Prevalence of Hypertension, Dyslipidemia, and Dyslipidemic Hypertension

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Background. It has been proposed that dyslipidemic hypertension is part of a distinct metabolic syndrome related to insulin resistance. This paper describes the prevalence and cross-sectional relations of dyslipidemic hypertension in a population-based sample of men and women.

Methods. In two southeastern New England communities, 11,199 randomly selected participants were evaluated as part of a cross-sectional surveillance program of coronary heart disease risk factors between 1981 and 1990.

Results. The frequency of dyslipidemia was 38% and of hypertension was 26.5%; the conjoint frequency (dyslipidemic hypertension) was 15.0%, which is 1.49 times the expected value if the two diseases were independent $P < .05$). Using a discrete multivariate model, dyslipidemia and hypertension were associated with sex, obesity, and diabetes mellitus. The excess association of dyslipidemic hypertension, compared with individual effects of dyslipidemia and hypertension, was not related to these factors.

Conclusions. This study suggests that dyslipidemic hypertension is common but may not be a unique entity associated with a distinct metabolic syndrome.

Key words. Hypertension; hypercholesterolemia; coronary disease; risk factors; cross-sectional studies.
(*J Fam Pract 1993; 36:17-23*)

While it is well accepted that low-density lipoprotein (LDL) cholesterol is involved in the pathogenesis of atherosclerosis and is a risk factor for cardiovascular disease,[1,2] the role of triglyceride disorders is less clear.[3] Familial combined hyperlipidemia[4,5] and type III dysbetalipoproteinemia[6] are lipid disorders associated with coronary heart disease that present as hypertriglyceridemia in many subjects. However, familial hypertriglyceridemia, which has the same degree of elevated triglycerides, demonstrates no increased association with cardiovascular disease.[7] Isolated low levels of high-density lipoprotein (HDL) cholesterol is a common lipid disorder and is a well-documented risk factor for early coronary artery disease.[3,7] Subjects on vegetarian and low-fat diets and those with certain inherited syndromes, however, both of whom have low HDL cholesterol,[3] have not shown an increased risk of coronary heart disease.

The term *dyslipidemia* has been coined to define subjects with either isolated elevated triglycerides, low HDL cholesterol or elevated LDL cholesterol, or a combination of the above that are associated with an increased incidence of coronary heart disease. The most widely recognized dyslipidemic syndromes associated with coronary heart disease are familial-combined hyperlipidemia and isolated low HDL cholesterol.[8] Atherogenic phenotype,[9] small, dense LDL cholesterol,[10–12] and apolipoprotein B excess[13–15] also have been used to describe dyslipidemic syndromes.

Submitted, revised, October 18, 1993.

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ISSN 0094-3509

Several investigators have noted increased frequency of dyslipidemia with familial hypertension and obesity.[4–5,9–14] Studies of diabetic and obese subjects have demonstrated a link between hypertension, insulin resistance, and body fat distribution.[16–22] Reaven[17,18] and Krauss[16] postulate that this interrelationship of elevated circulating triglycerides, low HDL cholesterol, central body fat distribution, diabetes mellitus, and blood pressure can be explained by insulin resistance, which they group as Syndrome X.

According to the investigators, Syndrome X consists of resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, increased very low density lipoprotein (VLDL), decreased HDL cholesterol, and hypertension.[16–18] Further evidence supporting the existence of Syndrome X has been presented by Haffner,[19] who adopted the term *insulin resistance syndrome*. In Mexican Americans and non-Hispanic whites, he showed that fasting insulin levels predicted the onset of hypertension, low HDL cholesterol, elevated triglycerides, and non–insulin-dependent diabetes mellitus (NIDDM) over the next 8 years. The same relation of insulin resistance to dyslipidemia and hypertension has been found in several cross-sectional studies[23–26] but not in others.[27–29]

Selby et al[30] also have provided evidence of Syndrome X in a study of 1028 male twins by demonstrating an increased prevalence of obesity and glucose intolerance in male twins with dyslipidemic hypertension. Importantly, this study demonstrated that twins with dyslipidemic hypertension also had increased mortality compared with twins with dyslipidemia only and twins with hypertension only. Since dysplipidemia and hypertension are both common entities associated with cardiovascular disease, it is not surprising that each is linked to early mortality. That the two conditions combined carry a greater risk of death than either individually, and that the two entities might be causally linked by insulin resistance, suggests an important clinical entity that needs further exploration.

