Abstract Service

Lipids and Lp(a) levels and coronary artery disease in subjects with non-insulin-dependent diabetes mellitus.

O'Brien T, Nguyen TT, Harrison JM, Bailey KR, Dyck PJ, Kottke BA. Mayo Clin Proc 1994; 69 : 430-5.

Objective: To determine whether increased Lp(a) levels are associated with either non-insulin-dependent diabetes mellitus (NIDDM) or coronary artery disease (CAD) in patients with NIDDM and to examine the relationship between Lp(a) levels and glycaemic control.

Design: We conducted a cross-sectional study of subjects with NIDDM who were participants in the Rochester Diabetic Neuropathy Study and healthy control subjects from the population of Rochester, Minnesota.

Material and methods: Lipids and Lp(a) levels were compared in 227 subjects with NIDDM and 163 control subjects and among the subjects with NIDDM, in those with (N=96) and without (N=131) CAD. The correlation between Lp(a) levels and glycosylated haemoglobin was investigated.

Results: Subjects with NIDDM had higher triglyceride and lower high density lipoprotein-cholesterol levels than did control subjects. Subjects with NIDDM and CAD had higher total cholesterol, triglyceride and low-density lipoprotein-cholesterol levels and lower high-density lipoprotein-cholesterol levels than did subjects with NIDDM without CAD. Subjects with NIDDM had significantly higher Lp(a) levels than did control subjects, but subjects with NIDDM and CAD did not have significantly higher Lp(a) levels than did those without CAD. Among subjects with NIDDM, the level of Lp(a) was not significantly correlated with glycosylated haemoglobin.

Conclusion: Although subjects with NIDDM have higher Lp(a) levels than do control subjects, Lp(a) does not seem to be associated with CAD in subjects with NIDDM. In this study, no association was found between Lp(a) level and glycaemic control.

Incidence of renal failure in NIDDM. The Oklahoma Indian Diabetes Study.

Lee ET, Lee VS, Lu M, Lee JS, Russell D, Yeh J. Diabetes 1994; 43 ; 572-9.

The incidence of and risk factors for renal failure were determined in 912 Oklahoma Indians with non-insulin-dependent diabetes mellitus in a follow-up study conducted between 1987 and 1990. The incidence rate was 15.7/1,000 person-years after an average follow-up time of 10.2 years. Among those who had no qualitatively positive proteinuria at baseline, the incidence of renal failure was 10.3/1,000 person-years compared with 19.3- and 56.2/1,000 person-years, respectively, in those with slight and heavy proteinuria at baseline. Fasting plasma glucose (FPG) $\geq$ 11.1 mM (200 mg/dl) increased the risk of renal failure to 2.9-fold (95% confidence interval [CI] = 1.9-4.6) higher than a level < 7.8 mM (140 mg/dl) and twofold (95% CI = 1.4-3.1) higher than a level between 7.8 (140 mg/dl) and 11.1 mM (200 mg/dl). The hypertensive patient had twice the incidence of renal failure than the normotensive subject (rate ratio = 2.1, 95% CI = 1.4-3.0). Patients with a lower blood pressure under antihypertensive medication had a lower incidence of renal failure than those whose hypertension remained uncontrolled with or without use of medication. Significant independent risk factors for renal failure, identified from Cox's proportional hazards model, were duration of diabetes, FPG, age, hypertension and insulin use ($P < 0.05$). In patients without proteinuria at baseline, FPG and hypertension were significant predictors of renal failure as identified by multivariate analyses, whereas in patients who had proteinuria at baseline, insulin use was significant. Thus, hyperglycaemic and hypertension control are suggested strongly for diabetic Oklahoma Indians as potential strategies to prevent the development of renal failure.

Insulin treatment improves microalbuminuria and other cardiovascular risk factors in patients with Type 2 diabetes mellitus.

Lindstrom T, Olsson AG, Von Schenck H, Wallentin L, Arnqvist HJ. J Intern Med 1994; 235 : 253-61.

