

Fibrinolytic Function in South Asians and Europeans with Coronary Heart Disease: Insights from the PRACTICE Registry

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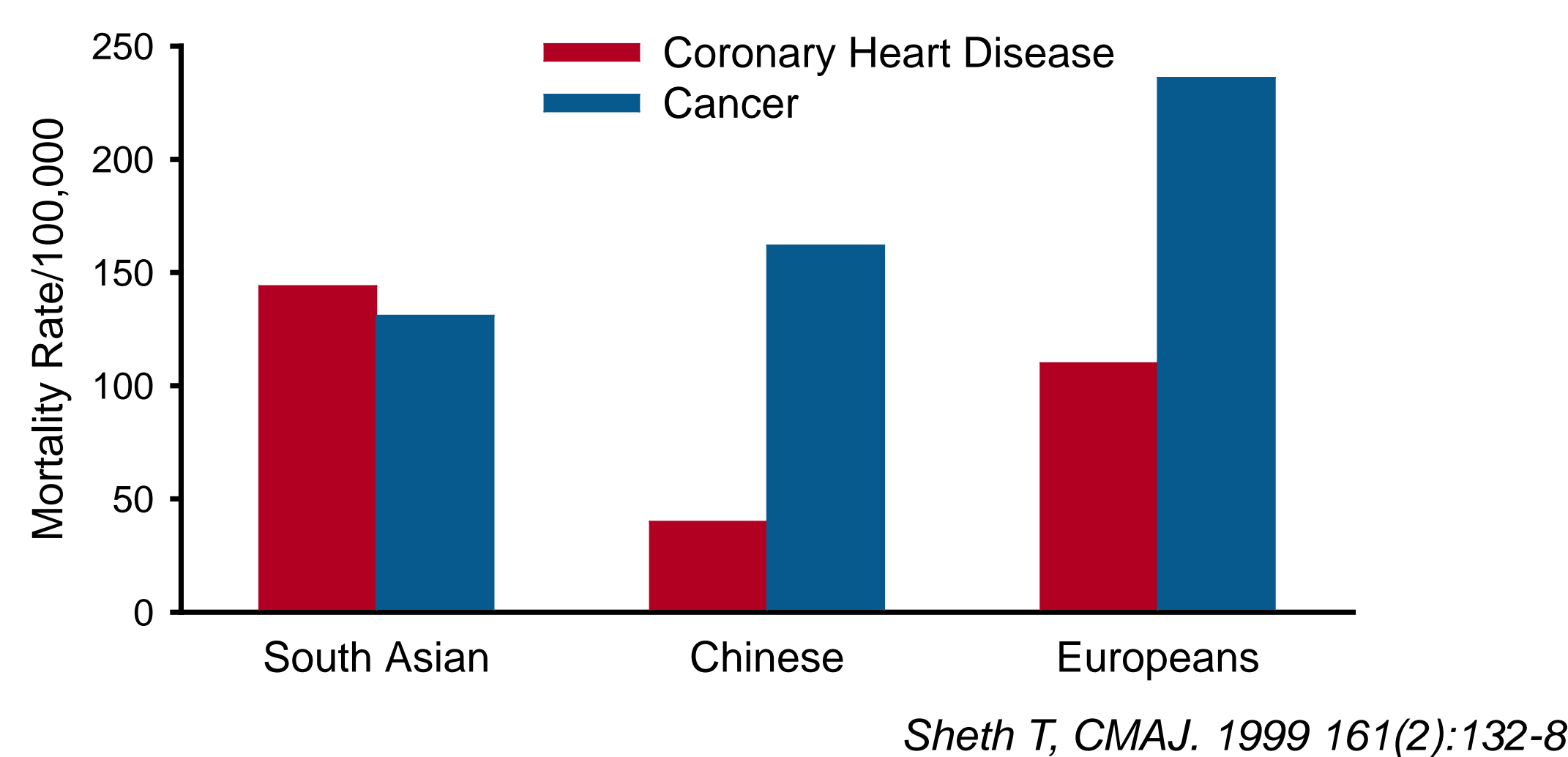
BACKGROUND

- According to the 2006 Canadian Census, South Asians (SA) are the country's largest and fastest growing visible minority group.

