



Four varieties of diabetes mellitus in acute myocardial infarction

Četiri tipa šećerne bolesti u akutnom infarktu miokarda

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Introduction

It is believed that 387 million patients (> 8% of the global population) have diabetes mellitus (DM), and almost one half of them are unaware of their diagnosis¹. DM is very important risk factor for acute myocardial infarction (AMI)². The patients with DM have a two- to four-fold increased risk of developing cardiovascular (CV) disease³, three-fold for the acute coronary syndrome (ACS)⁴, and they experience the CV events 15 years earlier than the general population^{4,5}. The patients with DM were believed to have as the high risk for the new AMI as the patients with previous myocardial infarction (MI), the “coronary artery disease (CAD) equivalent”^{6–8}. This is an overestimation as shown by the meta-analysis⁹. The Euro Heart Survey and other registries/studies found that a majority of ACS patients had dysglycaemia, including DM, which was not previously diagnosed^{1,8,10,11}. The patients with MI have the incidence of insulin resistance twice as often as the individuals with no history of myocardial infarction. Therefore, some authors consider a MI to be a pre-DM equivalent^{1,8}, or a DM risk equivalent¹², or a pre-DM risk equivalent¹³. Out of 2,036 DM-naïve CAD patients who were followed up for at least one year, AMI significantly increased the risk of “new-onset” DM after adjusting the covariates [hazard ratio (HR), 1.54; 95% confidence interval (CI), 1.14–2.07; $p < 0.01$]¹⁴.

Nevertheless, a short-term⁴ and a long-term mortality risk in the AMI patients with DM is almost doubled in comparison with the nondiabetic AMI patients^{2,4,7}. A systematic review and meta-regression of 1,614,174 AMI, or ACS patients showed that the patients with DM ($n = 432,066$) had the odds ratio (OR) [95% CI] of 1.66 [1.59–1.74] ($p < 0.0001$) for early mortality, and of 1.86 [1.75–1.97] ($p < 0.0001$) for 6–12 months mortality in comparison with 1,182,108 nondiabetic patients². The mortality risk after a 10-year follow-up in the patients with CAD and DM exceeds 70%¹⁵. Glycemia on admission of 108–126 mg/dL (6–7 mmol) in the AMI patients with DM is associated with 3 times higher mortality vs. the AMI patients without DM^{16,17}. In AMI, the risk for the repeated myocardial infarctions, heart failure, cardiogenic shock and stroke is also greater in the patients with concomitant DM, as compared to the AMI patients without DM^{4,18}. Increased mortality in the AMI patients vs. those without DM has remained constant over time (from 1970 to 2011), despite the important therapeutic advantages². The survival curves were persistently diverging for 20 years between the AMI patients with and without DM and the median survival was less than 3.3 years ($p < 0.0001$) in the DM patients following the AMI⁵. DM confers increased in-hospital mortality risk both in the ST-elevation myocardial infarction (STEMI) and the non-STEMI (NSTEMI) patients¹⁹.

Moreover, this dismal prognosis of patients with AMI and DM is not related to the body mass index, i.e., „obesity paradox“ is not relevant to them (in contrast to the AMI patients without DM)²⁰. Indeed, a meta-analysis of 21,759 DM patients (~29% of them were insulin-treated) revealed that both short-term and long-term mortality, and the incidence of new AMI, target lesion revascularization, major adverse cardiac effect (MACE), and stent thrombosis were significantly more frequent in the insulin-treated DM patients²¹. Also, among 243,861 patients with AMI the in-hospital mortality risk was higher in the insulin-treated DM patients (n = 20,051) vs. the DM patients who did not require insulin (n = 25,364)¹⁹. DM is prevalent in AMI, with usually quoted figures between 20%–30%^{7,22–24}, or 30%–40%²⁵, and the incidence and the prevalence of DM are expected to grow further^{2,26}. Another 300 million individuals are at a risk of developing DM²⁶. Even higher actual prevalence was published and a few recent papers reported almost doubled DM prevalence in AMI (47%)²⁷.

