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ACUTE CORONARY SYNDROMES PRESENTATIONS AND CARE ACCESS IN WHITE, SOUTH ASIAN, AND CHINESE PATIENTS: A COHORT STUDY

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ABSTRACT

Objectives. Successful treatment of acute coronary syndrome (ACS) relies on its rapid recognition. It is unclear whether the accepted presentation of chest pain applies to different ethnic groups. We aimed to examine potential ethnic variations in ACS symptoms in white, south Asian, and Chinese patients.

Design. Cross sectional survey.

Setting. Participants had been hospitalized at one of 12 Canadian centres across 4 provinces.

Participants. 1334 ACS patients (630 white; 488 south Asian; 216 Chinese).

Main outcome measures. ACS presentation symptoms (including classic/typical mid-sternal pain/discomfort or mid-sternal pain/discomfort with radiation to the left neck, shoulder or arm) were assessed by self-report. Clinical outcomes (time to emergency room (ER) presentation, cardiac catheterization; receipt of cardiac catheterization, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) were obtained by health record audit.

Results. The mean age of the sample was 62 years and 30% had STEMI. A substantial proportion of patients reported atypical symptoms (33% white, 19% south Asian, 20% Chinese; $p<0.006$). Yet, the most common presenting symptom was mid-sternal pain/discomfort of any intensity regardless of ethnic status. After adjustment for age, sex, education, current smoking, presence of diabetes or chronic kidney disease, STEMI vs non-STEMI/unstable angina, and education, south Asians were more likely to present with at least moderate intensity mid-sternal pain/discomfort (Adjusted Odds Ratio (AOR) 1.44; 95% Confidence Interval (CI) 1.05-1.98) whereas Chinese were less likely to present with radiating symptoms (AOR 0.53; 95% CI 0.38-0.74) compared with whites. South Asians with atypical pain (relative to those with mid-sternal

pain/discomfort) took significantly longer to present to the ER (p=0.037), and were less likely to receive PCI (p=0.008) or CABG (p=0.041).

Conclusions. Atypical presentations were associated with greater delays in arrival to the emergency department and reduced invasive cardiovascular care in south Asians.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This was a rigorously designed study which included participants who spoke a variety of languages and used highly systematic and validated translation and data collection processes.
- A number of mechanisms were used to obtain a data regarding participants' ACS symptoms.
- Only participants who survived their ACS event were included in this study. It is not possible to know if patients who succumbed to their ACS event or did not seek care had different symptoms than those who were diagnosed and survived.
- There was a noteworthy proportion of south Asian and Chinese patients approached to participate who refused.

INTRODUCTION

The burden of acute coronary syndrome (ACS) is substantial is now the leading cause of death and disability world-wide.[1,2] Life-saving therapies for ACS are dependent on early and timely recognition of symptoms. Atypical presentation of ACS symptoms leads to delays in recognizing symptoms by both patients and healthcare providers, and can result in misdiagnosis, delayed treatment, receipt of fewer evidence-based therapies, and higher in-hospital morbidity and mortality.[3]

The 'classic' ACS presentation, based on the presentation of men of European descent, includes moderate to severe intensity central chest with or without left arm, neck or jaw radiating pain or discomfort.[4,5] This description has been adopted internationally, though some studies suggest that ACS symptoms may differ by ethnicity.[6-11] Although these studies yielded discordant findings, some noted that non-white patients may present with additional symptoms (e.g., gastro-intestinal, dyspnea, nausea)[6-9,11] and south Asians may have more diffuse pain and more frequent back pain[10] than whites. It is difficult to draw robust conclusions from the current evidence given variable methods of data collection, inadequate cross cultural language adaptation, small sample sizes, and insufficient adjustment for other factors (e.g., sex, age, clinical factors) that may influence ACS presentation.

South Asians have a higher incidence of ACS and earlier onset relative to other ethnic groups.[13,14] Though Chinese currently have a lower incidence of acute myocardial infarction (AMI) relative to whites and south Asians,[15,16] cardiovascular events in China are expected to rise by more than 50% by 2030.[17] A rigorous investigation of ACS symptom presentation, time to arrival to the emergency department and cardiovascular care between these ethnic groups is warranted to ensure appropriate public health messaging and/or inappropriate stereotyping of

presenting symptoms. We thus aimed to examine potential ethnic variations in ACS symptoms using a rigorously cross-culturally adapted symptom questionnaire and visual identifiers in a multi-centre cohort of white, south Asian, and Chinese patients hospitalized in Canada.

METHODS

Study design

We conducted a cross-sectional survey of a cohort of white (i.e., of European descent), south Asian (i.e., descended from India, Pakistan, Bangladesh, Sri Lanka), and Chinese (i.e., descended from China, Hong Kong, Taiwan, Macau) patients hospitalized with physician-confirmed ACS (unstable angina, ST-elevation (STEMI) or non-ST-elevation (non-STEMI) myocardial infarction[5]).

Setting and sample

Following institutional ethics review at each participating hospital, participants were recruited consecutively from 12 urban hospitals in 4 Canadian provinces (>90% of Canada's immigrants reside in urban areas and the majority reside in these provinces[12]) between September 2010 and December 2015. Inclusion criteria were age $\geq$ 19 years; admission to hospital with a confirmed diagnosis of ACS (as identified on health record); self-reported ethnicity for either white (European), south Asian, or Chinese; and speaking English, Punjabi, Tamil, Urdu, Hindi, or Gujarati, (among the most common languages of Canadian residents from south Asia),[12] Cantonese, or Mandarin. Nearly 95% of south Asians and all Chinese residing in Canada would have been able to speak one or more of the languages used in this study.[12] Exclusion criteria were multiple ethnic origins (i.e., mixed-race) or known cognitive deficits (i.e., Alzheimer's Disease, dementia, uncontrolled psychiatric disorder), as identified on the health record. All participants provided informed consent to participate in this study.

Patient and Public Involvement

Patients were not involved in the conception, design or interpretation of this stuy. However, we have a detailed plan to disseminate this information widely to healthcare providers as well as potential patients, through traditional and social media.

Data collection

Data were collected while participants were in hospital (within the first 5 days), in the patient's preferred language (as listed above) by highly trained like-speaking research assistants. As reported elsewhere,[18] rigorous translation processes were undertaken for study materials.

Questionnaires were developed based on the current literature, and our earlier work.[10,19-21] We, like Teoh et al.,[10] asked participants to mark, on a gender-neutral torso silhouette (pictograph), all the locations of the pain/discomfort that brought them to hospital. Each participant used the same type of pen to 'colour in' the areas. Then, the participant was prompted to identify if he/she experienced other symptoms such as nausea, diaphoresis, dyspnea, dizziness or weakness. Next, they were asked to identify their 'chief' or 'main' symptom, describe its nature by pointing to pictorial identifiers (i.e., stabbing, heavy, shooting, burning, squeezing),[9,21] and finally identify its intensity (Likert-type scale, 0-10 where 0 was no pain). Pain/discomfort severity rated as < 5 was considered mild and ≥ 5 or higher was considered moderate to severe pain.

A health record audit was undertaken to collect additional demographic and as well as clinical data, once the participant had been discharged from hospital.

The outcomes of interest were symptom location and severity; time to emergency room (ER) presentation and cardiac catheterization; as well as receipt of cardiac catheterization, percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG). The

presence or absence of classic (typical) ACS presentation was defined as having mid-sternal or having mid-sternal with radiating left neck, shoulder or arm pain/discomfort of any or at least moderate intensity.

Statistical analysis

Descriptive statistics and Chi-Square tests were used to identify differences in participant characteristics, as well as symptoms and location(s) of pain/discomfort between ethnic groups. To analyze presenting symptoms data, a grid was placed over the original torso silhouette to identify the location(s) of pain/discomfort in a standardized manner.[10] These data were also presented as proportions of each participant group who identified any pain/discomfort in the various areas as well as moderate to severe pain/discomfort rated as $\geq$ 5/10 on a Likert-type scale. Crude and adjusted odds ratios with 95% confidence intervals were examined using logistic regression for south Asians and Chinese relative to whites having any mid-sternal pain/discomfort or any mid-sternal with radiating left neck, shoulder or arm pain/discomfort; as well as moderate to severe ($\geq$5/10) mid-sternal pain/discomfort or mid-sternal with radiating left neck, shoulder or arm pain/discomfort. Finally, crude and adjusted (as above) odds ratios with 95% confidence intervals were examined to determine the likelihood of receiving cardiac catheterization, PCI, and CABG for each ethnic group, based on having any mid-sternal pain/discomfort or any mid-sternal with radiating left neck, shoulder or arm pain/discomfort.

