Dyslipidemia in South Asian Patients

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South Asians around the globe have the highest rates of coronary artery disease (CAD). These rates are 50% to 300% higher than other populations, with a higher risk at younger ages. These high rates of CAD are accompanied by low or similar rates of major traditional risk factors. The prevalence of diabetes is three to six times higher among South Asians than Europeans, Americans, and other Asians but does not explain the "South Asian Paradox." A genetic predisposition to CAD, mediated by high levels of lipoprotein(a), markedly magnifies the adverse effects of traditional risk factors related to lifestyle and best explains the South Asian Paradox. Although the major modifiable risk factors do not fully explain the excess burden of CAD, they are doubly important and remain the foundation of preventive and therapeutic strategies in this population. A more aggressive approach to preventive therapy, especially dyslipidemia, at an earlier age and at a lower threshold is clearly warranted.

Introduction

The term "South Asian" refers to all people who have ancestral origins in the Indian subcontinent (the countries of India, Pakistan, Bangladesh, and Sri Lanka). The Indian subcontinent is home to 1.4 billion people, which constitutes 23% of the world's population. South Asians have the highest rates of coronary artery disease (CAD) in the world [1,2]. The terms "South Asians" and "Asian Indians" are used interchangeably in this paper.

The incidence, prevalence, hospitalization, morbidity, and mortality from CAD among South Asians are 50% to 300% higher than in Europeans, Americans, and other Asians, regardless of gender, religion, or social class [3••]. More than half of Asian Indians are lifelong vegetarians, but CAD rates are similar among vegetarians and those who are not [4,5]. CAD in South Asians is usually premature, aggressive, severe, diffuse, and often follows a malignant course in this population [1]. Three-vessel disease is common even among premenopausal Asian Indian women [6]. This article reviews the crucial role of dyslipidemia in malignant CAD among South Asians.

CAD in the Indian Subcontinent

The prevalence of CAD doubled to 3% to 4% in rural India and quadrupled to 9% to 11% in urban India over the past four decades. The prevalence of CAD in urban India is similar to overseas Indians and four times higher than the general US population [3••]. The prevalence is even higher in Pakistan, with 23.7% of men and 30.0% of women older than 40 years of age having CAD [7•]. CAD rates among South Asian women are higher than South Asian men, despite low rates of smoking [6,8].

CAD in the Indian Diaspora and the Coronary Artery Disease in Indians Study

In general, CAD rates among immigrants blend with that of the adopted country in two to three generations. When Japanese with very low rates of CAD came to the United States, CAD rates increased threefold but remained lower than the US population in general. When the Irish, who had high rates of CAD, came to Boston, their CAD remained high but not higher than the US population. Asian Indians have been a singular exception in having CAD rates higher than that of the host population in countries as diverse as the United States, Canada, the United Kingdom, South Africa, Singapore, Trinidad, Fiji, and Mauritius [2].

The Coronary Artery Disease in Indians (CADI) study [5] was the first systematic investigation of CAD among Asian Indians in the United States. The participants were physicians and the results showed for the first time that the high rates of CAD among South Asians also apply to physicians, including cardiologists. The age-adjusted prevalence of CAD among men was 10% in the CADI study compared with 2.5% in the Framingham Offspring Study [5]. This fourfold higher rate of CAD observed in the CADI Study is consistent with the fourfold higher rate of CAD among Asian Indians (compared with whites) in California [9].