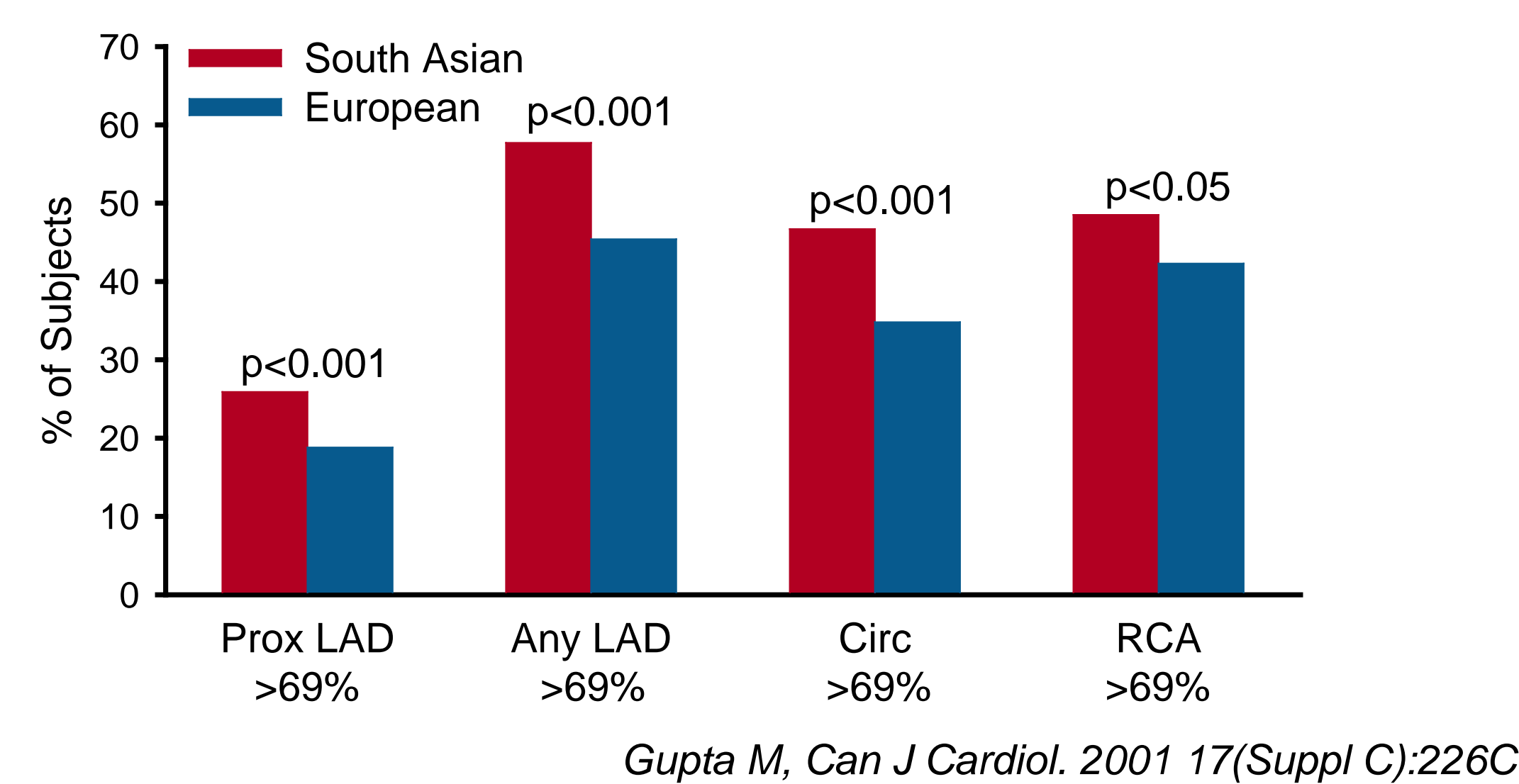
	All visible minorities	South Asian	% Pop'n	Δ '01-'06	Chinese	% Pop'n	Δ '01-'06
CA	5,068,090	1,262,865	4.0	37.7	1,216,570	3.9	18.2
ON	2,745,205	794,179	6.6	43.1	576,980	4.8	19.8
BC	1,008,855	262,290	6.4	24.7	407,225	10.0	11.4

- SA have a unique cardiovascular (CV) risk profile
Anand SS, Lancet. 2000 356(9226):279-84

- SA have a higher coronary heart disease mortality rate than other groups in Canada



- SA have more severe coronary artery disease at angiography



- SA ethnicity is an independent predictor of mortality following coronary artery bypass graft (CABG) surgery

