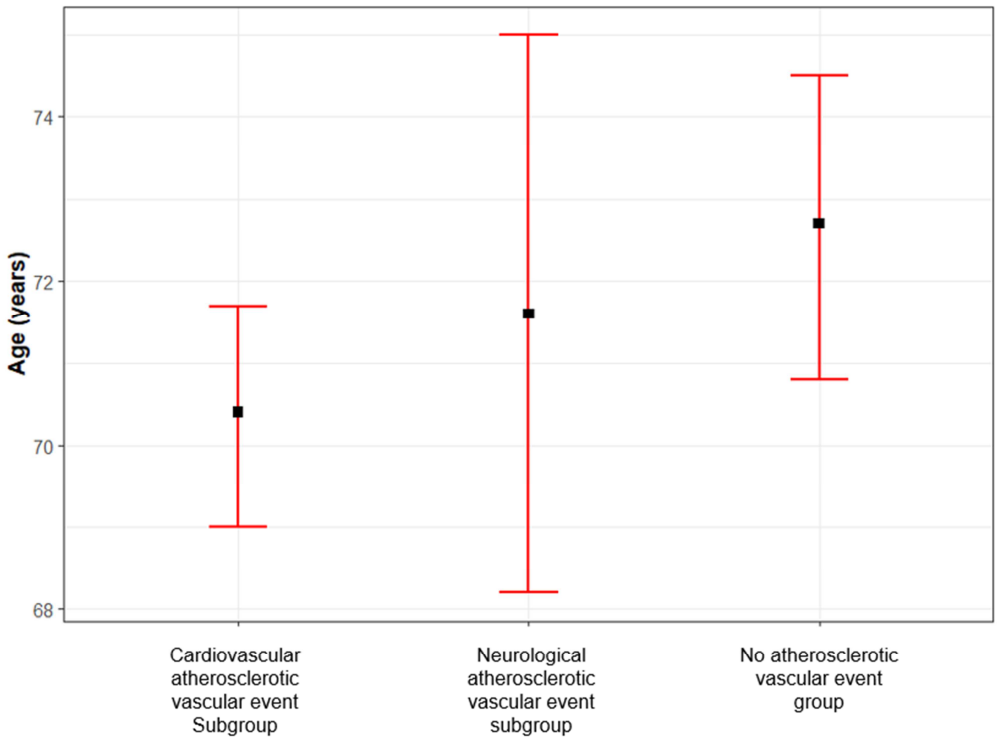
Table 1: Comparison of demographic variables over groups.

		Group-A		**Group-B**		
Variables	**Sub Category**	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value**
Age (years)	Mean ± SD Median (Min, Max)	70.38 ± 4.78 69.5 (65, 84)	71.6 ± 9.08 71 (42, 85)	72.66 ± 7.25 72 (65, 96)	71.63 ± 6.98 70 (42, 96)	0.3577
Gender	Female	12 (24%)	5 (16.67%)	29 (46.77%)	46 (32.39%)	**0.0044**
	Male	38 (76%)	25 (83.33%)	33 (53.23%)	96 (67.61%)	

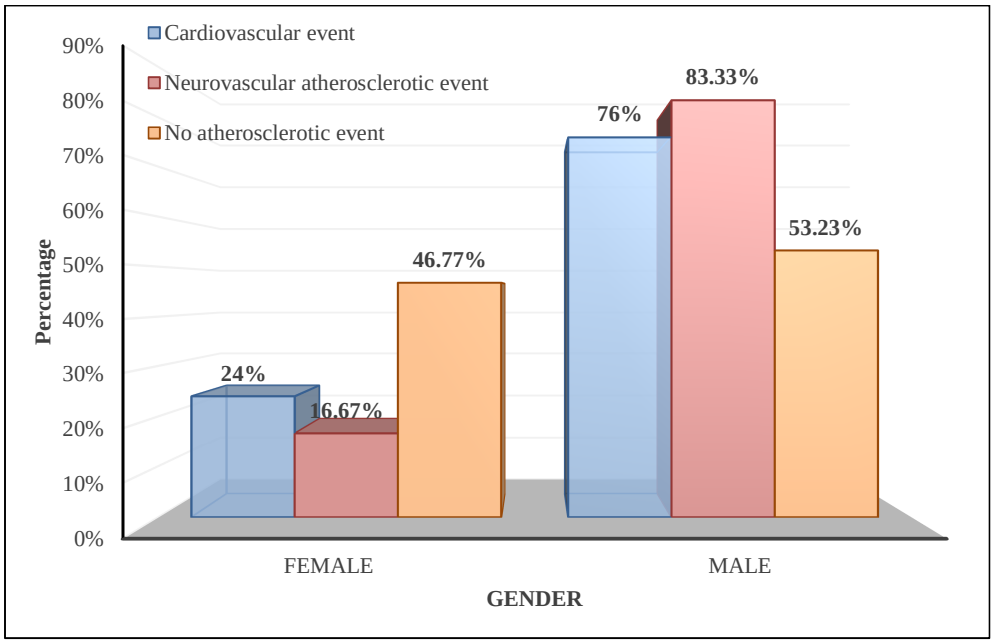
Abbreviation: K – Kruskal Wallis test, C – Chi square test

The mean age for the cardiovascular atherosclerotic vascular event subgroup is 70.38 ± 4.78 years, for the neurological atherosclerotic vascular event subgroup is 71.6 ± 9.08 years, and for the no atherosclerotic vascular event group is 72.66 ± 7.25 years. However, it was not statistically significant (p-value = 0.3577).

In the cardiovascular atherosclerotic vascular event subgroup, 24% are female and 76% are male. In the neurological atherosclerotic vascular event subgroup, 16.67% are female and 83.33% are male. Conversely, in the no atherosclerotic vascular event group, 46.77% are female and 53.23% are male. Gender distribution between the groups were statistically significant (p-value = 0.0044).



Graph 1: Mean plot of age between the groups.



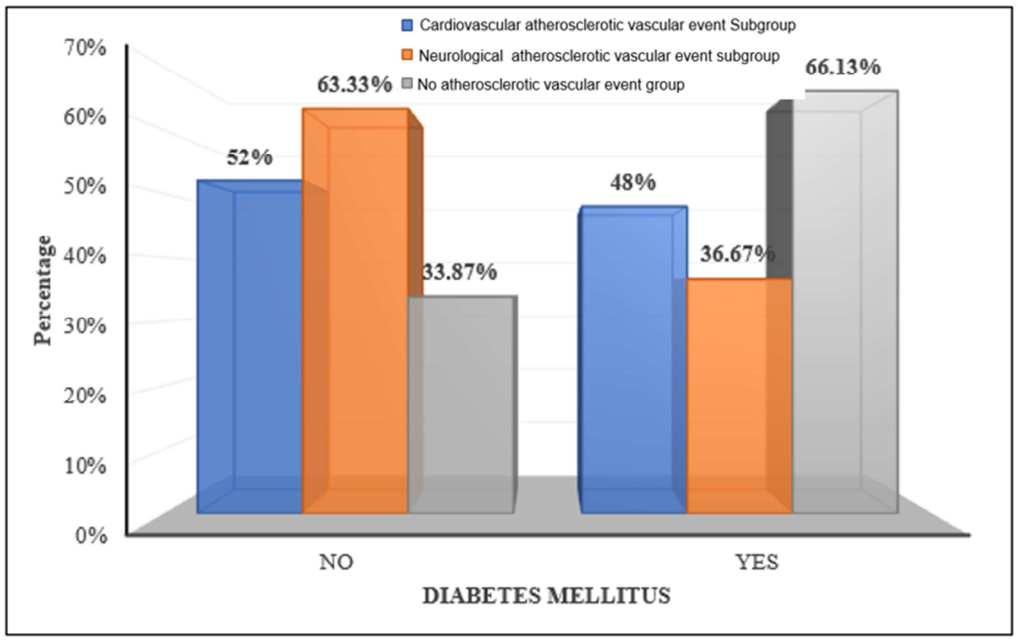
Graph 2: Distribution of gender between the groups.

Table 2: Comparison of comorbidities between the groups.

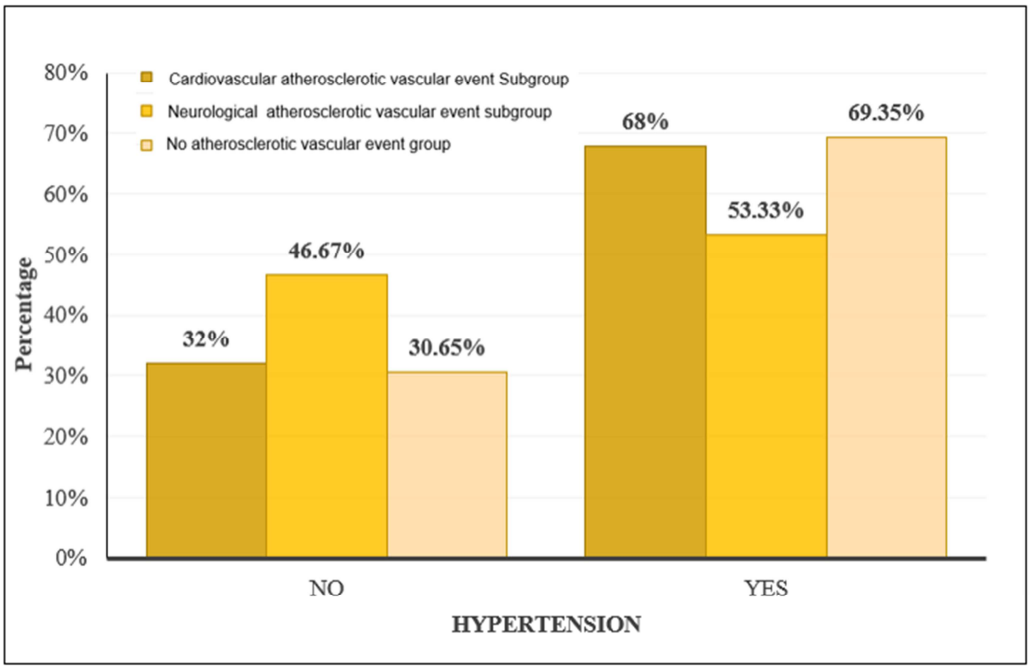
		Group-A		Group-B		
Variables	**Sub Category**	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value (Chi-square test)**
DM	No	26 (52%)	19 (63.33%)	21 (33.87%)	66 (46.48%)	**0.0183**
	Yes	24 (48%)	11 (36.67%)	41 (66.13%)	76 (53.52%)	
HTN	No	16 (32%)	14 (46.67%)	19 (30.65%)	49 (34.51%)	0.2849
	Yes	34 (68%)	16 (53.33%)	43 (69.35%)	93 (65.49%)	

In the cardiovascular atherosclerotic vascular event subgroup, 48% have DM, while 52% do not. In the neurological atherosclerotic vascular event subgroup, 36.67% have DM, and 63.33% do not. Conversely, in the no atherosclerotic vascular event group, 66.13% have DM, and 33.87% do not. Diabetes mellitus is statistically significant between the groups (p-value = 0.0183).

In the cardiovascular atherosclerotic vascular event subgroup, 68% have HTN, compared to 32% without HTN. In the neurological atherosclerotic vascular event subgroup, 53.33% have HTN, while 46.67% do not. In the no atherosclerotic vascular event subgroup, 69.35% have HTN, and 30.65% do not. There was no statistical significance noted in hypertension between the groups (p-value = 0.2849).



Graph 3: Distribution of DM between the groups.



Graph 4: Distribution of HTN between the groups.

The following table gives the comparison of lipoprotein (a) between the groups.

Table 3: Comparison of lipoprotein (a) across the groups.

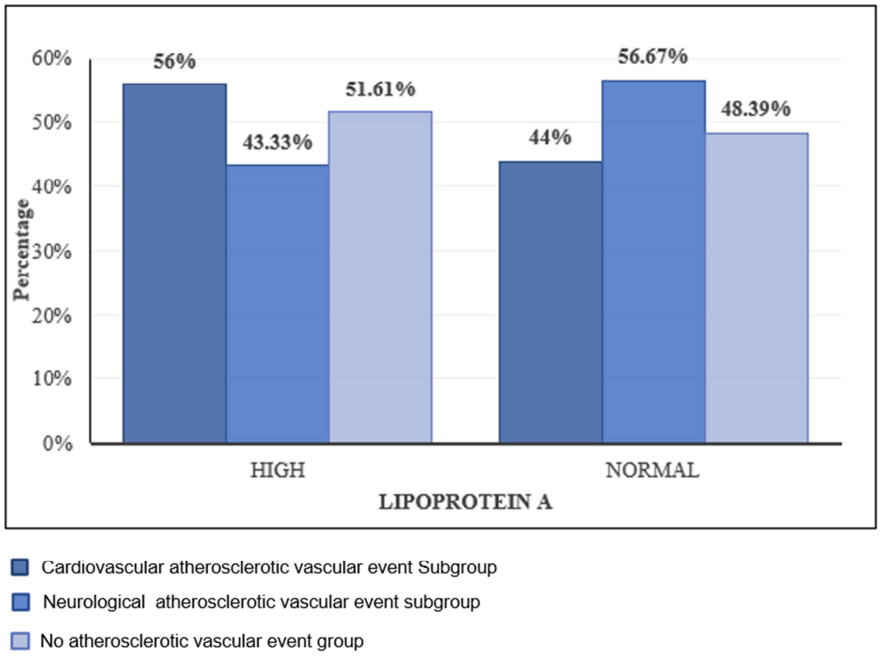
	Group-A		Group-B		
Lipoprotein (a)	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value**
High	28 (56%)	13 (43.33%)	32 (51.61%)	73 (51.41%)	0.5471
Normal	22 (44%)	17 (56.67%)	30 (48.39%)	69 (48.59%)	
Mean ± SD	55.74 ± 56.55	39.93 ± 46.42	45.67 ± 59.24	48 ± 55.77	0.2825
Median (Min, Max)	39.84 (4.24, 230)	21.35 (4.36, 210)	30 (2.44, 421.8)	30 (2.44, 421.8)	

Abbreviation: C – Chi square test, K – Kruskal Wallis test.

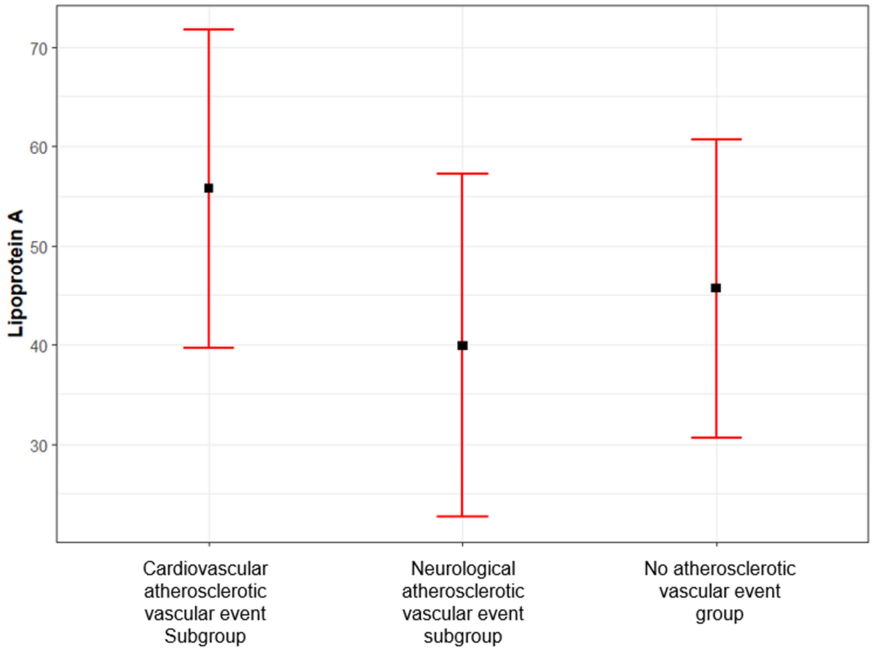
The percentage of individuals with high lipoprotein (a) levels is 56% in the cardiovascular atherosclerotic vascular event subgroup, 43.33% in the neurological atherosclerotic vascular event subgroup, and 51.61% in the no atherosclerotic vascular event group. The Chi-square test reveals no statistically significant difference in the distribution of high versus normal level of Lp(a) across the groups (p-value = 0.5471).

The mean lipoprotein (a) level for the cardiovascular atherosclerotic vascular event subgroup is 55.74 ± 56.55, with a median of 39.84 (ranging from 4.24 to 230). For the neurological atherosclerotic vascular event subgroup, the mean is 39.93 ± 46.42, with a median of 21.35 (ranging from 4.36 to 210). The no atherosclerotic vascular event group has a mean of 45.67 ± 59.24, with a median of 30 (ranging from

2.44 to 421.8). The Kruskal Wallis test indicates no statistically significant difference in the mean lipoprotein (a) levels across the groups (p-value = 0.2825).