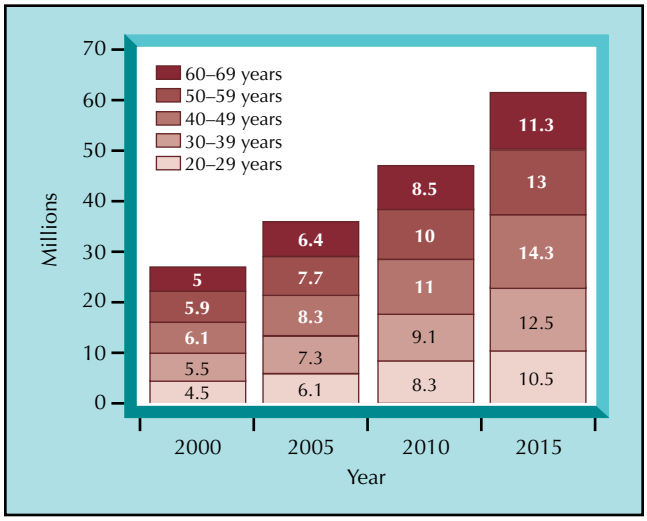

Figure 1. The increase in the projected number of coronary artery disease patients from year 2000 to 2015 by different age groups in India. (*Data from* Indrayan [11••].)

Palaniappan et al. [10•] have reported a higher CAD mortality rate among Asian Indians in California. Compared with the total population of the state, the standardized mortality ratio for CAD among Asian Indians was 74% higher in men and 64% higher in women. The proportionate mortality ratio for CAD was 61% higher for men and 44% higher for women. Furthermore, Asian Indian women experienced a 5% increase in CAD mortality from 1990 to 2000 compared with a decrease in all other ethnic groups.

Premature CAD among South Asians

Early development of malignant atherosclerosis results in premature myocardial infarction (MI) and death, with the first MI occurring about 7 to 10 years earlier [1]. Among South Asians younger than 30 years of age, the CAD mortality is threefold higher than whites in the United Kingdom and 10-fold higher than Chinese in Singapore [3••]. About 50% of the first heart attacks among men in India occur before the age of 55 years and 25% occur before the age of 40 years [3••]. An estimated 9.2 million productive years of life were lost in India in 2000, with an expected increase to 18 million years by 2030, which is almost 10 times the projected loss of productive life in the United States. India is a young population, with only 3% of the population older than 65 years of age, but by 2015 India is projected to have 62 million patients with CAD. Of these, 23 million will be younger than 40 years of age and only 11 million will be above 60 years of age (Fig. 1) [11••]. The projected number of deaths from CAD by 2015 is 2.95 million, of which 14% will be in people younger than 30 years of age, 31% will be in people younger than 40 years of age, and 50% will be in people younger than 50 years of age [11••].

Classification of CAD among South Asians

CAD among South Asians may be classified as type I (malignant), type II (usual), or type III (mixed) [3]. Type I CAD has a dismal prognosis and usually manifests before the age of 45 years. It is characterized by the absence or low rates of traditional risk factors but has a high prevalence of various emerging risk factors, particularly lipoprotein(a) (Lp(a)) excess. Type II is indistinguishable from CAD in other populations and is characterized by a high prevalence of traditional risk factors and has a good prognosis. Type III has a varying combination of traditional and emerging risk factors and typically manifests in middle age. Most of the excess burden of CAD among South Asians is due to a high prevalence of type I CAD, and to a lesser degree type III. Therefore, the risk factor profile may vary depending upon the age of the South Asian population studied.

South Asian Dyslipidemia

The excess burden of CAD among South Asians appears to be primarily due to dyslipidemia that is characterized by high levels of apolipoprotein (apo) B, triglycerides (TG), and Lp(a); borderline high levels of low-density lipoprotein cholesterol (LDL-C); and low levels of high-density lipoprotein cholesterol (HDL-C) and apoA1. Nearly half of Asian Indians (but not Pakistanis or Bangladeshis) are lifelong vegetarians. Unlike in other populations, Asian Indian vegetarians and nonvegetarians have a similar pattern of dyslipidemia and similar rates of CAD [5]. This appears to be due to "contaminated vegetarianism," wherein liberal amounts of saturated fats and trans fats are used in cooking vegetables, snacks, breads, rice, and curries. Deep frying is a favorite form of food preparation, resulting in increased consumption of trans fat [12]. Furthermore, overcooking of food is widely practiced among South Asians, which results in destruction of most nutrients, especially folate.