Models were adjusted for demographic and clinical characteristics associated with atypical symptoms (age, sex, education, current smoker, presence of diabetes or chronic kidney disease (CKD), STEMI vs non-STEMI/unstable angina, and level of education). All data were analyzed using SAS version 9.4.

Pictographic analysis

We used a heat-mapping technology to portray where participants identified that they pain/discomfort on the torso silhouettes.[10] Given that the numbers of participants varied by ethnic group, the mapping was based on proportion of participants who coloured areas on the torsos versus the absolute number.

RESULTS

Of 3243 persons screened for eligibility, 1042 did not meet eligibility criteria, and 903 patients declined enrolment in the study. Of the final 1334 patients (58.8% men), 47.2% were white; 36.6% were south Asian and 16.2% were Chinese (see Table 1).

Table 1. Patient characteristics by ethnicity

	white (n=630)	south Asian (n=488)	Chinese (n=216)	p-value
Age, mean (SD), years	65.9 (13.0)	62.2 (12.5)	65.1 (12.6)	<0.0001
Male	276 (43.8%)	355 (72.8%)	154 (71.3%)	<0.0001
English Language Survey	630 (100%)	440 (90.2%)	161 (74.5%)	<0.0001
Immigration Status				<0.0001
Canadian-born	455 (72.1%)	11 (2.3%)	10 (4.6%)	
Immigrant < 20 yrs	15 (2.4%)	189 (38.8%)	81 (36.6%)	
Immigrant ≥20 yrs	160 (25.4%)	288 (59.0%)	123 (56.9%)	
None documented	1 (0.25)	0	2 (0.9%)	
Marital Status				<0.0001
Married/Common law	362 (57.4%)	383 (78.5%)	174 (80.6%)	
Other	269 (42.7%)	105 (21.6%)	42 (19.5%)	
Highest level education				0.0001

None	8 (1.3%)	31 (6.4%)	7 (3.2%)	
< High School	94 (14.9%)	83 (17.0%)	41 (19.0%)	
≥High School	529 (83.9%)	374 (76.7%)	168 (77.8%)	
None documented	0	0	0	
Current smoker	123 (19.5%)	53 (10.9%)	27 (12.5%)	0.0002
Diabetes	193 (30.6%)	224 (45.9%)	64 (29.6%)	<0.0001
Chronic renal disease	74 (11.7%)	45 (9.2%)	18 (8.3%)	0.229
Acute Coronary Syndrome				0.187
Unstable Angina	205 (32.5%)	132 (27.1%)	61 (28.2%)	
Non-STEMI*	228 (36.2%)	208 (42.6%)	83 (38.4%)	
STEMI	188 (29.8%)	145 (29.7%)	68 (31.5%)	
Unspecified	9 (1.5%)	3 (0.6%)	4 (1.8%)	

*STEMI=ST elevation myocardial infarction

Baseline characteristics

Over 72% of whites were Canadian-born whereas the majority of south Asians and Chinese had immigrated to Canada ≥ 20 years earlier. Among these three ethic groups, whites were most likely to be a current smoker; south Asians were most likely to have diabetes; and most all participants were admitted with non-STEMI.

ACS symptom presentation

The most common presenting symptom in each ethnic group was mid-sternal pain/discomfort of any intensity (90.4%) followed by left shoulder pain/discomfort (47.2%) (Table 2). Most of the pain or discomfort was rated as moderate to severe (≥ 5/10) across ethnicities. Over 75% of all patients reported the classic presentation of at least moderate

intensity mid-sternal pain/discomfort, and more than 50% of all patients reported moderate to severe intensity mid-sternal chest with any of radiating left neck, shoulder or arm pain/discomfort. Chinese were less likely to report having either symptom profile relative to whites or south Asians.

Most patients described their pain or discomfort as pressure, squeezing or burning although south Asians reported significantly more stabbing pain than their counterparts. Other symptoms were also prevalent among all ethnic groups: shortness of breath (62.4%), diaphoresis (49.8%), dizziness (49.3%), and nausea/vomiting (33.1%). There were significant differences between groups in reporting these symptoms with south Asians reporting more shortness of breath, and whites reporting more diaphoresis, dizziness, and nausea and vomiting.

Table 2. Reported ACS symptoms by ethnicity

	white (n=630)	south Asian (n=488)	Chinese (n=216)	p-value
Pain/Discomfort Location				
Mid-Sternal	559 (88.7%)	438 (89.9%)	194 (89.8%)	0.828
Left Shoulder	310 (49.1%)	239 (49.0%)	72 (33.3%)	0.0006
Left Arm	206 (32.7%)	140 (28.7%)	22 (10.2%)	<0.0001
Left Jaw	122 (19.3%)	67 (13.7%)	21 (9.7%)	0.003
Left Neck	114 (18.1%)	69 (14.1%)	19 (8.8%)	0.0006
Mid-Sternal, with Radiating Left Neck, Shoulder or Arm Pain/Discomfort	435 (69.0%)	316 (63.8%)	123 (57.0%)	<0.0001
Mid-sternal Pain/Discomfort with	482 (76.5%)	394 (80.7%)	172 (79.6%)	0.0435

Intensity ☹ ≥ 5				
Mid-Sternal, with Radiating Left Neck, Shoulder or Arm Pain/Discomfort with Intensity ☹ ≥ 5	385 (61.6%)	285 (58.4%)	111 (51.4%)	<0.0001
Nature of Pain/Discomfort				
Pressure	312 (49.5%)	174 (35.7%)	93 (43.1%)	<0.0001
Squeezing	118 (18.7%)	120 (24.6%)	57 (26.4%)	0.016
Burning	82 (13.0%)	71 (14.6%)	25 (11.6%)	0.533
Stabbing	48 (7.6%)	68 (14.0%)	17 (7.9%)	0.001
Shooting/Moving	30 (4.8%)	39 (8.0%)	11 (5.1%)	0.065
None	40 (6.4%)	16 (3.3%)	13 (6.0%)	0.059
Not documented	0	0	0	----
Other Symptoms				
Shortness of breath	386 (61.2%)	303 (62.1%)	132 (61.1%)	0.952
Diaphoresis	313 (49.7%)	239 (49.0%)	103 (47.7%)	0.877
Dizziness	329 (52.2%)	221 (45.3%)	99 (45.8%)	0.047
Nausea or vomiting	235 (37.3%)	145 (29.7%)	56 (25.9%)	0.002

The pictographic analysis of the torsos (Figure 1) shows that the profiles were very similar for whites and south Asians, whereas the Chinese tended to report more central as well as less back or left arm pain/discomfort.

In the analysis stratified by ethnic group, ethnicity was not significantly associated with reporting mid-sternal pain/discomfort of any intensity. However, south Asians were significantly

more likely to report having mid-sternal pain/discomfort of moderate to severe intensity in adjusted (age and sex; age sex, education, diabetes, CKD, and STEMI versus non-STEMI/unstable angina) models (Table 3). The Chinese participants were less likely to report having radiating ACS symptoms (i.e., mid-sternal, with left neck, shoulder or arm pain or discomfort) of any as well as moderate to severe intensity, relative to whites in crude and adjusted models.