Objectives: Insulin treatment of patients with type 2 diabetes causes hyperinsulinaemia and improves glycaemic control. We have studied how this affects risk factors for cardiovascular disease.

Design: Patients with secondary failure to oral hypoglycaemic agents were studied whilst still taking oral agents and after insulin treatment for 8 weeks in an open study.

Setting: Department of Internal Medicine, University Hospital, Linkoping.

Subjects: Ten consecutive patients with Type 2 diabetes and secondary failure to oral hypoglycaemic agents.

Interventions: Switching oral treatment to insulin treatment.

Main outcome measures: Effect on several cardiovascular risk factors.

Results: Fasting and postprandial plasma insulin concentrations were increased by insulin treatment whereas C-peptide concentrations were lowered. HbA^{1c} was reduced from 8.9 ± 0.3% (mean ± SEM) to 6.3 ± 0.2% after 8 weeks. There was a weight gain of 2.8 ± 0.7 kg. Plasma concentrations of total and very low density lipoprotein (VLDL)-cholesterol, VLDL, low density lipoprotein and high density lipoprotein triglycerides were all reduced. The plasma concentration of apolipoprotein B was also lowered. Tissue plasminogen activator antigen measured after venous occlusion showed a significant reduction whilst plasminogen activator inhibitor 1 activity was 26.0 ±9.8 IU ml^{-1} on oral treatment and 18.2 ± 4.7 IU ml^{-1} on insulin treatment (*NS*). Albumin excretion in the urine was reduced and the percentage reduction correlated with the percentage lowering of the tissue plasminogen activator antigen concentration after venous occlusion but not with the percentage change of basal tissue plasminogen activator antigen concentration.

Conclusions: Insulin treatment of patients with Type 2 diabetes and secondary failure to oral hypoglycaemic agents causes hyperinsulinaemia and improves or has no unfavourable effect on several cardiovascular risk factors.

Felodipine therapy may not alter glucose and lipid metabolism in hypertensives. Felodipine Multicenter Prospective Study Group in Japan.

Shionoiri H, Takizawa T, Ohyama Y, Ishii J, Katayama S, Nagasawa T, Kitamoto K, Nagasawa K, Hariya Y, Sato R et al. Hypertension 1994; 23(1 Suppl): 1215-9.

The effects of long-term monotherapy with filodipine, a calcium antagonist, on blood pressure, glucose tolerance and serum lipid profiles were prospectively investigated in 51 hypertensive patients: 13 with normal glucose tolerance and 38 with glucose intolerance. The levels of plasma glucose, serum lipids and glycosylated haemoglobin A^{1c} were determined before and during long-term (7.5 ± 0.5 months; range, 6 to 9 months) therapy with felodipine. A 75-g oral glucose tolerance test was performed before and during long-term felodipine therapy. Significant decreases in both systolic and diastolic blood pressures in both patient groups were maintained during the therapy. Neither fasting nor post-glucose load venous plasma glucose levels were altered in either group of patients and no patients with normal glucose tolerance developed diabetes mellitus during the study,

Serum lipid levels did not change significantly in either group of patients except for significant decreases in high density lipoprotein-cholesterol and apolipoprotein A-1 in the group with normal glucose tolerance tests, but those changes remained within the normal range. Furthermore, neither serum lipid nor apolipoprotein levels were altered, even in patients with hypercholesterolaemia (total cholesterol levels > 5.69 mmol/l = 220 mg/dl). These results suggest that long-term therapy with felodipine may not alter glucose and lipid metabolism in hypertensive patients and felodipine appears to be useful as an antihypertensive agent for hypertensive patients with either dyslipidaemia or impaired glucose metabolism.

Augmentation of the synthesis of plasminogen activator inhibitor type-1 by precursors of insulin. A potential risk factor for vascular disease.

Nordt TK, Schneider DJ, Sobel BE. Circulation 1994; 89 : 321-30.