Small dense HDL-C

Low HDL-C is a strong predictor of severity of CAD, including left main and three-vessel disease, as well as premature MI and stroke. Low HDL-C is two times more common among Asian Indian men and three times more common among Asian Indian women compared with whites [5]. Approximately half of Asian Indian men and two thirds of Asian Indian women have low HDL-C.

HDL particles are heterogeneous, with large particles (HDL2) conferring most of the reverse cholesterol transport and protection against CAD. Small HDL particles are associated with less efficient reverse cholesterol transport and less protection against CAD. Patients with CAD or low HDL levels have a significant decrease in large HDL particles and an increase in small HDL particles [13,14]. HDL particle size among Asian Indians is significantly smaller than in whites [15••]. HDL2b, the most protective component of HDL, is low in more than 90% of Asian

Indians, indicating dysfunctional HDL [16]. Physical activity is associated with a significant increase in large HDL among Asian Indians. Potent statins such as atorvastatin and rosuvastatin, as well as niacin, are known to selectively increase the large HDL particles and decrease small HDL particles [17].

Total cholesterol and LDL

LDL levels as low as 25 to 40 mg/dL are physiologically sufficient, and the optimum level is currently set at 40 mg/dL [18]. The CAD risk increases 30% for every 30-mg/dL increase [18]. LDL levels among Asian Indians in the United States are similar to whites. Furthermore, over the past decade the LDL levels in urban India have increased by 25 mg/dL and are now similar to those in the United States. Also, some regions have very high total cholesterol (TC) levels, with a mean of 229 mg/dL, and 32% of patients have levels greater than 239 mg/dL [19].

TG, small dense LDL, and non–HDL-C

TG levels higher than 150 mg/dL are found in nearly half of Asian Indian men, which is partly due to a high glycemic load [12]. High TG levels make LDL small, dense, and more atherogenic, although recent studies question the greater atherogenicity of small dense LDL [20]. A TG/HDL ratio of greater than 3.8 is highly predictive of small dense LDL among Asian Indians [21•]. Despite having high TG and low HDL, several studies have failed to show a higher rate of small dense LDL among Asian Indians [16].

High TG levels are associated with a heightened risk of CAD only when accompanied by a modest elevation of non–HDL-C, which is a better predictor of CAD than LDL and LDL particle numbers. The non–HDL-C goal is set at 30 mg/dL higher than the LDL goal, and Asian Indians have similar levels compared with Americans and Europeans [5].

TC/HDL-C ratio and apoB/apoA-I ratio

The ratio of TC to HDL (TC/HDL) is a better predictor of myocardial infarction (MI) and CAD severity compared with other lipid levels among diverse populations, including Asian Indians [22•]. This ratio is higher among Asian Indian men than whites (5.44 vs 3.90) and among Asian Indian women than whites (4.64 vs. 3.37) [23]. Patients with a TC/HDL ratio of 5 have a twofold risk of CAD compared with those with a ratio of less than 4. A TC/HDL ratio greater than 5 was found in 60% of Asian Indians compared with only 14% having LDL greater than 160 mg/dL. Thus, a high TC/HDL ratio helps identify more high-risk Asian Indians [5].

ApoB represents all the atherogenic particles contained in LDL, very low-density lipoprotein (VLDL), and Lp(a), whereas apoA-I is the primary protein component in HDL that is responsible for most of the protective effects of HDL. In a large prospective study, TC/HDL ratio was the strongest predictor of major acute coronary events (MACE), with an odds ratio of 3.81 compared with 1.62 for LDL, 2.32 for TC, 2.51 for non–HDL-C, 2.50 for apoB, and 3.01 for apoB/A-I ratio [24]. South Asians have higher apoB/apoA-I ratio than whites [23], and this ratio was the single largest contributor of MI in Asian Indians, with a population-attributable risk of 46.8% in the INTERHEART Study [25••].

