

**To understand why coronary heart disease is more common in people with diabetes, we need to thoroughly investigate how oxidized LDL from various subgroups affects endothelium-dependent relaxation.**

XIONGZIZENG<sup>1</sup>, DR. SURIYAKALA<sup>2a</sup>

<sup>1</sup>PhD. Research Scholar in Medical Science, Lincoln University College, Malaysia

<sup>2</sup>Professor in Lincoln University College, Malaysia

Contact Details: <sup>a</sup>suriyakala@lincoln.edu.my

**Abstract**

There will be no Apolipoprotein B in this study, and the possibility of a second coronary ischemia event will not be taken into account because it is a case control study and the atorvastatin dosage will not

be increased to the maximum effective dose. The term "low density cholesterol" refers to a metric, but the low-density cholesterol particle will not be precisely measured.

**Keyword:** Cholesterol, Control Study, Effective Dose

**INTRODUCTION**

LDL cholesterol has long been known to play a role in determining the risk of heart attack and stroke. Atherogenic particles other than low-density lipoprotein (LDL) are well-documented currently. The importance of other apoprotein B-containing particles, such as VLDL and its remains, IDL, and Chylomicron remnants, cannot be understated. Non HDL cholesterol, a straightforward metric, captures this. A fasting specimen is not necessary. Subtracting total cholesterol from high-density lipoprotein (HDL) cholesterol Even if the LDL cholesterol in people using statins is lower, many of them still experience a second coronary or cerebral vascular incident. Patients with high triglyceride levels, poor HDL cholesterol, and other remnant lipoproteins in their lipid profile are at risk. Non HDL cholesterol, a phrase that encompasses all lipids other than HDL, is critical in determining the second level of risk for coronary or cerebral vascular events in people on statins. The purpose of the study will be to emphasise the usefulness of other lipid profile factors in reducing ischemia episodes.

Death from atherosclerosis and its complications is the leading cause of death in the globe at this time. Because of sedentary lifestyles and fast food culture, early-onset obesity is becoming more common. A growing number of people are taking statins as a result of public education. A reduction in cardiovascular disease, however, has not occurred. The purpose of this study will be to look at lipids other than LDL.

**TO UNDERSTAND WHY CORONARY HEART DISEASE IS MORE COMMON IN PEOPLE WITH DIABETES, WE NEED TO THOROUGHLY INVESTIGATE HOW OXIDIZED LDL FROM VARIOUS SUBGROUPS AFFECTS ENDOTHELIUM-DEPENDENT RELAXATION.**

---

## **LITERATURE REVIEW**

It was based on their medical history that CAD patients were identified. Measurements of height, weight, waist and hip circumference, blood pressures, and a lipid profile were taken for each participant. Age-standardized coronary artery disease anomalies were in the following order. Following non-HDL cholesterol and systolic blood pressure were abdominal obesity and non-HDL cholesterol.

The triglycerides, total cholesterol readings, low density lipoproteins, and HDL cholesterol had less relevance and a declining value of correlation in that sequence of importance. For the purposes of assessing coronary vascular risk, non-high density lipoprotein cholesterol serves as a screening tool for individuals with the metabolic syndrome.

Non-HDL cholesterol will be studied by Sigedel et al. to see whether it might be used as an indicator of CAD risk. There has been a long history of using total cholesterol measurements and low density lipoprotein cholesterol values as correlational indicators. Because non-HDL cholesterol may be computed by subtracting HDL cholesterol from total cholesterol, numerous studies have described this as an important and straightforward marker.

## **STATEMENT OF THE PROBLEM**

In lipid-lowering treatment, lowering low-density lipoprotein cholesterol levels is widely regarded as a means of reducing coronary artery disease risk. There are, of course, exceptions to this rule. A large number of people don't have elevated levels of LDL cholesterol. Non-high density lipoprotein cholesterol is becoming more widely accepted as a risk factor for cardiovascular disease. HDL cholesterol may be subtracted from total cholesterol to get non-HDL cholesterol, which comprises all the atherogenic lipoprotein particles' components of cholesterol. People with diabetes, for example, who have dyslipidemia (a condition characterised by low HDL cholesterol levels and high triglyceride levels) are more vulnerable to non HDL cholesterol. It is envisaged that the danger associated with triglyceride-rich particles will be captured by measuring non-HDL cholesterol. Cardiovascular disease mortality can be predicted by non-HDL Cholesterol, which has been proven to correspond with coronary artery disease severity. Non HDL Cholesterol treatment options include lifestyle changes and medication. Only rosuvastatin and simvastatin significantly lower non HDL cholesterol among statins as a group. Triglycerides and non-HDL Cholesterol are reduced by fibrates as a class of medications. LDL cholesterol is predicted using the FRIEDWALDS equation whereas non-HDL cholesterol is estimated using total cholesterol and HDL both of which are derived from direct measurements. Non-HDL cholesterol contains all of the lipid particles that contribute to cardiovascular disease. Since it has a better predictive value, it is widely accepted.

