

Impact of dyslipidemia on cardiovascular risk stratification of hypertensive patients and association of lipid profile with other cardiovascular risk factors: results from the ICEBERG study

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Background: Hypertension, dyslipidemia, and other cardiovascular risk factors are linked epidemiologically, clinically, and metabolically. Intensive/Initial Cardiovascular Examination regarding Blood Pressure levels, Evaluation of Risk Groups (ICEBERG) study focuses on the effect of dyslipidemia on cardiovascular risk evaluation and association of lipid profile with other risk factors.

Patients and methods: The ICEBERG study consisted of two sub-protocols: ICEBERG-1, conducted at 20 university hospitals (Referral Group) and ICEBERG-2, conducted at 197 primary healthcare centers (Primary Care Group). Sub-protocol had two patient profiles: patients previously diagnosed with essential hypertension and under medical treatment (Treated Group) and patients with systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, with no antihypertensive treatment for at least 3 months before inclusion (Untreated Group). Dyslipidemia was evaluated and cardiovascular risk stratification was performed according to ESC/ESH guidelines.

Results: More than half of the treated and untreated subjects were classified into high or very high cardiovascular risk groups. In a total of 1817 patients, the percentage of patients in “high” plus “very high” added risk groups increased to 55.2% in Treated Referral Group ($p < 0.001$), to 62.6% in Untreated Referral Group ($p = 0.25$) and to 60.7% in Untreated Primary Care Group ($p < 0.001$), by re-evaluation of patients’ lipid values.

Conclusions: Serum lipid levels are useful in stratifying hypertensive patients into cardiovascular risk groups more accurately, for appropriate antihypertensive treatment.

Keywords: hypertension, dyslipidemia, cardiovascular disease

Introduction

Dyslipidemia is characterized by elevated low-density lipoprotein (LDL) cholesterol, and triglycerides (TG), and decreased high-density lipoprotein (HDL) cholesterol. There is considerable evidence that hypertension (HT), dyslipidemia, and other cardiovascular (CV) risk factors are linked epidemiologically, clinically, and metabolically (Eaton et al 1994; Thomas et al 2001, 2002; O’Meara et al 2004; Liao et al 2004).

It is well known that high serum total and LDL cholesterol are particularly important risk factors for coronary artery disease (Brown et al 1997; Gould et al 1998; Ballantyne 1998). Many prospective and case-control studies have shown a positive association between serum TG and coronary artery disease risk and demonstrated the importance of fasting TG level as an independent risk factor

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(Austin 1991; Hokanson and Austin 1996). A number of clinical trials including The Framingham Heart Study have concluded that a low HDL cholesterol level predicts the risk for coronary artery disease independently of other risk factors (Castelli et al 1986; Kwiterovich 1998). Each 1 mg/dL decrease in HDL cholesterol has been shown to increase risk for coronary artery disease by 2% and 3% in men and women, respectively (Gordon et al 1989). The Veterans Affairs High-Density Lipoprotein Cholesterol Interventional Trial, investigating the impact of fibrate therapy on CV risk, demonstrated that 6% increase in HDL cholesterol was associated with a 22% decrease in coronary events (Rubins et al 1999).

Individuals with high blood cholesterol levels have a higher prevalence of HT and those with high blood pressure have a higher prevalence of hypercholesterolemia (Johnson et al 2004; O'Brien et al 2003; European Society of Hypertension-European Society of Cardiology Guidelines Committee 2003). A recent epidemiologic study revealed that 56.5% of patients with HT also had concomitant dyslipidemia and the percentage of patients with HT and dyslipidemia in the total population was estimated to be 15% (Eaton et al 1994). The clustering of these two conditions is important, because individuals with co-existing HT and dyslipidemia are particularly likely to develop atherosclerosis. This interplay is now known to produce a marked increase in CV disease risk (Thomas et al 2002; Liao et al 2004). The prevalence of stroke and peripheral arterial disease similarly increased among patients having both conditions (Johnson et al 2004).

The “Intensive/initial Cardiovascular Examination Regarding Blood pressure levels: Evaluation of Risk Groups (ICEBERG)” study aimed to determine CV risk evaluation and stratification of subjects with high normal or high blood pressure and also to evaluate the impact of different laboratory tests on patients' stratification. The objective of this article was to evaluate the serum lipid profiles of the ICEBERG study population, impact of lipid profile on CV risk stratification of patients and the association of serum lipid levels with other CV risk factors.