Metabolic Syndrome and Diabetes Do Not Explain the South Asian Paradox

Genetically susceptible South Asians develop abdominal obesity, metabolic syndrome, and diabetes when exposed to a reduced energy expenditure and increased caloric consumption, which occur in parallel with urbanization [2,23]. Because health risk associated with abdominal obesity is occurring at a lower waist circumference, the International Diabetes Federation (IDF) has proposed lower cut-points among South Asian men (> 90 cm) and women (> 80 cm) [26]. The abdominal obesity rates among South Asians are as high as 40% to 50%, with higher rates among women. The prevalence of metabolic syndrome in India is 27% using National Cholesterol Education Program (NCEP) criteria, and the prevalence increases to 35% when IDF waist cut-points are used [27••].

Asian Indians develop diabetes at a younger age and at a lower body mass index (BMI) and waist circumference. The prevalence of diabetes varies from 3% to 6% in rural India and 12% to 17% in urban India [27••]. The prevalence of diabetes among immigrant South Asians is greater than 20% and three to six times higher than the host population after standardizing for age [28••].

Prospective studies have shown that the incidence and mortality from CAD is twofold higher among South Asians, even when adjusted for standard risk factors including diabetes [29,30••]. Forouhi et al. [30••] examined prospectively whether measured risk factors can explain the higher CAD mortality in South Asians compared with Europeans in the United Kingdom. Conventional CAD risk factors and those associated with insulin resistance were measured in 1787 European men and 1420 South Asian men aged 40 to 69 years at baseline in a population-based study between 1988 and 1990. By February 2006, there were 202 CAD deaths (94 European and 108 South Asian). Despite universal access to health care, South Asian men had double the CAD mortality of European men in Cox regression analyses adjusted for age, smoking, and cholesterol (hazard ratio of 2.14; 95% CI, 1.56–2.94; $P < 0.001$). The odds ratio increased to 2.20 when adjusted for socioeconomic status (Fig. 2) [30••]. The study did not measure Lp(a) and, therefore, its role could not be assessed.

Lp(a) Excess? The Genetic Risk Factor for Malignant CAD among South Asians

Genetically determined elevations in Lp(a) play an important role in accelerating atherosclerosis, which results in

