Endocrinology & Metabolic Syndrome

Tarcin et al., Endocrinol Metab Synd 2012, S:5
DOI: 10.4172/2161-1017.S5-006

Research Article Open Access

Glycemic Profiles and Their Diagnostic Value among Inpatients in a Cardiology Clinic

Ozlem Tarcin[1]*, Mahmut Uluganyan[2], Zeynep Tartan[3] and Ibrahim Yekeler[4]

[1]Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Endocrinology and Metabolism, Istanbul, Turkey
[2]Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Cardiology, Istanbul, Turkey
[3]Memorial Atasehir Hospitals, Cardiology, Istanbul, Turkey
[4]Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Cardiovascular Surgery, Istanbul, Turkey

Abstract

Background: Most patients in cardiology clinics have diabetes mellitus (DM). Therefore, glucose monitoring is very important for these patients. Routinely, only fasting glucose is measured but not postprandial glucose and HbA1c; thus, the correlation between diabetes frequency and cardiac diagnosis in cardiology inpatients is unknown. The aim of this study was to determine the glucose abnormalities in inpatient cardiology clinics and their relationship with the diagnosis of heart disease.

Material and method: 309 patients (107 F/202 M; mean age 63.4 ± 13 years) hospitalized in cardiology clinic between December 2009 and February 2010 was recruited to the study. Admission glucose level, body mass index (BMI), fasting glucose level after stabilization, 2-hour postprandial glucose levels, HbA1c and diagnosis were recorded for all subjects. Patients were evaluated as DM (+), DM (-), and new-onset DM. Cardiac diagnoses were classified as acute coronary syndrome (ACS) and others. Pre-diabetes was defined based on fasting/random glucose and HbA1c concentrations among the non-diabetic patients.

Results: 108 (35%) of patients had DM, whereas 39 patients (12.6%) had unknown diabetes. Glucose profile of subjects with new-onset DM was similar to that of DM (+) patients. The remaining 162 patients (52.4%) were free of DM although 53 of them (32.7%) had prediabetes. Prediabetes was diagnosed in 17.1% of all patients. No difference was detected between ACS and Others regarding DM frequency. Admission/fasting glucose and HbA1c levels were found to be higher in ACS patients (p: 0.02). Prediabetic patients with ACS had higher admission and fasting glucose and also HbA1c levels than those with others.

Keywords: Cardiology; Acute coronary syndrome; Diabetes; Impaired glucose tolerance; Impaired fasting glucose; HbA1c

Introduction

Diabetes mellitus (DM) is one of the most important causes of coronary artery disease (CAD). In addition, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), classified as prediabetes, are also risk factors for cardiovascular disease [1]. Recent studies show that undiagnosed disorders of the glucose metabolism increase the cardiovascular mortality and morbidity in patients with a history of acute myocardial infarction and underscore the importance of early diagnosis in such patients [2-4]. The prevalence of diabetes among acute coronary syndrome (ACS) patients varies between 19.2-37% [1,5,6]. In a study conducted in the Dr. Siyami Ersek Hospital on patients monitored for ACS, 24.6% had known diabetes, and cardiovascular mortality was higher among non-diabetic patients who had presented to the Emergency Department with a blood sugar level above 200 mg/dL compared with the diabetic patients [5]. Generally, cardiologic studies focusing on diabetes investigate the relationship between ACS and hyperglycemia. However, since fasting blood glucose (FBG) levels and HbA1c are not evaluated, there is a lack of studies concerning the prevalence of undiagnosed diabetes and prediabetes as well as the association of diabetes with other cardiologic diseases.

The aim of this study was to determine DM and prediabetes prevalence in patients hospitalized and monitored in the cardiology department, to identify undetected diabetes by evaluating FBG and HbA1c levels in light of the latest diagnostic criteria for diabetes [7], and to investigate its relationship with the cause of inpatient admission in cardiology patients.

Material and Method

Study protocol and patient selection

In this observational study, we evaluated 309 patients (107 female and 202 male; mean age: 63.4 ± 13 years) who were admitted as inpatients to the Cardiology Clinics of *Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Training and Research Hospital* between December 2009 and February 2010. Cause of inpatient admission, height, weight, and admission blood glucose (ABG) levels were evaluated in all patients. Following achievement of a stable condition after the admission, the patients were evaluated for fasting blood glucose (FBG, after at least 8 hours of fasting), HbA1c, and postprandial blood glucose (PPBG, 2 hours after a meal) levels. The patients were split into two groups as the ones who had been diagnosed with DM previously, namely DM (+), and the ones who had no DM, namely DM (-). The diagnosis of DM in some of the reportedly non-diabetic patients was established according to the criteria of 2010 Diagnostic Guideline for Diabetes Mellitus; the patients with FBG≥126 mg/dL, random blood glucose≥200 mg/dL, or HbA1c≥6.5% were categorized in another group called newly diagnosed DM.

