CLINICAL CHARACTERISTICS OF SOUTH ASIAN PATIENTS HOSPITALIZED WITH HEART FAILURE

Narendra Singh, MD; Milan Gupta, MD

Ethnic variations in prevalence, presentation characteristics, and mortality have been identified in Canadian patients with coronary artery disease. Similar data with respect to heart failure do not exist. A retrospective sequential chart review of South Asians and non-South Asian Whites in Canada hospitalized with a primary diagnosis of congestive heart failure between 1997 and 1999 showed South Asians were significantly younger, of lower body mass index, were more often diabetic, and were less often smokers. In-hospital mortality was not different between groups, although South Asians were more likely to experience ventricular arrhythmias. Despite presenting at a younger age, South Asians had more high-risk features at hospital discharge. Since South Asians are at high risk of developing premature coronary artery disease, a more aggressive approach to prevention strategies in this ethnic group may reduce the subsequent burden of heart failure. (*Ethn Dis.* 2005;15:615–619)

Key Words: Diabetes, Ethnicity, Heart Failure, Population Health, South Asian

From Emory University School of Medicine, Division of Cardiology, Atlanta, Georgia (NS); McMaster University, Dept of Medicine, Hamilton, and Division of Cardiology, William Osler Health Centre, Brampton (MG), Ontario.

Address correspondence and reprint requests to Narendra Singh, MD; Northside Cardiology P.C.; 960 Johnson Ferry Road, Suite 500; Atlanta, GA 30342; 404-256-2525; 404-256-2535 (fax); mnsingh@yahoo.com

INTRODUCTION

South Asians are a diverse ethnic group whose ancestry originates from the Indian sub-continent that includes India, Pakistan, Nepal, Bangladesh, and Sri Lanka. South Asians have migrated to all parts of the world, and in Canada, they are the second-largest visible minority, numbering almost one million in the last census.[1] Previous studies have shown significant differences in cause-specific mortality between groups of differing ethnic origin in Canada. Cardiovascular disease mortality is more common in the South Asian and European Canadian populations and relatively less common among Chinese Canadians. Conversely, cancer mortality is more common in the Chinese Canadian population.[2] Since these diseases share certain risk factors in common, differing mortality rates suggest an important influence of ethnicity on outcome. In a random sampling of Canadians of European, South Asian, and Chinese ancestry, South Asian ethnicity was identified as an independent risk factor for cardiovascular disease.[3] South Asians develop acute myocardial infarction at a younger age compared to Europeans.[4] We have recently shown that South Asians are more likely to have an anterior wall myocardial infarction and present to the hospital later during an acute myocardial infarction than matched controls.[5]

Since South Asians develop coronary artery disease at an earlier age than non-South Asian Whites, they may also develop heart failure prematurely. To evaluate this hypothesis, we performed a retrospective comparison of baseline characteristics, processes of care, and in-hospital outcomes between South Asians and non-South Asian Whites in Canada who were hospitalized with a primary diagnosis of heart failure.

In a random sampling of Canadians of European, South Asian, and Chinese ancestry, South Asian ethnicity was identified as an independent risk factor for cardiovascular disease.[3]

METHODS

A retrospective sequential chart review of all patients hospitalized with a primary diagnosis of heart failure between 1997 and 1999 at two Toronto-area community hospitals was performed (William Osler Health Centre, Brampton Campus and the Rouge Valley Health System – Centenary Site in Scarborough). Both communities served by these hospitals have large South Asian populations. As well, these two hospitals are comparable in size, patient volumes, subspecialty services, and clinical quality indicators.[6] Surname analysis and self-reported ethnicity or country of birth, extracted from the medical record, were used to determine ethnicity. When coupled with country of birth, this method of determining ethnicity has 98% accuracy.[7] People of Southeast Asian, Arabic, African, Hispanic, and aboriginal descent were excluded. All remaining cases were used as the comparator group and were presumed to be non-South Asian Whites.

In cases where a patient had multiple admissions for heart failure during the study period, only the initial hospitalization was included for analysis. Cases were excluded if heart failure was a complication of a myocardial infarction defined as any cardiac enzyme/biomarker elevation >2× normal. Charts were reviewed for the following information: patient demographics, presence of self-reported conventional cardiac risk factors at admission, relevant laboratory results, processes of care including medical therapies, in-hospital revascularization, arrhythmias, need for mechanical ventilation, other complications, discharge medications, vital status, left ventricular ejection fraction (where available), and heart failure etiology (based on the attending physician's assessment).