## **OBJECTIVE OF THE STUDY**

- The effect of L-arginine and BH4 on I/R-induced endothelial dysfunction in patients with type 2 diabetes and coronary artery disease.

## **Research Questions**

- In individuals with type 2 diabetes and coronary artery disease, what are the effects of L-arginine and BH4 on I/R-induced endothelial dysfunction?

**TO UNDERSTAND WHY CORONARY HEART DISEASE IS MORE COMMON IN PEOPLE WITH DIABETES, WE NEED TO THOROUGHLY INVESTIGATE HOW OXIDIZED LDL FROM VARIOUS SUBGROUPS AFFECTS ENDOTHELIUM-DEPENDENT RELAXATION.**

---

**RESEARCH METHODOLOGY**

Atorvastatin-treated patients with coronary artery disease who suffered an ischemic stroke within five years after the onset of the first coronary event will be included in this study.

Cases in Group 1 comprised patients who had been on regular atorvastatin medication 10 mg daily for more than one year and had a cerebrovascular event, such as stroke, within five years of their first coronary event, and had ECG or ECHO confirmation of coronary disease.

As a control group, we recruited another set of patients who had coronary artery disease and had been taking atorvastatin 10 mg for more than five years as an appropriate control. A normal CT brain scan and no prior history of transient ischemic episodes are required for these individuals to be diagnosed.

**RESEARCH DESIGN**

There will be a wide variety of ages involved, from 40 to 80, and both sexes will be represented. A committee within the institution authorised the research. Both modifiable and non-modifiable risk variables such as cigarette smoking, alcohol intake, hypertension, diabetes mellitus, and obesity (BMI) will be included in the study. The risk factors of smoking and drinking will be discovered through a thorough history-taking procedure. Diabetic mellitus and high blood pressure (DM and HT) risk factors will be discovered by medical history and normal lab tests and BP measurements.

Total cholesterol, HDL cholesterol, and triglycerides will be tested at 7 a.m. in the morning using a Hitachi 704 Analyser after an overnight fast of 10 hours. Low density lipoprotein Cholesterol will be estimated using the FRIEDWALD formula, which is widely recognised in the medical community. To compute non-HDL cholesterol, the total cholesterol will be divided by the HDL content. The ECG and ECHO confirmed the presence of coronary artery disease in both patients and controls.

Metabolic syndrome will be ruled out based on the results of all of the patient's standard blood tests. Excluded from the research will be those with increased renal parameters or abnormal liver function tests.

**DATA ANALYSIS**

Descriptive statistics, including frequency, mean, median, and standard deviation will be generated, and unpaired t tests will be used to identify statistically significant differences in means across groups for any variables with a normal distribution. The chi-squared test will be used to compare independent variables.

And in contrast to Study, "data are presented as median and quartiles instead of mean and standard deviation (SEM). Categorical information is typically represented numerically. Both sides will be considered significant if their respective p-values are less than 0.05. The effects of treatment on biochemical markers and FMD will be analysed using Wilcoxon's signed rank test (within- group comparison). Using clinical characteristics, laboratory data, and FMD as dependent variables, the Mann-Whitney rank sum test will be performed to compare groups. We will compare the means of the plethysmographic responses to different doses of Ach using the Wilcoxon signed-rank test to look for statistically significant differences. In the Spearman "The correlation between the variables will be analysed using rank. Different time points reveal

**TO UNDERSTAND WHY CORONARY HEART DISEASE IS MORE COMMON IN PEOPLE WITH DIABETES, WE NEED TO THOROUGHLY INVESTIGATE HOW OXIDIZED LDL FROM VARIOUS SUBGROUPS AFFECTS ENDOTHELIUM-DEPENDENT RELAXATION.**

---

distinct differences between the Ach and SNP dose response curves "In Study IV, a two-way ANOVA will be used to compare the effects of the two treatments on endpoints such FBF, MAP, and P-glucose after reperfusion. Based on the findings of Study I, we can infer that we will need about 22 patients in each group to detect a difference of 2% in FMD using 80% power and a two-tailed test at the 5% level. Due to the inherently speculative character of Studies, reliable power estimates cannot be made. This is how we plan to use historical data to make predictions. I count 59, 145, and 157. Based on the data, there might be a sizable distinction between groups of 10 and 12 "as evidenced by these results.