According to the criteria of the *American Diabetes Association* (ADA), people with a FBG level between 100-125 mg/dL are recognized as IFG cases, whereas individuals who exhibit a blood glucose level between 140–199 mg/dL despite having a normal FBG are

***Corresponding author:** Ozlem Tarcin, Zuhtupasa mah, Yeni yol sok No: 4, Kuleli Kosk Konutlari C-Blok D: 17, Kiziltoprak Kadikoy, Istanbul-34724, Turkey, Tel: 00-90-216-450-51-44; E-mail: ozlemtarcin@yahoo.com

Received December 27, 2012; **Accepted** May 18, 2012; **Published** May 22, 2012

Citation: Tarcin O, Uluganyan M, Tartan Z, Yekeler I (2012) Glycemic Profiles and Their Diagnostic Value among Inpatients in a Cardiology Clinic. Endocrinol Metab Synd S5:005. doi:10.4172/2161-1017.S5-006

recognized as IGT cases; patients in both of those groups are deemed as prediabetes cases. Moreover, patients with HbA1c levels between 5.7–6.4% are deemed as a risky group for diabetes development as per 2010 Guidelines of the *American Diabetes Association* (ADA) [7]. However, because the specificity and sensitivity of diagnostic methods for prediabetes are low when used alone, we preferred to use 2 of the 3 criteria for the diagnosis of prediabetes. Since we could not apply OGTT to the patients, 2 hours PPBG levels within 140-199 mg/dL were recognized as IGT. Thus, IFG+IGT, IFG+HbA1c, and IGT+HbA1c were evaluated as prediabetes.

When evaluating the study group with regard to cause of inpatient admission, the patients were divided into 2 groups: ACS and Others. ACS group included patients hospitalized due to acute myocardial infarction (MI), non-ST elevation MI (non-STEMI) and unstable angina pectoris (USAP). The Others group was comprised of patients hospitalized due to reasons other than CAD such as decompensate heart failure, arrhythmia, valvular heart disease, and endocarditic.

Biochemical parameters

Blood sugar levels were measured quantitatively from the venous blood samples collected from the patients by an enzymatic colorimetric assay (Roche Diagnostic GmbH, Mannheim, Germany). Reproducibility rates for the glucose kit were 0.9% for intra-study and 1.8% for inter-study measurements. HbA1c evaluation was performed with turbidimetric inhibition immunologic test (TINIA) (Roche Diagnostic GmbH, Mannheim, Germany) and the percentage of HbA1c concentration was calculated with the following formula: HbA1c% = HbA1c/Hb×100. Intra-study and inter-study reproducibility rates for HbA1c were 2.3% and 3.2%, respectively.

Statistical analysis

All statistical analyses were performed by the InStat 3 statistics program. Inter-group comparisons were carried out using the student's t-test and ANOVA was applied in cases where it would be helpful. $p<0.05$ was recognized as statistically significant. All the results were expressed as mean ± standard deviation (SD) values.

Results

309 (107 female and 202 male) patients requiring inpatient admission to the cardiology department were evaluated. The mean age of the patients was 63.4 ± 13 years, and similar to other studies, the number of men was approximately twice the number of women. When categorized in terms of diabetic condition, 108 (35%) patients had known diabetes and the mean duration of diabetes was 10.6 ± 8.4 years among them. Thirty-nine patients (12.6%) without a history of diabetes were newly diagnosed with DM based on the HbA1c concentrations as well as FBG and PPBG levels. The remaining 162 patients (52.4%) had no diabetes, however, 53 (32.7%) of them were found to have prediabetes. The prediabetes rate was 17.1% among the entire cardiology patients (Figure 1).

The comparison of DM (+), newly diagnosed DM, and DM (-) groups showed that females were predominant in diabetics ($p<0.05$). Newly diagnosed DM and non-diabetic groups displayed a significant predominance of males (Table 1). There was no difference between the groups with regard to age and body mass index (BMI). Admission blood glucose (ABG) level was significantly elevated in the DM (+) group compared with the others ($p<0.001$). Newly diagnosed DM group had a statistically significantly higher ABG compared with the DM (-) group. FBG, PPBG, and HbA1c values were higher in the DM (+) group than in the DM (-) group ($p<0.01$). Newly diagnosed DM and DM (+) groups had similar values and they were significantly higher than those of the DM (-) group ($p<0.01$) (Table 1).