STATISTICS

Data were collected by two trained medical students and reviewed for quality control by the authors. All categorical variables were analyzed by using the chi-squared test. Continuous variables were compared by using the Student *t* test, and Cox proportional hazard analysis was used to separate the effect of age and other traditional risk factors from ethnicity. A *P* value <0.05 was considered significant.

RESULTS

A total of 887 consecutive patients with a primary diagnosis of heart failure were identified and entered into the database. Of these, 60 (6.8%) were excluded for other ethnicity. Of the remaining, 99 (12%) were classified as South Asian and 728 (88%) were classified as non-South Asian Whites (Table 1). Sex was similar in both groups (51% vs 50% male). At hospital admission, South Asians were significantly younger than Europeans (69.1 ± 12 vs 75.1 ± 13 years, *P*=.000017). This difference was further accentuated between South Asians and non-South Asian Whites presenting with their first heart failure hospitalization (67.1 ± 14 vs 73.7 ± 19 years, *P*=.02). South Asians had a significantly lower body mass index (24.4 vs 26.7 kg/m^2, *P*=.003) which was mainly a function of weight (67 ± 17 vs 74 ± 20 kg) rather than height (165 ± 9 vs 166 ± 15 cm). South Asians were more often diabetic (57% vs 39%, *P*=.00065) and were less likely to be current or former smokers (24% vs 41%, *P*=.0014). Rates of hypertension (62% vs 59%) and treated hyperlipidemia (27% vs 22%) were similar between the two groups. Prior history of myocardial infarction (53% vs 50%) and prior heart failure presentation (57% vs 58%) were also similar between groups.

Table 1. Baseline Characteristics

	South Asians (*N*=99)	Non-South Asian Whites (*N*=728)	*P* value
Age (years)	69.1±12	75.1±13	0.000017
Males (%)	51	50	ns
Weight (kg)	66.7±17	73.9±20	0.0031
Height (cm)	165±9	167±15	ns
Hypertension (%)	62	59	ns
Diabetes (%)	57	39	<0.001
Hyperlipidemia (%)	27	22	ns
Current/former smoker (%)	24	41	<0.001
Previous myocardial infarction (%)	53	50	ns
Previous congestive heart failure (%)	57	58	ns
Heart failure etiology			
Ischemic (%)	49	48	ns
Dilated cardiomyopathy (%)	10	7	ns
Valvular (%)	7	5	ns
Undefined or mixed (%)	20	16	ns

The etiology of heart failure was similar between South Asians and non-South Asian Whites. Ischemic heart disease was the most common cause (49% vs 48%) followed by cardiomyopathy (10% vs 7%) and then valvular heart disease (7% vs 5%). In a small and similar proportion of patients, the etiology of heart failure was either mixed or not clearly identifiable (20% vs 16%, *P*=ns for all comparisons).

Serum sodium level (Table 2) at admission was significantly lower in South Asians (135 ± 6 vs 137 ± 5 mmol/L, *P*=.002). The serum creatinine level was higher in South Asians at

Table 2. Biochemical and hemodynamic markers of risk

	South Asians (*N*=99)	Non-South Asian Whites (*N*=728)	*P* value
On Admission:			
Heart rate (bpm)	98±26	96±25	0.38
Systolic blood pressure (mm Hg)	139±20	138±47	0.83
Diastolic blood pressure (mm Hg)	82±21	77±17	0.015
Sodium (mmol/L)	135±6	137±5	0.002
Creatinine (mmol/L)	150±131	135±82	0.07
Hemoglobin (g/dL)	123±23	122±22	0.88
Ejection fraction (%)	40	42	0.41
On Discharge:			
Sodium (mmol/L)	136±13	137±4	0.14
Creatinine (mmol/L)	172±166	144±89	0.014

presentation (150 ± 131 vs 135 ± 82 mmol/L, *P*=.07), but this difference did not reach statistical significance. At the time of admission, no difference was seen in serum hemoglobin (123 ± 23 vs 122 ± 22 mg/dL). The mean systolic blood pressure (139 ± 30 vs 138 ± 47 mm Hg, *P*=.83) was similar although the mean diastolic pressure (82 ± 21 vs 77 ± 17 mm Hg, *P*=.015) was higher in South Asians. The mean heart rate (98 ± 26 vs 96 ± 25 beats/min, *P*=.38) was also similar. At discharge the serum sodium level remained lower in South Asians (136 ± 13 vs 137 ± 4 mmol/L), however this difference was no longer significant (*P*=.14). Serum creatinine increased more in South Asians during hospitalization and was significantly higher at discharge in South Asians (172 ± 166 vs 144 ± 89 mmol/L, *P*=.014).

