

A Retrospective Cohort Study on Changes in Proteinuria and Myocardial Infarction in Diabetic or Pre-Diabetic Patients

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Abstract

Introduction: Proteinuria, a frequent and significant sign of chronic kidney disease, is widely acknowledged as an independent predictor of cardiovascular disease in a variety of groups. In persons with diabetes or pre-diabetes, the association between changes in proteinuria and myocardial infarction (MI) is unknown. In this study, we intend to see if changes in proteinuria over a year may predict the occurrence of MI in persons with diabetes or pre-diabetes. We also investigate all patient data who had been first hospitalized for acute myocardial infarction and assessed the prevalence of non-diabetics, prediabetics, and diabetics among them.

Methodology: The patients with an acute myocardial infarction were included in this study. Several physiological (such as heart rate, pulse, blood pressure and respiratory rate) and biochemical (such as HbA1c, lipid profile, plasma glucose, and cardiac markers) indicators were investigated. The study looked at the proportion of diabetics, pre-diabetics, and non-diabetics who experienced myocardial infarction as well as the relationship between aberrant blood glucose levels and the severity of myocardial infarction. SSPE 21.0 was used to do the statistical analysis. P values less than 0.05 were deemed statistically significant.

Result: Among the 200 patients, 76 (38%) had no diabetes, compared to 74 (37%) and 50 (25%) who had pre-diabetes and diabetes, respectively. There was no statistically significant difference in the mean age of patients with diabetes, pre-diabetes, and those without diabetes ($P > 0.05$). The gender distribution revealed a M:F ratio of 1:0.26, with 71 (79.78%) men and 18 (20.50%) females. Diabetes patients were shown to have greater heart rates, systolic and diastolic blood pressure, and total cholesterol levels than pre-diabetic and non-diabetic individuals. Myocardial enzyme levels (CK-MB and Troponin I) analysis revealed that diabetes patients also had greater levels than pre-diabetic and non-diabetic individuals. Diabetes patients' mortality was shown to be statistically substantially higher ($P < 0.05$).

Conclusion: Diabetic patients with AMI had higher diastolic blood pressure, total cholesterol, triglycerides, LDL cholesterol, CK-MB, and Troponin I levels. Although the average age of myocardial infarction across diabetic, pre-diabetic, and non-diabetic patients was found to be similar, diabetic patients with myocardial infarction had statistically significantly higher fatality rates.

Keywords: Proteinuria, myocardial infarction, diabetes, cardiovascular, diastolic blood pressure.

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Introduction

A major global health issue is chronic kidney disease (CKD) and its related morbidity. 10–16% of adults worldwide have CKD, which has been linked to a variety of adverse clinical outcomes, including kidney failure, cardiovascular disease, and all-cause mortality [1]. Individuals with CKD are three times more likely to get a myocardial infarction (MI), as well as increased morbidity and death. Proteinuria, a frequent and significant sign of CKD, is widely acknowledged as an independent predictor of cardiovascular disease (CVD) in a variety of groups [2-7]. Acute myocardial infarction (AMI) is one of the leading global causes of death and morbidity [8]. According to data from the World Health Organization, AMI claims the lives of 3.4 million women and 3.8 million men per year. Since myocardial infarction (MI) occurs so often in developing nations like India, ischemic heart disease alone accounted for 32% of deaths in 2021[9]. The main cause of mortality in India is now MI. In India, MI has grown to be a significant cause of death by 2022[10].

Diabetes is linked to an increase in atherosclerotic macrovascular disease, which affects the arteries that supply the heart, brain, and lower limbs. As a result, diabetic individuals are at a substantially increased risk of myocardial infarction, stroke, and limb amputation [11]. Hyperglycemia and insulin resistance both appear to play crucial roles in the development of macrovascular problems. Cardiovascular disease (CVD), along with retinopathy, nephropathy, neuropathy, peripheral vascular disease (PVD), stroke, and other sequelae of macro and microvascular pathology, is one of the major consequences of diabetes mellitus [12]. Long-term abnormalities in glucose homeostasis, sometimes known as pre-