### **CONCLUSION**

Reducing triglycerides is more important than the statins' pleiotropic benefits of increasing macrovascular endothelial function, microvascular function, and reducing inflammatory activity in those with diabetes and coronary artery disease.

Those who suffer from diabetes "individuals with eosinophilic thrombocytopenia-1 (ET-1) deficiency have impaired cutaneous microcirculation. Diabetic microangiopathy may benefit from treatment that involves inhibiting ET receptors.

L-arginine and BH4 inhibit I/R-induced endothelial dysfunction in people with type 2 diabetes and CAD, as compared to placebo. Supplements including L-arginine and BH4 may help these patients deal with the "threat of I/R malfunction.

### **LIMITATIONS OF THE STUDY**

Due to the fact that this will be a case control study, the atorvastatin dosage will be not increased to the maximum effective dose. The term "low density cholesterol" refers to a metric. The low density cholesterol particle will be not precisely measured. There will be no Apolipoprotein B included in the research. No consideration will be given to the possibility of a second ischemia event inside the coronary system in this investigation. Even though the LDL Cholesterol levels in the research population will be low, they did not meet the threshold established by the ATP 3 recommendations. Despite the fact that non HDL cholesterol levels in controls will be low, they did not meet the ATP 3 criteria for non HDL cholesterol levels. There is no need for a placebo group in this study because it will be meant to examine the effects of the two treatment regimens on endothelial function. Furthermore, the current recommendations for statin therapy in individuals with established cardiovascular disease (CVD) and type 2 diabetes do not support the inclusion of a placebo group.

### **REFERENCES**

1. Amarenc Rosengar A, et al. "Anterior inferior cerebellar artery territory infarcts. Mechanisms and clinical features." *Archieve Neurology* 1993;50:154 -161
2. Andy Jones, Graham Bentham "EPIC-Norfolk prospective population"; MRC epidemiology unit: 2012
3. Badimon L, Badimon JJ, Turitto VT, Vallabhajosula S, Fuster V. mechanism of platelet aggregation using type one collagen to strengthen. A description of how trauma to vessel heals. Its impact on how blood cells move about, v WF& blood clotting and movement *Circulatory physiology*. 1988;78(6):1431–1442. [PMID: 3263902]

**TO UNDERSTAND WHY CORONARY HEART DISEASE IS MORE COMMON IN PEOPLE WITH DIABETES, WE NEED TO THOROUGHLY INVESTIGATE HOW OXIDIZED LDL FROM VARIOUS SUBGROUPS AFFECTS ENDOTHELIUM-DEPENDENT RELAXATION.**

4. Badimon L, Badimon JJ. "Procedures for thrombus formation large arteries in non parallel lines. Platelets aggregate and thrombus increases in size at the tip of the wall of arteries that are maximally affected." *J Clin Invest* 1989; 84(4):1134–1144. [PMID: 2794050]
5. Boekholdt SM, Arsenault BJ "Mora S, relationship between LDL cholesterol, non HDL cholesterol, and apolipoprotein B levels a meta analytical study indicating increase in coronary events.." *JAMA*. 2012 Mar 28;307(12):1302-9. doi: 10.1001/jama.2012.366.
6. Bogousslavsky J, Regli F. "infarcts due to anterior cerebral artery in the registry by Lausanne". *Archieve Neurology* 1990;47:144â€“150.
7. Chapman M.J "is there relevance in the effect on low density lipoprotein cholesterol by statins?" *European Heart Journal Supplements Volume 6: Issue supplC: 710* 2012.
8. Cholesterol in Adults "(Adult Treatment Panel III): Final Report.US Curr Atheroscler Rep. 2012" Apr; 14(2):130-4. doi: 10.1007/s11883-011-0224-x
9. Cholesterol in Adults "(Adult Treatment Panel III): Final Report.US Curr Atheroscler Rep. 2012" Apr;14(2):130-4. doi: 10.1007/s11883-011-0224-x
10. Elizabeth Barrett-Connor, MD "Sex Differences in Coronary Heart Disease" *CIRCULATION*;1997 95; 252-264.
11. "Expert Panel on Detection Evaluation, &Treatment of High Blood Fuster V. Cardiovascular disease and the United nations Millennium Development Goals: a significant need for analysis." *Nat Clin Pract Cardiovasc Med* 2006;3:401. [PMID: 16874332]
12. Garg PR, Kaabita 1 S, "a study on cholesterol" *Ann Human Biol*: 2012 Nov 30.
13. Havarkate F, Thomson SG JR, Pepys MB. Synthesis of CRP &increased incidence of heart problems in angina with and without enzyme elevations: "European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study" [NIH Publication No. 02-5215. September 2002.] *Circulation*. 2002;106:3143–3420
14. Hoseini K, Saedeghian S, Mamoudian M, Hamiidian R, Abasi A. "Family history of cardiovascular disease as a risk factor for coronary artery disease in adult offspring." *Monaaldi Archieve Chest Disease*. 2008 Jun;70(2):84-7.
15. Jeremy A. Kelley, MSN, RN, CRNP1 "CORONARY ARTERY DISEASE AND SMOKING CESSATION INTERVENTION" *Online Journal of Health Care*, vol. 9, no.2, Fall 2009
16. John C. M. Brust , Merritt's Neurology, "Cerebral Infarction"11th Edition, Lippincott Williams & [NIH Publication No. 02-5215. September 2002.] *Circulation*. 2002;106:3143–3420
17. KruthHS, "Sequestration of aggregated low density lipoproteins because of macrophages":*CurrOpinLipidol*: 2002; 13:483
18. Langile BL, "part in generation and progression of thrombus formation the circulatory system and atherothrombosis of heart". In: Fuuster V, "Atherothrombosis and Coronary Artery Disease", 2d edition Philadelphia: Lippincott Williams & Wilkins, 2005:561–568 : *Lancet* 1997:349:462–466.
19. Liby P, "Act local, act global: Inflammation and the multiplicity of "vulnerable" coronary plaques." *J Am. ColCardiology* 2005; 45:1600

