RISK FACTOR ASSESSMENT

Risk factor assessment in South African Black patients presenting with acute myocardial infarction at R.K. Khan Hospital, Durban

S.C. Masina*, N. Ranjith# and B. Sartorius[†]

ABSTRACT

*Department of Medicine, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa

[#]Department of Medicine, Coronary Care Unit, R.K. Khan Hospital, Durban, South Africa

[†]Department of Public Health Medicine, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa,

Address for correspondence:

Prof N. Ranjith R.K. Khan Hospital Department of Medicine Coronary Care Unit Private Bag X004 Chatsworth Durban 4030 South Africa

Email: ranjith@lantic.co.za

INTRODUCTION

Coronary Artery Disease (CAD) is a major cause of death and disability, worldwide. Similarly, in South Africa, which is a multiethnic society with a large range of cultures and life styles, CAD is also a major cause of morbidity and mortality, particularly amongst the White and Indian populations.⁽¹⁻³⁾ In contrast, earlier studies found that CAD was relatively uncommon in the Black population, and this low incidence was suggested to be due to lower serum cholesterol and increased high-density lipoprotein (HDL) cholesterol levels.⁽⁴⁾ In addition, assessment of selected risk factors for CAD in young South African male scholars by Seftel, et al. showed that both Indian and White scholars had a much higher prevalence and severity of CAD risk factors than Black youths.⁽⁵⁾

However, recently the INTERHEART Africa study reported that more premature acute myocardial infarctions (AMI) occur in sub-saharan Africa than in any of the other 52 countries participating in the INTERHEART study.^(6,7) This is due largely to the modeling of 5 risk factors (smoking, diabetes, hypertension, abdominal obesity and dyslipidaemia), which provide a population attributable risk of 89.2% for AMI. These results are consistent with the overall INTERHEART Study. Of note is that the prevalence of CAD is also increasing in the South African Black population because they are exposed to a similar risk

Objective: To assess various risk factors in Black South African patients presenting with acute myocardial infarction (AMI) to the Coronary Care Unit (CCU) at R.K. Khan Hospital, Durban, South Africa.

Methods and results: The study population was recruited from consecutive patients from a multi-ethnic background with a diagnosis of AMI over a 4 year period (2008 - 2012). Only patients who were of Black South African origin (n=94) were eligible for analysis. Demographic data stored in an electronic database were extracted from all patients. The mean age of the participants was 54.3 ± 11.0 years of whom 85% were males. The majority presented with ST elevation myocardial infarction (STEMI) (83%) whilst 17% had Non ST elevation myocardial infarction (NSTEMI). Smoking (48%) and hypertension (46%) were the most commonly observed risk factors. Thirty six percent of patients developed one or more major adverse cardiac events (MACE). Recurrence of infarction and death occurred more frequently in females compared to males (14% vs. 2%, p=0.04).

No significant difference in MACE was found between patients who were human immunodeficiency virus (HIV) positive (18%) compared to those who were HIV negative (82%). Metabolic syndrome, as defined by the International Diabetes Federation (IDF) criteria, was found in 35 (45%) of patients. The number of patients presenting with hypertension and diabetes was significantly higher in our study compared to the INTER-HEART Africa study (73% vs. 50%, p<0.01; and 40% vs. 24%, p<0.01).

Conclusion: South African Blacks have multiple risk factors, similar to other ethnic groups in the country, which contribute to the development of AMI. Recurrence of infarction and death occurred more frequently in females compared to males. In addition to conventional risk factors for CAD, an increased heart rate, STEMI, obesity, family history of cerebrovascular disease and hyperuricaemia are strongly associated with the presence of MACE. SAHeart 2016;13:12-18

profile, due to greater urbanisation and the adoption of an unhealthy life style. $\ensuremath{^{(8)}}$

Another important contributor to the increase in CAD in this ethnic group may be related to the human immunodeficiency virus (HIV), as South Africa is the country with the highest number of HIV infections in the world.^(?) It has been suggested that HIV infection per se should count as a coronary risk factor, similar to the traditional cardiovascular risk factors, since HIV infections may promote early atherosclerosis independently of these classical vascular risk factors.(10)

The prevalence rate of the metabolic syndrome is also increasing in Black South Africans, which could be another factor contributing to their increase in CAD.(11) Despite the growing burden of CAD in the Black population, there is still a paucity of information concerning the association between CAD and its known risk factors. The primary objective of this study, therefore, was to assess various risk factors in Black South African patients presenting with AMI to the Coronary Care Unit (CCU) at R.K. Khan Hospital, Durban.