Diagnosing DM in AMI has been clearly suboptimal

In a recent research paper, of the 3,778 AMI patients who had no history of DM before admission, 18.7% had the criteria for DM during hospitalization: fasting glucose level of at least 126 mg/dL (7 mmol/L), random plasma glucose (RPG) of at least 200 mg/dL (11.1 mmol/L), or glycated hemoglobin [HbA1c] level of at least 6.5%. Out of the AMI patients with the criteria for a new-onset DM, only 30% were clinically diagnosed (as having DM) in the hospital and were treated instantly²⁷. Similarly, in a study of 1,566 patients, insulin, or oral agents were prescribed at discharge for 80% of patients with known DM and only 25.4% of patients with newly diagnosed DM¹. Therefore, the great majority of newly diagnosed DM remained without an appropriate hypoglycemic treatment, which is very important finding. Indeed, the AMI patients who met the criteria for DM, but were not diagnosed, had a significantly higher risk for a MACE, 1 year following discharge, compared with the patients without previous diagnosis of DM (OR, 1.5; 95% CI, 1.3–1.7; $p < 0.0001$). On the other hand, there was no a statistically significant difference between the patients with properly newly diagnosed DM and the patients without DM (OR, 1.3; 95% CI, 0.9–1.7; $p = 0.15$)²⁷. The authors divided their DM patients into only three groups: 1) with a history of DM (34%); 2) without a history of DM, diagnosed during hospitalization (4%); with the criteria for DM, but undiagnosed during their intrahospital stay (9%)²⁷.

How many kinds of DM can be observed in AMI?

We believe that it is important to recognize that there were actually four kinds of DM in ACS: A) Previously diagnosed DM¹; B) Newly diagnosed (previously present, but not diagnosed until this admission) DM with HbA1c > 6.5%^{1,28}; C) New-onset DM with HbA1c < 6.5% and with either C1. Fasting blood glucose (FBG) ≥ 126 mg/dL (7 mmol/L), or C2. A RPG ≥ 200 mg/dL (11.1 mmol/L), or C3.

The positive oral glucose tolerance test (OGTT) before discharge with 2-hr plasma glucose (PG) ≥ 200 mg/dL (11.1 mmol/L)¹; D) Undetected DM, i.e., some of the four 2016 American Diabetes Association (ADA) criteria [in terms of FBG ≥ 126 mg/dL (7 mmol/L), or a RPG ≥ 200 mg/dL (11.1 mmol/L) or HbA1c $\geq 6.5\%$ (48 mmol/mol), or 2-hr PG ≥ 200 mg/dL (11.1 mmol/L) during OGTT (75 g)] not fulfilled and the other analysis not performed²⁹.

Some frequent mistakes in categorizing DM and stress hyperglycemia in AMI

The forth group (D) is missing in the aforementioned work²⁷ and with this group, the number of DM patients in AMI would be even higher. Consequently, as these patients were neither diagnosed nor treated – the real number of adequately diagnosed and treated DM patients in AMI may be therefore even lower than 30%. This should call to action. Regarding the terminology used in writing on this topic, there is a mistake with labeling “newly diagnosed” DM as “new-onset”. In AMI, the patients without known (previously diagnosed) DM can be considered as having “new-onset”, which frequently is not true, because they may have unrecognized DM for some time. It is not difficult to distinguish “new onset DM” from undiagnosed DM, because HbA1c is normal in the first and elevated in the second case.

Common methodological error for decades was to use the same cut-off in the AMI patients for the subgroup with the glycometabolic disease (DM) and without it. This single cut-off was artificially low for the DM patients (and high for non-DM ones) and decreased somewhat the predictive accuracy of stress hyperglycemia (SH). It is particularly true for the DM patients, because they are less represented in AMI, so that their cut-off value for SH is more remote from the artificial single cut-off of the whole AMI group³⁰. Hyperglycemia is common, valid both for risk stratification and treatment initiation and adjustments, but is often the underestimated parameter in critical illnesses, including AMI³¹. The importance of hyperglycemia in AMI stems from two facts: AMI is one of the most common lethal diseases and glycemia is undoubtedly one of the basic parameters in general and in AMI¹⁷. Hyperglycemia in AMI has different cut-offs for the prognostic and therapeutic purposes. The common mistake is to take therapeutic threshold e.g., 11 mmol/L (198 mg/dl) for the prognostic one, because the AMI patients without DM have far less prognostic cut-off ~8 mmol/L (144 mg/dl)³². Post-prandial hyperglycaemia contributed more to the CAD genesis as compared to fasting hyperglycemia³³. No less than 84% of AMI patients with abnormal glucose tolerance had normal plasma glucose (FPG)³⁴.

