EJMI

DOI: 10.14744/ejmi.2018.76486
EJMI 2018;2(1):1–7

Review

Risk Factors for Acute Myocardial Infarction: A Review

Vedika Rathore, Neelima Singh, Roshan Kumar Mahat

Department of Biochemistry, Gajra Raja Medical College, Gwalior, India

Abstract

Acute myocardial infarction (AMI) remains a leading cause of morbidity and mortality worldwide. It occurs when myocardial ischemia, a diminished blood supply to the heart, exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms designed to maintain normal operating function and homeostasis. This review highlights risk factors that are responsible for the onset of AMI. Among the most important are physical inactivity, smoking, alcohol consumption, dyslipidemia, diabetes mellitus, hypertension, and obesity. Hence, management of these risk factors is important in order to prevent the development of AMI, and should also be taken into consideration during the treatment of AMI.

Keywords: Acute myocardial infarction, dyslipidemia, risk factors

Acute myocardial infarction (AMI) is one of the most common diseases among the developing countries.[1] It is commonly known as a heart attack, which occurs when there is a sudden block in blood flow in one or more of the coronary arteries and this cut off blood supply to a part of the heart muscle, causing necrosis (massive cell death, a permanent damage). If the block is severe, the heart can stop beating (cardiac arrest). This is most commonly due to occlusion or blockage of a coronary artery following the rupture of a vulnerable atherosclerotic plaque which is an unstable collection of lipids (cholesterol and fatty acids) and white blood cells (especially macrophages) in the wall of an artery. Myocardial infarction usually begins in the endocardium and spread towards the epicardium.[2-5] There are many symptoms of acute myocardial infarction but the most common is chest pain, which may travel into the shoulder, arm, back, neck or jaw. This type of pain always starts from the center or left side of the chest and remains for few minutes. The onset of symptoms in acute myocardial infarction is usually gradual, over several minutes and rarely instantaneous.[6-8]

The incidence of myocardial infarction in the world varies greatly. In the United States and United Kingdom, nearly 650.000 and 180.000 patients get an acute myocardial infarction every year, respectively.[9] Worldwide, more than 3 million people have STEMIs and 4 million have NSTEMIs.[10] Indians are four time more prone to AMI as compared to the people of other countries due to a combination of the genetic and lifestyle factors that promote metabolic dysfunction.[11] The incidence of myocardial infarction in India is 64.37/1000 people.[12] The mortality rate of myocardial infarction is approximately 30% and for every 1 in 25 patients who survive the initial hospitalization, dies in the first year after AMI.[11] In India, 31.7% of deaths occur due to myocardial infarction. Incidence of cardiovascular diseases was about 7% in 1970 and increased upto 32% in 2011 in India.[13]

Address for correspondence: Vedika Rathore, Ph.D. Biyokimya Anabilim Dali, Gajra Raja Tip Fakultesi, Gwalior, India
Phone: +91 9713555241 **E-mail:** ved_sin26@rediffmail.com
Submitted Date: January 05, 2018 **Accepted Date:** January 28, 2018 **Available Online Date:** February 20, 2018

Risk Factors

There are various risk factors of AMI. Among them, some are modifiable (treatable) and others are non-modifiable (can not be changed). The major risk factors of AMI are described hereunder;

Physical activity:

Inactive people with multiple cardiac risk factors are more likely to develop AMI.[14] Physical activity may contribute up to 20%-30% reduced risk of coronary heart disease.[15, 16] However, studies have shown that different types of physical activities may have different effects on the risk of cardiovascular disease (CVD) and may interact together. For example, some leisure time activities such as walking, stair climbing, and cycling provide protection against CVD[17-22] whereas others, such as intensive domestic physical activity, may not offer protection against CVD.[21] There are also interactive effects between lack of exercise and sitting at work and between demanding household work and sitting at work on the association with increased risk of acute myocardial infarction (AMI).[19] D'Avanzo et al., examined the relationship between physical activity and acute myocardial infarction (AMI) and confirm that low physical activity is an indicator of subsequent risk of AMI.[23] Similarly, Gong et al., suggested that a light indoor activity pattern is associated with reduced AMI risk.[16]

Smoking:

Smoking is considered to be strong risk factor of myocardial infarction, premature atherosclerosis and sudden cardiac death. Smoking results in early STEMI especially in otherwise healthier patients.[24, 25] Cigarette smoking increases the risk for AMI by multiple and complex mechanisms.[26] With respect to atherogenesis, smoking increases serum LDL-cholesterol and triglyceride concentrations and reduces serum HDL-cholesterol. Furthermore, cigarette smoke promotes free radical damage to LDL, leading to accumulation of oxidized LDL-cholesterol within the arterial wall. Smoking appears to contribute vascular inflammation characteristic of atherosclerosis, as reflected by higher serum C-reactive protein levels in smokers than in non-smokers.[27] Smoking, mainly through its nicotine content, activates the sympathetic nervous system (SNS), increasing both heart rate and systolic blood pressure. This increase in the rate-pressure product results in increased myocardial oxygen demands. Increased in activity of SNS also leads to coronary arterial vasoconstriction,[28] decreasing myocardial blood flow at a time when oxygen demand is increasing. In addition to increasing myocardial oxygen demand and reducing coronary blood flow, cigarette smoking also causes increase in the levels of carboxyhemoglobin in the blood, with the potential to further reduce myocardial oxygen delivery from oxyhemoglobin.[26]

Alcohol Consumption:

Alcohol consumption is associated with an acutely higher risk of myocardial infarction in the subsequent hour among people who do not typically drink alcohol daily. There is consistent evidence that moderate habitual alcohol consumption is associated with a lower risk of cardiovascular events in subsequent months and years[29] and that heavy episodic (binge) drinking is associated with higher cardiovascular risk.[30]

As reviewed by McKee and Britton[31] and further sources,[32, 33] a number of possible mechanisms have been discussed explaining the acute effects of binge drinking on CHD events. These include: (i) Binge drinking has been shown to increase low-density lipoproteins, which in turn are linked to cardiovascular morbidity and mortality. However, low to moderate steady drinking, heavy irregular drinking has not been associated with increased levels of high-density lipoproteins, which are linked to favorable cardiovascular outcomes. (ii) Binge drinking has been associated with an increased risk of thrombosis, occurring after cessation of a heavy drinking episode. (iii) Binge drinking appears to predispose drinkers to histological changes in the myocardium and conducting system, as well as to a reduction in the threshold for ventricular fibrillation.[34]

However, there is a controversy regarding consumption of alcohol and risk of AMI. Most researches showed that alcohol consumption can increase high density lipoprotein cholesterol (HDL-C), apolipoprotein-a1 and adiponectin and reduce fibrinogen level, in which the HDL-C was the main protective factor which could explain about 50% of the causal relationship.[35-38] But, some researchers believed that the value of HDL-C was low, which could only explain about 16% of the causal relationship.[39, 40] Besides, some researchers found that alcohol consumption could increase the prostacyclin of blood vessel wall, improve functions of vascular endothelial cells, increase insulin sensitivity and resist thrombosis.[41, 42] Moreover, long-term regular alcohol consumption could improve heart rate variability[43, 44] and thus reduce MI onset risks. Most researches showed that alcohol consumption could increase LDH-C, triglyceride, heart rate, blood pressure[45-47] and thus increase the risks of atherosclerosis, atrial fibrillation and anoxia, resulting in damaging cardiac muscle cells and cardiovascular system and producing fibrinolytic enzyme inhibitor.[48]

Saremi et al.,[49] stated that moderate alcohol consumption is not associated with any significant morbidity; however,

three or more drinks per day is associated with hypertriglyceridemia, cardiomyopathy, hypertension, and stroke.