If dyslipidemic hypertension is causally linked to insulin resistance, as suggested by Reaven,[17–18] Krauss,[16] and Haffner,[19] treatment of hypertension or dyslipidemia might differ from standard therapy. Treating hypertension would not focus on antihypertensive agents, and treating dyslipidemia would not focus on lipid-altering agents. Rather, treatment would concentrate on reversing insulin resistance with exercise, weight loss, and perhaps upregulation of insulin receptors with metaformin or other pharmacologic agents.

Williams et al[31] have demonstrated a familial association of dyslipidemia and hypertension in 58 Utah families at high risk for coronary heart disease (CHD), and labeled this entity *familial dyslipidemic hypertension*. They calculated that the prevalence of familial dyslipidemic hypertension would be 12% of all patients with essential hypertension.

The research reported here focuses on these questions:

1. What is the prevalence of dyslipidemic hypertension in a population-based sample?
2. Is the prevalence of dyslipidemic hypertension more than what we would expect by chance alone based on the prevalence of two common entities, dyslipidemia and hypertension?
3. What are the influences of sex, smoking, obesity, and diabetes mellitus on dyslipidemic hypertension contrasted with the influences on dyslipidemia and hypertension alone?
4. Are these cross-sectional relationships consistent with a distinct metabolic disorder, Syndrome X, or insulin resistance syndrome?

Methods

The data analyzed in this study were derived from five cross-sectional surveys, conducted as part of the evaluation activities of the Pawtucket Heart Health Program,[32–34] in two communities in southeastern New England. The Pawtucket Heart Health Program is a community-based intervention project funded by the National Heart, Lung, and Blood Institute, the purpose of which is to reduce elevated levels of risk factors for cardiovascular disease.

From 1981 to 1990, five successive and independent random samples of households were chosen. A single age-eligible person was then randomly selected from each household. Interviewers made home visits to collect sociodemographic information and physiological measurements on 13,186 persons aged 18 through 64 years. Blood samples were drawn without regard to time of prior food ingestion. Since subjects with missing lipid or blood pressure measurements were excluded, 11,199 subjects comprised the final sample evaluated for analysis.

Physiologic Measurements

Lipids. Serum cholesterol, HDL cholesterol, and triglycerides were measured on blood samples drawn and were analyzed at a standardized laboratory of the Centers for Disease Control and Prevention using enzymatic methods. Since blood samples were drawn at the time of home visits, only 15.9% of the respondents had fasted for at least 4 hours.

Blood pressure. Two blood pressure measurements were taken 20 minutes apart on the right arm using a mercury sphygmomanometer with an appropriate cuff size. The second measurements were used for ascertaining the systolic and diastolic (fifth phase) readings.

Height. Height was measured following protocol recommended by the Centers for Disease Control.[33]

Weight. Body weight was measured on a portable scale with outer garments and shoes removed. Body mass index (BMI) was calculated using the following formula: BMI = weight/(height)^2 in kg/m^2.

Definitions. NIDDM was defined by self-report of physician diagnosis or by use of oral hypoglycemic agents. Glucose levels were not measured and therefore are not used in our definition of diabetes mellitus.

Dyslipidemia was defined using sex-specific percentiles based on fasting specimens. Triglycerides >90th percentile, HDL <10th percentile, or LDL cholesterol >75th percentile were used to define dyslipidemia. For men, the values used for dyslipidemia were: triglycerides >307 mg/dL, HDL cholesterol <32 mg/dL, and LDL cholesterol >154 mg/dL. For women, the values used to define dyslipidemia were: triglycerides >222 mg/dL, HDL <37 mg/dL and LDL cholesterol >150 mg/dL.

Hypertension was defined as a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg, or use of blood pressure medication. Obesity was defined using the National Health and Nutrition Examination Survey (NHANES)[35] criteria for overweight as BMI values of >27.8 kg/m^2 for men and >27.3 kg/m^2 for women.[34] Medication use was determined by self-report and validated by trained interviewers, who recorded the name of the medication directly from the respondents' prescription bottles.

Current cigarette smoking was determined by self-report and validated by serum cotinine levels. Sedentary lifestyle was defined by self-report of less than once-a-week frequency of either aerobic exercise or regular physical activity such as brisk walking, jogging, or bicycling sufficient to work up a sweat.