diabetes, can occur before insulin resistant DM. Pre-diabetes has recently been linked to a higher risk of cardiovascular illnesses. Pre-diabetic syndrome is characterized by fasting plasma glucose levels of less than 100 mg/dl (5.6 mM/L) but greater than 125 mg/dl (7.0 mM/L) and/or postprandial 2-hour plasma glucose levels of less than 140 mg/dl (7.8 mM/L) but greater than 199 mg/dl (11.1 mM/L)[13]. Pre-diabetes is a term that has been used by the American Diabetes Association (ADA) and the Department of Health and Human Services (HHS) to refer to an increasingly common condition where blood glucose levels are higher than normal but not yet diabetic, such as impaired glucose tolerance and impaired fasting glucose. It is popularly known that people with diabetes and pre-diabetes have an increased risk of cardiovascular problems, such as myocardial infarction. In addition to sedentary lifestyle and family history, other risk factors for coronary artery disease include hypertension, obesity, hyperlipidemia, and hypertension.

Therefore, in this study, we studied the data of all patients admitted for the first time for acute myocardial infarction (MI) and assessed the burden of non-diabetics, pre-diabetics, and diabetics. We evaluated acute MI patients admitted to our center in the years 2021-2022, and patients' biochemical and physiological characteristics, as well as cardiac markers, were measured at the time of admission.

Methodology

The current research was conducted in the Department of Biochemistry, Nalanda Medical College and Hospital, Patna, India. The research was conducted over a one-year period, from February 2022 to January 2023. A total of 200 patients hospitalized to our

hospital's Coronary Care Unit with the diagnosis of Acute Myocardial Infarction (AMI) were included in this study based on predetermined inclusion and exclusion criteria. The study was authorized by the institutional ethics committee, and all patients or their carers provided written informed permission. All patients' demographic information was recorded, and a thorough clinical examination was performed. A proforma was used to record relevant physiological and biochemical characteristics. In all patients, physiological data such as pulse rate, respiration rate, heart rate, and blood pressure were monitored. In all patients, biochemical measures such as HbA1C, plasma glucose, serum lipid profile, and cardiac markers such as CK-MB and Troponin I were also measured. On the basis of blood pressure measurements, patients were classified as normal (SBP < 120 or DBP < 80), pre-hypertension (SBP 130-139 or DBP 85-89), stage I hypertension (SBP 140-159 or DBP 90-99), and stage II hypertension (SBP \geq 160 or DBP 100). We choose diagnosed instances of Acute Myocardial Infarction (AMI) that met the aforementioned criteria. The patients in this study were further classified as non-diabetics, pre-diabetics, and diabetics based on the following criteria. The Statistical Package for

Social Science (SPSS 21.0) for Windows Software and Microsoft Excel 2010 were used for statistical analysis. The findings were presented as Mean Standard Deviation (SD). The unpaired t - test was performed to compare the groups, and a P value less than 0.05 was considered significant.

Results

The current investigation sought to ascertain the relationship between aberrant glucose levels and the severity of myocardial infarction. The levels of glycohemoglobin (HbA1C), plasma fasting and postprandial glucose (F and PP), creatine kinase-MB isoenzyme (CK-MB), and troponin I (cTnI), lipid profile (triglyceride, total cholesterol, LDL cholesterol, VLDL cholesterol, HDL cholesterol), blood pressure, pulse rate, and respiratory rate were all measured. 200 patients were separated into three groups: nondiabetics, prediabetics, and diabetics, and their values were compared [Figure 1]. The mean age of the AMI patients in nondiabetic group (n=76) was 57.36 ± 8.35 years, in prediabetic group (n=74) was 56.86 ± 6.35 years and in diabetic group (n=50) age was 59.74 ± 5.79 years. The patients' mean ages in the three groups were found to be equivalent, with no statistically significant difference ($P > 0.05$) [Table1].