Comparison of the most important tools to detect DM in AMI (in addition to FPG and RPG)

HbA1c is a marker of an increased CV risk in the patients with and without DM³⁵. ADA recommended the HbA1c with a threshold of 6.5%, to diagnose DM, due to its preanalytical stability, convenience (fasting not required),

and less day-to-day variability²⁸. Moreover, HbA1c is currently used to guide the management decisions⁴. The ACS patients with HbA1c of 6.0%–6.4% should have an OGTT 6–8 weeks after discharge⁴. HbA1c reflects the average glycemia, including postprandial spikes during last 3 months³⁶. The relation of postprandial hyperglycemia and a risk of CV diseases was demonstrated in a meta-analysis of 95,783 individuals^{3,37}. HbA1c has a low intraindividual variability and is not influenced by the stress caused by ACS^{25,36}. A single measurement of HbA1c is not sufficient to diagnose DM³⁸. Using HbA1c, FPG, and RPG newly diagnosed DM was found in ~1/5 of all AMI patients and pre-DM in 14%³⁹.

OGTT has been often recommended for the AMI patients^{23,25,26}. But neither from ADA²⁸ nor from NICE⁴⁰, OGTT is a valid screening tool for both DM and a high CV risk⁴¹. OGTT in the patients with ACS has comparable accuracy to that in the general population. Therefore, it is sound to perform OGTT in the ACS patients to improve search for such an important disease as DM⁴². Bronisz et al.⁴³ reported that a substantial proportion of AMI patients with the abnormal result of OGTT soon after AMI, can have a normal glucose tolerance 3 months after AMI. To the contrary, a meta-analysis found that < 10% of ACS patients diagnosed with DM by means of an OGTT before discharge will have a different result at the follow-up OGTT⁴². Moreover, HbA1c is more expensive, it is not available so widely, and does not correlate adequately with the average glycemia in certain individuals⁴⁴.

Comparing all three glycemic parameters, FPG, OGTT and HbA1c simultaneously for mortality and CV disease risk reveals that the association is strongest for 2-hour plasma glucose concentration (2hPG) in OGTT²⁶. In addition to FPG and HbA1c, OGTT reveals much more cases of DM, both in the general population and CAD⁴⁵. A portion of AMI patients with new-diagnosed AMI by means of OGTT was not negligible⁸. The OGTT showed that 27.4% of CAD patients without known DM at admission actually had DM. Moreover, 33.5% were found to have impaired glucose tolerance (IGT) and another 11.2% were found to have both IGT and impaired fasting glucose (IFG)⁴⁶. On one hand, HbA1c $\geq 6.5\%$ can predict the DM values on OGTT (2hPG value ≥ 11.1 mmol/L) with the positive predictive value of no less than 100% and could, therefore, replace OGTT to diagnose DM following ACS²⁵. To the contrary, OGTT or HbA1c may not diagnose the same patients; evidence of discrepancies between the two modalities to classify abnormal glyco-

regulation accumulated²⁵. OGTT is likely needed, but there is a dilemma when to perform it, during the initial hospitalization, or later (e.g., within 30 days, or at three months).

Variable practice reflects directly the lack of consensus – some authors used to perform OGTT: as early as on the day one of hospitalization⁴⁷, on the day three from the admission^{34,48,49}; on the day four of hospitalization⁵⁰ (the ESC guidelines also recommend delaying the test for 4 to 5 days after ACS to minimize the false positive results^{51,52}, because the results of OGTT could be somewhat falsified by stress hyperglycemia⁵²); from one to 3 days following the hospital discharge⁵³; from 7 to 28 days after ACS²⁵; or 3 months after discharge^{42,46}.