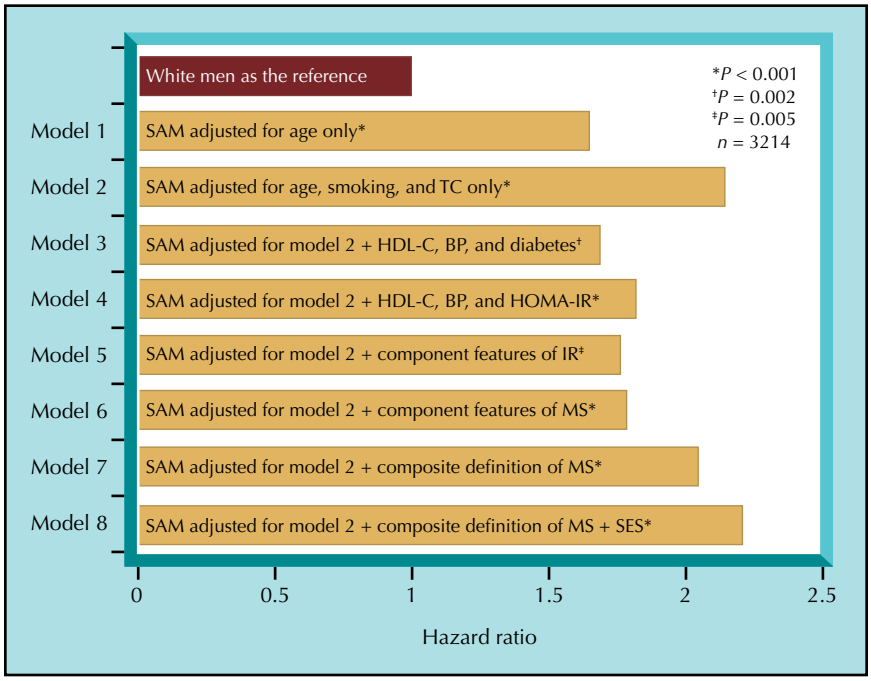

Figure 2. Odds ratios for coronary artery disease mortality among South Asian men (SAM) compared with white men. BP—blood pressure; HDL-C—high-density lipoprotein cholesterol; HOMA—homeostasis model; IR—insulin resistance; MS—metabolic syndrome; SES—socioeconomic status (*ie*, years of education and occupational social class); TC—total cholesterol. (*Data from* Forouhi et al. [30••].)

premature MI and stroke [31••]. Whereas earlier studies focused primarily on the role of Lp(a) as an independent risk factor in the absence of other risk factors, more recent studies have highlighted the important role of Lp(a) in accentuating the risk associated with virtually all conventional and emerging risk factors. Among patients with Lp(a) excess, the CAD risk is increased by threefold in the absence of other risk factors. However, the risk increases to eightfold with low HDL, 12-fold with high LDL, 16-fold with diabetes, and 25-fold with high TC/HDL ratio. When high levels of Lp(a) were combined with other risk factors, such as hypertension, diabetes, smoking, hyperhomocysteinemia, and/or a high TC/HDL ratio, the relative odds for premature CAD ranged from threefold to 122-fold depending on the number of risk factors present and their severity. This risk, which appears to be limited to premature vascular disease, is strongest before the age of 45 years, declines after the age of 55 years, and often disappears after the age of 65 years. The higher the Lp(a) level the lower the age of first heart attack, and most affected individuals develop MI by the third to fifth decade of life [31••].

Asian Indians around the world have high levels of Lp(a), second only to African Americans. Among Asian Indians, the mean level of Lp(a) is 20 mg/dL and the median level is 15 mg/dL. Approximately 30% to 40% of Asian Indians have levels greater than 20 to 30 mg/dL, which is generally considered as the threshold for high risk of CAD. High levels of Lp(a) correlate with the prematurity, severity, extent, and progression of coronary atherosclerosis as well as the occurrence and recurrence of MI among Asian Indians [31••,32]. Thus, Lp(a) provides the crucial link between the two hallmarks of CAD among South Asians, which are extreme prematurity and severity. Increased levels of Lp(a) are independently associated with risk of CAD among patients with diabetes, and the combination of diabetes and excess Lp(a) portends malignant CAD with a dismal prognosis [31••].

The impact of elevated Lp(a) levels is heterogeneous, with greater risk for Asian Indians and lower risk for African Americans. Nonetheless, among African Americans the atherogenic effects of elevated Lp(a) are significantly mitigated by their otherwise antiatherogenic lipid profile (high HDL and low TG and LDL) [31••]. In sharp contrast, the pathogenicity of elevated Lp(a) in Asian Indians is magnified as a result of a highly atherogenic metabolic milieu consisting of dysfunctional HDL and high levels of TG, non–HDL-C, and homocysteine. A combination of high Lp(a) and low HDL was found in 42% of Asian Indians [16]. It appears that Lp(a) excess is a risk factor of outstanding importance in Asian Indians, similar to diabetes among native Americans and hypertension in African Americans. Therefore, testing for Lp(a) is warranted in all Asian Indians being evaluated for the risk of premature CAD, regardless of the presence of other risk factors.

Double Jeopardy from Nature and Nurture

Many Asian Indians are in double jeopardy from nature and nurture, with nature being the genetically determined Lp(a) excess and nurture being the unhealthy lifestyle associated with affluence, urbanization, and mechanization. The adverse effects of the modifiable risk factors related to lifestyle, such as smoking, hypertension, atherogenic diet, physical inactivity, abdominal obesity, and diabetes, are markedly magnified in those with Lp(a) excess. This synergy between nature and nurture best explains the South Asian Paradox.

