

# Long-term prognosis of south Asians following acute coronary syndromes

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**BACKGROUND:** South Asians (SAs) have a higher prevalence of coronary artery disease than Caucasians. The long-term prognosis following acute coronary syndromes (ACS) in SA compared with non-SA patients is unclear.

**OBJECTIVES:** To compare the long-term adverse cardiovascular outcomes between SA and non-SA patients who have ACS.

**METHODS:** A case-control study of 65 consecutive SA patients admitted with ACS to the McGill University Health Centre (Montreal, Quebec) between 1995 and 2000 was conducted. Control subjects included 65 non-SA patients admitted to the same hospital with ACS matched by age, sex and year of hospitalization.

**RESULTS:** The mean  $\pm$  SD age was 59.7 $\pm$ 9.9 years and 12% of patients were women. There were more cases of diabetes mellitus among the SA patients than non-SA patients (43% versus 23%, respectively). Only 19% of SA patients were active smokers, compared with 34% of non-SA patients. At one year, 35% of SA patients had undergone coronary artery bypass graft surgery, compared with 22% of non-SA patients. One-year mortality was increased among the SA patients compared with the non-SA patients (6% versus 2%, respectively). However, SA ethnicity was not an independent predictor of one-year adverse cardiovascular outcomes.

**CONCLUSIONS:** The present study demonstrated an increased prevalence of diabetes mellitus among the SA patients with ACS compared with non-SA patients. SA patients had increased one-year mortality compared with non-SA patients. However, SA ethnicity was not an independent predictor of one-year mortality and coronary intervention.

**Key Words:** *Acute coronary syndromes; Acute myocardial infarction; Coronary artery bypass graft; Ethnicity; Percutaneous coronary intervention; South Asian; Unstable angina*

Coronary artery disease (CAD) remains a significant worldwide health problem. Despite its global implications, most studies have investigated the burden, prevention and treatment strategies traditionally in Caucasian populations. However, there are important racial variations in the prevalence of CAD (1-4), with a high prevalence in the south Asian (SA) population and a low prevalence in the Chinese population (5). These variations persist despite immigration of these populations, suggesting a genetic influence on the risk of CAD. These variations of CAD among populations are also accentuated by migration to urban centres, suggesting a possible involvement of diet and environmental effects (6).

There is a paucity of studies examining the prognosis of SA patients admitted with acute coronary syndromes (ACS). Gupta et al (7) showed similar rates of in-hospital mortalities among SA and non-SA patients admitted for myocardial infarction (MI). Other studies examining long-term outcomes of SA patients were completed before the era of aggressive coronary intervention and potent antiplatelet therapies

## Le pronostic à long terme des Asiatiques du Sud après un syndrome coronarien aigu

**HISTORIQUE :** Les Asiatiques du Sud (AS) ont une plus forte prévalence de coronaropathie que les Blancs. On ne connaît pas le pronostic à long terme d'un syndrome coronarien aigu (SCA) chez les AS par rapport aux non-AS.

**OBJECTIFS :** Comparer les issues cardiovasculaires négatives à long terme chez les AS par rapport aux patients non AS atteints d'un SCA.

**MÉTHODOLOGIE :** Les auteurs ont mené une étude cas-témoin auprès de 65 patients AS consécutifs hospitalisés au Centre de santé de l'Université McGill (de Montréal, au Québec) à cause d'un SCA entre 1995 et 2000. Les sujets témoins étaient 65 patients non AS hospitalisés dans le même hôpital à cause d'un SCA et appariés selon l'âge, le sexe et l'année d'hospitalisation.

**RÉSULTATS :** L'âge moyen  $\pm$  ÉT était de 59,7 $\pm$ 9,9 ans et 12 % des patients étaient des femmes. Il y avait plus de cas de diabète chez les patients AS que non AS (43 % par rapport à 23 %, respectivement). Seulement 19 % des patients AS étaient des fumeurs actifs, par rapport à 34 % des patients non AS. Au bout d'un an, 35 % des patients AS avaient subi un pontage aortocoronarien, par rapport à 22 % des patients non AS. La mortalité au bout d'un an était plus élevée chez les patients AS que non AS (6 % par rapport à 2 %, respectivement). Cependant, l'ethnie AS n'était pas un prédicteur indépendant d'issue cardiovasculaire négative au bout d'un an.