Graph 5: Distribution of lipoprotein (a) between the groups.



Graph 6: Mean plot of lipoprotein (a) between the groups.

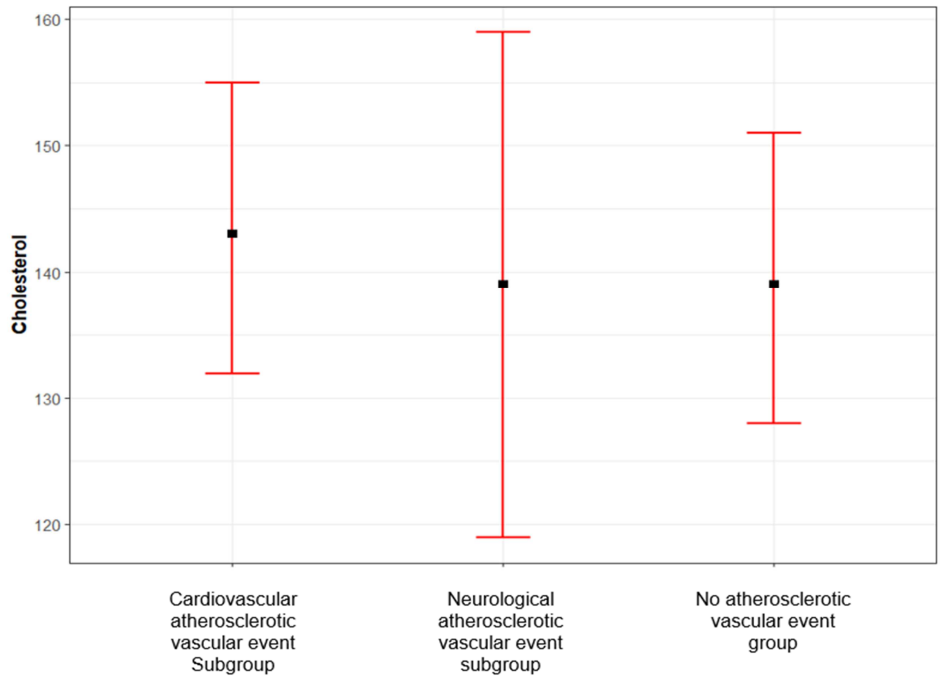
The following table gives the comparison of lipid profile between the groups.

Table 4: Comparison of lipid profile between the groups.

	Group-A		**Group-B**		
Variables	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value**
Cholesterol	143.32 ± 41.14 145.5 (75, 243)	138.97 ± 52.53 144 (54, 246)	139.34 ± 45.97 131 (53, 276)	140.66 ± 45.54 136.5 (53, 276)	0.7510
TG	133.18 ± 73.4 114.5 (55, 510)	108.87 ± 35.7 113.5 (19, 228)	140.87 ± 118.75 106.5 (51, 806)	131.4 ± 91.57 108.5 (19, 806)	0.4700
LDL	89.9 ± 51.44 81.5 (21, 336)	90.7 ± 41.87 100 (11, 174)	80.08 ± 31.64 79 (18, 168)	85.78 ± 41.7 82.5 (11, 336)	0.3188
HDL	37.42 ± 9.06 36.5 (22, 59)	38.3 ± 20.83 38.5 (10, 120)	37.84 ± 16.25 39.5 (8, 110)	37.79 ± 15.23 38.5 (8, 120)	0.9457

Abbreviation: K – Kruskal Wallis test.

No statistical significance was found in lipid profile between groups.



Graph 7: Mean plot of cholesterol between the groups.

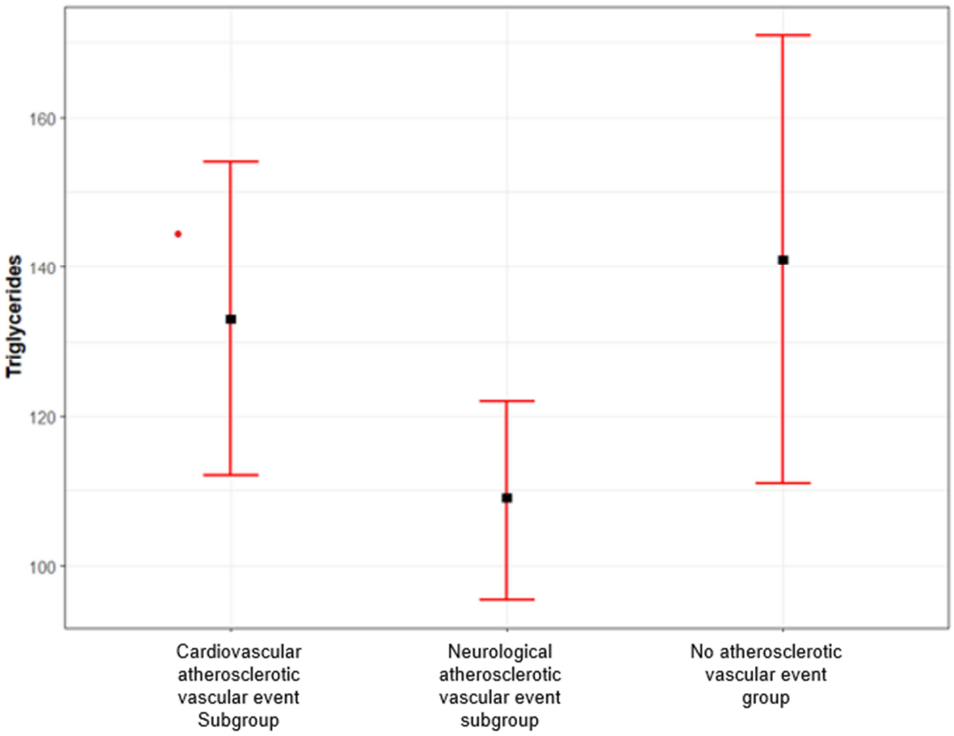
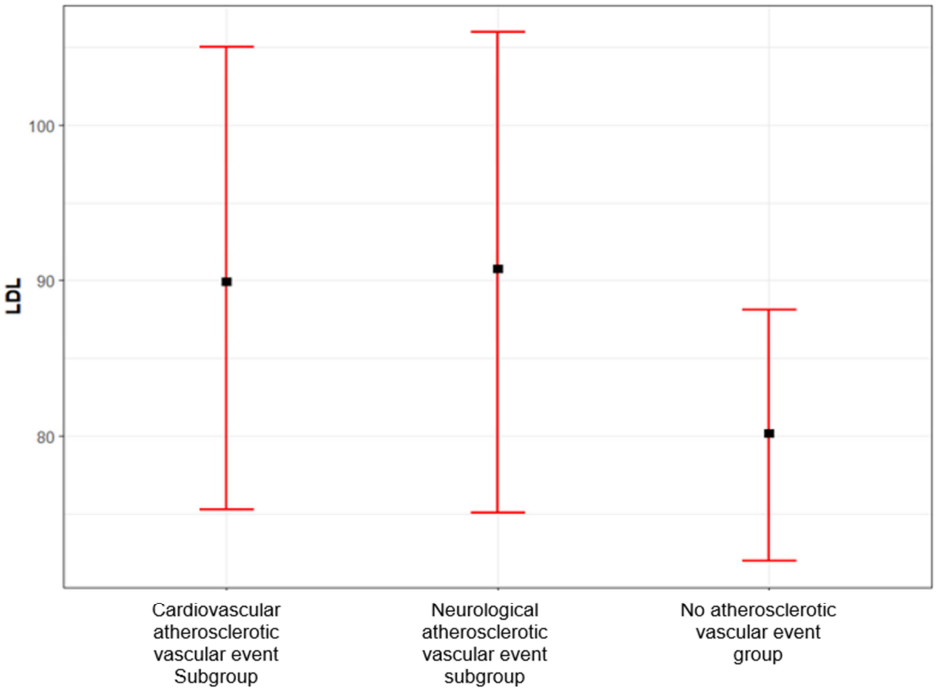
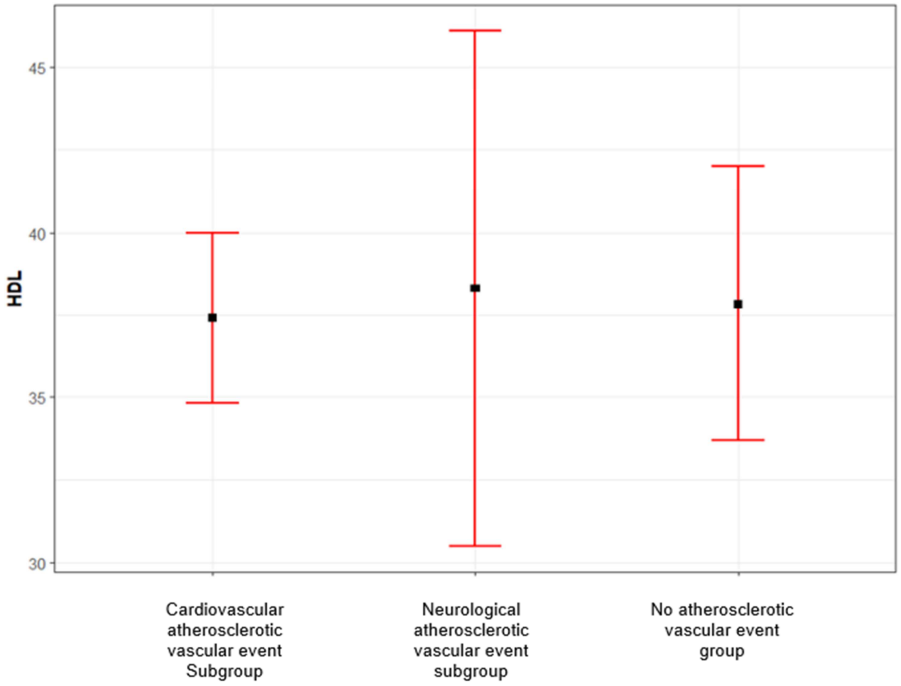


Figure 8: Mean plot of TG between the groups



Graph 9: Mean plot of LDL between the groups



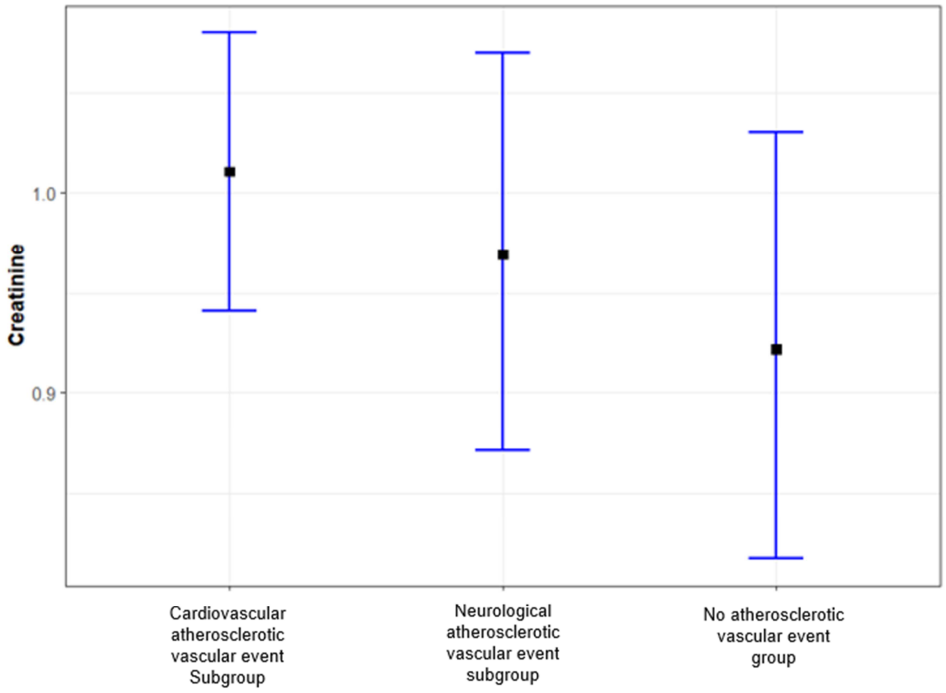
Graph 10: Mean plot of HDL between the groups

The following table gives the comparison of creatinine between the groups.

Table 5: Comparison of creatinine between the groups

	Group-A		**Group-B**		
Variable	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value (Kruskal Wallis test)**
Creatinine	1.01 ± 0.24 1.04 (0.32, 1.8)	0.97 ± 0.26 0.98 (0.54, 1.43)	0.92 ± 0.41 0.96 (0.22, 3.4)	0.96 ± 0.33 0.99 (0.22, 3.4)	**0.0202**

Individuals in the cardiovascular atherosclerotic vascular event subgroup have a mean creatinine level of 1.01 ± 0.24 mg/dL, with a median of 1.04 mg/dL and a range from 0.32 to 1.8 mg/dL. In contrast, those in the neurological atherosclerotic vascular event subgroup exhibit a mean creatinine level of 0.97 ± 0.26 mg/dL, a median of 0.98 mg/dL, and a range from 0.54 to 1.43 mg/dL. Similarly, individuals in the no atherosclerotic vascular event group show a mean creatinine level of 0.92 ± 0.41 mg/dL, a median of 0.96 mg/dL, and a range from 0.22 to 3.4 mg/dL. Kruskal Wallis test reveals a statistically significant difference in creatinine levels among the groups (p-value = 0.0202). Further, statistical significance of creatinine between no atherosclerotic vascular event group was found and the cardiovascular atherosclerotic vascular event subgroup (p-value = 0.0190).



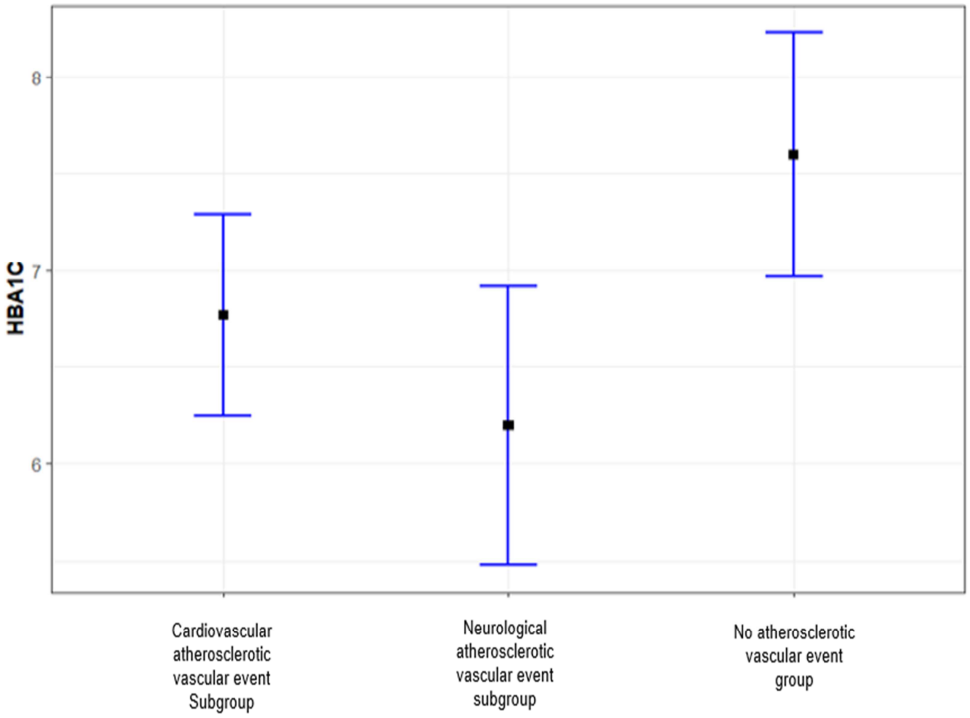
Graph 11: Mean plot of creatinine between the groups

The following table gives the comparison of HBA1C between the groups

Table 6: Comparison of HBA1C between the Group-A and Group-B

	Group-A		**Group-B**		
Variable	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value (Kruskal Wallis test)**
HBA1C	6.77 ± 1.84 6 (4.6, 10.9)	6.2 ± 1.93 5.5 (4.3, 12.5)	7.6 ± 2.47 7 (4.5, 15)	7.01 ± 2.21 6.3 (4.3, 15)	**0.0027**

individuals with cardiovascular atherosclerotic vascular events have a mean HBA1C level of 6.77 ± 1.84%, with a median of 6% and a range from 4.6 to 10.9%. Those with neurological atherosclerotic vascular events exhibit a mean HBA1C level of 6.2 ± 1.93%, a median of 5.5%, and a range from 4.3 to 12.5%. Conversely, individuals without atherosclerotic vascular events have a higher mean HBA1C level of 7.6 ± 2.47%, with a median of 7% and a range from 4.5 to 15%. Kruskal Wallis test reveals a statistically significant difference in HBA1C levels among the groups (p-value = 0.0027). Further from Dunn test, it is observed that there is significant difference in distribution of HBA1C between no atherosclerotic vascular event group and the Neurological atherosclerotic vascular event subgroup (p-value = 0.0022).