Dyslipidemia:

Dyslipidemia, a major risk factor of cardiovascular disease, is generally defined as the total cholesterol, LDL, triglycerides, apo B or Lp (a) levels above the 90th percentile or HDL and apo A levels below the 10th percentile of the general population.[50, 51] Increased triglyceride levels and dense, small LDL particles act as predisposing risk factors for myocardial infarction. Non fasting triglyceride level appears to be a strong and independent predictor of future risk of AMI, particularly when the total cholesterol level is also increased. The reason behind it is that decreased HDL-C levels and increased triglyceride levels cause metabolic perturbations and thus causing adverse consequences.[52] Ali et al.,[53] concluded that there is a high frequency of dyslipidemia in young patients presenting with acute myocardial infarction, with descending order hypertriglyceridemia followed by hypercholesterolemia, raised LDL and low HDL. The prospective studies such as those of Framingham study established the relationship of dyslipidemia and coronary artery disease. High levels of total cholesterol, LDL and low level of HDL are major risk factors for coronary atherosclerosis. Correction of dyslipidemia can reduce the risk of myocardial infarction.[54]

Diabetes Mellitus:

Type 2 diabetes mellitus is on the verge of becoming a pandemic in India.[55] It is a chronic condition that occurs when the body can not produce enough or effectively use of insulin, and are induced by a genetic predisposition coupled with environmental factors.[56] As type 2 diabetes shares several risk factors in common with coronary artery disease (CAD), such as age, hypertension, dyslipidemia, obesity, physical inactivity and stress, an increase in the prevalence of diabetes indirectly implicates an escalating risk of CAD as well.[36, 57] Diabetes mellitus is a well-established risk factor for cardiovascular disease (CVD). People with type 2 diabetes mellitus have a higher cardiovascular morbidity and mortality and are disproportionately affected by CVD compared with non-diabetic subjects.[58] Diabetes increases risk of coronary heart disease (CHD) by two to four times.[59] Patients with diabetes bear greater risk of atherosclerotic vascular disease in the heart as well as in other vascularized areas.

The life expectancy of people with diabetes is reduced by nearly eight years due to increased mortality.[60] Coronary artery disease accounts for more than 80% of all deaths and 75% of all hospitalizations in diabetic subjects.[61, 62] It is also reported that plaques are more vulnerable to rupture among patients with diabetes.[63] The protective female gender effect is lost in diabetic subjects, and indeed, women with diabetes are possibly more prone to develop CAD than men with diabetes.[58]

Diabetes increases the risk of myocardial infarction because it increases the rate of atherosclerotic progression and adversely affects the lipid profile and facilitates formation of atherosclerotic plaque.[64] In a hospital based case control study, conducted in a rural population of India, cases of AMI were twice as likely to have history of diabetes compared to controls.[65] Bibbins et al., says that diabetes mellitus is the biggest individual risk factor of heart disease.[66] Diabetes is also a risk factor for myocardial infarction case fatality: that is, myocardial infarction is more often fatal in people with diabetes compared with myocardial infarction in those without diabetes.[67-69]

Hypertension:

Both systolic and diastolic hypertension increase the risk of a myocardial infarction and the higher the pressure, the greater the risk.[70] It is major risk factor of causing atherosclerosis in coronary blood vessels, result in heart attack or myocardial infarction. Hypertension and myocardial infarction are closely linked. In old age, hypertension is even worse to heart and responsible for at least 70 percent of heart disease.[71] Several mechanisms can account for the increased coronary risk in hypertensive patients. Hypertension accelerates the effects on atheroma, increases shear stress on plaques, exerts adverse functional effects on the coronary circulation, and impairs endothelial function and control of sympathetic tone.[72] Ciruzzi et al.,[73] reported that in Argentine population, hypertension is a strong and independent risk factor for acute myocardial infarction. The control of hypertension with strict compliance of proper medication and adoption of lifestyle modifications reduce the risk of myocardial infarction significantly.[64]

Obesity/BMI:

Increased BMI is directly related to incidence of myocardial infarction. Infarction is greatly enhanced by extreme obesity because it is a recognized risk factor for myocardial infarction. Zhu et al.,[74] performed the meta-analysis of previous studies and suggested that overweight and obesity are associated with higher risk of AMI. Overweight and obesity may affect health, and it is necessary to control one's BMI to prevent AMI. Schargrodsky et al.,[75] demonstrated that overweight is an independent risk factor for MI. Yusuf et al.,[27] demonstrated that abdominal obesity increased the risk of AMI in both ages and sexes in all regions.