**CONCLUSIONS :** La présente étude démontre une prévalence de diabète plus élevée chez les patients AS atteints d'un SCA que chez les patients non AS. Les patients AS présentaient une mortalité plus élevée au bout d'un an que les patients non AS. Cependant, l'ethnie AS n'était pas un prédicteur indépendant d'issue cardiovasculaire négative et d'intervention coronaire au bout d'un an.

(8,9). It is unclear whether the long-term outcomes of SAs are similar to those of the non-SAs with ACS in this contemporary era. This issue is particularly important as ethnic diversity in the Canadian population increases. The primary objective of the present study was to compare the long-term prognosis of SA with non-SA patients following ACS.

## METHODS

The charts of all patients with ACS admitted to the two coronary care units of the McGill University Health Centre (Montreal, Quebec), from 1995 to 2000 were reviewed. The two coronary care units involved (Royal Victoria Hospital and Montreal General Hospital, both in Montreal) are tertiary care cardiac centres with onsite facilities for percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery. All patients with a final discharge diagnosis of nonatherosclerotic CAD and those who were transferred from other hospitals were excluded. SA patients were identified by the country of origin and/or by surnames, and included patients whose

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**TABLE 1**  
**Risk factor profile among south Asian (SA) and non-SA patients**

	SAs (n=65)	Non-SAs (n=65)
Age, years (mean $\pm$ SD)	59.7 $\pm$ 9.9	59.7 $\pm$ 9.9
Female sex, n (%)	8 (12.3)	8 (12.3)
Diabetes mellitus, n (%)	28 (43.1)	15 (23.1)
Hypertension, n (%)	30 (46.2)	27 (41.5)
Active smoking, n (%)	12 (18.5)	22 (33.8)

**TABLE 2**  
**Mortality and coronary intervention**

	In-hospital		One-year	
	SAs (n=65)	Non-SAs (n=65)	SAs (n=65)	Non-SAs (n=65)
All-cause mortality, n (%)	3 (4.6)	1 (1.5)	4 (6.1)	1 (1.5)
PCI, n (%)	17 (26.1)	22 (33.8)	31 (47.6)	40 (61.5)
CABG, n (%)	21 (32.3)	12 (18.5)	23 (35.3)	14 (21.5)

CABG Coronary artery bypass graft; PCI Percutaneous coronary intervention; SAs South Asians

country of birth was India, Pakistan, Bangladesh or Sri Lanka. This method has been validated by Sheth et al (10). For each case, one control subject was selected at random among all non-SA and non-Chinese patients, matched with the case by age ( $\pm 5$  years), sex and year of hospitalization. Patients of Chinese origin were excluded because this population has a lower prevalence of CAD and, possibly, less ischemic burden (5). Chinese patients were identified by the same method of examining the country of origin and/or surnames.

All charts were reviewed for the following patient characteristics: age, sex, smoking history, history of hypertension, diabetes mellitus, previous MI, lipid profile, intervention and in-hospital outcomes. All-cause mortality, reinfarction and revascularization (PCI or CABG) were examined during hospitalization and one year following the index hospitalization. MI was defined as having ischemic symptoms associated with creatine kinase (myocardial band) elevation and/or new Q waves on electrocardiogram. Unstable angina was defined as having ischemic symptoms without any elevation of serum creatine kinase (myocardial band) and with at least one of the following: electrocardiogram changes, positive stress test, or 50% or greater major epicardial coronary stenosis documented by coronary angiography. One-year outcomes were obtained through review of clinic and emergency room visits. The study was approved by the local director of professional services.

#### Statistical analysis

Patient characteristics on admission were summarized using mean  $\pm$  SD and proportions as appropriate. McNemar's test was used to compare categorical data between cases and controls, and paired Student's two-tailed *t* test was used for continuous data. A multivariable conditional logistic regression model was used to assess the association of cardiovascular risk factors, including diabetes, hypertension and hyperlipidemia, to ethnicity (SA versus non-SA). First, univariate analyses were conducted, and variables with  $P \leq 0.25$  were entered into the multivariable model. A backward selection was performed, in which an independent variable was kept in the model if it was statistically significant at a 0.10 level of significance. The age- and sex-adjusted risks of mortality, reinfarction and revascularization, and the risk of the combined outcome of reinfarction/revascularization/mortality were calculated for cases and controls one year following the index ACS. McNemar's test was used to compare these risks between cases and controls. All analyses were performed using SAS version 8.2 (SAS Institute Inc, USA).