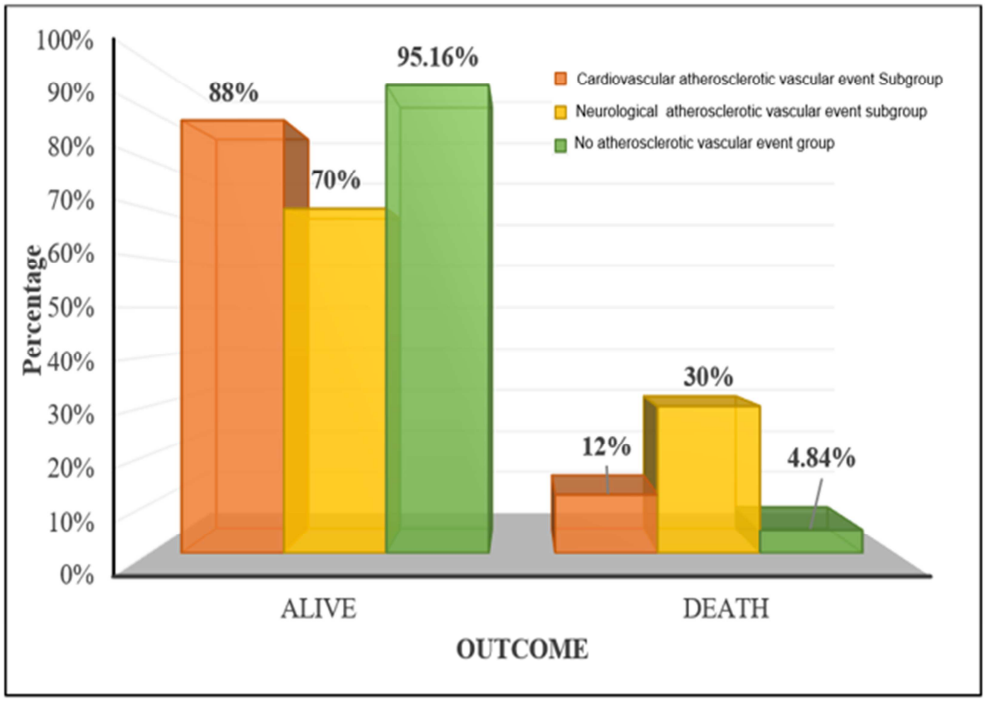
Graph 12: Mean plot of HBA1C between the groups

The following table gives the comparison of outcome between the groups

Table 7: Comparison of outcome between the groups

	Group-A		**Group-B**		
Outcome of patient	**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value (Chi square test)**
Alive	44 (88%)	21 (70%)	59 (95.16%)	124 (87.32%)	**0.0025**
Death	6 (12%)	9 (30%)	3 (4.84%)	18 (12.68%)	

In the cardiovascular atherosclerotic vascular event subgroup, 88% of patients are reported as alive, contrasting with 12% who have deceased. The neurological atherosclerotic vascular event subgroup shows 70% of patients alive, with a higher mortality rate of 30%. Remarkably, the no atherosclerotic vascular event group exhibits a substantially higher survival rate, with 95.16% of patients alive and only 4.84% having succumbed. From Chi square test, it is observed that there is a significant difference in the distribution of outcome of patients over groups (p-value = 0.0025).



Graph 13: Distribution of outcome between the group

The following table gives the comparison of addictions between the groups

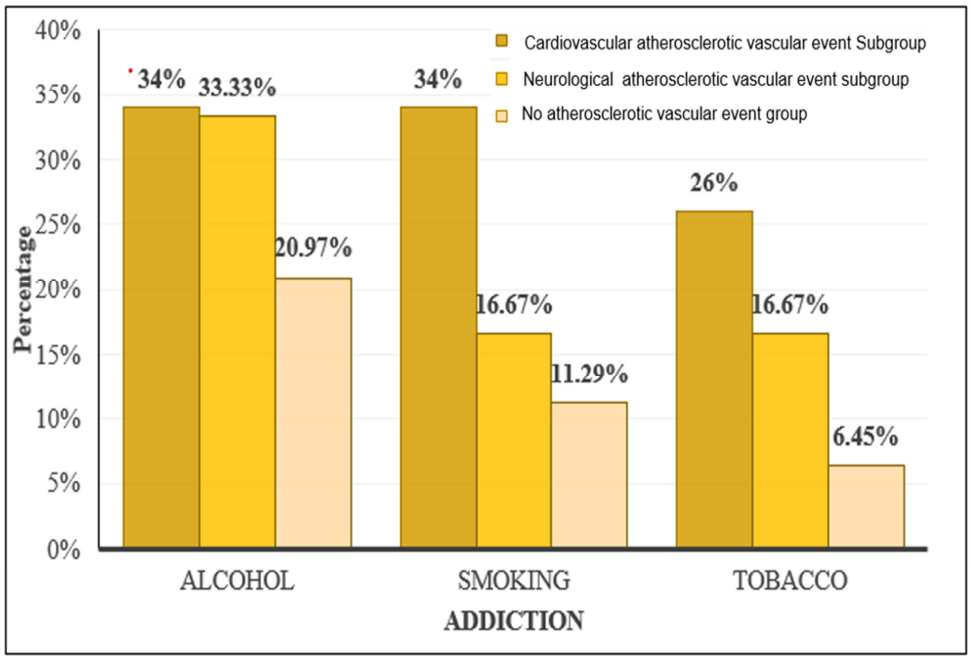
Table 8: Comparison of addictions between the groups

		Group-A		Group-B		
Addictions		**Cardiovascular atherosclerotic vascular event Subgroup**	**Neurological atherosclerotic vascular event subgroup**	**No atherosclerotic vascular event group**	**Total**	**p-value**
Alcohol	No	33 (66%)	20 (66.67%)	49 (79.03%)	102 (71.83%)	0.2436
	Yes	17 (34%)	10 (33.33%)	13 (20.97%)	40 (28.17%)	
Smoking	No	33 (66%)	25 (83.33%)	55 (88.71%)	113 (79.58%)	**0.0105**
	Yes	17 (34%)	5 (16.67%)	7 (11.29%)	29 (20.42%)	
Tobacco	No	37 (74%)	25 (83.33%)	58 (93.55%)	120 (84.51%)	**0.0190**
	Yes	13 (26%)	5 (16.67%)	4 (6.45%)	22 (15.49%)	
Anyone addiction	No	14 (28%)	16 (53.33%)	46 (74.19%)	76 (53.52%)	**< 0.001**
	Yes	36 (72%)	14 (46.67%)	16 (25.81%)	66 (46.48%)	

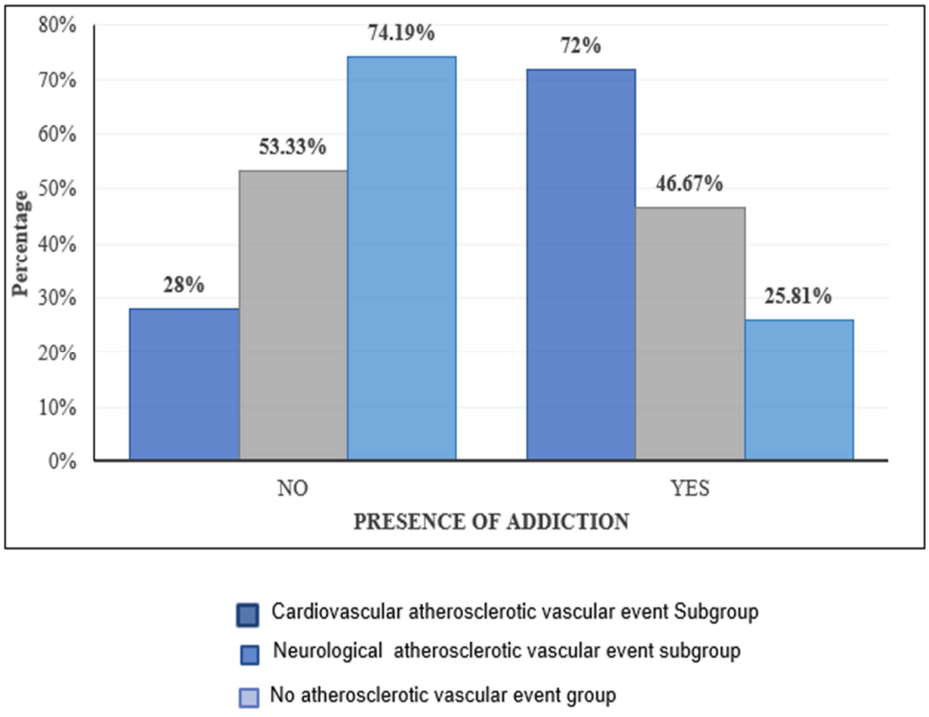
Abbreviation: C – Chi square test, MC – Chi square test with Monte Carlo simulation

From Chi square test, it is observed that, there is no statistically significant difference in alcohol consumption among the groups (p-value = 0.2436). A statistically significant difference is observed in smoking habits among the groups (p-value = 0.0105). Notably, fewer individuals with neurological atherosclerotic vascular events (16.67%) and no atherosclerotic vascular events (11.29%) report smoking compared to those with cardiovascular atherosclerotic vascular events (34%). Similarly, there is a significant difference in tobacco use among the groups (p-value = 0.0190). Individuals with cardiovascular atherosclerotic vascular events (26%) exhibit higher rates of tobacco use compared to those with neurological atherosclerotic vascular events (16.67%) and no atherosclerotic vascular events (6.45%).

Individuals with cardiovascular atherosclerotic vascular events (72%) have a higher prevalence of any addiction compared to those with neurological atherosclerotic vascular events (46.67%) and no atherosclerotic vascular events (25.81%). Hence, it is observed that, there is a significant difference in the presence of any addiction among the groups (p-value < 0.001).



Graph 14: Distribution of different addiction between the groups



Graph 15: Distribution of presence of addiction between the groups

The following table gives the correlation of blood profile with lipoprotein (a) in different groups.

Table 9: Correlation of blood profile with lipoprotein (a) in different groups.

	Group-A		**Group-B**			
Variables	**Cardiovascular atherosclerotic vascular event Subgroup**		**Neurological atherosclerotic vascular event subgroup**		**No atherosclerotic vascular event group**	
	Correlation coefficient	**p-value ^{SP}**	**Correlation coefficient**	**p-value ^{SP}**	**Correlation coefficient**	**p-value ^{SP}**
Cholesterol	0.1185	0.4123	0.3519	0.0565	0.1880	0.1434
TG	0.1884	0.1902	0.1225	0.5188	-0.1496	0.2457
LDL	0.1923	0.1809	0.2967	0.1114	0.2024	0.1146
HDL	-0.0681	0.6382	0.3167	0.0882	0.3337	**0.0080**
Creatinine	0.2219	0.1214	-0.0198	0.9172	-0.1995	0.1200
HBA1C	0.0004	0.9980	0.0459	0.8093	-0.3051	**0.0159**

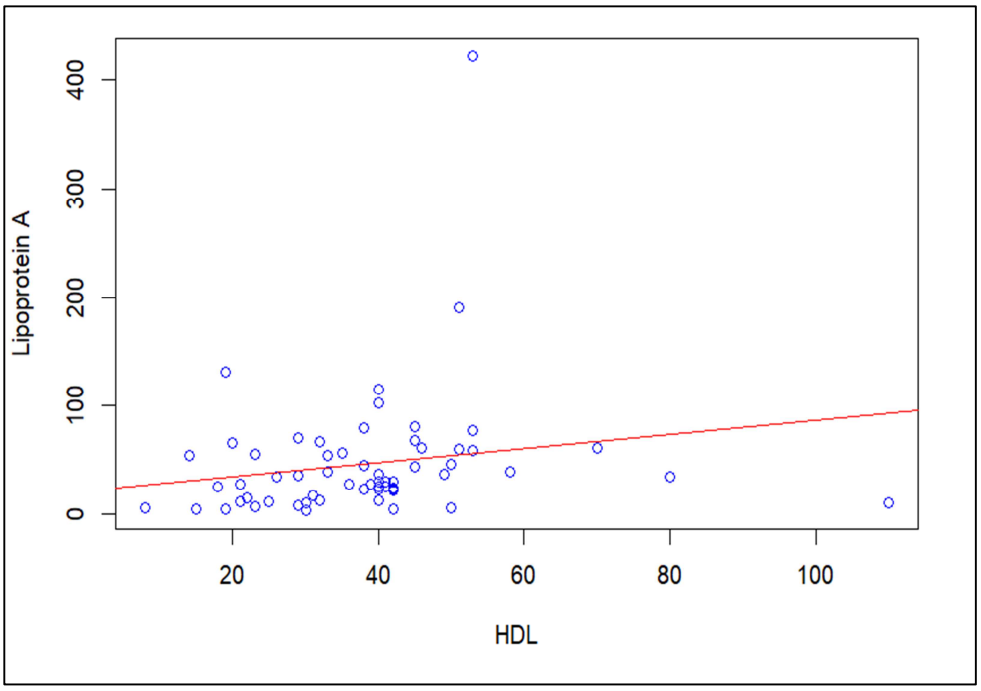
Abbreviation: SP – Spearman's rank correlation coefficient

For individuals experiencing cardiovascular atherosclerotic vascular events, there are weak positive correlations between cholesterol, TG, LDL, and creatinine

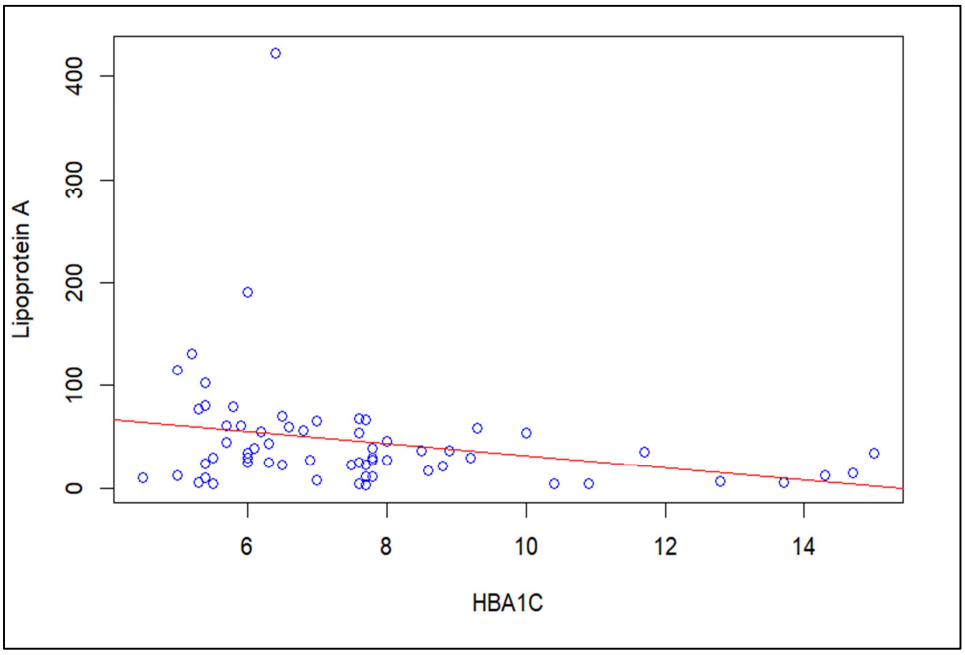
levels with lipoprotein (a) levels, but none are statistically significant. HDL levels show a weak negative correlation with lipoprotein (a) levels, but it is not significant. HBA1C levels demonstrate an extremely weak positive correlation with lipoprotein(a) levels, which is not significant.

In the neurological atherosclerotic vascular event subgroup, there is a weak positive correlation between cholesterol levels and lipoprotein (a) levels, but it is not significant. TG and LDL levels also exhibit weak positive correlations with lipoprotein(a) levels, but again, they are not significant. HDL levels show a positive correlation with lipoprotein (a) levels, which is not statistically significant. There is no significant correlation between creatinine or HBA1C levels and lipoprotein (a) levels in this group.

In the group without atherosclerotic vascular events, there are weak positive correlations between cholesterol and LDL levels with lipoprotein (a) levels, but they are not statistically significant. TG and Creatinine levels demonstrate a weak negative correlation with lipoprotein (a) levels, but it is not significant. HDL levels show a strong positive correlation with lipoprotein (a) levels, which is statistically significant (p-value = 0.0080). HBA1C levels have a weak negative correlation with lipoprotein (a) levels, which is statistically significant (p-value = 0.0159).