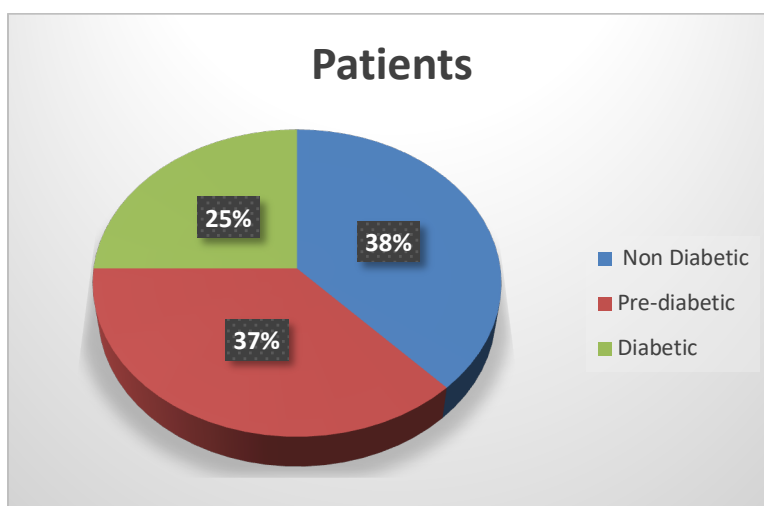


Figure 1: Distributions of Patients into groups

Table 1: Mean age of patients

Groups	Age (Years)	(Mean±SD)	P Value
Nondiabetic (n = 76)	57.36±8.35		0.785
Prediabetic (n = 74)	59.74±5.79		0.107
Diabetic (n = 50)	56.86±6.35		0.255

In the nondiabetic group, 69 (91%) of the 76 AMI patients were men, whereas 7 (9.0%) were females. In the prediabetic group, 58 (79%) of the 74 AMI patients were men, whereas 16 (21.88%) were females. There were 19 men (63.04%) and 31 females (37.06%) among the 50 diabetic AMI patients.

Table 2: Sex distribution of patients

	Male	Female
Nondiabetic (N = 76)	69 (91%)	7 (9.0%)
Prediabetic (N = 74)	58 (79%)	16 (21.88%)
Diabetic (N = 50)	19 (63.04%)	31 (37.06%)

The nondiabetic group (n=76) had a mean heart rate of 82.32±10.13, the prediabetic group (n=74) had a mean heart rate of 85.46±9.04, and the diabetic group (n=50) had a mean heart rate of 87.00±12.58. The nondiabetic group (n=76) had a mean systolic blood pressure of 130.94±51.58 mm of Hg and a mean diastolic blood pressure of 80.06±10.51 mm of Hg. Mean systolic blood pressure was 131.85±03.89 mm of Hg and mean diastolic blood pressure was 81.30±13.82 mm of Hg in the prediabetics group (n=74) and 89.73±13.91 mm of Hg in the diabetic group (n=50). Diastolic blood pressure (DBP) was considerably greater in diabetics compared to prediabetics or nondiabetics. The differences between prediabetics and nondiabetics were not statistically significant.

The nondiabetic group (n=76) had a respiratory rate/minute of 26.94±6.47, the prediabetic group (n=74) had a respiratory rate of 27.42±8.15, and the diabetic group (n=50) had a respiratory rate of 31.36±12.40. Diastolic blood pressure was considerably

higher in diabetes individuals than in prediabetic and non-diabetic patients (P<0.05). The other parameters were determined to be equivalent across all three groups, with no statistically significant difference (P>0.05).

TROPONIN I had a mean value of 1.07±0.49 in the nondiabetic group (n=76), 1.29±0.72 in the prediabetic group (n=77), and 2.62±0.70 in the diabetic group (n=50). TROPONIN-I serum levels were significantly higher (p<0.001) in diabetics than in prediabetics or nondiabetics. On statistical analysis, the differences between prediabetics and nondiabetics are not significant (p value 0.125). HbA1C was 5.02±0.28 in the nondiabetic group (n=76), 6.08±0.3 in the prediabetic group (n=74), and 8.47±1.24 in the diabetic group (n=50). TROPONIN I levels rise with increasing HBA1C levels in three groups. TROPONIN I had a mean value of 1.07±0.49 in the nondiabetic group (n=76), 1.38±0.72 in the prediabetic group (n=74), and 2.53±0.70 in the diabetic group (n=50).