Stress:

Chronic life stress, social isolation and anxiety increase the risk of heart attack and stroke.[25] Acute psychological stress also is associated with increased risk for coronary heart disease, and it has been reported that intense grief in the days after death of a significant person may trigger the onset of myocardial infarction.[76] The pathophysiological mechanism of acute emotional stress remains unclear, but it is assumed to be related to hemodynamic stress in the coronary arteries and rupture of an atherosclerotic plaque, with consequent thrombosis.[77]

Gout:

Patients with gout have an increased risk of myocardial infarction. In gout patients, the inflammatory response associated with gout plays a key role in the initiation and progression of atherosclerosis, and promotion of a pro-thrombotic environment that leads to acute coronary events such as angina or myocardial infarction.[78-80]

Periodontal Diseases:

Periodontal diseases are a group of inflammatory diseases in which bacteria and their by-products are the principal aetiologic agents.[81] The first indication of association between dental disease and atherosclerosis was given in 1963.[82] Since then, there is growing evidence that poor dental health, especially the presence of periodontal disease, increases the risk of occurrence of CHD.[83, 84] The study done by Kaisare et al.,[85] also indicates an association between periodontal disease and acute myocardial infarction.

Family history:

Family history of myocardial infarction is an independent risk factor for AMI. Several genetic variants are associated with increased risk of AMI and family history of AMI in a first-degree relative doubles AMI risk. A recent combined analysis of 12 cohort studies found a combined relative risk of 1.6 for future events in persons with a first-degree relative with cardiovascular disease, compared with persons without an affected first-degree relative.[86] Ciruzzi et al., reported that family history of acute myocardial infarction was a strong and independent risk factor in a study of 1.060 cases and 1.071 controls from Argentina. The antecedent of ≥1 first-degree relative with acute myocardial infarction increased the risk about twofold in men and nearly threefold in women, with a significant trend in risk in the number of relatives affected.[87] Friedlander et al.,[88] reported that family history of AMI is positively associated with the risk of early AMI in women. If a father develops heart attack before the age of 55 and mother before the age of 65 years, this positive family history becomes very significant for the next generation and mere presence of parental and maternal history for premature myocardial infarction may increase the risk to 7 folds in descendents.[89, 90]

Age:

Advanced age is associated with an increased mortality in acute myocardial infarction.[91, 92] The mechanism by which increasing age contributes so dramatically to mortality is unknown.[93] About 80% of heart disease deaths occur in people aged 65 or older.[25]

Gender:

Men tend to have heart attacks earlier in life than women. Women's rate of heart attack increases after menopause but does not equal men's rate. Even so, heart disease is the leading cause of death for both men and women.[25]

Conclusion

There are various risk factors of acute myocardial infarction which should be taken into consideration while treating patients of AMI.

Disclosures

Ethics Committee Approval: Ethics committee approval was not requested for this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – V.R., N.S., R.K.M.; Design – V.R., N.S., R.K.M.; Supervision – N.S.; Materials – V.R., N.S., R.K.M.; Data collection &/or processing – V.R., N.S., R.K.M.; Analysis and/or interpretation – V.R., N.S., R.K.M.; Literature search – V.R., R.K.M.; Writing – V.R., N.S., R.K.M.; Critical review – V.R., N.S., R.K.M.

References

1. Sathisha TG, Manjunatha GBK, Avinash SS, Shetty J, Devi OS, Devaki RN. Microalbunuria in non diabetic, non hypertensive myocardial infarction in south Indian patients with relation to lipid profile and cardiac markers. J Clin Diag Res 2011;5:1158–1160.
2. Nigam PK. Biochemical markers of myocardial injury. Indian J Clin Biochem 2007;22:10–7.
3. Rathore V, Singh N, Rastogi P, Mahat RK, Mishra MK, Shrivastava R. Lipid profile and its correlation with C-reactive protein in patients of acute myocardial infarction. Int J Res Med Sci 2017;5:2182–6.
4. Naik P. Biochemistry. 3rd. New Delhi: Jaypee Brothers Medical publishers; 2010.p.575–591.
5. Bhagwat K, Padmini H. Co-relation between lactate dehydrogenase and creatine kinase-MB in acute myocardial infarction. IJARPB 2014;4:–16.