Table 3. Crude and adjusted odds ratios for ACS symptom presentation

	Any Intensity			Moderate to Severe Intensity		
Ethnic Group	**Crude OR (95%CI)**	**Adjusted* OR (95%CI)**	**Adjusted† OR (95%CI)**	**Crude OR (95%CI)**	**Adjusted* OR (95%CI)**	**Adjusted† OR (95%CI)**
At least moderate intensity mid-sternal pain/discomfort						
white	1.0	1.0	1.0	1.0	1.0	1.0
south Asian	1.11 (0.76, 1.63)	1.04 (0.70, 1.56)	1.03 (0.68, 1.56)	1.29 (0.96, 1.72)	1.44 (1.06, 1.96)	1.55 (1.13, 2.13)
Chinese	1.12 (0.68, 1.86)	1.12 (0.67, 1.89)	1.15 (0.68, 1.93)	1.20 (0.82, 1.75)	1.40 (0.95, 2.07)	1.48 (0.99, 2.19)
At least moderate mid-sternal, with left neck, shoulder, or arm pain/discomfort						
white	1.0	1.0	1.0	1.0	1.0	1.0
south Asian	0.86 (0.68, 1.10)	0.83 (0.64, 1.06)	0.81 (0.63, 1.05)	0.94 (0.74, 1.19)	0.95 (0.74, 1.21)	0.83 (0.64, 1.08)
Chinese	0.44 (0.32, 0.61)	0.45 (0.32, 0.62)	0.45 (0.32, 0.63)	0.50 (0.36, 0.69)	0.53 (0.38, 0.74)	0.46 (0.33, 0.64)

*adjusted for age & sex; †adjusted for age, sex, education, current smoker, diabetes, CKD, and STEMI vs Non-STEMI/unstable angina

Time to emergency room presentation and cardiac catheterization, and care outcomes

The mean time to emergency room presentation, for those who had a distinct time of symptom onset, was 5.53 to 7.41 hours (Table 4). South Asians with atypical symptoms had significantly longer delays in arrival to the emergency department than those who had any typical symptoms. The mean time to receipt of cardiac catheterization following emergency room presentation was 3.00-3.93 hours. Whites with atypical symptoms had significantly longer delays in time to receipt of cardiac catheterization than those with typical symptoms. South Asian participants who had any typical mid-sternal pain/discomfort were more likely to receive

PCI but less likely to receive CABG than those with atypical symptoms. Table 4 also shows that south Asian participants who had any typical mid-sternal with left neck, shoulder, or arm pain/discomfort were more likely to receive PCI than those who had atypical symptoms.

Table 4. Time to emergency room presentation and cardiac catheterization, and care outcomes by symptoms and ethnicity

	white			**south Asian**			**Chinese**		
	Typical (n=482)	**Atypical (n=148)**	**p-value**	**Typical (n=394)**	**Atypical (n=94)**	**p-value**	**Typical (n=172)**	**Atypical (n=44)**	**p-value**
Any mid-sternal pain/discomfort	n=451	n=116		n=359	n=71		n=144	n=32	
Time to ER presentation (hours; if distinct time of onset) Mean (SD)	6.43 (5.77)	6.11 (5.53)	0.591	5.69 (5.35)	7.17 (5.94)	0.037	5.92 (5.49)	7.41 (6.10)	0.176
Median (IQR)	3.0 (6.5)	3.0 (6.0)	0.872	3.0 (6.0)	5.0 (6.5)	0.127	3.0 (6.0)	6.0 (6.5)	0.318
Time to CATH* (hours) Mean (SD)	3.35 (1.76)	3.93 (1.57)	0.001	3.10 (1.80)	3.10 (1.72)	0.975	3.09 (1.82)	3.58 (1.72)	0.134
Median (IQR)	4.0 (2.0)	5.0 (1.0)	0.002	3.0 (2.0)	2.0 (2.0)	0.862	3.0 (2.0)	5.0 (1.5)	0.109
	n (%)	n (%)		n (%)	n (%)		N (%)	n (%)	
CATH	402 (83.4%)	124 (83.8%)	0.913	359 (91.1%)	81 (86.2%)	0.148	151 (87.8%)	38 (86.4%)	0.826
PCI†	228 (47.3%)	60 (40.5%)	0.149	211 (53.6%)	36 (38.3%)	0.008	81 (47.1%)	19 (43.2%)	0.777
CABG§	44 (9.1%)	17 (11.5%)	0.396	38 (9.6%)	16 (17.0%)	0.041	13 (7.6%)	5 (11.4%)	0.636
Any mid-sternal, with left neck, shoulder, or arm pain/discomfort	n=330	n=237		n=234	n=196		n=68	n=108	
Time to ER presentation (hours; if distinct time of onset) Mean (SD)	6.41 (5.82)	6.31 (5.57)	0.836	5.53 (5.35)	6.42 (5.60)	0.092	6.0 (5.65)	6.31 (5.62)	0.726
Median (IQR)	3.0 (6.5)	3.0 (3.0)	0.926	2.0 (6.0)	3.0 (6.5)	0.037	3.0 (6.0)	3.0 (6.0)	0.649
Time to CATH* (hours) Mean (SD)	3.40 (1.76)	3.61 (1.68)	0.154	3.0 (1.77)	3.2 (1.79)	0.241	3.28 (1.81)	3.14 (1.81)	0.615
Median (IQR)	4.0 (2.0)	5.0 (1.5)	0.192	3.0 (2.0)	3.0 (2.0)	0.202	4.0 (2.0)	3.0 (2.0)	0.635
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
CATH	306 (86.0%)	220 (80.3%)	0.058	235 (91.1%)	205 (89.1%)	0.469	65 (82.3%)	124 (90.5%)	0.126
PCI	172 (48.3%)	116 (42.3%)	0.135	143 (55.4%)	104 (45.2%)	0.024	41 (51.9%)	59 (43.1%)	0.361
CABG	33 (9.3%)	28 (10.2%)	0.690	30 (11.6%)	24 (10.4%)	0.675	4 (5.1%)	14 (10.2%)	0.307

*CATH=catheterization; † PCI=percutaneous coronary intervention; §CABG=coronary artery bypass graft surgery

However, after adjustment for potential confounding, south Asians with atypical symptoms were less likely to receive PCI than those with typical symptoms (Table 5).

Table 5. Crude and adjusted odds ratios for care outcomes

Atypical vs typical	**Crude OR (95% CI)**	**Adjusted* OR (95% CI)**
Any mid-sternal pain/discomfort		
CATH[†]		
white	1.03 (0.62, 1.69)	1.11 (0.64, 1.95)
south Asian	0.61 (0.31, 1.20)	0.71 (0.34, 1.48)
Chinese	0.89 (0.33, 2.35)	0.77 (0.27, 2.14)
PCI[§]		
white	0.76 (0.52, 1.10)	0.82 (0.54, 1.24)
south Asian	0.54 (0.34, 0.85)	0.56 (0.33, 0.94)
Chinese	0.87 (0.45, 1.69)	0.81 (0.38, 1.72)
CABG[**]		
white	1.29 (0.71, 2.34)	1.24 (0.67, 2.30)
south Asian	1.92 (1.02, 3.62)	1.84 (0.95, 3.56)
Chinese	1.63 (0.56, 4.73)	1.42 (0.45, 4.47)
Any mid-sternal, with left neck, shoulder, or arm pain/discomfort		
CATH		
white	0.67 (0.44, 1.02)	0.74 (0.46, 1.17)
south Asian	0.80 (0.44, 1.46)	0.93 (0.49, 1.76)
Chinese	2.08 (0.92, 4.68)	2.37 (0.98, 5.72)
PCI		
white	0.79 (0.57, 1.08)	0.79 (0.56, 1.12)
south Asian	0.66 (0.46, 0.95)	0.72 (0.48, 1.08)
Chinese	0.69 (0.40, 1.21)	0.60 (0.32, 1.14)
CABG		
white	1.11 (0.66, 1.89)	1.09 (0.63, 1.87)
south Asian	0.89 (0.50, 1.56)	0.90 (0.49, 1.64)
Chinese	1.82 (0.63, 5.31)	2.11 (0.68, 6.56)

*adjusted for age, sex, education, current smoker, diabetes, CKD, and STEMI vs Non-STEMI/unstable angina
[†]CATH=catheterization; [§] PCI=percutaneous coronary intervention; [**]CABG=coronary artery bypass graft surgery

DISCUSSION

The classic (typical) presentation of moderate to severe intensity mid-sternal chest pain or discomfort was the most common presenting ACS symptom across ethnic groups. Yet, a substantial proportion of patients, up to one third, in each group studied had non-classic (atypical) ACS presentations. Differences in ACS symptom presentation among whites, south

Asians, and Chinese patients were statistically and clinically significant, as south Asians were more likely to present with classic ACS symptoms and Chinese were less likely to present with radiating symptoms in all models relative to whites. Our study extends the findings from previous work by employing rigorous cross cultural and language adaptation of study questionnaires, and including visual diagrams across multiple centers.