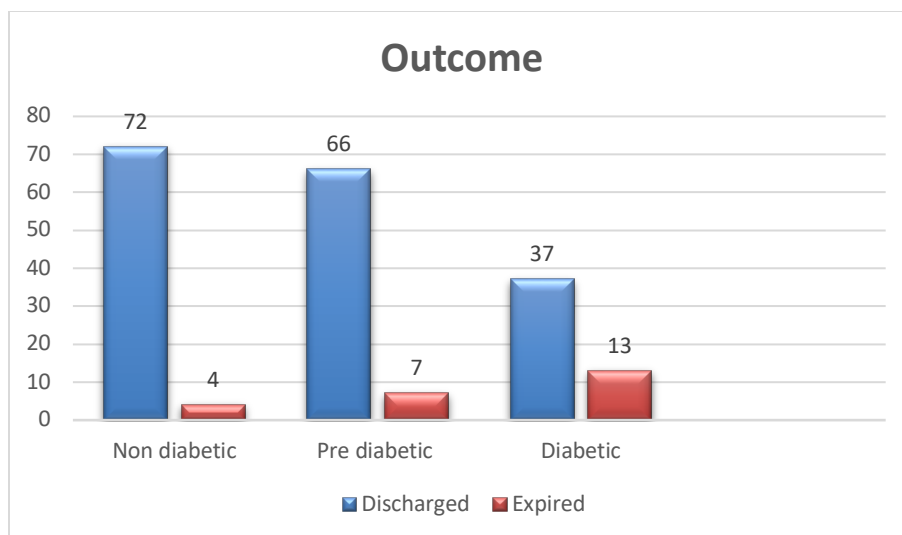


Figure 2: Outcome of patients

Of 76 nondiabetic patients, 46 develop CHF, 20 develop arrhythmias, and 4 develop both CHF and arrhythmias. Of 74 prediabetic individuals, 50 develop CHF, 17 develop arrhythmias, and 7 develop both CHF and arrhythmias. In 50 diabetic patients, 27 develop CHF, 21 develop arrhythmias, and 8 develop both CHF and arrhythmias. 22 of the 76 nondiabetic patients had hospital stays of less than 7 days, whereas 26 had hospital stays of more than 7 days. 35 prediabetic patients spent fewer than seven days in the hospital, whereas 23 spent more than seven days. And, out of 50 diabetes patients, 12 hospital stays of less than 7 days and 34 had hospital stays of more than 7 days.

As a result, 72 nondiabetic patients were improved and released, but four patients died. 66 prediabetic patients were improved and released, while 7 died. 37 diabetic patients were improved and released, whereas 13 patients died. Diabetic individuals died at a higher rate than nondiabetic and prediabetic patients [Figure 2].

Discussion

In the current study, the average age of AMI patients in the nondiabetic group was 57.36 ± 8.35 years. Prediabetics were 59.74 ± 5.79 years old, whereas diabetes were

56.86 ± 6.35 years old. In the nondiabetic group, out of the 76 AMI patients 69 were men, whereas 7 were girls. There were 58 men and 16 females among the 74 patients with AMI in the prediabetic group. There were 19 men and 31 females among the 50 AMI patients in the diabetic group. Our findings were consistent with those of other population-based studies, including Seeman T *et al* [14], Deborah RZ *et al* [15], Nahid R *et al* [16], and Nishiyama S *et al* [17], which indicated a higher overall incidence of AMI in men. In India, the frequency is 66.5 and 48.9 per 1000 males and females, respectively.

In the current study, the blood levels of total cholesterol, triglycerides, and LDL cholesterol are higher in the diabetic group when compared to the prediabetic or nondiabetic groups, although this difference is not statistically significant ($p > 0.05$). Hypercholesterolemia is universally recognised as a major risk factor for atherosclerosis, but there is variability in the occurrence of cardiovascular events at any given concentration of plasma cholesterol, as Heinecke JW *et al* [19] demonstrated that oxidative modification of LDL may be a crucially important step in the development of atherosclerotic plaque.

In three groups of nondiabetics, prediabetics, and diabetic MI patients, we discovered that when HbA1c and blood glucose levels rise, so do Troponin I levels. This is congruent with the findings of Bjornholt JV *et al* [22], who revealed that individuals with high fasting blood sugars that are not diagnostic of diabetes yet have an increased long-term risk of severe cardiac events. In our study, diabetics had significantly higher serum Troponin levels as compared to prediabetics or nondiabetics. Troponin I levels do not differ significantly between prediabetics and nondiabetics. This is consistent with Marfella Raffaele's [23] study, which found that hyperglycemia was related with greater troponin I levels and bigger infarct size, as well as myocardial TNF- α , NF κ B-activated, caspase-3, and nitrotyrosine levels as compared to normoglycemic patients.