The patients were divided into 2 groups according to the cause of inpatient admission. There was no difference between the patients hospitalized due to ACS and patients admitted due to other reasons in terms of diabetes presence and development (Figure 2). The comparison of those groups with regard to demographic and biochemical data revealed that men were significantly predominant among the patients admitted due to ACS (70.2%), whereas gender distribution was almost even in patients admitted because of other diagnoses ($p<0.01$) (Table 2). There was no difference between the groups in terms of age and BMI. ABG and FBG levels were significantly higher in ACS patients ($p=0.02$), however, there was no difference between the PPBG levels. ACS patients had statistically significantly higher mean HbA1c

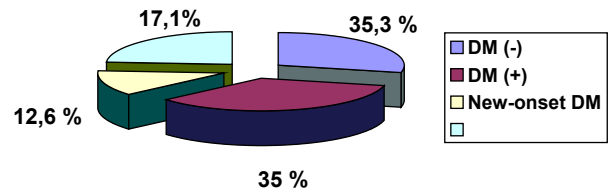

Figure 1: Glycemic profiles of cardiology inpatients.

	DM (+) (n:108)	New-onset DM (n:39)	DM (-) (n:162)	p
Gender (M / F)	58 / 50	30 / 9	114 / 48	0.005#
Age (Year)	65.5 ± 9.2	62.4 ± 14.7	62.3 ± 14.7	NS
median	65.5	67	61.5	
BMI (kg/m²)	28.9 ± 5.2	27.9 ± 4.9	27.5 ± 4.2	NS
median	27.8	27.5	27.1	
Admission BG	213.7 ± 89.7*	163.7 ± 70.2*§	123.8 ± 32.3	<0.001
median	191	141	116	
Fasting BG	141 ± 47.5*	124.7 ± 37.6*	96.9 ± 11.6	<0.001
median	133.5	109	95	
Postprandial BG	194.5 ± 50.9*	187.6 ± 49.9*	128.9 ± 22.1	<0.001
median	191	191	125.5	
HbA1c (%)	7.9 ± 1.6*	7.1 ± 1.1*	5.8 ± 0.4	<0.001
median	7.7	6.8	5.8	

*Compared to non-diabetic group $p<0.05$
§Compared to diabetic group $p<0.05$
#Chi square: 7.26
BG: blood glucose

Table 1: Demographic and biochemical parameters of cardiology inpatients.

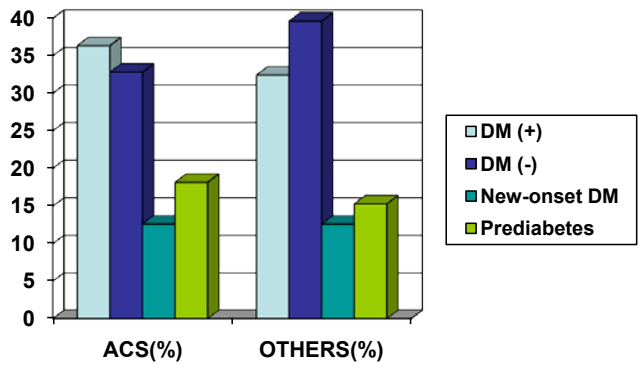

Figure 2: Glycemic profiles dispersion of inpatients according to diagnosis.

concentrations (p=0.01). However, there was no difference between the ACS and Others' patients with regard to diabetes presence (36.4% and 32.4%, respectively). While the percentage of newly diagnosed DM cases was 12.6% in both of the groups, the percentage of prediabetic patients was 18.2% in the ACS group and 15.3% in the others group (Figure 2).

When the DM (-) patients were evaluated in two groups as those with prediabetes and normal glucose tolerance (NGT), NGT patients admitted with ACS diagnosis showed significantly higher HbA1c concentrations as well as elevated ABG, FBG, and PPBG levels compared with the Others group (Table 3). Among patients admitted with other diagnoses, only FBG levels were found to be elevated in prediabetic patients and no difference was determined regarding the other parameters.