OGTT at the discharge performed in the patients with AMI detected a high proportion of patients with previously unknown abnormal glycoregulation that was significantly and independently related to a dismal long-term prognosis⁴¹. Within 7 days following AMI, OGTT can detect many patients with previously unknown either newly detected DM or IGT, indicating a high risk for the CV events in the next decade. OGTT was a better prognosticator as compared to FBG or HbA1c⁴¹.

Characteristics of most important methods detection of DM in AMI patients are given in Table 1.

The combination of HbA1c and OGTT to diagnose DM in the AMI patients

To obtain the diagnosis of DM as soon as possible, HbA1c and FBG should be analysed during the first days of hospitalization, but both of them will leave an undetected group of patients with glucometabolic abnormalities⁴¹. Indeed, OGTT should be performed when HbA1c and FPG are inconclusive⁵¹. Moreover, a combination of tests (both HbA1c and OGTT) in addition to simple FBG can be used to the better risk-stratification of AMI patients. The OGTT is more sensitive than fasting plasma glucose and HbA1c. The AMI patients categorized as newly diagnosed DM by OGTT, although HbA1c < 6.5%, have a poor long-term prognosis compared to the patients with HbA1c < 6.5%, and an IFG, or normal glucose tolerance (NGT)/IGT by OGTT³⁷. The combination of HbA1c and OGTT seems sound. For example, in the AMI patients treated invasively with IGT and newly diagnosed DM (detected by OGTT), an increase of HbA1c was one of the strongest independent risk markers of death⁵⁴.

Table 1

Detection of diabetes mellitus (DM) in the acute myocardial infarction patients

Method	Advantage
RPG > 11.1 mmol/L	routine, always available ^{1,27}
FBG > 7 mmol/L	routine, always available ^{1,46}
HbA1C > 6.5%	widely available, within 24 hours ^{1,28}
OGTT 2-hr PG ≥ 11.1 mmol/L	improves DM detection additionally ^{26,45}
All above	provides optimal result in DM detection ^{36,41,51}

RPG – random plasma glucose; FBG – fasting blood glucose; HbA1C – glycated haemoglobin A1c; OGTT – oral glucose tolerance test; PG – plasma glucose.

OGTT in a combination with HbA1c provides the additional prognostic information on all-cause mortality, as this identifies a group of high-risk patients, who would remain undetected if using an OGTT, or HbA1c only³⁸. Regretably, in practice, the HbA1c levels were not available in about 3/4 of AMI patients without DM¹⁹. Moreover, the frequency of performing HbA1c varied widely; it was quite different among hospitals (capturing from 7.7% to 87.6% of hospitalized patients)⁵⁵.

The real world underutilization of evidence-based therapies for DM may contribute to worse outcome of patients with DM and ACS⁷. Early diagnosis and treatment of dysglycemia may slow down, or even reverse the adverse effects on the CV system¹¹. Improved glycaemic control in the DM patients following the AMI results in the reduced long-term mortality⁵⁵. A greater benefit could be obtained from treating the ACS patients with newly diagnosed DM more intensively⁴. Some of the important advantages of measuring HbA1c and performing OGTT are timely detection of abnormal glucose regulation (during the AMI hospitalization, or shortly after it) which could give rise to the prevention strategies, such as lifestyle and pharmacological interventions that can help to prevent DM^{45,46}, and the detection of pre-DM which can be used to avoid drugs known to impair glucoregulation, such as diuretics, non-vasodilatory and non-selective beta blockers, some types of statins, etc.⁵⁶⁻⁵⁸. When DM is diagnosed, the appropriate diet, anti-DM drugs, exercise programs, etc., can be planned to improve quality of life and prognosis²⁹. Moreover, in the newly diagnosed DM, the prevention of CV diseases can be improved, such as introduction/intensification of treatment (e.g., renin-angiotensin system inhibitor, statin, aspirin, etc.), as a risk category changes substantially with the diagnosis of DM. Timely made DM diagnosis can improve even the mode of reperfusion, as the diabetic status influence the choice between a coronary artery by-pass graft (CABG) and a stent, and further – the choice of stent, as well as antiplatelet therapy. For example, < 20% of the patients with dysglycemia, detected by OGTT, received drug-eluting stents, since they were