According to Philip R *et al.* [24], diabetic people had a greater incidence of congestive heart failure (relative ratio = 2.2, 95% CI 1.7-2.8), more severe short-term and long-term prognosis scores, and a longer average hospital stay (12.1 vs. 8.9 days, $P < 0.01$). Our investigation likewise produced similar findings. Higher blood sugar concentrations in people with diabetes, including those who were previously undiagnosed, are significantly predictive of poorer outcome, as demonstrated by Dormandy JA *et al.*, [25] Norhammar AM *et al.*, [26] Fava S *et al.*, [27] Malmberg K *et al.*, [28] and Otter W *et al.*, [29]. According to Vivas D *et al.* [30], plasma glucose and initial fasting blood glucose levels at the time of admission can predict the bad prognosis of acute coronary syndrome patients.

Conclusion

Diastolic blood pressure, total cholesterol, triglycerides, LDL cholesterol, CK-MB, and Troponin I levels were observed to be higher in AMI patients who were diabetic. Diabetic patients with MI had a longer average

hospital stay and a greater death rate when compared to non-diabetics and prediabetics patients. Although the average age of myocardial infarction across diabetic, prediabetic, and non-diabetic patients was found to be similar, diabetic patients with myocardial infarction had statistically significantly higher fatality rates.

References

1. Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J, Chen M, He Q, Liao Y, Yu X, *et al.* Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet.* 2012;379(9818):815–50.
2. Pugliese G, Penno G, Natali A, Barutta F, Di Paolo S, Reboldi G, Gesualdo L, De Nicola L: Diabetic kidney disease: New clinical and therapeutic issues. *Nutrition, metabolism, and cardiovascular diseases: NMCD.* 2019; 29(11):1127–1150.
3. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA. Kidney disease as a risk factor for development of cardiovascular disease. *Hypertension (Dallas, Tex: 1979).* 2003; 42(5):1050–1065.
4. Kannel WB, Stampfer MJ, Castelli WP, Verter J. The prognostic significance of proteinuria: the Framingham study. *American heart journal.* 1984; 108(5): 1767–52.
5. Chang SH, Tsai CT, Yen AM, Lei MH, Chen HH, Tseng CD. Proteinuria and Reduced Estimated Glomerular Filtration Rate Independently Predict Risk for Acute Myocardial Infarction: Findings from a Population-Based Study in Keelung, Taiwan. *Acta Cardiologica Sinica.* 2015;31(2):106–12.
6. Vinnakota S, Scott CG, Rodeheffer RJ, Chen HH: Estimated Glomerular Filtration Rate, Activation of Cardiac Biomarkers and Long-Term Cardiovascular Outcomes: A Population-Based Cohort. *Mayo Clinic proceedings.* 2019; 94(11):2189–2198.