METHODS

The study population was recruited from consecutive patients from a multi-ethnic background, with a diagnosis of AMI within 24 hours of onset of symptoms to the CCU at R.K. Khan Hospital, Durban, over a four year period (2008 - 2012). Of the I 200 patients admitted with AMI, 87% were of Asian Indian origin, 7.8% Blacks, 4.4% Whites, and 0.8% Coloureds. Only patients of South African Black origin (n=94) were eligible for analysis. The study was carried out according to the principles of the Declaration of Helsinki and was approved by the local ethics committee. Acute myocardial infarction was defined by prolonged chest discomfort, typical electrocardiographic (ECG) changes, and elevated cardiac troponin T (cTnT) levels as outlined by the Joint European Society of Cardiology/American College of Cardiology Committee.⁽¹²⁾

Clinical assessment

Demographic data stored in an electronic database were extracted for all eligible patients. Every patient underwent an initial assessment that included clinical history, physical examination, and 12-lead surface ECG. Current smokers were defined as those individuals who had smoked any tobacco in the previous 12 months, and former smokers as those who had not smoked for a period of at least a year. A family history of premature atherosclerosis was defined by a history of myocardial infarction in either parents, or in siblings, or first degree relatives at the age of 55 years or younger, for males, and 65 years or younger, in females, whilst a family history of diabetes, hypertension, and cerebrovascular disease was defined as these conditions occurring at any age. Additional clinical data included a detailed description of major adverse cardiac events (MACE) encountered during hospital admission until 6 months followup, such as ventricular arrhythmias, complete heart block, cardiac failure, cardiogenic shock, recurrence of angina or myocardial infarction and death.

In keeping with standard acute coronary syndrome guidelines, all patients were counseled and offered coronary angiograms, which were performed at another referral hospital. Patients were required to consent to both coronary angiography and cardiac revascularisation procedures such as percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), should there be a need to perform these procedures. This type of triage is necessary due to the large volume of work and the lack of adequate facilities in the public sector (only I government-based hospital in the province of KwaZulu-Natal offers these specialised facilities). Consequently, only a limited number of patients underwent coronary angiography because the majority declined cardiac revascularisation. Patients who were eligible were thrombolysed with metalyse as a reperfusion therapy.

Since the INTERHEART Africa Study is probably the most comprehensive case-control study conducted among patients with AMI in sub-saharan Africa (SSA), we also explored the association of known cardiovascular risk factors and AMI between the Black African group of this study (n=144) and our study population.

Anthropometric measurements

The body mass index (BMI) was calculated as weight (kilograms) divided by height² (meters) according to the World Health Organisation guidelines.⁽¹³⁾

A BMI≥30kg/m² was used to define adult obesity. Waist circumference, which is considered the most practical way to assess central obesity, was measured midway between the lowest rib and the iliac crest on standing subjects, using a soft tape. The presence of the metabolic syndrome, as outlined by the International Diabetes Federation (IDF), was defined as central obesity (waist circumference: males ≥94cm, females \geq 80cm) plus any 2 of the criteria shown in Table 2.⁽¹⁴⁾

Biochemical Analyses

Blood samples for routine biochemistry were collected from all subjects on hospital admission and carried out using standard methods. Troponin T measured on the Elecsys 2010 (Roche Diagnostics) was considered positive at a cut-off value greater than 0.03ng/ml. Blood samples were also collected within 48 hours of admission after an overnight fast for total cholesterol, triglycerides and HDL cholesterol, which were measured on the Beckman Synchron CX7 auto analyser. Low-density lipoprotein (LDL) cholesterol levels were calculated utilising the formula of Friedewald. The HIV status of every patient was determined using the Enzyme linked immunosorbent assay (ELISA).

Statistical analyses

Data were processed and analysed using Stata 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Differences in means of continuous variables by dichotomous classification (e.g. gender, HIV status and adverse cardiac events) were assessed using t-tests (or the non-para-metric equivalent, namely the Wilcoxon Rank Sum Test). Differences in frequencies of categorical demographic variable by metabolic syndrome status and other categorical outcomes were assessed using the Pearson chi-square (χ 2) test. If an expected cell count has fewer than 5 observations, then the Fishers Exact Test P-values are presented instead.