Graph 16: Scatter plot of HDL with lipoprotein (a).



Graph 17: Scatter plot of HBA1C with lipoprotein (a).

The following table gives the comparison of lipoprotein (a) over comorbidities in different groups.

Table 10: Comparison of lipoprotein (a) over comorbidities in different groups.

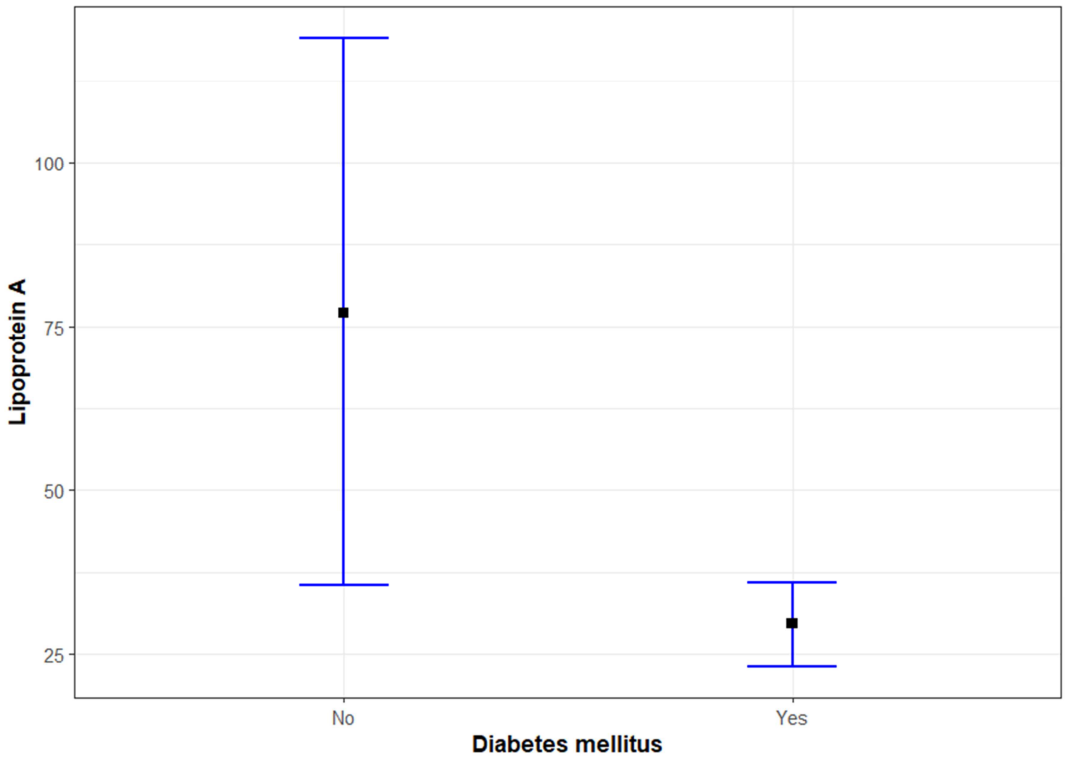
Variables		Group-A				Group-B	
		Cardiovascular atherosclerotic vascular event Subgroup		Neurological atherosclerotic vascular event subgroup		No atherosclerotic vascular event group	
		Mean ± SD Median (Min, Max)	p-value	Mean ± SD Median (Min, Max)	p-value	Mean ± SD Median (Min, Max)	p-value
DM	No	57 ± 59.87 35.5 (7.59, 230)	0.9999	30.09 ± 25.98 18 (4.36, 78)	0.3011	77.1 ± 91.25 59 (4.07, 421.8)	**0.0035**
	Yes	54.38 ± 53.97 44 (4.24, 223)		56.93 ± 67.32 24.2 (5, 210)		29.57 ± 20.12 26.7 (2.44, 78.8)	
HTN	No	65.84 ± 73.8 35.84 (4.24, 230)	0.9337	38.82 ± 53.38 17 (4.36, 210)	0.6029	72.35 ± 96.88 35.5 (4.6, 421.8)	0.1039
	Yes	50.99 ± 46.9 40 (6, 223)		40.9 ± 41.16 27.1 (5, 159)		33.88 ± 24.71 27 (2.44, 102)	

Abbreviation: MW – Mann Whitney U test,

From Mann Whitney U test, it is observed that there is a statistically significant difference in lipoprotein (a) levels between those with and without DM in

the no atherosclerotic vascular event group (p-value = 0.0035). However, no significant differences are observed in the cardiovascular atherosclerotic vascular event and neurological atherosclerotic vascular event subgroups.

No significant differences are found in lipoprotein (a) levels between individuals with and without HTN across all three groups.



Graph 18: Mean plot of lipoprotein (a) over diabetes mellitus in No atherosclerotic event group.

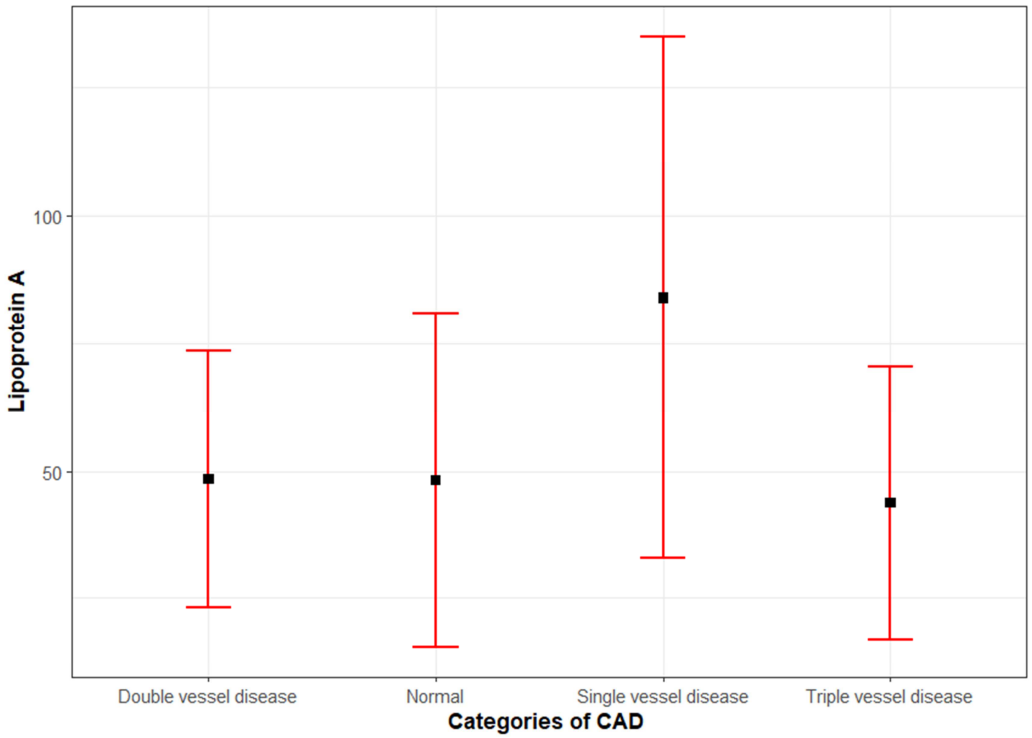
The following table gives the comparison of lipoprotein (a) over categories of CAD in cardiovascular atherosclerotic vascular event subgroup.

Table11: Comparison of lipoprotein (a) over subgroups of CAD in cardiovascular atherosclerotic vascular event subgroup.

CAD	Mean ± SD	Median (Min, Max)	p-value
Single vessel disease	83.83 ± 80.14	58.5 (6.00, 230.0)	0.6199
Double vessel disease	48.35 ± 50.53	36.34 (27.06, 4.24)	
Triple vessel disease	43.72 ± 41.96	25.35 (8.04, 147)	
Normal	48.27 ± 38.95	35.25 (10, 100)	

Abbreviation: K – Kruskal Wallis test.

Individuals with single vessel disease have a mean lipoprotein (a) level of 83.83 ± 80.14, those with double vessel disease have a mean lipoprotein(a) level of 48.35 ± 50.53, and those with triple vessel disease have a mean lipoprotein (a) level of 43.72 ± 41.96. Additionally, individuals with normal coronary arteries exhibit a mean lipoprotein (a) level of 48.27 ± 38.95. From Kruskal Wallis test, it is observed that, there is no statistically significant differences in lipoprotein (a) levels among the different categories of CAD (p-value = 0.6199).



Graph 19: Mean plot of lipoprotein (a) over categories of CAD in cardiovascular atherosclerotic vascular event group.

The following table gives the comparison of lipoprotein(a) over comorbidities in different groups.

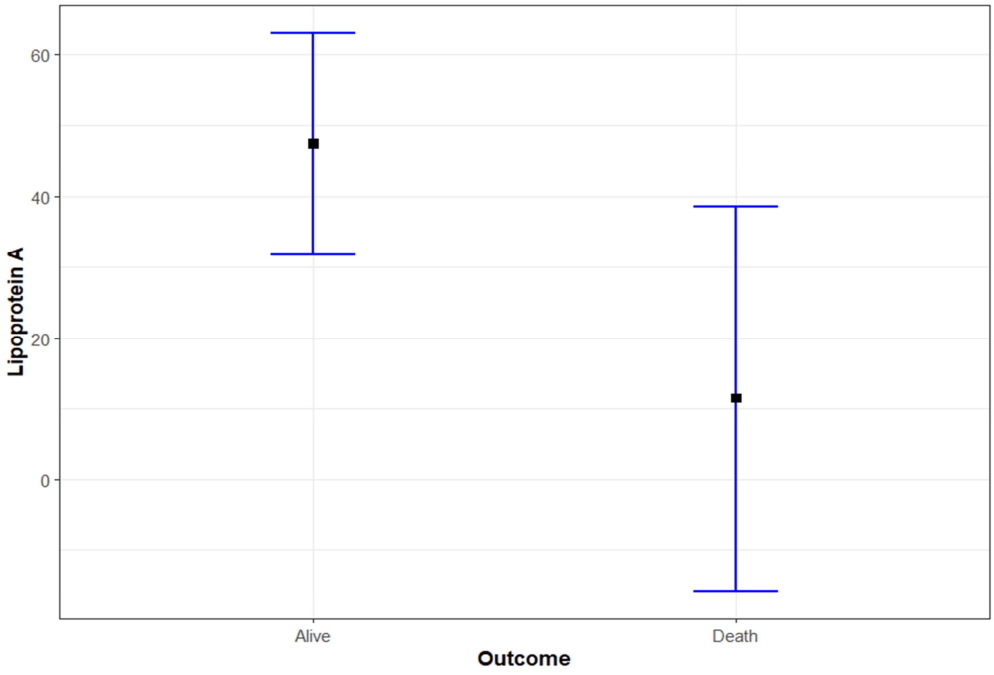
Table 12: Comparison of lipoprotein (a) over comorbidities in different groups.

	Group-A				**Group-B**	
Outcome	**Cardiovascular atherosclerotic vascular event Subgroup**		**Neurological atherosclerotic vascular event subgroup**		**No atherosclerotic vascular event group**	
	Mean ± SD **Median (Min, Max)**	**p-value**	**Mean ± SD** **Median (Min, Max)**	**p-value**	**Mean ± SD** **Median (Min, Max)**	**p-value**
Alive	58.06 ± 58.67 39.84 (4.24, 230)	0.3948	43.19 ± 53.47 18.5 (5, 210)	0.8208	47.41 ± 60.19 33.6 (2.44, 421.8)	**0.0454**
Dead	38.74 ± 36.63 31 (7.59, 100)		32.33 ± 23.86 30 (4.36, 60.1)		11.4 ± 10.92 5.6 (4.6, 24)	

Abbreviation: MW – Mann Whitney U test,

In No atherosclerotic vascular event group, individuals who are alive exhibit a notably higher mean lipoprotein (a) level of 47.41 ± 60.19 compared to those who have deceased, with a mean level of 11.4 ± 10.92. Further from Mann Whitney U test, it is observed that, there is a statistically significant difference in lipoprotein (a) levels

between individuals who are alive and those who have deceased (p-value = 0.0454). Conversely, in the neurological atherosclerotic vascular event subgroup and the Cardiovascular atherosclerotic vascular event subgroup, there are no significant differences in lipoprotein (a) levels between individuals who are alive and those who are deceased (p-values = 0.8208 and 0.3948, respectively).



Graph 20: Mean plot of lipoprotein (a) over outcome in No atherosclerotic vascular event group.

The following table gives the comparison of lipoprotein (a) over gender in different groups.

Table 13: Comparison of lipoprotein (a) over gender in different groups.

	Group-A				**Group-B**	
Gender	**Cardiovascular atherosclerotic vascular event Subgroup**		**Neurological atherosclerotic vascular event subgroup**		**No atherosclerotic vascular event group**	
	Mean ± SD **Median (Min, Max)**	**p-value**	**Mean ± SD** **Median (Min, Max)**	**p-value**	**Mean ± SD** **Median (Min, Max)**	**p-value**
Female	67.11 ± 76.15 36.5 (8.67, 223)	0.7504	32.94 ± 23.23 41 (5, 60)	0.9113	59.36 ± 79.67 36 (2.44, 421.8)	0.0931
Male	52.16 ± 49.55 39.84 (4.24, 230)		41.33 ± 50.01 18.5 (4.36, 210)		33.63 ± 28.58 27 (4.07, 130)	

Abbreviation: MW – Mann Whitney U test.

From Mann Whitney U test, it is observed that, there are no significant differences in lipoprotein (a) levels between females and males in any of the groups (p-values > 0.05).

DISCUSSION

Our study involves comparison of different groups including cardiovascular atherosclerotic vascular event subgroup, neurological atherosclerotic vascular event group and control group. The mean Lp(a) in our study was 48 ± 55.76 and median Lp(a) was 30 mg/ dL. Median Lipoprotein(a) in a meta-analysis conducted in Austria was 11 mg/ dL which was low-to-normal value (72).

Lp(a) was found to be a more reliable indicator of future ASCVD occurrences in individuals without prior ASCVD over a follow-up of eleven years than in patients with prior ASCVD in the sizable UK Biobank cohort. There were similar absolute risk differences of 1.8% and 1.7%, for those individuals without prior ASCVD and those with prior ASVD. Nevertheless, risks between greater and lower primary preventive groups were not compared in this study (73).

Furthermore, among over eight thousand participants from the general population in Denmark, with up to seventeen years of follow-up, 23% ($P < 0.001$) of myocardial infarction events and 12% ($P < 0.001$) of chronic heart disease events were correctly reclassified when Lp(a) levels were ≥80th percentile (≥47 mg/dL). The multivariable HRs for MI and CHD were 2.0 (95% CI: 1.5–2.7) and 1.5 (95% CI: 1.3–1.8), respectively, when compared to those with lower plasma lipoprotein (a) levels (74).

In conclusion, the BiomarCaRE (Biomarkers for Cardiovascular Risk Assessment in Europe) project, which involved over fifty six thousand participants from seven prospective study groups across Europe, found that participants at the

≥90th percentile for Lp(a) (43.5 mg/dL) had the highest rates of major cardiovascular and coronary events over a nine year follow-up. (75).

Risk persists in individuals with elevated serum Lipoprotein(a) despite high-intensity statin treatment, according to data collected in the FOURIER (Further Cardiovascular Outcomes Research with PCSK9 [proprotein convertase subtilisin/kexin 9] Inhibition in Subjects with Elevated Risk) as well as ODYSSEY Outcomes (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment with Alirocumab) trials (76, 77).

Research indicates that Lp(a) predicts ASCVD in participants of the same race or ethnicity as well as in females relative to males (73, 78). Our study showed similar results. In our study, gender was significantly associated with occurrence of atherosclerotic vascular events and no atherosclerotic vascular events (p=0.0044). It revealed that while comparing White, South Asian, and Black participants, as well as female and male participants in the "Emerging Risk Factors collaboration", there was a similarity in the strength of association of serum Lipoprotein (a) in predicting ASCVD events across race or ethnicity (79). While ≥50 mg/dL may be more appropriate for White and Hispanic individuals, it has been suggested that a Lipoprotein(a) cutoff point of more than or equal to 30 mg/dL should be used for Black individuals to identify increased risk (80). Nevertheless, other studies have suggested that varying thresholds should not be used because the proportional risk of elevated Lp(a) does not vary considerably across race or ethnicity (81).

According to a study, those with DM who had Lp(a) levels at or above the 90th percentile have a roughly two-fold higher risk of ASCVD events. This suggests that Lp(a) is a particularly good predictor of cardiovascular atherosclerotic vascular

events risk in this population which is contrary to our study (78). In our study, diabetes mellitus was significantly associated between the groups, that is, between the atherosclerotic vascular events (cardiovascular and neurological) and no atherosclerotic vascular events group (p=0.0183).