Statistical Methods

Differences among mean levels of coronary heart disease risk factors and the frequency of demographic factors between dyslipidemic and hypertensive categories were evaluated by analysis of variance and chi-square tests, respectively. The data also were analyzed by standard methods of discrete multivariate analysis using a generalized linear model.[36] Three response variables associated with the overall odds of dyslipidemia, hypertension, and the excess odds of hypertension attributable to dyslipidemia were calculated. Four binary predictors (sex, overweight, diabetes, and smoking) were modeled with the analyses stratified by age. Binary covariates including use of beta blockers, diuretics, insulin, and lipid-lowering drugs were added to the model to control for possible confounding. Ninety-five percent confidence intervals were calculated for the binary predictors using standard methods, ie, $e^{b \pm 1.96\ SE}$. The model was fitted by generalized least-squares using the Categorical Data Modeling procedure of the SAS Institute.[37] Goodness-of-fit was assessed by the residual chi-squared statistic. Individual terms were tested for significance by the Wald chi-squared statistic.

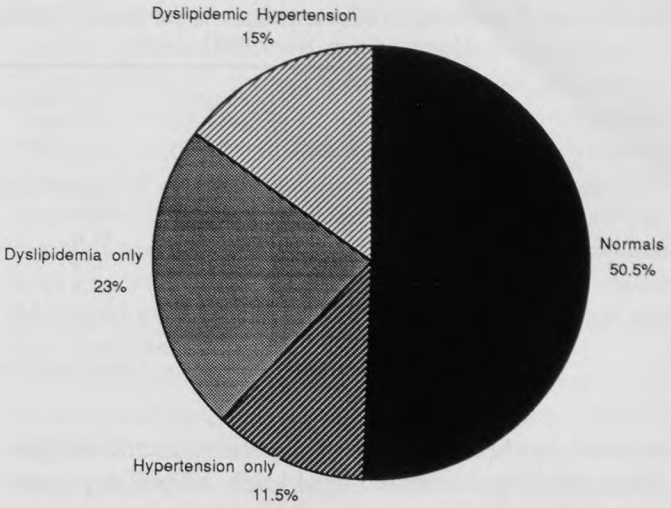

Figure. Percentage of dyslipidemic hypertension in two southeastern New England communities from 1981 to 1989.

Results

The figure shows the frequency of dyslipidemia only, hypertension only, and dyslipidemic hypertension only in our population-based sample. As shown, 23% of the sample had dyslipidemia only, 11.5% were hypertensive only, and 15% had dyslipidemic hypertension. The independent association of dyslipidemia with or without hypertension (38%) and hypertension with or without dyslipidemia (26.5%) would give an expected frequency of 10.1% for dyslipidemic hypertension. Thus, the frequency of 15% for dyslipidemic hypertension was 1.49 times greater than expected, a statistically significant difference ($P < .05$). Of hypertensive subjects, 56.5% have dyslipidemia. Of dyslipidemic subjects, 39.4% also have hypertension.

Table 1 identifies the descriptive characteristics of the entire sample (N = 11,199) and of individuals in each of four categories: dyslipidemic hypertension, dyslipidemia only, hypertension only, and normal. As

Table 1. Characteristics of the Study Population in Two Southeastern New England Communities, from 1981–1989

Characteristic	Dyslipidemic Hypertension (n = 1675)	Dyslipidemia Only (n = 2577)	Hypertension Only (n = 1290)	Normal (n = 5657)	Total (N = 11,199)
Age (y)*	51.6 ± 10.8	41.2 ± 13.0	46.2 ± 13.2	33.6 ± 11.3	39.5 ± 13.6
Male, %	48.8	42.2	61.0	38.6	43.5
Obesity, %	60.7	41.6	44.9	21.0	34.4
NIDDM, %	13.4	6.4	7.5	3.5	6.1
Sedentary, %	61.1	57.5	55.7	50.2	54.2
BMI (kg/m^2)*	29.6 ± 5.6	27.2 ± 5.0	27.9 ± 5.6	24.8 ± 4.6	26.4 ± 5.3

**Values are means ± standard deviations.*
NIDDM denotes non–insulin-dependent diabetes mellitus; BMI, body mass index.

expected by the definitions of hypertension and dyslipidemia, blood pressure and lipid levels differed appropriately among the groups. The dyslipidemic-hypertensive and hypertensive-only subjects were older, and the hypertensive-only group was predominantly male. All three groups (dyslipidemic hypertension, dyslipidemia only, hypertension only) were more likely to be obese and had a greater frequency of NIDDM than normal subjects. Smoking status also appeared to differ among the groups.