6. Aghaeishahsavari M, Noroozianavval M, Veisi P, Parizad R, Samadikhah J. Cardiovascular disease risk factors in patients with confirmed cardiovascular disease. Saudi Med J 2006;27:1358–61.
7. AlSaraj F, McDermott JH, Cawood T, McAteer S, Ali M, Tormey W, et al. Prevalence of the metabolic syndrome in patients with diabetes mellitus. Ir J Med Sci 2009;178:309–13.
8. Anwar A, Khan HA, Hafeez S, Firdous K. A comparative study of creatine kinase- MB and Troponin levels among diabetic and non diabetic patients with acute MI. Pak J Med Health Sci 2016;10:296–298.
9. Braunwald E. Approach to the patient with cardiovascular disease. In: Kasper DL, Braunwald E, Fauci AS,Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 16th. New York: McGraw-Hill;2005.p.1301–1494.
10. White HD, Chew DP. Acute myocardial infarction. Lancet 2008;372:570–84.
11. Venkateshwarlu M, Gayathri C. Study of significance of estimation of lipid profile in patient with acute myocardial infarction. Int J Inf Res Rev 2015;2:1028–1030.
12. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2224–60.
13. Goyal A, Yusuf S. The burden of cardiovascular disease in the Indian subcontinent. Indian J Med Res 2006;124:235–44.
14. Giri S, Thompson PD, Kiernan FJ, Clive J, Fram DB, Mitchel JF, et al. Clinical and angiographic characteristics of exertion-related acute myocardial infarction. JAMA 1999;282:1731–6.
15. Sofi F, Capalbo A, Cesari F, Abbate R, Gensini GF. Physical activity during leisure time and primary prevention of coronary heart disease: an updated meta-analysis of cohort studies. Eur J Cardiovasc Prev Rehabil 2008;15:247–57.
16. Gong J, Campos H, Fiecas JM, McGarvey ST, Goldberg R, Richardson C, et al. A case-control study of physical activity patterns and risk of non-fatal myocardial infarction. BMC Public Health 2013;13:122.
17. Barengo NC, Hu G, Lakka TA, Pekkarinen H, Nissinen A, Tuomilehto J. Low physical activity as a predictor for total and cardiovascular disease mortality in middle-aged men and women in Finland. Eur Heart J 2004;25:2204–11.
18. Boreham CA, Kennedy RA, Murphy MH, Tully M, Wallace WF, Young I. Training effects of short bouts of stair climbing on cardiorespiratory fitness, blood lipids, and homocysteine in sedentary young women. Br J Sports Med 2005;39:590–3.
19. Fransson E, De Faire U, Ahlbom A, Reuterwall C, Hallqvist J, Alfredsson L. The risk of acute myocardial infarction: interactions of types of physical activity. Epidemiology 2004;15:573–82.
20. Fransson EI, Alfredsson LS, de Faire UH, Knutsson A, Westerholm PJ; WOLF Study. Leisure time, occupational and household physical activity, and risk factors for cardiovascular disease in working men and women: the WOLF study. Scand J Public Health 2003;31:324–33.
21. Stamatakis E, Hamer M, Lawlor DA. Physical activity, mortality, and cardiovascular disease: is domestic physical activity beneficial? The Scottish Health Survey -- 1995, 1998, and 2003. Am J Epidemiol 2009;169:1191–200.
22. Yu S, Yarnell JW, Sweetnam PM, Murray L; Caerphilly study. What level of physical activity protects against premature cardiovascular death? The Caerphilly study. Heart 2003;89:502–6.
23. D'Avanzo B, Santoro L, La Vecchia C, Maggioni A, Nobili A, Iacuitti G, et al. Physical activity and the risk of acute myocardial infarction. GISSI-EFRIM Investigators. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto-Epidemiologia dei Fattori di Rischio dell'Infarto Miocardico. Ann Epidemiol 1993;3:645–51.
24. Zhang H, Sun S, Tong L, Li R, Cao XH, Zhang BH, et al. Effect of cigarette smoking on clinical outcomes of hospitalized Chinese male smokers with acute myocardial infarction. Chin Med J (Engl) 2010;123:2807–11.
25. Huma S, Tariq R, Amin F, Mahmood KT. Modifiable and non-modifiable predisposing risk factors of myocardial infarction -A review. J Pharm Sci Res 2012;4:1649–1653.
26. Alemu R, Fuller EE, Harper JF, Feldman M. Influence of smoking on the location of acute myocardial infarctions. ISRN Cardiol 2011;2011:174358.
27. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937–52.
28. Moliterno DJ, Willard JE, Lange RA, Negus BH, Boehrer JD, Glamann DB, et al. Coronary-artery vasoconstriction induced by cocaine, cigarette smoking, or both. N Engl J Med 1994;330:454–9.
29. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ 2011;342:d671.
30. Mostofsky E, van der Bom JG, Mukamal KJ, Maclure M, Tofler GH, Muller JE, et al. Risk of myocardial infarction immediately after alcohol consumption. Epidemiology. 2015;26:143–50.
31. McKee M, Britton A. The positive relationship between alcohol and heart disease in eastern Europe: potential physiological mechanisms. J R Soc Med 1998;91:402–7.
32. Puddey IB, Rakic V, Dimmitt SB, Beilin LJ. Influence of pattern of drinking on cardiovascular disease and cardiovascular risk factors- a review. Addiction 1999;94:649–63.
33. Rehm J, Sempos CT, Trevisan M. Alcohol and cardiovascular disease- more than one paradox to consider. Average volume of alcohol consumption, patterns of drinking and risk of coro-