Patients on statin therapy and having elevated lipoprotein(a) concentrations—mostly those with values >50 mg/dL—have a markedly increased risk of cardiovascular disease, according to a meta-analysis of Lp(a) and ASVD. Conventional cardiovascular disease risk variables have little bearing on the connection with cardiovascular events. Very weak or null cross-sectional associations between lipoprotein(a) and various risk variables supported this observation even more. Significantly, the hazard ratio for high lipoprotein(a) at baseline and while taking statins were similar in size, indicating that statin therapy may not significantly alter lipoprotein(a)-mediated risk in people with elevated lipoprotein(a) levels. All things considered, these datas imply that even while taking statins, patients with elevated lipoprotein(a) concentrations roughly 25% of those with a history of cardiovascular disease or a recommendation for statins remain significantly at risk (72).

Our study did not show any association between stroke and Lp(a) levels. Despite conflicting findings, lipoprotein (a) was thought to be a risk factor for ischemic stroke. A higher risk of ischemic stroke was linked to raised Lp(a) levels, according to a meta-analysis (82). According to a Mendelian randomization research, a 1-SD genetically reduced Lp(a) level was linked to a 13% decreased risk of stroke (83). According to recent research, Lp(a) may have distinct functions in various stroke subtypes. Large artery atherosclerosis (LAA) stroke was found to have substantially

higher Lp(a) levels than the other four subtypes, and elevated Lp(a) levels were linked to a significant burden of intracranial and extracranial vascular steno-occlusive lesions, according to a prospective stroke registry study conducted in Korea (84). Furthermore, higher Lp(a) levels may increase the chances of occurrence of large vessel stroke but lower the risk of small vessel stroke, according to a Mendelian randomization analysis based on data from a large-scale GWAS investigation (85).

An independent risk factor for ischemic stroke was discovered to be elevated Lp(a) in a recent meta-analysis included 90,904 individuals and 5029 stroke occurrences (59). There has been little research done on the relationship between Lp(a) concentrations and the risk of a particular ischemic stroke etiological subtype.

The work adds evidence of the causative relationship between genetic predicted Lp(a) concentrations and the risk of ischemic stroke and its subtypes using MR analysis. Higher Lp(a) concentrations may raise the risk of large artery stroke while lowering the risk of small vessel stroke. This could also help in explaining the inconsistent findings from earlier research. The unique correlation between Lp(a) and both large artery stroke (positive association) and small vessel stroke (inverse association) may lead to inconsistent findings when all ischemic stroke subtypes are examined collectively in prior research (85).

High levels of Lp(a) may be an independent predictor of an increased risk of stroke, mortality from vascular disease and death from all causes in men, but not in women, according to the analysis of a sizable research in elderly Americans. Our results offer fresh, pertinent evidence of risk in older males as well as thorough details on the binary relationship between sex and Lp(a). The significance of Lipoprotein(a) in the prognosis of vascular disease in older adults, a population for whom the validity

of several conventional risk factors has been questioned and is clarified by this prospective study. This study discovered a strong correlation between Lipoprotein(a) and atherosclerotic vascular events in men, with a risk magnitude that was comparable to that observed in young individuals in earlier investigations (66).

Lp(a) has been linked to atherogenic, thrombogenic, vascular inflammatory, and antifibrinolytic properties. It is composed of the glycoprotein Apo(a) and the LDL-like core lipoprotein. Due to its structural homology with plasminogen and resemblance to LDL, lipoprotein (a) stimulates atherosclerotic stenosis and the ischemic vascular events that follow (86). A higher serum Lp(a) is associated with a higher risk of carotid plaque burden and progression, according to a different previously published study that also demonstrated a steady increase in Lp(a) level with the amount of intracranial major artery stenoses (87, 88). A study confirms that the enhanced Lp(a) that was anticipated by genetics was only linked to a higher risk of LAS.

In the cardiovascular atherosclerotic vascular event subgroup, 88% of patients are reported as alive, contrasting with 12% who have deceased. The neurological atherosclerotic vascular event subgroup shows 70% of patients alive, with a higher mortality rate of 30%. Remarkably, the no atherosclerotic vascular event group exhibits a substantially higher survival rate, with 95.16% of patients alive and only 4.84% succumbed. From Chi square test, it is observed that there is a significant difference in the distribution of outcome of patients over groups ($p=0.0025$). Berman AN et al showed 21% increased hazard of MACE (major adverse cardiovascular events) with increasing Lp(a). Myocardial infarction, coronary revascularization, ischemic stroke, and cardiovascular death were significantly associated among

individuals with history of ASCVD. Higher Lp(a) had increased risk of cardiovascular death ($p<0.001$). Higher Lp(a) is also had higher risk of development of ischemic stroke ($p=0.016$) (89).

Higher Lp(a) level was significantly associated with hyperlipidemia ($p<0.001$). Median values of HDL, LDL, TG and TC were 46 (37-56.5), 97 (74-123.5), 173 (145-203.3), and 115 (81-166) respectively. These were statistically significant between ASCVD and non-ASCVD groups (89). In our study, TC, TG, LDL and HDL mean values were 140.66 ± 45.54, 131.4 ± 91.57, 85.78 ± 41.7 and 37.79 ± 15.23 respectively. There was no statistical significance among lipid profile and the groups in our study. Similar results were found in a comparative study. (90).

Serum Lp(a) is largely stable throughout an individual's life and is determined by genetics. Modifications in lifestyle and traditional lipid-lowering treatments don't seem to be able to lower elevated Lp(a) levels. It has been established that inflammation and oxidative stress are key factors in the development of atherosclerosis and thrombosis (89).

There are various limitations in our study. Lesser sample size was included in the study. Follow-up data of the study participants were not available. One important strength of this study is, it included a control group and compared the results with the other two groups.

LIMITATIONS

1. Lesser sample size was included in the study.
2. Our study was a cross-sectional study, not a prospective study and hence no follow up of study participants were done
3. Single center study

CONCLUSION

- In our study we reported a high lipoprotein (a) in 51.4% study participants. High lipoprotein (a) levels were seen in 56% study participants in cardiovascular atherosclerotic event subgroup, 43.33% study participants in neurological atherosclerotic vascular event subgroup and 51.61% in no atherosclerotic event group.
- Our study demonstrated that a higher serum lipoprotein (a) is not associated with higher risk of development of atherosclerotic vascular events in elderly.
- Our study we also noted :
    1. In the no atherosclerotic vascular event group HDL level showed a strong postive correlation with lipoprotein (a) levels and also a weak negative correlation between HBA1C and lipoprotein(a) levels.
    2. Statistically significant correlation of lipoprotein (a) levels and prevalence of diabetes in no atherosclerotic vascular event group.
    3. In the no atherosclerotic vascular event group the indivduals who were alive exhibit a notably high lipoprotein a levels, and this correlation was statistically significant. This also supports our study that high lipoprotein (a) levels are not asscociated with higher risk of atherosclerotic vascular events in elderly (age >65years).
- Therefore our study concludes that Lipoprotein (a) may not be used to infer any clinical significance nor may have a role to play as a risk factor for atherosclerotic vascular events in elderly (age >65 years)

SUMMARY

In our study we aimed to estimate and correlate the clinical significance of lipoprotein (a) as a risk factor of atherosclerotic vascular events in elderly in a yearlong cross-sectional study in a tertiary care centre in Karnataka.

142 study participants included in the study were divided into 2 groups atherosclerotic vascular event group (include 2 subgroups Cardiovascular Atherosclerotic vascular event subgroup and Neurological atherosclerotic vascular event subgroup) and no atherosclerotic vascular event group. We excluded those with active infections, neoplasia, renal dysfunction, hepatic dysfunctions.

Detailed history and examination were done on the day of enrolment into the study. Fasting Blood sample was withdrawn from each study participant for serum lipoprotein (a), serum HDL, LDL, total cholesterol, triglycerides, HBA1C, creatinine.

A total of 142 study participants were included in the study. Majority of study participants were male (n=96, 67.6%). The mean age of the study participants was 71.63 years.

The following study variables like age, gender, comorbidities, addictions, mortality, serum lipoprotein (a), serum HDL, LDL, total cholesterol, triglycerides, HBA1C, creatinine were compared across the study groups and also serum lipoprotein (a) was correlated and compared with all the other study variables. The lipoprotein (a) level in the cardiovascular atherosclerotic event subgroup was also compared and correlated with the types of coronary artery disease on coronary angiography.

A high lipoprotein (a) in 51.4% study participants. High lipoprotein (a) levels were seen in 56% study participants in cardiovascular atherosclerotic vascular event subgroup, 43.33% study participants in neurological atherosclerotic vascular event subgroup and 51.61% in no atherosclerotic vascular event group .

Our study demonstrated that a higher levels of lipoprotein (a) may not be associated with higher risk of development of atheroclerotic vascular events in elderly.

Our study also noted:

1. In the no atherosclerotic event group HDL level showed a strong postive correlation with lipoprotein (a) levels and also a weak negative correlation between HBA1C and lipoprotein(a) levels.
2. Statistically significant correlation of lipoprotein (a) levels and prevalence of diabetes in no athreosclerotic event group.
3. In the no atherosclerotic vascular event group the indivduals who were alive exhibit a notably high lipoprotein a levels and this correlation was statistically significant. This also supports our study that high lipoprotein (a) levels may not be asscociated with higher risk of atherosclerotic vascular events in elderly (age >65years).

Therefore our study concludes that Lipoprotein (a) may not infer any clinical significance nor may not have any role to play as a risk factor for atherosclerotic vascular events in elderly (age >65 years).

BIBLIOGRAPHY

1. Schmidt K, Noureen A, Kronenberg F, Utermann G. Structure, function, and genetics of lipoprotein (a). Journal of Lipid Research. 2016 Apr 13;57(8):1339–59.
2. Utermann G, Menzel HJ, Kraft HG, Duba HC, Kemmler HG, Seitz C. Lp(a) glycoprotein phenotypes. Inheritance and relation to Lp(a)-lipoprotein concentrations in plasma. Journal of Clinical Investigation. 1987 Aug 1;80(2):458–65.
3. Maranhão RC, Carvalho PO, Strunz CC, Pileggi F. Lipoprotein (a): Structure, Pathophysiology and Clinical Implications. Arquivos Brasileiros de Cardiologia [Internet]. 2014 Jul 1;103(1):76–84. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126764/
4. Klausen IC, Sjøl A, Hansen PS, Gerdes LU, Møller L, Lemming L, et al. Apolipoprotein(a) isoforms and coronary heart disease in men: a nested case-control study. Atherosclerosis [Internet]. 1997 Jul 11;132(1):77–84. Available from: https://pubmed.ncbi.nlm.nih.gov/9247362/
5. Farzam K, Senthilkumaran S. Lipoprotein A [Internet]. PubMed. Treasure Island (FL): StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK570621/
6. Scipione CA, Koschinsky ML, Boffa MB. Lipoprotein(a) in clinical practice: New perspectives from basic and translational science. Critical Reviews in Clinical Laboratory Sciences [Internet]. 2018 Jan 1;55(1):33–54. Available from: https://pubmed.ncbi.nlm.nih.gov/29262744/

7. Nordestgaard BG, Chapman MJ, Ray K, Borén J, Andreotti F, Watts GF, et al. Lipoprotein(a) as a cardiovascular risk factor: current status. European Heart Journal [Internet]. 2010 Dec 1;31(23):2844–53. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295201/
8. Tsimikas S, Brilakis ES, Miller ER, McConnell JP, Lennon RJ, Kornman KS, et al. Oxidized Phospholipids, Lp(a) Lipoprotein, and Coronary Artery Disease. New England Journal of Medicine. 2005 Jul 7;353(1):46–57.
9. Wilson DP, Jacobson TA, Jones PH, Koschinsky ML, McNeal CJ, Nordestgaard BG, et al. Use of Lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. Journal of Clinical Lipidology [Internet]. 2019 May;13(3):374–92. Available from: https://www.lipid.org/sites/default/files/files/Use%20of%20lipoprotein(a)%20in%20clinical%20practice(1).pdf
10. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ ASPC/ NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary. Journal of the American College of Cardiology. 2019 Jun;73(24):3168–209.
11. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the Management of dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk. European Heart Journal [Internet]. 2019 Aug 31;41(1). Available from: https://academic.oup.com/eurheartj/article/41/1/111/5556353

12. None eClinicalMedicine. The rising global burden of stroke. EClinicalMedicine. 2023 May 1;59:102028–8.
13. Kamalakannan S, Gudlavalleti AashraiSV, Gudlavalleti VenkataSM, Goenka S, Kuper H. Incidence & prevalence of stroke in India: A systematic review. Indian Journal of Medical Research. 2017;146(2):175.
14. Salari N, Morddarvanjoghi F, Abdolmaleki A, Rasoulpoor S, Khaleghi AA, Hezarkhani LA, et al. The global prevalence of myocardial infarction: a systematic review and meta-analysis. BMC Cardiovascular Disorders [Internet]. 2023 Apr 22;23(1). Available from: https://bmccardiovascdisord.biomedcentral.com/articles/10.1186/s12872-023-03231-w
15. Kalra A, Jose AP, Prabhakaran P, Kumar A, Agrawal A, Roy A, et al. The burgeoning cardiovascular disease epidemic in Indians – perspectives on contextual factors and potential solutions. The Lancet Regional Health - Southeast Asia. 2023 Feb;12:100156.
16. World Health Organization. Cardiovascular diseases (CVDs) [Internet]. World Health Organization. World Health Organization; 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
17. McCormick SPA. Lipoprotein(a): Biology and Clinical Importance. The Clinical Biochemist Reviews [Internet]. 2004 Feb 1;25(1):69–80. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1853362/
18. Brunner C, Kraft HG, Utermann G, Müller HJ. Cys4057 of apolipoprotein(a) is essential for lipoprotein(a) assembly. Proceedings of the National Academy of Sciences of the United States of America [Internet]. 1993 Dec 15 [cited

2024 Feb 4];90(24):11643–7. Available from: https://pubmed.ncbi.nlm.nih.gov/7505444/

19. Koschinsky ML, Côté GP, Gabel B, van der Hoek YY. Identification of the cysteine residue in apolipoprotein(a) that mediates extracellular coupling with apolipoprotein B-100. The Journal of Biological Chemistry [Internet]. 1993 Sep 15;268(26):19819–25. Available from: https://pubmed.ncbi.nlm.nih.gov/8366120/
20. McCormick SP, Ng JK, Taylor S, Flynn LM, Hammer RE, Young SG. Mutagenesis of the human apolipoprotein B gene in a yeast artificial chromosome reveals the site of attachment for apolipoprotein(a). Proceedings of the National Academy of Sciences of the United States of America [Internet]. 1995 Oct 24 [cited 2024 Feb 4];92(22):10147–51. Available from: https://pubmed.ncbi.nlm.nih.gov/7479743/
21. Phillips M, Lembertas AV, Schumaker VN, Lawn RM, Shire SJ, Zioncheck TF. Physical properties of recombinant apolipoprotein(a) and its association with LDL to form an Lp(a)-like complex. Biochemistry. 1993 Apr 13;32(14):3722–8.
22. Weisel JW, Chandrasekaran Nagaswami, Woodhead JL, Abd Al-Roof Higazi, Cain WJ, Marcovina SM, et al. The Structure of Lipoprotein(a) and Ligand-Induced Conformational Changes. Biochemistry. 2001 Aug 7;40(35):10424–35.
23. Su W, Campos H, Judge H, Walsh BW, Sacks FM. Metabolism of Apo(a) and ApoB100 of Lipoprotein(a) in Women: Effect of Postmenopausal Estrogen Replacement1. The Journal of Clinical Endocrinology & Metabolism. 1998 Sep;83(9):3267–76.