Left ventricular ejection fraction measured within three months of hospital admission was available in 44% of patients. This measure was mainly obtained by echocardiography (94%). In this subset of patients with a documented ejection fraction, no difference was seen in global ejection fraction (40 vs 42%, *P*=.41).

Comparing South Asians to non-South Asian White patients, in-hospital procedures such as coronary angiography (8% vs 5%), pacemaker insertion (3% vs 2%), revascularization (1% vs 1%), or mechanical ventilation (5% vs 4%) were infrequent and not significantly different between groups (Table 3). In-hospital arrhythmias differed between the two groups. South Asians were twice as likely to experience ventricular tachycardia or ventricular fibrillation requiring treatment (10% vs 5%, *P*<.05), whereas non-South Asian Whites were more likely to have atrial fibrillation requiring treatment (15% vs 24%, *P*<.05). The incidence of stroke (1% vs 1%) or death (6% vs 10%) did not significantly differ during the hospitalization phase. The unadjusted odds ratio for death was 0.52 (95% confidence interval [CI] 0.22–1.19). This ratio did not change with age adjustment 0.67 (95% CI 0.28–1.61).

Table 3. In-hospital procedures and complications

	South Asians (*N*=99)	Non-South Asian Whites (*N*=728)	*P* value
Cardiac catheterization (%)	8	5	ns
Pacemaker insertion (%)	3	2	ns
PCI/CABG (%)	1	1	ns
Mechanical ventilation (%)	5	4	ns
Atrial fibrillation (%)	15	24	<0.05
Ventricular tachycardia/fibrillation (%)	10	5	<0.05
Stroke (%)	1	1	ns
Myocardial infarction (%)	10	12	ns
Death (%)	6	11	ns

PCI—percutaneous coronary intervention, CABG—coronary artery bypass graft.

In the hospital, no significant differences between South Asians and non-South Asian Whites were seen in the use of intravenous diuretics (87% vs 86%) inotropes (14% vs 13%), or vasodilators (9% vs 8%). Similarly at discharge, no significant differences were noted in the use of antiplatelet and antithrombotic therapy (62% vs 59%), beta-blockers (21% vs 20%), diuretics (88% vs 84%), angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (70% vs 66%), hydroxy-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (14% vs 11%), or amiodarone (14% vs 16%). Digoxin use was significantly higher in non-South Asian Whites (30% vs 42%, *P*<.05).

DISCUSSION

This study demonstrates that important differences at presentation and discharge exist between South Asians and non-South Asian Whites in Canada hospitalized with a primary diagnosis of heart failure. South Asians, on average, were six years younger than non-South Asian Whites when hospitalized for heart failure, and those South Asians hospitalized for the first time with heart failure were almost seven years younger. Despite having a lower body mass index (actually within the normal range), South Asians were much more likely to be diabetic. In fact, most South Asians in our study were diabetic (57%). This paradoxical finding is consistent with previous studies of South Asians with coronary artery disease[5] and supports the concept of a "thrifty genotype" leading to greater development of the metabolic syndrome and diabetes[8,9] in this patient population.

The etiology of heart failure was similar between the two groups; ischemic heart disease was the predominant factor. South Asians were more likely to have serious ventricular arrhythmias. Prior studies have shown a higher incidence of anterior wall myocardial infarctions and a trend toward larger infarctions in South Asians[5] This finding may be a possible explanation for

South Asians, on average, were six years younger than non-South Asian Whites when hospitalized for heart failure, and those South Asians hospitalized for the first time with heart failure were almost seven years younger.

the higher incidence of ventricular arrhythmias, although global ejection fraction was not different between the subgroups evaluated by echocardiography in this study. An alternative explanation for the higher frequency of serious ventricular arrhythmias may relate to the greater degree of renal dysfunction noted in the South Asian patients. Non-South Asian Whites were more likely to have atrial fibrillation, a common complication associated with heart failure. The explanation for this is not clear, although atrial fibrillation is known to be more common in older patients.[10] This finding warrants further evaluation but has been confirmed in a recent paper from the United Kingdom.[11] The higher digoxin use in non-South Asian Whites may be due to higher rates of atrial fibrillation, or alternatively, doctors may have had safety concerns with digoxin in South Asians because of their higher serum creatinine levels.