Variable	Odds Ratio	95% CI
Increasing age	1.1	1.05-1.15
Unstable angina	1.9	1.2-3.0
Hypertension	2.5	1.0-6.8
LVEF <40%	12.2	3.3-44.9
South Asian ethnicity	3.1	1.4-6.8

Brister SJ, J Thorac Cardiovasc Surg. 2007 133(1):150-154

- Plasminogen activator inhibitor-1 (PAI-1) is an adipokine that is released in response to tumour necrosis factor, insulin, transforming growth factor-β, cortisol, the renin-angiotensin-aldosterone system and oxidative stress
- PAI-1 regulates fibrinolysis and elevated PAI-1 levels are associated with atherothrombosis and increased risk of myocardial infarction (MI)
- Ethnic differences in PAI-1 levels may account for the differential susceptibilities of populations to the development of CV disease (CVD)

OBJECTIVES

- To determine if PAI-1 levels differ between SA and European (EU) Canadians with coronary artery disease (CAD)
- To determine if levels of high sensitivity C-reactive protein (hsCRP), a marker of inflammation, differ between SA and EU with CAD

METHODOLOGY

Study Setting and Cohort

- 257 patients (111 SA, 146 EU) from the single centre, ongoing PRACTICE registry of patients with stable CAD enrolled since January 2003

- Inclusion Criteria (any one of):

- Prior MI
- Prior percutaneous coronary intervention (PCI)
- Prior CABG surgery
- Angiographic stenosis >50%

- Annual visits documented and reviewed:

- Cardiac medical history
- Any hospitalization or adverse events last year
- Physical measurements (blood pressure, heart rate, weight, waist and hip measurements)
- Medications
- Laboratory (lipids, CBC, Chem-7, liver function tests, hsCRP)
- Any imaging data collected over last year

PAI-1 Measurements

- Blood samples were drawn in trisodium citrate and the isolated plasma stored at -20°C
- Plasma PAI-1 levels were analyzed in a single laboratory using the TintElize® PAI-1 ELISA kit (Biopool). The average intraassay and interassay coefficient of variation were 1.9% and 3.3% respectively

Metabolic Syndrome

Defined as the presence of ≥3 of the following:

- Waist circumference
 - SA Men >90cm Women >80cm
 - EU Men >102 cm Women >88 cm
- Triglycerides ≥1.7 mmol/L
- HDL
 - Men <1.04 mmol/L Women <1.29 mmol/L
- Blood pressure
 - Systolic ≥130 mmHg OR Diastolic ≥ 85 mmHg OR Treated for hypertension
- Fasting glucose ≥6.1 mmol/L

Statistical Analysis

Statistical analyses were performed with an SAS software package (SAS1.3). Categorical variables are presented as frequencies and percentages, and continuous variables are summarized as means with standard deviations. Differences between SA and EC were compared using the chi-square test for categorical variables and the Student's t-test or the Wilcoxon signed-rank test for continuous variables. Linear model analysis was conducted to find expected differences in PAI-1 levels between South Asians and European Caucasians with potential confounding factors controlled. A 2-sided P value of ≤0.05 was considered statistically significant.

RESULTS

Table 1. Baseline characteristics

	South Asian N=111	European N=146	P-value
Age (yrs)	65	67	0.19
Males (%)	80.2	82.9	0.57
Hypertension (%)	61.3	48.6	0.04
Diabetes (%)	43.6	21.2	0.0001
Current Smoker (%)	4.5	11.0	0.01
Metabolic Syndrome (%)	73.0	48.6	0.0001
BMI (kg/m ²)	26.3	28.6	0.002
Waist Circumference (cm)	96.4	100.0	0.009
Hip Circumference (cm)	99.2	105.5	0.0001
HDL (mmol/L)	1.2	1.2	0.97
LDL (mmol/L)	2.1	2.2	0.11
Ln TG (mmol/L)	1.5	1.4	0.18
Systolic BP (mm Hg)	133	133	0.98
Diastolic BP (mm Hg)	77	76	0.41
HgA1c (%)	0.08	0.06	0.013
Ln Glucose (mmol/L)	6.9	6.3	0.008
% Antiplatelet Agents	82	88	0.20
% Beta Blockers	66	61	0.44
% RAS Inhibitors	76	71	0.43
% Statins	89	88	0.71