24. Trieu VN, McConathy WJ. A Two-step Model for Lipoprotein(a) Formation. Journal of Biological Chemistry. 1995 Jun;270(26):15471–4.
25. Chiesa G, Hobbs HH, Koschinsky ML, Lawn RM, Maika SD, Hammer RE. Reconstitution of lipoprotein(a) by infusion of human low density lipoprotein into transgenic mice expressing human apolipoprotein(a). The Journal of Biological Chemistry [Internet]. 1992 Dec 5;267(34):24369–74. Available from: https://pubmed.ncbi.nlm.nih.gov/1280258/
26. Gabel BR, Koschinsky ML. Sequences within apolipoprotein(a) kringle IV types 6-8 bind directly to low-density lipoprotein and mediate noncovalent association of apolipoprotein(a) with apolipoprotein B-100. Biochemistry [Internet]. 1998 May 26;37(21):7892–8. Available from: https://pubmed.ncbi.nlm.nih.gov/9601051/
27. Becker L, P. Michael Cook, Wright TG, Koschinsky ML. Quantitative Evaluation of the Contribution of Weak Lysine-binding Sites Present within Apolipoprotein(a) Kringle IV Types 6–8 to Lipoprotein(a) Assembly. J Biol Chem . 2004 Jan 1;279(4):2679–88.
28. Becker L, McLeod RS, Marcovina SM, Yao Z, Koschinsky ML. Identification of a critical lysine residue in apolipoprotein B-100 that mediates noncovalent interaction with apolipoprotein(a). The Journal of Biological Chemistry [Internet]. 2001 Sep 28;276(39):36155–62. Available from: https://pubmed.ncbi.nlm.nih.gov/11473115/
29. McCormick SP, Ng JK, Cham CM, Taylor S, Marcovina SM, Segrest JP, et al. Transgenic mice expressing human ApoB95 and ApoB97. Evidence that sequences within the carboxyl-terminal portion of human apoB100 are important for the assembly of lipoprotein. The Journal of Biological

Chemistry [Internet]. 1997 Sep 19;272(38):23616–22. Available from: https://pubmed.ncbi.nlm.nih.gov/9295301/

30. Sharp RJ, Perugini MA, Marcovina SM, McCormick SPA. A Synthetic Peptide That Inhibits Lipoprotein(a) Assembly. Arteriosclerosis, Thrombosis, and Vascular Biology. 2003 Mar;23(3):502–7..
31. Liu CYY, Broadhurst R, Marcovina SM, McCormick SPA. Mutation of lysine residues in apolipoprotein B-100 causes defective lipoprotein[a] formation. Journal of Lipid Research. 2004 Jan;45(1):63–70.
32. Utermann G, Hoppichler F, Dieplinger H, Seed M, Thompson G, Boerwinkle E. Defects in the low density lipoprotein receptor gene affect lipoprotein (a) levels: multiplicative interaction of two gene loci associated with premature atherosclerosis. Proceedings of the National Academy of Sciences. 1989 Jun 1;86(11):4171–4.
33. Kraft HG, Lingenhel A, Raal FJ, Hohenegger M, Utermann G. Lipoprotein(a) in Homozygous Familial Hypercholesterolemia. Arteriosclerosis, Thrombosis, and Vascular Biology. 2000 Feb;20(2):522–8.
34. Rader DJ, Mann WA, Cain W, Kraft HG, Usher D, Zech LA, et al. The low density lipoprotein receptor is not required for normal catabolism of Lp(a) in humans. Journal of Clinical Investigation [Internet]. 1995 Mar 1;95(3):1403–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC441483/
35. Hofmann SL, Eaton DL, Brown MS, McConathy WJ, Goldstein JL, Hammer RE. Overexpression of human low density lipoprotein receptors leads to accelerated catabolism of Lp(a) lipoprotein in transgenic mice. Journal of Clinical Investigation [Internet]. 1990 May 1 [cited 2024 Feb 4];85(5):1542–7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC296603/

36. Kostner GM, Gavish D, Leopold B, Bolzano K, Weintraub MS, Breslow JL. HMG CoA reductase inhibitors lower LDL cholesterol without reducing Lp(a) levels. Circulation. 1989 Nov;80(5):1313–9.
37. Maartmann-Moe K, Berg K. Lp(a) lipoprotein enters cultured fibroblasts independently of the plasma membrane low density lipoprotein receptor. Clinical Genetics. 2008 Apr 23;20(5):352–62.
38. Liu R, Saku K, Kostner GM, Hirata K, Zhang B, Shiomi M, et al. In vivo kinetics of lipoprotein(a) in homozygous Watanabe heritable hyperlipidaemic rabbits. European Journal of Clinical Investigation [Internet]. 1993 Sep 1;23(9):561–5. Available from: https://pubmed.ncbi.nlm.nih.gov/8243527/
39. Kostner KM, Maurer G, Huber K, Stefenelli T, Dieplinger H, Steyrer E, et al. Urinary Excretion of Apo(a) Fragments. Arteriosclerosis, Thrombosis, and Vascular Biology. 1996 Aug;16(8):905–11.
40. Dieplinger H. Lipoprotein(a) in health and disease. Biochemical Society Transactions. 1999 Aug 1;27(4):439–47.
41. HRZENJAK A, FRANK S, WO X, ZHOU Y, van BERKEL T, KOSTNER GM. Galactose-specific asialoglycoprotein receptor is involved in lipoprotein (a) catabolism. Biochemical Journal. 2003 Dec 15;376(3):765–71.
42. Berg K, Dahlén G, Christophersen B, Cook T, Kjekshus J, Pedersen T. Lp(a) lipoprotein level predicts survival and major coronary events in the Scandinavian Simvastatin Survival Study. Clinical Genetics. 2008 Apr 23;52(5):254–61.
43. Seman LJ, DeLuca C, Jenner JL, Cupples LA, McNamara JR, Wilson PW, et al. Lipoprotein(a)-cholesterol and coronary heart disease in the Framingham

Heart Study. Clinical Chemistry [Internet]. 1999 Jul 1;45(7):1039–46. Available from: https://pubmed.ncbi.nlm.nih.gov/10388480/

44. Danesh J, Collins R, Peto R. Lipoprotein(a) and Coronary Heart Disease. Circulation. 2000 Sep 5;102(10):1082–5.
45. Luc G, Bard JM, Arveiler D, Ferrieres J, Evans A, Amouyel P, et al. Lipoprotein (a) as a predictor of coronary heart disease: the PRIME Study. Atherosclerosis [Internet]. 2002 Aug 1;163(2):377–84. Available from: https://www.sciencedirect.com/science/article/pii/S0021915002000266?casa_token=4ennR7yOLW0AAAAA:8C1cyRA0v4n7cJ-No71fnAoa9UCmM_39o9JiORh-S4LgFGtB_BAzB8VkBjWqU_DSQ1mgfLDXBAw
46. Arnold von Eckardstein, Schulte H, Cullen P, Assmann G. Lipoprotein(a) further increases the risk of coronary events in men with high global cardiovascular risk. Journal of the American College of Cardiology. 2001 Feb 1;37(2):434–9.
47. Jürgens G, Chen Q, Esterbauer H, Mair S, Ledinski G, Dinges HP. Immunostaining of human autopsy aortas with antibodies to modified apolipoprotein B and apoprotein(a). Arteriosclerosis and Thrombosis: A Journal of Vascular Biology. 1993 Nov;13(11):1689–99.
48. Rath M, Niendorf A, Reblin T, Dietel M, Hans-Joachim Krebber, Beisiegel U. Detection and quantification of lipoprotein(a) in the arterial wall of 107 coronary bypass patients. Arteriosclerosis. 1989 Sep 1;9(5):579–92.
49. Jamieson DG, Usher DC, Rader DJ, Lavi E. Apolipoprotein(a) deposition in atherosclerotic plaques of cerebral vessels. A potential role for endothelial cells in lesion formation. The American Journal of Pathology [Internet]. 1995

Dec 1 [cited 2024 Jun 1];147(6):1567–74. Available from: https://pubmed.ncbi.nlm.nih.gov/7495281/

50. Cambillau M, Simon A, Amar J, Giral P, Atger V, Segond P, et al. Serum Lp(a) as a discriminant marker of early atherosclerotic plaque at three extracoronary sites in hypercholesterolemic men. The PCVMETRA Group. Arteriosclerosis and Thrombosis: A Journal of Vascular Biology. 1992 Nov;12(11):1346–52.
51. Nielsen LB, Stender S, Kjeldsen K, Nordestgaard BG. Specific Accumulation of Lipoprotein(a) in Balloon-Injured Rabbit Aorta In Vivo. Circulation Research. 1996 Apr;78(4):615–26.
52. van der Hoek YY, Sangrar W, Côté GP, Kastelein JJ, Koschinsky ML. Binding of recombinant apolipoprotein(a) to extracellular matrix proteins. Arteriosclerosis and Thrombosis: A Journal of Vascular Biology [Internet]. 1994 Nov 1;14(11):1792–8. Available from: https://pubmed.ncbi.nlm.nih.gov/7947605/
53. Hughes SD, Lou XJ, Ighani S, Verstuyft J, Grainger DJ, Lawn RM, et al. Lipoprotein(a) vascular accumulation in mice. In vivo analysis of the role of lysine binding sites using recombinant adenovirus. The Journal of Clinical Investigation [Internet]. 1997 Sep 15;100(6):1493–500. Available from: https://pubmed.ncbi.nlm.nih.gov/9294116/
54. Scanu AM. Atherothrombogenicity of lipoprotein(a): the debate. The American Journal of Cardiology [Internet]. 1998 Nov 5;82(9A):26Q33Q. Available from: https://pubmed.ncbi.nlm.nih.gov/9819101/
55. Kario K, Matsuo T, Imiya M, Kayaba K, Kuroda T, Nago N, et al. Close relation between lipoprotein (a) levels and atherothrombotic disease in

Japanese subjects > 75 years of age. The American Journal of Cardiology [Internet]. 1994 Jun 15;73(16):1187–90. Available from: https://pubmed.ncbi.nlm.nih.gov/8203336/

56. Heinimann K, Stähelin HB, Perrig-Chiello P, Perrig WO, Ehrsam R, Meier B, et al. [Lipoprotein(a) and plasma lipids in 429 elderly and very old subjects: significance as risk factor, effect of nutrition and life style]. Schweizerische Medizinische Wochenschrift [Internet]. 1996 Aug 31;126(35):1487. Available from: https://pubmed.ncbi.nlm.nih.gov/8927952/
57. Cicek H, Bayil S, Zer Y, Celik A, Geyikli I. Comparison of Lipoprotein(a) levels between elderly and middle-aged men with coronary artery disease. Annals of the New York Academy of Sciences [Internet]. 2007 Apr 1;1100:179–84. Available from: https://pubmed.ncbi.nlm.nih.gov/17460176/
58. Van Kooten F, van Krimpen J, Dippel DW, Hoogerbrugge N, Koudstaal PJ. Lipoprotein(a) in patients with acute cerebral ischemia. Stroke [Internet]. 1996 Jul 1;27(7):1231–5. Available from: https://pubmed.ncbi.nlm.nih.gov/8685934/
59. Nave AH, Lange KS, Leonards CO, Siegerink B, Doehner W, Landmesser U, et al. Lipoprotein (a) as a risk factor for ischemic stroke: A meta-analysis. Atherosclerosis. 2015 Oct;242(2):496–503.
60. Smolders B, Lemmens R, Thijs V. Lipoprotein (a) and Stroke. Stroke. 2007 Jun;38(6):1959–66.
61. Kumar P, Swarnkar P, Misra S, Nath M. Lipoprotein (a) level as a risk factor for stroke and its subtype: A systematic review and meta-analysis. Scientific Reports. 2021 Aug 2;11(1).

62. Arora P, Kalra R, Callas PW, Alexander KS, Zakai NA, Wadley V, et al. Lipoprotein(a) and Risk of Ischemic Stroke in the REGARDS Study. Arteriosclerosis, Thrombosis, and Vascular Biology. 2019 Apr;39(4):810–8.
63. Langsted A, Nordestgaard BG, Kamstrup PR. Elevated Lipoprotein(a) and Risk of Ischemic Stroke. Journal of the American College of Cardiology. 2019 Jul;74(1):54–66..
64. Boden-Albala B, Kargman DE, Lin I-Feng, Paik MC, Sacco RL, Berglund L. Increased Stroke Risk and Lipoprotein(a) in a Multiethnic Community: The Northern Manhattan Stroke Study. Cerebrovascular Diseases. 2010;30(3):237–43.
65. Baggio G, S. Donazzan, Monti D, Mari D, Martini S, C. Gabelli, et al. Lipoprotein(a) and lipoprotein profile in healthy centenarians: a reappraisal of vascular risk factors. The FASEB Journal. 1998 Apr 1;12(6):433–7.
66. Ariyo AA, Thach C, Tracy RP. Lp(a) Lipoprotein, Vascular Disease, and Mortality in the Elderly. The New England Journal of Medicine. 2003 Nov 27;349(22):2108–15.
67. Ammara Abid, Amina Nadeem. Association of lipoprotein (a) with lipid profile and response to statin treatment in hyperlipidemic patients. Journal of the Pakistan Medical Association. 2022 Jan 28;
68. Habib SS, Aslam M. Lipids and lipoprotein(a) concentrations in Pakistani patients with type 2 diabetes mellitus. Diabetes, Obesity and Metabolism. 2004 Sep;6(5):338–43.
69. Stürzebecher PE, Uttinger KL, Vogel M, Schlingmann M, Ceglarek U, Isermann B, et al. Lipoprotein(a) serum concentrations in children in relation to body mass index, age and sex. Pediatric Research [Internet]. 2024 Feb 28

[cited 2024 Jun 1];1–7. Available from: https://www.nature.com/articles/s41390-024-03108-4#:~:text=Distribution%20of%20Lp(a)%20serum%20concentrations%20in%20children&text=The%20median%20Lp(a)%20level

70. Raitakari O, Kartiosuo N, Pahkala K, Hutri-Kähönen N, Bazzano LA, Chen W, et al. Lipoprotein(a) in Youth and Prediction of Major Cardiovascular Outcomes in Adulthood. Circulation. 2023 Jan 3;147(1):23–31.
71. Minami Y, Kinoshita D, Muramatsu Y, Nagata T, Ako J. Role of Lipoprotein(a) in Cardiovascular Disease: A Review of Clinical Practice. Journal of Asian Pacific Society of Cardiology. 2022 May 13;1.
72. Willeit P, Ridker PM, Nestel PJ, Simes J, Tonkin AM, Pedersen TR, et al. Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. The Lancet [Internet]. 2018 Oct 13;392(10155):1311–20. Available from: https://www.sciencedirect.com/science/article/pii/S0140673618316520
73. Patel AP, Wang M, Pirruccello JP, Ellinor PT, Ng K, Kathiresan S, et al. Lp(a) (Lipoprotein[a]) Concentrations and Incident Atherosclerotic Cardiovascular Disease. Arteriosclerosis, Thrombosis, and Vascular Biology. 2020 Oct 29;
74. Kamstrup PR, Tybjærg-Hansen A, Nordestgaard BG. Extreme lipoprotein(a) levels and improved cardiovascular risk prediction. Journal of the American College of Cardiology [Internet]. 2013 Mar 19;61(11):1146–56. Available from: https://pubmed.ncbi.nlm.nih.gov/23375930/
75. Waldeyer C, Makarova N, Zeller T, Schnabel RB, Brunner FJ, Jørgensen T, et al. Lipoprotein(a) and the risk of cardiovascular disease in the European population: results from the BiomarCaRE consortium. European Heart Journal

[Internet]. 2017 Aug 21 [cited 2020 Sep 4];38(32):2490–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5837491/

76. O'Donoghue ML, Fazio S, Giugliano RP, Stroes ESG, Kanevsky E, Gouni-Berthold I, et al. Lipoprotein(a), PCSK9 Inhibition, and Cardiovascular Risk. Circulation. 2019 Mar 19;139(12):1483–92.
77. Szarek M, Bittner VA, Aylward P, Baccara-Dinet M, Bhatt DL, Diaz R, et al. Lipoprotein(a) lowering by alirocumab reduces the total burden of cardiovascular events independent of low-density lipoprotein cholesterol lowering: ODYSSEY OUTCOMES trial. European Heart Journal [Internet]. 2020 Nov 21;41(44):4245–55. Available from: https://academic.oup.com/eurheartj/article/41/44/4245/5922803?login=false
78. Wong ND, Fan W, Hu X, Ballantyne C, Hoodgeveen RC, Tsai MY, et al. Lipoprotein(a) and Long-Term Cardiovascular Risk in a Multi-Ethnic Pooled Prospective Cohort. Journal of the American College of Cardiology [Internet]. 2024 Apr 23 [cited 2024 May 6];83(16):1511–25. Available from: https://pubmed.ncbi.nlm.nih.gov/38631771/
79. Emerging Risk Factors Collaboration. Lipoprotein(a) Concentration and the Risk of Coronary Heart Disease, Stroke, and Nonvascular Mortality. JAMA. 2009 Jul 22;302(4):412.
80. Guan W, Cao J, Steffen BT, Post WS, Stein JH, Tattersall MC, et al. Race is a key variable in assigning lipoprotein(a) cutoff values for coronary heart disease risk assessment: the Multi-Ethnic Study of Atherosclerosis. Arteriosclerosis, thrombosis, and vascular biology [Internet]. 2015 Apr 1;35(4):996–1001. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4377643/

81. Tsimikas S, Marcovina SM. Ancestry, Lipoprotein(a), and Cardiovascular Risk Thresholds: JACC Review Topic of the Week. Journal of the American College of Cardiology [Internet]. 2022 Aug 30 [cited 2023 Oct 13];80(9):934–46. Available from: https://www.sciencedirect.com/science/article/pii/S0735109722054286
82. Ugovšek S, Šebeštjen M. Lipoprotein(a)—The Crossroads of Atherosclerosis, Atherothrombosis and Inflammation. Biomolecules. 2021 Dec 24;12(1):26.
83. Wang Y, Jing J, Meng X, Pan Y, Wang Y, Wang W, et al. The Third China National Stroke Registry (CNSR-III) for patients with acute ischaemic stroke or transient ischaemic attack: design, rationale and baseline patient characteristics. Stroke and vascular neurology. 2019 Jun 29;4(3):158–64.
84. Kim BS, Jung HS, Bang OY, Chung CS, Lee KH, Kim GM. Elevated serum lipoprotein(a) as a potential predictor for combined intracranial and extracranial artery stenosis in patients with ischemic stroke. Atherosclerosis. 2010 Oct;212(2):682–8.
85. Pan Y, Li H, Wang Y, Meng X, Wang Y. Causal Effect of Lp(a) [Lipoprotein(a)] Level on Ischemic Stroke and Alzheimer Disease. Stroke. 2019 Dec;50(12):3532–9.
86. Kotani K, Serban MC, Penson P, Lippi G, Banach M. Evidence-based assessment of lipoprotein(a) as a risk biomarker for cardiovascular diseases – Some answers and still many questions. Critical Reviews in Clinical Laboratory Sciences. 2016 Jun 26;53(6):370–8.
87. Arenillas JF, Molina CA, Chacón P, Rovira A, Montaner J, Coscojuela P, et al. High lipoprotein (a), diabetes, and the extent of symptomatic intracranial

atherosclerosis. Neurology [Internet]. 2004 Jul 13 [cited 2024 Jun 1];63(1):27–32. Available from: https://pubmed.ncbi.nlm.nih.gov/15249606/

88. Steffen BT, Thanassoulis G, Duprez D, Stein JH, Karger AB, Tattersall MC, et al. Race-Based Differences in Lipoprotein(a)-Associated Risk of Carotid Atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology. 2019 Mar;39(3):523–9.
89. Li J, Li S, Pan Y, Wang M, Meng X, Wang Y, et al. Relationship Between Lipoprotein (a) [Lp(a)] and Cognition in Different Ischemic Stroke Subtypes. Frontiers in Neurology. 2021 Dec 3;12.