The prevalence of standard risk factors is similar or lower among South Asians than whites [33••]. In the CADI study, prevalence of smoking was 3%, obesity 3%, hypertension 14%, and high LDL 14% [5]. However, in the INTERHEART study [25••], prevalence of modifiable risk factors, especially sedentary lifestyle and low intake of fruits and vegetables, was high in India. This and other studies indicate that the increased cardiovascular risk in South Asians may be preventable through lifestyle interventions and the judicious use of medication to attain optimal levels of blood pressure, lipids, and glucose.

Statins and LDL-lowering Therapy

LDL-lowering therapy with statins is the main stay of treatment of dyslipidemia, with an LDL goal of less than 100 mg/dL in high-risk patients and less than 70 mg/dL for very high-risk patients, goals that are readily achievable with today's medicines. For example, a combination of 10 mg/d of ezetimibe and 40 mg/d of rosuvastatin achieved LDL lowering of 70%. This combination allowed 80% of patients to achieve an LDL goal of less than 70 mg/dL [34].

Several Japanese studies demonstrated that treatment with low doses of statins (5 mg/d of simvastatin or 10–20 mg/d of pravastatin) reduced LDL by 27% to 29%, an LDL reduction that is usually achieved with 20 mg/d of simvastatin or 40 mg/d of pravastatin in Europe and the United States [35,36]. The potential mechanisms of heightened response to statins in Japanese are related to genetically based differences in the metabolism of statins at the level of hepatic enzymes and drug transporters and not the BMI. In sharp contrast, the efficacy and side-effect profile of statins among Asian Indians appear to be similar to that of whites (LDL reduction of 30%–39% with 10 mg/d of atorvastatin and 40%–44% reduction with 10 mg/d of rosuvastatin) [37–39].

In a pharmacokinetic study involving a diverse population of Asians, including Asian Indians, rosuvastatin drug levels were found to be elevated approximately twofold compared with a white control group [40]. However, post-marketing data for all statins have not identified any particular safety issues, even when statins are given at equivalent doses. Nonetheless, it is advisable not to use the maximum dose of any statins among Asians, including Asian Indians, because of risk of increased blood levels and anecdotal information of markedly increased myalgia.

Niacin Treatment for Lp(a) Excess and Low HDL

Even when LDL is lowered to less than 70 mg/dL, approximately 60% to 65% of MACEs are not prevented. This residual risk was 86% among those patients who had combined elevations of LDL and Lp(a) in the Scandinavian Simvastatin Survival Study (4S) [41]. In this study, compared with placebo, simvastatin therapy achieved an LDL-C reduction of 35% [41]. A total of 1042 MACEs, including 432 deaths, were observed among 4444 patients during 24,455 patient-years of follow-up. There was a highly significant 30% relative reduction in overall mortality with simvastatin therapy. Lp(a) was a strong predictor of MACEs and death in both placebo and treatment groups. More importantly, the numbers of deaths differed significantly in the simvastatin groups between quartiles of Lp(a). The reduction in mortality was almost double in those with low Lp(a) levels (58%) and only half in those in the highest quartile of Lp(a) (14%). The 4S results underscore the limitations of LDL-lowering therapy and the need for treatment directed at other lipoproteins, such as low HDL and high Lp(a). However, no outcome studies have been performed to assess the benefits of lowering Lp(a).

Niacin, a unique broad-spectrum antilipemic agent that modestly lowers LDL and robustly lowers VLDL and Lp(a), is by far the most potent agent to raise HDL. Niacin at 4 g/d can reduce Lp(a) by 38% [42]. Niacin has also been shown to produce regression of atherosclerosis and reduce MACEs and total mortality with long-term use. Extended-release niacin (niacin-ER [Niaspan; Kos Pharmaceuticals, Cranbury, NJ]) is approved for treatment of dyslipidemia, and at a dose of 2 g/d it reduces LDL by 16%, apoB by 15%, TG by 32%, and Lp(a) by 25%, and it increases HDL by 40% [43].

