Does being “South Asian” increase the risk of CAD?

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Since many disease aetiologies have a genetic contribution, the use of ethnic categories (or “geographical ancestries”) can be a useful way of integrating a range of cultural and genetic attributes in order to elucidate the association between such factors and disease susceptibility. "South Asia" is usually defined as the area encompassing Pakistan, Nepal, Bangladesh, India, and Sri Lanka. Numerous observational studies have been done showing that South Asians, both in situ in South Asia and in South Asian diaspora communities, are at increased risk for cardiovascular disease, especially coronary artery disease (CAD), a finding with major implications for clinical practice in countries such as Canada, where South Asians are the third most populous immigrant group. While not every South Asian may develop CAD-related morbidity, one approach to preventive medicine is the application of interventions in an entire at-risk population, rather than targeting interventions to individuals on a case-by-case basis. Such population-wide interventions might, however, do more harm than good if their risks and costs outweigh their benefits, and if they cause the clinician or the patient to neglect modifiable independent risk factors with a proven causative role in disease aetiology. We therefore present a critical look at literature suggesting the use of South Asian ethnicity as an independent risk factor in the development of CAD.

Epidemiology of CAD in South Asian Populations

Unfortunately, there are no large multi-centre studies performed in regions of South Asia, and the national figures available from India are based on pooling of studies taken from different centres at different time points. More importantly, such data are not directly comparable with those from South Asian diaspora communities, for which disease prevalence estimates are sometimes more scarce and less reliable than mortality rates. World Health Organization (WHO) data are typically expressed as DALYs, but this is a flawed measure of disease burden, and not necessarily a good indicator of risk. Mortality from CAD in India has been calculated to be 0.85 million in men and 0.74 million in women, totaling 1.59 million deaths in 2000.\(^1\) For an Indian population of 1.05 billion in 2000, this translates to a mortality rate of 151 CAD deaths/100000 people. Global mortality from ischaemic heart disease, which correlates closely with symptomatic CAD, stands at 115 deaths/100,000.\(^2\) Like the DALY, mortality is highly subject to local socioeconomic conditions, and is therefore not a good indicator of risk. Similar challenges exist in surveillance of South Asian populations outside of South Asia, though these are mitigated by smaller overall population size. For instance, in Canada, ischaemic heart disease mortality is roughly similar between South Asian men and European-origin men: approximately 320 deaths/100000 per year between 1979 and- 1993,\(^3\) but is increased for South Asian versus European-origin women: 145 versus 109.9 deaths per year between 1979 and 1993. The comparison is more valid than at the international level, given more uniform social conditions within Canada. Furthermore, prevalence estimates within Canada between ethnic groups were made in the Study of Health Assessment and Risk in Ethnic groups (SHARE), which showed a prevalence of 8.6% in the South Asian origin cohort compared to 4.9% in the European origin one.\(^4\) Data in UK and US cohorts show similar trends.\(^5-6\)

Is risk genetic?

While the epidemiological data may support increased cardiovascular disease risk in South Asians versus other populations, this does not necessarily imply that genetic factors in the group described as “South Asians” are of primary importance. Culture – including diet, activity and social factors – while "heritable,” is unlike the genome in that the consequences of
cultural factors in determining risk might be more amenable to modification through education and counseling. Some authors, however, assert that the degree to which risk is increased amongst South Asians is too high to be accounted for only by lifestyle factors. This has led to considerable discussion of whether or not South Asian origin should be considered an independent risk factor for CVD disease.

The attempt to find biochemical markers for genetically determined risk is in its infancy and has met mixed results. Some work has been done associating polymorphisms in homocysteine metabolic pathways with carotid atherosclerosis, but a causative link has not been well-described. Thus far, the only biochemical marker with a clear association with South Asian origin that is based in genetics, and not the environment, is a high plasma level of Lipoprotein (a), which has been considered as an emerging risk factor by the U.S. National Cholesterol Education Program (NCEP). Both clinical and basic science data strongly suggest both that Lp(a) is under genetic control and that expression of particular alleles plays a causative role in atherosclerosis and the aetiology of thrombogenic conditions.

This alone does not necessitate that elevated plasma Lp(a), or any other independent risk factor associated with South Asian origin, is primarily to blame for the increased prevalence and mortality of CAD in South Asians. The importance of environment and lifestyle over genetics was highlighted in a study by Bhatnagar et al in the Lancet, that showed significant differences in cardiovascular disease risk factors between siblings of South Asian origin who lived in either West London or Punjab state. While some risk factors, such as Lp(a), were similar between the cohorts, indicating a genetic component, blood glucose, beta cell function, serum apo B, and body mass index (BMI) were all appreciably worse in the UK cohort.