Findings from other studies have some similar conclusions. Like the south Asian and Chinese participants in our study, Blacks have been reported to have a similar prevalence of chest pain relative to whites.[6-9] Yet, other studies suggest that non-white patients with ACS are more likely to have chest pain than whites. A study from a single hospital in the United Kingdom reported south Asians are more frequently to have 'classic chest pain with radiation' than whites (90 vs. 82%).[10] A study of 390 ACS patients residing in the Asia-Pacific rim revealed patients from India, China and Korea were significantly more likely to report typical pain than their white counterparts.[11] A small study of whites, Blacks (US-residents), and Koreans (Korea-residents) revealed Koreans reported significantly more frequent and greater radiation of chest pain.[8] Yet, our earlier study from a single health region, revealed that south Asian and Chinese AMI patients were less likely to report classic symptom presentation.[19] These inconsistencies may be explained by the controlled analyses we used, and the lack of cross cultural (and language) adaptation in other studies.

We found significant differences among ethnic groups in the nature of the pain/discomfort as well as the presence of additional symptoms. Culture may influence patients identifying, recognizing, and acknowledging urgent symptoms as such, as well as making the decision to seek care. Single centre studies revealed that south Asians and Chinese with AMI tended to report atypical symptoms and did not recognize or accept their symptoms as

'urgent'.[19,22] Studies[23-26] suggest that expression of symptoms, and language and semantic differences of symptom descriptors may account for discrepancies in reporting symptoms. Further, pain/discomfort are subjective experiences, thus how they are identified and portrayed are culturally bound.[25,26] For example, the Worchester Heart Attack Study revealed that south Asian participants were significantly less accepting of overtly expressing pain, but showed no difference in reporting pain intensity than white participants.[21]

We identified little overall ethnic variation in time to emergency room presentation, though south Asians who had atypical symptoms were more likely to have a longer time to presentation to the emergency room (mean of 1.48 hours longer) relative to those who had typical symptoms. In a study of 440,398 registry patients, Ting et al.[27] demonstrated that delays from symptom onset to emergency room presentation were associated with reduced likelihoods of receiving any reperfusion therapy in the general population. Authors of other American studies have demonstrated ethnic (e.g., African Americans, Hispanics, Pacific Islanders) differences relative to whites in longer time to emergency room presentation and reduced access to treatment (reperfusion therapies) for ACS events.[28-30]

South Asians who had typical mid-sternal pain/discomfort symptoms were more likely to receive PCI and significantly less likely to receive CABG than those who had atypical symptoms. Overall, and after adjustment, south Asians with atypical symptoms were less likely to receive PCI than those with typical symptoms. The reasons for this difference are not clear. It is possible that south Asians with atypical presentations arrive too late for emergent coronary revascularization; there are biases from health care providers; or this population may be more likely to refuse invasive cardiovascular procedures.

Study limitations

We employed a rigorous approach to comparing symptom presentation between cultural groups in this large cross-sectional study. We included participants who spoke a variety of languages, used highly systematic and validated translation and data collection processes, and had a large sample size. However, there were some limitations. First, we studied participants who survived their ACS event. It is not possible to know if patients who succumbed to their ACS event or did not seek care had different symptoms than those who were diagnosed and survived. Second, we studied only those who agreed to participate. The proportion of south Asian and Chinese patients approached to participate and who refused was noteworthy. Third, we studied only patients in Canada who were admitted to selected hospitals.

Conclusions

A substantial proportion of white, south Asian and Chinese patients with ACS do not report classic ACS symptoms. Differences in ACS symptoms presentation among whites, south Asians, and Chinese patients are significant with south Asians being more likely to report mid-sternal pain/discomfort and Chinese being less likely to report radiating pain/discomfort, relative to whites. On the whole, the mean time to emergency room presentation was unacceptably long for each ethnic group and especially so for south Asians. These delays can reduce the opportunity to receive evidence-based reperfusion therapies. From a public health perspective, we need to include non-chest pain symptoms for screening and public awareness campaigns for ACS among south Asian, Chinese and white persons.

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COMPETING INTERESTS

RT reports grants from Merck Canada, personal fees from Merck Canada, outside the submitted work.

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AUTHORS' CONTRIBUTION

All authors have met the ICMJE recommendations regarding authorship.

KKS, HQ and NK conceived the study.

KKS, HQ, RT, and NK made substantial contributions to the design of the work.

MK, LA, SB, and NK made substantial contributions to the acquisition of data.

KKS, HQ, RT, DS, and NK made substantial contributions to the analysis

KKS, HQ, MK, RT, LA, SB, DS, and NK made substantial contributions to the interpretation of the data

KKS, HQ, MK, RT, LA, SB, DS, and NK made substantial contributions to drafting the work or revising it critically for important intellectual content, and made final approval of the version to be published.

KKS, HQ, MK, RT, LA, SB, DS, and NK agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA SHARING STATEMENT

Data are housed at the University of Calgary and are not available at this time.

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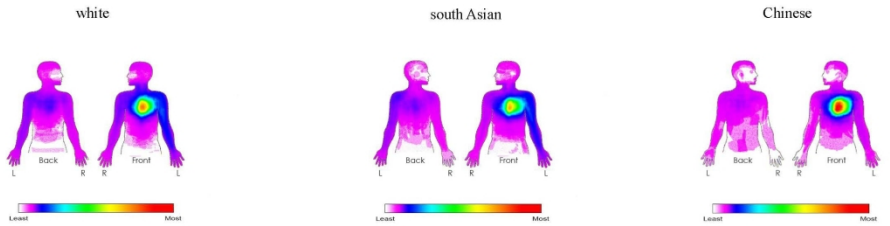
Figure 1. Pictographic for Each Ethnic Group

The colour gradient (white/purple to red) indicates no/few participants to most (>65%) of participants identified pain/discomfort in that location.



279x215mm (220 x 220 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓ pg 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓ pg 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓ pp. 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	✓ pg 5
Methods			
Study design	4	Present key elements of study design early in the paper	✓ pg 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓ pp 5-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	✓ ✓
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓ pp 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓ pp. 5-7
Bias	9	Describe any efforts to address potential sources of bias	✓ p. 7
Study size	10	Explain how the study size was arrived at	✓ p. 8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓ p. 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓ pp. 7-8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	✓
		(*e*) Describe any sensitivity analyses	none

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓ pg 8
		(b) Give reasons for non-participation at each stage	✓ pg 8
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓ pp 8-10
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	✓ pp. 9-14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓ pp 9-14
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓ pp 14-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓ pg 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓ pg 17
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓ pg 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓ pg 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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ACUTE CORONARY SYNDROMES PRESENTATIONS AND CARE OUTCOMES IN WHITE, SOUTH ASIAN, AND CHINESE PATIENTS: A COHORT STUDY

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ACUTE CORONARY SYNDROMES PRESENTATIONS AND CARE OUTCOMES IN WHITE, SOUTH ASIAN, AND CHINESE PATIENTS: A COHORT STUDY

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ABSTRACT

Objectives. Successful treatment of acute coronary syndrome (ACS) relies on its rapid recognition. It is unclear whether the accepted presentation of chest pain applies to different ethnic groups. We thus examined potential ethnic variations in ACS symptoms and clinical care outcomes in white, south Asian, and Chinese patients.

Design. Cross sectional survey.

Setting. Participants were hospitalized at one of 12 Canadian centres across 4 provinces.

Participants. 1334 ACS patients (630 white; 488 south Asian; 216 Chinese).

Main outcome measures. ACS presentation symptoms (classic/typical mid-sternal pain/discomfort with or without radiation to the left neck, shoulder or arm) were assessed by self-report. Clinical **care** outcomes (time to emergency room (ER) presentation, cardiac catheterization; receipt of cardiac catheterization, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) were obtained by health record audit.