Bivariate and multivariable logistic regression was employed to estimate the association between clinical and laboratory parameters and MACE. Coefficients were exponentiated to represent odds ratios (ORs) and 95% confidence intervals. An adjusted P-value of <0.05 was deemed statistically significant.

RESULTS

Of the 94 patients in the study cohort, 58 (85%) were males. The mean age of the study population was 54.3 ± 11.0 years, with the majority presenting with ST elevation myocardial infarction (STEMI) (83%), whilst 17% had Non ST elevation myocardial infarction (NSTEMI) (Table 1). Previous and current smoking (48%) and hypertension (46%) were the most commonly observed risk factors. A significantly greater number of men had a history of smoking compared to their female counterparts [72% vs. 8%, OR 28.87 (95% CI 7.75 - 107.52); p<0.01], while females in contrast were found to have a higher incidence of hypertension [67% vs. 33%, OR 0.24 (95% CI 0.1 - 0.59); p<0.01]. Although haemoglobin levels were significantly lower in female patients (12.38 \pm 1.91g/dl vs. 14.06 \pm 1.9g/dl, p<0.01), male patients had higher creatinine values (101.24 \pm 27.85umol/L vs. 83.08 \pm 21.3umol/L, p<0.01).

From index hospitalisation until 6-month follow-up, 36% of patients developed one or more MACE. Recurrence of infarction and death occurred more frequently in females compared to males [14% vs. 2%, OR 0.11 (95% Cl 0.01 - 0.97); p=0.04]. No significant difference was found in traditional cardiovascular risk factors and MACE between patients who were HIV positive (18%) compared to those who were HIV negative (82%, data not shown). Only 23 patients had coronary angiograms performed at another referral hospital because most patients declined coronary revascularisation. Thirty five percent presented with triple vessel disease, 22% with double vessel, and 26% with single vessel disease while 17% had normal coronary angiograms.

Metabolic syndrome, as defined by the IDF criteria, was found in 35 (45%) of the study population (Table 2). Central obesity was the major IDF determinant in patients with or without the metabolic syndrome (100% vs. 61%, p<0.01), while elevated blood pressure (83%), low HDL cholesterol levels (80%), raised triglyceride (48%), and fasting blood glucose values (46%) occurred significantly more frequently in patients with the metabolic syndrome.

Table 3 compares the risk profile for AMI between the Black population of the INTERHEART Africa study and the R.K. Khan Hospital study. The number of patients presenting with hypertension and diabetes was significantly higher in our study compared to the INTERHEART Africa study (73% vs. 50%, p<0.01; and 40% vs. 24%, p<0.01), respectively. The lipid profiles were similar for the 2 study groups.

Figure 1 illustrates the presence of various combinations of any 6 risk factors for AMI, namely diabetes, smoking, family history

of vascular disease, dyslipidaemia, hypertension and central obesity. Of note is that 32% of patients had 4 risk factors, 20% presented with 5 risk factors, and overall 89% had 2 or more risk factors for AMI.

A multivariable analysis for factors associated with MACE by logistic regression was done (Table 4). After multivariable adjustment, an increased heart rate (>100 beats per minute) (OR 1.06 [95% CI 1.01 - 1.10]; p=0.01), STEMI (OR 5.89 [95% CI 1.22 - 28.51]; p=0.03), obesity (OR 3.86 [95% CI 1.18 - 12.63]; p=0.03), a family history of cerebrovascular disease (OR 14.83 [95% CI 1.10 - 200.82]; p=0.04) and hyperuricaemia (OR 3.64 [95% CI 1.05 - 12.66]; p=0.04) was significantly associated with MACE.

DISCUSSION

In this study, South African Black patients were characterised by the presence of multiple risk factors for AMI. Previous and current smoking (48%), hypertension (46%), and diabetes (40%) were the most commonly observed risk factors. Of note is that 89% of patients had 2 or more risk factors for AMI, with 32% presenting with 4 risk factors while 20% had 5 risk factors. These results are consistent with the INTERHEART Africa Study and confirm that people from Africa, particularly Black South Africans who, when exposed to known major CAD risk factors, are at risk to develop AMI, as are people across the globe.⁽¹⁵⁾