treated as the non-diabetic patients at the time of percutaneous coronary intervention (PCI)^{1,11}. In the multivariate analysis, the ACS patients with pre-DM (OR, 1.58, 95%:1.08–2.31) and undiagnosed DM (OR, 1.51, 95%:1.01–2.26) also had reduced kidney function more frequently, in comparison with the AMI patients who had normal glycoregulation²³.

Consequently, the detection of pre-DM and previously undiagnosed DM could enable us to pay more attention to the kidney function and prevent its deterioration. It may be useful to have information about pre-DM and newly detected DM prior to imaging techniques requiring contrast, in order to better prevention of contrast induced nephropathy, i.e., acute kidney injury. Moreover, an additional care should be taken to avoid potentially nephrotoxic drugs, such as, e.g., aminoglycosides.

Conclusion

There are four different DM varieties in ACS. The real number of the DM patients in AMI, who are adequately diagnosed and treated, could be even less than 30%. It is important to measure HbA1c on admission to detect the unrecognized patients with glycometabolic abnormalities. OGTT before discharge, or within the next 3 months is recommended in the majority of guidelines, but not in all. It is reasonable not to omit OGTT at least if HbA1c is not conclusive. DM and pre-DM are important prognostically, they can be prevented, or treated only if detected. There is no excuse to avoid at least one of such routine tests as it frequently occurred in practice with probable serious clinical consequence (see Table 1).