To better understand the unique associations of dyslipidemic hypertension as opposed to the associations of dyslipidemia and hypertension individually, the odds ratio for dyslipidemia, for hypertension, and for the excess odds of dyslipidemic hypertension were calculated using generalized linear models. The influence of sex, obesity, smoking, and diabetes mellitus on dyslipidemic hypertension was contrasted with the influence of those factors on dyslipidemia and hypertension individually for two age groups, consisting of persons between the ages of 18 and 49 years and those between 50 and 64 years (Table 2). To control for the effect of beta blockers, diuretics, insulin, and cholesterol-lowering medications on the proposed relationships, they were added as covariates to the model.

Sex differences were found in the odds of dyslipidemia and hypertension but not the excess odds of dyslipidemic hypertension. For the younger group, men were more likely to have dyslipidemia or hypertension than women. In the older group, women were more likely to have dyslipidemia, whereas men had higher odds of hypertension.

Overweight was associated with increased odds of dyslipidemia and hypertension but not with the excess odds of dyslipidemic hypertension in both age groups. The odds of dyslipidemia and hypertension associated with overweight, however, were much higher in the younger group.

Smoking was associated with increased odds of dyslipidemia in the younger group but not in the older group. Smoking was not associated with hypertension or excess odds of dyslipidemic hypertension in either age group.

NIDDM in the younger group was associated with increased odds of dyslipidemia and hypertension but not

Table 2. Influence of Sex, Overweight, Smoking, and Diabetes Mellitus on Dyslipidemic Hypertension, Contrasted with Influences on Dyslipidemia and Hypertension Independently*

Predictor	Form of Ratio	Odds Ratio (95% Confidence Interval)		
		Odds of Dyslipidemia	Odds of Hypertension	Excess Odds of Dyslipidemic Hypertension
Patients 18–49 years of age				
Sex	Female:male	0.72† (0.65–1.05)	0.33† (0.29–0.38)	1.20 (0.90–1.60)
Overweight	Overweight:not overweight	2.90† (2.61–3.21)	2.61† (2.30–2.97)	0.88 (0.67–1.15)
Smoking	Smoking:nonsmoking	1.56† (1.44–1.73)	1.01 (0.90–1.16)	1.05 (0.79–1.38)
NIDDM	Diabetic:not diabetic	1.82† (1.45–2.27)	1.69† (1.29–2.20)	1.27 (0.71–2.25)
Patients 50–64 years of age				
Sex	Female:male	1.50† (1.31–1.72)	0.72† (0.63–0.84)	1.14 (0.84–1.55)
Overweight	Overweight:not overweight	1.57† (1.36–1.80)	1.60† (1.39–1.85)	0.85 (0.63–1.16)
Smoking	Smoking:nonsmoking	1.11 (0.96–1.28)	0.90 (0.77–1.05)	0.78 (0.56–1.07)
NIDDM	Diabetic:not diabetic	0.99 (0.80–1.22)	0.93 (0.75–1.17)	0.97 (0.59–1.58)

**Adjusted for sex, overweight, smoking, diabetes mellitus, use of insulin, beta blockers, and diuretics and cholesterol-lowering medications.*
†P < .05.
NIDDM denotes non–insulin-dependent diabetes mellitus.

the excess odds of dyslipidemic hypertension. No significant relation was found in the older group between NIDDM and dyslipidemic hypertension or the excess odds of dyslipidemic hypertension.

Discussion

The prevalence of dyslipidemic hypertension, based on our definitions, was 15%, which, coupled with the fact that 56.5% of the hypertensives in our sample had this syndrome, suggests that it occurs frequently. Williams et al[8] calculated that familial dyslipidemic hypertension would occur in 12% of subjects with essential hypertension. Our study demonstrated four times the frequency calculated by Williams and colleagues, which can probably be attributed to the contrast between the small number of families at high risk for CHD used by Williams et al in evaluating familial dyslipidemic hypertension vs the representative community sample on which we based our estimates of prevalence.

Although it could be argued that the definitions of dyslipidemia and hypertension used in this study are arbitrary, they are consistent with other published studies. In the NHANES study,[38] the prevalence of hypertension was 41% in white men and 32% in white women when the same definition of hypertension was applied as that in our study. Dyslipidemia (defined as the top 25th percentile of LDL cholesterol, the top 10th percentile of triglycerides, or the lowest 10th percentile for HDL cholesterol) could represent 45% of the population if the lipid fractions were independent. The prevalence of dyslipidemia in this study (38%) suggests that the lipid fractions are not independent, which is consistent with the known role of HDL cholesterol in triglyceride metabolism. Although the combined prevalence of dyslipidemia and hypertension (49.5%) may seem high, it is not unreasonable, considering that 50% of the population will develop CHD.