Patients and methods

Study design

ICEBERG was a healthcare organization-based epidemiological study with two sub-protocols. ICEBERG-1 was conducted at 20 referral hospitals (Referral Group) and ICEBERG-2 was conducted at 197 primary healthcare centers (Primary Care Group).

Study population and procedures

Both Referral and Primary Care Groups consisted of two profiles of patients: risk profile A and B. Risk profile A consisted of patients who were under medical treatment for essential HT (Treated Patients). Risk profile B included patients diagnosed with high-normal or high blood pressure [systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg] who have not received any anti-hypertensive medication for at least the last 3 months before inclusion (Untreated Patients). Patients with secondary HT, pregnant patients and patients younger than 18 years of age were not included in the study. Signed informed consent was obtained from each patient who accepted to participate in the study. The study was approved by the Ethics Committee of Istanbul University, Istanbul School of Medicine.

Treated Primary Care Group patients were not analyzed in this article, since laboratory evaluation was not practical and not performed in this group, because of its largest size ($n = 8496$).

Routine clinical evaluation

All patients were evaluated initially by medical history and a complete physical examination. At least two sitting blood pressure measurements were performed as described previously (O'Brien et al 2003). In addition to demographic data and anti-hypertensive treatment history, hypertensive risk profile, concomitant diseases and target organ damage data, waist circumference and body mass index measurements were collected as described in European Society of Cardiology Guidelines (2003) and routine serum and urine analysis were performed.

Evaluation of the patients' lipid profile

The lipid profile of the patients was determined by measuring serum total cholesterol, HDL cholesterol, LDL cholesterol and TG levels. Dyslipidemia was diagnosed when serum total cholesterol and LDL cholesterol levels were >250 mg/dL, >155 mg/dL, respectively and HDL cholesterol level was <40 mg/dL in men and <48 mg/dL in women (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001). In addition, apolipoprotein-A and -B levels were also measured as indicators of dyslipidemia. Evaluation of dyslipidemia was performed in Treated and Untreated Referral Groups and in Untreated Primary Care Group.

Stratification of patients by absolute cardiovascular risk factor

Regarding overall absolute CV disease risk assessment, European Society of Cardiology Guidelines Committee

classified the patients into “low”, “moderate”, “high” and “very high” added risk groups. In the present study, the target organ damage was assessed by the following approaches: 1) routine procedures [medical history, physical examination, electrocardiography (ECG), serum creatinine and urine analysis]; 2) routine procedures along with subsequent reassessment by serum high sensitive C-reactive protein (hs-CRP) levels and urinary albumin excretion (plus echocardiography (ECHO) and carotid ultrasonography, in the Untreated Referral Group). Patient stratification was performed separately and cumulatively by using data on the following: 1) medical history plus physical examination including blood pressure measurements, 2) routine laboratory tests (fasting blood glucose, lipid profile, serum potassium, serum and urine creatinine, complete urine test), 3) presence of microalbuminuria, 4) high plasma hs-CRP levels, 5) presence of left ventricular hypertrophy by ECG, 6) presence of left ventricular hypertrophy by ECHO, and 7) presence of vascular end organ damage by carotid ultrasonography.

Statistical analysis

The statistical analyses presented the demographic, physical and laboratory findings, the presence of risk factors, concomitant diseases, target organ damage and the blood pressure levels in the study groups descriptively, using mean and standard deviation and/or median for the numeric variables and percent distributions for the categorical ones.

The analyses used to compare non-normally and normally distributed dependent variables between groups were Kruskal Wallis non-parametric ANOVA, Mann-Whitney U test, Chi-square test and Fisher's exact test; and one-way ANOVA, Tukey HSD test and Student's t test, respectively. Values of $p < 0.05$ were considered as statistically significant.

Results

Study population profile

The numbers of patients in Referral Group, Treated and Untreated study arms, were 765 (60.9% females; mean age 58.4 ± 10.4 years) and 164 (56.4% females; mean age 50.1 ± 11.3 years), and in Untreated Primary Care Group, 888 (54.9% females; mean age 51.1 ± 12.1 years), respectively.