Background: Both vascular disease and elevated concentrations in plasma of plasminogen activator inhibitor type-1 (PAI-1) are prominent in patients with non-insulin-dependent diabetes mellitus (NIDDM). We and others have hypothesised that the increased PAI-1 may contribute to acceleration of atherosclerosis in this condition and in other states characterised by insulin resistance as well. Surprisingly, however, elevations of PAI-1 decrease when Type 2 diabetic patients are treated with exogenous insulin, as do circulating concentrations of the precursor of insulin, proinsulin, in plasma. Accordingly, the increased PAI-1 in patients with NIDDM may reflect effects of precursors of insulin rather than or in addition to those of insulin itself. To assess this possibility directly, this study was performed to identify potential direct effects of proinsulin and proinsulin split products on synthesis of PAI-1 in lever cells, thought to be the major source of circulating PAI-1 in vivo.

Methods and results: Help G2 cells (highly differentiated human hepatoma cells) were exposed to human proinsulin, des (31,32) proinsulin and des (64,65) proinsulin (split products of proinsulin) or C-peptide. Accumulation of PAI-1 in conditioned media increased in a time and concentration-depenent fashion in response to the two des-intermediates [3.3-fold with des(31,32) proinsulin and 4.5-fold with des (64,65) proinsulin]. C-peptide elicited no increase. Stimulation was transduced at least in part by the insulin receptor as shown by inhibition of stimulation by insulin receptor antibodies, mediated at the level of PAI-1 gene expression as shown by the 2.2 to 2.9-fold increases in steady state concentrations of PAI-1 mRNA and indicative of newly synthesized protein as shown by results in metabolic labeling experiments.

Conclusions: Our results are consistent with the hypothesis that precursors of insulin (proinsulin and proinsulin split products), known to be present in relatively high concentrations in plasma in patients with NIDDM and conditions characterised by insulin resistance, may directly stimulate PAI-1 synthesis, thereby attenuating fibrinolysis and accelerating atherogenesis.

MEDLINE (R) 1/95-10/95

Calcium antagonist antihypertensive treatment of non-insulin-dependent diabetics: efficacy and safety of lacidipine versus nifedipine SR.

Gulizia M, Valenti R, Platania F, D'Onofrio V, Rizzini P, Circo A. J Cardiovasc Pharmacol 1994; 23 suppl 5:S101-4.

Arterial hypertension is a chronic condition regarded as one of the main risk factors for development of coronary antherosclerosis. As dyslipidaemia and reduced glucose tolerance are also risk factors for coronary disease, it is considered important to use antihypertensive drugs having no negative effects on lipid and glucose metabolism when diabetic patients are treated for hypertension. Lacidipine, a new dihydropyridine-like calcium antagonist, has been shown in vivo and in vitro preclinical studies to possess potent, long-lasting antihypertensive activity. The present study compared the efficacy and safety of once-daily treatment with lacidipine versus nifedipine SR given twice-daily in non-insulin-dependent diabetic patients. Results have shown a similar efficacy of the two treatments: 6 months later, both drugs had reduced blood pressure values [lacidipine from 184.8/105.2 mm Hg to 144.4/87.1 mm Hg; nifedipine slow-release (SR) from 182.3/106.8 mm Hg to 143.6/89.4 mmHg]. However, lacidipine exhibited a lower incidence of adverse events (particularly ankle edema and tachycardia) than nifedipine SR. Finally, both treatments showed no negative effect on metabolic parameters (total cholesterol, high density lipoprotein-cholesterol, triglycerides and blood glucose).

LDL particle size in mildy hypertriglyceridaemic subjects: no relation to insulin resistance or diabetes.

Lahdenpera S, Sane T, Vuorinen Markkola H, Knudsen P, Taskinen MR. Atherosclerosis 1995; 113 : 227-36.