nary heart disease- a review. J Cardiovasc Risk 2003;10:15–20.
34. Gerlich MG, Krämer A, Gmel G, Maggiorini M, Lüscher TF, Rickli H, et al. Patterns of alcohol consumption and acute myocardial infarction: a case-crossover analysis. Eur Addict Res 2009;15:143–9.
35. Ikeoka D, Mader JK, Pieber TR. Adipose tissue, inflammation and cardiovascular disease. Rev Assoc Med Bras (1992) 2010;56:116–21.
36. Kannel WB, Wolf PA, Castelli WP, D'Agostino RB. Fibrinogen and risk of cardiovascular disease. The Framingham Study. JAMA 1987;258:1183–6.
37. Kannel WB. Overview of hemostatic factors involved in atherosclerotic cardiovascular disease. Lipids 2005;40:1215–20.
38. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, et al. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med 2004;351:2599–610.
39. Magnus P, Bakke E, Hoff DA, Høiseth G, Graff-Iversen S, Knudsen GP, et al. Controlling for high-density lipoprotein cholesterol does not affect the magnitude of the relationship between alcohol and coronary heart disease. Circulation 2011;124:2296–302.
40. Mänttäri M, Tenkanen L, Alikoski T, Manninen V. Alcohol and coronary heart disease: the roles of HDL-cholesterol and smoking. J Intern Med 1997;241:157–63.
41. Moncada S, Radomski MW. The problems and the promise of prostaglandin influences in atherogenesis. Ann N Y Acad Sci 1985;454:121–30.
42. Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies. BMJ 2011;342:d636.
43. Janszky I, Ericson M, Blom M, Georgiades A, Magnusson JO, Alinagizadeh H, et al. Wine drinking is associated with increased heart rate variability in women with coronary heart disease. Heart 2005;91:314–8.
44. Quintana DS, Guastella AJ, McGregor IS, Hickie IB, Kemp AH. Moderate alcohol intake is related to increased heart rate variability in young adults: implications for health and well-being. Psychophysiology 2013;50:1202–8.
45. Spaak J, Merlocco AC, Soleas GJ, Tomlinson G, Morris BL, Picton P, et al. Dose-related effects of red wine and alcohol on hemodynamics, sympathetic nerve activity, and arterial diameter. Am J Physiol Heart Circ Physiol 2008;294:H605–12.
46. Sengul C, Cevik C, Ozveren O, Sunbul A, Oduncu V, Akgun T, et al. Acute alcohol consumption is associated with increased interatrial electromechanical delay in healthy men. Cardiol J 2011;18:682–6.
47. Briasoulis A, Agarwal V, Messerli FH. Alcohol consumption and the risk of hypertension in men and women: a systematic review and meta-analysis. J Clin Hypertens (Greenwich) 2012;14:792–8.
48. Hendriks HF, Veenstra J, Velthuis-te Wierik EJ, Schaafsma G, Kluft C. Effect of moderate dose of alcohol with evening meal on fibrinolytic factors. BMJ 1994;308:1003–6.
49. Saremi A, Arora R. The cardiovascular implications of alcohol and red wine. Am J Ther 2008;15:265–77.
50. Dobson A, Filipiak B, Kuulasmaa K, Beaglehole R, Stewart A, Hobbs M, et al. Relations of changes in coronary disease rates and changes in risk factor levels: methodological issues and a practical example. Am J Epidemiol 1996;143:1025–34.
51. Falk E, Shah PK, Fuster V. Coronary plaque disruption. Circulation 1995;92:657–71.
52. Stampfer MJ, Krauss RM, Ma J, Blanche PJ, Holl LG, Sacks FM, et al. A prospective study of triglyceride level, low-density lipoprotein particle diameter, and risk of myocardial infarction. JAMA 1996;276:882–8.
53. Ali SN, Bashir M, Sherwani M. Pattern of dyslipidemia in young patients with acute ST elevation myocardial infarction. J Sheikh Zayed Med Coll 2016;7:998–1001.
54. Borgia MC, Medici F. Perspectives in the treatment of dyslipidemias in the prevention of coronary heart disease. Angiology 1998;49:339–48.
55. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047–53.
56. Harris M, Zimmet P. Classification of diabetes mellitus and other categories of glucose intolerance. In: Alberti K, Zimmet P, De Fronzo R, editors. International Textbook of Diabetes Mellitus. 2nd. New York: John Willey and Sons;1997.p.9–23.
57. Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339:229–34.
58. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA 1999;281:1291–7.
59. Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971-1993. Diabetes Care 1998;21:1138–45.
60. Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H. Mortality from coronary heart disease and stroke in relation to degree of glycaemia: the Whitehall study. Br Med J (Clin Res Ed) 1983;287:867–70.
61. Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, Hunt D, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000;102:1014–9.
62. Nesto RW, Rutter MK. Impact of the atherosclerotic process in patients with diabetes. Acta Diabetol 2002;39:S22–8.
63. Moreno PR, Murcia AM, Palacios IF, Leon MN, Bernardi VH, Fuster V, et al. Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes melli-