Discussion

In this observational and cross-sectional study, we aimed to reveal the distribution of DM and prediabetes according to the admitting diagnoses and to determine the prevalence of known and undetected DM in patients hospitalized in the cardiology department due to various reasons. Many studies with large sample sizes report that nearly 25% of patients under monitorization for ACS have known diabetes [8-10]. In our study, the prevalence of known DM was 35% and it was higher than the rates reported by other studies. As shown by the recent Turdep-II study, the reason behind this high rate was deemed to be the rapid increase in obesity and DM rates [11]. This higher prevalence in the Turkish population could be explained by insufficient population-based screening programs and increasing bad eating habits in Turkey. Although Turkey is a Mediterranean country, due to the industrial development, people tend to consume high-fat and high-calorie meals (i.e. fast-food type). Unfortunately, exercise is not a routine among Turkish people, which contributes to increase in obesity rate and development of metabolic syndrome. While female gender was predominant in diabetic cases, the number of men was significantly higher among patients admitted with ACS diagnosis. This finding supports the fact that CAD has a higher incidence in men. New-onset diabetes was also higher in men which could be related to higher incidence of CAD. TURDEP-II study has shown a slightly higher prevalence of diabetes and obesity in women which was not statistically significant, but smoking was more common among men compared to women. Thus, the higher new-onset diabetes prevalence in men could be because in Turkey, men usually refuse their health problems and do not accept to participate in screening programs. Thus, glucose metabolism disorders are often detected incidentally when these patients present with CAD.

	ACS (n: 198)	Others (n: 111)	p
Gender (M / F)	139 / 59	48 / 63	**0.01***
Age (year)	62.5 ± 12.4	65 ± 14.2	NS
median	62.5	68	
BMI (kg/m^2)	27.8 ± 4.4	28.5 ± 5.3	NS
median	27.5	27.7	
AdmissionBG (mg/dL)	166.5 ± 72.8	149.7 ± 78.5	**0.02**
median	143	118	
Fasting BG (mg/dL)	119.2 ± 40.9	110.3 ± 31.9	**0.02**
median	107	99.5	
Postprandial BG	164.1 ± 49.7	158 ± 52.4	NS
median	154	140	
HbA1c (%)	6.8 ± 1.6	6.5 ± 1.2	**0.01**
median	6.2	6.1	

*RR: 0.8 95% CI: 0.65 to 0.97
NS: Non-significant

Table 2: Demographic and biochemical properties of cardiology inpatients according to the primary diagnosis.

	ACS		OTHERS	
	Prediabetes (n:36)	Normal (n:65)	Prediabetes (n:17)	Normal (n:44)
Admission BG	143.7 ± 36.5*	120.7 ± 25.1	123 ± 26.2	113 ± 34
Fasting BG	106.6 ± 10.8*	94 ± 10	101.7 ± 9.8**	91.5 ± 9.4
Postprandial BG	138.3 ± 21*	124.9 ± 18.4	136.8 ± 32	122.3 ± 18.8
HbA1c (%)	6.1 ± 0.2*	5.6 ± 0.4	5.9 ± 0.3	5.7 ± 0.4

*Comparison of ACS-prediabetes with ACS-normal and Others-normal p<0.05
**Comparison of Others-prediabetes and Others-normal p<0.05

Table 3: Comparison of non-diabetic patients with prediabetes and normal glucose metabolism according to the primary diagnosis.

Norhammar et al. [3], conducted a study on 181 non-diabetic patients with acute MI, in which discharge OGTT values revealed that 31% of them had DM and 35% had IGT. Three months after the discharge, reassessment by OGTT showed that 25% still had diabetes and 40% had IGT. However, they also noted that using FBG as the sole diagnostic measure indicated diabetes in only 10% at discharge and in 13% at 3-month follow-up. Additionally, they evaluated the HbA1c levels as well and showed that HbA1c and FBG levels were independent predictors indicating the glucose anomalies to be encountered 3 months later. According to the results of this study, the risk of diabetes development can be determined by HbA1c concentration, FBG level measured 4 or 5 days after the hospitalization, and discharge OGTT. In our study, 12.6% of the patients were newly diagnosed with diabetes based on the FBG and HbA1c levels, whereas prediabetes was diagnosed in 32.7% of the non-diabetic patients. In short, when we evaluated known diabetes, newly diagnosed diabetes, and prediabetes groups together, 64.7% of the entire inpatient population in the cardiology department (67.2% in the ACS and 60.4% in the Others group) was determined to have a glucose metabolism disorder. In other words, 30% of the inpatients had undetected diabetes or a glucose metabolism disorder. In addition, DM diagnosis could be higher in our study than in previous studies because HbA1c is a new diagnostic criterion which may cause a rise in DM or prediabetes diagnosis. In our study, some people had only high HbA1c although they had normal FBG which lead to the diagnosis of DM. Similarly, other studies underscore the importance of FBG, HbA1c, and OGTT in the early diagnosis of glucose metabolism disorders, particularly during the post-infarction period, with regard to reduction of cardiovascular mortality and morbidity [3,12,13]. Those results show that cardiology patients should be investigated in a more detailed fashion in terms of glucose metabolism disorders.