Since environment, and therefore lifestyle, obviously contributes to the growth of CAD amongst South Asians in Western countries, research is required to determine whether or not genetics, environment, or an interaction between them fundamentally explains the increased risk. Unfortunately, to date no study claiming an increase in independent risk factors amongst South Asians has properly controlled for lifestyle factors – instead indirect biochemical or anthropometric surrogates such as insulin sensitivity, dyslipidemia, or central adiposity have been used to argue that South Asians are more susceptible to the effects of a sedentary lifestyle, perhaps by virtue of genetics. Cultural attitudes towards diet and exercise are, however, heritable or perhaps learned, and could result in increased exposure of South Asians to negative lifestyle factors, explaining the increase in risk without the need to invoke genetics.

Culture can and does have a profound impact upon how a group views health-related lifestyle choices, such as frequency of exercise or the content of the diet. On the question of exercise, a small study (n = 56) published by Lip and coworkers showed South Asians presenting with acute MI were much less likely than their Caucasian counterparts to have engaged in regular exercise. At least 12 other studies on the general population of South Asians in the UK have been done. A systematic review revealed that British South Asians were generally less physically active than their "white" or "European" counterparts.

In the field of diet and nutrition, the data leave much to be desired in terms of inter-ethnic comparisons. Recent evidence, however, shows that Canadian South Asians on average consume a higher proportion of calories as carbohydrate than Europeans, Aboriginals, or Chinese persons. In the same cohort, consumption of carbohydrates was inversely related to serum HDL, a potent protective factor against CAD. In preliminary data from schoolchildren in the UK, South Asian students consumed less fresh fruit and vegetables than white children did. South Asian cooking, particularly from northern India and Pakistan does not typically involve the use of raw vegetables, and there is a strong reliance upon saturated fats for cooking, evidenced by the widespread use of ghee (clarified butter) and khoya or mawa (precipitated whole milk) in traditional food.
The validity of the concept of "Ethnicity"
The current literature does not recognize potential genetic heterogeneity amongst South Asians. Whilst this overall categorization of “South Asian” may be useful “shorthand” that might simplify data collection, it is predisposes studies to sampling error: there might be substrata in a sample labelled as being “South Asian” that have different risk than others so classified, but which would be falsely seen as representative of the whole population.

India, Pakistan, Bangladesh, Nepal, and Sri Lanka each have genetically and culturally distinct sub-populations, and cultural differences need not track with genetics. Even in the relatively confined space of Sri Lanka, 5 genetically distinct populations are discernible, and Tamils and Sinhalese, the two largest groups, both have the least in common, from a genetic perspective, with India’s Veddahs, Gujaratis and Punjabis.

Whether genetic or cultural, heterogeneity can be shown to manifest itself in different cardiovascular risks between population substrata. For instance, Bangladeshis in the UK have been shown to have the highest cardiovascular risk of any South Asian group, both from biochemical data, and from self-reported lifestyle factors, with Pakistanis also having demonstrably higher risk than Indians. These national groupings (“geographical ancestries”) may themselves be further misleading, given the significant cultural and genetic overlap between North India and Pakistan, as well as the over-representation of certain ethnic groups within those countries in the UK.

Given the history and ethnology of the "South Asian" region, such use of generalized ethnic origin as a risk factor cannot be justified based upon the current evidence, which is as imprecise as studies in “Europeans” that have not differentiated between such diverse subpopulations as Italians, Finns, Icelanders or Ashkenazim.

Conclusions
Despite the volume of studies published, there is no definitive evidence that South Asian origin can be yet used as an independent risk factor when considering a patient’s CAD risk in order to plan interventions. As with most individual patients, biochemical and biometric data may be useful as "red flags" for the physician, and more precise indicators of risk for the specific patient since they more directly reflect potential underlying disease processes. Clinicians do not treat populations, they treat individuals, and each individual's risk profile is still related to behaviour, regardless of the genetic contribution. Since genetic risk factors are not amenable to modification, the sensible course of action is to base treatment strategies upon the individual patient's history and circumstances, and to make the same key recommendation to South Asian patients as is made to all other patients – the adoption of a healthy diet and regular exercise.

References


