Original Article

Cardiovascular Risk Factors and Specific Coronary Artery Calcification in Postmenopausal Women

Siamak Sabour, MD, PhD[1,2], Marie Louise Bartelink, MD, PhD[1], Annemarieke Rutten, MD[3], Diederick E Grobbee, MD, PhD[1], Mathias Prokop, MD, PhD[3], Yvonne T van der Schouw, PhD[1], Michiel L Bots, MD, PhD[1]

[1]*Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands.*
[2]*Tabriz University of Medical Sciences, Tabriz, I. R. Iran.*
[3]*Radiology Department, University Medical Center Utrecht, Utrecht, the Netherlands.*

Received 4 December 2008; Accepted 28 April 2009

Abstract

Background: *Myocardial infarctions at different locations have been related to different sets of risk factors. This study was designed to examine the association between cardiovascular risk factors and specific coronary artery calcification (CAC).*

Methods: *The study population comprised 573 postmenopausal women selected from a population-based cohort study. Established vascular risk factors were measured. The women underwent a multi detector-row computed tomography (16-MDCT) (Philips Mx 8000 IDT 16) to assess coronary calcium. The Agatston score was used to quantify coronary calcium. Logistic regression models were utilized to assess the relations.*

Results: *The prevalence of coronary artery calcification (Agatston score>0) was 61.5% (n=348). CAC was most common in the left anterior descending (LAD) artery with a prevalence of 43.9%; and the rates of prevalence in the right coronary artery (RCA), the circumflex (LCX), the left main artery (LM), and the posterior descending artery (PDA) were 23.1%, 19.4%, 15.8%, and 0.3%, respectively. In the multivariate regression models, age was predominantly related to the calcification in the LAD and LCX, low density lipoprotein to calcification in the LAD, and cholesterol to the calcification of the RCA. Hypertension and systolic & diastolic blood pressures were related to the calcification of the LCX, whereas smoking was predominantly related to the calcification of both LAD and RCA. Finally, age, body mass index, and systolic blood pressure were significantly related to the calcification in the LM.*

Conclusion: *Our findings showed that the consequences of elevated risk factor levels on the development of atherosclerosis appeared to be different across the segments of the coronary arteries.*

J Teh Univ Heart Ctr 3 (2009) 171-176

Keywords: *Cardiovascular diseases • Atherosclerosis • Calcification, physiologic • Women • Postmenopause*

Introduction

Acute myocardial infarction (MI) occurs in varying anatomical locations, ranging from anteroseptal to the inferolateral zone.[1] In general, the left circumflex artery (LCX) serves the lateral and posterior walls of the myocardium, and the right coronary artery (RCA) serves the inferior wall. In an anterior MI, the left anterior descending artery (LAD), which serves the left ventricle as well as parts of the septum and papillary muscles, is obstructed.[2] Different locations of

[*]**Corresponding Author:** ***Siamak Sabour,*** *Assistant Professor of Clinical Epidemiology & Medicine, Department of Epidemiology & Biostatistics, Faculty of Health & Nutrition, Tabriz University of Medical Sciences, Tabriz, I. R. Iran. 5166614711. Tel: +98 411 3357580-3. Fax: +98 411 3340634. Email: sabours@tbzmed.ac.ir.*

an MI are expected to be due to atherosclerosis development at different coronary segments. Furthermore, MIs at different locations have been related to different sets of risk factors. Age over 65 and hypercholesterolemia are independent risk factors for anterior MI, whereas smoking and diabetes are independent risk factors for inferior MI.[3] In a retrospective study over a 7-year period, common finding on angiography was single-vessel disease causing infarction of the inferior wall (62%), and the major risk factor was tobacco use (81%), followed by family history (40%), hypertension (26%), and hyperlipidemia.[4]

These findings indicate that risk factors differently affect different parts of the coronary arteries. Since atherosclerosis is one of the main underlying abnormalities leading to coronary heart disease, we hypothesized that risk factors differed in their relation with the development of atherosclerosis in specific coronary arteries. Coronary atherosclerosis can be validly and non-invasively assessed using computer tomography. For example, Multi-Detector-Row Computed Tomography (MDCT) has been shown to be an accurate, non-invasive, and reproducible method to quantify coronary artery calcification (CAC).[5]

We set out to study the relation of vascular established risk factors to specific CAC in a population-based sample of postmenopausal women.