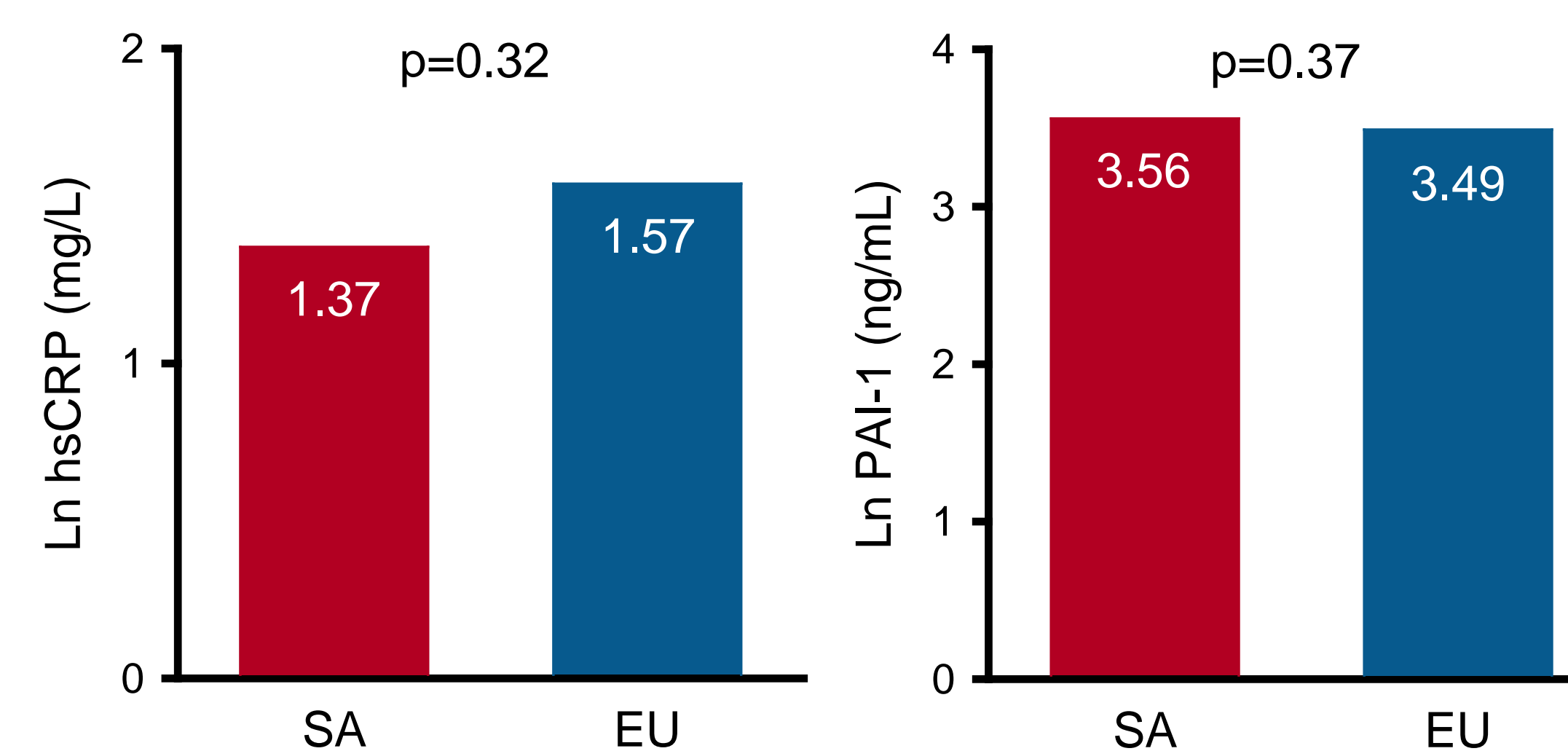


Fig. 1. Unadjusted hsCRP and PAI-1 levels

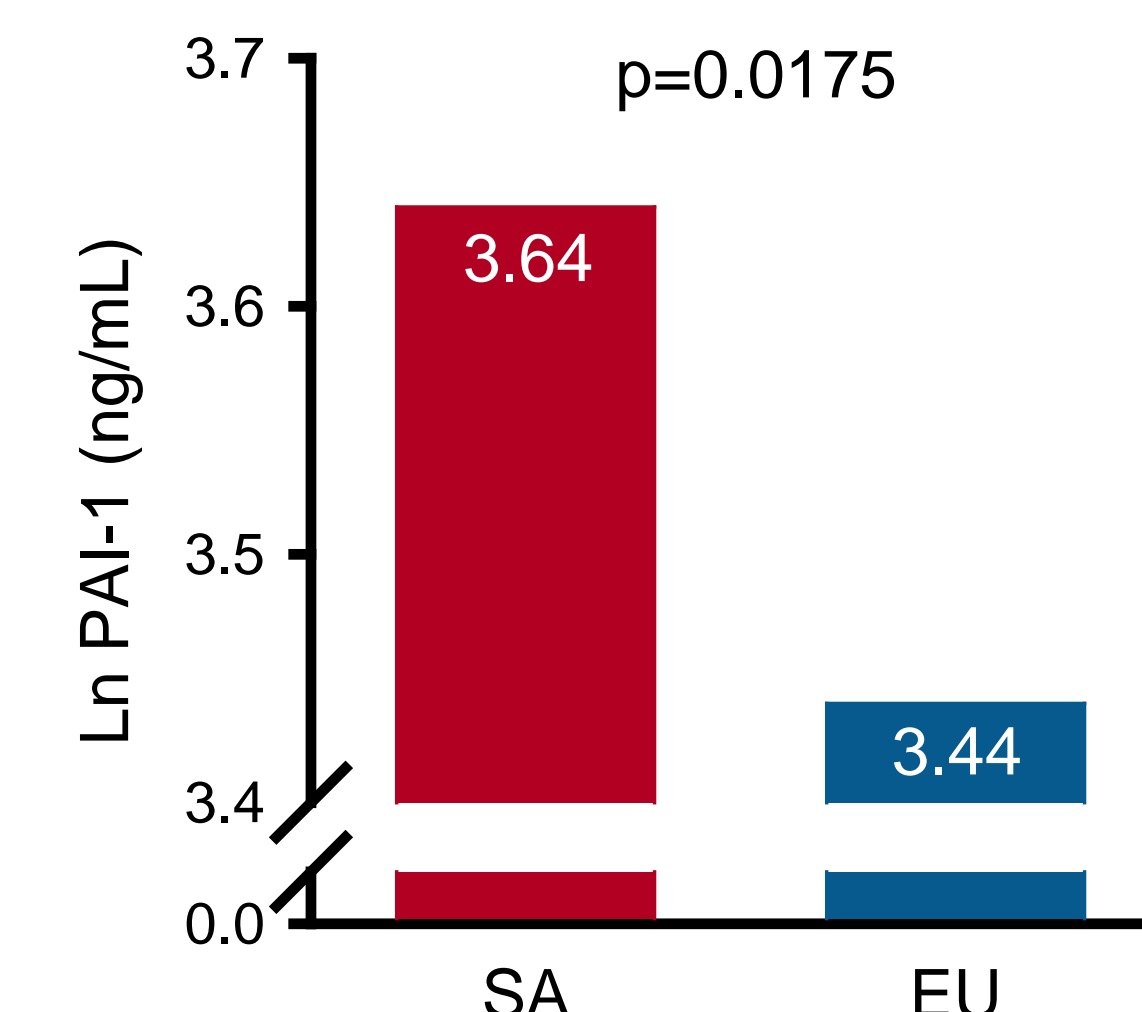


Fig. 2. PAI-1 levels adjusted for age, gender, hsCRP, HbA1c, waist, hip, height, weight and glucose