**TABLE 3**  
**Association of south Asian ethnicity with one-year mortality and coronary intervention, adjusted for diabetes mellitus**

	OR	95% CI
All-cause mortality	0.98	(0.95–1.02)
Myocardial infarction	0.91	(0.63–1.31)
Percutaneous coronary intervention	0.98	(0.68–1.43)
Coronary artery bypass graft	1.03	(0.78–1.35)

## RESULTS

Sixty-five SA patients with ACS were identified and matched to 65 non-SA control patients. All had survival status determined at one year. The mean age in cases and controls was 59.7 $\pm$ 9.9 years, and 12% were women. There were significant differences in risk factors; 43% of subjects in the SA group were diabetic, while only 23% of subjects in the control group were diabetic (Table 1). In the SA group, only 19% of patients were smokers compared with 34% in the control group. The prevalence of hypertension was similar between SA and non-SA patients. The prevalence of dyslipidemia could not be reliably assessed because of inconsistent recording of lipid profiles at the McGill University Health Centre during the study period.

There were fewer PCI (26% versus 34%) and more CABG (32% versus 18%) procedures among SA patients than non-SA patients, respectively during the index hospitalization. SA patients had higher in-hospital mortality than non-SA patients (5% versus 2%) (Table 2). At one year, SA patients underwent fewer PCI (48% versus 62%) and more CABG (35% versus 22%) procedures than non-SA patients. One-year mortality was higher among SA patients than non-SA patients (6.1% versus 1.5%) (Table 2). However, SA ethnicity was not an independent predictor of one-year cardiovascular outcomes (Table 3).

## DISCUSSION

The SA patients had different risk factor profiles from the non-SA patients in our cohort. SA patients had higher prevalence of diabetes mellitus and were less active smokers compared with non-SA patients. This difference in risk factor profile was in agreement with previous reports (11–13). SAs have an increased concentration of adipose tissue metabolites such as leptin, resulting in an increased risk of insulin resistance and CAD even in the absence of obesity (14). SA patients also have increased levels of other risk factors for CAD. In particular, the increased levels of lipoprotein(a), fibrinogen, homocysteine and plasminogen activator inhibitor-1, as documented in SA patients (15–17), can potentially further increase the risk of CAD. Elevated inflammatory markers, such as C-reactive protein, may also be associated with increased prevalence of CAD in this population (18). More than one-half of the SA patients in our study had undergone coronary revascularization one year following the index ACS. CABG was more frequent at one year among the SA patients compared with the non-SA patients. In general, CABG is indicated for symptom relief in patients with disabling angina, and for survival benefit in patients with left main CAD and triple-vessel disease (or double-vessel disease including a proximal left anterior descending stenosis) combined with left ventricular systolic dysfunction (19). Thus, the increased use of CABG in SA patients may be a marker of increased CAD burden. Dhawan and Bray (20) demonstrated that SA patients were more likely to present with triple-vessel disease than Caucasians. Furthermore, the high prevalence of diabetes mellitus in SAs may have led clinicians to favour CABG in this population because it offers more survival benefit than PCI in diabetic patients (21).

Our in-hospital CABG and mortality rates were in agreement with those of Gupta et al (7), who showed that the need for urgent CABG was doubled in SA patients compared with control patients (4.2%

versus 2.2%). They found no difference in in-hospital mortality between the two groups (9.6% versus 7.8%;  $P=0.27$ ). Data of long-term outcomes were not available in this study.

Wilkinson et al (8) showed similar six-month mortality after adjustment for diabetes among 149 SA patients compared with 313 Caucasian patients (adjusted hazard ratio 1.26, 95% CI 0.68 to 2.33). Mukhtar et al (22) showed no significant survival difference in 102 SA and 102 matched Caucasian patients following an acute MI. Data concerning revascularization were not available from these studies. Both of these studies were completed from 1993 to 1995, and treatment of ACS has evolved with the introduction of more aggressive antiplatelet therapies and coronary interventions. It is unclear whether aggressive coronary intervention would improve the long-term outcomes among SA patients.

#### Limitations

The main limitation of the present study is the small number of patients, which limited its statistical power to show significant differences in major cardiovascular outcomes among the two groups of patients. Second, the study's retrospective design, with its inherent problem of missing data, is also a major limitation. Third, dyslipidemia,

which may be more prevalent in SA patients, might have confounded the outcomes in these patients. Because we were unable to obtain complete data on dyslipidemia in our cohort, this further limited our assessment of whether SA ethnicity was an independent predictor of adverse long-term outcomes. Nevertheless, this study's strengths lied in the completeness of data concerning one-year outcomes. It provided additional insight into the long-term prognosis of SA patients in this era of aggressive medical and coronary intervention following ACS.