The most common risk factors were abdominal obesity (72.2%), sedentary life style (62.8%), age (>55 for men, >65 for women) (30.4%), and hs-CRP (≥ 1 mg/dL) (50.4%) and the most common concomitant diseases were heart disease (22.0%) and diabetes mellitus (20.4%).

In terms of renal disease, 9.0%, 5.5% and 6.0% of Treated Referral, Untreated Referral and Untreated Primary Care patients, respectively, have renal disease according to laboratory findings (ie, slight increase in serum creatinine level, presence of proteinuria). For Treated patients, monotherapies with the angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers, angiotensin receptor blockers, diuretics or B-adrenergic blockers and combined therapies with the angiotensin receptor blockers + diuretics or ACE inhibitors + calcium channel blockers were the most commonly prescribed antihypertensive therapies. Table 1 summarizes the major population characteristics in study groups.

Blood pressure measurements and severity of hypertension

The patients were stratified into different degrees of increased blood pressure according to European Society of Cardiology Guidelines (2003) (Figure 1A). The patients in all groups were stratified into high normal (SBP 130–139 mmHg and/or DBP 85–89 mmHg), Grade 1 (mild) HT (SBP 140–159 mmHg and/or DBP 90–99 mmHg), Grade 2 (moderate) HT (SBP 160–179 mmHg and/or DBP 100–109 mmHg), Grade 3 (severe) HT (SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg), isolated systolic HT (SBP ≥ 140 mmHg and DBP < 90 mmHg).

The distribution of patients to different blood pressure groups was significantly different among sub-groups ($p < 0.001$). As could be expected, the percentage of patients with Grade 3 HT was smallest in Treated Referral group.

Evaluation of dyslipidemia according to serum lipid profile

As given in Table 2, 45.8% (41.8% males, 48.5% females) of the Treated Referral, 42.5% (40.3% males, 44.6% females) of the Untreated Referral and 47.6% (43.1% males, 51.4% females) of the Untreated Primary Care patients had dyslipidemia according to laboratory results. The percentages of patients having dyslipidemia according to history in the same study groups were 39.9% (35.2% males, 43.1% females), 18.9% (19.7% males, 18.5% females) and 19.4% (17.8% males, 20.6% females), respectively. Thus, dyslipidemia was diagnosed in a total of 65.0% of the Treated patients (Referral) and 54.6% of the Untreated patients (both Referral and Primary Care). In a total of 29.2% of patients who had dyslipidemia according to history, 20.6% of them had elevated total cholesterol, 9.2% had elevated LDL cholesterol and 6.8% had reduced HDL cholesterol levels.

Table 1 The mean age, gender distribution and percentages of patients with the most common risk factors and concomitant diseases in the study groups. Data are given as mean \pm standard deviation

	Referral groups		Primary Care group
	Treated (n = 765)	Untreated (n = 164)	Untreated (n =888)
Age (years)	58.4 \pm 10.4	50.1 \pm 11.3	51.1 \pm 12.1
Gender (F/M)	464/298	92/71	485/398
Physical findings			
SBP (mmHg)	142.5 \pm 21.1	154.6 \pm 18.4	158.0 \pm 19.9
DBP (mmHg)	86.1 \pm 11.1	93.9 \pm 10.6	96.3 \pm 10.7
BMI (kg/m ²)	29.3 \pm 4.9	28.4 \pm 4.4	29.1 \pm 4.9
Waist circumference (cm)			
Males	99.3 \pm 11.9	99.9 \pm 14.0	99.5 \pm 12.5
Females	99.0 \pm 14.3	93.2 \pm 12.5	98.5 \pm 14.0
Percentage of patients with dyslipidemia according to medical history			
Increased total cholesterol	25.6%	12.2%	11.8%
Increased LDL cholesterol	16.2%	6.7%	5.0%
Reduced HDL cholesterol	8.2%	1.8%	5.6%
Percentage of patients with dyslipidemia according to lipid profile			
Increased total cholesterol	9.2%	11.3%	11.7%
Increased LDL cholesterol	11.0%	11.3%	13.5%
Reduced HDL cholesterol	35.8%	30.2%	35.6%
Percentage of patients with risk factors or concomitant diseases			
Age (>55 for men; >65 for women)	40.2%	25.6%	22.7%
Smoking	15.4%	20.1%	23.9%
Alcohol consumption	7.5%	10.4%	12.2%
Sedentary life style	61.4%	59.8%	64.6%
hs-CRP (\geq 1 mg/dL)	48.9%	57.6%	55.1%
Abdominal obesity	74.5%	61.3%	72.3%
Heart disease	37.9%	20.7%	8.4%
Diabetes mellitus	22.7%	15.6%	19.2%
Renal disease	9.0%	5.5%	6.0%

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein.