tus. Circulation 2000;102:2180–4.
64. Khan MZ, Pervaiz MK, Javed I. Biostatistical study of clinical risk factors of myocardial infarction: a case-control study from Pakistan. Pak Armed Forces Med J 2016;66:354–60.
65. Patil SS, Joshi R, Gupta G, Reddy MV, Pai M, Kalantri SP. Risk factors for acute myocardial infarction in a rural population of central India: a hospital-based case-control study. Natl Med J India 2004;17:189–94.
66. Bibbins-Domingo K, Lin F, Vittinghoff E, Barrett-Connor E, Hulley SB, Grady D, et al. Predictors of heart failure among women with coronary disease. Circulation 2004;110:1424–30.
67. Cooper RS, Pacold IV, Ford ES. Age-related differences in case-fatality rates among diabetic patients with myocardial infarction. Findings from National Hospital Discharge Survey, 1979-1987. Diabetes Care 1991;14:903–8.
68. Davis TM, Parsons RW, Broadhurst RJ, Hobbs MS, Jamrozik K. Arrhythmias and mortality after myocardial infarction in diabetic patients. Relationship to diabetes treatment. Diabetes Care 1998;21:637–40.
69. Gaba MK, Gaba S, Clark LT. Cardiovascular disease in patients with diabetes: clinical considerations. J Assoc Acad Minor Phys 1999;10:15–22.
70. Kannel WB, Gordon T, Schwartz MJ. Systolic versus diastolic blood pressure and risk of coronary heart disease. The Framingham study. Am J Cardiol 1971;27:335–46.
71. Kannel WB. Incidence and epidemiology of heart failure. Heart Fail Rev 2000;5:167–73.
72. Julius S. Coronary disease in hypertension: a new mosaic. J Hypertens Suppl 1997;15:S3–10.
73. Ciruzzi M, Pramparo P, Rozlosnik J, Zylberstjn H, Delmonte H, Haquim M, et al. Hypertension and the risk of acute myocardial infarction in Argentina. The Argentine Factores de Riesgo Coronario en America del Sur (FRICAS) Investigators. Prev Cardiol 2001;4:57–64.
74. Zhu J, Su X, Li G, Chen J, Tang B, Yang Y. The incidence of acute myocardial infarction in relation to overweight and obesity: a meta-analysis. Arch Med Sci 2014;10:855–62.
75. Schargrodsky H, Rozlosnik J, Ciruzzi M, Ruffa R, Paterno C, Ardariz M, et al. Body weight and nonfatal myocardial infarction in a case-control study from Argentina. Soz Praventivmed 1994;39:126–33.
76. Mostofsky E, Maclure M, Sherwood JB, Tofler GH, Muller JE, Mittleman MA. Risk of acute myocardial infarction after the death of a significant person in one's life: the Determinants of Myocardial Infarction Onset Study. Circulation 2012;125:491–6.
77. Muller JE, Abela GS, Nesto RW, Tofler GH. Triggers, acute risk factors and vulnerable plaques: the lexicon of a new frontier. J Am Coll Cardiol 1994;23:809–13.
78. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation 2005;111:3481–8.