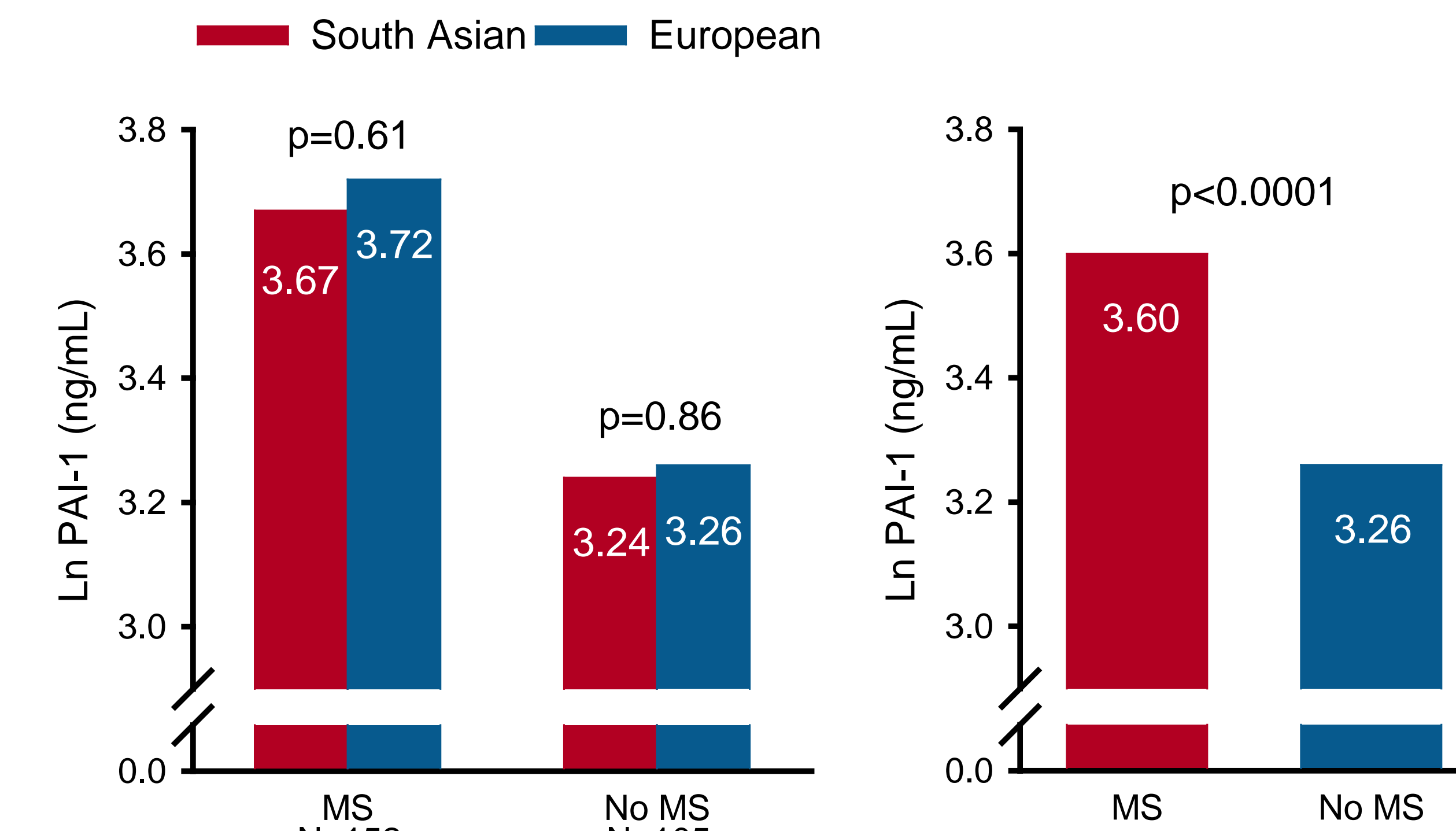


Fig. 3. PAI-1 levels adjusted for metabolic syndrome (MS)

LIMITATIONS

- Spectrum of CAD at entry was variable but balanced

	% MI	% PCI	% CABG	% Abn Cath
South Asian	77	38	49	85
European	71	39	45	89

- Time from the sentinel inclusion event varied
- Adjustments may not fully correct for differences in baseline characteristics
- Single site may affect generalizability of findings

SUMMARY

- Our results confirm the higher prevalence of traditional CV risk factors among SA compared with EU Canadians with CAD
- PAI-1 levels are higher in SA following multivariate adjustment
- Ethnic differences in PAI-1 levels appear to be closely linked with the presence of the metabolic syndrome
- Impaired fibrinolytic function may be an additional marker of CV risk in patients with established CAD

IMPLICATIONS

- These findings are concordant with the SHARE study population of healthy individuals
- This suggests that PAI-1 may play a causal role in the transition from subclinical atherosclerosis to overt CVD and may be particularly important in people of South Asian origin
- Further studies are needed to understand the relationship between PAI-1 levels and the metabolic syndrome.
- Future preventive strategies should assess whether modification of the metabolic syndrome and/or improved fibrinolytic function are associated with improved clinical outcomes

CONFLICTS OF INTEREST

JWE has received consulting fees from AstraZeneca. NS has received research funding from AstraZeneca. No other relevant disclosures.

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