Among all patients, 5.9% (6.5% males, 5.5% females) of them were currently using antilipidemic drugs. The percentages of patients using antilipidemic drugs were as follows: 12.5% in Treated Referral, 0.6% in Untreated Referral, and 2.1% in Untreated Primary Care study groups.

Association between serum lipid profile and other cardiovascular risk factors

As shown in Table 3, serum total cholesterol levels correlated with blood pressure values, obesity parameters (ie, body mass index and waist circumference) and microalbuminuria in Treated Referral patients. On the other hand, total serum

cholesterol level correlated with only systolic pressure in Untreated patients. LDL cholesterol levels revealed a positive correlation with blood pressure values and obesity parameters in Treated Referral patients but no correlation was observed in Untreated patients (Table 3). HDL cholesterol levels showed negative correlations with waist circumference and hs-CRP levels in both Treated and Untreated patients (Table 3). HDL cholesterol levels also correlated negatively with ECG and ECHO parameters (Sokolow index and left ventricular mass index values, respectively) as indicators of left ventricular hypertrophy in these patients. Serum TG levels correlated positively with almost all other CV risk

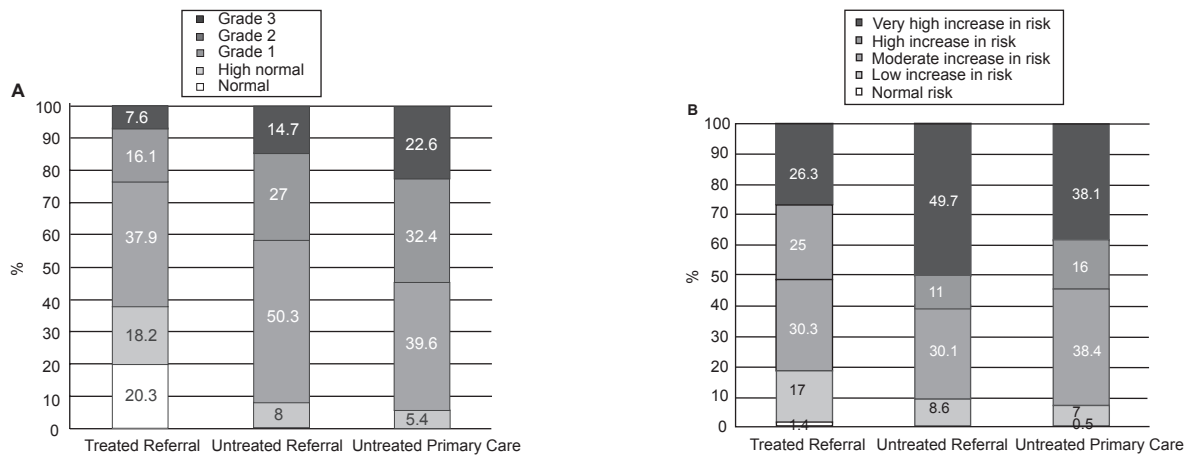


Figure 1 Distribution of patients in study groups into different grades of hypertension (A) and into CV risk groups according to existing risk factors before additional tests (B). Distribution into different groups showed significantly different patterns for both panels ($p < 0.001$, by Kruskal-Wallis test). Group comparisons were as follows: (A) $p < 0.001$ for Treated Referral Group vs other groups; $p = 0.001$ for Untreated Referral vs Untreated Primary Care Groups; (B) $p < 0.001$ for Treated Referral vs Untreated Primary Care groups, and $p = 0.06$ for Treated vs Untreated Referral Groups by Mann-Whitney U test.

factors in Treated patients whereas in Untreated patients only obesity parameters and hs-CRP levels correlated with TG levels significantly (Table 3).