Results. The mean age of the sample was 62 years and 30% had ST-elevation myocardial infarction (STEMI). The most common presenting symptom was mid-sternal pain/discomfort of any intensity regardless of ethnic status. Yet, a substantial proportion of patients reported atypical symptoms (33% white, 19% south Asian, 20% Chinese; $p<0.006$). After adjustment for age, sex, education, current smoking, extent of coronary artery disease, presence of diabetes or chronic kidney disease, and STEMI vs non-STEMI/unstable angina, south Asians were more likely to present with at least moderate intensity mid-sternal pain/discomfort (Adjusted Odds Ratio (AOR) 1.44; 95% Confidence Interval (CI) 1.05-1.98) whereas Chinese were less likely to present with radiating symptoms (AOR 0.53; 95% CI 0.38-0.74) compared with whites. South Asians with atypical pain (relative to those with mid-sternal pain/discomfort) took significantly

longer to present to the ER (p=0.037), and were less likely to receive PCI (p=0.008) or CABG (p=0.041).

Conclusions. Atypical presentations were associated with greater delays in arrival to the emergency department and reduced invasive cardiovascular care in south Asians.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This was a rigorously designed study which included participants who spoke a variety of languages and used highly systematic and validated translation and data collection processes.
- A number of mechanisms were used to obtain a data regarding participants' ACS symptoms.
- Only participants who survived their ACS event were included in this study. It is not possible to know if patients who succumbed to their ACS event or did not seek care had different symptoms than those who were diagnosed and survived.
- There was a noteworthy proportion of south Asian and Chinese patients approached to participate who refused.

INTRODUCTION

The burden of acute coronary syndrome (ACS) is substantial and it is now the leading cause of death and disability world-wide.[1,2] Life-saving therapies for ACS are dependent on early and timely recognition of symptoms. Atypical presentation of ACS symptoms leads to delays in recognizing symptoms by both patients and healthcare providers, and can result in misdiagnosis, delayed treatment, receipt of fewer evidence-based therapies, and higher in-hospital morbidity and mortality.[3]

The 'classic' ACS presentation, based on the presentation of men of European descent, includes moderate to severe intensity central chest with or without left arm, neck or jaw radiating pain or discomfort.[4,5] This description has been adopted internationally, though some studies suggest that ACS symptoms may differ by ethnicity.[6-11] Although these studies yielded discordant findings, some noted that non-white patients may present with additional symptoms (e.g., gastro-intestinal, dyspnea, nausea)[6-9,11] and south Asians may have more diffuse pain and more frequent back pain[10] than whites. It is difficult to draw robust conclusions from the current evidence given variable methods of data collection, inadequate cross cultural language adaptation, small sample sizes, and insufficient adjustment for other factors (e.g., sex, age, clinical factors) that may influence ACS presentation.

South Asians have a higher incidence of ACS and earlier onset relative to other ethnic groups.[12,13] Though Chinese currently have a lower incidence of acute myocardial infarction (AMI) relative to whites and south Asians,[14,15] cardiovascular events in China are expected to rise by more than 50% by 2030.[16] A rigorous investigation of ACS symptom presentation, time to arrival to the emergency department and clinical care outcomes between these ethnic groups is warranted to ensure appropriate public health messaging and/or inappropriate stereotyping of

presenting symptoms. We thus aimed to examine potential ethnic variations in ACS symptoms using a rigorously cross-culturally adapted symptom questionnaire and visual identifiers in a multi-centre cohort of white, south Asian, and Chinese patients hospitalized in Canada.

METHODS

Study design

We conducted a cross-sectional survey of a cohort of white (i.e., of European descent), south Asian (i.e., descended from India, Pakistan, Bangladesh, Sri Lanka), and Chinese (i.e., descended from China, Hong Kong, Taiwan, Macau) patients hospitalized with physician-confirmed ACS (unstable angina, ST-elevation (STEMI) or non-STEMI) myocardial infarction[5]).

Setting and sample

Following institutional ethics review at each participating hospital, participants were recruited consecutively from 12 urban hospitals in 4 Canadian provinces (>90% of Canada's immigrants reside in urban areas and the majority reside in these provinces[17]) between September 2010 and December 2015. Inclusion criteria were age ≥ 19 years; admission to hospital with a confirmed diagnosis of ACS (as identified on health record); self-reported ethnicity for either white (European), south Asian, or Chinese; and speaking English, Punjabi, Tamil, Urdu, Hindi, or Gujarati, (among the most common languages of Canadian residents from south Asia),[17] Cantonese, or Mandarin. Nearly 95% of south Asians and all Chinese residing in Canada would have been able to speak one or more of the languages used in this study.[17] Exclusion criteria were multiple ethnic origins (i.e., mixed-race) or known cognitive deficits (i.e., Alzheimer's Disease, dementia, uncontrolled psychiatric disorder), as identified on the health record. All participants provided informed consent to participate in this study.

Patient and Public Involvement

Patients were not involved in the conception, design or interpretation of this study. However, we have a detailed plan to disseminate this information widely to healthcare providers as well as potential patients, through traditional and social media.

Data collection

Data were collected while participants were in hospital (within the first 5 days), in the patient's preferred language (as listed above) by highly trained like-speaking research assistants. As reported elsewhere,[18] rigorous translation processes were undertaken for study materials.

Questionnaires were developed based on the current literature, and our earlier work.[10,19-21] We, like Teoh et al.,[10] asked participants to mark, on a gender-neutral torso silhouette (pictograph), all the locations of the pain/discomfort that brought them to hospital. Each participant used the same type of pen to 'colour in' the areas. Then, the participant was prompted to identify if he/she experienced other symptoms such as nausea, diaphoresis, dyspnea, dizziness or weakness. Next, they were asked to identify their 'chief' or 'main' symptom, describe its nature by pointing to pictorial identifiers (i.e., stabbing, heavy, shooting, burning, squeezing),[9,21] and finally identify its intensity (Likert-type scale, 0-10 where 0 was no pain). Pain/discomfort severity rated as < 5 was considered mild and ≥ 5 or higher was considered moderate to severe pain.

A health record audit was undertaken to collect additional demographic and as well as clinical data, once the participant had been discharged from hospital.

The presence or absence of classic (typical) ACS presentation was defined as having mid-sternal or having mid-sternal with radiating left neck, shoulder or arm pain/discomfort of any or at least moderate intensity. The clinical care outcomes of interest were time to emergency

room (ER) presentation and cardiac catheterization; as well as receipt of cardiac catheterization, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

There was potential for bias when using this design and data collection method. This was a self-selected group of patients (i.e., selection bias) who agreed to participate in the study. Also, the retrospective nature of the design could lead to recall bias given that patients were asked about their symptoms up to 5 days following hospital admission.

Statistical analysis

Descriptive statistics and Chi-Square tests were used to identify differences in participant characteristics, as well as symptoms and location(s) of pain/discomfort between ethnic groups. Each variable had a 'not entered' category. In binary variables of present/not present, 'not entered' was assumed to be not present. To analyze presenting symptoms data, a grid was placed over the original torso silhouette to identify the location(s) of pain/discomfort in a standardized manner.[10] These data were also presented as proportions of each participant group who identified any pain/discomfort in the various areas as well as moderate to severe pain/discomfort rated as $\geq$ 5/10 on a Likert-type scale. Crude and adjusted odds ratios with 95% confidence intervals were examined using logistic regression for south Asians and Chinese relative to whites having any mid-sternal pain/discomfort or any mid-sternal with radiating left neck, shoulder or arm pain/discomfort; as well as moderate to severe ($\geq$5/10) mid-sternal pain/discomfort or mid-sternal with radiating left neck, shoulder or arm pain/discomfort. Finally, crude and adjusted (as above) odds ratios with 95% confidence intervals were examined to determine the likelihood of receiving cardiac catheterization, PCI, and CABG for each ethnic group, based on having any mid-sternal pain/discomfort or any mid-sternal with radiating left neck, shoulder or arm pain/discomfort.