Methods

We used data from a cross-sectional study among 573 postmenopausal women as has been described previously.[6] In short, these women were selected from participants of the PROSPECT study, one of the two Dutch cohorts participating in the European Prospective Investigation into Cancer and Nutrition (EPIC). In PROSPECT 17,357 participants of a nationwide population-based breast-cancer screening programme, aged 49-70 years, were enrolled between 1993 and 1997. Between October 2002 and April 2004, 1996 women were randomly selected from 5844 participants of the PROSPECT study who were postmenopausal and did not use contraceptives or hormone-replacement therapy, and 1000 agreed to participate. Of these 1000 women, a random selection of 573 underwent a multislice CT examination at a second visit between January and December 2004. Information on CAC was present in 566 women. The Institutional Review Board of the University Medical Center Utrecht approved the study, and written informed consent was obtained from all the participants before enrolment.

At the re-examination visit, smoking behavior and family history of cardiovascular diseases were assessed through a questionnaire. Smoking was categorized as current versus past and never. Age was calculated from birth date and date of investigation. Height and weight were measured, and body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Waist-to-hip ratio (WHR) was assessed. Systolic and diastolic blood pressures (SBP & DBP) were measured at both arms with an automated and calibrated blood pressure device (DINAMAP™ XL, Critikon, Johnson & Johnson, Tampa, Florida, USA) with the subject in supine position. A venous blood sample was drawn after an overnight fast of at least eight hours. Plasma total cholesterol, plasma triglycerides, and plasma glucose were measured using standard enzymatic procedures. High density lipoproteins (HDL) cholesterol was measured by the direct method (inhibition, enzymatic). Low density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula. We defined hypertension as being under hypertensive therapy or a systolic blood pressure equal or higher than 140 mmHg or a diastolic blood pressure equal or higher than 90 mmHg. Pulse pressure (PP) was defined as SBP-DBP.

The amount of calcium in the coronary arteries was assessed with a multi-detector computed tomography (MDCT) scanner (Mx 8000 IDT 16, Philips Medical Systems, Best, The Netherlands). The subjects were positioned within the gantry of the MDCT scanner in supine position. A 16-slice scanner with 0.42 seconds rotation time was used to obtain 1.5 mm thick sections. During a single-breath hold, images of the heart, from the level of the tracheal bifurcation to below the base of the heart, were acquired employing prospective ECG triggering at 50-80% of the RR-interval, depending on the heart rate. Scan parameters were 16x1.5 mm collimation, 205 mm field of view (FOV), 0.42 s rotation time, 0.28 s scan time per table position, 120 kVp and 40-70 mAs (patient weight <70 kg: 40 mAs; 70-90 kg: 55 mAs; >90 kg: 70 mAs). Scan duration was approximately 10 seconds, depending on heart rate and patient size. From the acquired raw data, 3 mm thick sections were reconstructed. Quantification of CAC was performed on a separate workstation with software for calcium scoring (Heartbeat-CS, EBW, Philips Medical Systems, Best, The Netherlands). All the regions with a density over 130 Hounsfield units were identified as potential calcifications. After completing a training program, a trained scan reader, blinded for the results of cardiovascular risk factors, manually selected only the calcifications within one of the coronary arteries [left main (LM), left anterior descending (LAD), left circumflex (LCX), right coronary artery (RCA) , or posterior descending artery (PDA)]. It has recently been shown that inter- and intra-observer as well as inter-scan reproducibilility of coronary calcium measurement using MDCT is excellent, irrespective of slice thickness and type of calcium parameter.[7] To reduce the influence of noise, the minimum size of a calcified lesion was set at 0.5 mm^2. The peak density in Hounsfield units and the area in mm^2 of each selected region were calculated. An overall Agatston[8] calcium score was obtained by multiplying the area by a weighting factor that is dependent on the peak signal anywhere in the lesion. The scores of individual lesions were added to obtain the Agatston calcium score for individual

segments and for the entire coronary tree.