Impact of serum lipid profile on cardiovascular risk stratification

The patients in study groups were stratified into CV risk groups according to European Society of Cardiology

Guidelines (2003) regarding existing risk factors in history and concomitant diseases before additional tests (Figure 1B). There were significant differences between sub-groups regarding distribution of patients into different risk groups ($p < 0.001$). More than half of the treated and untreated subjects were classified into high or very high cardiovascular risk groups. Patients with “high” plus “very high” added risk was significantly higher in Untreated

Table 2 The serum lipid profile of patients in study groups

	Referral groups		p value	Primary care group
	Treated (n = 749–470)	Untreated (n = 160–119)		Untreated (n = 870–540)
Total cholesterol (mg/dL)				
Males	187.7 ± 39.6	196.8 ± 40.8		203.0 ± 50.3
Females	200.2 ± 40.8	206.9 ± 43.4	0.041	204.1 ± 42.8
LDL cholesterol (mg/dL)				
Males	111.4 ± 33.0	117.6 ± 32.3		119.3 ± 34.6
Females	118.4 ± 32.3	122.8 ± 34.2	0.08	119.1 ± 35.5
HDL cholesterol (mg/dL)				
Males	44.2 ± 10.8	47.2 ± 12.3		44.3 ± 9.2
Females	52.4 ± 12.8	54.8 ± 13.2	0.035	51.4 ± 13.7
Triglyceride (mg/dL)				
Males	167.5 ± 117.0	164.7 ± 109.4		192.3 ± 130.4
Females	151.0 ± 85.5	144.0 ± 88.1	0.58	160.3 ± 108.6
Apolipoprotein-A (mg/dL)				
Males	147.5 ± 29.1	155.5 ± 27.6		152.4 ± 26.3
Females	168.1 ± 33.7	174.3 ± 29.8	0.07	168.9 ± 32.5
Apolipoprotein-B (mg/dL)				
Males	95.2 ± 27.5	102.8 ± 28.8		101.1 ± 26.3
Females	99.5 ± 28.3	99.3 ± 25.7	0.27	98.9 ± 30.9

Notes: Data are given as mean ± standard deviation. P values indicate the statistical difference between Treated and Untreated Referral Groups.

Table 3 Correlation between lipid profile and other cardiovascular risk factors in study groups

	Treated (Referral)		Untreated (Referral and primary care)	
	r	p	r	P
Total cholesterol				
Systolic blood pressure	0.124	<0.001	0.073	0.019
Diastolic blood pressure	0.123	<0.001	0.037	0.240
Body mass index	0.048	0.001	0.037	0.244
Waist circumference	0.030	0.047	0.053	0.109
Microalbuminuria (qualitative)	0.043	0.006	–	–
LDL cholesterol				
Systolic blood pressure	0.074	<0.001	0.042	0.179
Diastolic blood pressure	0.071	<0.001	0.034	0.284
Body mass index	0.042	0.012	0.041	0.194
Waist circumference	0.045	0.010	0.064	0.053
HDL cholesterol				
Waist circumference	–0.038	0.027	–0.119	<0.001
Microalbuminuria (qualitative)	–0.073	<0.001	–	–
Microalbuminuria (quantitative)	–0.104	0.005	–0.025	0.425
hs-CRP	–0.088	0.001	–0.128	<0.001
Sokolow index	–0.121	0.002	–0.052	0.156
Left ventricular mass index	–	–	–0.254	0.002
Triglyceride				
Systolic blood pressure	0.062	<0.001	0.020	0.533
Diastolic blood pressure	0.070	<0.001	0.023	0.454
Body mass index	0.075	<0.001	0.110	<0.001
Waist circumference	0.093	<0.001	0.159	<0.001
Microalbuminuria (qualitative)	0.079	<0.001	–	–
Microalbuminuria (quantitative)	0.120	0.001	0.057	0.076
hs-CRP	0.047	0.075	0.114	<0.001

Abbreviation: hs-CRP, high sensitivity C-reactive protein.

Groups (Referral + Primary Care) compared to Treated Group (Referral) ($p < 0.001$).