Models were adjusted for demographic and clinical characteristics associated with atypical symptoms (age, sex, education, current smoker, extent of coronary artery disease (based on cardiac catheterization), presence of diabetes or chronic kidney disease (CKD; as defined by the Charlson Co-Morbidity Index[22]), and STEMI vs non-STEMI/unstable angina). All data were analyzed using SAS version 9.4.

Pictographic analysis

We used a heat-mapping technology to portray where participants identified that they pain/discomfort on the torso silhouettes.[10] Given that the numbers of participants varied by ethnic group, the mapping was based on proportion of participants who coloured areas on the torsos versus the absolute number.

RESULTS

Of 3243 persons screened for eligibility, 1042 did not meet eligibility criteria, and 903 patients declined enrolment in the study. Of the final 1334 patients (58.8% men), 47.2% were white; 36.6% were south Asian and 16.2% were Chinese (see Table 1).

Table 1. Patient characteristics by ethnicity

	white (n=630)	south Asian (n=488)	Chinese (n=216)	p-value
Age, mean (SD), years	65.9 (13.0)	62.2 (12.5)	65.1 (12.6)	<0.0001
Male	276 (43.8%)	355 (72.8%)	154 (71.3%)	<0.0001
English Language Survey	630 (100%)	440 (90.2%)	161 (74.5%)	<0.0001
Immigration Status				<0.0001
Canadian-born	455 (72.1%)	11 (2.3%)	10 (4.6%)	
Immigrant < 20 yrs	15 (2.4%)	189 (38.8%)	81 (36.6%)	

Immigrant ≥20 yrs	160 (25.4%)	288 (59.0%)	123 (56.9%)	
None documented	1 (0.25)	0	2 (0.9%)	
Marital Status				<0.0001
Married/Common law	362 (57.4%)	383 (78.5%)	174 (80.6%)	
Other	269 (42.7%)	105 (21.6%)	42 (19.5%)	
Highest level education				0.0001
None	8 (1.3%)	31 (6.4%)	7 (3.2%)	
< High School	94 (14.9%)	83 (17.0%)	41 (19.0%)	
≥High School	529 (83.9%)	374 (76.7%)	168 (77.8%)	
None documented	0	0	0	
Current smoker	123 (19.5%)	53 (10.9%)	27 (12.5%)	0.0002
Extent of coronary artery disease				<0.0001
Normal/<50% disease	92 (14.6%)	50 (10.3%)	36 (16.7%)	
1-2 vessel disease	148 (23.5%)	91 (18.7%)	33 (15.3%)	
3 vessel disease/LAD	272 (43.2%)	293 (60.0%)	109 (50.5%)	
Left main	11 (1.8%)	4 (0.8%)	10 (4.6%)	
Not entered/missing	107 (17.0%)	50 (10.3%)	28 (13.0%)	
Diabetes	193 (30.6%)	224 (45.9%)	64 (29.6%)	<0.0001
Chronic renal disease	74 (11.7%)	45 (9.2%)	18 (8.3%)	0.229
Acute Coronary Syndrome				0.187
Unstable Angina	205 (32.5%)	132 (27.1%)	61 (28.2%)	
Non-STEMI*	228 (36.2%)	208 (42.6%)	83 (38.4%)	
STEMI	188 (29.8%)	145 (29.7%)	68 (31.5%)	

Unspecified	9 (1.5%)	3 (0.6%)	4 (1.8%)	

*STEMI=ST elevation myocardial infarction

Baseline characteristics

Over 72% of whites were Canadian-born whereas the majority of south Asians and Chinese had immigrated to Canada ≥ 20 years earlier. Among these three ethic groups, whites were most likely to be a current smoker and have 1-2 vessel disease; south Asians were most likely to have 3-vessel disease and diabetes; and the greatest proportion of each patient group (36.2% whites, 42.6% south Asian, 38.4% Chinese) were admitted with non-STEMI.

ACS symptom presentation

The most common presenting symptom **across** ethnic groups was mid-sternal pain/discomfort of any intensity (89.3%) followed by left shoulder pain/discomfort (46.6%) (Table 2). Most of the pain or discomfort was rated as moderate to severe (≥ 5/10) across ethnicities. More than 78% of all patients reported the classic presentation of at least moderate intensity mid-sternal pain/discomfort, and more than 58% of all patients reported moderate to severe intensity mid-sternal chest with any of radiating left neck, shoulder or arm pain/discomfort. In these unadjusted analyses, whites were less likely to report having the classic presentation of at least moderate intensity mid-sternal pain/discomfort while the Chinese were less likely to report having at least moderate intensity mid-sternal pain/discomfort with radiation to left neck, shoulder or arm. Extent of coronary artery disease was not associated with having classic symptoms in whites (p=0.973), south Asians (p=0.562), or Chinese (p=0.304) patients.

The majority of patients described their pain or discomfort as pressure, squeezing or burning (81.3% whites, 74.8% south Asians, 81.0% Chinese), although south Asians reported significantly more stabbing pain than their counterparts. Other symptoms were also prevalent

among all ethnic groups: shortness of breath (62.4%), diaphoresis (49.8%), dizziness (49.3%), and nausea/vomiting (33.1%). There were significant differences between groups in reporting these symptoms with whites reporting more dizziness, and nausea or vomiting.

Table 2. Reported ACS symptoms by ethnicity

	white (n=630)	south Asian (n=488)	Chinese (n=216)	p-value
Pain/Discomfort Location				
Mid-Sternal	559 (88.7%)	438 (89.9%)	194 (89.8%)	0.828
Left Shoulder	310 (49.1%)	239 (49.0%)	72 (33.3%)	0.0006
Left Arm	206 (32.7%)	140 (28.7%)	22 (10.2%)	<0.0001
Left Jaw	122 (19.3%)	67 (13.7%)	21 (9.7%)	0.003
Left Neck	114 (18.1%)	69 (14.1%)	19 (8.8%)	0.0006
Mid-Sternal, with Radiating Left Neck, Shoulder or Arm Pain/Discomfort	435 (69.0%)	316 (63.8%)	123 (57.0%)	<0.0001
Mid-sternal Pain/Discomfort with Intensity ☹ ≥ 5	482 (76.5%)	394 (80.7%)	172 (79.6%)	0.0435
Mid-Sternal, with Radiating Left Neck, Shoulder or Arm Pain/Discomfort with Intensity ☹ ≥ 5	385 (61.6%)	285 (58.4%)	111 (51.4%)	<0.0001
Nature of Pain/Discomfort				
Pressure	312 (49.5%)	174 (35.7%)	93 (43.1%)	<0.0001

Squeezing	118 (18.7%)	120 (24.6%)	57 (26.4%)	0.016
Burning	82 (13.0%)	71 (14.6%)	25 (11.6%)	0.533
Stabbing	48 (7.6%)	68 (14.0%)	17 (7.9%)	0.001
Shooting/Moving	30 (4.8%)	39 (8.0%)	11 (5.1%)	0.065
None	40 (6.4%)	16 (3.3%)	13 (6.0%)	0.059
Not documented	0	0	0	----
Other Symptoms				
Shortness of breath	386 (61.2%)	303 (62.1%)	132 (61.1%)	0.952
Diaphoresis	313 (49.7%)	239 (49.0%)	103 (47.7%)	0.877
Dizziness	329 (52.2%)	221 (45.3%)	99 (45.8%)	0.047
Nausea or vomiting	235 (37.3%)	145 (29.7%)	56 (25.9%)	0.002

The pictographic analysis of the torsos (Figure 1) shows that the profiles were very similar for whites and south Asians, whereas the Chinese tended to report more central as well as less back or left arm pain/discomfort.

In the analysis stratified by ethnic group (Table 2), ethnicity was not significantly associated with reporting mid-sternal pain/discomfort of any intensity. However, in adjusted (age and sex; age sex, education, current smoker, extent of coronary artery disease, diabetes, CKD, and STEMI versus non-STEMI/unstable angina) models (Table 3), south Asians were significantly more likely to report having mid-sternal pain/discomfort of moderate to severe intensity. The Chinese participants were less likely to report having radiating ACS symptoms (i.e., mid-sternal, with left neck, shoulder or arm pain or discomfort) of any as well as moderate to severe intensity, relative to whites in crude and adjusted models.