We examined 18 Type 2 diabetic and 19 non-diabetic subjects in order to determine the association between insulin resistance and LDL particle size distribution in mildly hypertriglyceridaemic and hyperinsulinaemic subjects with and with out Type 2 diabetes. Insulin sensitivity of the patients was characterized by their insulin-stimulated glucose uptake rate determined by euglycaemic clamp technique. LDL particle size distribution was determined by non-denaturing polyacrylamide gradient gel electrophoresis. Type 2 diabetic and non-diabetic subjects had closely similar serum lipid and lipoprotein concentrations as well as the mean particle diameters of the major LDL peak (246 ± 6 A and 244 ± 6 A respectively). To evaluate the effect of insulin resistance on LDL particle size the participants were categorized into two subgroups using the median of their insulin-stimulated glucose uptake rate (14.67 mumol/kg/min) as a cut-off point. Neither lipid and lipoprotein concentrations nor the LDL particle size distributions differed between the more insulin resistant group (nine diabetic and nine non-diabetic subjects) and less insulin resistant group (nine diabetic and ten non-diabetic subjects). LDL particle size was not associated with the insulin-stimulated glucose uptake rate or with the mean 24-h concentration of serum insulin. Mean 24-h concentration of serum triglycerides was the strongest discriminator for LDL particle size ($r=-0.44$, $p<0.01$). In conclusion, neither Type 2 diabetes nor insulin resistance seem to have any direct effect on LDL particle size in mildly hypertriglyceridaemic subjects. The fact that LDL particle size was associated with serum triglycerides indicates that the effect of diabetes and insulin resistance on LDL particle size could be explained by the effects of insulin resistance and/or hyperinsulinism on VLDL metabolism.

Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin and carotid arterial wall thickness: the ARIC study [Atherosclerosis Risk in Communities Study].

Ma J, Folsom AR, Melnick SL, Eckfeldt JH, Sharrett AR, Nabulsi AA, Hutchinson RG, Metcalf PA. J Clin Epidemiol 1995; 48 : 927-40.

The objective of this study was to examine the relationships of serum and dietary magnesium (Mg) with prevalent cardiovascular disease (CVD), hypertension, diabetes mellitus, fasting insulin and average carotid intimal-medial wall thickness measured by B-mode ultrasound. A cross-sectional design was used. The setting was the Atherosclerosis Risk in Communities (ARIC) Study in four US communities. A total of 15,248 participants took part, male and female, black and whit, aged 45-64 years. Fasting serum Mg, lipids, fasting glucose and insulin were measured; as was usual dietary intake by food frequency questionnaire and carotid intima-edia thickness by standardized B-mode ultrasound methods. The results showed that serum Mg levels and dietary Mg intake were both lower in blacks than whites. Mean serum Mg levels were significantly lower in participants with prevalent CVD, hypertension and diabetes than in those free of these

diseases. In participants without CVD, serum Mg levels were also inversely associated with fasting serum insulin, glucose, systolic blood pressure and smoking. Dietary Mg intake was inversely associated with fasting serum insulin, plasma high density lipoprotein-cholesterol, systolic and diastolic blood pressure. Adjusted for age, race, body mass index, smoking, hypertension, low density lipoprotein-cholesterol and field centre mean carotid wall thickness increased in women by 0.0118 mm (p=0.006) in diuretic users and 0.0048 mm (p=0.017) in non-users for each 0.1 mmol/l decrease in serum Mg level; the multivariate association in men was not significant. In conclusion, low serum and dietary Mg may be related to the etiologies of CVD, hypertension, diabetes and atherosclerosis.

Effect of intensive diabetes management on macrovascular events and risk factors in the Diabetes Control and Complications Trial.

Am J Cardiol 1995; 75 : 894-903.