In ACS, diabetic patients are known to have a higher mortality than non-diabetic patients [14,15]. However, in many studies, mortality has been shown to be higher in patients having no history of diabetes and presenting with hyperglycemia [5,16]. In ACS, presence of hyperglycemia at admission increases the mortality independently from the diagnosis of diabetes. Prominent authors in this field note that hyperglycemic individuals with no diagnosis of diabetes generally have a history of prior glucose anomalies and advocate that although the prevalence of diabetes is reported to be 20% in the non-ACS patient group, it might rise up to 45% [3,17,18].

Many studies show that CAD prevalence and post-ACS mortality are increased in prediabetics [19,20]. There are studies which indicate that particularly IGT and elevated PPBG level have a significant

correlation with ACS [1,17,19]. Similarly, in our study, the ABG levels of patients hospitalized with the diagnosis of ACS were higher than those admitted with other diagnoses. Moreover, FBG and HbA1c levels were found to be higher in patients admitted due to ACS. When non-diabetic patients admitted with ACS were evaluated, prediabetic patients had significantly higher ABG, HbA1c, FBG, and PPBG values compared with the ones having a normal glucose metabolism. This is a finding which supports that the risk of CAD is higher in prediabetic patients than in patients with other cardiologic diseases. In Europe, authorities recommend that patients diagnosed with cardiovascular diseases should be evaluated by early OGTT [21].

We divided our patients according to their admission diagnosis because we have already known that ACS may cause extreme hyperglycemia in patients who has undetermined IGT, IFG or DM. Although the high frequency of glucose metabolism abnormalities in ACS or CAD is well established, to our knowledge, there is no any study reporting the frequency in other heart diseases like congestive heart failure, valvular diseases or cardiac arrhythmia. Thus, we aimed to compare the frequency of glucose metabolism abnormalities in different heart diseases. As a result, both new-onset DM and prediabetes in ACS were as high as in the other heart diseases which mean that glucose metabolism abnormalities are not a risk factor only for ACS but also for all other heart problems.

When patients are categorized based on the cause of inpatient admission, majority of the patients hospitalized with ACS diagnosis are males. This finding was consistent with the other studies and there are many studies reporting predominance of male gender in CAD [3,5,22]. There was no difference between the groups in terms of known and newly diagnosed diabetes prevalence. This suggests that diabetes prevalence is increasing similarly in all cardiologic patients.

The most important limitation of our study was the low number of patients and the absence of OGTT evaluation which was compensated by PPBG assessment. However, if we had performed OGTT on our patients, the number of diabetes and prediabetes diagnoses could have been higher. That would be a factor influencing the aim of our study in a positive way.

In conclusion, 2/3 of our inpatients admitted due to cardiologic indications had a glucose metabolism disorder and 30% of them were previously undiagnosed patients. Therefore, we can estimate that nearly 65% of all cardiac patients have a glucose metabolism disorder, and that this condition is more clearly observed in patients with a cardiovascular disease. We aimed in this study to put the attention on high frequency of diabetes and glucose metabolism abnormalities among all patients with heart diseases and to encourage the cardiologists to consider the diagnosis of diabetes and other glucose metabolism abnormalities, a world-wide growing problem. In view of the inclusion of HbA1c level assessment in the diagnostic criteria of diabetes in 2010, the evaluation of HbA1c concentration as well as FBG and PPBG levels in patients hospitalized in cardiology departments and outpatient clinics can be recommended. Because diabetes is accompanied mostly by cardiovascular diseases and patients present first to cardiologists and then they see endocrinologists, cardiologists should be aware of this disease. Finally, evaluation of patients with a cardiologic problem (even those with no reported diabetes) by their primary physician in terms of glucose metabolism disorders bears importance relative to the prevention of new cardiac problems and early recognition of diabetes for starting the treatment without any delay.