South Asians presented to the hospital with a lower serum sodium concentration and a higher creatinine level, both known markers of increased risk for adverse outcomes in the setting of heart failure.[12,13] The difference in renal impairment between groups persisted at discharge and suggests that South Asians may have a worse long-term prognosis, although our study was unable to determine outcomes beyond hospital discharge.

The unadjusted in-hospital mortality rate was not different between groups, but the absolute event rate was very small. This finding made adjusting for age and differences in traditional cardiac risk factors difficult with the Cox-proportional hazards model. With adjustment however, the in-hospital mortality remained statistically insignificant between groups. Longer follow-up and a larger sample size are required to more reliably determine if South Asians and non-South Asian Whites hospitalized with heart failure have similar outcomes.

As with all retrospective analyses, this study had some limitations. Assignment of ethnicity was retrospective and has the potential for error. However, cross-contamination by ethnicity assignment was likely bidirectional and therefore should not have influenced our findings to any significant degree. Race-based research has been challenged in recent editorials[14,15] highlighting the difficulty and subjectivity of such categorizations. Unlike race, the authors[14] point out that ethnicity incorporates socioeconomic and cultural values of a group of people and thus is more likely to be a relevant grouping for comparison. Both groups of authors conclude that racial and ethnic background should not be ignored, but by managing its downside, can serve as a starting point for future research. Left ventricular function data were incomplete, although to the same degree in both groups. B-type natriuretic peptide (BNP) levels were not routinely available to help confirm the clinical diagnosis of heart failure. To date, no studies have looked at potential differences in BNP levels in South Asians. Finally, post-discharge rates of intervention and outcomes were unavailable.

The key finding of this paper, a younger age of heart failure hospitalization in South Asians, was supported in a large historical cohort study from the United Kingdom.[11] We therefore believe that the results of this study are generalizable and may have important implications for clinicians treating South Asian patients. Despite presenting at a younger age, South Asians with heart failure have similar in-hospital morbidity and mortality. However, they leave the hospital with a higher risk profile, and they may be at higher risk for serious ventricular arrhythmias and progressive renal dysfunction. Since ischemic heart disease was the most common etiology, we hypothesize that the younger age of heart failure presentation is likely explained by the younger age at which South Asians develop coronary artery disease. South Asians are also more likely to present to the hospital later in the course of an acute myocardial infarction,[5] have an anterior myocardial infarction,[5] and have a greater burden of coronary artery disease at the time of coronary angiography.[16] These factors cumulatively could result in earlier left ventricular dysfunction leading to clinically apparent heart failure at a younger age.

Our findings suggest that the target for intervention in preventing heart failure should be at the level of preventing the acute coronary event from occurring in this high-risk patient population or at least diagnosing and treating LV dysfunction before it becomes symptomatic. We have previously shown in outpatients with stable coronary artery disease that assessment by a cardiologist can improve the use of evidence-based pharmacotherapy and potentially reduce the risk of subsequent events.[17] We believe that an aggressive strategy of risk factor intervention is likely to yield greater benefit compared to aggressive management once heart failure has manifested itself clinically.

This study also demonstrates that better use of proven heart failure therapies in all patient populations is needed. While ACE inhibitor/angiotensin receptor blocker use was reasonable, the use of beta-blockers and statins was low. This finding confirms those of many other investigators regarding such treatment gaps.[18] However, our data collection was carried out between 1997–1999 and predated the publication of the CIBIS II[19] and MERIT-HF[20] trials, and use of beta-blockers has improved since then.[21]

In summary, important differences at presentation and discharge exist between South Asians and non-South Asian Whites hospitalized for heart failure in Canada. Since South Asians are at high risk of developing premature coronary artery disease, a more aggressive approach to prevention strategies in

this ethnic group may reduce the subsequent burden of heart failure.

ACKNOWLEDGMENTS

We would like to acknowledge the tremendous work of Tuhina Biswas, Quoc Nguyen, and Kelly Ali in gathering and tabulating these data. We acknowledge the valuable statistical assistance of Steven Hawken. We acknowledge partial funding support by Roche Canada through an unrestricted research grant.