Mixed Dyslipidemia and Combination Therapy

Combination therapy is required for the management of most patients with hypertension and diabetes. This is equally true for dyslipidemia, especially among Asian Indians, who often have qualitative and quantitative abnormalities in various lipoproteins. Niacin can be safely combined with statins and resins with augmented changes in lipoprotein levels. Simvastatin plus niacin was shown to provide marked clinical and angiographically measurable benefits in patients with CAD and low HDL levels, with a 60% to 90% reduction in MACEs.

The US Food and Drug Administration (FDA) has approved a combination of niacin-ER plus lovastatin (Advicor; Kos Pharmaceuticals, Cranbury, NJ) for the treatment of dyslipidemia. The effect of this fixed-dose combination was studied in 131 patients in India with LDL-C greater than 130 mg/dL. All subjects were administered a combination of lovastatin (20 mg) and niacin-ER (500 mg) once daily for 24 weeks. Dose escalation (niacin-ER, 1 g) on the basis of lipid parameters and NCEP goals were needed only in 11 patients. The percentage of decline was as follows: LDL-C 38%; TG 21%; Lp(a) 44.5% ($P < 0.01$). HDL-C increased by 18.2% and the apoA1/apoB ratio increased by 51.6% ($P < 0.01$) (Table 1) [44••]. Target LDL levels were achieved in 80.7% of the patients. The efficacy of this fixed combination appears to be higher than reported in other populations [45]. Various combinations of statins, fenofibrate, ezetemibe, and fish oil have been shown to improve lipoproteins more than statin monotherapy alone.

Table 1. Effects of 20 mg/d of lovastatin plus 500 mg/d* of niacin over 24 weeks

	Baseline	24 weeks	Change	*P* value
Total cholesterol	239.9 ± 27.4 mg/dL	174.9 ± 27.2 mg/dL	-25.2%	< 0.05
Low-density lipoprotein	153.4 ± 21.9 mg/dL	95.1 ± 23.1 mg/dL	-38.0%	< 0.05
Triglycerides	171.1 ± 72.2 mg/dL	135.2 ± 40.5 mg/dL	-21.0%	< 0.05
High-density lipoprotein	45.6 ± 7.4 mg/dL	53.9 ± 9.5 mg/dL	+18.2%	< 0.05
Lipoprotein(a)	48.5 ± 26.4 mg/dL	26.9 ± 19 mg/dL	-44.5%	< 0.05
ApoA-1/apoB	0.96 ± 0.67 mg/dL	1.45 ± 0.5 mg/dL	+51.6%	< 0.05

*11 patients received 1000 mg/d of extended-release niacin.
Apo—apolipoprotein.
(*Data from* Sharma et al. [44••].)

Rationale for Aggressive Preventive Therapy for South Asians

"Normal" ranges for risk factors such as blood pressure, lipid profile, and BMI derived from studies in white populations may not be applicable to populations such as Chinese, Japanese, and South Asians. The Framingham Risk Score under-estimates the risk among Asian Indians by as much as 200% (Fig. 2) [30••]. Various adjustments that have been proposed to compensate for this underestimation of risk in nondiabetic South Asians include adding 10 years to age, 50 mm Hg to systolic blood pressure, 100 mg/dL to TC levels, or multiplying the TC/HDL ratio by 1.5 [46••]. Whereas the New Zealand Guidelines recommend moving up by one risk category (10-year risk of 10%) [28••], the Joint British Society and South Asian Health Foundation [47••] recommend that the 10-year CAD risk calculated from the Framingham Risk Score be multiplied by 1.4 among South Asians. Others have recommended multiplication of the Framingham Risk Score by a factor of 1.8 [28••], and the author [3••] recommends multiplying by 2.0. All these recommendations essentially gravitate to using a lower CAD risk threshold for lifestyle and pharmacologic intervention.