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R E F E R E N C E S

1. Aggarwal B, Shah GK, Randhava M, Ellis SG, Lincoff AM, Menon V. Utility of glycated hemoglobin for assessment of glucose metabolism in patients with ST-segment elevation myocardial infarction. *Am J Cardiol* 2016; 117(5): 749–53.
2. Banters C, Lemesle G, de Groot P, Lamblin N. A systematic review and meta-regression of temporal trends in the excess mortality associated with diabetes mellitus after myocardial infarction. *Int J Cardiol* 2016; 217: 109–21.
3. Madsbad S. Impact of postprandial glucose control on diabetes-related complications: How is the evidence evolving? *J Diabetes Complications* 2016; 30(2): 374–85.
4. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. *Methods. Can J Diabetes* 2013; 37(Suppl 1): S1–212.
5. Patel PA, Cubbon RM, Sapsford RJ, Gillott RG, Grant PJ, Witte KK, et al. An evaluation of 20 year survival in patients with diabetes mellitus and acute myocardial infarction. *Int J Cardiol* 2016; 203: 141–4.
6. Witt DM, Clark NP, Kaatz S, Schnurr T, Ansell JE. Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. *J Thromb Thrombolysis* 2016; 41(1): 187–205.
7. Wei CC, Shyu KG, Cheng JJ, Lo HM, Chiu CZ. Diabetes and Adverse Cardiovascular Outcomes in Patients with Acute Coronary Syndrome - Data from Taiwan's Acute Coronary Syndrome Full Spectrum Data Registry. *Acta Cardiol Sin* 2016; 32(1): 31–8.
8. Mazurek M, Kowalczyk J, Lenarczyk R, Zielinska T, Sedkowska A, Pruszkowska-Skerzyp P, et al. The prognostic value of different glucose abnormalities in patients with acute myocardial infarction treated invasively. *Cardiovasc Diabetol* 2012; 11: 78.
9. Bulugabapitiya U, Sijambalapitiya S, Sithole J, Idris I. Is diabetes a coronary risk equivalent? Systematic review and meta-analysis. *Diabet Med* 2009; 26(2): 142–8.
10. Bartnik M, Ryden L, Ferrari R, Malmberg K, Pyörälä K, Simoons-Schouten M, et al. 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* 2004; 25(21): 1880–90.
11. Kuhl J, Jörneskog G, Wemmingen M, Bengtsson M, Lundman P, Kalani M. Long-term clinical outcome in patients with acute coronary syndrome and dysglycaemia. *Cardiovasc Diabetol* 2015; 14: 120.
 12. Usami M, Sakata Y, Nakatani D, Suna S, Matsumoto S, Hara M, et al. Clinical impact of acute hyperglycemia on development of diabetes mellitus in non-diabetic patients with acute myocardial infarction. *J Cardiol* 2014; 63(4): 274–80.
 13. Mozaffarian D, Marfisi R, Levantesi G, Silletta MG, Tavazzoli L, Tognoni G, et al. Incidence of new-onset diabetes and impaired fasting glucose in patients with recent myocardial infarction and the effect of clinical and lifestyle risk factors. *Lancet* 2007; 370(9588): 667–75.
 14. Park CS, Chung WB, Choi YS, Kim PJ, Lee JM, Baek K, et al. Acute Myocardial Infarction Is a Risk Factor for New Onset Diabetes in Patients with Coronary Artery Disease. *PLoS One* 2015; 10(8): e0136354.
 15. Tavares CA, Wajsbjerg BL, Rochitte C, Lerario AC. Screening for asymptomatic coronary artery disease in patients with type 2 diabetes mellitus. *Arch Endocrinol Metab* 2016; 60(2): 143–51.
 16. Ishihara M. Acute hyperglycemia in patients with acute myocardial infarction. *Circ J* 2012; 76(3): 563–71.
 17. Koracevic GP. Proposal of a new approach to study and categorize stress hyperglycemia in acute myocardial infarction. *J Emerg Med* 2016; 51(1): 31–6.
 18. Gomez-Arbelaes D, Sanchez-Vallejo G, Perez M, Garcia RG, Arguello JF, Peñaberrera E, et al. Hyperglycaemia is associated with worse outcomes in Latin-American individuals with acute myocardial infarction. *Clin Investig Arterioscler* 2016; 28(1): 9–18. (Spanish)
 19. Rousan TA, Pappay RM, Chen AY, Roe MT, Saucedo JF. Impact of diabetes mellitus on clinical characteristics, management, and in-hospital outcomes in patients with acute myocardial infarction (from the ncd). *Am J Cardiol* 2014; 114(8): 1136–44.
 20. Colombo MG, Meisinger C, Amann U, Heier M, von Scheidt W, Kuch B, et al. Association of obesity and long-term mortality in patients with acute myocardial infarction with and without diabetes mellitus: results from the MONICA/KORA myocardial infarction registry. *Cardiovasc Diabetol* 2015; 14(1): 24.
 21. Bundhun PK, Li N, Chen M. Adverse cardiovascular outcomes between insulin-treated and non-insulin treated diabetic patients after percutaneous coronary intervention: a systematic review and meta-analysis. *Cardiovasc Diabetol* 2015; 14(1): 135.
 22. Arnold SV, Spertus JA, Lipska KJ, Tang F, Goyal A, McGuire DK, et al. Association between diabetes mellitus and angina after acute myocardial infarction: analysis of the TRIUMPH prospective cohort study. *Eur J Prev Cardiol* 2015; 22(6): 779–87.