Dyslipidemic hypertension was found in this study with a prevalence 1.49 times the expected value of the frequency of dyslipidemia and hypertension acting independently. Other investigators have found that dyslipidemia was two to four times more frequent than expected in subjects with familial hypertension, which is consistent with our findings.

Although cross-sectional studies are limited in their ability to define causal relationships, they do allow associations found in highly selected clinical studies to be tested in a larger population relatively free of selection bias. Therefore, in this large cross-sectional study, we evaluated the independent influences of sex, smoking, obesity, and NIDDM on dyslipidemia, hypertension, and the excess association of dyslipidemic hypertension using a discrete multivariate model, which controlled for the potentially confounding effects of insulin, beta blockers, cholesterol-lowering medications, and diuretics. Multiple studies have demonstrated the association of obesity and diabetes mellitus with dyslipidemia and hypertension,[19–26] but none to our knowledge have attempted to discern whether these factors were associated with the interaction of dyslipidemia and hypertension compared with the individual effects of dyslipidemia and hypertension.

Our study demonstrated that both dyslipidemia and hypertension were associated with sex, obesity, and diabetes mellitus, and that their association varied somewhat by age. However, the excess association of dyslipidemic hypertension was not related to these factors. This finding suggests that dyslipidemic hypertension as a unique interaction may not be related to physiologic states associated with insulin resistance and brings into question the unique role dyslipidemic hypertension plays in human disease other than the individual effects of dyslipidemia and hypertension alone. This does not rule out an important role for familial dyslipidemic hypertension, which is only a subgroup of the general population with dyslipidemic hypertension.

Several cautions should be noted in interpreting the present study. First, the lipid determinations used to define dyslipidemia were performed on convenience samples of blood drawn throughout the day without regard to meals. It is well known that triglyceride levels may vary 10% to 20% or greater in relation to meals. Recent data concerning the relation of postprandial triglyceride-rich VLDL particles to CHD, however, suggest that nonfasting triglyceride levels may be a better indicator of this dyslipidemic state than are fasting levels.[39–41] Adjusting analysis for fasting status did not change any inferences discussed in this paper. It could be argued that the definition of dyslipidemia is arbitrary. We performed several alternative analyses using different definitions. One adjusted the lipid values for beta blockers and for diuretic use directly rather than in the discrete multivariate model. Another used clinical cutoffs of HDL <35 mg/dL, triglycerides >200 mg/dL, and LDL <160 mg/dL. Although changing the definitions slightly changed the prevalence of dyslipidemia and dyslipidemic hypertension, it did not alter any inferences discussed in the paper. We chose to present the most conservative estimate using sex-specific specimen percentiles, unadjusted for beta blockers and diuretic use.

A second caution is that basing our definition of NIDDM on self-report of physician diagnosis or on the use of oral hypoglycemic agents is potentially prone to misclassification. The prevalence of diabetes mellitus in

our study (5.2% for NIDDM) is consistent with the prevalence found in a study in southern California (6.4%),[42] which used World Health Organization criteria, including fasting glucose and postglucose challenge testing. The prevalence of diabetes mellitus in our study also is consistent with that found in NHANES II (6.6%)[43] and the Israeli diabetes prevalence study (4.1%).[44]

Third, this study relied on self-report for smoking and physical activity, which also are prone to misclassification.

Fourth, the multivariate model used to evaluate the odds of the unique excess of dyslipidemic hypertension makes several mathematical assumptions, including that interaction of dyslipidemic hypertension is "multiplicative," or a ratio of exponents.[45] An interaction of potential biologic importance that does not conform to this model thus may be overlooked.

Conclusions

Dyslipidemic hypertension is common and found more often than would be dictated by chance alone, which is consistent with a distinct syndrome. Although dyslipidemia and hypertension were associated with potential insulin-resistant states of obesity and diabetes mellitus in this study, the unique interaction of dyslipidemia and hypertension found in dyslipidemic hypertensives was not associated with these states. Further prospective study of the unique relation between dyslipidemic hypertension and insulin resistance, as opposed to the role of dyslipidemia and hypertension independently, appears warranted.

Given our present state of knowledge about the possible cause of dyslipidemic hypertension, coupled with the association of exercise and weight loss with increased insulin sensitivity,[44] lower levels of triglycerides,[46] reduced blood pressure in moderately hypertensive subjects,[47] and higher HDL cholesterol,[48,49] it seems prudent that the treatment of dyslipidemic hypertensive patients should focus on weight loss and exercise.

Acknowledgments

Special thanks to Joy Reynes for work on the early statistical analysis and to Irene Reis for typing the manuscript.

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