Furthermore, our data show that patients in the R.K. Khan Hospital study had a significantly higher prevalence of hypertension (p<0.01) and diabetes (p<0.01) compared to the Black patients in the INTERHEART Africa study. These results assume greater importance since it was reported that a history of hypertension was significantly stronger in the total African population compared to the global INTERHEART population (p=0.002 for tests of heterogeneity of effects).⁽⁶⁾ What was once considered a rare disease in this ethnic group,^(16,17) is now observed more frequently, suggesting that uncontrolled major CAD risk factors will have a larger impact on the burden of CAD in Africa than elsewhere. This is supported by the fact that although only 25% of patients in the study cohort underwent cardiac catheterisation studies, most patients presented with advanced triple vessel disease (35%), with 17% having normal coronary angiograms. In addition, 36% of subjects experienced MACE during the study follow-up period, with recurrence of myocardial infarction (p=0.04) and death (p=0.04) occurring more often in females compared to their male counterparts.

Several studies have reported an association between HIV disease and CAD, which may occur because of dyslipidaemia, glucose intolerance and endothelial dysfunction secondary to some antiretroviral drugs.^(18,19) This is of particular importance in the South African setting, since it is the country with the highest number of HIV infections in the world.⁽⁹⁾ Eighteen percent of the study population were found to be HIV positive but none

Characteristics	All patients % (n=94)	Males % (n=58)	Females % (n=36)	OR (95% CI) Males vs. Females	P-value
STEMI	83	85	81		0.42
NSTEMI	17	15	19	1.31 (0.44 - 3.91)	0.62
Body mass index					
Normal (≤25kg/m²)	26	38	6	10.39 (2.27 - 47.57)	< 0.0
Pre-obese (26 - 29kg/m²)	35	36	33	1.14 (0.47 - 2.73)	0.78
Obese (≥30kg/m²)	31	24	42	0.45 (0.18 - 1.09)	0.08
Risk Factors					
Previous and current smoking	48	72	8	28.87 (7.75 - 107.52)	<0.01
Hypertension	46	33	67	0.24 (0.1 - 0.59)	< 0.01
Diabetes	40	33	53	0.44 (0.19 - 1.02)	0.06
Previous angina	5	5	6	0.93 (0.15 - 5.84)	0.94
Previous myocardial infarction	4	5	3	1.91 (0.19 - 19.09)	0.58
Family History of vascular disease					
Hypertension	18	16	22	0.64 (0.22 - 1.85)	0.41
Diabetes	17	12	25	0.41 (0.14 - 1.23)	0.11
Coronary Artery disease	9	7	11	0.59 (0.14 - 2.53)	0.48
Cerebrovascular disease	5	4	8	0.39 (0.06 - 2.47)	0.32
•				OR (95% CI)	
Continuous variables	Mean (SD)	Mean (SD)	Mean (SD)	Males vs. Females	P-value
Age (years)	54.3 (11.0)	53.02 (9.9)	56.31(12.37)	0.97 (0.93 - 1.01)	0.16
Systolic blood pressure (mmHg)	142.29 (29.04)	138.03 (26.4)	149.14 (32.05)	0.99 (0.97 - 1.0)	0.08
Diastolic blood pressure (mmHg)	88.33 (20.56)	87.31 (19.01)	89.97 (23.04)	0.99 (0.97 - 1.01)	0.54
Abdominal girth (cm)	99.88 (13.5)	97.98 (14.27)	102.94 (11.72)	0.97 (0.94 - 1.01)	0.11
Biochemical Data					
Haemoglobin (g/dl)	I 3.42 (2.06)	14.06 (1.9)	12.38 (1.91)	1.66 (1.25 - 2.2)	< 0.0
Blood glucose (mmol/L)	8.87 (5.76)	8.22 (5.11)	9.92 (6.61)	0.95 (0.88 - 1.02)	0.17
Creatinine (umol/L)	94.29 (26.96)	101.24 (27.85)	83.08 (21.3)	1.04 (1.01 - 1.07)	< 0.0
Uric acid (mmol/L)	0.39 (0.13)	0.39 (0.14)	0.39 (0.12)	1.03 (0.04 - 25.96)	0.99
Total cholesterol (mmol/L)	4.8 (1.74)	4.77 (1.86)	4.85 (1.54)	0.97 (0.77 - 1.23)	0.82
LDL cholesterol (mmol/L)	3.20 (1.12)	2.9 (1.01)	3.22 (1.28)	0.77 (0.52 - 1.15)	0.20
HDL cholesterol (mmol/L)	1.30 (0.35)	1.01 (0.34)	1.05 (0.37)	0.71 (0.21 - 2.41)	0.58
Triglycerides (mmol/L)	1.48 (1.41)	1.58 (1.63)	1.32 (0.97)	1.17 (0.81 - 1.69)	0.40
MACE	36	31	44	0.56 (0.24 - 1.33)	0.19
Cardiac failure	18	4	25	0.48 (0.17 - 1.39)	0.18
Death	6	2	4	0.11 (0.01 - 0.97)	0.04
Recurrence of infarction	6	2	4	0.11 (0.01 - 0.97)	0.04
Ventricular arrhythmia	6	9	3	3.3 (0.37 - 29.48)	0.29
Atrial fibrillation	4	3	6	0.61 (0.08 - 4.51)	0.63
Cardiogenic shock	4	5	3	1.91 (0.19 - 19.09)	0.58
Recurrence of angina	3	2	6	0.3 (0.03 - 3.41)	0.33
Cerebrovascular accident	3	3	3	1.25 (0.11 - 14.3)	0.86
Heart block	2	3	0	NC	0.52
Medication at discharge					
Nitrates	100	100	100	NC	
Disprin	100	100	100	NC	
Statins	94	93	94	0.79 (0.14 - 4.57)	0.80
ACEI/ARB	89	86	94	0.37 (0.07 - 1.84)	0.22
Beta blockers	56	55	58	0.88 (0.38 - 2.04)	0.76
Calcium antagonist	6	5	8	0.60 (0.11 - 3.15)	0.55
Coronary Angiogram	n=23	n=14	n=9		
Single vessel disease	26	21	33	1.61 (0.35 - 4.48)	0.54
Double vessel disease	22	29	11	(
Triple vessel disease	35	36	33		
CABG	17	14	22	0.58 (0.07 - 5.11)	0.63
PCI	0	0	0	NC	