The ratios of patients in “high” plus “very high” added risk groups assessed by medical history and physical examination were 51.2%, 60.7% and 54.2% in Treated Referral, Untreated Referral and Untreated Primary Care patients, respectively. Upon stepwise re-stratification, the percentage of patients in “high” plus “very high” added risk groups increased to 55.2% in Treated Referral Group ($p < 0.001$), to 62.6% in Untreated Referral Group ($p = 0.25$) and to 60.7% in Untreated Primary Care Group ($p < 0.001$), by re-evaluation with patients’ serum lipid values (Figure 2). When all risk groups are considered, additional shifts to upper risk group by including lipid profile data to medical history were 5.5% in Treated

Referral, 3.7% in Untreated Referral, and 9.3% in Untreated Primary Care Groups.

Discussion

Patients with multiple CV risk factors are at much greater risk for CV disease-related events than those with a single factor. Abnormalities in plasma lipoprotein metabolism play a central role in the pathogenesis of atherosclerosis, and arterial HT with elevated systolic or diastolic blood pressure is positively and independently associated with coronary heart disease (Shurtleff 1970; SHEP Cooperative Research Group 1991). Data from the Framingham Study demonstrated that HT tends to occur in association with other atherogenic risk factors (eg, 78% of hypertensive men and 82% of hypertensive women had multiple CV risk factors) (Kannel 2000).

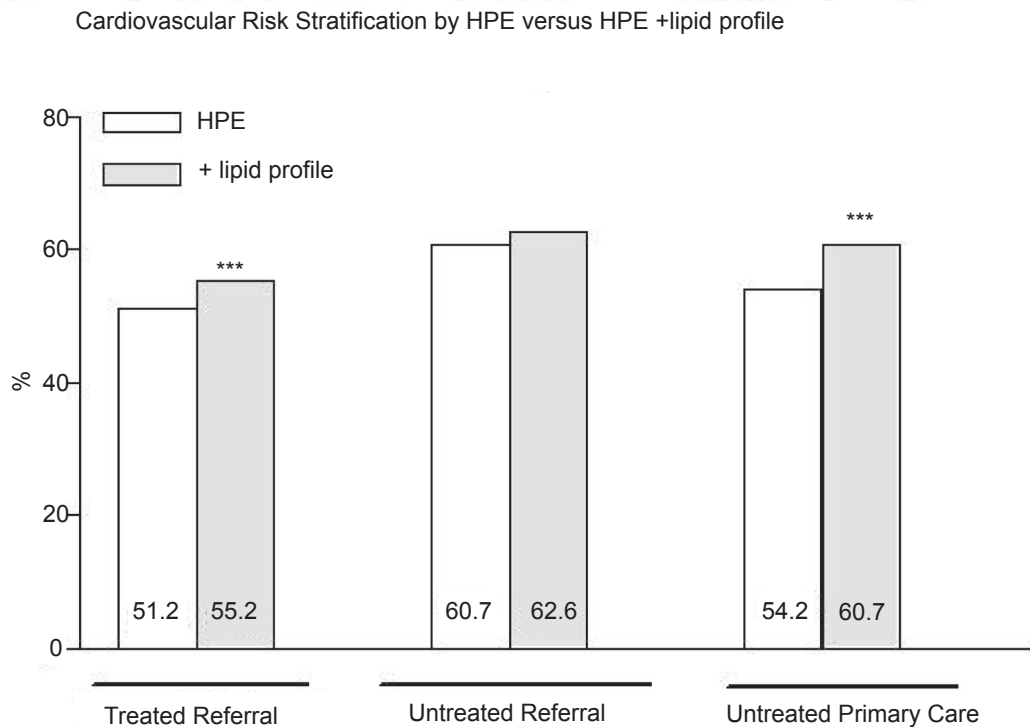


Figure 2 The percentages of Treated, Untreated Referral and Untreated Primary Care patients in "high" plus "very high" added risk groups according to medical history and physical examination (HPE), and medical history and physical examination plus serum lipid profile (plus lipid profile). *** $p < 0.001$ vs HPE (McNemar test).