The main objective of the present study was to characterize the relation between coronary risk factors and specific CAC. The dependent variable for the analysis was the presence or the absence of CAC in a particular coronary artery as measured by MDCT. The independent variables were coronary risk factors.

First, the general characteristics of the study population were described. Then, the relation between cardiovascular risk factors and total coronary calcification was examined using logistic regression models. Age-adjusted relations between the risk factors and specific CAC were thereafter assessed. Finally, the relation between the risk factors and specific CAC was investigated adjusted for age and coronary calcification in the other segments.

The relations were quantified by odds ratio with corresponding 95% confidence limits. A significance level of 0.05 was used for all analysis. Data analysis was performed using SPSS for Windows version 13.0.

Results

Table 1 describes the general characteristics of our population. In our study population (n=573), information on coronary calcification was present in 566 women. The prevalence of coronary artery calcification was 61.5% (n=348) in 1.5 mm and 52% in 3 mm slice thicknesses.

Of those, 15.8% (n=90) had coronary calcification in the LM, 43.9% (n=249) in the LAD, 23.1% (n=131) in the RCA, 19.4% (n=110) in the LCX, and 0.3% (n=2) had calcification in the PDA. In our study population, 13.3% (n=75) had an Agatston score of less than 10 and 8.3% (n=47) of greater than 400.

Table 1. General characteristics of study population (n=573)*

Age (y)	66.8±5.5
Body mass index (Kg/ m^2)	26.7±4.4
Waist to hip ratio	0.84±0.07
Systolic blood pressure (mmHg)	136±21
Diastolic blood pressure (mmHg)	72±9
Pulse pressure (mmHg)	64±16
Total cholesterol (mmol/l)	6.1±1.0
Low density lipoprotein cholesterol (mmol/l)	4.2±0.9
High density lipoprotein cholesterol (mmol/l)	1.4±0.4
Triglycerides (mmol/l)	1.2±0.6
Glucose (mmol/l)	5.6±1.0
Current smoking	11
Former smoking	44
Hypertension	35
Diabetes	6
Previous cardiovascular diseases	4
Family history of cardiovascular diseases	11

*Data are presented as mean±SD or related percentage

The age-adjusted relations between the risk factors and coronary calcification are given in Table 2. Increased age itself, increased levels of WHR, SBP, DBP, PP, LDL, current smoking, and previous cardiovascular diseases were significantly related to increased levels of CAC. Current smokers had more than an eight-fold increase in the risk of coronary calcification compared to non-smokers [OR=8.50 (4.15-17.43)]. The risk of CAC in postmenopausal women with cardiovascular diseases was more than six fold compared to those without previous cardiovascular diseases [OR=6.29 (1.74-22.76)]. Decreased level of HDL was also significantly related to increased CAC.

Table 2. Age-adjusted relation between cardiovascular risk factors and coronary calcification