The Diabetes Control and Complications Trial (DCCT), a multicentre, randomized, controlled clinical trial, demonstrated that intensive diabetes therapy delays the onset and slows the progression of retinopathy, nephropathy and neuropathy in patients with insulin-dependent diabetes mellitus. This study presents the effect of intensive therapy on atherosclerosis-related events and associated risk factors. Patients (n=1,441) between the ages of 13 and 39 years with insulin-dependent diabetes mellitus were randomly assigned to conventional or intensive diabetes treatment. The patients were free of cardiovascular disease at baseline. Patients with hypertension, hypercholesterolaemia, or obesity were excluded. Average length of follow-up was 6.5 years (range 3.5 to 9). The study used standardized definitions of macrovascular events, verification of such events and central laboratories for determination of lipids and the grading of electrocardiograms. The number of combined major macrovascular events was almost twice as high in the conventionally treated group (40 events) as in the intensive-treatment group (23 events), although the differences were not statistically significant (p=0.08). There were no differences in the cumulative incidence of hypertension. Mean total serum cholesterol, calculated low density lipoprotein-cholesterol and triglycerides were significantly reduced in the intensive-treatment group (p < or = 0.01), as was the development of low density lipoprotein-cholesterol levels > 160 mg/dl. Weight gain was significantly increased in the intensive-treatment group (p < 0.001). There were no differences in cigarette smoking habits, consumption of alcohol or aspirin use between treatment groups. The reduction in some, but not all, cardiovascular risk factors suggests a potential beneficial effect of intensive therapy on macrovascular disease in insulin-dependent-diabetes mellitus.

Prospective study of lipoprotein(a) as a risk factor for atherosclerotic cardiovascular disease in patients with diabetes.

Hiraga T, Kobayashi T, Okubo M, Nakanishi K, Sugimoto T,Ohashi Y, Murase T. Diabetes Care 1995; 18 : 241-4.

Objective: To assess whether lipoprotein(a) [Lp(a)] is a risk factor for atherosclerotic cardiovascular disease in diabetes.

Research design and methods: We studied 221 patients with non-insulin-dependent diabetes mellitus (NIDDM) without diabetic complications who were followed for 2.2 to 3.1 years. Their serum Lp(a) levels were semi-quantified by a rapid electrophoretic method that accurately discriminates high from low serum Lp(a) at the 20 mg/dl level.

Results: Seven of 105 diabetic patients with a high serum Lp(a) experienced a clinical event related to atherosclerotic cardiovascular disease. This incidence was significantly higher than that of the 110 diabetic patients with a low serum Lp(a). The logistic regression analysis revealed that Lp(a) was an independent risk factor for the event.

Conclusions: Lp(a) is a significant risk factor for atherosclerotic cardiovascular disease in NIDDM.

Subgroup analyses of the major clinical endpoints in the Programme on the Surgical Control of the hyperlipidaemias (POSCH): overall mortality, atherosclerotic coronary heart disease (ACHD) mortality and ACHD mortality or myocardial infarction.

Matts JP, Buchwald H, Fitch LL, Campos CT, Varco RL, Campbell GS, Pearce MB, Yellin AE, Smink RD Jr, Sawin HS Jr et al. J Clin Epidemiol 1995; 48 : 389-405.

The Programme on the Surgical Control of the Hyperlipidaemias (POSCH) was a secondary atherosclerosis intervention trial employing partial ileal bypass surgery as the intervention modality. For this report, we analysed 105 subgroups in 35 variables in POSCH, chosen pre-dominantly for their potential relationship to the risk of atherosclerotic coronary heart disease (ACHD). We defined potential differential effects as those with: (1) an absolute z-value $\geq$ 2.0 for the subgroup, if the absolute z-value for the overall effect was < 2.0 and (2) an absolute z-value $\geq$ 3.0 for the subgroup and a relative risk < or =0.5, if the absolute z-value for the overall effect was $\geq$ 2.0. For each of three major POSCH endpoints of overall mortality, ACHD mortality and ACHD mortality or confirmed non-fatal myocardial infarction, we found seven subgroups with a differential risk reduction in the surgery group as compared to the control group. Allowing for identical subgroups for more than one endpoint, there were 13 individual subgroups with differential effects. Of these, 7 demonstrated internal consistency across endpoints and 5 of these 7 displaced external consistency with known ACHD risk factors and for biological plausibility: triglyceride concentration $\geq$ 200 mg/dl; cigarette smoking; overt or borderline diabetes mellitus; a Minnesota ECG Q-QS code of 1-1; and obesity. A greater risk reduction, in comparison to the overall treatment effect, by the reduction of a single risk factor, hypercholesterolaemia, in patients with at least two major ACHD risk factors was a provocative and an hypothesis-generating outcome of this analysis. The clinical implications of this finding may lead to more aggressive cholesterol intervention in patients with multiple ACHD risk factors.