#### CONCLUSIONS

Our study demonstrated increased prevalence of diabetes mellitus among SA patients compared with non-SA patients with ACS. SA patients had increased one-year mortality compared with non-SA patients. However, SA ethnicity was not an independent predictor of one-year mortality or coronary intervention.

This manuscript was presented, in part, at the Canadian Cardiovascular Congress in Halifax, Nova Scotia (2001), and in Edmonton, Alberta (2002), as well as at the American Heart Asian Pacific Congress in Hawaii (2003).

#### REFERENCES

- Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998;97:596-601.
- Lanza GA. Ethnic variations in acute coronary syndromes. *Heart* 2004;90:595-7.
- Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part I: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001;104:2746-53.
- Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Indian Heart J* 1996;48:343-53.
- Sheth T, Nair C, Nargundkar M, Anand S, Yusuf S. Cardiovascular and cancer mortality among Canadians of European, south Asian and Chinese origin from 1979 to 1993: An analysis of 1.2 million deaths. *CMAJ* 1999;161:132-8. (Erratum in 1999;161:489).
- Pais P, Pogue J, Gerstein H, et al. Risk factors for acute myocardial infarction in Indians: A case-control study. *Lancet* 1996;348:358-63.
- Gupta M, Doobay AV, Singh N, et al. Risk factors, hospital management and outcomes after acute myocardial infarction in South Asian Canadians and matched control subjects. *CMAJ* 2002;166:717-22.
- Wilkinson P, Sayer J, Laji K, et al. Comparison of case fatality in south Asian and white patients after acute myocardial infarction: Observational study. *BMJ* 1996;312:1330-3.
- Mukhtar HT, Littler WA. Survival after acute myocardial infarction in Asian and white patients in Birmingham. *Br Heart J* 1995;73:122-4.
- Sheth T, Nargundkar M, Chagani K, Anand S, Nair C, Yusuf S. Classifying ethnicity utilizing the Canadian Mortality Data Base. *Ethn Health* 1997;2:287-95.
- Anand SS, Yusuf S, Vuksan V, et al. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: The Study of Health Assessment and Risk in Ethnic groups (SHARE). *Lancet* 2000;356:279-84.
- McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. *Circulation* 1993;87:152-61.
- Dhawan J. Coronary heart disease risks in Asian Indians. *Curr Opin Lipidol* 1996;7:196-8.
- Abate N, Chandalia M, Snell PG, Grundy SM. Adipose tissue metabolites and insulin resistance in nondiabetic Asian Indian men. *J Clin Endocrinol Metab* 2004;89:2750-5.
- Anand SS, Yusuf S, Vuksan V, et al. Differences in risk factors, atherosclerosis and cardiovascular disease between ethnic groups in Canada: The study of health assessment and risk in ethnic groups (SHARE). *Indian Heart J* 2000;52(7 Suppl):S35-43.
- Anand SS, Enas EA, Pogue J, Haffner S, Pearson T, Yusuf S. Elevated lipoprotein(a) levels in South Asians in North America. *Metabolism* 1998;47:182-4.
- Mohan V, Deepa R, Haranath SP, et al. Lipoprotein(a) is an independent risk factor for coronary artery disease in NIDDM patients in South India. *Diabetes Care* 1998;21:1819-23.
- Anand SS, Razak F, Yi Q, Davis B et al. C-Reactive Protein as a Screening Test for Cardiovascular Risk in a Multiethnic Population. *Arterioscler Thromb Vasc Biol* 2004;24:1-7.
- Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA Guidelines for Coronary Artery Bypass Graft Surgery: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). American College of Cardiology/American Heart Association. *J Am Coll Cardiol* 1999;34:1262-347.
- Dhawan J, Bray CL. Angiographic comparison of coronary artery disease between Asians and Caucasians. *Postgrad Med J* 1994;70:625-30.
- Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: The Bypass Angioplasty Revascularization Investigation (BARI). *Circulation* 1997;96:1761-9.
- Cannon CP, Weintraub WS, Demopoulos LA, et al; TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy) – Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 2001;344:1879-87.