ANNEXURE-I

INFORMED CONSENT

Title Of Research Study:

''Estimation and correlation of clinical significance of lipoprotein (a) as a risk factor of atherosclerotic vascular events in elderly: A One Year Cross-sectional Study in KLE's Dr Prabhakar Kore hospital and Medical Research Centre, Belagavi''.

Principal Investigator:

Guide:

Introduction and Purpose:

To estimate and correlate the clinical significance of lipoprotein (a) as a risk factor for atherosclerotic vascular events in elderly.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn. You may not benefit by these investigations, but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study.

If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing

In case of the queries during study or in future you may contact following persons:

Dr MD (General Medicine) Professor of General Medicine and Unit Chief. Jawaharlal Nehru Medical College, Belagavi	**Dr.** Post Graduate Student, Department Of General Medicine, JNMC, Belagavi. 9422644631.

Dr.
Chairman,
College Ethical Dissertation
Research Committee
J. N. Medical. College
Nehru Nagar, Belagavi 590010

ANNEXURE-II

PROFORMA

Estimation and correlation of clinical significance of lipoprotein(a) as a risk factor of atherosclerotic vascular event in elderly: A ne Yeas Cross Sections in KLE's Dr. Prabhakar Kore hospital and Medical Research Centre, Belagavi.

Case No.	
Name	
IP No.	
Age	
Sex	
Address	
Occupation	

Complaints at Presentation	
Past History	
Family History	
Personal History	
Treatment History	

Vitals:

Temperature	
Pulse	
Respiratory rate	
Blood Pressure	

Physical Examination:

Pallor	
Icterus	
Lymphadenopathy	
Cyanosis	
Clubbing	
Edema	

Systemic Examination:

C.V.S	
R.S	
C.N.S	
Per Abdomen	

Investigations:

Serum Lipoprotein (a)	
Serum LDL Cholesterol	
Serum HDL Cholesterol	
Serum Triacylglycerol	
Serum Total Cholesterol	
Random Plasma Glucose	
Serum Creatinine	
HBA1C	
Troponin-T	

Risk Factors:

Hypertension	
Type-1/Type-2 Diabetes Mellitus	
Ischemic Heart Disease	
History of stroke or Transient ischemic attack	
Chronic Obstructive Pulmonary Disease	
History of Cancer	
Family History of Stroke for Myocardial Infarction	
Former/Current Smoking	
Alcohol Consumption	
Body Mass Index	

Additional Investigations:

2D Echocardiography	
Coronary Angiography	
MRI/CT Brain Plain Screening	
Treatment Given	

ANNEXURE III (MASTER CHART)

Neurological atherosclerotic vascular event subgroup (Group-A)

SR NO	AGE	DIAGNOSIS	LP (a)	CHOLES	TG	LDL	HDL	CREAT	HBA1C	Outcome	Addictions
1	65/M	RIGHT MCA INFARCT , HTN	62	151	82	96	39	0.74	5.6	Alive	alcoholic
2	65/M	OLD PTB,SUACUTE LEFT MCA TERRITORY EMBOLIC INARCT WITH HEMORRAGIC TRANSFORMATION, INFECTIVE ENDOCARDITIS	18	56	79	124	38	1.18	5.4	Alive	no
3	66/M	LEFT HEMIPARESIS RECURRENT CVA,DEMENTIA, SEIZURE DISORDER	28.3	100	130	120	44	0.62	6	Alive	no
4	65/F	MULTIPLE LACUNAR INFARCT IN RIGHT FRONTAL LOBE AND CORONA RADIATA, TYPE 2DM, HTN,	41	202	100	139	40	0.66	8.7	Alive	alcoholic, smoking
5	67/F	RIGHT CEREBELLAR STROKE	46	88	156	71	36	0.63	4.5	Alive	no
6	72/M	SEIZURE DISORDER WITH LEFT MCA TERRITORY INFARCT, HTN	70	124	72	70	40	1.28	5.7	Alive	no
7	69/M	LEFT MCA SUBCORTICAL INFARCT HTN, TYPE 2DM, VERTIGO IHD S/P CABG	74	101	87	50	34	1.07	5.4	Alive	tobacco chewer
8	79/M	MULTIFOCAL EMBOLIC INFACRT IN LEFT FRONTAL LOBE IN MCA TERRITORY,HTN, TYPE 2DM	13	159	108	111	36	1.14	6.5	Alive	no
9	76/M	LEFT CEREBELLAR INFARCT , HTN , TYPE 2 DM	5	180	73	118	37	0.84	7.3	Alive	alcohol
10	79/M	LARGE RT POSTERIOR PARITO-OCCIPTO-TEMPORAL INFARCT (ACUTE ON CHRONIC), IHD S/P CARDIAC ARREST,HTN	30	138	76	87	36	1.08	5.4	death	tobacco chewer
11	65/M	LEFT FRONTOPARIETOTEMPORAL HEMORRAGE WITH MASS EFFECT,TYPE 2DM	16	125	140	76	31	1.09	5.8	death	smoking, alcoholic
12	69/M	DEMENTIA,PARKINSION,HTN,RIGHT MCA TERRITORY INFARCT	5	161	117	128	40	0.67	5.4	alive	no
13	65/F	HYPERACUTE INFARCT IN MCA,PCA WATERSHED, HTN,	60	246	228	130	30	0.91	4.3	death	no
14	67/M	SUBACUTE INFARCT IN RIGHT PCA WITH MULTIPLE EMBOLIC INFARCT IN B/L HEMISPHERE, IHD-TVD S/P CABG, AVR	5	175	192	136	41	0.95	5.8	alive	tobacco chewer
15	79/M	RIGHT FRONTAL INFARCT	10.4	129	82	64	54	1.11	5.4	alive	no
16	42/M	ACUTE PONTINE ISCHEMIC STROKE (RT HEMIPARESIS WITH LEFT LMN FACIAL PALSY) , HTN,	6.24	120	130	133	120	0.97	4.8	alive	no
17	81/M	ACUTE NON HEMORRHAGIC LEFT MCA INFARCT	15.5	163	90	82	60	1.21	5.3	alive	no
18	75/M	ACUTE ISCHEMIC STROKE ,B/L CAROTID ARTERY DISEASE, RIGHT ICA OCCLUSION, HTN	78	211	141	138	52	0.78	4.5	alive	tobacco chewer
19	72/M	B/L CEREBELLAR INFARCT, OLD IHD EF 25%, CCF, ACUTE POLYRADICULOPATHY	60.1	79	112	30	22	0.54	5.4	death	alcoholic , smoking
20	85/M	RIGHT HEMIPONS INFARCT, LEFT ICA OCCLUSION, HEMETEMSIS,DM,HTN	24.2	184	125	129	30	1.11	6.9	alive	alcoholic
21	78/M	RIGHT MCA,PCA,ACA TERRITORY,DCM,	50	160	134	100	43	1.33	4.6	death	alcoholism , smoking
22	65/M	ACUTE EMBOLIC INFARCT IN RIGHT POSTERIOR PARIETAL REGION, TYPE 2 DM, IHD S/P PTCA	210	204	121	131	39	1.19	7.8	alive	no
23	85/M	MULTIPLE SUBACUTE EMBOLIC INFARCTS, LEFT THALAMUS BLEED,TYPE2DM, HTN	18.5	129	106	62	40	1.43	8.2	alive	no
24	78/M	ACUTE RIGHT CEREBELLAR INFARCT,OCCIPITAL INFARCT, THROMBOCYTOPENIA	5.07	54	117	11	20	0.58	6.5	alive	no
25	60/F	MULTIPLE EMBOLIC INFARCTS IN FRONTAL TEMPORAL PARIETAL, FLOATING THROMBUS IN AORTIC ARCH	12.7	171	115	110	30	0.8	4.7	alive	no
26	70/F	MULTIPLE LACUNAR INFARCTS,HTN,HYPOTHYROIDISM	5	171	131	112	33	1.13	5.6	death	no
27	74/M	LEFT FRONTOPARIETOTEMPORAL INFARCT WITH HEMORRHAGIC TRANSFORMATION, HTN, TYPE 2 DM	54	224	126	174	40	0.85	10.3	death	alcoholic, smoking
28	82/M	SUBACUTE INFARCT IN RIGHT FRONTAL, RIGHT PARIETAL SUBCORTICAL WHITE MATTER, HTN, TYPE 2 DM	159	152	131	101	39	0.98	9.2	alive	no
29	85/M	RIGHT LATERAL MEDULLARY SYNDROME, HTN, TYPE 2 DM	11.5	150	120	100	38	0.66	12.5	death	alcoholic
30	68/M	PULMONARY EMBOLISM, PAROXYSOMAL AF, IWMI, L FRONTOTEMPOROPARIETAL SDH S/P DECOMPRESSIVE CRANIOTOMY,SYMTOMATIC SEIZURES	4.36	62	105	18	10	1.23	4.6	death	alcoholic, tobacco chewer

Cardiovascular atherosclerotic vascular event subgroup (Group-A)