79. Tiong AY, Brieger D. Inflammation and coronary artery disease. Am Heart J 2005;150:11–8.
80. Liu SC, Xia L, Zhang J, Lu XH, Hu DK, Zhang HT, et al. Gout and Risk of Myocardial Infarction: A Systematic Review and Meta-Analysis of Cohort Studies. PLoS One 2015;10:e0134088.
81. Listgarten MA. Nature of periodontal diseases: pathogenic mechanisms. J Periodontal Res 1987;22:172–8.
82. Mackenzie R S, Millard H D. Interrelated effects of diabetes, arteriosclerosis and calculus on alveolar bone loss. J Am Dent Assoc 1963;66:192–198.
83. Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. J Periodontol 1996;67:1123–37.
84. Joshipura KJ, Rimm EB, Douglass CW, Trichopoulos D, Ascherio A, Willett WC. Poor oral health and coronary heart disease. J Dent Res 1996;75:1631–6.
85. Kaisare S, Rao J, Dubashi N. Periodontal disease as a risk factor for acute myocardial infarction. A case-control study in Goans highlighting a review of the literature. Br Dent J 2007;203:E5.
86. Prabhakaran D, Jeemon P. Should your family history of coronary heart disease scare you? Mt Sinai J Med 2012;79:721–32.
87. Ciruzzi M, Schargrodsky H, Rozlosnik J, Pramparo P, Delmonte H, Rudich V, et al. Frequency of family history of acute myocardial infarction in patients with acute myocardial infarction. Argentine FRICAS (Factores de Riesgo Coronario en America del Sur) Investigators. Am J Cardiol 1997;80:122–7.
88. Friedlander Y, Arbogast P, Schwartz SM, Marcovina SM, Austin MA, Rosendaal FR, et al. Family history as a risk factor for early onset myocardial infarction in young women. Atherosclerosis 2001;156:201–7.
89. Simon J, Rosolová H. Family history--and independent risk factors for coronary heart disease, it is time to be practical. Eur Heart J 2002;23:1637–8.
90. Khan SA, Safdar S, Ijaz A, Taseer I. Acute myocardial infarction patients; fre-quency of family history of ischemic heart disease (IHD) and related risk fac¬tors in the first degree relatives. Professional Med J 2014;21:1200–3.
91. Yoshida T, Kawano H, Miyamoto S, Motoyama T, Fukushima H, Hirai N, et al. Prognostic value of flow-mediated dilation of the brachial artery in patients with cardiovascular disease. Intern Med 2006;45:575–9.
92. Brevetti G, Silvestro A, Schiano V, Chiariello M. Endothelial dysfunction and cardiovascular risk prediction in peripheral arterial disease: additive value of flow-mediated dilation to ankle-brachial pressure index. Circulation 2003;108:2093–8.
93. Guo F, Wang X, Li G, Chen X, Jin Y. Risk factors of acute myocardial infarction following primary percutaneous coronary intervention among elderly patients. J Geriatr Cardiol 2009;6:67–70.