7. Puddu PE, Bilancio G, Terradura Vagnarelli O, Lombardi C, Mancini M, Zanchetti A, Menotti A. Serum uric acid and eGFR_CKDEPI differently predict long-term cardiovascular events and all causes of deaths in a residential cohort. *Int J Cardiol.* 2014;171(3):361–7.
8. Mukherjee AK. Prediction of coronary heart disease using risk factor categories. *J Ind Med Assoc.* 1995; 93: 312–315.
9. Ghaffar A, Reddy KS, Singhi M. Burden of noncommunicable diseases in South Asia. *BMJ.* 2004; 328: 807–810.
10. Gupta R. Escalating coronary heart disease and risk factors in South Asians. *Indian Heart J.* 2007; 59: 214–217.
11. UK Retrospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 74). *Lancet.* 1998; 352, 837–853.
12. Wei, M., Gaskill, S. P., Haffner, S. M. & Stern, M. P. Effects of diabetes and level of glycemia on all-cause and cardiovascular mortality. The San Antonio Heart Study. *Diabetes Care.* 1998; 7: 1167–1172.
13. Expert committee on the diagnosis and classification of diabetes mellitus- follow up report on the diagnosis of diabetes mellitus. *Diabetes Care.* 2003; 26: 701–710.
14. Seeman T, Mendes de Leon C, Berkman L, Ostfeld A. Risk factors for coronary heart disease among older men and women: a retrospective study of community-dwelling elderly. *Am J Epidemiol.* 1993; 138(2):1037–49.
15. Deborah RZ, John LG, Joni RB, Harry PS. Presentations of Acute Myocardial Infarction in Men and Women. *J Gen Intern Med.* 1997; 12(2): 79–87.
16. Nahid R, Yoshikuni K, Tanvir CT. Trend of Increase in the Incidence of Acute Myocardial Infarction in a Japanese Population, *Am J Epidemiol.* 2008; 167: 1358–1364.
17. Nishiyama S, Watanabe T, Arimoto T. Trends in coronary risk factors among patients with acute myocardial infarction over the last decade *J Atheroscler Thromb.* 2010; 30;17 (9):989.
18. Turin TC, Jun M, James MT, Tonelli M, Coresh J, Manns BJ, Hemmelgarn BR. Magnitude of rate of change in kidney function and future risk of cardiovascular events. *Int J Cardiol.* 2016; 202:657–65.
19. Heinecke JW. Mechanism of oxidative damage of low-density lipoproteins in human atherosclerosis. *Curr. Opin. Lipidol.* 1997; 8: 268- 274.
20. Turin TC, Coresh J, Tonelli M, Stevens PE, de Jong PE, Farmer CK, Matsushita K, Hemmelgarn BR. Change in the estimated glomerular filtration rate over time and risk of all-cause mortality. *Kidney international.* 2013;83(4):684–91.
21. Schiffrin EL, Lipman ML, Mann JF. Chronic kidney disease: effects on the cardiovascular system. *Circulation.* 2007;116(1):85–97.
22. Bjornholt JV, Erikssen G, Aaser E. Fasting blood glucose: an underestimated risk factor for cardiovascular death. Results from a 22- year follow-up of healthy nondiabetic men. *Diabetes Care.* 1999; 22:45–49.
23. Marfella R, Di Filippo C, Portoghese M. Tight glycemic control reduces heart inflammation and remodeling during acute myocardial infarction in hyperglycemic patients. *Am J Coll Cardiol.* 2009;53(16):1425–36.
24. Philip R. Orlander, David C. Goff, Marilyn Morrissey, David J. Ramsey, Mary L. Wear, Darwin R. Labarthe, and Milton Z. Nichaman. The Relation of Diabetes to the Severity of Acute Myocardial Infarction and Post-

- Myocardial Infarction Survival in Mexican Americans and Non-Hispanic Whites The Corpus Christi Heart Project 1994; *Diabetes*. 43:897-902.
25. Dormandy JA, Charbonnel B, Eckland DJ. Secondary prevention of macrovascular events in patients with type 2 diabetes in the Proactive Study (Retrospective Pioglitazone Clinical Trial in Macrovascular Events): a randomised controlled trial. *Lancet*. 2005; 366:1279–1289.
 26. Norhammar AM, Ryden L, Malmberg K. Admission plasma glucose independent risk factor for long-term prognosis after myocardial infarction even in nondiabetic patients. *Diabetes Care*. 1999; 22:1827–31.
 27. Fava S, Aquilina O, Azzopardi J. The prognostic value of blood glucose in diabetic patients with acute myocardial infarction. *Diabet Med*. 1996; 13:80–83.
 28. Malmberg K, Norhammar A, Wedel H *et al*. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study. *Circulation*. 1999; 25:2626–2632.
 29. Otter W, Kleybrink S, Doering W. Hospital outcome of acute myocardial infarction in patients with and without diabetes mellitus. *Diabet Med*. 2004; 21:183–187.
 30. Vivas D, Gracia-Rubira JC, Gonzalez-Ferrar JJ. Prognostic value of first fasting glucose measurement compared with admission glucose level in patients with acute coronary syndrome. *Rev Esp Cardiol*. 2008; 61: 458– 464.
 31. Ostergren J, Poulter NR, Sever PS. The Anglo-Scandinavian Cardiac Outcomes Trial: blood pressure-lowering limb: effects in patients with type II diabetes. *J Hypertens*. 2008; 26:2103— 11.