Risk Factors	OR (95% CI)
Age (y)	1.13 (1.10-1.17)
Body mass index (Kg/ m^2)	1.01 (0.97-1.05)
Waist to hip ratio	1.78 (1.26-2.50)
Systolic blood pressure (mmHg)	1.01 (1.00-1.02)
Diastolic blood pressure (mmHg)	1.03 (1.01-1.05)
Pulse pressure (mmHg)	1.01 (1.00-1.02)
Total cholesterol (mmol/l)	1.17 (0.98-1.40)
Low density lipoprotein cholesterol (mmol/l)	1.24 (1.02-1.51)
High density lipoprotein cholesterol (mmol/l)	0.48 (0.30-0.80)
Triglycerides (mmol/l)	1.38 (1.03-1.85)
Glucose (mmol/l)	1.05 (0.90-1.24)
Current smoking	8.50 (4.15-17.43)
Former smoking	1.40 (0.95-2.03)
Hypertension	1.30 (0.85-1.98)
Diabetes	1.16 (0.56-2.40)
Previous cardiovascular diseases	6.29 (1.74-22.76)
Family history of cardiovascular diseases	1.68 (0.96-2.93)

The age-adjusted relations of the risk factors with specific CAC are given in Table 3. After extra adjustment for calcification of the other coronary segments (Table 4), increased SBP and DBP were significantly related to the calcification of the circumflex branch [OR=1.01 (1.00-1.02)] and [OR=1.04 (1.01-1.07)] per mmHg, respectively. The age relation remained significant for the LAD and circumflex [OR=1.09 (1.05-1.13) and 1.08 (1.03-1.13)]. BMI, SBP, and family history of cardiovascular diseases were statistically significantly related to the calcification of the LM [OR=1.05 (1.00-1.10) per kg/m^2, 1.01 (1.00-1.02) mmHg and 2.25 (1.10-4.57)], respectively. Previous cardiovascular disease was related to the RCA [OR=3.79 (1.23-11.63)] and LDL cholesterol with the LAD [OR=1.36 (1.09-1.71)]; however, total cholesterol was related to the RCA [OR=1.25 (1.00-1.57)]. A strong significant relation was found between current smoking and coronary calcification but only in the LAD [OR=3.21 (1.60-6.45)] and the RCA [OR=2.99 (1.48-6.02)]. The relation of the other risk factors with calcification in a specific branch of the coronary artery did not reach statistical significance.

Table 3. Age-adjusted relation between cardiovascular risk factors and specific coronary artery calcification

Risk factors	Specific coronary artery calcification OR (95% CI)			
	LM n=90	LAD n=249	LCX n=110	RCA n=131
Body Mass Index (Kg/ m^2)	1.05 (1.00-1.10)*	0.99 (0.95-1.03)	1.01 (0.97-1.06)	1.04 (0.99-1.08)
Waist to Hip Ratio	1.42 (0.93-2.16)	1.59 (1.13-2.23)*	1.81 (1.20-2.73)*	1.81 (1.24-2.65)*
Systolic blood pressure (mmHg)	1.01 (1.00-1.02)*	1.00 (1.00-1.01)*	1.01 (1.00-1.02)*	1.00 (0.99-1.01)
Diastolic blood pressure (mmHg)	1.01 (0.98-1.03)	1.02 (1.00-1.04)*	1.03 (1.01-1.06)*	1.02 (1.00-1.04)
Cholesterol (mmol/l)	1.12 (0.98-1.38)	1.10 (0.93-1.31)	1.04 (0.84-1.28)	1.25 (1.02-1.52)
Low density lipoprotein (mmol/l)	1.00 (0.78-1.29)	1.27 (1.04-1.55)*	0.97 (0.76-1.24)	1.00 (0.80-1.25)
High density lipoprotein (mmol/l)	0.58 (0.29 -1.16)	0.44 (0.26-0.74)	0.48 (0.24-0.93)	0.67 (0.37-1.21)
Triglycerides (mmol/l)	1.42 (1.01-2.01)*	1.35 (1.02-1.81)*	1.18 (0.83-1.67)	1.30 (0.95-1.79)
Glucose (mmol/l)	0.97 (0.76-1.24)	1.09 (0.93-1.29)	1.05 (0.85-1.31)	0.82 (0.63-1.08)
Current smoking	3.39 (1.68-6.84)*	5.41 (2.88-10.17)	2.80 (1.44-5.45)*	5.12 (2.74-9.57)*
Past smoking	1.82 (1.08-3.07)*	1.35 (0.92-1.98)	1.04 (0.64-1.67)	1.57 (0.99-2.47)
Hypertension	2.15 (1.25-3.70)*	1.34 (0.87-2.05)	2.58 (1.49-4.46)*	1.75 (1.08-2.83)*
Diabetes	1.12 (0.44-2.84)	1.20 (0.57-2.51)	0.88 (0.34-2.29)	0.42 (0.14-1.23)
Previous CVD	3.22 (1.25-8.30)*	6.14 (1.93-19.56)*	6.35 (2.38-16.89)*	7.42 (2.81-19.59)*
Family history of CVD	2.13 (1.11-4.10)*	1.14 (0.65-1.98)	1.07 (0.52-2.21)	1.63 (0.89-2.99)