MACE = Major Adverse Cardiac Events, NC = Not Calculated.

TABLE 2: Prevalence of the metabolic syndrome according to the IDF definition and frequency of individual criteria.

IDF Criteria	All patients % (n=81)	Patients with Metabolic Syndrome % (n=35)	Patients without Metabolic Syndrome % (n=46)	P-value
Waist circumference (male ≥94cm, females ≥80cm)	78	100	61	<0.01
Fasting glucose ≥5.6mmol/L*	26	46	П	<0.01
Triglycerides >1.7mmol/L	27	48	13	<0.01
HDL (males <1.03mmol/L) (females <1.29mmol/L)	63	80	50	0.01
Blood pressure (≥130/≥85mmHg)*	52	83	28	<0.01

*Patients on specific treatment for blood pressure and fasting plasma glucose were included, irrespective of the value obtained.

TABLE 3: Comparison of Cardiovascular Risk Factors between INTERHEART Africa Study and R.K. Khan Hospital Study.

Characteristics	INTERHEART Africa % (n=144)	R. K. Khan % (n=94)	OR (95% CI)	P-value
Male	64	62	0.91 (0.51 - 1.62)	0.73
Hypertension	50	73	2.76 (1.52 - 5.06)	<0.01
Diabetes	24	40	2.11 (1.16 - 3.85)	<0.01
Smoker (current/former)	45	48	1.12 (0.64 - 1.94)	0.68
Continuous variables	Mean (SD)	Mean (SD)	P-value	
Age	52.3 (12.3)	54.3 (11.0)	0.20	
Total cholesterol	4.50 (1.18)	4.80 (1.74)	0.11	
HDL cholesterol	0.99 (0.45)	1.03 (0.35)	0.46	
LDL cholesterol	2.83 (0.97)	3.02 (1.12)	0.16	
BMI	28.4 (5.2)	28.1 (5.9)	0.68	

were on highly active antiretroviral therapy (HAART). This presented us with the unique opportunity of studying a HAART- naïve population, thus negating the potential effects of HAART on thrombotic risk. Consistent with the study by Becker, et al.⁽²⁰⁾ our treatment-naïve HIV positive patients with AMI presented at a young age and had a high prevalence of smoking. In contrast, however, we did not find any significant difference in traditional cardiovascular risk factors between HIV positive and HIV negative patients. In addition, we found no significant difference in MACE between the 2 groups.