Table 3. Crude and adjusted odds ratios for ACS symptom presentation

	Any Intensity			Moderate to Severe Intensity		
Ethnic Group	**Crude OR (95%CI)**	**Adjusted* OR (95%CI)**	**Adjusted† OR (95%CI)**	**Crude OR (95%CI)**	**Adjusted* OR (95%CI)**	**Adjusted† OR (95%CI)**
At least moderate intensity mid-sternal pain/discomfort						
white	1.0	1.0	1.0	1.0	1.0	1.0
south Asian	1.11 (0.76, 1.63)	1.04 (0.70, 1.56)	1.04 (0.68, 1.57)	1.29 (0.96, 1.72)	1.44 (1.06, 1.96)	1.43 (1.04, 1.97)
Chinese	1.12 (0.68, 1.86)	1.12 (0.67, 1.89)	1.18 (0.70, 2.00)	1.20 (0.82, 1.75)	1.40 (0.95, 2.07)	1.41 (0.95, 2.09)
At least moderate mid-sternal, with left neck, shoulder, or arm pain/discomfort						
white	1.0	1.0	1.0	1.0	1.0	1.0
south Asian	0.86 (0.68, 1.10)	0.83 (0.64, 1.06)	0.81 (0.62, 1.05)	0.94 (0.74, 1.19)	0.95 (0.74, 1.21)	0.92 (0.71, 1.75)
Chinese	0.44 (0.32, 0.61)	0.45 (0.32, 0.62)	0.46 (0.33, 0.63)	0.50 (0.36, 0.69)	0.53 (0.38, 0.74)	0.53 (0.38, 0.75)

*adjusted for age and sex; †adjusted for age, sex, education, current smoker, extent of coronary artery disease (no disease vs low risk or high risk), diabetes, CKD, and STEMI vs non-STEMI/unstable angina

Clinical care outcomes

The mean time to emergency room presentation, for those who had a distinct time of symptom onset, was 5.53 to 7.41 hours (Table 4). South Asians with atypical symptoms had significantly longer delays in arrival to the emergency department than those who had any typical symptoms. The mean time to receipt of cardiac catheterization following emergency room presentation was 3.00-3.93 hours. Whites with atypical symptoms had significantly longer delays in time to receipt of cardiac catheterization than those with typical symptoms. South Asian participants who had any typical mid-sternal pain/discomfort were more likely to receive PCI but less likely to receive CABG than those with atypical symptoms. Table 4 also shows that south Asian participants who had any typical mid-sternal with left neck, shoulder, or arm pain/discomfort were more likely to receive PCI than those who had atypical symptoms.

Table 4. Clinical care outcomes by symptoms and ethnicity

	white			south Asian			Chinese		
	Typical (n=482)	**Atypical (n=148)**	**p-value**	**Typical (n=394)**	**Atypical (n=94)**	**p-value**	**Typical (n=172)**	**Atypical (n=44)**	**p-value**

Any mid-sternal pain/discomfort	n=451	n=116		n=359	n=71		n=144	n=32	
Time to ER presentation (hours; if distinct time of onset) Mean (SD)	6.43 (5.77)	6.11 (5.53)	0.591	5.69 (5.35)	7.17 (5.94)	0.037	5.92 (5.49)	7.41 (6.10)	0.176
Median (IQR)	3.0 (6.5)	3.0 (6.0)	0.872	3.0 (6.0)	5.0 (6.5)	0.127	3.0 (6.0)	6.0 (6.5)	0.318
Time to CATH* (hours) Mean (SD)	3.35 (1.76)	3.93 (1.57)	0.001	3.10 (1.80)	3.10 (1.72)	0.975	3.09 (1.82)	3.58 (1.72)	0.134
Median (IQR)	4.0 (2.0)	5.0 (1.0)	0.002	3.0 (2.0)	2.0 (2.0)	0.862	3.0 (2.0)	5.0 (1.5)	0.109
	n (%)	n (%)		n (%)	n (%)		N (%)	n (%)	
CATH	402 (83.4%)	124 (83.8%)	0.913	359 (91.1%)	81 (86.2%)	0.148	151 (87.8%)	38 (86.4%)	0.826
PCI†	228 (47.3%)	60 (40.5%)	0.149	211 (53.6%)	36 (38.3%)	0.008	81 (47.1%)	19 (43.2%)	0.777
CABG§	44 (9.1%)	17 (11.5%)	0.396	38 (9.6%)	16 (17.0%)	0.041	13 (7.6%)	5 (11.4%)	0.636
Any mid-sternal, with left neck, shoulder, or arm pain/discomfort	n=330	n=237		n=234	n=196		n=68	n=108	
Time to ER presentation (hours; if distinct time of onset) Mean (SD)	6.41 (5.82)	6.31 (5.57)	0.836	5.53 (5.35)	6.42 (5.60)	0.092	6.0 (5.65)	6.31 (5.62)	0.726
Median (IQR)	3.0 (6.5)	3.0 (3.0)	0.926	2.0 (6.0)	3.0 (6.5)	0.037	3.0 (6.0)	3.0 (6.0)	0.649
Time to CATH* (hours) Mean (SD)	3.40 (1.76)	3.61 (1.68)	0.154	3.0 (1.77)	3.2 (1.79)	0.241	3.28 (1.81)	3.14 (1.81)	0.615
Median (IQR)	4.0 (2.0)	5.0 (1.5)	0.192	3.0 (2.0)	3.0 (2.0)	0.202	4.0 (2.0)	3.0 (2.0)	0.635
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
CATH	306 (86.0%)	220 (80.3%)	0.058	235 (91.1%)	205 (89.1%)	0.469	65 (82.3%)	124 (90.5%)	0.126
PCI	172 (48.3%)	116 (42.3%)	0.135	143 (55.4%)	104 (45.2%)	0.024	41 (51.9%)	59 (43.1%)	0.361
CABG	33 (9.3%)	28 (10.2%)	0.690	30 (11.6%)	24 (10.4%)	0.675	4 (5.1%)	14 (10.2%)	0.307

*CATH=catheterization; † PCI=percutaneous coronary intervention; §CABG=coronary artery bypass graft surgery

However, after adjustment, south Asians with atypical symptoms were least likely to receive PCI than those with typical symptoms (Table 5).

Table 5. Crude and adjusted odds ratios for **clinical** care outcomes

Atypical vs typical	**Crude OR (95% CI)**	**Adjusted† OR (95% CI)**
Any mid-sternal pain/discomfort		
CATH†		
white	1.03 (0.62, 1.69)	1.15 (0.53, 2.49)
south Asian	0.61 (0.31, 1.20)	0.66 (0.22, 1.98)
Chinese	0.89 (0.33, 2.35)	2.77 (0.64, 11.90)
PCI§		
white	0.76 (0.52, 1.10)	0.73 (0.45, 1.19)
south Asian	0.54 (0.34, 0.85)	0.57 (0.32, 1.00)

Chinese	0.87 (0.45, 1.69)	1.10 (0.45, 2.68)
CABG**		
white	1.29 (0.71, 2.34)	1.59 (0.81, 3.09)
south Asian	1.92 (1.02, 3.62)	1.90 (0.96, 3.77)
Chinese	1.63 (0.56, 4.73)	1.76 (0.53, 5.80)
Any mid-sternal, with left neck, shoulder, or arm pain/discomfort		
CATH		
white	0.67 (0.44, 1.02)	0.90 (0.47, 1.73)
south Asian	0.80 (0.44, 1.46)	1.37 (0.55, 3.41)
Chinese	2.08 (0.92, 4.68)	4.94 (1.41, 17.31)
PCI		
white	0.79 (0.57, 1.08)	0.84 (0.56, 1.26)
south Asian	0.66 (0.46, 0.95)	0.74 (0.47, 1.18)
Chinese	0.69 (0.40, 1.21)	0.49 (0.23, 1.05)
CABG		
white	1.11 (0.66, 1.89)	1.24 (0.69, 2.21)
south Asian	0.89 (0.50, 1.56)	0.92 (0.50, 1.70)
Chinese	1.82 (0.63, 5.31)	2.10 (0.65, 6.85)

*adjusted for age and sex; †adjusted for age, sex, education, current smoker, extent of coronary artery disease (no disease vs low risk or high risk), diabetes, CKD, and STEMI vs non-STEMI/unstable angina; †CATH= catheterization; § PCI=percutaneous coronary intervention; **CABG=coronary artery bypass graft surgery

DISCUSSION

The classic (typical) presentation of moderate to severe intensity mid-sternal chest pain or discomfort was the most common presenting ACS symptom across ethnic groups. Yet, a substantial proportion of patients, up to one third, in each group studied had non-classic (atypical) ACS presentations. Differences in ACS symptom presentation among whites, south Asians, and Chinese patients were statistically and clinically significant, as south Asians were more likely to present with classic ACS symptoms and Chinese were less likely to present with radiating symptoms in all models relative to whites. Our study extends the findings from previous work by employing rigorous cross cultural and language adaptation of study questionnaires, and including visual diagrams across multiple centers.