*p< 0.05
LM, Left main; LAD, Left anterior descending; LCX, Left circumflex; RCA, Right coronary artery; CVD, Cardiovascular diseases

Table 4. Relation between cardiovascular risk factors and specific coronary artery calcification adjusted for age and calcification of the other segments of coronary arteries

Risk factors	Specific coronary artery calcification OR (95% CI)			
	LM n=90	LAD n=249	LCX n=110	RCA n=131
Age (y)	1.03 (0.98-1.08)	1.09 (1.05-1.13)*	1.08 (1.03-1.13)*	1.02 (0.98-1.07)
Body Mass Index (Kg/ m^2)	1.05 (1.00-1.10)*	0.97 (0.93-1.02)	1.00 (0.95-1.06)	1.04 (0.99-1.09)
Waist to Hip Ratio	1.04 (0.66-1.64)	1.26 (0.87-1.85)	1.43 (0.90-2.28)	1.48 (0.96-2.27)
Systolic blood pressure (mmHg)	1.01 (1.00-1.02)*	1.00 (0.99-1.01)	1.01 (1.00-1.02)*	1.00 (0.99-1.01)
Diastolic blood pressure (mmHg)	1.00 (0.97-1.03)	1.00 (0.98-1.02)	1.04 (1.01-1.07)*	1.01 (0.99-1.04)
Cholesterol (mmol/l)	1.06 (0.83-1.35)	1.02 (0.84-1.24)	0.93 (0.73-1.18)	1.25 (1.00-1.57)*
Low density lipoprotein (mmol/l)	1.00 (0.77-1.30)	1.36 (1.09-1.71)*	0.90 (0.69-1.17)	0.94 (0.74-1.20)
High density lipoprotein (mmol/l)	0.83 (0.40-1.71)	0.51 (0.30-0.91)	0.72 (0.35-1.50)	1.08 (0.56-2.11)
Triglycerides (mmol/l)	1.29 (0.90-1.87)	1.26 (0.91-1.75)	0.93 (0.63-1.39)	1.13 (0.78-1.63)
Glucose (mmol/l)	0.92 (0.69-1.23)	1.14 (0.96-1.36)	1.09 (0.88-1.35)	0.77 (0.57-1.05)
Current smoking	1.66 (0.77-3.61)	3.21 (1.60-6.45)*	1.03 (0.48-2.20)	2.99 (1.48-6.02)*
Past smoking	1.70 (0.97-2.97)	1.22 (0.80-1.87)	0.70 (0.40-1.22)	1.43 (0.85-2.39)
Hypertension	1.48 (0.81-2.74)	0.91 (0.55-1.51)	2.00 (1.06-3.76)*	1.24 (0.70-2.20)
Diabetes	1.18 (0.41-3.36)	1.47 (0.66-3.25)	1.00 (0.35-2.87)	0.37 (0.12-1.15)
Previous CVD	1.26 (0.45-3.51)	2.26 (0.67-10.32)	2.49 (0.80-7.85)	3.79 (1.23-11.63)*
Family history of CVD	2.25 (1.10-4.57)*	0.91 (0.49-1.71)	0.91 (0.40-2.08)	1.58 (0.78-3.16)

*p< 0.05
LM, Left main; LAD, Left anterior descending; LCX, Left circumflex; RCA, Right coronary artery; CVD, Cardiovascular diseases

Discussion

We found that different cardiovascular risk factors had different relations with the calcification of a particular branch in the coronary arteries.