This report presents the data of ICEBERG study which has been conducted in patients with high normal/high blood pressure levels either under hypertensive treatment or not and focuses on the evaluation of dyslipidemia as a CV risk factor. The diagnosis of dyslipidemia was based on the patients' medical history and measured serum lipid profile values. The data revealed that a total of 65.0% of the Treated and 54.6% of the Untreated patients had dyslipidemia. In all study groups, the majority of the patients had a reduced HDL cholesterol level. This finding is in accordance with the data of the TEKHARF cohort of 2001/02 which revealed prevalence of low HDL cholesterol level as 64% and 35.5% in men and women, respectively (Onat et al 2003). Elevated LDL cholesterol and triglyceride levels were the second and the third most common impaired lipid status, respectively. Among all patients, only 5.9% of them were currently using antilipidemic drugs.

The risk of CV disease associated with the presence of concomitant HT and dyslipidemia has been demonstrated to be greater than the sum of the CV risks for HT and dyslipidemia alone (Borghetti 2002). Gaziano et al (1999) noted a potential interaction between elevated cholesterol and HT in the development of myocardial infarction. Thus, the need to quantify a person's overall CV risk is of great importance.

In a recent retrospective cohort study aiming to estimate the prevalence of concurrent HT and dyslipidemia among a veteran population and to compare the prevalence of CV disease among groups with isolated versus concurrent HT and dyslipidemia, it has been found that 57.8% of all patients had HT or dyslipidemia and that nearly one third (30.7%) of all patients had both (Johnson et al 2004). Moreover, patients with these two conditions were found to have 3 to 4 times the prevalence of myocardial infarction than patients with either condition alone, and 2 to 3 times the prevalence of coronary artery disease, peripheral arterial disease and cerebrovascular disease (Johnson et al 2004).

Estimates from the National Health and Nutrition Examination Survey III found that the prevalence of HT was 32.8% and the proportion of patients with LDL cholesterol above 130 mg/dL was 49% for men and 43% for women (American Heart Association 2003). Johnson et al have found a 52.1% prevalence of HT and a 36.3% prevalence of dyslipidemia in their study populations (Johnson et al 2004).

In the current study, the analysis of the correlation of serum lipid profile with other major CV risk factors demonstrated statistical significance at different levels. Impairment of the lipid profile mostly correlated with elevated blood pressure levels (systolic and/or diastolic)

and with obesity parameters (body mass index and/or waist circumference). Significant correlations between reduced HDL cholesterol and microalbuminuria, hs-CRP and left ventricular hypertrophy parameters are of particular importance. Although correlation coefficients (r values) are relatively low and statistical significance might be due to large sample size, our observations are in accordance with the findings of Castelli and Anderson who noted that blood pressure and serum cholesterol were strongly correlated among hypertensive patients and recommended early treatment of hypercholesterolemia in patients with HT (Castelli and Anderson 1986).

The other important observation of our study was that when we included lipid profile data to CV risk stratification in addition to routine clinical evaluation with medical history and physical examination, we observed marked upward shifts to “high and very high added risk” groups in all study groups. Moreover, when all risk groups were considered, we observed marked additional shifts to upper risk group by including lipid profile data to routine clinical evaluation in all study groups. These observations may suggest that the use of serum lipid data in screening is useful in stratifying patients with high normal and high blood pressure levels into risk groups at both Referral and Primary Health Care settings.

Recent studies have suggested that substantial reductions in the risk of coronary heart disease, stroke, and death can be achieved by targeting HT and dyslipidemia (Wald and Law 2003; Wong et al 2003). For instance, it has been estimated that 79% of ischemic heart disease events and 69% of strokes would be prevented if LDL cholesterol levels decreased by 70 mg/dL and diastolic pressure by 11 mmHg (Wald and Law 2003).

As a conclusion, an important fraction of ICEBERG patients with high normal and high blood pressure levels, either under antihypertensive therapy or not was found to have dyslipidemia. The serum lipid profile of these patients correlated significantly with other major CV risk factors. These observations taken together with the data demonstrating the importance of dyslipidemia in patients’ risk stratification imply that patients who have high blood pressure and impaired lipid profile are at high risk and should be the target of aggressive primary preventive strategies to reduce the burden of HT and subsequent CV disease.