References

1. Uçucu M, Alibaz Öner F, Yurdakul S, Ergüney M (2010) In hospital mortality in patients with impaired fasting glucose and acute coronary syndrome. Marmara Medical Journal 23: 257-262.
2. Bartnik M, Malmberg K, Norhammar A, Tenerz A, Ohrvik J, et al. (2004) Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction. Eur Heart J 25: 1990-1997.
3. Norhammar A, Tenerz A, Nilsson G, Hamsten A, Efendic S, et al. (2002) Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study. Lancet 359: 2140-2144.
4. Lenzen M, Ryden L, Ohrvik J, Bartnik M, Malmberg K, et al. (2006) Diabetes known or newly detected, but not impaired glucose regulation, has a negative influence on 1-year outcome in patients with coronary artery disease: a report from the Euro Heart Survey on diabetes and the heart. Eur Heart J 27: 2969-2974.
5. Ergelen M, Uyarel H, Cicek G, Isik T, Osmonov D, et al. (2010) Which is worst in patients undergoing primary angioplasty for acute myocardial infarction? Hyperglycaemia? Diabetes mellitus? Or both? Acta Cardiol 65: 415-423.
6. Panduranga P, Sulaiman KJ, Al-Zakwani IS, Al-Lawati JA (2010) Characteristics, management, and in-hospital outcomes of diabetic acute coronary syndrome patients in Oman. Saudi Med J 31: 520-524.
7. American Diabetes Association (2010) Diagnosis and classification of diabetes mellitus. Diabetes Care 33: S62-S69.
8. Hasin T, Hochadel M, Gitt AK, Behar S, Bueno H, et al. (2009) Comparison of treatment and outcome of acute coronary syndrome in patients with versus patients without diabetes mellitus. Am J Cardiol 103: 772-778.
9. Bakhai A, Collinson J, Flather MD, de Arenaza DP, Shibata MC, et al. (2005) Diabetic patients with acute coronary syndromes in the UK: high risk and under treated. Results from the prospective registry of acute ischaemic syndromes in the UK (PRAIS-UK). Int J Cardiol 100: 79-84.
10. Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, et al. (2000) 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 102: 1014-1019.
11. http://www.itf.istanbul.edu.tr/attachments/021_turdep.2.sonuclarinin.aciklamasi.pdf
12. Wallander M, Malmberg K, Norhammar A, Ryden L, Tenerz A (2008) Oral glucose tolerance test: a reliable tool for early detection of glucose abnormalities in patients with acute myocardial infarction in clinical practice: a report on repeated oral glucose tolerance tests from the GAMI study. Diabetes Care 31: 36-38.
13. Bartnik M, Ryden L, Ferrari R, Malmberg K, Pyorala K, et al. (2004) The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe. The Euro Heart Survey on diabetes and the heart. Eur Heart J 25: 1880-1890.
14. Abbud Z, Schindler D, Wilson A, Kostis J (1995) Effect of diabetes mellitus on short- and long-term mortality rates of patients with acute myocardial infarction: a statewide study. Myocardial Infarction Data Acquisition System Study Group. Am Heart J 130: 51-58.
15. Woodfield SL, Lundergan CF, Reiner JS, Greenhouse SW, Thompson MA, et al. (1996) Angiographic findings and outcome in diabetic patients treated with thrombolytic therapy for acute myocardial infarction: the GUSTO-I experience. J Am Coll Cardiol 28: 1661-1669.
16. Monteiro S, Monteiro P, Goncalves F, Freitas M, Providencia LA (2010) Hyperglycaemia at admission in acute coronary syndrome patients: prognostic value in diabetics and non-diabetics. Eur J Cardiovasc Prev Rehabil 17: 155-159.
17. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK (1990) Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? JAMA 263: 2893-2898.
18. Malmberg K, Ryden L. (1988) Myocardial infarction in patients with diabetes mellitus. Eur Heart J 9: 256-264.
19. Fuller J, Shipley M, Rose G, Jarret R, Keen H (1980) Coronary heart disease risk and impaired glucose tolerance: The Whitehall study. Lancet 1: 1373-1376.
20. Tuomilehto J (1999) Glucose tolerance and mortality: comparison of WHO and American Diabetic Association diagnostic criteria. Lancet 354: 617-621.

21. Ryden L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, et al. (2007) Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J 28: 88-136.

22. Abbot R, Donahue R, Kannel W, Wilson P (1988) The impact of diabetes on survival following myocardial infarction in men vs women. The Framingham Study. JAMA 260: 3456-3460.

This article was originally published in a special issue, **Diabetes & Types** handled by Editor(s). Dr. Teik Chye Ooi, University of Ottawa, Canada; Dr. Panagiotis Anagnosti, Hippokration Hospital, Greece