The metabolic syndrome contributes to an increased risk of cardiovascular disease.⁽²¹⁾ Many of the metabolic abnormalities common to this syndrome such as insulin resistance, central obesity, dyslipidaemia and hypertension are all independent risk factors for the development of cardiovascular disease, which when grouped together, amplify this risk. It is also well recognised that the incidence of the metabolic syndrome varies among different ethnic groups.⁽²²⁾ The prevalence of the meta-

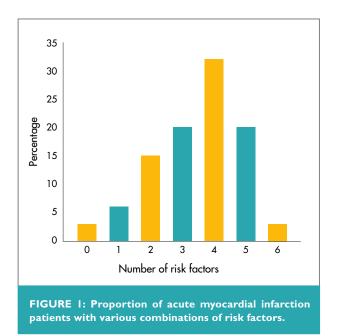
bolic syndrome in Asian Indians presenting with AMI to the CCU at R.K. Khan Hospital was reported to be 57% according to the IDF criteria.⁽²³⁾

Similarly, in Black patients with AMI, the metabolic syndrome was seen in 45% of the study population based on the IDF definition. These results concur with another study amongst South African Blacks with CAD in whom the metabolic syndrome was found to be highly prevalent (60%).⁽¹¹⁾ The metabolic syndrome, therefore, may be another factor contributing to the increase in AMI in the Black population.

More importantly, following multivariable analysis using logistic regression, our data showed that several clinical and laboratory parameters are significantly associated with MACE such as an increased heart rate (p=0.01), STEMI (p=0.03), obesity (p=0.03), a family history of cerebrovascular disease (p=0.04) and hyperuricaemia (p=0.04).

LIMITATIONS

Potential limitations of this study merit consideration. Firstly, because of the relatively small sample size, results for smaller subgroups should be interpreted with caution. Secondly, this was a single centre study and selection bias might exist. Finally, not all patients were subjected to cardiac catheterisation studies and data on angiographic severity of CAD and cardiac revascularisation was, therefore, tentative.



Includes any combination of diabetes, smoking, family history of vascular disease, dyslipidaemia, hypertension and visceral obesity.

CONCLUSION

This study demonstrates that South African Blacks have multiple risk factors, similar to other ethnic groups in the country, which contribute to the development of AMI. In addition to conventional risk factors for CAD, an increased heart rate, STEMI, obesity, a family history of cerebrovascular disease and hyperuricarmia are strongly associated with the presence of MACE. Furthermore, recurrence of infarction and death occurred more frequently in females compared to males. These results highlight the urgent need for lifestyle modification and effective treatment of CAD risk factors, particularly in the Black population.

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Conflict of interest: none declared.

TABLE 4: Bivariate and multivariate le	ogistic regression analysis of clinical and lab	boratory parameters associated with MACE.
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Characteristics	Bivariate OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Age	1.03 (0.99 - 1.08)	0.11	1.02 (0.96 - 1.08)	0.55
Male	0.56 (0.24 - 1.33)	0.19	0.72 (0.14 - 3.56)	0.68
Heart rate	1.03 (1.01 - 1.06)	0.02	1.06 (1.01 - 1.10)	0.01
HIV positive	0.69 (0.22 - 2.16)	0.52	0.65 (0.13 - 3.15)	0.59
STEMI vs. NSTEMI	2.0 (0.67 - 5.93)	0.21	5.98 (1.22 - 28.51)	0.03
Diabetes	1.54 (0.65 - 3.61)	0.33	1.03 (0.27 - 3.89)	0.97
Hypertension	1.01 (0.39 - 2.62)	0.98	0.95 (0.23 - 3.93)	0.95
Smoking	0.54 (0.23 - 1.28)	0.16	0.60 (0.13 - 2.78)	0.51
Obesity	1.05 (0.43 - 2.56)	0.92	3.86 (1.18 - 12.63)	0.03
Family history of cerebrovascular disease	7.87 (0.84 - 73.52)	0.07	14.83 (1.10 - 200.82)	0.04
Metabolic syndrome	0.86 (0.34 - 2.19)	0.75	0.66 (0.18 - 2.43)	0.53
Creatinine	1.02 (1.0 - 1.04)	0.04	1.02 (0.99 -1.04)	0.13
Blood glucose	1.06 (0.99 - 1.14)	0.11	1.0 (0.88 -1.12)	0.94
Uric acid	2.53 (1.05 - 6.07)	0.04	3.64 (1.05 -12.66)	0.04
Triglycerides	0.86 (0.59 - 1.25)	0.42	0.82 (0.48 - 1.40)	0.47

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