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Disclosures

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References

- American Heart Association. Heart Disease and Stroke Statistics: 2004 Update. 2003. Dallas: American Heart Association.
- Austin MA. 1991. Plasma triglyceride and coronary heart disease. *Arterioscler Thromb*, 11:2–14.
- Ballantyne CM. 1998. Low-density lipoproteins and risk for coronary artery disease. *Am J Cardiol*, 82:3Q–12Q.
- Borghgi C. 2002. Interactions between hypercholesterolemia and hypertension: implications for therapy. *Curr Opin Nephrol Hypertens*, 11:489–96.
- Brown BG, Zhao XQ, Bardsley J, et al. 1997. Secondary prevention of heart disease amongst patients with lipid abnormalities: practice and trends in the United States. *J Intern Med*, 241:283–94.
- Castelli WP, Anderson K. 1986. A population at risk. Prevalence of high cholesterol levels in hypertensive patients in the Framingham Study. *Am J Med*, 80: 23–32.
- Castelli WP, Garrison RJ, Wilson PW, et al. 1986. Incidence of coronary heart disease and lipoprotein cholesterol levels: The Framingham Study. *JAMA*, 256:2835–8.
- Eaton CB, Feldman HA, Assaf AR, et al. 1994. Prevalence of hypertension, dyslipidemia, and dyslipidemic hypertension. *J Fam Pract*, 38:17–23.
- European Society of Hypertension-European Society of Cardiology Guidelines Committee. 2003. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens*, 21:1011–53.
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 2001. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*, 285:2486–97.
- Gaziano JM, Sesso HD, Breslow JL, et al. 1999. Relation between systemic hypertension and blood lipids on the risk of myocardial infarction. *Am J Cardiol*, 84:768–73.
- Gordon DJ, Probstfield JL, Garrison RJ, et al. 1989. High-density lipoprotein cholesterol and cardiovascular disease: Four prospective American studies. *Circulation*, 79:8–15.
- Gould AL, Ressouw JE, Santanello NC, et al. 1998. Cholesterol reduction yields clinical benefit: impact of statin trials. *Circulation*, 97:946–52.
- Hokanson JE, Austin MA. 1996. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. *J Cardiovasc Risk*, 3:213–9.
- Johnson ML, Pietz K, Battleman DS. 2004. Prevalence of comorbid hypertension and dyslipidemia and associated cardiovascular disease. *Am J Manag Care*, 10:926–32.

- Kannel WB. 2000. Fifty years of Framingham Study contributions to understanding hypertension. *J Hum Hypertens*, 14:83–90.
- Kwiterovich PO Jr. 1998. The antiatherogenic role of high-density lipoprotein cholesterol. *Am J Cardiol*, 82:13Q–21Q.
- Liao D, Mo J, Duan Y, et al. 2004. The Joint Effect of Hypertension and Elevated LDL-Cholesterol on CHD are beyond Additive (abstract). *Eur Heart J*, 25(Suppl):235.
- O'Brien E, Asmar R, Beilin L, et al. 2003. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*, 21:821–48.
- O'Meara JG, Kardia SL, Armon JJ, et al. 2004. Ethnic and sex differences in the prevalence, treatment, and control of dyslipidemia among hypertensive adults in the GENOA study. *Arch Intern Med*, 164:1313–8.
- Onat A, Hergenc G, Uzunlar B, et al. 2003. Determinants of HDL-cholesterol and its prediction of coronary disease among Turks. *Arch Turk Soc Cardiol*, 31:9–16.
- Rubins HB, Robins SJ, Collins D, et al. 1999. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med*, 341:410–8.
- SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. 1991. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA*, 265:3255–64.
- Shurtleff D. 1970. The Framingham Study: An Epidemiologic Investigation of Cardiovascular Disease, Section 26, Washington, DC: US Government Printing Office.
- Thomas F, Bean K, Guize L, et al. 2002. Combined effects of systolic blood pressure and serum cholesterol on cardiovascular mortality in young (<55 years) men and women. *Eur Heart J*, 23:528–35.
- Thomas F, Rudnichi A, Bacri AM, et al. 2001. Cardiovascular mortality in hypertensive men according to presence of associated risk factors. *Hypertension*, 37:1256–61.
- Wald NJ, Law MR. 2003. A strategy to reduce cardiovascular disease by more than 80%. *BMJ*, 326:1419–23.
- Wong ND, Pio JR, Franklin SS, et al. 2003. Preventing coronary events by optimal control of blood pressure and lipids in patients with the metabolic syndrome. *Am J Cardiol*, 91:1421–6.