Asymptomatic coronary artery disease in diabetes: relation to common risk factors, lipoproteins, apoproteins and apo E polymorphism.

Koistinen MJ, Huikuri HV, Korhonen UR, Linnaluoto MK, Kuusi T, Takkunen JT, Taskinen MR. Acta Diabetol 1994; 31 : 210-4.

The risk factors for asymptomatic coronary artery disease (CAD) were examined in 138 diabetic patients. Following non-invasive screening examinations (exercise electrocardiography, dynamic thallium scintigraphy, 24-h electrocardiographic recording), CAD was confirmed angiographically in 21 symptom-free diabetic subjects with an ischaemic finding in at least one of the non-invasive tests. The prevalence of asymptomatic CAD in this cohort of diabetic patients was 21/132 (16%), which may be an underestimation because 6 patients refused angiography. Risk factors (age, diabetes, smoking, hypertension, serum lipoproteins, apoproteins and apo E phenotypes) were analysed according to the presence or absence of CAD. Multivariate logistic stepwise analysis did not show any definite changes of serum lipids, lipoproteins and apoproteins in Type 1 (n=72) and Type 2 (n=66) diabetic patients with or without asymptomatic CAD. The only factors associated with asymptomatic CAD were the duration of diabetes (p < 0.005) and the age of the patient (p < 0.05). These results suggest that in diabetic patients the major risk factor for premature coronary atherosclerosis is diabetes itself. Assessment of other risk factors does not seem to define any subgroup with asymptomatic CAD.

Non-insulin-dependent diabetes mellitus and fasting glucose and insulin concentrations are associated with arterial

stiffness indexes. The ARIC Study. Atherosclerosis Risk in Communities Study.

Salomaa V, Riley W, Kark JD, Nardo C, Folsom AR. Circulation 1995; 91 : 1432-43.

Background: Cardiovascular diseases are the most common cause of disability and death among subjects with non-insulin-dependent diabetes mellitus (NIDDM). The atherosclerotic process begins during the pre-diabetic phase characterised by impaired glucose tolerance, hyperinsulinaemia and insulin resistance. In vitro studies have suggested that glucose and insulin can substantially alter the atructure and function of the arterial wall and affect the development of atherosclerosis.

Methods and results: We performed a cross-sectional study of the relation of arterial stiffness indexes with glucose tolerance and serum insulin concentrations. Several indexes of common carotid artery stiffness were assessed with non-invasive ultrasound methods in a biracial sample of 4701 men and women, 45 to 64 years of age in the Atherosclerosis Risk in Communities (ARIC) Study. Arterial compliance (AC), stiffness index (SI), pressure-strain elastic modulus (Ep) and young's elastic modulus (YEM) were calculated. YEM includes wall (intima-media) thickness and thus gives an estimate of arterial stiffness controlling for wall thickness. All indexes of arterial stiffness were higher with increasing concentrations of fasting glucose. This finding was consistent in both black and white examines and in both sexes. A 25% increase in fasting glucose (approximately 1 SD) was associated in non-diabetic white men with a 5.8% (95% CI,-9.6% to -1.9%; P=.004) decrease in AC and increases of 5.8% (95%CI, 2.0% to 9.7%;P=.002) in SI, 11.3% (95% CI, 6.9% to 15.9%; P < .001) in Ep and 11.2% (95% CI, 6.2% to 16.6%; P < .001) in YEM. In non-diabetic white women, the corresponding predicted changes were a decrease of 15.0% (95% CI, -18.2% to -11.7%; P < .001) in AC and increases of 16.6% (95% CI, 12.5% to 20.8%; P < .001) in SI, 23.2% (95% CI, 18.4% to 28.2%; P < .001) in Ep and 19.2% (95% CI, 14.0% to 24.7%; P < .001) in YEM. Glucose and insulin contributed synergistically to the increase in stiffness indexes. Insulin and triglycerides also had a synergistic association with stiffness indexes.