Findings from other studies have some similar conclusions. Like the south Asian and Chinese participants in our study, Blacks have been reported to have a similar prevalence of

chest pain relative to whites,[6-9] while other studies suggest that non-white patients with ACS are more likely to have chest pain than whites. A study from a single hospital in the United Kingdom reported south Asians are more frequently to have 'classic chest pain with radiation' than whites (90 vs. 82%).[10] A study of 390 ACS patients residing in the Asia-Pacific rim revealed patients from India, China and Korea were significantly more likely to report typical pain than their white counterparts.[11] A small study of whites, Blacks (US-residents), and Koreans (Korea-residents) revealed Koreans reported significantly more frequent and greater radiation of chest pain.[8] Yet, our earlier study from a single health region, revealed that south Asian and Chinese AMI patients were less likely to report classic symptom presentation.[19] These inconsistencies may be explained by the controlled analyses we used, and the lack of cross cultural (and language) adaptation in other studies.

We found significant differences among ethnic groups in the intensity and nature of the pain/discomfort as well as the presence of additional symptoms. Ethnicity and culture may influence patients identifying, recognizing, and acknowledging urgent symptoms as such, as well as making the decision to seek care. Though not consistent, study findings suggest that people who represent ethnic minorities (who are not residing in their country of origin) have greater pain sensitivity in both clinical and experimental conditions relative to the ethnic majority (e.g., whites). Though most of this research has been undertaken in African Americans and Hispanics relative to whites,[23] what little research that has focused on south Asians or Chinese suggests that both groups may report less pain tolerance relative to whites.[24,25] Single centre studies have revealed that south Asians and Chinese with AMI tended to report atypical symptoms and did not recognize or accept their symptoms as 'urgent'.[19,26] Research findings suggest that expression of symptoms, and language and semantic differences of symptom descriptors may

also account for discrepancies in reporting symptoms. Given that pain/discomfort are subjective experiences, how they are portrayed are culturally bound.[23-30] For example, the Worchester Heart Attack Study revealed that south Asian participants were significantly less accepting of overtly expressing pain,[21] and both south Asians and Chinese are viewed as more stoic in their presentations.[29]

We identified little overall ethnic variation in time to emergency room presentation, though south Asians who had atypical symptoms were more likely to have a longer time to presentation to the emergency room (mean of 1.48 hours longer) relative to those who had typical symptoms. In a study of 440,398 registry patients, Ting et al.[31] demonstrated that delays from symptom onset to emergency room presentation were associated with reduced likelihoods of receiving any reperfusion therapy in the general population. Authors of other American studies have demonstrated ethnic (e.g., African Americans, Hispanics, Pacific Islanders) differences relative to whites in longer time to emergency room presentation and reduced access to treatment (reperfusion therapies) for ACS events.[30-33]

Overall, and after adjustment, south Asians with atypical symptoms were least likely of the ethnic groups to receive PCI than those with typical symptoms. The reasons for this difference are not clear. It is possible that south Asians with atypical presentations arrive too late for emergent coronary revascularization; there are biases from health care providers; or this population may be more likely to refuse invasive cardiovascular procedures.

Study limitations

There were some limitations to this study. First, we studied participants who survived their ACS event. It is not possible to know if patients who succumbed to their ACS event or did not seek care had different symptoms than those who were diagnosed and survived. Second, we

studied only those who agreed to participate. The proportion of south Asian and Chinese patients approached to participate and who refused was noteworthy. Third, we studied only patients in Canada who were admitted to selected hospitals. Finally, the cross sectional design renders only observations and no basis for attributing causation. We undertook the following to balance these limitations: we employed a rigorous approach to comparing symptom presentation between cultural groups in this large cross-sectional study; we included participants who spoke a variety of languages, using highly systematic and validated translation and data collection processes; and had a large sample size.

Conclusions

A substantial proportion of white, south Asian and Chinese patients with ACS do not report classic ACS symptoms. Differences in ACS symptoms presentation among whites, south Asians, and Chinese patients are significant with south Asians being more likely to report mid-sternal pain/discomfort and Chinese being less likely to report radiating pain/discomfort, relative to whites. On the whole, the mean time to emergency room presentation was unacceptably long for each ethnic group and especially so for south Asians. These delays can reduce the opportunity to receive evidence-based reperfusion therapies. From a public health perspective, we need to include non-chest pain symptoms for screening and public awareness campaigns for ACS among south Asian, Chinese and white persons.

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COMPETING INTERESTS

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AUTHORS' CONTRIBUTION

All authors have met the ICMJE recommendations regarding authorship.

KKS, HQ and NK conceived the study.

KKS, HQ, RT, and NK made substantial contributions to the design of the work.

MK, LA, SB, and NK made substantial contributions to the acquisition of data.

KKS, HQ, RT, DS, and NK made substantial contributions to the analysis

KKS, HQ, MK, RT, LA, SB, DS, and NK made substantial contributions to the interpretation of the data

KKS, HQ, MK, RT, LA, SB, DS, and NK made substantial contributions to drafting the work or revising it critically for important intellectual content, and made final approval of the version to be published.

KKS, HQ, MK, RT, LA, SB, DS, and NK agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA SHARING STATEMENT

Data are housed at the University of Calgary and are not available at this time.

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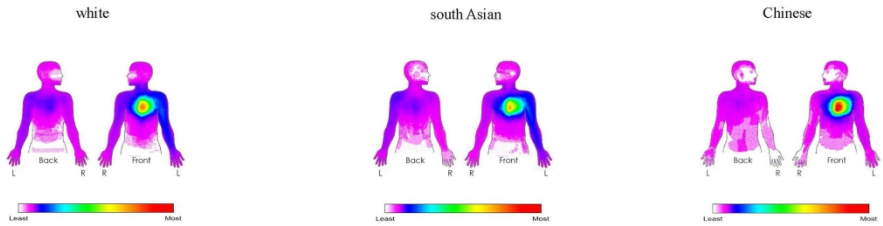
Figure 1. Pictographic for Each Ethnic Group

The colour gradient (white/purple to red) indicates no/few participants to most (>65%) of participants identified pain/discomfort in that location.



Pictographic for Each Ethnic Group

279x215mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓ pg 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓ pg 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓ pp. 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	✓ pg 5
Methods			
Study design	4	Present key elements of study design early in the paper	✓ pg 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓ pp 5-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	✓ ✓
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓ pp 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓ pp. 5-7
Bias	9	Describe any efforts to address potential sources of bias	✓ p. 7
Study size	10	Explain how the study size was arrived at	✓ p. 8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓ p. 7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓ pp. 7-8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	✓
		(*e*) Describe any sensitivity analyses	none

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed ✓ pg 8
		(b) Give reasons for non-participation at each stage ✓ pg 8
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders ✓ pp 8-10
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures ✓ pp. 9-14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included ✓ pp 9-14
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives ✓ pp 14-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias ✓ pg 17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence ✓ pg 17
Generalisability	21	Discuss the generalisability (external validity) of the study results ✓ pg 17
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based ✓ pg 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.