To appreciate our findings, some limitations of our study need to be addressed. First, a causal interpretation of our findings is inherently restricted by the cross-sectional nature of the study design. Also, our study population comprised only postmenopausal women and thus our results should be confirmed by other studies with a large number of both male and female patients.

Although heritability plays a significant role in coronary calcification at the LM and the proximal part of coronary arteries,[9] it has been shown that also non-genetic factors such as age over 65 and hypercholesterolemia are

independent risk factors for anterior MI, whereas smoking and diabetes are independent risk factors for inferior MI. In a retrospective study over a 7-year period to define the risk factors and clinical presentation of patients with an acute MI, a common finding on angiography was single-vessel disease (62%) causing infarction of the inferior wall (LCX and RCA), and the major risk factor was tobacco use (81%), followed by family history (40%), hypertension (26%), and hyperlipidemia (20%).[10] Our results extended the present knowledge on the relation between risk factors and location of MI with segment-specific coronary atherosclerosis and different risk factors.

Age is an independent predictor of CHD event fatality[11] having a strong association with total coronary calcification. However, in our study, after adjusting for the calcification of the other coronary segments, this relation remained significant just for the LAD and LCX. In other words, age is significantly related to the location of MI (anterior) and the calcification of particular coronary segments (LAD and LCX). It seems the higher our age, the higher the likelihood of developing CAC in the LAD and LCX as well as anterior MI.

Since the location of current and prior MI predicts short- and long-term risk of death,[12] there have been efforts to predict the location of a future MI based on the location of ischemia.[13] Although in the setting of severely depressed ejection fraction (≤30%), inferior MI has been shown to be associated with a significantly higher risk of mortality than anterior MI (hazard ratio 1.58, p=0.048),[14] it has been shown that the rate of reinfarction or death is almost two times higher in patients with anterior than that in those with inferior infarction.[15] Also, in patients with an LAD lesion, proximal lesion location correlates with adverse outcomes even after adjustment for coronary blood flow and other covariates.[16] However, there is evidence that adverse prognosis associated with anterior MI is related to differences in etiology rather than to infarction size.[17] Therefore, regarding the adverse prognosis of MI, not only the location and size of the MI but also different risk factors are related to the outcome.

We found a significant association between hypertension and coronary calcification. Our results indicated that after adjusting for the calcification of other segments, both systolic and diastolic blood pressures as well as hypertension, according to our definition, had a significant relation with the calcification of the LCX, which serves the lateral and posterior walls of the myocardium; and the relation between LDL cholesterol and coronary calcification is significant just for the LAD, which is obstructed in anterior MI.

It has been reported that after adjustment for other risk factors, smokers are more likely to have more advanced atherosclerosis in the LAD than non-smokers. This is true for the RCA as well.[18] We confirmed previous results by showing that indeed among coronary segments, only the calcifications of the LAD and RCA were related to smoking. Finally, our results showed that a family history of cardiovascular disease was related to LM calcification, whereas previous cardiovascular disease had a significant relation with the calcification of the RCA.

Conclusion

In conclusion, our study showed that the consequences of elevated risk factor levels on the development of atherosclerosis appeared to be different across the segments of the coronary arteries.

Acknowledgements

This study was approved and was supported by University Medical Center Utrecht, the Netherlands. The first author was supported by the health ministry of Iran.