 23. Liu H, Zhou C, Yu J, Jiang Q, Hu D. Reduced kidney function in acute coronary syndrome patients with undiagnosed diabetes or pre-diabetes. *Nephrology (Carlton)* 2013; 18(4): 263–8.
 24. Koracevic GP, Petrovic S, Damjanovic M, Stanojlovic T. Association of stress hyperglycemia and atrial fibrillation in myocardial infarction. *Wien Klin Wochenschr* 2008; 120(13–14): 409–13.
 25. Vergès B, Arignon A, Bonnet F, Catargi B, Cattan S, Cosson E, et al. Diabetes and cardiovascular Disease study group of the Société française de diabète (SFD), in collaboration with the Société française de cardiologie (SFC). Consensus statement on the care of the hyperglycaemic/diabetic patient during and in the immediate follow-up of acute coronary syndrome. *Diabetes Metab* 2012; 38(2): 113–27.
 26. Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, et al. Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC); European Association for the Study of Diabetes (EASD). ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD - summary. *Diab Vasc Dis Res* 2014; 11(3): 133–73.
 27. Le VT, Knight S, Anderson JL, Lappé DL, May HT, Horne BD, et al. Undiagnosed diabetes at the time of acute myocardial infarction is frequent and associated with poor cardiovascular outcomes. *Circulation* 2015; 132: A15117.
 28. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2010; 33(Suppl 1): S62–9.
 29. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 2016; 39(Suppl 1): S1–S106.
 30. Koracevic GP. Using a single cut-off for stress hyperglycemia in myocardial infarction decreases its prognostic value particularly in diabetes. *Am J Emerg Med* 2014; 32(1): 103–4.
 31. Koraćević G, Vasiljević S, Veličković-Radovanović R, Sakac D, Obradović S, Damjanović M, et al. Stress hyperglycemia in acute myocardial infarction. *Vojnosanit Pregl* 2014; 71(9): 858–69.
 32. Koracevic GP. Various admission glucose cut-offs for prognostication and for therapeutic threshold in acute myocardial infarction. *Am J Emerg Med* 2015; 33(1): 108–9.
 33. Henareh L, Agewall S. 2-h postchallenge plasma glucose predicts cardiovascular events in patients with myocardial infarction without known diabetes mellitus. *Cardiovasc Diabetol* 2012; 11: 93.
 34. George A, Bhatia RT, Buchanan GL, Whiteside A, Moisey RS, Beer SF, et al. Impaired glucose tolerance or newly diagnosed diabetes mellitus diagnosed during admission adversely affects prognosis after myocardial infarction: an observational study. *PLoS One* 2015; 10(11): e0142045.
 35. Naito R, Miyauchi K, Ogita M, Kasai T, Kawaguchi Y, Tsuboi S, et al. Impact of admission glycemia and glycosylated hemoglobin A1c on long-term clinical outcomes of non-diabetic patients with acute coronary syndrome. *J Cardiol* 2014; 63(2): 106–11.
 36. Pararajasingam G, Hofsten DE, Logstrup BB, Egstrup M, Henriksen FL, Hangaard J, et al. Newly detected abnormal glucose regulation and long-term prognosis after acute myocardial infarction: Comparison of an oral glucose tolerance test and glycosylated haemoglobin A1c. *Int J Cardiol* 2016; 214: 310–5.
 37. Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A meta-regression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* 1999; 22(2): 233–40.
 38. American Diabetes Association. Standards of medical care in diabetes - 2012. *Diabetes Care* 2012; 35(Suppl 1): S11–63.
 39. Abdullatef WK, Al-Aqeedi RF, Dabdoob W, Hajar HA, Bener A, Gebani AA. Prevalence of unrecognized diabetes mellitus in patients admitted with acute coronary syndrome. *Angiology* 2013; 64(1): 26–30.
 40. Sentbinathan A, Kelly V, Dzingina M, Jones D, Baker M, Longson D. Hyperglycaemia in acute coronary syndromes: summary of NICE guidance. *BMJ* 2011; 343: d6646.
 41. Ritsinger V, Tanoglicidi E, Malmberg K, Näsman P, Rydén L, Tenerz Å, et al. Sustained prognostic implications of newly detected glucose abnormalities in patients with acute myocardial infarction: long-term follow-up of the Glucose Tolerance in Patients with Acute Myocardial Infarction cohort. *Diab Vasc Dis Res* 2015; 12(1): 23–32.
 42. Ye Y, Xie H, Zhao X, Zhang S. The oral glucose tolerance test for the diagnosis of diabetes mellitus in patients during acute coronary syndrome hospitalization: a meta-analysis of diagnostic test accuracy. *Cardiovasc Diabetol* 2012; 11(1): 155.
 43. Bronisz A, Kozłowski M, Magielski P, Fabiszak T, Gierach J, Świątkiewicz I, et al. Value of oral glucose tolerance test in the acute phase of myocardial infarction. *Cardiovasc Diabetol* 2011; 10(1): 21.
 44. American Diabetes Association (ADA). Standards of medical care in diabetes *Diabetes Care* 2015; 38(Suppl 1): S1–S90.