Conclusions: Our findings are compatible with the view that persons with NIDDM or borderline glucose intolerance have stiffer arteries than their counterparts with normal glucose tolerance and that the decreased elasticity is independent of artery wall thickness. The joint effect of elevated glucose, insulin and triglycerides can have a considerable impact on arterial stiffness and play an important role in the early pathophysiology of macrovascular disease in NIDDM.

Lipoprotein (a) and other risk factors in patients with non-insulin-dependent diabetes mellitus.

Martinez Triguero-ML, Salvador A, Samper MJ, Almela M, Vega L, Mora A, Martinez Diago V. Coron Artery Dis 1994; 5 : 755-60.

BACKGROUND: Studies have established a relationship between lipoprotein (a) [Lp(a)] levels and cardiovascular disease, but few have studied Lp(a) in patients with non-insulin-dependent diabetes mellitus (NIDDM).

Methods: We determined Lp(a) concentrations, levels of glycated haemoglobin and the personal and family history of atherosclerosis in 88 patients with NIDDM (53 men and 35 women; age 33-70 years) and 90 age and sex-matched controls. Twenty-three patients with NIDDM had cardiovascular disease (CVD group) and 65 did not (non-CVD group).

Results: Lp(a) levels were higher in CVD than non-CVD patients ($p < 0.01$). Triglyceride levels negatively correlated with Lp(a) ($r=-0.51$, $p < 0.05$), independently of the metabolic control of diabetes. Patients with poor metabolic control (glycated haemoglobin > 7.5%) had higher Lp(a) levels than the control group ($p < 0.05$). Lp(a) levels were higher than 0.30 milligram in 11% of patients without CVD and 55% of those with CVD ($p < 0.05$). Cluster analysis showed that Lp(a) as well as total cholesterol, triglycerides, apolipoprotein B100 and age were independently related to CVD in patients with NIDDM ($p < 0.001$ for triglycerides and $p < 0.05$ for the other variables).

Conclusions: Lp(a) levels can be considered an independent risk factor for the development of atherosclerosis in NIDDM.

Atherosclerotic risk factors for peripheral vascular disease in non-insulin-dependent diabetic patients.

Tseng CH, Chong CK, Lin BJ, Chen CJ, Tai TY. J Formos Med Assoc 1994; 93 : 663-7.

The purpose of this study was to evaluate risk factors associated with peripheral vascular disease (PVD) in patients with non-insulin-dependent diabetes mellitus (NIDDM). A group of 100 patients (50 men and 50 women) aged 50 years or over with PVD and another group of 200 age-sex-matched patients (100 men and 100 women) without PVD were studied. The mean ± standard error of ages for subjects with and without PVD were 60.8 ± 0.6 years and 59.7 ± 0.3 years respectively. Doppler ultrasound was used to measure the systolic pressures of the brachial, posterior tibial and dorsal pedal arteries bilaterally. The diagnosis of PVD was made by an ankle-brachial index (ABI) < 0.90 and the diagnosis of non-PVD by an ABI >1.00. The association of PVD with diabetic duration, body mass index (BMI), cerebral infarction (CI), coronary heart disease (CHD), proteinuria, diabetic retinopathy, neuropathy, hypertension and cigarette smoking was evaluated. In addition, biochemical data including fasting plasma glucose, haemoglobin (HD) Alc, cholesterol, triacylglycerol, high and low density lipoprotein-cholesterol, uric acid, blood urea nitrogen (BUN) and creatinine (Cr) were studied. In univariate analysis, PVD was associated with an increased level of systolic blood pressure (SBP), BUN and Cr, cigarette smoking, CI, CHD, proteinuria and retinopathy. In stepwise logistic regression analysis, the level of SBP, cigarette smoking and CI remained statistically significant. The log odds of PVD could be expressed as: -2.834 + 0.013 (SBP in mmHg) + 0.577 (cigarette smoking) + 1.320 (CI). PVD is the result of aggregation of atherosclerotic risk factors; among those factors noted in this study, SBP, cigarette smoking and CI are important.