SR NO	AGE	DIAGNOSIS	CORONARY ANGIOGRAPHY	LP(a)	CHOLES	TG	LDL	HDL	CREAT	TROP I	HBA1C	Outcome	Addictions
1	65/F	ACUTE CORONARY SYNDROME, CAD-TRIPLE VESSLE DISEASE, TYPE 2DM,COPD	CORONARY ARTERY DISEASE-TRIPLE VESSEL DISEASE	62	114	80	67	31	1.03	0.41	6.1	alive	no
2	66/M	ACS-NSTEMI, CAD-SINGLE VESSEL DISEASE	MILD CORONARY ARTERY DISEASE	81	153	100	93	40	0.88	0.89	5.5	alive	no
3	73/M	IHD-UNSTABLE ANGINA, CAD- SINGLE VESSEL DISEASE, HTN	MILD CAD	10	148	105	95	31	0.86	0.01	7.1	alive	smoking, alcohol
4	75/M	IHD-INFERIOR WALL MYOCARDIAL INFARCTION,CAD- TRIPLE VESSEL DISEASE	CAD-TRIPLE VESSEL DISEASE	147	146	141	82	36	1.34	1.66	5.6	alive	tobacco
5	67/M	IHD-UNSTABLE ANGINA,HTN	NORMAL EPICARDIAL CORONARIES	100	89	100	67	24	1.04	0.01	5.4	alive	alcohol
6	70/M	IHD, COPD, TYPE2DM, HTN, CAD-TVD S/P PTCA STENT TO OM1 AND PROXIMAL LAD	CAD- TRIPLE VESSEL DISEASE	24	105	87	33	35	1.26	0.9	5.3	alive	smoking
7	69/M	IHD, CAD-TVD, TPE 2 DM, HTN, ACS EF 20%	CAD-TRIPLE VESSEL DISEASE	100	130	55	87	32	1.08	0.33	7.6	death	alcohol, smoking
8	75/M	ACS-NSTEMI, CAD-DOUBLE VESSEL DISEASE,HTN,TYPE 2DM	DOUBLE VESSEL DISEASE	20	120	90	100	42	0.91	0.79	8.6	alive	smoking
9	82/M	IHD-UNSTABLE ANGINA, CAD-DOUBLE VESSEL DISEASE,HTN,TYPE 2DM,BPH	CORONARY ARTERY DISEASE-DOUBLE VESSEL DISEASE	55	156	162	83	43	1.06	0.02	7.8	alive	no
10	74/M	IHD- EVOLVED AWMI,CAD-SINGLE VESSEL DISEASE, TYPE 2DM,HTN	CAD- SINGLE VESSEL DISEASE	62	151	185	90	24	1.11	1.6	6.6	alive	alcohol
11	65/M	IHD-EVOLVED AWMI, CAD- DOUBLE VESSEL DISEASE,TYPE 2 DM	CAD DOUBLE VESSEL DISEASE	28	242	131	160	56	1.2	2.58	9.1	alive	alcohol
12	65/F	IHD-S/P PTCA(2014), UNSTABLE ANGINA WITH LBBB, CAD- DOUBLE VESSEL DISEASE,HTN,TYPE 2DM	CAD- TRIPLE VESSEL DISEASE	44	170	140	100	40	1.01	1.04	10.9	alive	smoking
13	66/M	IHD-S/P PTCA (2014), CAD- SINGLE VESSEL DISEASE,HTN, TYPE 2DM	CAD- SINGLE VESSEL DISEASE	55	89	129	37	26	1.27	2.7	9.3	alive	tobacco chewing
14	76/M	IHD- POST PTCA WITH STENTING TO LAD(2011) WITH UNSTABLE ANGINA, CAD- MID LAD STENT PATENT, HTN	CAD- MID LAD STENT PATENT, NORMAL LCX RCA	28	158	109	114	22	1.8	0.05	4.6	alive	no
15	69/M	IHD-TVT POSTIVE FOR INDUCIBLE ISCHEMIA, CAD- DOUBLE VESSEL DISEASE, HTN	CAD- DOUBLE VESSEL DISEASE	11	121	85	74	30	0.87	0.02	5.5	alive	alcohol
16	76/M	IHD-S/P PTCA (2021) PROXIMAL LAD, HTN,BPH	CAD SINGLE VESSEL DISEASE	36	122	89	67	37	1.26	0.03	6.7	alive	alcohol smoking
17	76/M	IHD-S/P PTCA,HTN,TYPE2DM	CAD- SINGLE VESSEL DISEASE	6	118	68	48	56	1.02	0.01	8.5	alive	no
18	84/M	ACUTE CORONARY SYNDROME-POST PTCA (2018) WITH EXTENSIVE ANTERIOR WALL MI S/P THROMBOLYSIS WITH STREPTOKINASE, CAD- TRIPLE VESSEL DISEASE	CAD- TRIPLE VESSEL DISEASE	12	149	80	74	59	0.97	0.66	6	death	alcohol, smoking,tobacco
19	80/M	IHD, METABOLIC ENCEPHALOPATHY-HYPONATREMIA, TYPE 2 DM,HTN,WEDGE COMPRESSION FRACTURE OF L1, CHRONIC LACUNAR INFARCT IN LEFT THALAMUS	CAD- TRIPLE VESSEL DISEASE	14	135	152	72	33	0.79	0.07	4.8	alive	alcohol, smoking.
20	77/M	IHD- EVOLVED IWMI, CAD-DOUBLE VESSEL DISEASE, HTN	CAD- DOUBLE VESSEL DISEASE	12.3	119	130	63	30	0.82	1.88	8.5	alive	no
21	72/F	TMT POSITIVE INDUCIBLE ISCHEMIA, MILD CAD, HTN	MILD CAD	50	100	120	80	46	0.32	2.01	9.9	death	alcohol
22	65/M	ACS-IWMI S/P THROMBOLYSIS, TYPE 2DM	CAD- TRIPLE VESSEL DISEASE	82.9	176	308	109	33	1.09	0.03	5.8	alive	smoking
23	69/M	IHD- CHRONIC STABLE ANGINA, CAD DOUBLE VESSEL DISEASE,TYPE 2DM,BPH,REFLUX ESOPHAGITIS	CAD- DOUBLE VESSEL DISEASE	223	132	200	81	34	1.08	1.55	8	alive	tobacco
24	71/M	IHD- NSTEMI, CAD- DOUBLE VESSEL DISEASE, RETROVIRAL DISEASE	CAD- DOUBLE VESSEL DISEASE	22.9	200	211	88	39	1.02	1.8	5.5	alive	smoking
25	65/M	IHD-TVT POSTIVE FOR INDUCIBLE ISCHEMIA, CAD- DOUBLE VESSEL DISEASE, TYPE 2 DM	CAD-DOUBLE VESSEL DISEASE	56	118	170	88	48	1.24	0.02	5.1	alive	no
26	66/M	IHD-AWMI (THROMBOLYSED WITH RETEPLASE), CAD SINGLE VESSLE DISEASE	CAD- SINGLE VESSEL DISEASE	63.5	152	189	63	51	1.16	0.03	4.6	alive	alcohol
27	68/M	ACUTE CORONARY SYNDROME-AWMI S/P THROMBOLYSIS WITH STREPTOKINASE, CAD DOUBLE VESSEL DISEASE-HTN	CAD- DOUBLE VESSEL DISEASE	26.7	80	84	21	42	1	2.41	5.1	alive	tobacco
28	68/F	IHD-S/P PTCA TO LAD , ACS-AWMI,CAD-SVD,HTN,TYPE 2 DM	CAD- SINGLE VESSLE DISEASE	35.5	150	88	100	45	1.26	0.01	5	alive	smoking
29	65/M	IHD CAD- TRIPLE VESSEL DISEASE, HYPOTHYROIDISM	CAD- TRIPLE VESSEL DISEASE	4.24	183	510	44	27	0.81	0.59	6.5	alive	no
30	72/M	IHD- TMT+ FOR INDUCIBLE ISCHEMIA, CAD- TRIPLE VESSEL DISEASE,HTN	CAD- TRIPLE VESSEL DISEASE	18.7	214	64	177	41	0.66	1.8	8.8	alive	tobacco
31	74/M	IHD-TMT+ FOR INDUCIBLE ISCHEMIA,CAD- DOUBLE VESSEL DISEASE, HTN	CAD-DOUBLE VESSEL DISEASE	7.59	243	122	152	52	1.26	1.59	5.7	death	alcohol, tobacco
32	70/F	IHD-EVOLVED ANTERIOR WALL MI, HYPERTENTION	CAD- SINGLE VESSEL DISEASE	230	145	206	99	32	1.21	0.01	5.3	alive	tobacco chewing
33	65/M	IHD-NSTEMI,CAD-TRIPLE VESSEL DISEASE,ACCELERATED HTN, HBSAG+	CAD- TRIPLE VESSEL DISEASE	9.77	93	78	35	49	1.02	0.08	9.5	alive	no
34	72/M	IHD-S/P PTCA (2007),TYPE 2DM,HTN,OLD CVA,BPH.	NORMAL EPICARDIAL CORONARIES	91.9	75	82	35	28	0.93	0.01	4.6	alive	alcohol, smoking
35	69/M	IHD- NSTEMI,CAD-DOUBLE VESSEL DISEASE, TYPE 2DM	CAD-DOUBLE VESSEL DISEASE	29	119	59	67	40	0.74	0.52	5.1	alive	smoking
36	72/F	IHD- NSTEMI, CAD-DOUBLE VESSEL DISEASE,HTN,TYPE 2DM	CAD- DOUBLE VESSEL DISEASE	8.04	86	101	43	28	1.11	0.02	5	alive	tobacco
37	65/M	ACS-EXTENSIVE AWMI(THROMBOLYSED WITH RETEFUSE), CAD-SINGLE VESSEL DISEASE	CAD- SINGLE VESSEL DISEASE	44	145	95	80	46	1.33	0.11	6.7	alive	alcohol
38	65/M	IHD-EVOLVED IWMI WITH COMPLETE HEART BLOCK,CAD-SINGLE VESSEL	CAD- SINGLE VESSEL DISEASE	51.2	82	93	31	32	0.7	1.77	6	alive	tobacco
39	68/M	IHD-NSTEMI,CAD-SINGLE VESSEL DISEASE,HTN, TYPE 2DM	CAD- SINGLE VESSEL DISEASE	11.8	150	188	92	34	1.14	0.05	7.8	alive	alcohol, smoking
40	65/M	IHD- CHRONIC STABLE ANGINA,CAD- TRIPLE VESSEL DISEASE,HTN	CAD- SINGLE VESSEL DISEASE	116	166	121	116	39	1.06	0.76	10.5	alive	tobacco
41	67/M	ACS-EVOLVED AWMI WITH LV APICAL CLOT, CAD-DOUBLE VESSEL DISEASE,OLD CVA	CAD-DOUBLE VESSEL DISEASE	216	177	100	77	40	1.04	0.66	6.6	alive	no
42	67/F	IHD-UNSTABLE ANGINA, DOUBLE VESSEL DISEASE,HTN	CAD- DOUBLE VESSEL DISEASE	8.67	94	97	42	30	0.6	0.43	5.7	death	alcohol smoking
43	66/M	IHD-ANTEROLATERAL MI,CAD-TRIPLE VESSEL DISEASE,TYPE 2DM, HTN	CAD- TRIPLE VESSEL DISEASE	35	161	143	128	26	0.76	0.01	6	alive	no
44	72/F	IHD- POST PTCCA (2012), CAD- TRIPLE VESSEL DISEASE, RHEUMATOID ARTHRITIS	CAD- TRIPLE VESSEL DISEASE	98.9	174	135	128	33	0.86	0.07	5.8	alive	smoking
45	74/M	IHD-UNSTABLE ANGINA, CAD-SINGLE VESSEL DISEASE, HTN, TYPE 2 DM.	CAD- SINGLE VESSEL DISEASE	170	188	100	88	42	0.75	0.02	10.1	alive	no
46	67/F	UNSTABLE ANGINA, OBSTRUCTIVE SLEEP APNEA SYNDROME, MORBID OBESITY, HTN, TYPE 2DM	MILD CORONARY ARTERY DISEASE	15.7	127	98	69	49	0.7	0.77	5.5	alive	no
47	67/M	ACS-EVOLVED AWMI WITH qRBBB, CAD-SINGLE VESSEL DISEASE, HTN	CAD- SINGLE VESSEL DISEASE	170	150	148	39	39	1.07	0.69	5	alive	no
48	67/F	IHD-NTEMI, HTN, TYPE 2 DM.	NORMAL EPICARDIAL CORONARIES	43.69	223	170	152	40	0.84	0.02	10.9	alive	tobacco
49	73/M	ACS- IWMI RVMI THROMBOLYSED WITH STK ,POST CABG, CAD- DOUBLE VESSEL DISEASE, TYPE 2 DM	CAD- DOUBLE VESSEL DISEASE	54.2	195	196	336	34	1.06	0.69	5.3	death	smoking, alcohol
50	70/F	IHD- NSTEMI,CAD- DOUBLE VESSEL DISEASE	CAD- DOUBLE VESSEL DISEASE	8.99	113	163	77	25	1.06	1.66	7.6	alive	tobacco

Group-B-No atherosclerotic vascular events (Control Group)

SR NO	AGE	DIAGNOSIS	LP(a)	CHOLES	TG	LDL	HDL	CREAT	HBA1C	TSH	Outcome	Addictions
1	73/M	TYPE 2 DM, NEUROGENIC BLADDER	53	107	198	53	14	1.13	10	3.4	alive	no
2	74/M	TYPE DM,	27	150	74	96	39	0.94	6.9	2.24	alive	alcohol
3	66/M	TYPE 2 DM , HTN	65	149	195	90	20	0.99	7	1.9	alive	no
4	67/M	UNCONTROLLED TYPE 2DM	5	276	806	107	18	1.06	13.7	2.24	alive	no
5	72/F	GRADE B OESOPHAGITIS WITH GASTRIC EROSIONS	190	199	67	135	51	0.22	6	2.66	alive	tobacco chewer
6	75/M	HTN, TYPE 2 DM, VASULITIS	54	142	107	88	33	1.01	7.6	0.66	alive	alcohol
7	72/F	HYPOTHYROIDISM, ANEMIA	30	145	70	65	40	1.08	5.5	1.07	alive	no
8	84/M	TYPE 2DM. HTN	58	166	69	99	53	1.08	9.3	2.5	alive	no
9	70/M	TYPE 2DM, HTN ,S/P AORTIC VALVE REPLACEMENT I/V/O SEVERE SCLEROTIC AORTIC STENOSIS	43	160	112	93	45	0.9	6.3	6.4	alive	no
10	82/F	TYPE 2DM, HTN	36	104	76	40	49	1.04	8.5	0.84	alive	no
11	72/F	UNCONTROLLED TYPE 2DM, HTN, NON PROLIFERATIVE DIABETIC	7	109	125	61	23	0.97	12.8	1.77	alive	no
12	68/F	PERIPHERAL ARTERY DISEASE (ARCH OF AORTA LEFT AXILLARY ARTERY THROMBOSIS)	421.8	146	92	75	53	0.6	6.4	2.2	alive	NO
13	74/F	DIABETIC NEUROPATHY, TYPE 2DM, HTN	27	141	135	93	21	0.7	7.8	0.69	alive	no
14	66/M	HTN ,COSTOCONDRITIS	102	147	190	69	40	0.79	5.4	0.79	alive	no
15	83/M	TYPE 2DM, HTN,CHOLELITHIASIS	45	134	63	71	50	1.06	8	3.66	alive	no
16	96/M	HTN, TYPE 2 DM	130	91	70	38	19	0.99	5.2	2.7	alive	alcohol
17	66/F	TYPE 2 DM	30	220	107	157	42	0.88	6	3.5	alive	no
18	65/M	TYPE 2DM, OHA INDUCED HYPOGLYCEMIA, HTN	10.2	212	71	88	38	0.74	4.5	4.5	alive	no
19	72/F	IATROGENIC CUSHINGS SYNDROME, PERICARDIAL EFFUSION, RAYNAUDS PHENOMENON,	115	135	100	85	40	0.67	5	3.5	alive	no
20	70/M	ANEMIA, TYPE 2 DM, HYPERTHYROIDISM	38.1	202	124	138	42	0.85	7.8	0.33	alive	no
21	72/F	POSTURAL HYPOTENSION	76.3	194	243	114	44	0.55	5.3	2.63	alive	no
22	68/M	HTN, TYPE 2 DM	16.9	161	121	115	31	0.66	8.6	3.5	alive	no
23	76/M	TYPE 2 DM, HTN, HYPOTHYROISDM	25	90	62	45	40	0.85	7.6	10.6	alive	no
24	74/M	HTN, HYPERTENSIVE RETINOPATHY, TYPE 2DM	4.48	95	51	40	42	1.36	7.6	1.06	alive	no
25	75/M	RIGHT LL DVT,LEFT TOE ULCER TYPE 2 DM,HTN,FACIAL NERVE PALSY	11.4	72	70	31	25	0.43	7.7	0.98	alive	no
26	77/M	HYPONATREMIA, SEIZURE DISORDER,HTN,ANEMIA,DM	4.6	98	145	81	35	1.01	10.9	1.77	alive	alcohol
27	70/M	SEVERE ANEMIA, HCV+, TYPE 2 DM	10.6	98	145	100	39	1.04	10.4	0.63	death	alcohol
28	66/F	ANEMIA, TYPE 2DM	21	249	394	128	42	0.49	8.8	2.78	alive	no
29	90/F	HYPERTENSIVE URGENCY, HYPOTHYROIDISM,HYPERTENSION	5.6	160	110	78	40	0.97	5.3	10.7	death	no
30	65/M	UNCONTROLLED TYPE 2 DM,HTN	14	113	185	47	22	0.75	14.7	2.5	alive	smoking alcohol
31	66/M	TYPE 2DM, HTN, SEIZURE DISORDER	29	130	72	77	41	0.92	9.2	3.5	alive	no
32	85/M	TYPE 2DM, HTN, HYPERTENSIVE RETINOPATHY	10.8	71	148	108	31	0.63	7.8	3.6	alive	no
33	65/M	HTN, TYPE 2DM	7.2	94	84	90	40	1.04	7	4	alive	no
34	72/F	HTN,RHEUMATOID ARTHRITIS	10	100	120	90	30	0.4	5.4	3.5	alive	no
35	82/M	HTN, TYPE 2DM, DIABETIC NEURPATHY	23	128	102	65	38	1.05	6.5	2.6	alive	no
36	78/M	HYPOTHYROIDISM, HTN, UNCONTROLLED TYPE 2DM	33.6	130	80	73	35	1.33	15	3.6	alive	no
37	68/M	HTN EMERGENCY	39	195	332	96	33	0.91	6.1	4.5	alive	no
38	75/M	COPD, SEVERE PAH, HTN	4.07	153	100	68	40	0.81	5.5	3	alive	SMOKING
39	66/M	BRONCHIAL ASTHAMA	12.3	100	86	72	40	1.04	5	3.6	alive	no
40	67/M	UNCNTROLLED TYPE 2 DM WITH PIVD, DIABETIC GASTROPATHY	35.5	169	403	112	29	0.64	11.7	1.43	alive	smoking
41	68/F	HTN,TYPE 2 DM	29	130	230	70	40	0.99	7.8	3.5	alive	no
42	65/M	COPD, OBSTRUCTIVE SLEEP APNEA,HTN, HYPOTHYROIDISM, METABOLIC SYNDROME	55	117	85	91	23	0.49	6.2	25	alive	smoking, alcohol
43	65/F	ACHALASIA CARDIA S/P PNEUMATIC DIALATATION, HTN	60	151	70	85	40	1.02	5.9	0.66	alive	no
44	65/F	TYPE 2 DM, HTN	23	120	77	60	40	0.65	7.7	3.6	alive	tobacco chewer
45	71/F	LEFT LOWER LIMB NON HEALING ULCER, ACUTE EXACERBATION OF COPD, TYPE 2DM,HTN	2.44	216	168	103	30	0.73	7.7	0.3	alive	alcohol. Tobacco
46	65/F	TYPE 2 DM, TRIGGER FINGER	25	141	120	94	41	0.75	6.3	3.12	alive	no
47	94/F	NSAIDS INDUCED GASTRITIS, HTN, OSTEOARTHRITIS	60	102	59	52	40	1	5.7	1.78	alive	no
48	65/M	TYPE 2 DM, HTN	25	145	234	92	38	1.17	6	1.96	alive	no
49	70/F	RHEUMATOID ARTHRITIS, IATROGENIC CUSHINGS SECONDARY TO STEROIDS, STEROID INDUCED HYPERGLYCEMIA,	59	213	119	168	40	0.59	6.6	0.61	alive	no
50	73/F	UNCONTROLLED TYPE 2 DM WITH MODERATE NPDR, HYPERTENSION WITH GRADE 2 HYPERTENSIVE RETINOPATHY WITH DYSTHYMIA	12.4	231	412	142	32	1	14.3	0.83	alive	no
51	81/F	TYPE 2DM HTN	36	124	100	80	40	1.02	8.9	1.89	alive	no
52	72/M	HYPERTENSIVE URGENCY, TYPE 2DM	22.45	109	114	80	42	0.98	7.5	3.33	alive	no
53	66/M	DIMORPHIC ANEMIA SECONDARY TO VITAMIN B 12 DEFIENCY	67	120	112	88	40	0.85	5.6	3.66	alive	no
54	68/F	IRON DEFIENCY ANEMIA, TYPE 2DM HTN	26.7	139	106	98	36	0.54	8	2.29	alive	no
55	77/F	HYPERPARATHYROIDISM SECONDARY TO SEVERE VIT D DEFICIENCY,HTN,TYPE 2 DM	56	120	100	78	35	1	6.8	4.09	alive	no
56	70/F	HYPOTHYROIDISM, HTN, TYPE 2DM	70	132	135	89	29	1.15	6.5	13.7	alive	no
57	74/M	COPD, TYPE 2 DM, HTN	66	86	79	46	32	1.02	7.7	1.5	alive	alcohol.smoking
58	76/M	RHO 52+ MIXED CONNECTIVE TISSUE DISORDER	34	120	197	76	36	1.04	6	2.38	alive	alcohol, smoking
59	80/M	TYPE 2DM, HTN	32	134	100	88	38	1	8	3.3	alive	no
60	77/F	HYPOTHYROIDISM, HTN	21	156	107	79	40	0.87	4.6	10	alive	no
61	67/M	TYE 2 DM , BPH	34	108	100	80	38	0.77	10	3.7	ALIVE	no
62	72/F	HTN, TYPE 2 DM	40	177	102	90	41	0.88	11	4	alive	no