45. *de la Hera JM, García-Ruiz JM, Martínez-Cambor P, Martín M, Tellería AL, Corros C*, et al. Real incidence of diabetes mellitus in a coronary disease population. *Am J Cardiol* 2013; 111(3): 333–8.
46. *Colomo N, Linares F, Rubio-Martín E, Moreno MJ, de Mora M, García AM*, et al. Stress hyperglycaemia in hospitalized patients with coronary artery disease and type 2 diabetes risk. *Eur J Clin Invest* 2013; 43(10): 1060–8.
47. *Knudsen EC, Seljeflot I, Abdelnoor M, Eritsland J, Mangschau A, Arnesen H*, et al. Abnormal glucose regulation in patients with acute ST- elevation myocardial infarction-a cohort study on 224 patients. *Cardiovasc Diabetol* 2009; 8: 6.
48. *Gierach J, Gierach M, Świątkiewicz I, Woźnicki M, Grześek G, Su-kiennik A*, et al. Admission glucose and left ventricular systolic function in non-diabetic patients with acute myocardial infarction. *Heart Vessels* 2016; 31(3): 298–307.
49. *Bronisz A, Kozjński M, Magielski P, Fabiszak T, Bronisz M, Świątkiewicz I*, et al. Stress hyperglycaemia in patients with first myocardial infarction. *Int J Clin Pract* 2012; 66(6): 592–601.
50. *Gitt A, Bramlage P, Towae F, Papp A, Deeg E, Senges J*, et al. Newly diagnosed diabetes and prediabetes in patients after acute myocardial infarction predicts adverse outcomes during a three-year follow-up: results of the sweetheart registry. *JACC* 2013; 61(10): E176.
51. Task Force Members. *Ryden L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N*, et al. ESC Guidelines on diabetes, prediabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2013; 34(39): 3035–87.
52. Task Force of the SEC for the ESC Guidelines on Diabetes, Prediabetes and Cardiovascular Disease; Expert Reviewers for the ESC Guidelines on Diabetes, Prediabetes And Cardiovascular Disease; Guideliness Committee of the SEC. Comments on the ESC guidelines on diabetes, prediabetes, and cardiovascular diseases developed in collaboration with the european society for the study of diabetes. *Rev Esp Cardiol (Engl Ed)* 2014; 67(2): 87–93.
53. *Monteiro CM, Oliveira L, Izar MC, Helfenstein T, Santos AO, Fischer SM*, et al. Early glucometabolic profile in patients with acute coronary syndromes and metabolic syndrome. *Arq Bras Cardiol* 2009; 92(2): 89–99. (English, Portuguese, Spanish)
54. *Kowalczyk J, Mazurek M, Zielinska T, Lenarczyk R, Sedkowska A, Świątkowski A*, et al. Prognostic significance of HbA1c in patients with AMI treated invasively and newly detected glucose abnormalities. *Eur J Prev Cardiol* 2015; 22(6): 798–806.
55. *Snir A, Dabin B, Hyun K, Yamen E, Ryan M, Aliprandi-Costa B*, et al. Glycosylated haemoglobin assessment in diabetic patients with acute coronary syndromes. *Intern Med J* 2016; 46(5): 574–82.
56. *Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M*, et al. Task Force for the Management of Arterial Hypertension of the European Society of Hypertension and the European Society of Cardiology. 2013 ESH/ESC Practice Guidelines for the Management of Arterial Hypertension. *Blood Press* 2014; 23(1): 3–16.
57. *Sternlicht H, Bakeris GL*. Hydrochlorothiazide as the Diuretic of Choice for Hypertension: Time to Kick the Habit. *J Am Coll Cardiol* 2016; 67(4): 390–1
58. *Navarese EP, Buffon A, Andreotti F, Kozjński M, Welton N, Fabiszak T*, et al. Meta-analysis of impact of different types and doses of statins on new-onset diabetes mellitus. *Am J Cardiol* 2013; 111(8): 1123–30.

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