**TO UNDERSTAND WHY CORONARY HEART DISEASE IS MORE COMMON IN PEOPLE WITH DIABETES, WE NEED TO THOROUGHLY INVESTIGATE HOW OXIDIZED LDL FROM VARIOUS SUBGROUPS AFFECTS ENDOTHELIUM-DEPENDENT RELAXATION.**

20. Meenakshi Sharma, "Premature Coronary Artery Disease in Indians and its Associated Risk Factors" *Vascular Health Risk Management*. 2005 September; 1(3): 217–225.
21. Michal G Marrmota, "alcohol and heart disease" *Int. J. Epidemiology*. (2001) 30 (4): 724-729.
22. Michel Miler, MD, "What Are the Effects of Statins on Triglycerides and What Are the Results of Major Outcomes Studies?" *JAMA*. 2012 Mar 28;307(12):1302-9.
23. Mulvihill ER, Jager J, "smooth muscle cells in atherosclerotic plaques have a distinct phenotype". *Arteriosclerosis Thrombosis Vascular Biology* 2004; 24:1283
24. Napoli C, D'Armiento FP, Mancini FP, et al. "mechanism of formation of streak of fat in embryonic aorta & which causes severe increase because of increase in cholesterol levels in the mother increase in concentration of LDL and how its metabolism by oxidation cause influx of monocyte at the site of very early atherogenic plaques", *J Clin Invest* 1997;100:2680–2690. [PMID: 9389731]
25. Nilson J, "Atherogenesis regulated by immune mechanisms: prospects for the development of preventive medicines". *Arteriosclerosis Thromb Vascular Biol* 2005;25:18–28. [PMID: 15514204.
26. Pasterrkamp G, "Expansive arterial remodeling: Location, location, location". *Arteriosclerosis Thromb Vascular Biol* 2004; 24:650.Pp. C58-C63.
27. Rana JS, "The role of non-HDL cholesterol in risk stratification for coronary artery disease" Elsevier Ireland Ltd Nov 16:2012.
28. Sigdel M, "study on cholesterol" *B.BMC Res Notes*. 2012 Nov 17;5(1):640.
29. Stamler, J, "do we have a grading between cholesterol levels and risk of dying prematurely? "Findings in 356,222 primary screenees of the "Multiple Risk Factor Intervention Trial (MRFIT)": *JAMA*, 1986, 256:2823–2828. [PMID: 3773199]
30. Susan A, "Use of Statin" *Lipid-Lowering Drugs Compared With Guidelines*" *JAMA* January 2001:Vol 161, No.1234.
31. The Expert Panel. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, & Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). The end report." *Circulation*, 2002, 106:3143–3421.
32. "Third report of the National Cholesterol Education Program (NCEP) :Tuzcu EM, "High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: Evidence from intravascular ultrasound." *Circulation* 2001; 103:2705.
33. Vaccaro JA KELLEY, *New England journal of medicine* 2012;2012:916816. doi: 0.1155/2012/916816.
34. Robert C. Byrd ,Sniderman AD , "Discordance analysis of Apolipoprotein B and non-high density lipoprotein cholesterol as markers of cardiovascular risk in the INTERHEART study *Atherosclerosis*." 2012 Dec;225(2):444-9.