REFERENCES

1. *1996 Census: Population by Ethnic Origin*. Ottawa: Statistics Canada; 1997.
2. 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: analysis of 1.2 million deaths. *CMAJ*. 1999;161(2):132–138.
3. Anand S, Yusuf S, Vladmir 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;356:279–284.
4. Enas E, Garg A, Davidson M, Nair V, Huet B, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Ital Heart J*. 1996;48(4):343–353.
5. Gupta M, Doobay A, Singh N, et al. A comparison of risk factors, hospital management, and outcomes after acute myocardial infarction between South Asian and European Canadians. *CMAJ*. 2002;166(6): 717–722.
6. Tu JV, Austin P, Naylor D, Iron K, Zhang H. Acute myocardial infarction outcomes in Ontario. In: Naylor CD, Slaughter PM, eds. *Cardiovascular Health and Services in Ontario: An ICES Atlas*. Toronto: Institute for Clinical Evaluative Sciences, 1999;83–110.
7. Sheth T, Nargundkar M, Chagani K, Anand S, Nair C, Yusuf S. Classifying ethnicity utilizing the Canadian Mortality Data Base. *Ethn Health*. 1997;2(4):287–295.
8. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular disease: part 1: general considerations, the epidemiological transition, risk factors, and the impact of urbanization. *Circulation*. 2001;104:2746–2753.
9. Hales CN, Barker DJ. Thrifty genotype type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologica*. 1992;35:595–601.
10. Furburg CD, Psaty BM, Manolio TA, et al. Prevalence of atrial fibrillation in elderly subjects (The Cardiovascular Health Study). *Am J Cardiol*. 1994;74:236–241.
11. Blackledge HM, Newton J, Squire IB. Prognosis for South Asian and White patients newly admitted to hospital with heart failure in the United Kingdom: historical cohort study. *BMJ*. 2003;327:526–532.
12. Packer M, Lee WH, Kessler PD, et al. Role of neurohormone mechanisms in determining survival in patients with severe heart failure. *Circulation*. 1987;75(suppl 4):80–84.
13. Badr KF, Ichikawa II. Pre-renal failure. A deleterious shift from renal compensation to decompensation. *N Engl J Med*. 1988;319: 623–627.
14. Burchard EG, Ziv E, Coyle N, et al. The importance of race and ethnic background in biomedical research and clinical practice. *N Engl J Med*. 2003;348(12):1170–1175.
15. Bloche MG. Race-based therapeutics. *N Engl J Med*. 2004;351(10):2035–2037.
16. Gupta M, Singh N, Warsi M, Reiter N, Ali K. Canadian South Asians have more severe angiographic coronary disease than European Canadians despite having fewer risk factors [abstract]. *Can J Cardiol*. 2001;17(suppl C):68C.
17. Singh N, Gupta M, Jain A, Halperin D, Borts D. Differences in presentation and 1 yr outcomes in coronary artery disease (CAD) patients of South Asian versus European ethnicity treated in an outpatient cardiology practice [abstract]. *J Am Coll Cardiol*. 2001;37(suppl D):171D.
18. Tsuyuki RT, Ackman ML, Montague TJ, for the CQIN investigators. Effects of the 1994 Canadian Cardiovascular Society clinical practice guidelines for heart failure. *Can J Cardiol*. 2002;18(2):147–152.
19. CIBIS II Investigators and Committees. The Cardiac Insufficiency Bisoprolol Study II (CIBIS II): a randomized trial. *Lancet*. 1999;353:9–13.
20. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF). *Lancet*. 1999;353:2001–2007.
21. Johnson D, Jin Y, Quan H, Cujec B. Beta-blocker and angiotensin-converting enzyme inhibitors/receptor blockers prescriptions after hospital discharge for heart failure are associated with decreased mortality in Alberta, Canada. *J Am Coll Cardiol*. 2003;42(8): 1438–1445.

AUTHOR CONTRIBUTIONS

Design and concept of study: Singh, Gupta
Acquisition of data: Singh, Gupta
Data analysis and interpretation: Singh, Gupta
Manuscript draft: Singh, Gupta
Statistical expertise: Singh, Gupta
Acquisition of funding: Singh, Gupta
Supervision: Singh, Gupta