Although the major modifiable risk factors, such as smoking, high blood pressure, and high cholesterol, do not fully explain the excess burden of CAD among South Asians, these factors are doubly important and remain the principal targets for preventive therapy among South Asians. The alarming epidemic of CAD among South Asians underscores the need for early and aggressive preventive therapy, such as regular physical activity, lifetime tobacco abstinence, and increased intake of fruits and vegetables. Watching the saturated fat intake and waist size is more important than watching cholesterol intake and body weight.

Because the CAD risk from any given risk factor is higher among South Asians, the threshold of intervention and target goal of treatment should be at least 10% lower for various modifiable risk factors and 20% lower for LDL and non–HDL-C (similar to the recommendations for people with diabetes and CAD). The IDF has already proposed a lower waist circumference for South Asians. For Asians, the World Health Organization has also proposed lower BMI cut-points for overweight (> 23) and obesity (> 25). The American Association of Physicians of Indian origin (AAPI) recommends LDL less than 100 mg/dL and non–HDL-C less than 130 mg/dL for all Asian Indians without CAD and diabetes. The recommended goal is LDL less than 70 mg/dL and non–HDL-C less than 100 mg/dL for Asian Indians with diabetes or CAD [48••]. This is by far the simplest and most effective recommendation and is in agreement with the current literature [3••].

Consideration should also be given for treatment of other lipid abnormalities, especially HDL-C, Lp(a), and TG using FDA-approved medications. The benefits of optimal medical therapy in patients with CAD have been clearly documented [49]. Because of small dense dysfunctional HDL, raising the large HDL is likely to have greater benefit among South Asians than whites. It has been estimated that the aggressive treatment of all modifiable risk factors, including raising HDL-C, can reduce the CAD burden in South Asian men by 59% and women by 67% (Table 2) [33••].

Conclusions

The high rates of malignant CAD among South Asians are due to a combination of genetically determined Lp(a) excess and lifestyle factors, with the former magnifying the risk from the latter. Lifestyle and pharmacologic interventions are warranted for all modifiable risk factors at a younger age. The threshold of intervention and goal of treatment should be at least 10% lower for various modifiable risk factors and 20% lower for LDL and non–HDL-C. The target goals for South Asians without CAD or diabetes are less than 100 mg/dL for LDL and less than 130 mg/dL for non–HDL-C. Among those with diabetes or CAD, target goals are less than 70 mg/dL for LDL and less than 100 mg/dL for non–HDL-C. Many statins are approved for use among children and adolescents, and the safety and efficacy profile of statins among South Asians are no different from whites except for anecdotal information of increased myalgia. The current evidence of established safety and broad-spectrum lipoprotein benefits of statins and niacin would make these invaluable agents in the armamentarium against dyslipidemia in South Asians. Those with metabolic syndrome and

Table 2. Ethnic differences in predicted coronary artery disease risk reduction with aggressive control of risk factors in the United Kingdom

	Risk reduction			
	White men	**South Asian men**	**White women**	**South Asian women**
BP: 115 mm Hg	14%	5%	16%	14%
TC: 174 mg/dL	30%	28%	21%	19%
HDL: 50 mg/dL men	-3%	19%	NA	NA
HDL: 62 mg/dL women	NA	NA	0%	41%
No smoking	16%	15%	16%	1%
No diabetes	2%	9%	3%	16%
All changes	50%	59%	48%	67%

BP—blood pressure; HDL—high-density lipoprotein; NA—not applicable; TC—total cholesterol.
(*Data from* Bhopal et al. [33••].)

diabetes may need high-dose statins or low-dose statins in combination with fenofibrate, ezetemibe, or fish oil. Regular physical activity, lifetime abstinence of tobacco, avoidance in the consumption of trans fats (fried food), and reduced intake of saturated fats together with an increased intake of fruits and vegetables form the foundation of lifestyle changes that can both reduce the dose and need for medications.

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