References

1. Bayés de Luna A, Cino JM, Pujadas S, Cygankiewicz I, Carreras F, Garcia-Moll X, Noguero M, Fiol M, Elosua R, Cinca J, Pons-Lladó G. Concordance of electrocardiographic patterns and healed myocardial infarction location detected by cardiovascular magnetic resonance. Am J Cardiol 2006;97:443-451.
2. Ayling J. Ready to go. Emerg Med Serv 2003;32:97.
3. Fabijanic D, Giunio L, Culic V, Bozic I, Martinovic D, Miric D. Predictors of type and site of first acute myocardial infarction in men and women. Ann Saudi Med 2005;25:134-139.
4. Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. J Emerg Med 1996;14:139-145.
5. Thompson BH, Stanford W. Update on using coronary calcium screening by computed tomography to measure risk for coronary heart disease. Int J Cardiovasc Imaging 2005;21:39-53.
6. Sabour S, Franx A, Rutten A, Grobbee DE, Prokop M, Bartelink ML. High blood pressure in pregnancy and coronary calcification. Hypertension 2007;49:813-817.
7. Sabour S, Rutten A, van der Schouw YT, Atsma F, Grobbee DE, Mali WP, Bartelink ME, Bots ML, Prokop M. Inter-scan reproducibility of coronary calcium measurement using Multi Detector-Row Computed Tomography (MDCT). Eur J Epidemiol 2007;22:235-243.
8. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827-832.
9. Fischer M, Broeckel U, Holmer S, Baessler A, Hengstenberg C, Mayer B, Erdmann J, Klein G, Riegger G, Jacob HJ, Schunkert H. Distinct heritable patterns of angiographic coronary artery disease in families with myocardial infarction. Circulation 2005;111:855-862.
10. Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. J Emerg Med 1996;14:139-145.
11. Pearte CA, Furberg CD, O'Meara ES, Psaty BM, Kuller L, Powe NR, Manolio T. Characteristics and baseline clinical predictors of future fatal versus nonfatal coronary heart disease events in older adults: the cardiovascular health study. Circulation 2006;113:2177-

2185.
12. Brieger DB, Mak KH, Miller DP, Califf RM, Topol EJ. Benefit of early sustained reperfusion in patients with prior myocardial infarction (the GUSTO-I trial). Global utilization of streptokinase and TPA for occluded arteries. Am Heart J 2000;140:29-33.
13. Miller GL, Herman SD, Heller GV, Kalla S, Levin WA, Stillwell KM, Travin MI. Relation between perfusion defects on stress technetium-99m sestamibi SPECT scintigraphy and the location of a subsequent acute myocardial infarction. Am J Cardiol 1996;78:26-30.
14. Gomez JF, Zareba W, Moss AJ, McNitt S, Hall WJ. Prognostic value of location and type of myocardial infarction in the setting of advanced left ventricular dysfunction. Am J Cardiol 2007;99:642-646.
15. Welty FK, Mittleman MA, Lewis SM, Healy RW, Shubrooks SJ Jr, Muller JE. Significance of location (anterior versus inferior) and type (Q-wave versus non-Q-wave) of acute myocardial infarction in patients undergoing percutaneous transluminal coronary angioplasty for postinfarction ischemia. Am J Cardiol 1995;76:431-435.
16. Karha J, Murphy SA, Kirtane AJ, de Lemos JA, Aroesty JM, Cannon CP, Antman EM, Braunwald E, Gibson CM; TIMI Study Group. Evaluation of the association of proximal coronary culprit artery lesion location with clinical outcomes in acute myocardial infarction. Am J Cardiol 2003;92:913-918.
17. Bourke S, Conroy RM, Mulcahy R, Robinson K. Aetiological and prognostic correlates of site of myocardial infarction. Eur Heart J 1988;9:734-739.
18. Zieske AW, McMahan CA, McGill HC Jr, Homma S, Takei H, Malcom GT, Tracy RE, Strong JP. Smoking is associated with advanced coronary atherosclerosis in youth. Atherosclerosis 2005;180:87-92.